

DELAYED CONTRAST ENHANCEMENT

Scar detection by contrast-enhanced magnetic resonance imaging in chronic coronary artery disease: a comparison with nuclear imaging and echocardiography

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We compared contrast-enhanced MRI (CeMRI) with the most widely used imaging techniques for myocardial infarct (MI) diagnosis, SPECT and Echo, in unselected patients with chronic coronary artery disease (CAD). Two blinded operators assessed scars on MRI, SPECT and Echo images using a 16-segments LV model. We studied 105 consecutive patients: 50 had Q-wave MI (Q-MI), 19 non Q-wave MI or rest angina (nonQ-MI/RA) and 36 effort angina (EA) history. CeMRI was positive, respectively, in 96%, 37%, and 6%, SPECT in 90%, 53%, and 44%, and Echo in 84%, 32%, and 28% of patients (within Q-MI: CeMRI vs. SPECT $p < 0.03$, vs. Echo $p < 0.001$; within EA CeMRI vs. SPECT and ECHO $p < 0.001$; all trends $p < 0.001$, pseudo r-square: 0.56–0.75 for CeMRI, 0.18–0.28 for SPECT and 0.23–0.37 for Echo). CeMRI and SPECT agreed in 83 patients (79%); negative SPECT with 1 ± 0 segments subendocardial delayed enhancement (DE) was found in 4 (4%); negative CeMRI with 4 ± 3 segments perfusion defects in 18 (17%), 16 of whom were obese or showed LBB or sub-occlusion of related coronary. CeMRI and Echo agreed in 78 patients (75%); negative Echo with 2 ± 1 segments subendocardial DE was found in 13 (12%) and negative CeMRI with 11 ± 7 segments kinetic abnormalities in 14 (13%), in 10 confirmed by Cine-MRI. In Q-MI, CeMRI detects DE more frequently than perfusion defects and, especially, kinetic abnormalities are found by SPECT and Echo, respectively. CeMRI identifies small areas of DE also in some patients with nonQ-MI or RA but usually not in patients with EA. This biologically plausible decreasing trend is shown by CeMRI more clearly than by SPECT and Echo. Disagreement between CeMRI and SPECT or Echo may be reduced, but perhaps not fully eluded, performing dobutamine Echo and SPECT after maximal epicardial coronary dilatation.

Key Words: Magnetic resonance imaging; SPECT; Echocardiography; Myocardial infarction; Angina

1. Introduction

Necrotic myocardium and scar, resulting from myocardial infarct (MI), may be distinguished from normal myocardium by magnetic resonance imaging (MRI) (1,2), an operator independent technique, which does not expose the patient to ionizing radiations. Contrast enhanced MRI (CeMRI) seems to be clinically useful and reproducible in scar detection (1,3). In patients with MI history, CeMRI was able to detect subendocardial infarcts missed by SPECT (4). Also in patients without MI history, precisely after successful percutaneous coronary angioplasty, CeMRI was able to detect micro-infarcts in the presence of (mild) creatinine-kinase

elevation, also in absence of electrocardiographic (ECG) and left ventricle (LV) wall motion abnormalities (5).

Since SPECT and echocardiography (Echo) are the most widely used imaging techniques for MI diagnosis, we compared CeMRI, SPECT, and Echo scar detection ability in unselected patients with chronic CAD.

2. Methods

The study was approved by the Institutional Review Board. It was retrospective; patients referred to our division from December 1, 2001 to March 31, 2003 for chronic CAD evaluation, who routinely underwent SPECT and Echo, were the reference population. After informed consent, patients also underwent cardiac MRI. According to clinical history, which was recorded in the electronic database of our division, patients were divided into three groups: Q-wave MI (Q-MI), non Q-wave MI or rest angina (nonQ-MI/RA) and effort angina (EA). Q-MI was diagnosed if a Q wave (with duration

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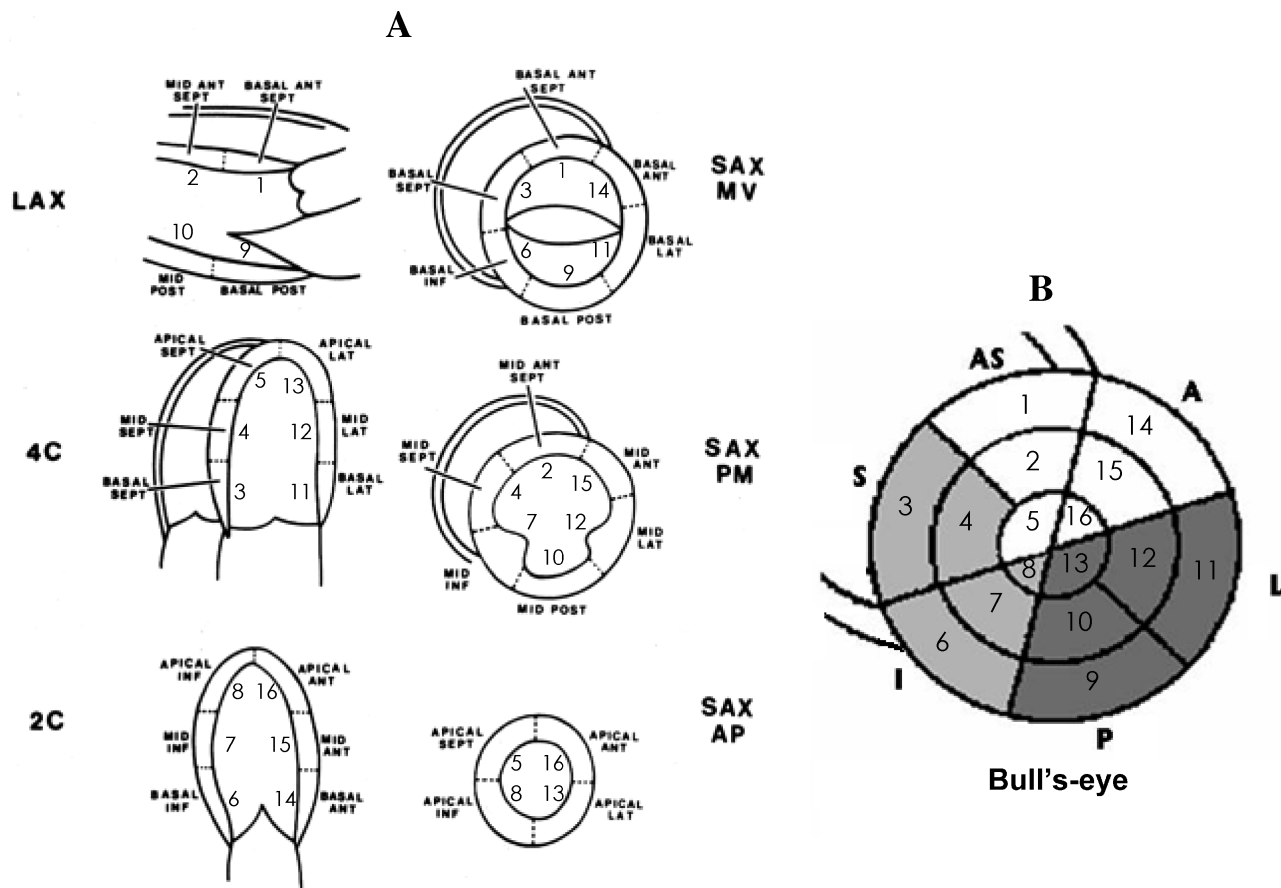


Figure 1. Sixteen segments model of LV used to evaluate CeMRI, SPECT, and Echo images. Panel A shows segmentation on the parasternal long-axis view (LAX), on the parasternal short-axis views at mitral valve (SAX MV), papillary muscles (SAX PM) and apex (SAX AP) levels and on the apical two-chamber (2C) and four-chamber (4C) views. Panel B shows the equivalent position of segments on a polar map. Different colours depicts “a priori” distribution of coronary arteries. Left anterior descending coronary artery territory includes 6 segments (white): anterior septum (segments 1–2), anterior wall (14–15), apical septum (5) and anterior apex (16). Circumflex coronary artery territory includes 5 segments (dark grey): lateral wall (11–12), posterior wall (9–10) and lateral apex (13). Right coronary artery territory includes 5 segments (light grey): inferior wall (6–7), septum (3–4) and inferior apex (8).

≥ 40 msec) was found on admission ECG in at least two contiguous leads.

A standard 16 segment partition of LV (6) was used for all imaging techniques (Fig. 1). A semi-quantitative assessment of segmental contractility, delayed enhancement and perfusion status was obtained by consensus of two skilled operators for each technique, blinded with respect to the other tests results and patients' history. For all evaluations MI area was calculated as the number of segments showing any morphologic, perfusion, or kinetic abnormality. We supposed an *a priori* distribution of coronary artery territories (Fig. 1, panel B). Scar was assigned to a coronary territory when the most part of delayed enhancement, rest perfusion defect, or kinetic abnormalities was located within it.

2.1. MRI

We used a 1.0 Tesla scanner (Magnetom Harmony, Siemens, Erlangen, Germany) with 20 mT gradient and a phased-array coil. We performed breath-hold ECG-gated cine gradient-echo sequen-

ces (repetition time 45 msec; Echo time [TE] 6.1 msec; flip angle [FA] 20°; matrix 126 × 256; field of view [FOV] 350 mm) for wall motion analysis, and inversion-recovery turboFLASH sequences (TE 2.6 msec, FA 8°, inversion time 260–360 msec, matrix 96 × 256; FOV 400 mm) for scar detection, 5 minutes after 0.15 mmol/kg intravenous injection of gadopentetate-dimeglumine or gadomenate-dimeglumine (Magnevist; Schering, Berlin, Germany; Multihance, Bracco, Milan, Italy). Full ventricle coverage was obtained with 10 mm thick multiple (usually 8) short-axis views. Moving from the base to the apex of LV, slice 1–3 were considered to cover basal portion, slice 4–6 mid portion and slice 7–8 the apex of LV. Transmural extent of delayed enhancement was scored using a four point scale (1) (Table 1). Score of each of the 16 segments was then calculated from the average of three values (two values for apical ones).

2.2. SPECT

SPECT study was performed 45–60 min after 740 MBq Tetrofosmin administration at rest. A large FOV tomographic

Table 1. Semi-quantitative assessment of segmental contractility, delayed enhancement, and perfusion

	Applied to	Segmental score			
		0	1	2	3
Wall thickening/radial shortening (10)	CineMRI and Echo	normal	hypokinesia (moderately reduced)	akinesia (severely reduced or absent)	dyskinesia or reduced thickness*
Delayed enhancement (% of wall thickness) (1)	CeMRI	absent	< 25%	25–75%	> 75%
Perfusion (7–9)	SPECT	normal	mildly reduced	moderately reduced	severely reduced or absent

CineMRI = kinetic magnetic resonance imaging; CeMRI = contrast-enhanced magnetic resonance imaging; SPECT = single photon emission tomography; Echo = echocardiography.

*Less than 5 mm.

gamma-camera (Apex-SP6, Elscint, Haifa, Israel) with high resolution collimator and a 20% window centred on the 140 KeV photo-peak of Technetium-99m was used. Images were reconstructed by filtered back-projection with no attenuation or scatter correction. Tracer activity was normalized on maximal LV activity. Colour encoded short axis images were used to build a bull's-eye display of activity. On bull's-eye polar plots the 16 segments model of LV was superimposed and tracer activity was scored using a 4-point system (7–9) (Table 1). Horizontal long axis, vertical long axis, and short axis slices were simultaneously available and used to confirm polar map assessments.

2.3. Echocardiography

Regional LV systolic function was evaluated by assessing wall thickening and endocardial excursion (radial shortening) with second harmonic two dimensional echocardiography (Sequoia, Acuson; Sonos 5500, Hewlett Packard, Philips, Andover, MA). A multi-views approach was used assessing parasternal short (at mitral valve, papillary muscles and apical level) and long axis views and 2 and 4 chamber apical views. In patients with very poor parasternal imaging windows, the apical 3 chamber view was used. Regional contractility was scored on a 4-point scale (10) (Table 1).

2.4. Statistical analysis

Continuous variables were expressed as means \pm standard deviation, discrete variables as counts or percentages. Between groups, differences for continuous variables were tested by one-way analysis of variance (ANOVA). CeMRI, SPECT and Echo outcomes, entered as binary variables (positive or negative test), were tested by chi-square for within groups difference and by ordinal logistic regression and likelihood ratios for trends between groups. Goodness of fit of the models was assessed by Cox & Snell and McFadden pseudo r-square calculation. Statistical significance was considered with P values < 0.05 .

3. Results

One hundred and ten consecutive patients were suitable for the study. Five of them (4%) were excluded for claustrophobia and 105 were evaluated: 50 had a history of Q-MI, 19 of RA or nonQ-MI, 36 of EA. MRI was performed within 7 ± 8 and 8 ± 9 days, respectively, of Echo and SPECT. In all patients, MRI image quality was adequate although breath holding was poor in 4 (4%) and ECG triggering difficult in 2 (2%). Clinical features in the three groups of patients are reported in Table 2. As expected, LV ejection fraction was

Table 2. Clinical features of study population

	Q-wave MI	Non Q-wave MI/rest angina	Effort angina	P
Sex (male/female)	38/12	16/3	22/14	n.s.
Age (years)	65 ± 9	64 ± 9	64 ± 13	n.s.
MI site				
Anterior	24	—	—	—
Inferior/lateral	26	—	—	—
Non-Q wave	—	5	—	—
LVEF (%)	48 ± 14	64 ± 7	61 ± 7	* $p < 0.001$

MI = myocardial infarction; LVEF = left ventricle ejection fraction.

*Q-MI vs. nonQ-MI/RA and Q-MI vs. EA.

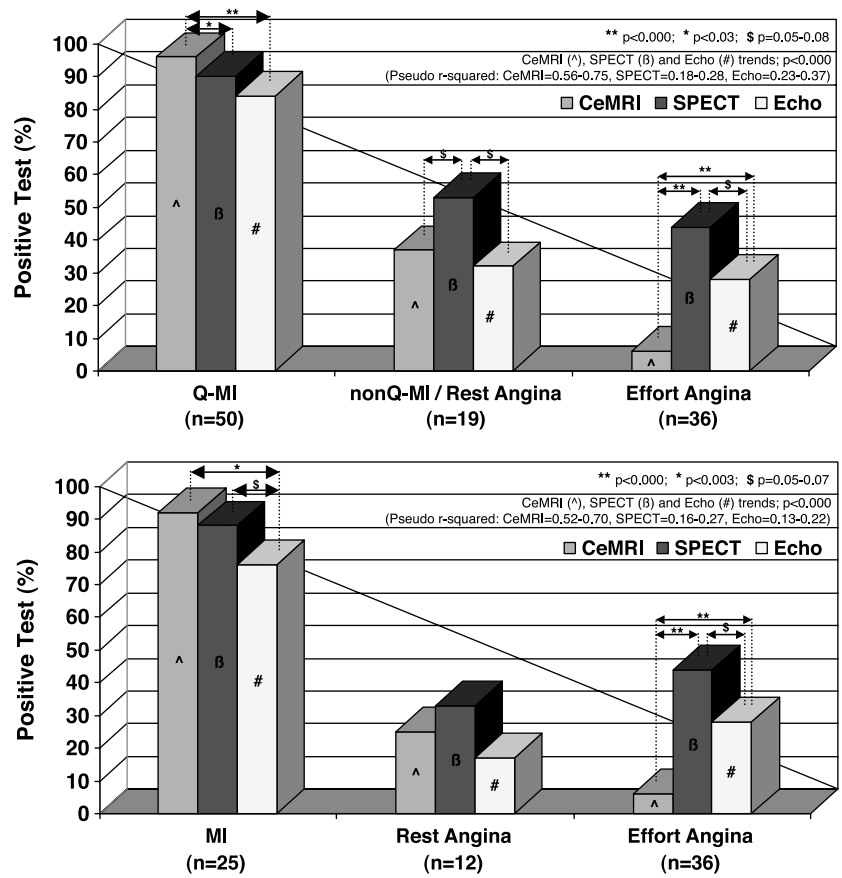


Figure 2. Proportions of positive CeMRI, SPECT, and Echo assessments in patients with Q-wave MI, non Q-wave MI/rest angina and effort angina history (upper part) and in patients with MI, rest angina, and effort angina history (lower part).

significantly lower in Q-MI patients than in the other two groups (ANOVA $p < 0.001$). There was also a difference in sex distribution but it had no statistical value.

3.1. CeMRI, SPECT and Echo scar detection

Forty-eight patients (96%) with Q-MI had a positive CeMRI study. Two patients without delayed enhancements and three more patients with 1 ± 0 segment subendocardial delayed enhancements (segmental score: 1.3 ± 0.5) had a negative SPECT. Thus, 45 patients with Q-MI (90%) showed rest perfusion defects at SPECT. Wall motion abnormalities were detected at Echo in 42 patients (84%), of which only one had a negative CeMRI. We found 2 ± 1 segments subendocardial (score: 1.6 ± 0.9) delayed enhancements when kinesis was normal.

In patients with nonQ-MI or RA history, CeMRI, SPECT and Echo were positive respectively in 7 (37%), 10 (53%) and 6 (32%) cases. Six of seven patients with positive CeMRI (2 ± 2 segments; score 1.9 ± 1.0) showed rest perfusion defects too (4 ± 2 segments; score 1.5 ± 0.6).

In patients with EA history, CeMRI, SPECT, and Echo were positive in 2 (6%), 16 (44%) and 10 (28%) cases, respectively. Both patients with positive CeMRI (1 ± 1 segments, score 1.6 ± 0.9) showed also rest perfusion defects at SPECT (2 ± 1 segments, score 1.3 ± 0.5).

Thus, in the three groups of patients (Q-MI history, nonQ-MI/RA and EA), CeMRI was positive in 96%, 37%, and 6%, SPECT in 90%, 53%, and 44%, and Echo in 84%, 32%, and 28% of cases, respectively (Fig. 2, upper part). A significant statistical difference was found between CeMRI and SPECT (chi-square $p < 0.03$) within Q-MI group of patients and,

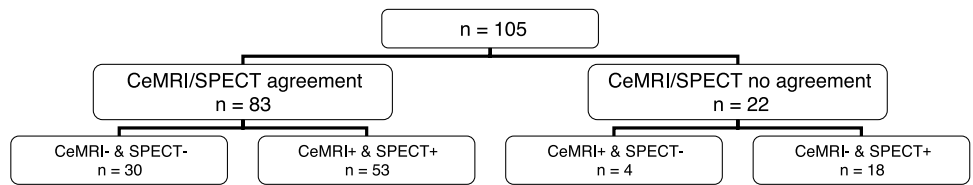


Figure 3. Agreement between CeMRI and SPECT results.

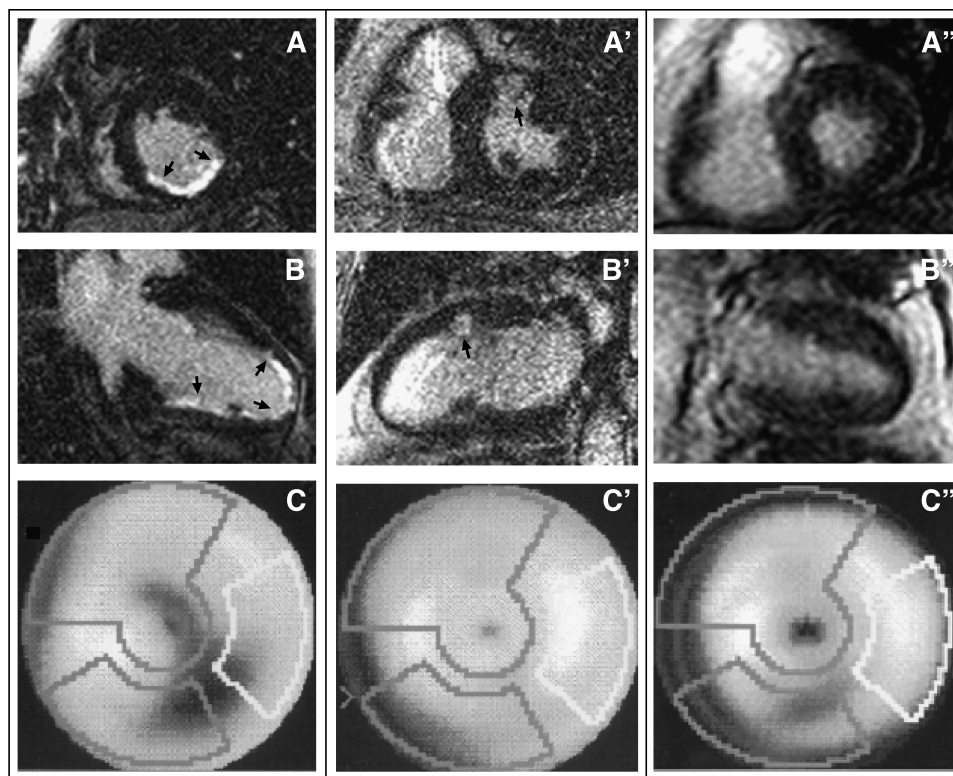


Figure 4. Examples of CeMRI and SPECT assessments: short-axis CeMRI view (panels A, A', A''), long-axis CeMRI view (B, B', B'') and rest SPECT bull's-eye (C, C', C'') are shown. First column: a patient with Q-MI history who showed a large inferior, posterior, and apical delayed enhancement (A and B) and a comparable perfusion defect (C). Second column: a patient with RA history who showed small mid-anterior delayed enhancement (A' and B') without perfusion defect (C'). Third column: an obese (BMI = 36) male patient with EA history who had not delayed enhancement (A'' and B'') and showed a mild inferior perfusion defect (C'').

above all, between CeMRI and Echo ($p < 0.001$) in the same group, and between CeMRI and SPECT ($p < 0.001$) and ECHO ($p < 0.001$) in EA group. A borderline statistical difference was found between CeMRI and SPECT in nonQ-MI/RA group ($p = 0.08$), and between SPECT and Echo in the same group ($p = 0.06$) and in EA group ($p = 0.05$). Between groups difference in proportion of positive tests was statistically significant for CeMRI (likelihood ratio of ordinal logistic regression; $p < 0.001$) as well as for SPECT ($p < 0.001$) and Echo ($p < 0.001$). However, model goodness

of fit was better for CeMRI (pseudo r-square: 0.56–0.75) than for SPECT (0.18–0.28) or Echo (0.23–0.37).

3.2. Comparison of CeMRI and SPECT

Agreement between CeMRI and SPECT (Figs. 3 and 4, Table 3) was found in 83 cases (79%). When CeMRI and SPECT were both positive ($n = 53$), scar was in the same coronary territory in 46 patients (87%). Four patients (4%), three with Q-MI and one with RA history, had a negative

Table 3. Clinical history and scar extent in patients with agreeing or disagreeing results of CeMRI and SPECT

	CeMRI – and SPECT –	CeMRI + and SPECT +	CeMRI + and SPECT –	CeMRI – and SPECT +
	n° patients			
Q-MI	2	44	1	–
nonQ-MI/Rest angina	8	6	3	4
Effort angina	20	3	–	14
	n° segments			
Delayed enhancement	–	5 ± 4	1 ± 0	
Perfusion defect	–	7 ± 4		4 ± 3

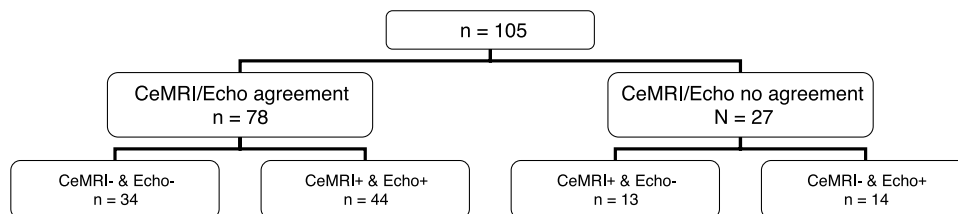


Figure 5. Agreement between CeMRI and Echo results.

SPECT but exhibited 1 ± 0 segment subendocardial (score: 1.3 ± 0.5) delayed enhancements at CeMRI. Eighteen patients (17%), of which only three with nonQ-MI and one with RA history, had a negative CeMRI but showed totally at SPECT twenty-five mild (score: 1.3 ± 0.6) rest perfusion defects of 4 ± 3 segments. Six defects were placed in the anterior septum or anterior wall in patients with left bundle block (LBB), with both female sex and body mass index (BMI) greater than 30 or with all these features. Ten defects of the inferior or posterior wall were found in male patients all with BMI greater than 25 (in two cases greater than 30). Five defects in the anterior wall, anterior septum, anterior-lateral or posterior walls and inferior wall were found in patients with a sub-occlusion of, respectively, the first diagonal branch, the left anterior descending, the circumflex, and the right coronary artery. Four defects had not a reasonable explanation.

In patients in whom CeMRI and SPECT were both positive, we looked for coarse disagreement of segmental scores, and we found delayed enhancements of less than 25% transmural extent (score 0 or 1) and severe perfusion defects (score 3) in 21 of 848 segments (2.5%). On the other hand, we found delayed enhancements of more than 75% transmural extent (score 3) and no or mild perfusion defects (score 0 or 1) in 28 of 848 segments (3.3%).

3.3. Comparison of CeMRI and Echo

Agreement between CeMRI and Echo (Fig. 5) was found in 78 cases (75%). When CeMRI and Echo were both positive ($n = 44$), scar was in the same coronary territory in 36 patients (81%). Thirteen patients (12%) presented 2 ± 1 segments subendocardial (score 1.4 ± 0.6) late enhancements without Echo contractile anomalies. Cine-MRI showed 2 ± 1 segments wall motion abnormality in 4 of them. Fourteen cases (13%) showed 11 ± 7 segments kinetic abnormalities (82% hypokinetic, 18% akinetic) at Echo without CeMRI scar evidence. Cine-MRI showed 8 ± 7 segments wall motion abnormalities in 10 of them.

In patients in whom CeMRI and Echo were both positive, we looked for coarse disagreement of segmental scores, and we found delayed enhancements of less than 25% transmural extent (score 0 or 1) and akinesia or dyskinesia (score 2 or 3) in 73 of 704 segments (10%). On the other hand, we found

delayed enhancements of more than 75% transmural extent (score 3) and normal contraction or hypokinesia (score 0 or 1) in 28 of 704 segments (4%).

4. Discussion

In patients with history of Q-MI, CeMRI, and SPECT showed high sensibility in detection of scar, confirming the results of Wagner et al. (4), who reported high concordance between CeMRI and SPECT in case of transmural scars. The relatively low sensibility of Echo is due to the possible absence of wall motion abnormalities in case of small subendocardial scars, rather commonly observed in clinical practice.

CeMRI identified subendocardial scars of small size (2 segments on the average) in about one third of patients with nonQ-MI or RA history. Very small subendocardial scars (1 segment) were found at CeMRI in a negligible proportion of patients with EA history.

Moving from a clinical setting of remarkable myocardial necrosis (Q-MI) to scenarios of minor or uncertain (nonQ-MI or RA) or generally absent (RA) myocardial damage, decreasing detection of scar tissue seems to have a biological plausibility. This was highlighted by trends analysis which showed a good correlation between CeMRI and clinical history. SPECT and Echo decreasing trends also were statistically significant. However, correlation with clinical history was much weaker because positive SPECTs were relatively high both in nonQ-MI/RA and EA groups and positive Echos were high in EA group.

Independently of patients' history, CeMRI and SPECT agreement for scar detection was incomplete (79% of cases). Few patients, all of them with MI or RA history, did not showed rest perfusion defect at SPECT but had a positive CeMRI. In these cases, scars, which were very small (1 segment) and subendocardial, might not be unmasked by SPECT because of its low spatial resolution as it has been shown by Wagner et al. (4) too. Most of incongruous cases, of whom only one fifth had nonQ-MI or RA history, did not showed delayed enhancements but had medium size (4 segments) rest perfusion defects at SPECT. The misleading identification of a scar segment in case of LBB, rest ischemia or tracer activity attenuation (above all in obese patients), might

account for an overestimation of scar at SPECT examination in most of them. Rest ischemia could be eluted by epicardial coronary dilatation with maximal IV nitrate therapy, whose application is unfortunately difficult in routine evaluations.

Agreement between CeMRI and Echo for scar detection was incomplete too (75% of cases). Half of incongruous cases showed delayed enhancements at CeMRI without wall motion abnormalities at Echo, probably because scars were very small (2 segment) and located in subendocardium. However high spatial resolution, high dynamic range and full LV coverage by cine-MRI allowed the detection of minor kinetic abnormalities in some of these patients. Another half of inconsistent cases did not show delayed enhancements but had wide wall motion abnormalities at Echo, mostly confirmed by cine-MRI. Although stunned myocardium was expected to be infrequent in a population of chronic MI, hibernation could not be excluded and might explain those kinetic abnormalities. Low dose dobutamine might be useful for assessing viable from scar segments but it is more difficult to perform than rest Echo.

Concordance between CeMRI and SPECT in location of scar in the same coronary territory was good (87%) and slightly higher than between CeMRI and Echo (81%). An adequate agreement of segmental score was seen in a higher proportion of segments comparing CeMRI with SPECT than comparing CeMRI with Echo (84% vs. 76%) too.

Comparing different techniques, imperfect overlapping of segments and of coronary territories might have occurred although the same segmentation of LV was used. Difference in diagnostic content of the various imaging technique must be considered too. Indeed when we compared Cine-MRI with Echo, both assessing LV contractility, MI site concordance was very good (92%).

4.1. Limits of the study

Patients with MI history included in the study had this diagnosis in a very wide period of time before MRI evaluation, ranging from 1 month to 30 years (about 50% less than 1 year; 25% from 1 to 10 years; and 25% more than 10 years before) so it was impossible for us to use an unique biochemical marker of myocardial necrosis to define them (furthermore this data lacked in half of patients). This is a limit of our study, which is related to its retrospective nature. However to assess data consistency, we repeated statistical analysis comparing patients with enzyme proved MI, rest angina, and effort angina, and we found similar results as comparing Q-MI, nonQ-MI/RA and EA (Fig. 2, lower part).

We did not use gated SPECT. This may be a limit of the study as in clinical practice rest defects without contraction abnormalities could be simply considered artefacts (attenuation, movement, conduction block, etc.) due to their low prognostic significance. However, this approximation is not acceptable if we are testing SPECT sensibility in

detecting scar, as subendocardial scars can sometimes not cause kinetic abnormalities but can be detected by SPECT as mild or moderate perfusion defects. Concordance between fixed perfusion defect and kinetic abnormalities at gated SPECT has been shown indeed to be variable (11–14) in patients with MI history. In our study, 8 of 50 patients (16%) with Q-MI did not showed kinetic abnormalities at Echo study, but perfusion defects (and delayed enhancements) were found in 6 of them. Then, adding contractility to perfusion data would have meant underestimated SPECT sensibility. Probably in patients with preceding acute coronary syndrome other than Q-MI contractility data also would not have been useful. In this setting, 4 of 8 patients showed perfusion defects without kinetic abnormalities but all of them had an enzyme proved MI history (and small delayed enhancements at CeMRI). Vice versa adding contractility data would rule out 14 of 16 perfusion defects (and work out 9 of 14 incongruities between CeMRI and SPECT) in patients with effort angina. So gated SPECT might be useful in a clinical setting of very low probability of scar (effort angina) but not when probability is moderate or high (acute coronary syndrome history).

We used a Technetium based rest perfusion study instead of a Thallium-201 (rest-redistribution or reinjection) based evaluation, which is considered the best SPECT method to distinguish viable myocardium from scar. However, many studies have demonstrated an equivalence of the two methods (15–19) above all after administration of nitrates (20,21). Indeed, guidelines for the clinical use of cardiac radionuclide imaging (22) classified both resting sestamibi and thallium rest-redistribution imaging as Class I, level of evidence B for assessment of myocardial viability. Although our patients were studied without wash-out from their coronary-active therapy, we did not administer nitrates before SPECT, and this might have caused an overestimation of scar.

5. Conclusions

Our study demonstrates that CeMRI almost always identifies areas with DE in patients with Q-MI history, in whom perfusion defects and, above all, kinetic abnormalities may not be found by SPECT and Echo, respectively. CeMRI identifies small amounts of scar tissue also in some patients with chronic CAD and previous nonQ-MI or RA but usually not in patient with EA history. This biologically plausible decreasing trend, in clinical settings with progressively reducing probability of myocardial necrosis, is disclosed by CeMRI more clearly than by SPECT and Echo.

Disagreement between CeMRI and SPECT as well as Echo may be reduced, but perhaps not fully eluded, performing low-dose dobutamine Echo and SPECT after maximal epicardial coronary dilatation, whose application is more

difficult in routine evaluations. Gated SPECT may be useful in patients without clinical history of acute coronary syndrome.

Findings of our study should be confirmed by properly designed prospective studies.

Abbreviations

BMI	body mass index (calculated as weight [kg] divided by the square of height [m])
CAD	coronary artery disease
Echo	trans-thoracic echocardiography
LBB	left bundle block
LV	left ventricle
SPECT	single-photon emission tomography

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