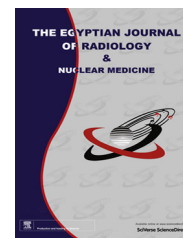




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ORIGINAL ARTICLE

Utility of cardiac MRI in the assessment of myocardial viability: Evaluating its role using 3-T machine in correlation with SPECT

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KEYWORDS

3 T magnetic resonance imaging;
 Single photon emission computed tomography;
 Coronary artery disease;
 Myocardial viability

Abstract *Background:* Assessment of viable myocardium has important prognostic value in patients with coronary artery disease (CAD). The aim of this study was to compare 3 T cardiac magnetic resonance (CMR) with single-photon emission computed tomography (SPECT).

Methods: Thirty-three patients with coronary artery disease were involved in this study. All patients were examined using coronary angiography to determine the degree of the coronary artery disease. Then, they underwent 3 T CMR examination, after administration of intravenous gadolinium and the segmental extent of myocardial enhancement was determined, followed by SPECT evaluation. Comparison of myocardial viability was performed in 99 coronary territories.

Results: Agreement between two modalities was obtained in 88 segments (88.9%), resulting in a kappa value of 0.725. In 99 segments, we had eleven discordant results. Eleven SPECT viable segments were non-viable according to CMR.

Conclusion: SPECT was comparable to 3 T CMR for myocardial viability assessment, C-MRI detected more non-viable segments with high definition to the thickness of the myocardial scar tissue than the SPECT.

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1. Introduction

Not every patient with coronary artery disease (CAD) can benefit from coronary revascularization so, assessment of viable myocardium has important prognostic implications.

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Only patients with a considerable amount of dysfunctional but viable myocardium benefit from revascularization procedures (1).

Imaging modalities such as positron emission tomography (PET) in combination with perfusion imaging or single-photon emission computed tomography (SPECT) have been used for the detection of myocardial viability (2). These techniques are relatively time-consuming and expose the patient to radiation.

During the last two decades, contrast enhanced cardiac MRI (CE-MRI) is considered as promising imaging modality that has been used for the assessment of myocardial viability. This technique provides direct imaging of necrotic tissue with high contrast and high spatial resolution (3). In patients with CAD, the transmural extent of the scar tissue predicts functional recovery after myocardial revascularization. Several studies suggest that areas of hyperenhancement represent irreversible ischemic injury (4).

There are many several advantages of 3 T MR over 1.5 T MR in cardiac imaging. First, 3 T has high signal-to-noise ratio (SNR) than 1.5 T that can be used to increase the spatial resolution or reduce the acquisition time by using parallel imaging. This issue is so important in better delineation of myocardial scarring with high image quality (5). In addition, the high spatial resolution of the 3 T can better discriminate infarct zones from peri-infarct regions, which may be a focus of ventricular arrhythmias and has been reported to be a strong predictor of future cardiovascular events. Second, the prolongation of the T1-relaxation times at 3.0 T is expected to improve the tissue enhancing properties of the T1-shortening contrast agents, and thus can reduce the dose of the contrast agent in cardiac examination (6). Third, stimulated echo acquisition mode (STEAM) MRI is recently newer methods at 3 T for black-blood LGE myocardial imaging. This method enhances the discrimination of the blood-infarct border than allowing measurement of infarct size accurately. In contrast, 3 T has strong static field inhomogeneities and short T2* that cause more artifacts with SSFP cine imaging than at lower field strengths (7,8).

This study was performed to assess the degree of the agreement between 3 T cardiac MR (CMR) and SPECT myocardial perfusion imaging (MPI), in the detection of myocardial viability.

2. Patients and methods

2.1. Patients

Thirty-three patients that were clinically diagnosed to have CAD were enrolled in that study after having their consent. They all were examined using coronary angiography to localize the affected coronary artery and to predict the affected myocardial segments (9).

The age of the patients ranges between 32 and 75 years with mean age 54 years (± 3.3). There were a total number of 29 males and 4 females.

The major inclusion criterion was scheduling for conventional coronary angiography. Other criteria were, sinus heart rhythm, ability to hold breath for 10–20 s and normal serum creatinine.

Exclusion criteria were hemodynamic instability, atrial fibrillation, contraindications for MR imaging, claustrophobia, applied pacemaker or metal implants, contraindication for contrast material including known allergy and renal insufficiency (serum creatinine more than 1.4 mg/dl). Characteristics of the patient population are shown in Table 1.

2.2. Methods

All patients were subjected to conventional coronary angiography, contrast enhanced MRI and SPECT. Written and verbal

Table 1 Characteristics of the patient population.

| Characteristics | Frequency |
|--|------------------|
| Number of patients (women) | 33 |
| Age (years) | 54 (± 3.3) |
| <i>Extent of coronary artery disease</i> | |
| Three vessel disease | 4 (12%) |
| Two vessel disease | 15 (45.5%) |
| One vessel disease | 14 (42.5%) |

consents were obtained from all patients as well as an agreement of the local ethics committee.

1. *Selective Conventional Coronary Angiography*: All patients were scheduled for diagnostic coronary angiography. Arterial catheterization and selective coronary angiography were performed within 3 weeks before or after the cardiac MRI study using a trans-femoral approach to selectively inject the left and right coronary systems sequentially. Different projections are used according to the standard techniques with at least four views of the left and two views of the right coronary artery systems were analyzed.

Images analysis: A reduction of the luminal diameter 70% or more in a major epicardial coronary artery or the major branches was considered to be a relevant stenosis. The angiographic results were classified as one-, two-, or three-vessel disease.

2. *SPECT study*: Patients underwent 2-day exercise/rest gated SPECT imaging with Tc-99 m sestamibi to allow adequate decay of myocardial activity from the first image and to minimize interference of the first with the second image.

On day 1: Stress study: The patients were instructed to be fasting and to wear comfortable shoes and loose fitting clothes. Calcium channel blockers and long acting nitrates were stopped 24 h before the test while beta blockers were stopped 48 h before the test. Tc-99 m sestamibi 20–25 mCi was intravenously injected at peak exercise or after injection of pharmacological agent and flushed with 5–10 ml saline solution and then the stress was continued for 1–2 min at the same workload.

Initial stress imaging was started approximately 30–60 min after injection. Cardiac gated SPECT was performed. 32 projection (30 s/projection) images were obtained over 1800 circular orbit, beginning from the 450 right anterior oblique views to the 450 left posterior oblique views. The images obtained were reconstructed as three sets of tomographic images oriented along the standard orthogonal planes of the left ventricle.

On day 2: Rest study: Patients were fasting for at least 4 h before the study. Rest gated SPECT imaging was started 60 min after intravenous injection of 20–25 mCi of Tc-99 m sestamibi and flushed with 5–10 ml saline solution in the same manner as in the stress study.

The reconstructed data were projected as tomographic slices in short, vertical and horizontal axis views in side-by-side display. In addition, the images were displayed as polar plots (bull's eye maps).

Images analysis:

- (1) All images were reviewed by experienced nuclear cardiologist.
- (2) Quantitative and semi-quantitative analysis from 60 min poststress and rest SPECT images were performed using the following:

Scintigraphic indices: A semi-quantitative visual interpretation was performed using 4 evenly spaced regions in the apical, midventricular and basal slices of the short axis views and apical segment on the midventricular long axis slices (17 segments totally).

Each segment was scored using 4-point scoring system (0 indicated normal; 1 mild; 2 moderate; 3 severe reduction of isotope uptake in segment).

The summed stress and rest score were obtained by adding the score of the 17 segments of the respective images. These indices were converted to percent as the total myocardium (% myocardium) involved with stress, ischemia or fixed defects by dividing the summed score by 51 the maximal potential score (3×17), and multiplying by 100.

Comparison between resting and exercise images is used to detect areas with fixed defects (scar), those with reversible defects (ischemic but still viable) and those with partially reversible defects (mixed scar and ischemia).

A defect was considered to be *fixed* when there was no change between the stress and rest images, *partially reversible* when there was an improvement in tracer uptake of at least 1 grade between stress and rest images, *totally reversible* when there was normalization of uptake at rest images.

3. *Cardiac MR examination*: No special instructions are required prior to the examination. Medications are not to be discontinued. All steps of the study were explained in detail for each patient with given instructions for breath hold.

A Philips Achiva, the Netherlands (3 T) superconducting magnet was used. All patients were examined in the supine position, head first using respiratory sensor and ECG gating. Additionally sensitivity encoding (SENSE) cardiac coil was used. All patients received wide bore intravenous line for the contrast agent. The patients underwent a standard MR examination that included the following steps:

1. *Scout images* were acquired in orthogonal orientations for planning of the final long-axis and short-axis views.
2. *First pass rest perfusion imaging* by using geometry is identical to that of the short axis cine views to carefully exclude any wraparound or trigger artifacts before starting the actual index test. It is performed by intravenous bolus injection of 0.025 mmol/kg of gadopentetate dimeglumine (Magnevist) at an injection rate of 5 mL/s followed by a flush of 20 mL of saline solution at the same rate. Scanning was started about 10 s after the starting of contrast injection and continues for about 1 min. Breath-hold first-pass perfusion MR imaging was performed by using a hybrid gradient echo-planar imaging pulse sequence. This pulse sequence yields three sections (at basal, mid-cavitary and apical levels) in the short-axis view covering the entire left ventricle every other heart beat with the following

parameters: TR/TE: 2.9/1.46, FOV: 350×350 mm², Phases: 25, NSA: 1, Matrix: 128×128 , Bandwidth: 125 kHz, Flip angle: 200, Scan Time: 1 s., Slice thickness: 8 mm, Slice number: 3.

3. *An additional bolus* of 0.2 mmol/kg gadopentetate dimeglumine immediately after ending of the rest perfusion scan.
4. *Functional cine images*: These images were acquired using electrocardiographic gated, breath hold balanced fast field echo (b-FFE) sequence in short axis view. Stack of eight to eleven sections in short-axis views, were obtained during repeated breath-holds, starting from the mitral valve insertion and covering the entire left ventricle with the following parameters: TR/TE: 4.4/2.5, FOV: 300×300 mm², Phases: 25, NSA: 1, Matrix: 128×128 , Slice thickness: 8 mm, Slice number: 8–11. This sequence was performed during the interval period between the aforementioned injection of additional bolus of contrast and the delayed gadolinium enhancement sequences.
5. *Standard delayed gadolinium enhancement imaging*, using segmental inversion recovery balanced turbo field echo (IR-b-TFE) was acquired with 10–15 min interval delay after the last injected intravenous bolus. Contrast-enhanced images were acquired in short axis plane and at least one of the long axis planes with the following parameters: TR/TE: 3.8/1.86, FOV: 300×300 mm², TI: 260–350, NSA: 1, Matrix: 128×128 , Bandwidth: 125 kHz, Flip angle: 15°, Scan Time: 9–15 s., Slice thickness: 8 mm, Slice number: 8–11.

The mean time of the MR imaging examination was about 30–35 min.

- *Image analysis*: Images (DICOM) were transferred to a workstation equipped with a dedicated cardiac software package (Brilliance 170 P workstation), for further analysis.

Segmental analysis: Images of delayed enhancement (DE) on MRI and SPECT were evaluated guided by the results of the coronary angiography to predict the affected segments using an identical 17-segment model (5). The basal, mid-ventricular, and apical segments were evaluated on short-axis images, whereas the apical cap was evaluated on a 2 or four-chamber long-axis planes.

Results of cardiac MRI were subdivided into two groups:

- (a) *Viable myocardial segment*: It was defined as no myocardial scarring or $\leq 50\%$ myocardial scarring. Subendocardial scarring was defined as 25% myocardial scarring and partial thickness scarring was defined as 50% myocardial scarring.
- (b) *Nonviable myocardial segment* was defined as $> 50\%$ thickness myocardial scarring. A no-reflow zone (microvascular obstruction) is evident on delayed-enhancement imaging as a dark region surrounded by hyperenhancing myocardium and/or first pass resting perfusional defect corresponding to delayed myocardial enhancement.

Findings of the cardiac MRI were compared to those of the corresponding conventional coronary angiograms and SPECT. The Kappa statistics was used to calculate the level of agreement between Cardiac MRI and SPECT in the distinction between viable and non-viable myocardium.

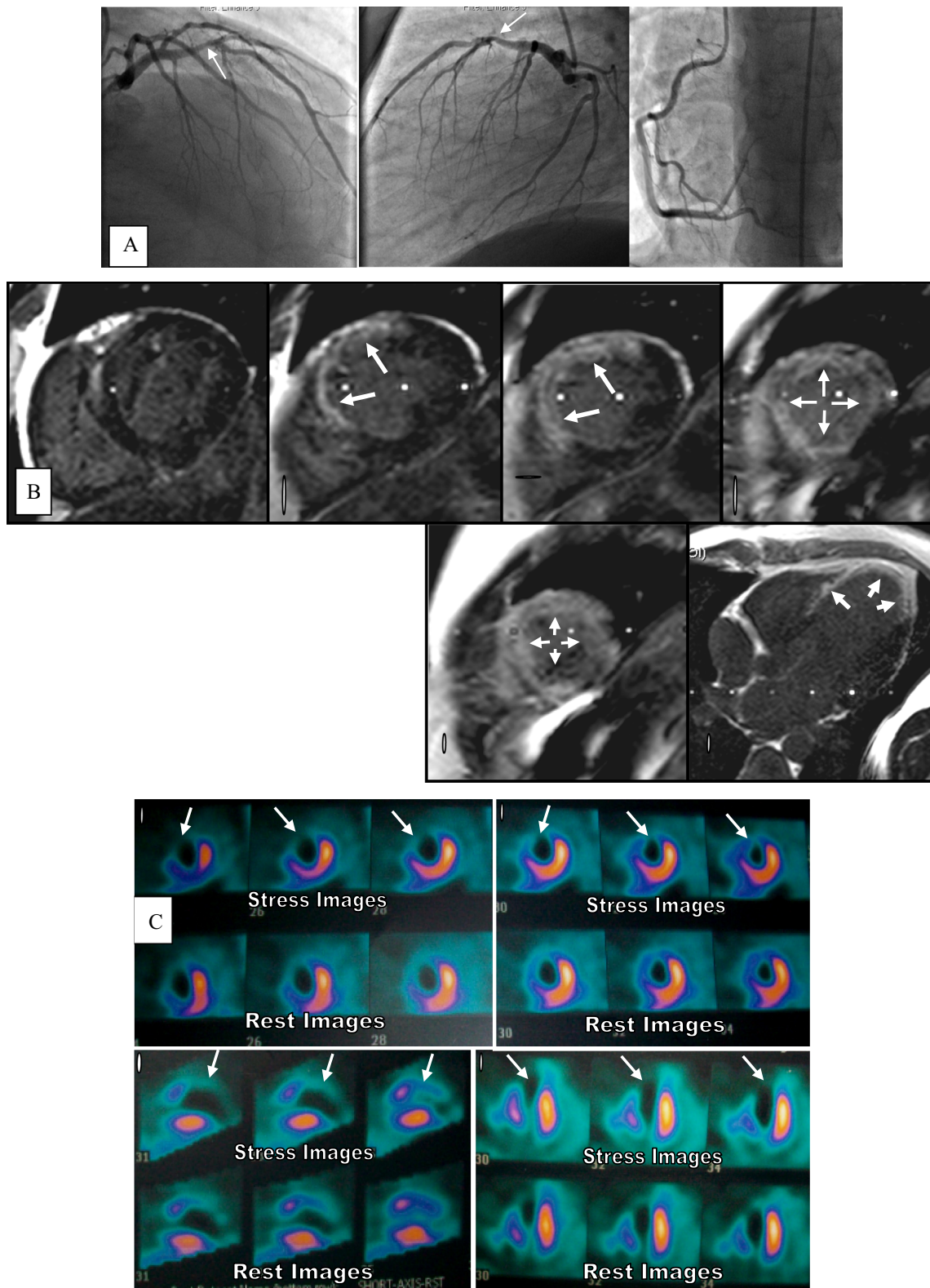


Fig. 1 35-year-old young male patient with clinical manifestations of CAD. (A) Coronary angiography showing moderately stenotic lesion at LAD territory, inducing about 40–50% luminal reduction. (B) In the 3D IR sequence, axial & four chamber images, showing transmural (75–100%) enhancing scar at the left ventricular wall involving anterior, anteroseptal and septal segments at the mid-cavity and apical levels and extends to involve the cardiac apex circumferentially). (C) SPECT study was performed that revealed large transmural myocardial scar along the apex, septum, anterior and inferoapical segments.

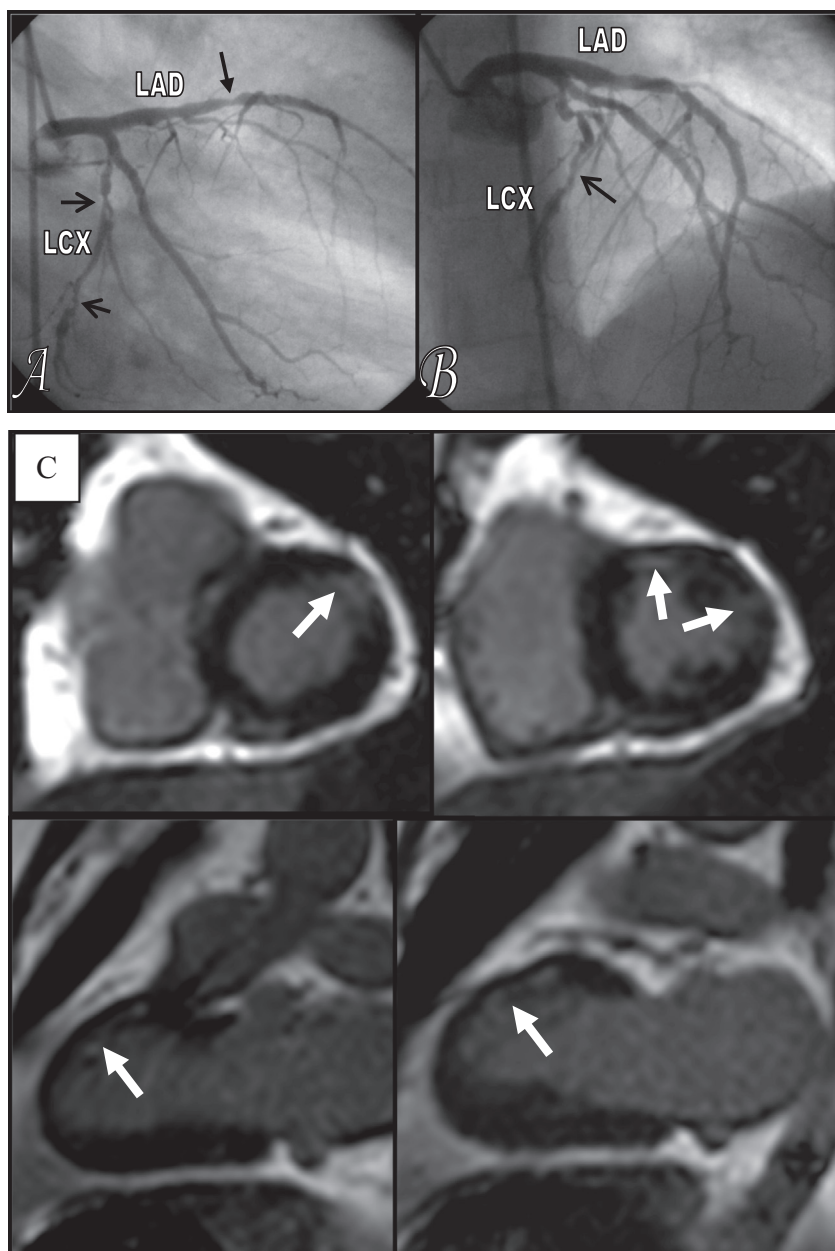


Fig. 2 52-year-old male patient with CAD. (A and B) Conventional coronary angiographic findings: LAD: shows mid course stenotic lesion, inducing about 60–70% luminal reduction (closed black arrow). LCx: shows proximal and mid portion stenotic lesions, inducing about 80% luminal reduction for each (opened black arrows). (C) In the delayed 3D IR sequence, there is multifocal patchy areas of enhancing scar tissue detected involving the following segments: Near transmural scarring along the anterolateral segments at the basal level and lateral segment at the mid-cavitary level respectively (upper images; right left) (LCx territory). Subendocardial scarring along the anterior segments at the mid-cavitary and apical levels (lower images; right left) (LAD territory). (D) Gated SPECT shows: Mild to moderate ischemia at the anterior wall (LAD territory). Stress images in short axis and Bull' eye images D–F: Rest images in short axis and Bull' eye images. The cardiac MRI detected subendocardial scarring along the LAD territory and focal small transmural scar along LCx territory. The SPECT study detects only ischemic insult along LAD territory. Yet it missed the focal small scar and subendocardial scar detected by cardiac MRI along the LCx and LAD territories respectively.

3. Results

Thirty-three patients were included in the study (characteristics of the study population are shown in Table 1) with corresponding 99 territories. The morphology, and global and

regional ventricular functions were assessed using the functional short axis cine images.

Cardiac MRI detected myocardial segments corresponding to 23 transmural scarred territories, matching with 12 transmural scarred territories detected by SPECT study (Fig. 1).

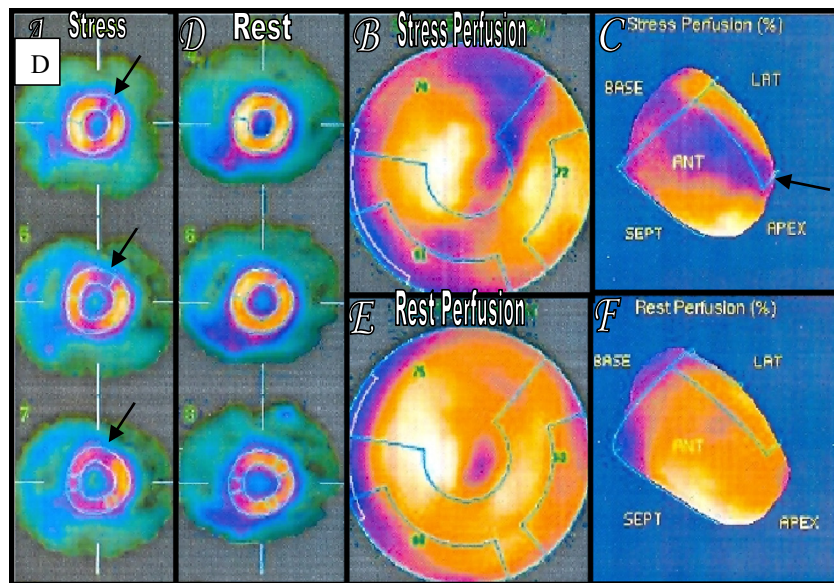


Fig. 2 (continued)

- The mismatched 11 territories are distributed as follows:
 1. Two territories of negative finding in SPECT study correspond to small scar at LCx and RCA territories detected by MRI (Fig. 2).
 2. Two territories of ischemic findings in SPECT study correspond to scarred myocardial segments along LAD and LCx territories detected by MRI.
 3. Seven territories of partial thickness scarring in SPECT study correspond to transmural scarred myocardial segments along LAD, LCx and RCA territories (Fig. 3).

Microvascular obstruction was detected in 5 territories among these 23 territories of transmural scarring (Fig. 3).

MRI detected myocardial segments corresponding to 9 partial thickness scarred territories, matching with 8 partial thickness scarred territories detected by SPECT study. The mismatched one territory was negative in SPECT.

SPECT detected myocardial segments corresponding to 15 of partial thickness scarred territories, matching with 8 partial thickness scarred territories in cardiac MRI. The other mismatched 7 territories correspond to 7 transmural scarred territories in cardiac MRI.

Among the examined 99 territories, subendocardial scarring of myocardial segments detected in cardiac MRI along 7 territories. From these diseased territories with subendocardial scarring, only 1 territory (14%) is matching with SPECT findings, and the other six territories were negative in SPECT (Fig. 2).

We considered delayed enhancing myocardial segment as scarred myocardial tissue. Among the 99 examined territories, variable thickness of myocardial scarring was detected at 39 territories (23 transmural, 9 partial thickness and 7 subendocardial scarring).

- Among the examined 99 territories, cardiac MRI detected 23.2% (23 out of 99) of nonviable (transmural scarred) diseased territories and 76.7% (76 out of 99) with still having variable degree of viable territory.

- In 89% of the examined viable and nonviable territories, we had an agreement between the CE-MRI and SPECT findings. All scarred (nonviable) territories detected by SPECT, were detected by CE-MRI. However, 11 nonviable territories detected by CE-MRI were shown to be viable by SPECT.
- So SPECT viable/CE-MRI non-viable territories were localized in 11 territories and this accounts for 48% (11 out of 23 nonviable territories) of all nonviable territories and 11.1% of all the examined territories (Table 2).

In 88.9% of the segments, we had an agreement between the two methods, which denotes a Kappa value of 0.725.

4. Discussion

In developed countries, coronary artery disease (CAD) continues to be a major cause of death and disability. Since introduction of the cardiac MRI as a non-invasive tool for depiction of the coronary artery disease, the clinical value of myocardial MRI has been the subject for research work. Several comparative studies for evaluation of cardiac MRI as a diagnostic tool for coronary artery disease using the conventional angiography as the gold standard have been published. The results of these researches concluded that cardiac MRI is considered as accurate imaging tool in detection of myocardial viability. Recently developed high field MR magnet (3 T) and improvements of the used MR protocols allow high spatial and temporal resolutions with considerably reduced acquisition times, reflecting on the image quality leading to better results.

The results of this study demonstrate a high agreement between CE-MRI and SPECT. It had previously been proved that 50% of the segmental extent of hyperenhancement in CE-MRI would be a good discriminator for functional recovery after revascularization (10), so we considered segments with >50% thickness of myocardial enhancement as non-viable.

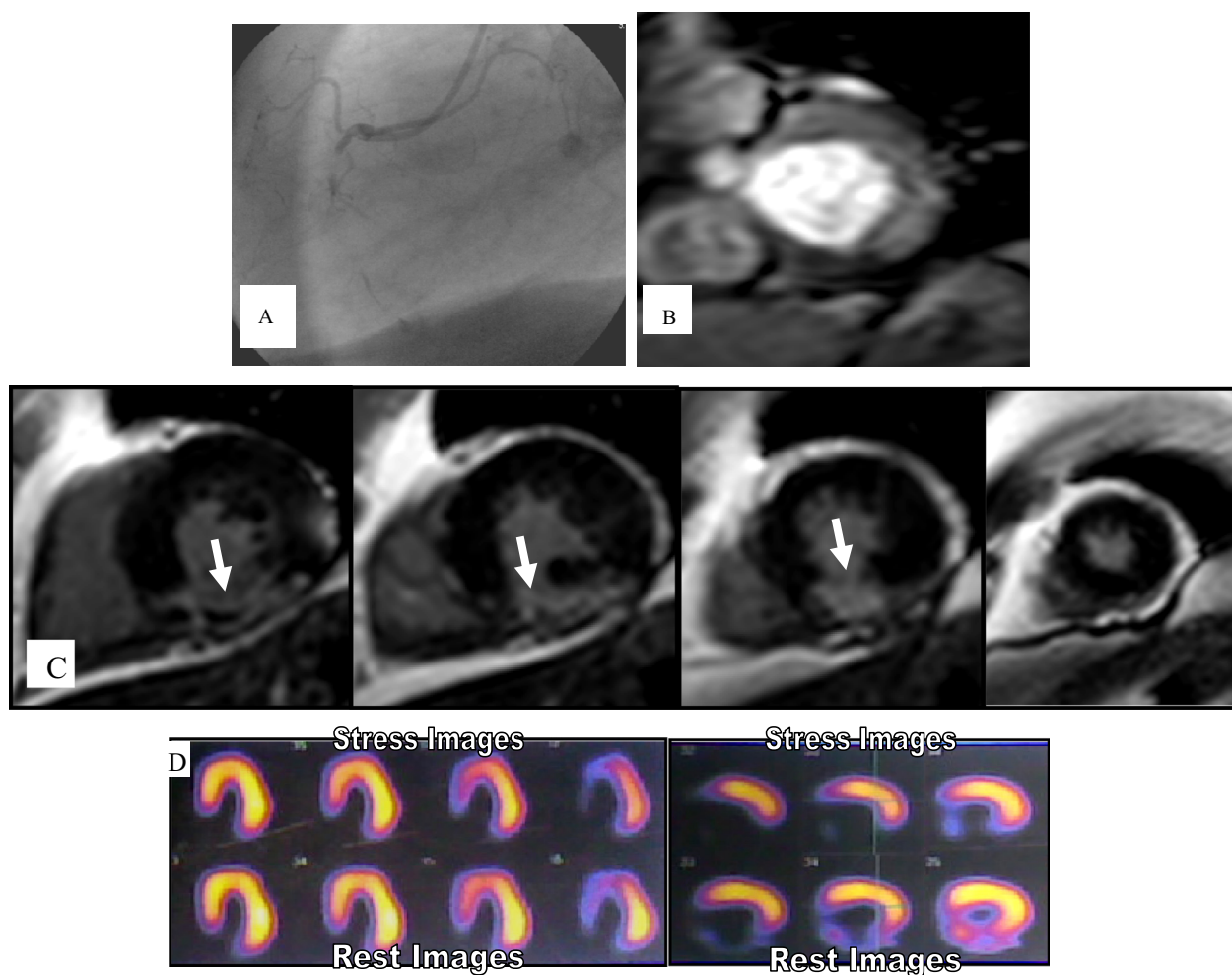


Fig. 3 62-year-old male patient with clinical manifestations of CAD. (A) Conventional coronary angiography showing total proximal RCA occlusion that fills faintly distally retrogradely from the left system collaterals (arrows). (B) In the dynamic 2D EPI sequence, the left ventricular inferior wall shows poorly defined small myocardial perfusional defect at the inferior segment at its basal ventricular level. (C) Short & long axis cardiac images in the 3D IR sequence, there is transmural (75–100%) enhancing scar seen along the inferior and inferolateral segments of the left ventricle at its mid-cavitary and basal levels with hypointense filling defect within its core, corresponding to the fore-mentioned resting perfusional defect, denoting superadded microvascular obstruction. (D) Gated SPECT Findings, shows Mixed scar and ischemia (predominant scarring) is seen involving most of the inferior wall with partial extension to the apical inferoapical segment.

Among the examined 99 territories, cardiac MRI detected 23.2% (23 out of 99) of nonviable (transmural scarred) diseased territories and 76.7% (76 out of 99) with still having variable degree of viable territory.

All scarred (nonviable) territories detected by SPECT, were detected by CE-MRI. However, 11 nonviable territories detected by CE-MRI were shown to be viable by SPECT. So SPECT viable/CE-MRI non-viable territories were localized in 11 territories and this accounts for 48% (11 out of 23 non-viable territories) of all nonviable territories and 11.1% of all the examined territories.

Agreement between two modalities was obtained in 88 segments (88.9%), resulting in a kappa value of 0.725. The discordant results can be attributed to both imaging artifacts. Thinning of the myocardium without irreversible damage may result in a viability defect in a SPECT study, while CE-MRI allows determining directly the amount of viable myocardium within the thin segment (11). Thus, CE-MRI

may be especially important in identifying myocardial viability in patients with a thin myocardial wall (12).

SPECT MPI has many limitations yet it is still widely available and validated in many cases. Its limitations include long acquisition time, using radio-active tracer agents, poor spatial resolution and high limitation in detection of subendocardial defects (10). The SPECT MPI can be partially degraded also by many motion artifacts related to the patient, diaphragmatic and gut motion. Soft tissue photon attenuation artifacts which are often observed in myocardial SPECT imaging might represent themselves as myocardial viability defects especially in the inferior and lateral myocardial wall (13,14). In previous study, overestimation of infarct size was reported by CE-MRI (16). This effect could explain some of our discordant results. The imaging hardware and iterative reconstruction of the SPECT MPI were developed in last decade, resulting in improvement of its spatial resolution contrast and imaging speed (15).

Table 2 Showing the results of ce-MRI and SPECT in the assessment of myocardial viability.

| Comparison of myocardial viability between ce-MRI and SPECT | | SPECT (n) | | |
|---|-----------|-----------|-----------|----|
| | | Viabile | Nonviable | |
| CE-MRI (n) | Viabile | 76 | 0 | 76 |
| | Nonviable | 11 | 12 | 23 |

Although different MR techniques were used in many previous studies in CAD, the cardiac MR considered as golden standard technique for proper diagnosis of acute or chronic MI. Delayed enhancement inversion techniques are considered the most widely used and accurate tool in differentiation between reversible and irreversible myocardial ischemic injury. The delayed enhancement technique has high capability to detect micro infarcts as little as 1 g of irreversibly damaged tissue (13). In addition, the delayed-enhancement technique has high sensitivity for identification of both acute (99%) and chronic (94%) MI and also has 97% accuracy for prediction of the vascular distribution of the scar (IV). Good correlation between the delayed-enhancement technique and histopathology regarding the detection of myocardial scarring was confirmed in previous animal studies (14).

Combination between the rest perfusion and delayed enhancement could be valuable in detection of coronary artery disease. In our study, 3 T CMR shows higher accuracy in assessment of myocardial viability compared to SPECT especially in the subendocardial and inferior left ventricular locations. This could be explained by its high spatial resolution, as the CMR can accurately determine the thickness of scarred myocardium with high definition within the diseased territory.

CMR is considered superior to single-photon-emission CT (SPECT) in identifying irreversibly damaged myocardium because of its high spatial resolution, especially in nonanterior locations (16). As a result, delayed-enhancement MR imaging findings are now being incorporated into diagnostic criteria for imaging patients with MI (17).

In addition, CMR was considered as the modality of choice in detection of microvascular obstruction, and it was detected within 5 diseased territories of transmural scarring in our study. In patients with a recent AMI, myocardial perfusion studies at rest frequently show the infarct territory perfusion deficit. These defects are subendocardially located and the transmural extent is variable (15). These defects are caused by microvascular obstruction in the subendocardium (no-reflow). Other way to detect microvascular obstruction is the presence of hypointense filling defect within the core of delayed myocardial enhancement.

This imaging abnormality reflects the impaired diffusion of the gadolinium tracer into the central core of the infarction. This finding is related to extensive microvascular obstruction produced by myocardial infarction that results not only in myocyte death, but also in extensive microvascular destruction. The presence of microvascular obstruction has been shown to correlate with a significantly increased risk of adverse outcomes from myocardial infarction, including adverse remodeling, diminished systolic function, and arrhythmia (14).

In our clinical practice, the short acquisition times and high spatial resolution of the 3 T CMR allowed to perform the cardiac examination in short time with high definition of myocardial scarring. Moreover, 3 T CMR had high capability in detection of resting perfusional defects or hypointense defects within the enhanced myocardial scarring. 3 T CMR was feasible for the routine assessment of myocardial viability with no need of stress agents or radiation exposure.

Potential role for cardiac MRI as a non-invasive modality in evaluation of the coronary artery disease, includes the following conditions:

- Detection of diseased coronary territory in patients suspecting or known to have CAD with high sensitivity and specificity.
- Differentiation between ischemic and dilated cardiomyopathy.
- The cardiac MR is considered as the most accurate method for assessment of myocardial viability, delineation and quantification of myocardial scarring, and thus it is necessary to preoperatively predict the functional recovery.
- Diagnosis of the associated complications of myocardial infarction (MI) in one examination setting.
- In addition, the time required to perform a viability study with MRI is usually less than one hour, whereas this time extends to about 3–24 h for SPECT, which is apparently an additional benefit of MRI compared with SPECT.

In conclusion, resting cardiac MR shows high accuracy as compared to stress SPECT study in detection and delineation of myocardial scarring, particularly the subendocardial scarring in one short time examination.

Conflict of interest

We have no conflict of interest to declare.

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