Critically appraising a cardiovascular magnetic resonance imaging article

Clinical practice should be informed by the application of critical analysis of methodologically sound research. Critically appraising a research article can only be effective if one is familiar with the methods used. This article provides information to allow the reader to critically review cardiovascular magnetic resonance imaging papers.

Background

Cardiovascular magnetic resonance imaging has become widely established in clinical and research settings for its ability to provide information on anatomy, function and tissue characterization. Ridgway (2010) has comprehensively reviewed the applied physics. This article describes:

1. The components and applications of cardiovascular magnetic resonance imaging
2. Imaging planes, sequences and protocols
3. Pharmacological agents used
4. Key considerations for appraising methodology.

The setup

Cardiovascular magnetic resonance imaging uses general magnetic resonance imaging hardware with specific software tailored to cardiovascular imaging (*Figure 1*). Papers should describe the type of magnetic resonance imaging scanner used, the strength of the magnet (most imaging uses 1.5 Tesla magnets, but some use 3 Tesla), which cardiac coil was used and the technique of image acquisition. The setup used in the study would ideally be described in a reference study. Differences in setup between the reference and current study should be clarified.

Figure 1. Basic setup of cardiac magnetic resonance imaging. The magnets generate a magnetic field with strength expressed in tesla (T). In the clinical setting, 1.5T or 3T are used. Gradient coils can be orientated to direct the field of the main magnetic coil. Radiofrequency coils are able to transmit or detect electromagnetic energy. Adapted from Ridgway (2010).

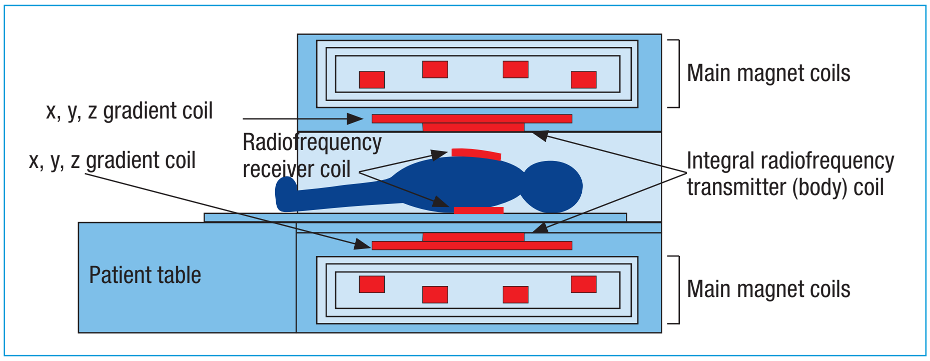

Table 1. Techniques used to obtain specific information

Feature	Technique
Morphology	Dark blood and bright blood static imaging
Function	Bright blood gated imaging. Cardiovascular magnetic resonance tagging (regions of myocardium grid marked and degree of deformation observed and/or quantified during the cardiac cycle)
Metabolism	Cardiac magnetic resonance spectroscopy (high energy substrate are measured)
Blood flow	Phase contrast imaging to determine peak velocity and flow parameters
Perfusion	First pass contrast enhancement of myocardium to detect areas of inducible ischaemia after application of a stress agent. Assessing vascularity of cardiac masses
Angiography	A vascular road map, arterial or venous either with or without contrast
Tissue characterization	T1 and T2 weighted images with or without fat suppression. T2* for detection of iron volume, T1 and T2 mapping. Early and late gadolinium enhancement

From Hundley et al (2010)

Applications

Cardiovascular magnetic resonance imaging is non-invasive with the ability to image in any plane. A wide variety of protocols is used to address clinical or research questions (*Table 1*). The Society of Cardiac Magnetic Resonance and the 2010 expert consensus document on cardiovascular magnetic resonance imaging have published guidance on protocols for given clinical scenarios (Hundley et al, 2010; Kramer et al, 2013). These outline the steps involved in studying specific structures as well as recommended protocols used to study disease states. Using these as a template, methodology can be assessed and should contain sufficient detail to allow reproduction of technique from the manuscript.

Pulse sequences

Pulse sequences are specific series of waveforms generated by gradient and radiofrequency coils used to obtain a magnetic resonance image (Bitar et al, 2006). These can delineate anatomy, function or tissue characterization.

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Table 2. Terminology based on vendor

	Spin echo		Gradient echo	
Vendor	RARE	HASTE	Spoiled gradient echo	Balanced steady state free precession
Siemens	Turbo spin echo	HASTE	Fast low-angle shot	True fast imaging with steady precession
Philips	Turbo spin echo	Single-shot fast spin echo	T1-weighted fast field echo	Balanced fast field echo
GE	Fast spin echo	Single-shot fast spin echo	Spoiled GRASS (gradient recalled acquisition in the steady state)	Fast imaging employing steady state acquisition
Hitachi	Fast spin echo	Fast spin echo, asymmetric data allocation with half scan	Gradient echo, normal, with low flip angle	Balanced spoiled steady state acquisition rewind gradient echo
Toshiba	Fast spin echo	Fast advanced spin echo	T1-weighted fast field echo	True-SSFP (steady state free precession)

From Boyle et al (2006). HASTE = half-fourier acquired single shot turbo spin echo; RARE = rapid acquisition with relaxation enhancement

Table 3. Contrast agents commonly used in cardiovascular magnetic resonance imaging

Contrast agent distribution	Trade names	Use
Intravascular or extracellular	Magnevist (gadopentetate dimeglumine) Omniscan (gadodiamide) ProHance (gadoteridol) Optimark (gadoversetamide) Gadovist (gadobutrol) Dotarem (gadoterate meglumine)	Gadolinium-based contrast agents are used to characterize tissue viability, masses and study first pass perfusion. The standard single dose of most gadolinium-based contrast agents is 0.1 mmol/kg. Double dose contrast is often used in stress testing protocols
Blood pool agents, commonly containing iron particles	Clariscan (PEG-feron) Supravist, Angiomark (ferucarbotran)	Blood pool agents are useful in angiography and perfusion studies. Some are also taken up by macrophages, and may be helpful in the study of vulnerable coronary plaques
Intracellular agents, i.e manganese chelates	Teslascan (mangafodipir trisodium)	Intracellular agents are taken up by normal myocardium. They can be used in delineating regions of 'at risk' myocardium

From Edelman (2004); Ni (2012)

There are two main types of pulse sequences: spin echoes (mainly used for anatomy rather than function, also called black blood sequences) and gradient echoes (used to study function, also called bright blood sequences). Spin sequences take longer but have a higher signal to noise ratio and are less susceptible to artefact. Gradient echoes are faster but have lower signal to noise and are more susceptible to artefacts. Sequences may be either two-dimensional (one section acquired at a time) or three-dimensional (multiple sections obtained simultaneously) (Bitar et al, 2006). Different vendors have specific names for these pulse sequences (*Table 2*)(Boyle et al, 2006).

Research applications

In clinical research cardiovascular magnetic resonance imaging may be used for primary work such as development of specific pulse sequences (e.g. magnetic resonance spectroscopy to measure metabolism; T1 and T2 mapping to measure the degree of fibrosis) and secondary work in clinical studies. In the latter, it can be used to select patients into trials, compare baseline characteristics between treatment arms and measure outcomes. Because of its high reproducibility cardiovascular magnetic resonance is very powerful for assessing surrogate endpoints in clinical trials (Pitcher et al, 2011). Use of cardiovascular magnetic resonance imaging may allow a reduction in study sample size. Bellenger et al (2000) reduced sample size by 81–97% compared to echocardiography, when measuring left ventricular mass, function and volume.

Imaging planes

The two main coordinate systems used are the body planes (coronal, axial and sagittal) and the cardiac planes (Ginat et al, 2011). The body planes help derive the scout images and inform the viewers which slice in one plane corresponds to that in another. Cardiac planes are also used as standard body planes are not sufficient to capture the dimensions of all chambers and ensure adequate visualization of each segment, owing to the oblique nature of the cardiac anatomy. The principal cardiac planes are the short axis, vertical long axis (two-chamber view), horizontal long axis, true four-chamber view, three-chamber view, left ventricular outflow tract and right ventricular outflow tract views.

Contrast agents

Blood and myocardial tissue have inherent relaxation properties, but contrast agents can affect these properties. Contrast agents can be divided into extracellular, blood-pool and non-gadolinium (Edelman, 2004; Ni, 2012). Most commonly used are gadolinium chelates, most of which are extracellular agents. *Table 3* summarizes the agents used and their applications.

Stress agents

To detect reduced myocardial perfusion reserve using cardiac magnetic resonance, first pass perfusion is combined with pharmacological stress, usually via a coronary vasodilator. At maximal hyperaemia or vasodilatation, regions of myocardium supplied by a significantly stenotic coronary artery appear hypoperfused. Stress sequences are compared to resting images for interpretation. Ensuring that a patient is adequately stressed is important as a false negative result can occur if this is suboptimal. In addition to monitoring heart rate and development of patient symptoms, 'splenic switch off' can be useful (Manisty et al, 2014). *Table 4* summarizes currently

KEY POINTS

- Critical appraisal is important when assessing the validity of a research paper.
- The reader needs sufficient knowledge of the techniques used and their limitations when assessing the quality of a study.
- The Society for Cardiovascular Magnetic Resonance website (www.scmr.org) lists cardiovascular magnetic resonance imaging protocols, which are tailored to specific clinical or research hypotheses.

used pharmacological stress agents in cardiovascular magnetic resonance imaging and potential adverse effects. Studies should state the criteria used to establish if patients were adequately stressed.

Appraising methodology

The setup and protocol should follow either recommended guidelines or a reference study to aid reproducibility. Images tend to be quantified on workstation software but can be reviewed on a patient archive and communication system (PACS) – these may be mentioned in the text. The manuscript should describe who quantified, reviewed and reported the studies, and if the reporter(s) were blinded. The paper should state the number of reviewers, their level of experience and accreditation, and if images were reviewed as a team or independently. These variables can be a source of bias. At a minimum, the reviewer of the images should not be directly involved in the study.

Conclusions

Cardiovascular magnetic resonance imaging has an established role in clinical practice, along with many developing research applications. To critically appraise a research paper in cardiovascular magnetic resonance imaging, the reader must have some knowledge of the components of a magnetic resonance imaging set up, the types of magnetic resonance imaging sequences, how they are used to create protocols for specific indications and whether appropriate methodology has been described and used. **BJHM**

Conflict of interest: none.

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Table 4. Properties of the commonly used stress agents in cardiovascular magnetic resonance imaging

	Adenosine	Dipyridamole	Regadenoson	Dobutamine
Mechanism of action	■ A1 and A2 receptor agonist ■ Vasodilation of coronary vessels (attenuated in diseased vessels) ■ Negatively chronotropic and inotropic ■ Net result is decrease in blood pressure with reflex tachycardia	■ Inhibits cellular reuptake of adenosine (indirect coronary vasodilator) ■ Results in increase in coronary blood flow	■ Adenosine (A2A) receptor agonist ■ Leads to coronary vasodilatation and increased coronary blood flow in normal vessels	■ Positive inotrope and chronotrope (β1, β2 receptor agonist with dose-related increase in heart rate, blood pressure and myocardial contractility) ■ Regional wall motion abnormalities occur as a result of reduced myocardial perfusion
Pharmaco-kinetics	Uptake by cell and cellular degradation	Metabolised and excreted through the liver (>95%)	>50% renally excreted unchanged	Renally excreted
	Half-life <10 seconds	Half-life approx. 30 minutes	Half-life 2–4 minutes	Half-life 2 minutes
Side effects	Transient first, second or third degree heart block, hypotension, bronchoconstriction, chest pain, lightheadedness, diaphoresis, nausea, facial flushing			
Dosing	140 μg/kg/min	Low dose protocol: infusion of 0.56 mg/kg in 4 minutes; high dose protocol: as well as the low dose infusion, a second injection of 0.28 mg/kg is given for 2 minutes	0.4 mg single injection	Usual peak dose 40 ug/kg/min (atropine may also be required to achieve target heart rate). Continuous infusion with 3-minute increments in dosage, aiming to achieve the calculated target heart rate

From Gerber et al (2008); Kramer et al (2013)