Advances in clinical applications of cardiovascular magnetic resonance imaging

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ABSTRACT
Cardiovascular magnetic resonance (CMR) is an evolving technology with growing indications within the clinical cardiology setting. This review article summarises the current clinical applications of CMR. The focus is on the use of CMR in the diagnosis of coronary artery disease with summaries of validation literature in CMR viability, myocardial perfusion, and dobutamine CMR. Practical uses of CMR in non-coronary diseases are also discussed.

The purpose of this review is to illustrate that cardiovascular magnetic resonance (CMR) has developed into a powerful non-invasive diagnostic tool that can routinely image myocardial anatomy, function, perfusion, and viability without need for ionising radiation.

WHAT CMR CAN DO
Assessment of right and left ventricular function and mass
Assessment of left ventricular size, function, and mass has been well validated in both autopsy and animal studies,10-12 and has excellent intraobserver and interobserver variability.13-18 This reproducibility allows for smaller sample size in studies requiring serial exams than other lower-resolution imaging such as echocardiography.

CMR can quantify regional wall motion and myocardial strain with techniques such as the harmonic phase method (HARP),19 displacement encoding with stimulated echoes (DENSE),20 21 and spatial modulation magnetisation (SPAMM).22 These techniques can assess myocardial strain independent of the effects of through-plane motion.

Real-time CMR can be used in situations where cardiac gating is not currently feasible. One example is the prenatal assessment of fetal cardiovascular abnormalities.23

Diagnosis of coronary artery disease
A single CMR study can provide information regarding the coronary arteries, left ventricular systolic function, myocardial perfusion, and viability (fig 1).

Viability assessment
One of the major breakthroughs for the use of CMR was the development of gadolinium delayed enhancement techniques to assess for myocardial infarction.24 Gadolinium shortens tissue T1 relaxation time, a magnetic property inherent to all tissues. The operator can select an inversion time that will “null” normal myocardium resulting in images where viable myocardium appears uniformly dark while a region of myocardial infarction or fibrotic scar appears bright (fig 2). Dysfunctional but viable myocardium is expected to have functional recovery if revascularised (in the case of hibernating myocardium), with time (in the case of stunned myocardium), or with resynchronisation (in the case of dyssynchronous myocardium).
In a seminal paper by Kim et al, the delayed enhancement of myocardial infarction by CMR closely correlated with the histopathological triphenyltetrazolium chloride (TTC) findings. Multiple studies have demonstrated the inverse relationship between the transmural extent of myocardial infarction and recovery of function, the higher spatial resolution of this technique compared with nuclear techniques, as well as the good correlation with biomarkers of necrosis. The reproducible nature of the delayed enhancement technique also makes it a natural choice for serial imaging of chronic infarctions.

Myocardial perfusion
Myocardial perfusion has been a CMR research focus. The challenge has been obtaining enough signal, temporal resolution, spatial resolution, and spatial coverage, while minimizing artifacts. Most groups use fast gradient recalled echo (FGRE), FGRE with echoplanar imaging (Hybrid EPI), and steady state free precession (SSFP) perfusion techniques, typically using adenosine or dipyridamole as the stressor. These sequences may be accelerated with parallel imaging techniques and performed with multiple gadolinium dosing schemes. The studies may be interpreted qualitatively, semi-quantitatively, or quantitatively. Despite the technical issues related to perfusion imaging, many papers document that CMR first-pass perfusion has comparable diagnostic accuracy to the alternative myocardial perfusion imaging standards.

Dobutamine CMR
Dobutamine stress CMR was first described in the same year that dobutamine stress echocardiography was described. Dobutamine CMR has good sensitivity and specificity in the detection of significant coronary artery disease (table 1) with a safety profile similar to dobutamine echocardiography. While the sensitivity and specificity of CMR are comparable to stress echocardiography in patients with good echocardiographic windows, CMR performs better than stress echocardiography in patients with suboptimal echocardiographic windows. Furthermore, dobutamine stress CMR has prognostic value above and beyond the baseline ejection fraction.

Acute chest pain in the hospital setting
Three major papers have looked at use of CMR in patients with acute coronary syndrome (ACS) or early diagnosis of chest pain in the emergency department. In a study of 161 patients presenting with chest pain not associated with ST elevation, Kwong et al found that CMR had 100% sensitivity for non-ST elevation myocardial infarction and was a better predictor of ACS than standard clinical tests including the composite TIMI risk score. In a higher risk group of 68 patients with possible or probable ACS scheduled for coronary angiography, Plein et al found that a multi-component CMR consisting of cine function, adenosine and rest perfusion, delayed enhancement, and coronary artery imaging yielded a sensitivity of 96% and a specificity of 83% in predicting the presence of significant coronary artery disease. In another emergency department study of 141 patients with myocardial infarction excluded by serial troponin assays, Ingkanisorn et al found that adenosine stress CMR had excellent prognostic value as 100% of patients with adverse cardiovascular outcomes were detected with an overall specificity of 91%.

Figure 1 Comprehensive cardiovascular magnetic resonance with cine function, dipyridamole perfusion, and delayed enhancement: A 77-year-old man presents with exertional angina and a past medical history significant for hypertension and a prior stroke. In the top row, cine function demonstrates normal global and regional left ventricular systolic function. The dipyridamole perfusion image on the lower left panel demonstrates a severe perfusion defect in a multivessel coronary distribution, while the delayed enhancement image on the right lower panel demonstrates only a small subendocardial myocardial infarction of the inferoseptal wall, indicating a large ischaemic region with a large territory of viable myocardium.
CMR is also helpful in patients with atypical chest pain. For example, many patients with myocarditis present with chest pain, ECG abnormalities, elevated biomarkers, but normal coronary arteries. This diagnosis is easily made with CMR. The presence of atypical mid-wall or epicardial delayed enhancement distinguishes myocarditis from MI. Stress CMR perfusion can detect diffuse subendocardial ischaemia in patients with syndrome X. Acute chest pain from acute aortitis will present with irregularly thickened aortic wall and bright enhancement of the aortic wall on delayed enhancement imaging. CMR has been used in the diagnosis of stress cardiomyopathy (tako tsubo, left ventricular apical ballooning syndrome, and broken heart syndrome). Despite the profound left ventricular apical systolic dysfunction, there is little delayed enhancement in these patients.

**Coronary artery imaging**

Although multidetector computed tomography (MSCT) is the most rapid and highest-resolution non-invasive technique for imaging the coronary arteries, CMR offers an alternative for imaging the coronary arteries. CMR does not require ionising radiation and can be combined with a multimodality CMR assessment of cardiac function, perfusion, and viability in a relatively short period of time. However, coronary imaging by CMR is still relatively complicated and many technical nuances require significant operator experience.

A few studies indicate that CMR is not as far from clinical feasibility as many physicians assume. A multicentre study of 109 patients who underwent coronary magnetic resonance angiography (MRA) reported a sensitivity of 100%, a specificity of 85%, and an accuracy of 87% in the detection of left main artery or three-vessel disease. Sakuma et al performed three-dimensional whole-heart coronary MRA in 131 patients with a mean acquisition time of 12.9 (SD 4.3) minutes and a per patient sensitivity of 82%, specificity of 90%, and accuracy of 87%. However, most experts and clinical guidelines only support the use of CMR in determining the proximal course of anomalous coronary arteries (fig 3, coronary MRA).

**Cardiomyopathy**

CMR can characterise cardiomyopathies in unique ways based on the magnetic properties of myocardium. Assomull et al succinctly review the use of CMR in the evaluation of congestive heart failure. In hypertrophic cardiomyopathy, CMR can detect patches of myocardial fibrosis with intermediate delayed enhancement. Stress CMR perfusion can detect diffuse subendocardial ischaemia in patients with syndrome X. Acute chest pain from acute aortitis will present with irregularly thickened aortic wall and bright enhancement of the aortic wall on delayed enhancement imaging. CMR has been used in the diagnosis of stress cardiomyopathy (tako tsubo, left ventricular apical ballooning syndrome, and broken heart syndrome). Despite the profound left ventricular apical systolic dysfunction, there is little delayed enhancement in these patients.

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In patients suspected of having arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C), CMR can detect global right ventricular abnormalities, right ventricular aneurysms, or regional wall motion abnormalities. Fibrofatty myocardial infiltration can be determined in patients suspected of having ARVD/C. Sen-Chowdhry et al have proposed modified criteria for the diagnosis of ARVD/C focusing on right ventricular size and function, right ventricular segmental dilatation, and regional right ventricular hypokinesis. These proposed criteria would improve the sensitivity in the detection of early or incompletely expressed disease.

CMR can measure iron overload in the heart, particularly as a result of thalassaemia. Iron overload shortens T2* relaxation properties of the myocardium and liver. Intriguingly, some patients with thalassaemia have iron overload in the heart but not in the liver and vice versa. Thus, CMR determinations of
iron overload may be better at assessing patient risk than relying on liver biopsy alone and may be used to follow therapy success.

CMR is good at differentiating constrictive from restrictive cardiomyopathy due to each entity’s unique presentation and physiology. Many of the infiltrative cardiomyopathies such as amyloidosis, sarcoidosis, Chagas’ disease, and endomyocardial fibroelastosis have characteristic abnormalities on delayed enhancement. CMR can identify thickened pericardium as well as abnormal motion of the heart in constrictive cardiomyopathy. While both CT and CMR can detect thickened pericardium, CMR is better able to distinguish between pericardial thickening and small effusion than CT. Real-time imaging to evaluate the septum may demonstrate interventricular dependence. Real-time cine imaging of the inferior vena cava during respiration can also separate constrictive from restrictive physiology.

**Congenital heart disease**

In a patient with congenital heart disease, anatomic connections or malformations may be identified, the direction of intracardiac shunts may be identified and quantified, and valvular anatomy and function may be assessed. Volumetric anatomic CMR depicts the complex vascular abnormalities associated with congenital syndromes and the surgical corrections. Echocardiography cannot always visualise the heart and great vessels in their entirety, particularly in adults with surgically corrected congenital heart disease. Repeated exposure to the radiation of CT is not desirable, especially in a paediatric population that is at greater risk for developing long-term radiation-related malignancies.

CMR can provide more than simply anatomical imaging. A saturated black band technique highlights intracardiac shunting. Velocity encoded phase contrast techniques can quantify the severity of intracardiac shunts. Measuring pulmonary blood flow (Qp) in the pulmonary artery and systemic blood flow (Qs) in the aorta provides a noninvasive estimate of Qp/Qs and thus quantifies the degree of intracardiac shunting (fig 4). CMR can quantify the amount of valvular regurgitation (eg, in patients with Tetralogy of Fallot).

**Valvular disease**

CMR provides non-invasive clear anatomical valvular information that can impact clinical management of a patient. It is

![Figure 3](image1)

**Figure 3** Whole heart coronary magnetic resonance angiography. Image provided courtesy of Vibhas Deshpande, MR Research & Development, Siemens Medical Solutions.

![Figure 4](image2)

**Figure 4** Pulmonic flow (Qp) and systemic flow (Qs) may be calculated non-invasively with cardiovascular magnetic resonance using simple phase-contrast techniques. This figure illustrates an abnormal Qp/Qs of 1.6:1 in a patient with an atrial septal defect.
possible to differentiate a bicuspid from a tricuspid aortic valve (figs 5 and 6). CMR reproducibly characterises aortic valve anatomy and the determined aortic valve area correlates well with cardiac catheterisation. \(^{117}\)

Phase contrast techniques can reliably measure peak velocity and thus peak gradient in aortic stenosis. Valvular information in combination with accurate left ventricular volumes and assessment of thoracic aortic dilatation can assist in planning valvular replacement and, importantly, determine whether the aorta needs intervention as well. Similar data can be obtained in an assessment of the pulmonic valve, which is not always well-defined by transthoracic echocardiography.

While most valvular lesions seen by echocardiography can be assessed by CMR, echocardiography has the advantages of widespread availability and validation. CMR provides additional information in patients who have poor echocardiographic windows and is useful in patients who are poor candidates for invasive transoesophageal echocardiography or when additional surgery beyond the valve is contemplated.

**Assessment of cardiac masses**

Through various tissue-characterising techniques (T2-weighted, T1-weighted, first-pass perfusion, and delayed enhancement), CMR can reliably distinguish between myocardium, fat, avascular tissue (eg, thrombus), and other tissue types, such as tumours (fig 7). CMR often aids in differentiating intracardiac masses from masses that externally compress the heart.

The ability to characterise normal structures or variants makes CMR superior to echocardiography in the assessment of intracardiac mass. Atrial structures such as Eustachian valve, crista terminalis, Chiari network, and lipomatous hypertrophy are commonly mistaken by echocardiography to be a mass, and CMR can help avoid more invasive diagnostic testing.\(^{116}\)

Contrast-enhanced CMR is twice as sensitive as echocardiography in the detection of ventricular thrombi.\(^{119-121}\)

**Non-coronary vascular imaging**

**Aorta and great vessels**

MRI and MRA can assess large and medium-sized vascular structures. Serial exams are particularly useful in the paediatric population with congenital abnormalities of the aorta. CMR is able to visualise congenital aortic abnormalities including right-sided aortic arch, cervical aortic arch, double aortic arch, and vascular ring. As many as 42% of surgically repaired coarctations present with restenosis, dissection, pseudoaneurysm, or aneurysm at a later date.\(^{122-124}\)

Other common indications for CMR include assessment of aortic dilation and aneurysm, aortic dissection, aortic ulcer, and intramural haematoma. While a contrast CT is the study of choice in the acutely ill, haemodynamically unstable patient, in a haemodynamically stable patient a focused CMR exam of the aorta may be performed within approximately 10–15 minutes with little cooperation from the patient (fig 8). CMR is more sensitive than CT, echocardiography, and transoesophageal echocardiography in the diagnosis of intramural haematoma. CMR can also distinguish between an acute intramural haematoma and a chronic haematoma based upon the T1 and T2 characteristics of the bleed.\(^{125}\)

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**Figure 5** Black-blood fast spin echo technique to visualise the aortic valve.

**Figure 6** During diastole cine imaging, an aortic valve appears tricuspid; however, during systole, it is apparent that the valve is functionally bicuspid with fusion of the right and left cusps.
Pulmonary veins
Three-dimensional MRA can help guide electrophysiological interventions and can detect pulmonary vein stenosis after the procedure. It is possible to merge 3D MRA with fluoroscopy in the electrophysiology lab to help guide catheter tip placement and the ablation. CMR is also useful for determining the flow patterns through vessels.126

FUTURE DIRECTIONS
CMR continues to develop rapidly. Contrast agents targeted to specific tissue types are in development. For example, thrombus-avid contrast agents are feasible.127–129 Lipid-specific agents have also been studied. Stem cells and macrophages have been identified with iron-based contrast agents and tracked in vivo.130–133

Interventional CMR is also a field with growing interest. A variety of percutaneous procedures used to treat vascular abnormalities and congenital heart disease are in development.134–137 Even CMR-guided percutaneous replacement of the aortic valve is feasible.138 CMR can help precisely guide delivery of drugs and stem cells.139–141

LIMITATIONS
There are many factors that have slowed the dissemination of CMR. CMR is expensive and requires a skilled multidisciplinary team. In-depth CMR training is not readily available. Insufficient numbers of adequately trained physicians limit utilisation and dissemination of CMR. In many countries, reimbursement of CMR is not well-established. Although gadolinium-based contrast

Figure 7  A 48-year-old woman presented with a markedly abnormal preoperative ECG and nuclear stress test indicating that she had an anteroseptal myocardial infarction. Cardiovascular magnetic resonance was able to demonstrate that the patient actually had an intraseptal mass (bright on the left) which was in fact a benign lipoma as demonstrated by fat saturation techniques (dark on the right after using a fat saturation technique to suppress the fat).

Figure 8  This magnetic resonance angiography was performed in a Turner’s Syndrome patient. Note on the anterior view the dilated size of the ascending aorta (red arrow) in comparison with the descending aorta, as well as the persistent left-sided superior vena cava (green arrow). The posterior view demonstrates the malformed aortic arch (red arrow).
Table 2  Summary of gadolinium delayed enhancement publications

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>n</th>
<th>Acute vs chronic</th>
<th>Major findings</th>
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<tr>
<td>2006</td>
<td>Gerber BL et al</td>
<td>16</td>
<td>Acute</td>
<td>Delayed enhancement correlated with MI size.</td>
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<td>2005</td>
<td>Bello D et al</td>
<td>48</td>
<td>Chronic</td>
<td>Delayed enhancement correlated with MI size and predicted inducibility of ventricular tachycardia.</td>
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<td>2005</td>
<td>Ibrahim T et al</td>
<td>33</td>
<td>Acute</td>
<td>Delayed enhancement correlated with MI size.</td>
</tr>
<tr>
<td>2005</td>
<td>Selvanayagam JB et al</td>
<td>50</td>
<td>Acute</td>
<td>Delayed enhancement correlated with biomarkers of necrosis.</td>
</tr>
<tr>
<td>2004</td>
<td>Ingkanisorn WP et al</td>
<td>33</td>
<td>Acute</td>
<td>Delayed enhancement predicted recovery of function and correlated with biomarkers of necrosis.</td>
</tr>
<tr>
<td>2004</td>
<td>Lund GK et al</td>
<td>60</td>
<td>Acute</td>
<td>Delayed enhancement correlated with MI size.</td>
</tr>
<tr>
<td>2004</td>
<td>Selvanayagam JB et al</td>
<td>52</td>
<td>Chronic</td>
<td>Delayed enhancement predicted recovery of function.</td>
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<td>2003</td>
<td>Wellhofer E et al</td>
<td>29</td>
<td>Chronic</td>
<td>Delayed enhancement and dobutamine CMR predicted recovery of function.</td>
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<td>Beek AM et al</td>
<td>30</td>
<td>Acute</td>
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<td>91</td>
<td>Chronic</td>
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<td>2002</td>
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<td>31</td>
<td>Chronic</td>
<td>Delayed enhancement correlated with MI size.</td>
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<td>2002</td>
<td>Mahrohldt H et al</td>
<td>20</td>
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<td>Delayed enhancement correlated with MI size and was reproducible in two separate scans.</td>
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<td>2002</td>
<td>Perin EC et al</td>
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<td>The unipolar voltage recorded during electromechanical mapping varied inversely with the amount of delayed enhancement.</td>
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<td>2001</td>
<td>Ricciardi MJ et al</td>
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<td>Chronic</td>
<td>Delayed enhancement correlated with biomarkers of necrosis. Microinfarcts were detected in patients who had PCI-related elevations in CKMB.</td>
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<td>2001</td>
<td>Wu E et al</td>
<td>82</td>
<td>Chronic</td>
<td>Delayed enhancement correlated with MI size.</td>
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</tbody>
</table>

CMR, cardiovascular magnetic resonance; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 3  Summary of vasodilator perfusion CMR validation publications

<table>
<thead>
<tr>
<th>Year</th>
<th>First author</th>
<th>n</th>
<th>Excluded</th>
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<th>Reference</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>2007</td>
<td>Merkle et al</td>
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<td>4</td>
<td>Adenosine</td>
<td>Cath &gt;70%</td>
<td>89</td>
<td>87</td>
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<tr>
<td>2006</td>
<td>Klem et al</td>
<td>92</td>
<td>3</td>
<td>Adenosine</td>
<td>Cath &gt;70%</td>
<td>89</td>
<td>87</td>
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<tr>
<td>2006</td>
<td>Pitz et al</td>
<td>176</td>
<td>5</td>
<td>Adenosine</td>
<td>Cath &gt;70%</td>
<td>96</td>
<td>83</td>
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<td>2006</td>
<td>Rieber et al</td>
<td>50</td>
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<td>Adenosine</td>
<td>Cath &gt;50% and FFR</td>
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<td>90</td>
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<td>2005</td>
<td>Okuda et al</td>
<td>33</td>
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<td>Dipyridamole</td>
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<td>84</td>
<td>87</td>
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<tr>
<td>2005</td>
<td>Plein et al</td>
<td>92</td>
<td></td>
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<td>Cath &gt;70%</td>
<td>88</td>
<td>82</td>
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<td>2005</td>
<td>Sakuma et al</td>
<td>40</td>
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<td>Cath &gt;70%</td>
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<td>68</td>
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<td>Bunce et al</td>
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<td>71</td>
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<td>Giang et al</td>
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<td>75</td>
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<td>2004</td>
<td>Kawase et al</td>
<td>50</td>
<td>0</td>
<td>Nicorandil</td>
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<td>Kinoshita et al</td>
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<td>Nagel et al</td>
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<td>88</td>
<td>90</td>
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<td>2002</td>
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<td>25</td>
<td></td>
<td>Adenosine</td>
<td>QCA &gt;50%</td>
<td>69</td>
<td>89</td>
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<td>Schwitter et al</td>
<td>48</td>
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</tbody>
</table>

CMR, cardiovascular magnetic resonance.
agents are in everyday clinical use worldwide, cardiovascular applications are not yet approved by the United States Food and Drug Administration. Currently it is easier to run an MRI for profit by doing non-cardiac applications. Thus, significant economic issues must be addressed.

MRI scanners trigger claustrophobia in many patients. Other patients cannot undergo MRI scans due to implanted devices like pacemakers or defibrillators. Arrhythmias and respiratory insufficiency compromise many of the highest quality CMR methods. Technology development can solve most of these issues.

**CONCLUSION**

With advances in CMR technology, multiple clinical indications have followed. Although there is overlap with other cardiac imaging modalities, CMR often works in a complementary fashion to these other techniques or resolves residual diagnostic dilemmas. The strengths of CMR lie in its ability to comprehensively image cardiac anatomy, function, perfusion, viability and physiology, and put this information in the context of the wide field of view of surrounding vascular and non-cardiac anatomy. At a time when serious concerns are being raised about the medical use of ionising radiation, it is reassuring to know that CMR provides high-quality diagnostic information without a need for radiation.

**Competing interests:** None.

**REFERENCES**

1. **Sodickson DK, McKenzie CA, Ohliger MA, et al.** Recent advances in image reconstruction, coil sensitivity calibration, and coil array design for SMASH and generalized parallel MRI. *Magma* 2002; **13**:158–63.


Technology and guidelines

Perfusion MR imaging with sensitivity encoding versus conventional angiography.


Multi-perforated atrial septum

A 61-year-old woman was referred owing to recent-onset, moderate dyspnoea on exertion. On physical examination the patient was in atrial fibrillation. The second heart sound was widely split with a prominent pulmonary component that was, however, moving with inspiration. A systolic ejection murmur was heard at the upper left sternal edge and there was also the impression of a diastolic rumble at the lower left sternal border. The patient was pink and the jugular venous pressure was not raised but there was mild bilateral ankle oedema.

Trans-thoracic echocardiography that had been performed elsewhere demonstrated a central jet through the atrial septum and the condition was deemed to be a typical atrial secundum atrial septal defect (ASD). On transoesophageal echocardiography, multiple jets were seen (panel A). The right ventricle was dilated, there was pulmonary hypertension (50 mm Hg) and the Qp/Qs was 2. The patient was referred for surgical repair. A multiperforated membranous atrial septum was found with a functional total cross-sectional area of approximately 3 cm² (panel B). It was resected and replaced by a patch of autologous pericardium.

Multiple ASDs are unusual, found in less than 5% of diagnosed cases of ASD,¹ and can be missed on trans-thoracic echocardiography. The effective shunt is the additive shunt of all the little holes.

REFERENCE
Advances in clinical applications of cardiovascular magnetic resonance imaging

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