



Přehledový článek | Review article

Imaging in coronary artery disease. Cardiac magnetic resonance

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SOUHRN

Zobrazovací metody u ischemické choroby srdeční je třeba považovat za nástroj podporující léčbu pacienta. Zobrazovací metody pomáhají lékařům stanovit diagnózu přesněji a následně je účinněji léčit. U pacientů s ischemickou chorobou srdeční je rozhodovací proces nutno stále zdokonalovat. Důvodem pro tento přehled možností uvedené metody jsou zvyšující se počty pracovišť s vybavením pro magnetickou rezonanci srdce (cardiac magnetic resonance, CMR), pacientů podstupujících vyšetření metodou CMR i množství důkazů pro použití CMR jak u pacientů se stabilní ischemickou chorobou srdeční, tak s akutními koronárními syndromy. I když jsou aplikace ve výzkumu a technický vývoj pro pokrok v oblasti zobrazování velmi významné, pro pacienty i lékaře jsou naprosto zásadní různé možnosti využití této metody v klinické praxi; tyto možnosti jsou předmětem tohoto článku.

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ABSTRACT

Imaging in coronary artery disease should be regarded as a tool supporting patients' management. Imaging helps physicians to diagnose patients more precisely and to treat them more effectively. There is a constant need to improve the decision-making process in patients with coronary artery disease. The growing number of cardiac magnetic resonance (CMR) centers, patients undergoing CMR studies and the plethora of evidence for the use of CMR both in patients with stable coronary artery disease, as well as acute coronary syndromes, justify reviewing its capabilities. Although research applications and technical developments are of particular value for progress being made in the field of imaging, clinical applications are the most crucial for patients and treating physicians, thus they will be discussed.

Keywords:

Acute coronary syndromes

Cardiac magnetic resonance imaging

Coronary artery disease

Introduction

Imaging in coronary artery disease (CAD) should be regarded as a tool supporting patients' management. Imaging helps physicians to diagnose patients more precisely and to treat them more effectively. Although in many cases the diagnosis or the exclusion of stable CAD can be made on the basis of clinical evaluation including patients' age,

sex and chest pain characteristics, in numerous patients the tool verifying the baseline clinical judgement is needed. Moreover, a physician needs information additional to clinical evaluation to make a decision about management strategy (conservative vs invasive treatment, percutaneous vs surgical treatment, etc.) [1,2].

In the case of acute coronary syndromes (ACS), in the vast majority of cases, there is no need (and no sense) to

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perform imaging test additional to clinical evaluation and ECG to confirm that the patient really has ACS [3,4]. Particularly, in patients with ST-segment elevation myocardial infarction (STEMI) coronary angiography should be performed without any delay [4]. Invasive imaging (coronary angiography) is crucial for patients' treatment, and non-invasive imaging is indispensable for determining complications, further treatment needs and options as well as patients' prognosis.

There is a constant need to improve the decision-making process in these situations. Among other imaging modalities, cardiac magnetic resonance (CMR) is being more and more commonly used not only in research projects, but also in normal clinical scenarios. The growing number of CMR centres, patients undergoing CMR studies and the plethora of evidence for the use of CMR both in patients with stable CAD, as well as ACS justify reviewing its capabilities [5]. Although research applications and technical developments are of particular value for progress being made in the field of imaging, clinical applications are the most crucial for patients and treating physicians, thus they will be discussed.

Stable coronary artery disease

The main questions that a physician treating a patient with suspected CAD needs to answer include the following [1,2]:

- Does a patient have CAD?
- Should a patient undergo revascularisation?
- Should a patient undergo percutaneous (percutaneous coronary intervention – PCI) or surgical treatment (coronary artery bypass grafting – CABG)?
- Is there any additional disease that should be treated simultaneously (valvular disease, dilated aorta)?
- If not CAD, what could be the cause of chest pain?

When we review diagnostic capabilities of each imaging modality, one should think whether it could answer these questions. Does CMR answer these questions? It does! (... well almost).

Does the patient have CAD?

CMR has emerged as a valuable tool in the assessment of patients with suspected CAD. The growing evidence supporting the use of CMR to diagnose the presence of CAD has led to the recognition of stress CMR as a method equal to well established methods of functional testing in the case of suspected CAD, namely stress echocardiography, nuclear imaging (single photon emission computed tomography – SPECT), and positron emission tomography (PET) perfusion [1,2]. But the very first imaging modality in patients with suspected CAD should be transthoracic echocardiography and determining left ventricular ejection fraction (LVEF) [1]. This guides further management:

- (A) Patients with typical angina and impaired LVEF (<50%) should undergo invasive coronary angiography without delay related to additional test.

Except for patients with poor acoustic window, in whom echocardiography is not able to provide reliable data on LVEF, there is no room for CMR at this initial diagnostic step in these patients. However, CMR (or other stress imaging test) may be needed after coronary angiography to assess the extent of ischaemia and/or myocardial viability.

- (B) In patients with LVEF <50% without typical angina, imaging stress test should be the initial test for diagnosing CAD.

- (C) In the remaining patients (i.e. those with LVEF ≥50%), a physician should determine pre-test probability of CAD. Stress testing for ischaemia is needed in patients with intermediate pre-test probability of the disease. Alternatively, anatomical detection of CAD with the use of computed tomography (CT) angiography may be applied in selected patients.

Stress CMR offers several stress agents and protocols that are similar to those used in nuclear imaging (vasodilators: adenosine, dipyridamole or regadenoson) or stress echocardiography (dobutamine-atropine protocol) [6–8]. Details in protocols as well as pharmacological agents used in stress CMR may vary between CMR centres.

Should the patient undergo revascularisation?

Perfusion defects or new wall motion abnormalities during stress testing confirm the diagnosis of stable CAD. This is, however, not enough to make a decision regarding revascularisation. Current guidelines for revascularisation require evidence that the extent of ischaemia is significant, since only in this group of patients revascularisation improves prognosis in terms of CAD and all-cause mortality [1,2]. The huge advantage of CMR as a modality for confirming diagnosis of stable CAD is the fact that simultaneously with the diagnosis of CAD, we receive the information concerning the extent of ischaemia (Fig. 1). This is a common advantage of imaging stress tests that is lacking in the case of ECG exercise test, coronary angiography or coronary CT angiography [1,2].

Although various imaging stress tests are able to provide the information on the extent of ischaemia, the definition of significant ischaemia varies between them [1,9,10]. Since there are no studies with the use of CMR determining the ischaemia burden threshold in terms of improved survival after revascularisation, the findings from stress nuclear imaging are interpolated in this field [9,10]. The question is, how to translate area of ischemia ≥10% of the left ventricular myocardium in SPECT into CMR perfusion or dobutamine study. According to the European Society of Cardiology guidelines, high risk in CMR ischaemia imaging means ≥2 out of 16 segments of the left ventricle being ischemic on stress perfusion or ≥3 segments of the left ventricle with dysfunction induced by dobutamine stress test [1]. This definition, however, is not based on randomised controlled trials. The precise answer to the question what a significant burden of ischaemia is in CMR perfusion studies and who benefits from revascularisation will be provided by two ongoing studies. The MR-INFORM study compares two strategies

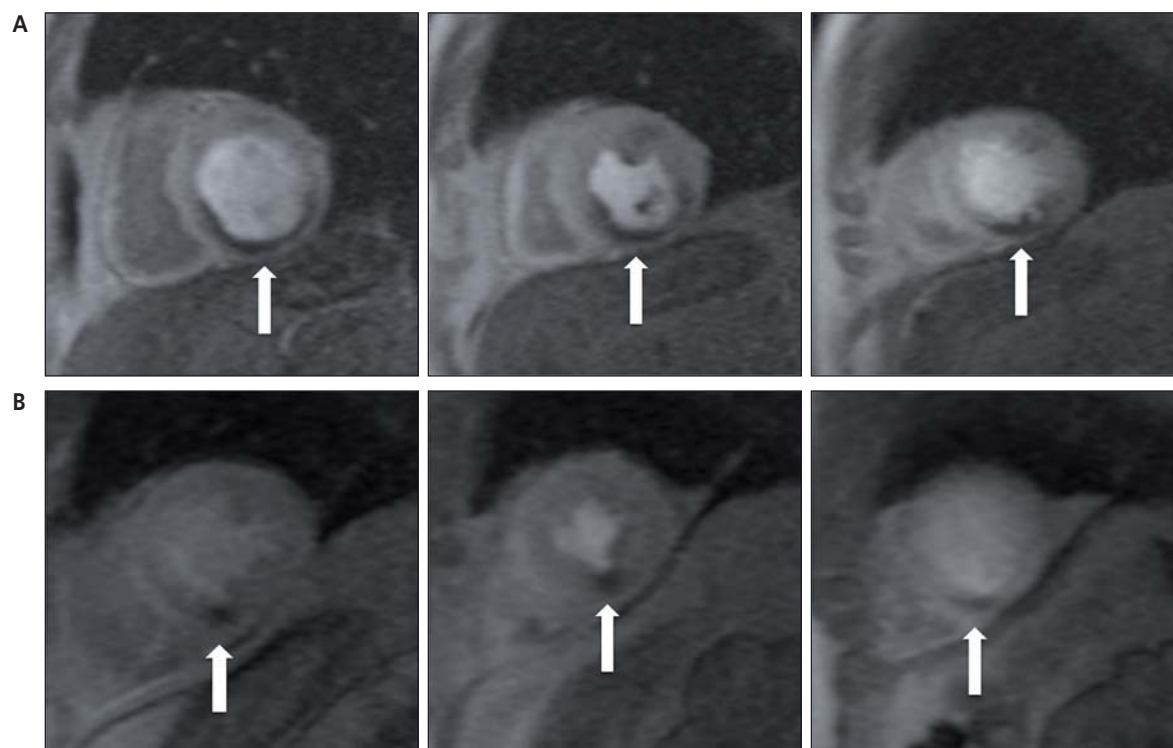


Fig. 1 – Stress perfusion cardiac magnetic resonance in three slices (left to right: basal, mid-ventricular, apical). (A) Large perfusion defect consistent with moderate–severe ischaemia is seen in the territory supplied by the right coronary artery (arrows). (B) Smaller perfusion defect seen in a different patient (arrows).

in patients with suspected CAD [10]. In one arm, the decisions about the need for revascularisation are guided by invasive fractional flow reserve. In the second arm, CMR perfusion-guided therapy is implemented. In patients in CMR arm, angiography (with intention to revascularise) is recommended in the case of perfusion defects in at least 2 segments of a 32-segment model. A 32-segment model means that each segment of a 16-segment model was divided into two halves: an endocardial and an epicardial one [10]. In the ISCHEMIA trial, the criteria for moderate–severe ischemia mean ≥ 4 of 32 subsegments with perfusion defects [9]. In a 32 segment model, each subsegment equals to approximately 3% of the myocardium, so 2 subsegments represent 6% of the myocardium, and 4 subsegments – 12%, respectively. Both thresholds are near to SPECT-derived 10% threshold. The future will show which criterion is more accurate for patients' management.

The next important question, next to ischaemia testing which needs to be solved prior to revascularisation is myocardial viability [2,11]. Although, the substudy of the STICH trial raised concerns about the impact of viability assessment on the outcomes after revascularisation, still viability needs to be taken into consideration when revascularisation in patients with heart failure due to ischaemic aetiology is planned [2,11–13]. CMR offers a simple and robust analysis of myocardial viability. It is based on prolonged wash out of gadolinium contrast agents from necrotic or fibrotic tissue, causing the phenomenon of late gadolinium enhancement (LGE) in these areas [14,15]. In the landmark study, Kim et al. showed that the transmural extent of LGE (expressed in percentages of the left ventricular

wall thickness) corresponds to the likelihood of function recovery after revascularisation [14]. The greater extent of LGE is associated with a lower likelihood of improving contractility after PCI or CABG (Fig. 2).

Should the patient undergo PCI or CABG?

This issue is a handicap of CMR. To make a decision about performing PCI or CABG, precise information on coronary artery anatomy is needed. In the case of multivessel disease, the Syntax Score is recommended as a valuable tool in the decision-making process for or against PCI or CABG in given cases [2,16]. Despite technical developments made in the last decade, CMR currently cannot be used in clinical practice for visualisation of coronary arteries in case of CAD or the assessment of the degree of stenosis [8,17]. Further progress is needed in this field.

Is there any additional disease that should be treated simultaneously (valvular disease, dilated aorta)?

Simultaneously with stress testing for ischaemia, CMR provides additional information on valvular status, aorta size, left ventricular function and myocardial viability [8,17]. The comprehensiveness and versatility of CMR provide superiority to other stress tests. Diagnosing aortic dilatation or significant valvular disease concomitant to newly diagnosed stable CAD with a significant extent of ischaemia, not only determines the extensiveness of surgery (e.g. CABG alone vs CABG plus valvular surgery), but also speaks for or against the given method of treatment (conservative management vs PCI vs CABG). All these information needs to be taken into consideration.

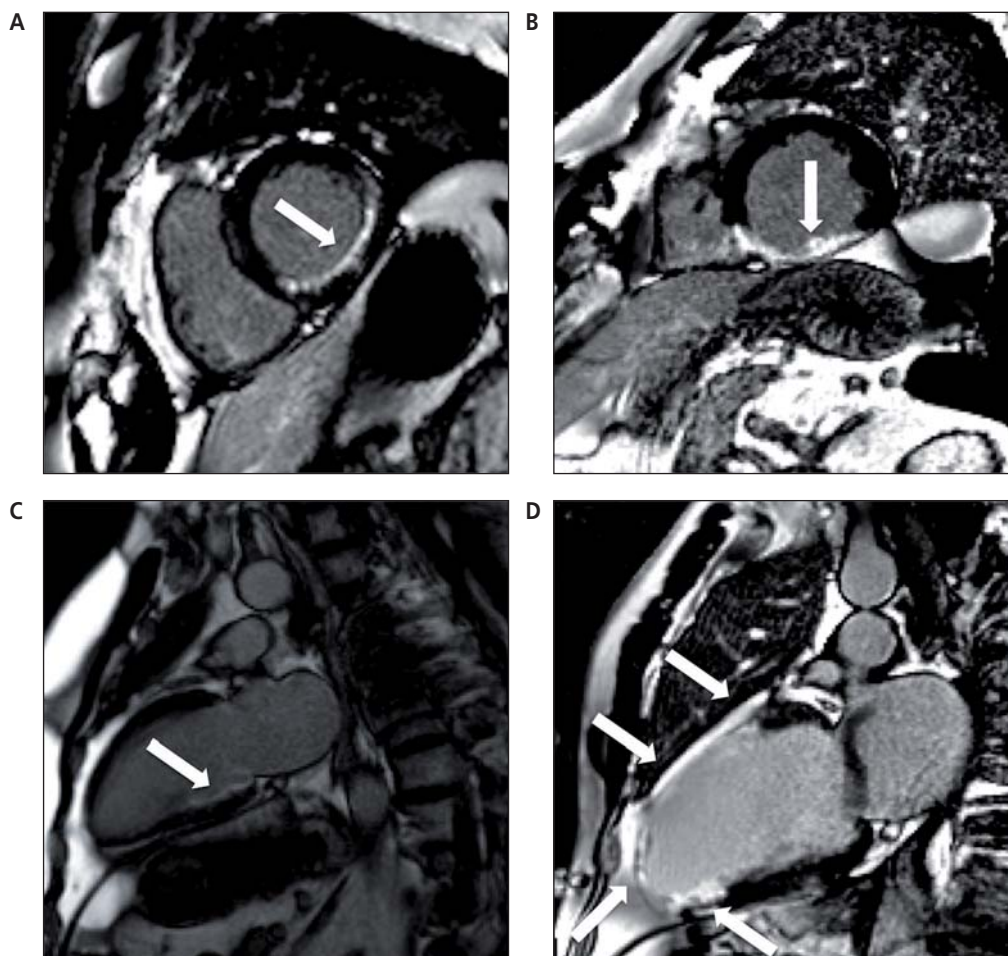


Fig. 2 – Viability imaging in cardiac magnetic resonance with the use of late gadolinium enhancement method. (A) Short axis slice demonstrating subendocardial infarction in the inferior wall (arrow). (B) Short axis slice demonstrating transmural infarction in the inferior wall (arrow). (C) Two-chamber view. Small subendocardial infarction in the basal slice of the inferior wall is seen (arrow). (D) Two-chamber view. Large transmural infarction in the anterior wall, the apex, and the apical segment of the inferior wall is seen (arrow).

If not CAD, what could be the cause of chest pain?

In some cases, CMR may be helpful in determining possible causes of chest pain in patients in whom the study excluded the presence of CAD. Hiatal hernia or spinal degenerative disease is among the most common possible causes of chest pain in patients without obstructive CAD.

Acute coronary syndromes

Contrary to stable CAD, invasive imaging is the first step in patients with myocardial infarction presenting with ST-segment elevation and high risk patients with non-ST elevation ACS [3,4]. The majority of crucial questions such as those concerning the infarct related artery, the extent of atherosclerosis in the remaining arteries, as well as the immediate results of restoring flow in the occluded artery are based on invasive angiography. Nevertheless, management of patients with ACS is not only limited to opening the occluded artery (although this is crucial step for short-term and long-term outcome). But what if no occluded artery is present and troponin levels are high? Is it really ACS? Which is the culprit lesion? Are there any complicati-

ons? CMR cannot be regarded as a routine imaging modality in patients with ACS. However, it provides useful and unique information influencing patients' treatment and outcomes and should be considered in selected patients [8,17]. Treating patients with ACS raises the aforementioned questions and CMR helps to answer them.

Is it really ACS?

There is a small group of patients with suspected ACS in whom a non-invasive imaging may be implemented. Performing CMR in patients with acute chest pain without obstructive CAD on invasive angiography demonstrated that myocarditis is the most common final diagnosis in this group of patients [18,19]. Differentiation of ischaemic aetiology (myocardial infarction – MI) from non-ischaemic causes (such as myocarditis) as a cause of troponin rise in patients with chest pain is based on the localisation of LGE and myocardial oedema [8,17–19]. In the case of MI, the localisation in subendocardial or transmural and corresponds to the coronary artery supply territories (Fig. 2). Myocarditis causes diffuse, patchy areas of LGE and myocardial oedema with subepicardial, intramyocardial, Which is the culprit artery?

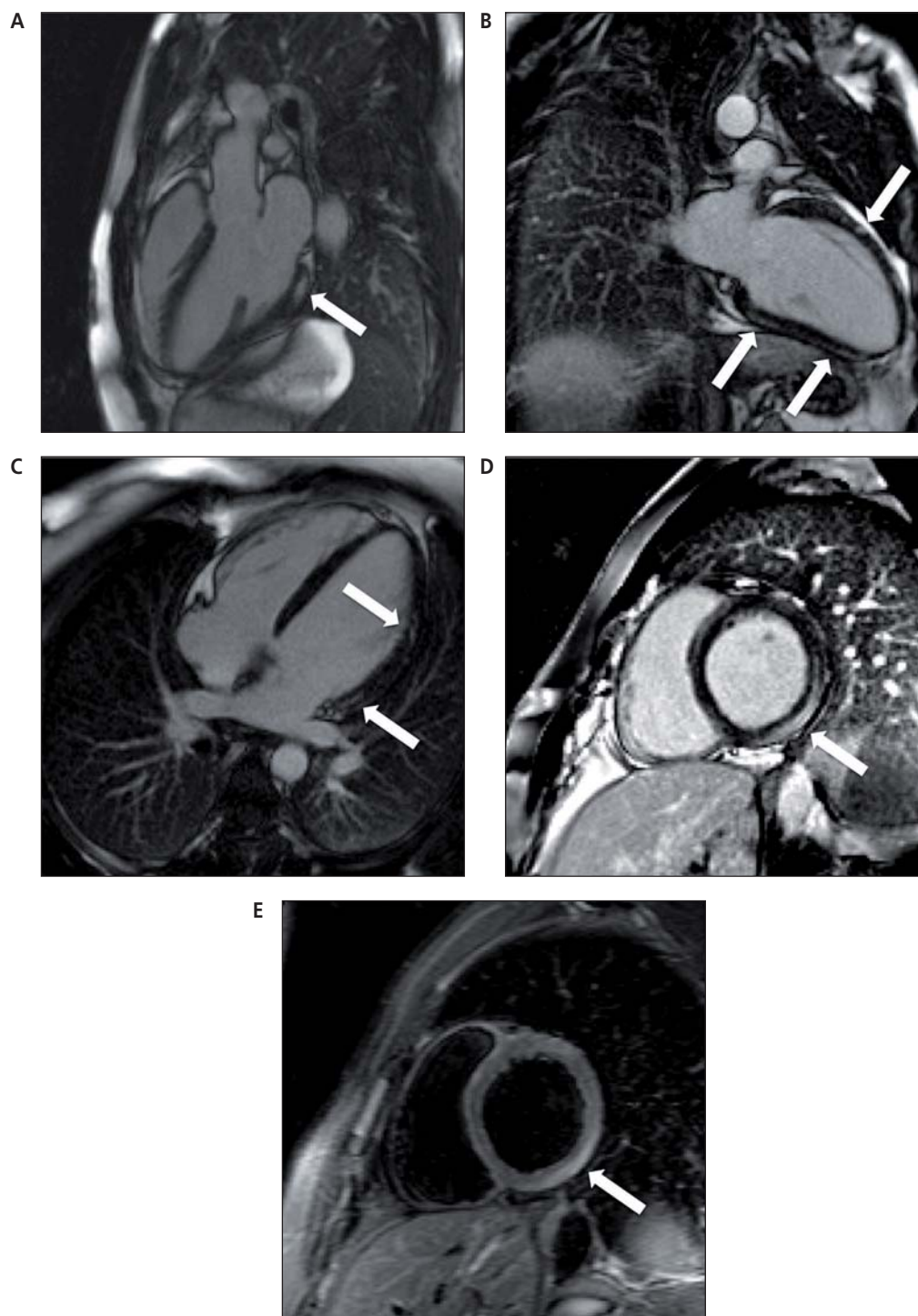


Fig. 3 – Cardiac magnetic resonance in a patient with myocarditis admitted with chest pain and ST segment changes suggestive of acute coronary syndrome. Diffuse subepicardial and intramyocardial areas of late gadolinium enhancement (LGE) are seen (arrows) in three chamber view (A), two chamber view (B), 4 chamber view (C) and short axis basal slice (D). Areas of LGE do not correspond to the coronary artery distribution. Additionally, myocardial oedema is seen in pre-contrast T2-weighted short axis image (E, arrow. The same slice as in Figure 3D).

The identification of the culprit artery is usually straightforward on the basis of coronary angiography. In some patients, however, coronary angiography reveals multivessel disease with no obvious culprit lesion. Implementing CMR with LGE imaging demonstrating infarct scar and T2-weighted imaging that demonstra-

tes myocardial oedema in the area supplied by the infarct related artery may be useful in these cases (Fig. 4) [20–23]. With this method, CMR has the ability to differentiate patients with acute and chronic myocardial infarction. One should note, that the progress of invasive imaging with the use of optical coherence tomography

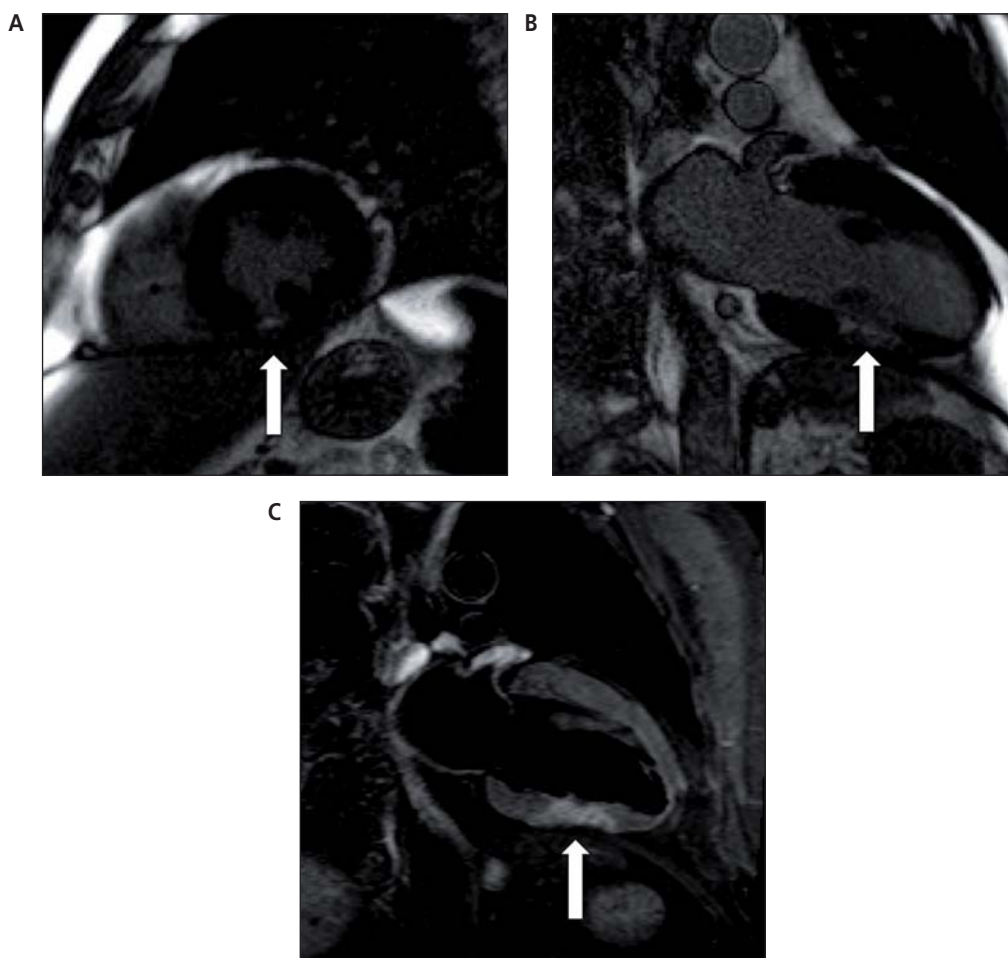


Fig. 4 – Cardiac magnetic resonance in acute myocardial infarction. Subendocardial scar is seen both in short axis as well as in two chamber view (A, B, arrows) consistent with the infarction in the area supplied by the right coronary artery. T2-weighted imaging demonstrates myocardial oedema (larger than the area of scar) consistent with the acute phase of the infarct (C, arrow).

in precise localisation of culprit lesions should be recognised [24–26].

Are there any complications?

The vast majority of MI complications are diagnosed with the use of echocardiography. However, CMR, additionally to the assessment of location and the extent of MI, has the ability to demonstrate various types of myocardial damage [27,28]. Although restoring flow in coronary artery is the main aim of treating MI, it does not necessarily reflect the restoration of normal tissue perfusion. No reflow phenomenon has been shown to significantly influence patients' prognosis and therapeutic success [29]. With the use of CMR it is possible to detect areas of irreversible microcirculation damage named microvascular obstruction (MVO) (Fig. 5) [28]. Additionally, myocardial haemorrhage may occur as the result of damage of endothelial cells, loss of their structural integrity leading to extravasation of blood cells in reperfused myocardium [28,30]. Finally, peri-infarct zone may be identified at the border between scar tissue and viable myocardium and represents arrhythmogenic substrate [31–33]. All these phenomena have been shown to have negative prognostic implications [28,32,33].

It has been shown that CMR is superior to echocardiography in detecting intracavitary thrombi in the left ventricle in patients with recent MI [34–36]. This issue is of particular importance since it requires antithrombotic treatment additional to antiplatelet therapy [4].

Contraindications to CMR and safety of the study

Prior to referring a patient for a CMR scan, a physician should consider whether there are any contraindications to CMR. Firstly, one should consider general contraindications for CMR such as electronic devices (e.g. conventional pacemakers or cardioverter-defibrillators, insulin pumps), metallic foreign bodies in the eyes and unknown implants [37]. Secondly, specific contraindications to stress CMR should be listed [6,7]:

- adenosine, dipyridamole: 2nd or 3rd degree atrio-ventricular block, sick sinus syndrome, chronic obstructive lung disease, severe hypotension, unstable angina, decompensated heart failure, allergy against vasodilator or contrast medium;

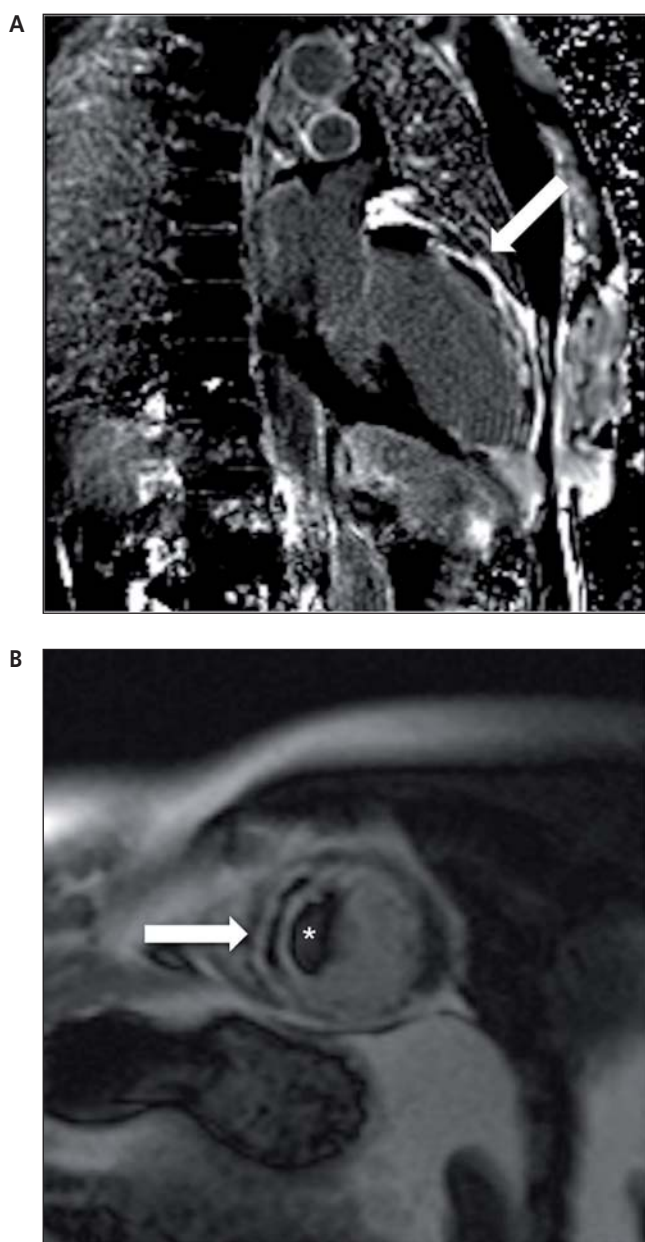


Fig. 5 – Cardiac magnetic resonance in acute myocardial infarction. Dark areas of microvascular obstruction inside the infarct core are seen in a patient with large antero-septal infarction (A, B, arrows). Additionally, thrombus in the left ventricle is seen (B, asterisk).

- regadenoson: 2nd or 3rd degree atrioventricular block, sinus node dysfunction;
- dobutamine: severe hypertension (>220/120 mmHg), unstable angina, acute myocardial infarction, severe aortic stenosis, hypertrophic obstructive cardiomyopathy, acute perimyocarditis or endocarditis, glaucoma.

Additionally, the administration of gadolinium-chelate contrast media is contraindicated in patients with severe renal failure (glomerular filtration rate <30 mL/min/1.73 m²). On the other hand, it should be underlined that neither coronary stents nor sternal suture wires are contraindications to CMR.

Summary

The final choice for stress testing for ischaemia should be based on patient's suitability for a given test, availability, and local expertise [1]. CMR is contraindicated in patients with pacemakers or cardioverter-defibrillators, stress echo is not a preferred imaging technique in patients with poor acoustic window, and SPECT – if radiation exposure should be avoided. Thus, there is no ideal imaging modality for patients with CAD. There are pros and cons to each of the methods. Providing information on ventricular size and function, ischaemia and viability, valvular function and aorta size, as well as aetiology of left ventricular dysfunction (e.g. myocardial infarction vs non-ischemic causes such as myocarditis), CMR seems to be close to the ideal imaging modality in coronary artery disease.

Conflict of interest

No conflict of interest.

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Ethical statement

I declare that the research was conducted according to Declaration of Helsinki.

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