How to measure myocardial infarct size by cardiac magnetic resonance imaging

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Abstract

In survivors of acute myocardial infarction (MI), the initial size of infarction is associated with long-term prognosis. This article addresses the role of contrast-enhanced cardiac magnetic resonance (CMR) imaging in determining the presence and extent of MI. Contrast-enhanced CMR is widely accepted as the reference method for imaging infarct size. The principles involved in contrast-enhanced CMR imaging of MI will be considered, including pathophysiology, gadolinium contrast kinetics, and imaging methods. The different approaches to measuring infarct size with CMR will also be discussed. ■ *Heart Metab*. 2016;70:14-18

Keywords: acute myocardial infarction; CMR imaging; infarct size

Introduction

In survivors of acute myocardial infarction (MI), the initial size of infarction is associated with long-term prognosis.[1-4] Myocardial infarct size can be assessed noninvasively with different methods, including measurement of cardiac biomarkers (eg, troponin), electrocardiography, nuclear imaging, and contrast-enhanced cardiac magnetic resonance (CMR) imaging.[5,6] Each of these methods have strengths and limitations; however, contrast-enhanced CMR is widely accepted as the reference method for imaging infarct size. In this article, the use of CMR to measure infarct size will be considered.

CMR for assessment of infarct size: an overview of general principles

Gadolinium chelates are extracellular contrast agents. After intravenous administration of gadolinium, the contrast agent perfuses locally through myocardium and diffuses within the interstitial compartment. In the presence of infarct tissue, the gadolinium distribution volume is increased due to the degradation of cardiac cells; the wash-in, wash-out kinetics are disturbed, and gadolinium persists within the infarct zone for a longer period of time and is revealed by a hyperintense (bright) area on T1-weighted imaging.[7-10] The regional retention of gadolinium spatially reflects the

Abbreviations

CMR: cardiac magnetic resonance; **LGE:** late gadolinium enhancement; **MI:** myocardial infarction; **MVO:** microvascular obstruction; **OAT:** Otsu-Auto-Threshold; **ROI:** region of interest; **SD:** standard deviation; **STEMI:** ST-segment elevation myocardial infarction; **FWHM:** full width at half maximum

territory of infarct tissue fibrosis at the near-cellular level.[11] Inversion-recovery T1-weighted methods allow optimized signal and contrast[12,13] and are used in clinical practice.[14]

Acquisition

A CMR scan should be conducted by appropriately trained staff in line with contemporary standardized protocols.[13] Infarct imaging with contrast-enhanced CMR involves a wide-bore clinical scanner, typically 1.5 or 3.0 Tesla, a phased-array chest surface coil, and retrospective electrocardiogram gating. Infarct tissue is revealed by late gadolinium enhancement (LGE) imaging. The method typically involves breath-hold inversion recovery imaging 10 to 15 minutes after intravenous administration of a gadolinium-based contrast agent (0.10-0.20 mmol/kg). Scans of the entire left ventricle should be acquired sequentially with short-axis slice positions and also with orthogonal long-axis positions. The slice positions should be spatially registered with other acquisitions for mass, function, and tissue characterization. If breath-holding is poor, then a "single-shot" acquisition method may be preferred. In order to ensure that uninjured myocardium appears black, the inversion times should be individually adjusted to optimize nulling of apparently normal myocardium (typical values, 200-300 ms). In order to rule out the possibility of artefact, scans should be repeated with "phase swops."

Timing after acute MI

Infarct size changes progressively after acute MI.[15] Initially, infarct tissue is expanded because of edema, inflammatory-cell infiltrates, and hemorrhage. As healing progresses, these acute infarct pathologies resolve and are replaced with collagen scar tissue such that the size of infarction diminishes with time. CMR with LGE can track these changes because gadolinium is an extracellular contrast agent. Due to these changes over time, the size of infarction as revealed by LGE within the first week after an acute MI may overestimate the actual size of infarction[15]; LGE may more closely approximate infarct size in the following days and weeks as injured tissue is replaced by collagen scar tissue.

The prognostic value of infarct size revealed by contrast-enhanced CMR may vary over time from the index event. A multivariable analysis carried out by Lønborg et al[16] showed that—beyond other clinical parameters of the severity of MI, including peak troponin T concentration—final infarct size measured at 3 months was associated with all-cause mortality and heart failure hospitalization.

Measurement of infarct size with CMR

LGE images should be analyzed by observers who have been trained to use software that is appropriate for measurement of infarct size.[14]

Where feasible, the presence of acute infarction should be established on the basis of abnormalities in cine wall motion, resting first-pass myocardial perfusion, and LGE imaging. If LGE imaging is used, the presence of acute infarction should be confirmed on both the axial and long-axis acquisitions. The epicardial and endocardial borders of the ventricle should be delineated by manual or semiautomated methods. The papillary muscles, trabeculae, and blood pool should be excluded from these contours. The apical short-axis slice may be excluded to rule out partial volume effects.

The myocardial mass of late gadolinium (grams) can be quantified with computer-assisted planimetry, and the approach to image analysis may be user defined (ie, manual) or fully automated.

Methods for estimation of infarct size

Delineation of the infarct territory involves identifying the border of the bright infarct zone, distinguished from the lower signal intensity of neighboring unaffected tissue and the remote zone. The main approaches include manual delineation based on visual assessment,[17] determination of the "full width at half maximum" (FWHM),[18,19] use of the Otsu-Auto-Threshold (OAT) method,[20] thresholding from the remote zone (eg, based on >5 standard deviations [SDs]),[19]

and automated methods.[21,22] An example of how the estimated extent of infarction may differ between methods is shown in *Figure 1*. Comparative studies of these methods have recently been performed.[23-25]
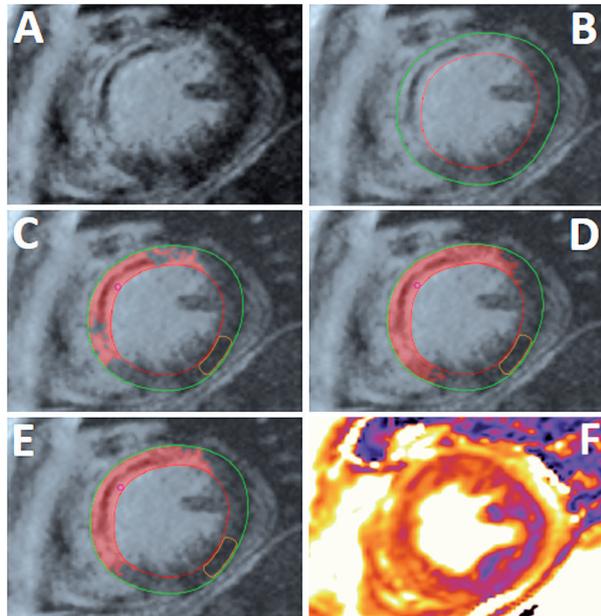

Fig. 1 *Cardiac magnetic resonance imaging applying different estimation methods to delineate extent of myocardial infarct territory. The images depict a basal short-axis slice from a 70-year-old male who was admitted with an anteroseptal ST-segment elevation myocardial infarction and treated with primary percutaneous coronary intervention to an occluded proximal left anterior descending artery. The procedure was complicated by the slow-flow phenomenon and persistent ST-segment elevation. Cardiac magnetic resonance was performed on a MAGNETOM Avanto (Siemens Healthcare, Erlangen, Germany) 1.5-Tesla scanner with a 12-element phased-array cardiac surface coil 48 hours after admission. **(A-E)** Delayed-enhancement phase-sensitive inversion recovery pulse sequences; **(F)** quantitative T2 parametric mapping sequence.*
(A) The uncontoured image demonstrates transmural late gadolinium enhancement of the mid anteroseptum (hyperenhanced region) with a central hypoenhanced region indicative of microvascular obstruction. (B) The endocardial (red) and epicardial (green) contours are then manually drawn. (C-E) A region of interest is placed in the remote (normal) myocardium (orange contour). The infarct area may then be automatically detected and manually corrected using the (C) full width at half maximum, (D) 2-SD, and (E) 5-SD methods. (F) A corresponding T2 parametric map is shown, which may be used to calculate the area at risk. The edematous myocardium is depicted by the color map in orange. The analysis was performed with QMass (Medis, Leiden, the Netherlands).

Manual delineation

The manual approach involves the observer drawing a border around the bright infarct zone to separate it from neighboring unaffected tissue. This approach is subjective, but it minimizes the potential for automated error.

Infarct border delineation based on thresholding (threshold set to a >5-SD difference in signal intensity versus remote-zone signal intensity)

For infarct-size delineation based on a greater than 5-SD difference in mean signal intensity in the infarct zone versus the remote zone, a region of interest (ROI) should be manually inserted within apparently unaffected myocardium in an area distant from the infarct zone, and the area of hyperenhancement calculated as the territory defined by a signal intensity more than 5 SDs above the mean within the ROI.[19] The size of the remote-zone ROI should be large enough to be representative; in general, a 2.0-cm^2 ROI is considered to be representative.

Full width at half maximum

The FWHM technique defines the threshold for boundary delineation as half the maximal signal within the scar.[18,19] An ROI should be drawn manually in the infarct zone (taking care not to involve the dark core of microvascular obstruction [MVO], if present); hyperenhancement is then calculated as pixels where signal intensity is greater than 50% of the automatically determined maximum signal intensity in the infarct zone. The FWHM method is unaffected by ROI size as it selects the threshold based on the single pixel with highest signal intensity.

Otsu-Auto-Threshold

OAT[20] automatically identifies hyperenhanced areas and has minimal user dependence. The OAT method involves automatic calculation of the signal-intensity threshold for each slice by dividing the signal-intensity histogram in each slice into two groups (enhanced, normal) according to the signal-intensity threshold that gives the least variance (lowest sum of variances) and, thus, the most homogeneity of signal intensities within each group. Endo- and epicardial contours are user defined, as is manual correction of noise artefact. OAT does not involve ROIs and so is more user independent than other approaches.

Overview of diagnostic performance

Flett et al[19] demonstrated that infarct size may be reliably delineated using thresholding greater than 5

SDs above a remote reference region and expressed as a percentage of total left ventricular mass. Use of a 2-SD threshold approach leads to an overestimation of infarct size, whereas the FWHM approach has good reproducibility.

McAlindon et al[24] measured infarct size repeatedly in 40 patients with recent ST-segment elevation MI (STEMI). They found that the manual and FWHM methods were associated with the lowest inter- and intraobserver variability for infarct size, with similar findings for interscan variability. Khan et al[25] assessed infarct size in 10 STEMI patients repeatedly at 1.5- and 3.0-Tesla field strengths. They found that the FWHM method was accurate and reproducible, whereas the threshold approach (5 SD) and OAT methods overestimated infarct size at both field strengths. Vermes et al[23] assessed 28 patients with acute MI and found no differences between the OAT and the 5-SD threshold methods.

One of the main limitations of these analyses is the lack of reference data for measurement of the absolute amount of infarct tissue. Experimental studies have shown that infarct size can be estimated with laboratory techniques such as tissue staining with the colorless dye triphenyltetrazolium chloride (TTC). With this dye, the area of dead cells will appear pale, and viable cells—which retain NADH—will be red, due to a color change in the dye when reduced by dehydrogenases.

Microvascular obstruction

MVO revealed by contrast-enhanced CMR represents failure of the intravenous contrast agent to penetrate within the infarct core.[26-28] Infarct regions with evidence of MVO are usually included within the infarct area, and the area of MVO can be separately assessed and expressed as a percentage of total left ventricular mass.[26,27] MVO occurs in about 40%-50% of STEMI survivors and is a prognostically important complication.[27-29] Noncontrast T1-mapping has emerging potential for imaging MVO with comparable prognostic significance to contrast-enhanced CMR.[30]

Infarct size and myocardial salvage

In survivors of acute MI, the amount of salvageable myocardium is represented by the amount of ischemically jeopardized tissue that is amenable to recovery.

Myocardial salvage can be calculated by subtraction of percent infarct size from percent area at risk, as revealed by T2-weighted edema imaging.[31-33]

Myocardial viability

The extent of LGE is a measure of the extent of viable myocardium after MI[34,35] and predicts the potential for recovery after coronary revascularization.[36,37] CMR has a Class 1A guideline recommendation for assessing ischemia and viability in STEMI survivors who have multivessel coronary disease.[6]

Conclusion

Contrast-enhanced CMR is widely accepted as the reference method for imaging infarct size and pathology. Because of acute tissue injury and swelling, the initial size of infarction revealed by CMR in the first week after STEMI overestimates actual (final) infarct size. A threshold approach based on a 5-SD difference in signal intensity versus the remote-zone signal intensity and the FWHM method have the best diagnostic performance overall. ■

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