

Delayed Enhancement Cardiac MRI In Ischemic and Non-Ischemic Heart Failure

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ABSTRACT

Background: In patients with left ventricular systolic dysfunction, the primary diagnostic issue is to differentiate the underlying cause whether related to coronary artery disease or dilated cardiomyopathy, for which coronary angiography was often used.

Aim of the Work: Using Delayed enhancement-magnetic resonance imaging (DE-MRI) to identify myocardial tissue characteristics through retention of gadolinium in areas with reduced density of viable myocytes so appear enhancing (bright). So, we can differentiate dilated from ischemic cardiomyopathy.

Patient and Method: Our study included 34 patients with left ventricular systolic dysfunction (ejection fraction less than 40% by echocardiography). All of them were submitted to DE-MRI using achievea 1.5 Tesla MRI machine.

Results: 15 patients (44%) showed infarct pattern of DE (presumed ischemic cardiomyopathy) while 19 patients (56%) showed no DE or non-infarct pattern of DE (presumed dilated cardiomyopathy).

Conclusion: DE-MRI could be considered as an effective non-invasive tool to differentiate ischemic from non-ischemic cardiomyopathy.

Key words: Delayed enhancement- MRI- Heart failure- Coronary artery disease- Dilated cardiomyopathy.

INTRODUCTION

Cardiovascular magnetic resonance imaging (CV MRI) has recently emerged as a new non-invasive imaging modality capable of providing high resolution images in any desired plane⁽¹⁾. It has evolved from an effective research tool into a clinically proven, safe and comprehensive imaging modality providing anatomic and functional information in acquired and congenital heart diseases⁽²⁾.

Over the last several years, CV MRI has undergone rapid evolution and tremendous advances in pulse sequence design, scanner hardware, and coil technology resulting in progressive expansion of the clinical applications⁽³⁾. For imaging cardiac structure and function, pulse sequence and hardware development has resulted in improvement in image quality with simultaneous acceleration of image acquisition, resulting in shorter but better examinations. Improved coil design now allows the use of parallel imaging technology, resulting in further reduction in acquisition time⁽⁴⁾.

In particular, new pulse sequences have enriched the inherently superior soft tissue contrast provided by MRI so that it now provides the reference standard for in vivo viability imaging⁽⁵⁾. Additionally, the pattern and distribution of scar as demonstrated by CV MRI often provide useful information regarding the specific etiology of various cardiac disorders⁽¹⁾.

This improvement has led to the recognition of CV MRI as the reference standard for the assessment of regional and global systolic function, the detection of myocardial infarction and viability as

well as the evaluation of pericardial diseases and cardiac masses. In some centers, CV MRI is emerging as the test of choice for the detection of ischemic heart disease, as well as for the initial work-up of patients presenting with heart failure⁽⁶⁾.

The treatment of patients with left ventricular systolic dysfunction is determined in part by the identification of the underlying disease process. The primary diagnostic issue centers on differentiating an underlying cause of the left ventricular dysfunction that is related to dilated cardiomyopathy or coronary artery disease⁽⁷⁾.

This differentiation is clinically important as ischemic cardiomyopathy is associated with shorter mean survival than non-ischemic cardiomyopathy. In addition, the patient management is altered as patients with ischemic heart disease may benefit from revascularization, and secondary preventive pharmacotherapy, whereas patients with non-ischemic cardiomyopathy may have better response to beta-blockade⁽¹⁾. In many centers, coronary angiography is routinely performed for this task⁽⁷⁾.

Contrast-enhanced CV MRI can play a role in the differentiation between primary dilated cardiomyopathy and ischemic cardiomyopathy through the identification of myocardial scarring or fibrosis as presence of delayed enhancement⁽⁸⁾. This would reduce the costs and inherent risk associated with invasive cardiac catheterization on which the diagnosis of dilated cardiomyopathy is still dependent⁽⁷⁾. In addition, CV MRI in non-ischemic cardiomyopathy patients strongly predicts adverse cardiac outcomes⁽⁹⁾.

Direct imaging of myocardial fibrosis is possible with the use of an inversion recovery T1-weighted gradient-echo sequence after the intravenous administration of a gadolinium-chelate. This cardiac magnetic resonance technique has been named "delayed enhancement" and demonstrates non-viable tissue as hyperenhanced or bright. This technique was developed primarily for characterization of myocardial scarring after myocardial infarction⁽¹⁰⁾.

It is suggested that the likely mechanism of myocardial scar enhancement is a combination of delayed wash-in and wash-out kinetics of non-viable tissue and different volumes of distribution of gadolinium in viable and non-viable regions. Because the presence of fibrotic tissue increases the interstitial space per unit volume and gadolinium diffuses rapidly into the interstitial, but not intracellular space; the infarcted myocardium has increased concentrations of gadolinium per unit volume of tissue resulting in hyperenhancement relative to the viable myocardium⁽¹⁰⁾.

AIM OF THE WORK

This study aims to identify the role and diagnostic potential of delayed enhancement cardiovascular magnetic resonance imaging to differentiate left ventricular systolic dysfunction related to dilated cardiomyopathy from that related to coronary artery disease.

DELAYED ENHANCEMENT CARDIAC MRI

Mechanism of delayed enhancement of myocardial infarction

Gadolinium produces its effect by becoming distributed in damaged cells and the engorged extracellular space in the acute setting and in the extracellular space of scar tissue in the chronic setting. In either case, the washout of gadolinium is slower in these areas, resulting in high signal intensity compared to normal myocardium on T1-weighted imaging⁽¹¹⁾.

The mechanism of myocardial hyperenhancement in the setting of infarction is demonstrated in figure 1. (The mechanism is based on two simple facts. First, gadolinium chelates are extracellular contrast agents that are inert and cannot cross myocyte cell membranes. Second, in normal myocardium, myocytes are densely packed and thus myocyte intracellular space forms the majority (~85%) of the volume. Conceptually, it then follows that the volume of distribution of

gadolinium in a hypothetical voxel of normal myocardium is small, and the overall number of gadolinium molecules is low. In the setting of acute infarction, there is myocyte membrane rupture, which allows additional gadolinium to diffuse into what was previously intracellular space. This in turn results in increased gadolinium concentration and therefore hyperenhancement. In the setting of chronic infarction, myocytes have been replaced with collagenous scar. In this situation, the interstitial space is expanded which again leads to increased gadolinium concentration and therefore hyperenhancement⁽¹⁾.

Accordingly, areas of prior infarction will have higher concentrations of contrast on delayed images (5 to 10 minutes after intravenous administration)⁽¹²⁾.

Technique of Delayed Enhancement Cardiac MRI.

The delayed-enhancement sequences used for infarct detection are designed to maximize the differential signal intensity between normal myocardium and infarcted myocardium. The standard delayed-enhancement imaging sequence incorporates a segmented gradient echo sequence and an inversion prepulse to produce heavy T1-weighting⁽¹³⁾.

PATIENTS AND METHODS

Patient Population: This study was conducted on 34 subjects (26 males and 8 females with mean age 48 ± 10 years). All of them had left ventricular systolic dysfunction with ejection fraction less than 40% by echocardiography. We excluded patients with acute myocarditis, congenital heart disease, hypertrophic cardiomyopathy, or infiltrative heart disease. A full medical history was taken including symptoms of heart failure, history of previous myocardial infarction, in addition cardiovascular risk factors like hypertension, diabetes mellitus, smoking and dyslipidemia were analyzed. **The study was approved by the Ethics Board of Al-Azhar University.**

Echocardiography was done to assess left ventricular systolic dysfunction as per American Society of Echocardiography recommendations⁽¹⁴⁾. All patients were submitted to MRI examination.

Magnetic Resonance Imager: A Philips Achieva (1.5 tesla) superconducting magnet was used in Al-hussein university hospital.

Patient Preparation and Set Up for the MR Study: The procedures of the MR examination were explained to the patient including breath hold instructions.

The patients were briefly interviewed with regard to MR contraindications, whether the patient has a pacemaker or any other implanted devices, or other foreign materials inside the body (in particular cerebral aneurysmal clips).

Sedation was not needed in any case. Most of the patients had regular sinus rhythm.

For delayed enhancement imaging: Intravenous gadolinium-DTPA is given (0.2 mmol/kg) followed 10 to 15 minutes later by breath-hold segmented inversion recovery balanced turbo field echo (IR-b-TFE) in the same short-axis locations as the cine images with the following parameters: TR/TE: 3.8/1.86 FOV: 300 NSA: 1 Flip angle: 15 TI: 260-350 msec.

Number of slices: 7 Slice thickness: 8 mm Scan time: 9-15 sec.

Data Analysis: Analysis of the CMR (DICOM) images was performed using workstation.

Left ventricular ejection fraction and volumes were quantified automatically from the cine images after manual tracing of the endocardial border of the left ventricle in the short axis images during end systole and end diastole for each slice position.

Determination of the presence or absence of late gadolinium enhancement was done by reviewing all contrast-enhanced images. Enhancement patterns were classified into subendocardial, transmural (more than 50% of wall thickness), subepicardial or midwall.

Statistical Analysis: The continuous variables were expressed as mean \pm SD; comparison between groups was made by means of unpaired t test. Chi square test was performed for non-continuous variables. A 2-tailed probability value of <0.05 was considered statistically significant.

RESULTS

Our study included 34 patients with left ventricular systolic dysfunction (ejection fraction less than 40 % by echocardiography). Male gender predominated our study population (male/female ratio=26/8) with mean age 48 ± 10 years (range from 32-70). All patients were subjected to delayed enhancement cardiac MRI and coronary angiography.

All population had history of shortness of breath. Eleven patients (32%) had history of myocardial infarction or unstable angina. Fourteen patients (41%) had electrocardiographic evidence of myocardial infarction.

Mean ejection fraction by echocardiography for the whole population was 23 ± 7 . Regional wall motion abnormalities were detected in 18 cases (53%).

Delayed enhancement cardiac MRI showed different patterns of myocardial enhancement in the examined patients. One of 34 patients (2.9 %) showed subendocardial enhancement in coronary artery territories (pattern I). Seven of 34 patients (20.6 %) showed transmural enhancement in coronary artery territories (pattern II). Seven of 34 patients (20.6 %) showed both subendocardial and transmural enhancement in coronary artery territories (pattern III). Six of 34 patients (17.6 %) showed midwall enhancement (pattern IV). One of 34 patients (2.9%) showed combined patchy subepicardial and transmural enhancement (not in a coronary artery territory) (pattern V). One of 34 patients (2.9%) showed combined patchy midwall and transmural enhancement (not in a coronary artery territory) (pattern VI). Eleven of 34 patients (32.5%) showed no delayed myocardial enhancement (pattern VII) (Table 1).

Table (1): Per case patterns of delayed myocardial enhancement.

	DE pattern	No of cases	Percentage of cases
Pattern I	Subendocardial territorial	1	2.9
Pattern II	Transmural territorial	7	20.6
Pattern III	Subendocardial and transmural territorial	7	20.6
Pattern IV	Midwall	6	17.6
Pattern V	Subepicardial and transmural (non territorial)	1	2.9
Pattern VI	Midwall and transmural (non territorial)	1	2.9
Pattern VII	No DE	11	32.5

(DE: Delayed enhancement, No: Number).

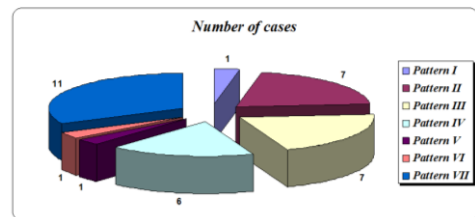


Fig. (1): Per case patterns of delayed myocardial enhancement.

Fifteen of 34 patients (44%) had subendocardial and/or transmural myocardial

enhancement in the territory of one or more major coronary artery (LAD, LCX, or RCA)” patterns I, II and III”, they were named as group A. This is the pattern of delayed enhancement of myocardial infarction, so this group is presumed to represent heart failure related to coronary artery disease.

Nineteen of 34 patients (56%) had either no delayed myocardial enhancement or other patterns of enhancement that differed from those of group A ”patterns IV, V, VI, VII”, they were named as group B. This group is presumed to represent heart failure due to dilated cardiomyopathy.

Table (2): Groups A and B.

	Group A	Group B
Patterns of DE	I, II, III	IV, V, VI, VII
Number of cases	15	19
Percentage of cases	44	56
Presumed cause of heart failure	Coronary artery disease	Dilated cardiomyopathy

(DE: Delayed enhancement).

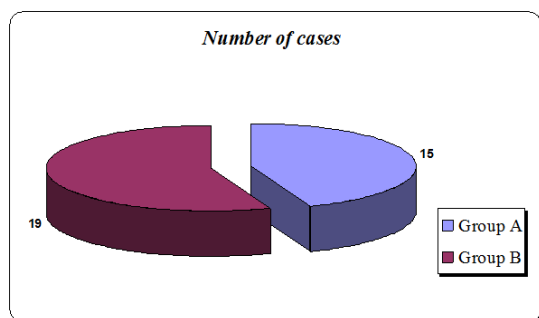


Fig. (2): Groups A and B.

REPRESENTATIVE CASE

History: Male patient 55 years old presented by shortness of breath. Echocardiography revealed EF of 28 %

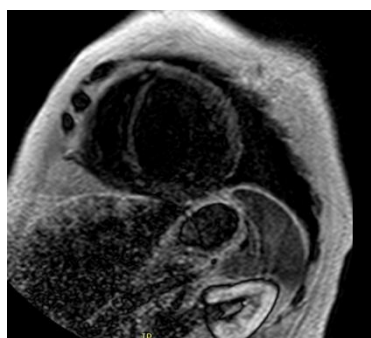


Fig. (3): Short axis view.

IR sequence at SA view showing LGE at the mid cavitary anteroseptal view involving the whole thickness of the myocardium

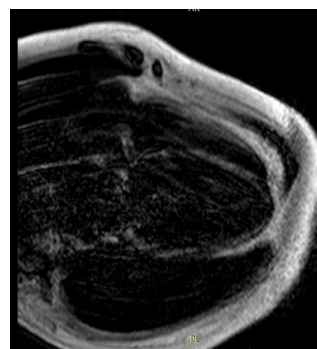


Fig. (4): Four-chamber view.

DISCUSSION

Cardiac MRI has become a clinically important tool for the evaluation of known or suspected heart diseases. Advances in both scanner hardware and novel pulse sequences continue to improve the diagnostic utility of cardiac MRI ⁽¹⁵⁾.

Delayed enhancement cardiac magnetic resonance imaging (DE-CMR) involves administration of gadolinium contrast material followed by an inversion-recovery preparatory pulse to null normal myocardium, then a segmented k-space gradient-echo acquisition. Retention of contrast material results in T1 shortening and thus increased signal intensity on T1-weighted images relative to that of the normal myocardium ⁽¹⁶⁾.

The mechanism of DE-CMR is likely based on the following: First, tissue volume in normal myocardium is predominantly intracellular (75 to 80% of the water space); and second, currently available gadolinium contrast media are “extracellular” agents because they do not cross cell membranes ⁽¹⁷⁾. Thus, the volume of distribution of gadolinium contrast in normal myocardium is quite small (about 20% of the water space), and one can consider viable myocytes as actively excluding contrast media ⁽¹⁸⁾.

Pathophysiological states that result in a reduced density of viable myocytes will then have an increased volume of distribution of gadolinium and a higher concentration ⁽¹²⁾. This mechanism is independent of the cause or etiology for nonviable myocardium. Whether the tissue consists of contraction-band necrosis in the setting of acute myocardial infarction, collagenous scar in chronic myocardial infarction, or fibrosis in various non-ischemic cardiomyopathies, the region will have an increased gadolinium concentration if there is a reduced density of viable myocytes ⁽¹⁸⁾. Studies in

animal models demonstrated an excellent match of infarcted regions by DE-CMR to histopathology⁽¹⁹⁾.

In patients with heart failure and depressed left ventricular systolic function, differentiation of ischemic from non-ischemic causes has important therapeutic and prognostic implications⁽²⁰⁾. This differentiation is clinically important as ischemic cardiomyopathy is associated with shorter mean survival than non-ischemic cardiomyopathy. In addition, patient management is altered⁽¹⁾.

In this study, DE-CMR was assessed for the ability to differentiate between dilated cardiomyopathy and coronary artery disease as the underlying cause of left ventricular systolic dysfunction in patients with stable heart failure after excluding acute myocarditis, congenital heart disease, hypertrophic cardiomyopathy, and infiltrative heart disease.

The patients in our study were classified according to the pattern of delayed myocardial enhancement into two groups: group A (15 patients, 44%) that showed subendocardial and/or transmural enhancement in a coronary artery territory (infarction pattern) and group B (19 patients, 56%) that showed no delayed enhancement or other enhancement patterns that differ from group A. According to this pattern, group A was supposed to represent cases of heart failure due to coronary artery disease while group B was supposed to represent cases of dilated cardiomyopathy.

In our study, DE-CMR could demonstrate myocardial infarctions in absence of clinical evidence or Q waves in ECG. This is in agreement with *Wu et al*, *Plein et al.*⁽²¹⁾ and *Kwong et al.*⁽²²⁾. Also *Schuster and Bulkley*⁽²³⁾ demonstrated that virtually all patients with congestive heart failure and significant coronary artery disease had gross myocardial scarring at autopsy, even in those without clinical history of myocardial infarction, angina, or Q-wave.

Absent mid wall enhancement pattern in *Wu*⁽²¹⁾ studies could be attributed to small sample size (32 patients in Wu study and 45 patients in Bello study), and also because only hyperenhancement patterns consistent with regions of prior myocardial infarction were included in the analysis, as explained by Mahrholdt⁽¹⁾.

Two other patterns of delayed enhancement were demonstrated in group B in our study. These patterns were subepicardial enhancement (1 patient, 5.3%) and non-territorial transmural enhancement (2 patients, 10.5%). These two patterns could result from

previous attacks of myocarditis⁽²⁴⁾. Dilated cardiomyopathy can result from asymptomatic or subclinical myocarditis⁽²⁵⁾, so these patients were not excluded from the study. Although dilated cardiomyopathy defined by the World Health Organization (WHO) was originally understood as being 'primary', several etiologic factors have been identified. A genetic disposition with a possible additional effect of inflammatory or toxic injuries to the myocardium may contribute to the pathogenesis of dilated cardiomyopathy⁽¹⁾.

Other conditions can cause gadolinium uptake in the myocardium, and this must be considered during interpretation of dilated cardiomyopathy⁽¹⁾. Amyloidosis, hyperesinophilic syndrome, and histiocytoid cardiomyopathy can cause subendocardial enhancement not in a coronary artery territory. Mid wall enhancement can result from hypertrophic cardiomyopathy, and pulmonary hypertension. Subepicardial and transmural enhancement can be caused by myocarditis and sarcoidosis⁽²⁴⁾.

CONCLUSION

DE-CMR is a valuable non-invasive imaging technique in patients with left ventricular systolic dysfunction. It helps identify the underlying cause, predict prognosis and responsiveness to therapy and determine myocardial viability in cases of coronary artery disease and accordingly chances for coronary revascularization.

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