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Magnetic resonance imaging in the diagnostics of myocardial infarction

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Summary

Cardiovascular magnetic resonance (CMR) has a growing application in the diagnostics of myocardial infarction (MI). It is a non-invasive method that can be used regardless of the shape of patient's body. A single study allows assessment of the morphology and function of the cardiac muscle. It visualizes many pathophysiologic changes such as edema, microvascular obstruction (MVO) or necrosis, and complications of MI, like myocardial hemorrhage (MH) or thrombus, which are very difficult to diagnose using other methods. An obvious advantage of CMR is the possibility to differentiate an acute MI from the chronic one and to identify the etiology of fibrosis. All the aforementioned features of CMR have made it a useful tool in planning the treatment and assessing the prognosis of patients after MI.

Key words: magnetic resonance • myocardial infarction • edema

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Background

Imaging of the heart and vessels with magnetic resonance (CMR) is gradually becoming commonly used in the field of cardiac diagnostics. In recent years, due to technological advances, image quality and therefore the sensitivity and specificity of this method have greatly improved. Nowadays, CMR is considered a gold standard in many situations involving the cardiovascular system. Indications include the assessment of the anatomy and of the global function of the left and right ventricle and its mass, the diagnostics of congenital heart diseases, cardiac tumors, pericardial diseases, and ischemic heart disease, as well as differentiation of cardiomyopathies.

Recently, CMR has gained significant recognition in the diagnostics of myocardial infarction (MI). Guidelines on MI diagnostics and viability assessment published by the European Society of Cardiology (ESC) recognize CMR as a Class-I method [1]. Sequences used before and after contrast administration allow clear visualization of myocardial

morphology and precise scar quantification [2–4]. The multitude of sequences used in CMR allow to differentiate among tissues (fat, fibrous) and physiological processes (edema, inflammation). Each sequence should be set up with different key parameters for an optimal picture quality. Therefore, the use of a standardized protocol helps to perform a complete examination.

Figure 1 shows standard parts of the examination in a patient with MI. Specific sequences are added to or subtracted from the examination, depending on either patient's ability to hold breath or because of the fact of revealing a new pathology, such as thrombus, during the examination. Depending on the sequence, CMR allows also to evaluate the pathologies of valves (stenosis or insufficiency) or fluid in the pericardial sack, to differentiate between a true and a false aneurysm of the left ventricle, or to assess coronary arteries. A significant advantage of this method is its potential to evaluate the right ventricle (RV) without any special sequences.

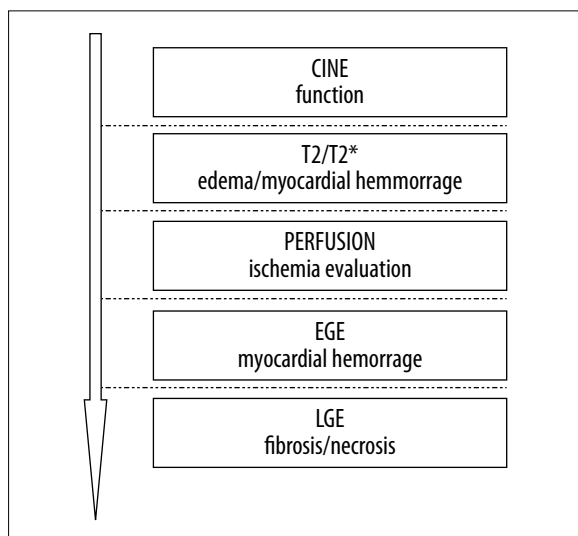


Figure 1. Parts of a standard examination in patients after myocardial infarction. CINE – sequences showing motion of the myocardium during the whole cardiac cycle; T2/T2* – T2/T2*-weighted imaging; EGE – early gadolinium enhancement; LGE – late gadolinium enhancement.

Function

Generally, CINE (gradient echo or Steady-State Free Precession – SSFP) sequences are used in all patients for the functional analysis of the heart. SSFP technique is characterized by a high contrast between myocardium (hypointense) and blood in the cardiac chambers (hyperintense). This allows clear visualization of myocardial borders. Further examination includes assessment of the left ventricular (LV) mass, end-diastolic and end-systolic volumes, and contractility of both ventricles. Images are taken in 2-, 3-, and 4-chamber views and short-axis stack from the base to the apex. The recommended thickness of a slice is 6-8 mm, the gap between slices 2-4 mm [5], with in-slice resolution of 1.5-2 mm, and temporal resolution of 35-45 ms [6]. The left and right ventricular function analysis is usually conducted with the use of specialized software. This method is based on a manual (or automatic) assessment of endo- and epicardial borders in the short axis from the base to the apex of the ventricle. There are no clear guidelines regarding papillary muscles and their inclusion to or exclusion from the endocardium. Because the choice of one or the other convention results in different outcomes, it is advised to always use the same method. This allows later comparisons of the results. MR provides the most precise and reproducible estimation of the LV mass and its function [2,7].

Myocardial Edema

Magnetic resonance is important in diagnosing patients with acute coronary syndrome (ACS), owing to its ability to visualize the so called ischemic area at risk (IAR). T₂-weighted images allow to identify this area being a part of a muscle with edema. A comparison of the IAR with the area of necrosis (estimated after several months following MI) shows the amount of salvaged myocardium. Moreover, the presence of edema allows to differentiate between an old and an acute MI [8].

Most MR imaging techniques show a contrast between tissues with a different proton relaxation after radiofrequency impulse. The relation between tissue relaxation time T₂ and water content in the myocardium was observed as early as in 1983 [9]. Prolongation of the relaxation time of tissues with a high density of protons bound to water molecules results in an increased signal intensity in T₂-weighted images. An increase in the water content in the myocardium is not the only mechanism responsible for a prolonged T₂ relaxation time. The relaxation time of free water molecules is 40 times longer than the one of molecules bound to proteins [10]. Therefore, their release into the intracellular space (as in acute MI) leads to a significant prolongation of TR and an increased signal intensity in T₂-weighted images. Visualization of edema is normally carried out with T₂-weighted imaging such as fast/turbo spin echo sequences with fast suppression (SPAIR – Spectral Adiabatic Inversion Recovery) and blood suppression, allowing a good delineation of endo- and epicardial borders (Figure 2). STIR (Short TI Triple Inversion Recovery Fast Spin Echo) is the most commonly used sequence. This method applies both fat and blood inversion impulses, which allows to obtain a higher contrast between the edema and the unchanged myocardium. Currently, much effort is put into developing new hybrid techniques. T₂-prepared SSFP is supposed to result in a better image quality with a similar contrast-to-noise ratio (CNR) [11]. Edema can also be evaluated by measuring T₂ relaxation time. T₂ maps are used for this purpose – a series of T₂ images with a different echo time (TE). The interdependence between signal intensity of the myocardium and TE allows for T₂ time estimation, which is much shorter for a healthy myocardium than for edematous tissue [12]. Despite the wide use of T₂-weighted imaging in edema evaluation, this method has certain limitations which must be taken into account during image interpretation. The main problem is the “slow flow” artifact which leads to a partial blood suppression within areas of a slow flow (apex of LV). This leads to the appearance of a hyperintense signal, often confused with sub-endocardial edema. Additionally, a relatively low contrast between edematous and healthy myocardium the occurrence of motion artifacts due to inadequate breath holding, very often lead to a diagnostic dilemma. Diagnosis of myocardial edema is still based mostly on a subjective estimation of the myocardial signal. The methods of T₂ signal quantification are being developed to standardize the diagnostic criteria independently of the sequence used. The edematous tissue should show signal intensity of at least 2× standard deviation (SD) of the mean signal intensity of a healthy tissue [4,13]. Moreover, edema has to be visualized in two perpendicular projections. The protocol used for edema should include T₂-weighted imaging in the long axis, in 2-, 3-, 4-chamber views and short-axis stack from base to apex [5]. Optimal SNR is achieved with the slice thickness of approx. 10 mm. Long TE (>60 ms) and TR, of at least 2× R-R intervals, lead to a maximal contrast between the healthy tissue and edema.

Perfusion and Viability

Ultrafast gradient-echo sequences or echo planar imaging (EPI) allow assessment of myocardial perfusion using the first-pass method. This method is based on the assessment of gadolinium distribution in the myocardium, right

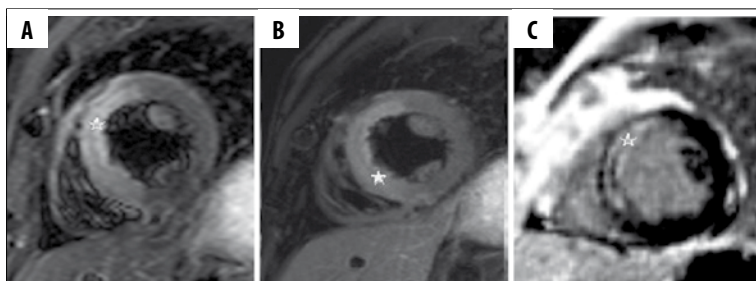


Figure 2. Edema (a hyperintense signal) in the interventricular septum and anterior wall of the left ventricle on (A) STIR and (B) T2-weighted images with fat suppression SPAIR. A myocardial scar after infarction in the area of edema shown in LGE sequences (C).

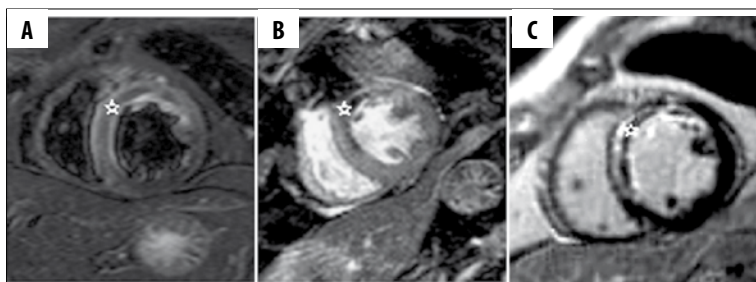


Figure 3. A hypointense signal showing the area of myocardial hemorrhage (A) STIR, (B) T2*-weighted images, (C) LGE.

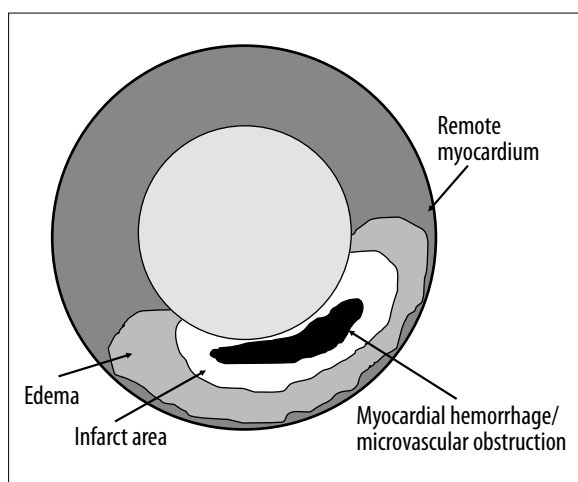


Figure 4. Area of myocardial infarction visualized with magnetic resonance [30].

after the intravenous injection. The signal intensity of the myocardium in areas with a good blood supply increases quickly, whereas segments with a worse blood supply stay hypointense. First-pass imaging is mostly used in three short-axis views (basal, mid, and apical segments) as well as 2- and 4-chamber views. As much as 0.05–0.10 mmol/kg of contrast medium should be injected at the injection rate of 3–7 ml/s. The slice thickness should amount to 8 mm, in-slice resolution to <3 mm, temporal resolution to 100–125 ms, while the whole sequence should cover 40–50 heart cycles to visualize the whole process of contrast passage into the myocardium [5]. The blood-oxygen-level-dependent (BOLD) method can also be used to assess myocardial perfusion. This method applies paramagnetic properties of unoxygenated hemoglobin (short TR) and diamagnetic properties of oxygenated hemoglobin (long TR). Signal differences in different segments are caused by changing levels of deoxyhemoglobin in myocardial microcirculation [14].

Late Gadolinium Enhancement (LGE) imaging allows visualization of irreversibly damaged myocardium (fibrosis,

necrosis). A great advantage of this method is its ability to identify the etiology of fibrosis. In the case of ischemic heart disease, the area of necrosis appears sub-endocardially or transmurally in typical areas of coronary supply. In non-ischemic diseases, the areas of necrosis appear intramurally, subepicardially, and subendocardially, but irrespectively of the coronary supply. MR also allows assessment of the RV infarction.

LGE utilizes two properties of gadolinium-based contrast media: decreasing longitudinal relaxation of tissues and increasing signal intensity of T₁-weighted images, as well as the fact of their being an extracellular compound. In a healthy muscle, the contrast does not enter the intracellular space and is quickly washed out to the intravascular space. In a damaged cell wall (acute MI), a paramagnetic contrast enters the myocytes and is washed out much more slowly than from the extracellular space. In the case of MI, the interstitial space is much larger due to scar formation, which leads to a prolonged contrast deposition in the damaged muscle. Both mechanisms result in a prolonged (lasting a few minutes) contrast deposition in the damaged myocardium. These regions exhibit a hyperintense (white) signal ("bright is dead"). To visualize this process, T₁-weighted images are used. The most often used sequences include the gradient echo with an inversion impulse suppressing the signal from the healthy muscle. Special pilot sequences help to choose the best inversion time (TI). A correct TI allows for a complete suppression of the signal from the healthy muscle, resulting in a high difference between the healthy (black) and the damaged (white) myocardium. Images are acquired after 10–15 min following contrast administration. The examination should include 2-, 3- and 4-chamber long-axis views and a short-axis stack from base to apex. The recommended slice thickness is 6–8 mm with a gap of 2–4 mm (a total of 10 mm), with special resolution of 1.4–1.8 mm [5]. Image acquisition should be performed in end-diastole with TR equal to 2× R-R interval (1× R-R in bradycardia and 3× R-R in tachycardia). In patients with arrhythmia or with breath-holding problems, single-shot sequences should be used (only

one R-R interval to acquire the whole image) [15]. New 3D sequences are also more commonly used in LGE visualization [16]. There are many methods applied to assess a myocardial scar using LGE. Visual assessment method is the most commonly used and the easiest one. The assessment includes a 17-segment model and a 5-point grading scale. The size of the infarct area is calculated as a percentage of the scar compared to the muscle thickness [17,18]. Because this is a very subjective method, new automatic and semi-automatic methods have been proposed. Early trials showed that using the brightness threshold of $2-3 \times$ SD of the signal from a healthy muscle allows measurement of the scar extension in a very similar manner as is used in measuring the histopathologic results [19,20]. This trial was performed for images $0.5 \times 0.5 \times 0.5$ mm. Images used in the daily practice have a much smaller resolution, which leads to so called partial volume effect (artifact caused by averaging the signal from a healthy and a necrotic tissue in one voxel) and overestimation of the scar area. The use of higher cut-off values ($5 \times$ SD) or "full width at maximum" techniques (cut-off value set at half the intensity of scar tissues) may help reduce the partial-volume effect. However, the choice of the cut-off value is still made on the basis of a subjective assessment [21,22]. Therefore, many leading centers continue to rely mostly on the visual assessment of scar tissue based on experience [23,24].

Myocardial Hemorrhage. Microvascular Obstruction

In the case of myocardial infarction, CMR allows visualization of other pathophysiological processes like MVO and MH (Figure 3). MVO is defined as an area of hypointense signal surrounded by LGE [6]. In practice, MVO assessment is performed by analyzing LGE, after 1–5 minutes following contrast administration, and then after 10–15 minutes.

Because the contrast agent enters damaged microvasculature very slowly, MVO decreases in size in LGE images after 10–15 minutes. Visualization of MH is also performed using T_2 - and T_2^* -weighted sequences [25–27]. As a result of hemorrhage, oxygenated hemoglobin is replaced by deoxyhemoglobin (with four unbound electrons), with strong paramagnetic properties. This leads to a shorter T_2 relaxation time and a hypointense signal in the area of hemorrhage [27].

Conclusions

The applications of CMR presented in this paper allow for a detailed and noninvasive diagnosis of acute coronary syndromes (ACS) without exposing the patient to ionizing radiation. An important advantage of MR is its potential to apply versatile imaging techniques for assessing processes that take place in the myocardium in the acute phase of MI (Figure 4). MR makes it possible to visualize the heart in any desired view, regardless of the anatomy of the chest wall or abundant fat tissue. Even though other diagnostic techniques (ECG, SPECT, echocardiography, necrotic markers) are well developed, in questionable cases, CMR allows clear differentiation between MI and Takotsubo cardiomyopathy or myocarditis [28,29]. The role of this method is limited because it is time-consuming, expensive (as compared to other methods) and less accessible (also in comparison to other methods). It should also be noted that this method requires a continuous cooperation of the patient, which instantly excludes patients in severe condition. Therefore, the diagnostic protocols should be as short as possible. This method has also certain limitations. Its contraindications include the presence of a metal shaving in the eyeball or an implanted ICD. It is also relatively contraindicated in women in their first trimester.

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