Cardiac MRI for Detection of Unrecognized Myocardial Infarction in Patients With End-Stage Renal Disease: Comparison With ECG and Scintigraphy

Joalbo M. Andrade[1]
Luís Henrique W. Gowdak
Maria C. P. Giorgi
Flavio J. de Paula
Roberto Kalil-Filho
José Jayme G. de Lima
Carlos E. Rochitte

OBJECTIVE. The purposes of this study were to use the myocardial delayed enhancement technique of cardiac MRI to investigate the frequency of unrecognized myocardial infarction (MI) in patients with end-stage renal disease, to compare the findings with those of ECG and SPECT, and to examine factors that may influence the utility of these methods in the detection of MI.

SUBJECTS AND METHODS. We prospectively performed cardiac MRI, ECG, and SPECT to detect unrecognized MI in 72 patients with end-stage renal disease at high risk of coronary artery disease but without a clinical history of MI.

RESULTS. Fifty-six patients (78%) were men (mean age, 56.2 ± 9.4 years) and 16 (22%) were women (mean age, 55.8 ± 11.4). The mean left ventricular mass index was 103.4 ± 27.3 g/m^2, and the mean ejection fraction was 60.6% ± 15.5%. Myocardial delayed enhancement imaging depicted unrecognized MI in 18 patients (25%). ECG findings were abnormal in five patients (7%), and SPECT findings were abnormal in 19 patients (26%). ECG findings were false-negative in 14 cases and false-positive in one case. The accuracy, sensitivity, and specificity of ECG were 79.2%, 22.2%, and 98.1% (p = 0.002). SPECT findings were false-negative in six cases and false-positive in seven cases. The accuracy, sensitivity, and specificity of SPECT were 81.9%, 66.7%, and 87.0% (not significant). During a period of 4.9–77.9 months, 19 cardiac deaths were documented, but no statistical significance was found in survival analysis.

CONCLUSION. Cardiac MRI with myocardial delayed enhancement can depict unrecognized MI in patients with end-stage renal disease. ECG and SPECT had low sensitivity in detection of MI. Infarct size and left ventricular mass can influence the utility of these methods in the detection of MI.

Keywords: coronary artery disease, ECG, kidney transplantation, MRI, myocardial infarction, scintigraphy

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J. M. Andrade and C. E. Rochitte contributed equally to this work.

[1]All authors: Department of Cardiology, Heart Institute (InCor), University of Sao Paulo Medical School, Av. Dr. Enéas de Carvalho Aguiar, 44, Cerqueira César, Setor de Ressonancia e Tomografia, Andar AB, São Paulo SP, Brazil 05403-000. Address correspondence to C. E. Rochitte (rochitte@incor.usp.br).

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Unrecognized myocardial infarction (MI) in patients without a clinical history of MI is usually diagnosed with surveillance ECG [1]. For many years, unrecognized MI has been perceived as having a prevalence ranging from 5% to 40%, depending on sex, age, and the presence of coronary artery disease (CAD). The prevalence may be higher among women, elderly persons, and persons with diabetes or hypertension [2–4]. Population-based studies [4, 5] have shown a 10-year mortality rate of 45–55% in groups of patients with unrecognized MI. This rate is comparable with or higher than that among patients with recognized MI. This finding highlights the importance of unrecognized MI as a major clinical problem [1].

Patients with end-stage renal disease (ESRD) are at high risk of CAD, which is the leading cause of death after renal transplantation. Thus preoperative risk evaluation is crucial to this population [6]. In patients undergoing renal transplantation, the mortality is higher among recipients with known CAD compared with those without clinically overt CAD before surgery [7]. Moreover, when only conventional tests are used for preoperative risk stratification, MI may be missed in renal transplantation candidates.

ECG and SPECT are the tests most frequently performed in the diagnosis of unrecognized MI. However, these methods have inherent limitations, such as the low sensitivity of ECG and the low spatial resolution for infarct detection of SPECT [1, 8, 9]. Another potential limitation may be related to small infarct size and infarct size relative to global or segmental left ventricular (LV) mass because these methods rely on the regional mass of live myocardium (electric and radioisotopic uptake by intact cells, respectively)

in the detection of segments with less or no myocardial activity. However, this hypothesis should be further investigated.

Myocardial delayed enhancement at contrast-enhanced cardiac MRI has been found to depict myocardial infarcts [10] and has greater accuracy than SPECT in the detection of small infarcts [8], which often are present in unrecognized MI. The primary objective of our study was to use myocardial delayed enhancement at cardiac MRI to investigate the frequency of unrecognized MI among patients with ESRD and to compare the findings with those of ECG and SPECT. We also sought to study factors that may influence the utility of these methods in the detection of MI.

Subjects and Methods

From 2002 to 2004, we enrolled 79 patients with ESRD who were being treated with hemodialysis and had no history of MI, myocarditis, Chagas disease, or cardiac surgery. All patients had chronic kidney disease classified grade 5, and the glomerular filtration rate was less than 10 mL/min/1.73 m^2 [11]. At the time of the study, the problem of contrast-related nephrogenic systemic fibrosis (NSF) was not known, and gadolinium-based agents were considered safe for this group of patients. Therefore, all data were acquired during the pre-NSF era. The main causes of renal failure were diabetes mellitus (34 patients, 43%) and nephrosclerosis (16 patients, 20%). Ten patients had other causes of renal failure (three, polycystic kidney disease; two, systemic lupus erythematosus; one, tuberculosis; one, lithiasis; one, chronic pyelonephritis; one, drug-induced nephropathy; one, reflux nephropathy), and 19 patients (24%) had no identified cause of renal failure.

We included only patients at high risk of CAD with at least one of the following: age 50 years or older; diabetes mellitus; and clinical evidence of previous cardiovascular disease (including stable CAD), but only if any clinical history of MI, prolonged chest pain (more than 30 minutes), or previous known changes in ECG findings (before enrollment) or cardiac enzyme levels suggestive of MI were absent. The protocol was approved by the institutional review board, and all patients provided signed informed consent. All patients prospectively underwent full cardiac MRI studies, resting ECG, resting and pharmacologic stress SPECT, and invasive coronary angiography as part of the clinical evaluation.

Cardiac MRI

All patients underwent a full cardiac MRI examination with a 1.5-T system (Signa CV/i, GE Healthcare), including assessment of LV function at rest, rest and stress myocardial perfusion with dipyridamole, and myocardial delayed enhancement for detection of MI. LV short- and long-axis images were acquired at rest with breath-hold cine cardiac MRI (gradient-recalled echo sequence with steady-state precession). The imaging parameters were as follows: TR/TE, 3.8/1.6; flip angle, 45°; receiver bandwidth, ± 125 kHz; rectangular field of view, 0.75, 34–36 cm; matrix size, 256 × 128; slice thickness, 8.0 mm; gap, 2.0 mm.

The patients received 0.56 mg/kg of dipyridamole (Persantin, Boehringer Ingelheim) IV over 4 minutes. After 3–4 minutes, stress cardiac MR perfusion images were obtained with 0.05 mmol/kg of a gadolinium-based contrast agent (gadoterate meglumine, Dotarem, Guerbet) infused at 5 mL/s followed by a saline flush. The pulse sequence used for myocardial perfusion was a hybrid sequence of fast gradient-recalled echo and echo-planar readouts. An additional 0.1 mmol/kg of contrast agent was injected for myocardial delayed enhancement 10–20 minutes later. A gradient-recalled echo with inversion recovery preparatory pulse was used to saturate the myocardial signal at the following parameters: 7.3/3.2; inversion time, 150–250 milliseconds; receiver bandwidth, 31.2 kHz; flip angle, 30°; acquisition every R-R interval; matrix size, 256 × 192; field of view, 34–38 cm; number of signals acquired, 2; slice thickness, 8.0 mm; slice gap, 2.0 mm. Inversion times are usually shorter with our choice of single R-R acquisition for myocardial delayed enhancement (typical value, 175–250 milliseconds [12]). Despite less time for signal recovery after the inversion recovery pulse, with 2 signals acquired and other parameters, image quality was good. The cardiac MRI examination time was 45 minutes. Blood pressure, heart rate, and signs of adverse reactions were continuously monitored throughout the examination.

Rest perfusion imaging was performed 48 hours after stress imaging with the same cardiac MRI parameters after a hemodialysis session. The objectives were avoiding interference of residual contrast material from stress perfusion imaging with rest perfusion imaging and decreasing the risks of adverse effects related to the contrast agent. Myocardial delayed enhancement imaging at cardiac MRI was the standard of reference for clinically silent MI against which other techniques were compared.

ECG, SPECT, and Invasive Coronary Angiography

All patients underwent 12-lead standard ECG and SPECT myocardial perfusion imaging with ^{99m}Tc-sestamibi or ^{201}Tl. Image acquisition began 45–60 minutes after sestamibi injection at rest (dose, 370 MBq) and stress (dose, 800 MBq) or immediately after thallium injection during stress (dose, 110 MBq) and 4 hours after stress (redistribution image) with a single-detector gamma camera system equipped with low-energy high-resolution collimator. All studies were performed with the following parameters: 64 projections; 180° noncircular orbit, 45° right anterior oblique to left posterior oblique angles; matrix size, 64 × 64 ; pixel size, 6.7 mm. Images were reconstructed by filtered back-projection with a Butterworth filter (order, 5; cutoff frequency, 0.6 Nyquist) and resliced into short-axis, vertical long-axis, and horizontal long-axis views that were used for qualitative analysis. All SPECT studies were performed with pharmacologic stress because of the large number of patients with ESRD unable to perform an efficacious exercise test. All patients underwent selective coronary angiography performed with the Sones or Judkins technique according to the usual routine of our catheterization laboratory [13].

Data Analysis

In all studies, including ECG, SPECT, and cardiac MRI, two experienced readers were asked to give a consensus report on the presence or absence of MI. For SPECT and cardiac MRI images, data (presence or absence of MI) also were recorded for each of the 17 LV segments on the basis of recommended LV segmentation [14], allowing for regional comparison between these two imaging methods. Readers using a specific method were blinded to the results of the other two methods of MI detection investigated in this protocol. The readers were an experienced cardiologist, nuclear cardiologist, and radiologist with more than 10 years of experience in their respective fields and active in many research projects. Readers of cardiac MR images had level 3 expertise according to the guidelines of the Society for Cardiovascular Magnetic Resonance.

Although the patients underwent a full cardiac MRI study, the myocardial perfusion data are not reported, except for the limited and specific data used for interpreting the false-positive SPECT findings. For the purpose of this study—detection of unrecognized MI—the full scope of cardiac MRI myocardial perfusion data would not increase the amount of useful information.

End-systolic and end-diastolic LV volumes, LV mass, and ejection fraction were measured on cine cardiac MRI images with MASS plus software (Medis) according to the method of Simpson. On the myocardial delayed enhancement images, infarcted areas were visually identified and quantified with planimetry after consensus was reached among the readers. Only areas of myocardial delayed enhancement that the observers considered

suggestive of MI were measured. Typically, subendocardial or focal and well-delineated areas of myocardial delayed enhancement were considered infarcts. Diffuse patterns of myocardial delayed enhancement, described previously [15], were not included as MI. Measurement and analysis of infarct size and LV mass was performed to investigate the influence of these parameters on the utility of the methods investigated in the detection of MI.

ECG criteria for MI were presence of major Q-wave (Q wave > 0.04 second) or minor Q-wave abnormalities combined with ST-segment or T-wave abnormalities. We adopted Cardiovascular Health Study criteria [16] with the best balanced sensitivity and specificity. Scintigraphic methods were considered indicative of MI if a fixed defect (rest and stress) of radioisotopic uptake was detected. Functional information derived from gated SPECT examinations were used only if a perfusion defect was considered equivocal. Findings at invasive coronary angiography were based on the presence or absence of ≥ 70% stenosis in the major coronary arteries and branches.

End Points and Follow-Up

The follow-up data were obtained by at least one of the following methods: the patient met with a cardiologist in the outpatient clinic, a cardiologist made a telephone call to the patient or relatives regarding the patient's health status, or the patient's hospital records were reviewed. In this study, cardiac death was the only end point. Two cardiologists adjudicated all cardiac deaths after careful review of all available data. Cardiac death required documentation of death attributable to congestive heart failure, MI, or a revascularization procedure. In case of death at the hospital, only sudden unexpected death was considered to have a cardiac cause. The average follow-up period was 34.1 ± 16.1 months (minimum and maximum, 6.9 and 71.7 months), and the median was 33.2 months.

Statistical Analysis

Results are expressed as the mean ± SD, and 95% CIs were calculated. The accuracy, sensitivity, and specificity of ECG and SPECT were calculated with myocardial delayed enhancement imaging as the reference method. The Kolmogorov-Smirnov test was used to assess the gaussian distribution of continuous data. The McNemar test was used to evaluate nominal paired data, and the Student's *t* test was used to assess continuous parametric data, both with two-tailed analysis. Survival distributions for the time to event were estimated with the Kaplan-Meier method, and differences between survival distributions were assessed with a log-rank test. Statistical significance was

TABLE 1: Patient Characteristics

Characteristic	All Patients (*n* = 72)	Myocardial Delayed Enhancement Imaging	
		Yes (*n* = 18)	No (*n* = 54)
Age (y)	56 ± 9	58 ± 8	56 ± 10
No. of men	56 (78)	14 (78)	42 (78)
No. of women	16 (22)	4 (22)	12 (22)
Family history of coronary artery disease	26 (36)	9 (50)	17 (31)
Medical history			
Smoking	24 (33)	9 (50)	15 (28)
Diabetes mellitus	34 (47)	10 (56)	24 (44)
Dyslipidemia	35 (49)	8 (44)	27 (50)
Peripheral arteriopathy	21 (29)	9 (50)	12 (22)
Cerebral ischemia	7 (10)	5 (28)	2 (4)[a]
Angina	14 (19)	4 (22)	10 (19)
Heart failure	11 (15)	5 (28)	6 (11)
Medication use			
Diuretics	17 (24)	4 (22)	13 (24)
Angiotensin-converting enzyme inhibitor	38 (53)	13 (72)	25 (46)
β-Blocker	20 (28)	5 (28)	15 (28)
Calcium channel blocker	28 (39)	6 (33)	22 (41)
Sympatholytic agent	12 (17)	2 (11)	10 (19)
Vasodilator	5 (7)	3 (17)	2 (4)

Note—Except for age, values are numbers of patients with percentages in parentheses.
[a] $p < 0.05$; otherwise difference not significant.

TABLE 2: Absolute and Relative Frequencies of Results of Each Diagnostic Technique Versus Findings of Myocardial Delayed Enhancement at Cardiac MRI

Evidence of Myocardial Infarction	Myocardial Delayed Enhancement (*n* = 18)	No Myocardial Delayed Enhancement (*n* = 54)	All (*n* = 72)
ECG			
Present	4 (22)	1 (2)	5 (7)
Absent	14 (78)	53 (98)	67 (93)
SPECT			
Present	12 (67)	7 (13)	19 (26)
Absent	6 (33)	47 (87)	53 (74)
Invasive coronary angiography (≥ 70% stenosis)			
Present	14 (78)	23 (43)	37 (51)
Absent	4 (22)	31 (57)	35 (49)
^{99m}Tc SPECT (*n* = 51)	11	40	51
Present	8 (73)	5 (13)	13 (25)
Absent	3 (27)	35 (87)	38 (75)
^{201}Tl SPECT (*n* = 21)	7	14	21
Present	3 (43)	2 (14)	5 (24)
Absent	4 (57)	12 (86)	16 (76)

Note—Values are numbers of patients with percentages in parentheses.

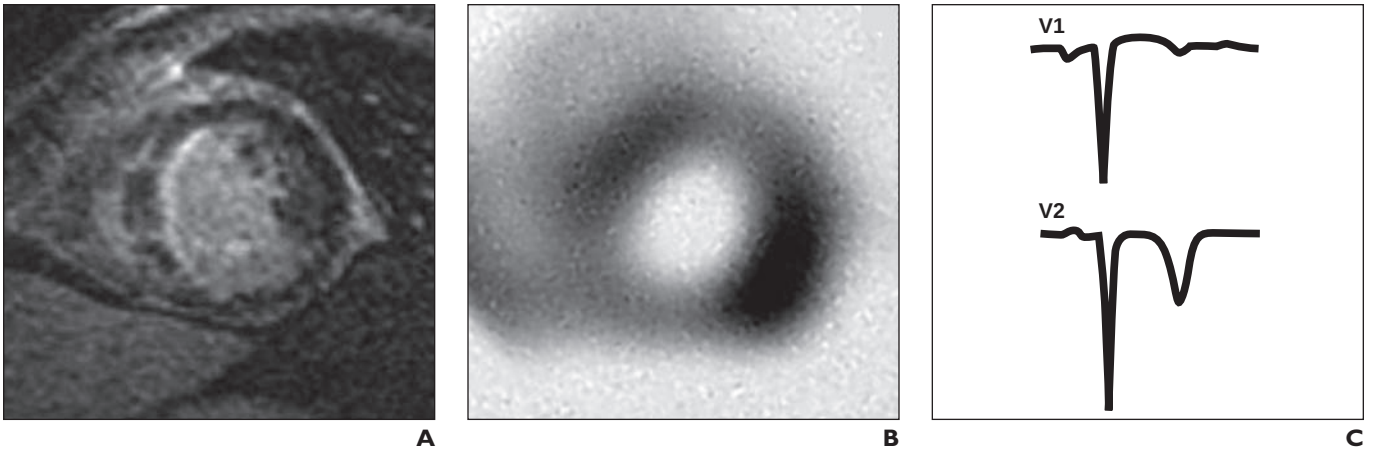

Fig. 1—68-year-old man with unrecognized myocardial infarction detected with all methods. Example of concordant findings.
A, Cardiac short-axis left ventricular myocardial delayed enhancement MR image shows area of myocardial infarction involving anterior, septal, and inferior walls of left ventricle.
B, Image from ^{99m}Tc sestamibi SPECT shows fixed perfusion defect corresponding to findings in **A.**
C, ECG tracing shows abnormal Q wave in V1 and V2 leads.

considered $p < 0.05$. The SPSS statistical package (version 15.0, SPSS) was used for all analyses.

Results

Of the 79 patients enrolled, two claustrophobic patients and five patients lost to follow-up were excluded. The baseline clinical characteristics of the 72 patients included in the study are shown in Table 1. All tests (cardiac MRI, ECG, SPECT, and invasive coronary angiography) were performed within a period of 4 months for each patient.

Cardiovascular MRI data showed the mean LV mass index was 103.4 ± 27.3 g/m^2 and the ejection fraction was 60.6% ± 15.5%. The mean end-systolic volume index was 42.1 ± 31.6 mL/m^2, and the mean end-diastolic volume index was 96.6 ± 32.7 mL/m^2. Typical areas of myocardial delayed enhancement indicating MI were detected in 18 patients (25%) (Table 2) in 26 coronary territories (12.1% of all coronary territories). No cases of diffuse myocardial delayed enhancement were found.

MI was detected with ECG in five patients (7%); 67 patients (93.1%) had no ECG signs of MI (Table 2). Fifty-one patients (71%) underwent ^{99m}Tc-sestamibi SPECT and 21 patients (29%) underwent ^{201}Tl SPECT during rest and pharmacologic stress (Figs. 1–3).

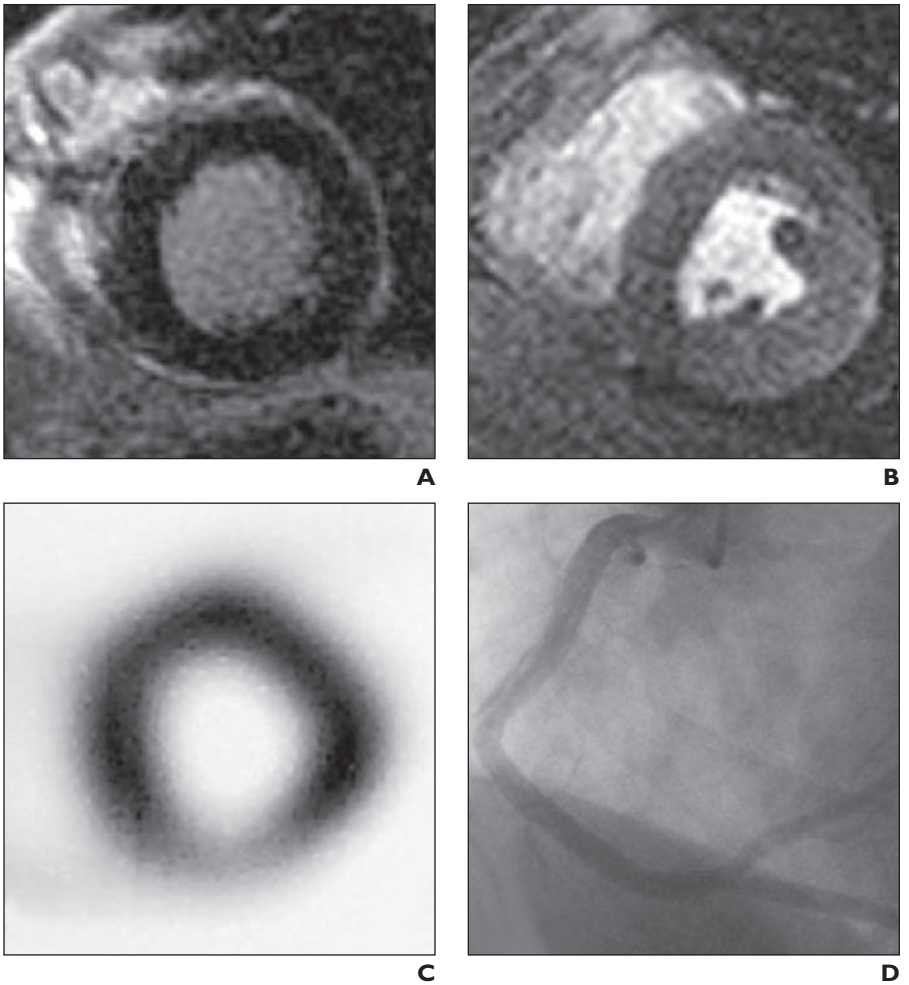

Fig. 2—53-year-old man with fixed defect only at ^{99m}Tc-sestamibi SPECT. Example of discordant false-positive findings.
A and **B,** Cardiac short-axis left ventricular myocardial delayed enhancement MR image (**A**) and first-pass myocardial stress image (**B**) show normal findings.
C, Left ventricular short-axis ^{99m}Tc-sestamibi SPECT image shows false-positive fixed perfusion defect in inferior left ventricular wall.
D, Invasive angiogram shows normal right coronary artery.

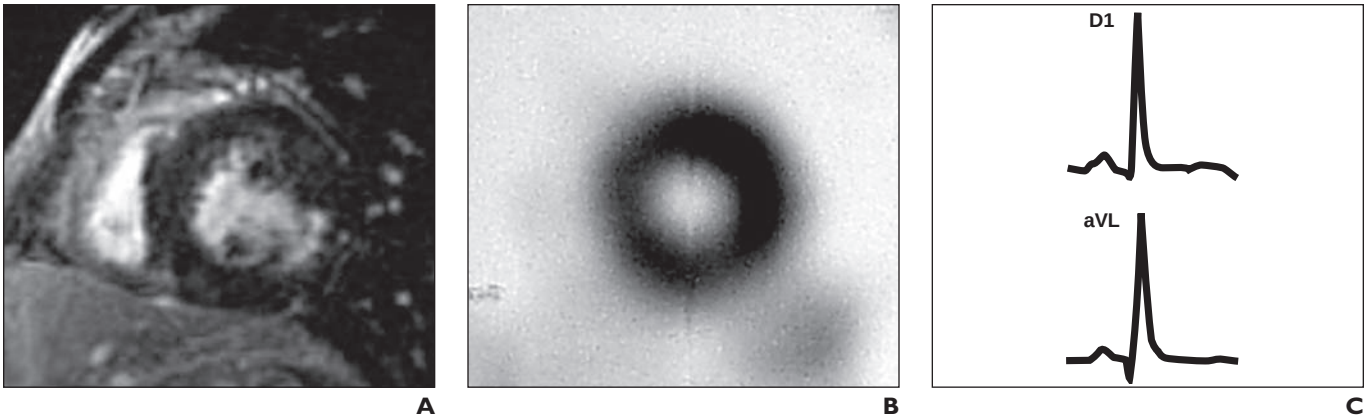

Fig. 3—43-year-old man with myocardial infarction. Example of false-negative ^{99m}Tc-sestamibi SPECT and ECG findings.
A, Cardiac short-axis left ventricular myocardial delayed enhancement MR image shows small area of myocardial infarction involving lateral left ventricular wall.
B and **C,** Images from ^{99m}Tc sestamibi SPECT (**B**) and ECG tracing (**C**) show findings considered normal.

SPECT images revealed unrecognized MI in 19 patients (26%) in 23 (11%) coronary territories (Table 2). Invasive coronary angiography revealed significant CAD (stenosis ≥ 70%) in 37 patients (51%). Significant CAD was present in 23 of the patients (43%) without myocardial delayed enhancement and 14 (78%) of the patients with myocardial delayed enhancement ($p < 0.05$) (Figs. 1–3, Table 2). Patients with unrecognized MI detected with cardiac MRI tended to have a greater mean LV mass than did patients without unrecognized MI, but the difference was not statistically significant (196.7 ± 49.5 g vs 171.3 ± 49.3 g). The mean mass of LV infarcts was 13.2 ± 7.9 g.

Cardiac MRI Versus ECG

Fourteen patients (78%) with myocardial delayed enhancement MRI evidence of MI had normal ECG findings. ECG showed Q waves indicative of MI in five patients, four of these patients having abnormal myocardial delayed enhancement (Table 2). Thus, ECG had 14 false-negative results and one false-positive result; the accuracy, sensitivity, and specificity in the detection of MI were 79.2%, 22.2%, and 98.1% ($p = 0.002$) (Table 3). In the four patients with abnormal myocardial delayed enhancement and abnormal ECG findings, the mean infarct size was 23.8 ± 9.1 g (12.6% ± 3.1% of LV mass). In the 14 patients with normal ECG findings and abnormal myocardial delayed enhancement, the mean infarct size was 11.6 ± 4.1 g (6.5% ± 3.1% of LV mass) ($p = 0.001$) (Fig. 4A). Among the 18 patients with abnormal myocardial delayed enhancement, the four patients with abnormal ECG findings had an LV mass less than that of the 14 patients with normal ECG findings, but the difference was not statistically significant (185 g vs 195 g) (Fig. 4B).

Cardiac MRI Versus SPECT

Six of 18 patients (33%) with MI at cardiac MRI performed with myocardial delayed enhancement technique had normal SPECT findings. In 19 patients, SPECT showed fixed myocardial defects; 12 of these patients had abnormal myocardial delayed enhancement (Table 2). Thus SPECT had six false-negative results and seven false-positive results. The accuracy, sensitivity, and specificity in detection of MI were 81.9%, 66.7%, and 87.0% (difference not significant) (Table 3).

The mean LV infarct size was 16.3 ± 7.9 g (9.5% ± 3.6% of LV mass) in the 12 patients with abnormal myocardial delayed enhancement and abnormal SPECT findings. In the six patients with normal SPECT findings and abnormal myocardial delayed enhancement, the mean LV infarct mass was 7.1 ± 3.1 g (3.0% ± 1.3% of LV mass). Therefore, significantly smaller infarcts were found in patients with normal SPECT findings ($p = 0.014$) (Fig. 5A). Among the 18 patients with abnormal myocardial delayed enhancement, the 12 patients with abnormal SPECT findings had less LV mass than the six patients with normal SPECT findings (171 g vs 238 g; $p = 0.003$) (Fig. 5B).

In the subgroup of 51 patients who underwent ^{99m}Tc SPECT, results were similar to the entire group of patients who underwent SPECT (Table 2). The mean LV infarct size for the 11 patients with abnormal myocardial delayed enhancement was 15.6 ± 9.3 g. Whereas infarct size among the eight patients with abnormal myocardial delayed enhancement and abnormal ^{99m}Tc SPECT findings was

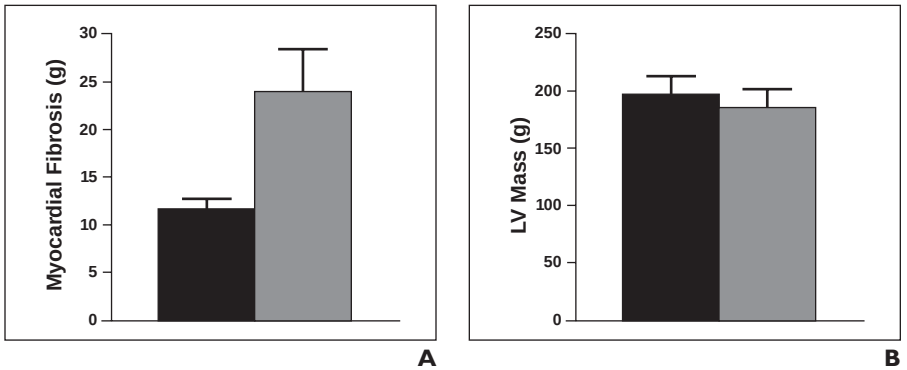

Fig. 4—Myocardial delayed enhancement versus ECG in diagnosis of unrecognized myocardial infarction.
A, Graph shows mass of myocardial infarcts was significantly higher in patients with abnormal ECG (*black bar*) than in patients with normal ECG (*gray bar*) findings ($p = 0.001$).
B, Graph shows left ventricular (LV) mass was similar in patients with abnormal ECG (*black bar*) and normal ECG (*gray bar*) findings (difference not significant).

TABLE 3: Diagnostic Test Values of ECG and SPECT in Detection of Myocardial Infarction With Myocardial Delayed Enhancement MRI as the Reference Method

Characteristic	ECG[a]	SPECT[b]
Accuracy (%)	79.2 (69.4–88.9)	81.9 (73.1–90.8)
Sensitivity (%)	22.2 (3.0–41.4)	66.7 (44.9–88.4)
Specificity (%)	98.1 (94.3–101.8)	87.0 (78.1–96.0)
Positive predictive value (%)	80.0 (44.9–115.1)	63.2 (41.5–84.8)
Negative predictive value (%)	79.7 (70.2–89.2)	88.7 (80.1–97.2)

Note—Values in parentheses are 95% CI.
[a] $p < 0.05$ myocardial delayed enhancement versus ECG, McNemar test.
[b] $p > 0.05$. myocardial delayed enhancement versus SPECT, McNemar test.

18.9 ± 8.5 g, in the three patients with normal ^{99m}Tc SPECT findings, the infarct size was only 6.7 ± 3.9 g ($p = 0.02$). In the subgroup of 21 patients who underwent ^{201}Tl SPECT, only seven patients had myocardial delayed enhancement indicating MI (Table 2). In this group of patients, we found greater LV mass in the four patients with normal ^{201}Tl SPECT findings ($p = 0.028$), but we did not find statistically different infarct sizes.

False-Positive Results of SPECT

Five patients with fixed defects on ^{99m}Tc SPECT images had normal myocardial delayed enhancement, constituting false-positive results. Two of these patients had normal invasive coronary angiographic and function–perfusion cardiac MRI findings and thus true ^{99m}Tc SPECT false-positive results. One patient had normal invasive coronary angiographic findings, but a perfusion defect, which may be an indication of microvascular disease, was found at cardiac MRI. The other two patients had a cardiac MRI perfusion defect in the anterior LV wall and significant stenosis on invasive coronary angiograms, probably suggesting substantial hibernating myocardium without MI (Table 4).

Two patients with a fixed defect on ^{201}Tl SPECT images had normal myocardial delayed enhancement, a false-positive result. One of these patients had normal function–perfusion cardiac MRI and invasive coronary angiographic findings. The other had a cardiac MRI perfusion defect and significant stenosis on invasive coronary angiograms, probably indicating the presence of transient myocardial defects interpreted as fixed (Table 4).

Cardiac Events

Among the 72 patients in this study, 19 cardiac deaths (26%) occurred over 4.9–77.9 months. In this small sample, Kaplan-Meier and log-rank test analyses showed that the presence of unrecognized MI at ECG, SPECT, and myocardial delayed enhancement MRI does not identify a higher probability of cardiac death (curves not shown).

Discussion

Myocardial delayed enhancement at cardiac MRI can depict unrecognized MI in high-risk patients with ESRD. This finding has been made in other subgroups of patients [17, 18]. Sensitivities were low for ECG and SPECT owing to the reduced utility of these techniques in the detection of small infarcts. To our knowledge, our study is the first comparison of myocardial delayed enhancement MRI with other methods in the detection of unrecognized MI in patients with ESRD. In a similar study with another high-risk subgroup of 70-year-old subjects without symptoms, investigators found a 20% prevalence of unrecognized MI [17], compared with 25% in our study.

Asymptomatic MI has been recognized for years, and although its initial prevalence was thought to be as low as less than 10% of all MI [19], more recent epidemiologic studies have shown the prevalence to be higher [2–5, 20]. The prevalence is higher among elderly persons [4] and persons with hypertension [20]. The prognosis and clinical and public health implications of unrecognized MI are as serious as those of recognized MI [1, 5]. The prevalence of unrecognized MI in our study was similar to that reported in the literature. Our patients had a high probability of CAD and unrecognized MI; patients at high risk or with known CAD are less likely to have unrecognized MI, however, because they are aware of their disease and its associated symptoms [21]. Among our patients, the prevalence of unrecognized MI was higher among patients with significant coronary stenosis at invasive coronary angiography.

Kim et al. [22–24] developed and validated the technique of myocardial delayed enhancement imaging for infarct detection [22, 23] and myocardial viability assessment [24]. This pulse sequence, described in detail by Simonetti et al. [10], allows visualization of myocardial infarcts with high spatial resolution [8, 25], good reproducibility [26], and excellent correlation with histologic findings on the global and transmural extent of infarction [8, 22, 23]. In addition, myocardial delayed enhancement imaging is less susceptible than radionuclide imaging to body habitus and wall-motion artifacts.

Although ECG is the most frequently used noninvasive method for detection of asymptomatic MI, limitations leading to underestimation of the diagnosis of silent MI include

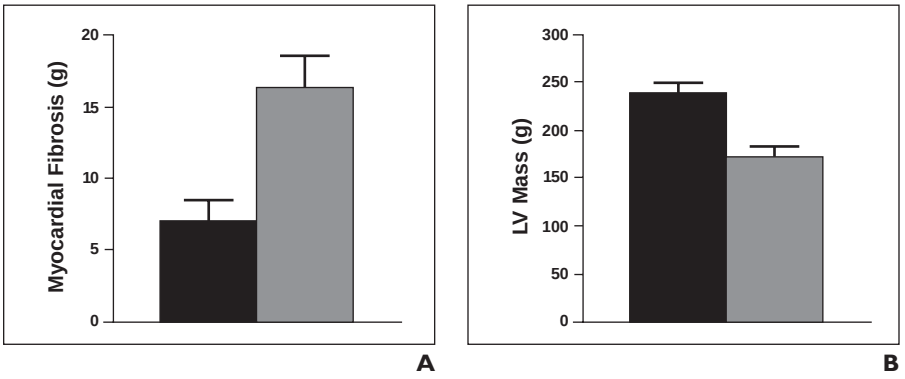

Fig. 5—Myocardial delayed enhancement versus SPECT in diagnosis of unrecognized myocardial infarction.
A, Graph shows mass of myocardial infarcts was significantly higher in patients with abnormal SPECT (*black bar*) than in patients with normal SPECT (*gray bar*) findings ($p = 0.014$).
B, Graph shows left ventricular (LV) mass was less in patients with abnormal SPECT (*black bar*) than in patients with normal SPECT (*gray bar*) findings ($p = 0.003$).

TABLE 4: Results of Evaluation of SPECT False-Positive Results in Detection of Myocardial Infarction With Myocardial Delayed Enhancement MRI as the Reference Method (*n* = 7)

Radionuclide	Defect at SPECT	Perfusion Defect at Cardiac MRI	Hypokinesis at Cardiac MRI	Stenosis at Invasive Coronary Angiography
^{99m}Tc-sestamibi	RCA	Normal	Normal	Normal
^{99m}Tc-sestamibi	RCA	LAD, RCA	Normal	Normal
^{99m}Tc-sestamibi	LAD	Normal	Normal	Normal
^{99m}Tc-sestamibi	LAD	LAD, RCA	LAD, RCA	LAD, RCA
^{99m}Tc-sestamibi	LAD	LAD, RCA	Normal	LAD
^{201}Tl	LAD	Normal	Normal	Normal
^{201}Tl	LAD, LCX	LAD, LCX, RCA	LAD, LCX, RCA	RCA

Note—RCA = right coronary artery, LAD = left anterior descending coronary artery, LCX = left circumflex coronary artery.

inability to detect non-Q-wave MI, MI resulting in sudden death, and lack of ECG soon after the event [1]. ECG features of MI disappear within 2 years in 10% of cases of anterior MI and 25% of cases of inferior MI [27]. Overall, 20% of MI patients who survive have normal ECG findings 4 years later [28]. Another issue is that the lack of standard criteria for the ECG diagnosis of MI leads to variable results in the literature and hampers direct comparisons [29]. In our study, ECG findings were abnormal in only 22% of patients with myocardial delayed enhancement and in patients with larger infarct sizes. Infarct sizes were smaller at myocardial delayed enhancement imaging of patients with normal ECG findings, indicating that ECG was not useful for detecting small infarcts.

Studies conducted with animal models of permanent occlusion [30] and reperfusion [31] have shown that the size of defects detected with ^{99m}Tc SPECT is an accurate measure of infarct size. Medrano et al. [32], in a study of hearts from patients who had undergone transplantation, found that ^{99m}Tc SPECT defect size measurements were 7% overestimates (mean value) of infarct size owing to the presence of hibernating myocardium. SPECT has important limitations, especially in the detection of small and subendocardial infarcts, because of low spatial resolution [33], degradation of image quality due to scatter and attenuation effects, and partial volume effect potentiated by abnormal wall motion [34]. The relatively low sensitivity of scintigraphy compared with myocardial delayed enhancement imaging is probably related to these limitations. Our data suggest that the utility of SPECT in the detection of areas of MI can be influenced by the ratio between infarcted myocardium and associated LV hypertrophy, both globally and regionally. For instance, a hypertrophic LV segment that has double the wall thickness of the opposite segment and harbors a myocardial infarct involving 50% of its volume will have counts at scintigraphy similar to those of the opposite wall, generating apparently normal homogeneous radioisotope distribution [8].

In our study, after SPECT-missed infarction, the infarct size was smaller and LV mass was greater than after SPECT-detected infarction. These findings suggest that not only the limited spatial resolution for detection of small infarcts but also the higher myocardial mass for radionuclide distribution contribute to the limited SPECT resolution for MI detection. In uremic cardiomyopathy, cardiac MRI has depicted LV abnormalities and two patterns of myocardial delayed enhancement, subendocardial and diffuse [15]. In our study, no case of diffuse myocardial delayed enhancement was detected.

Kwong et al. [18] found that detection of unrecognized MI at myocardial delayed enhancement imaging is a strong predictor of major adverse cardiac events and cardiac mortality and that findings at cardiac MRI can improve risk stratification and be a better standard for unrecognized MI than ECG in future population-based studies. In our study, myocardial delayed enhancement was not a predictor of cardiac death in ESRD, probably owing to the small number of patients in the study.

Several limitations of this study must be addressed. Some patients had a longer interval between examinations, but because no patient had clinical events during this period, we believe this limitation did not substantially influence our results. The use of two SPECT techniques can be viewed as a limitation, but it added to the comparison with cardiac MRI radioisotopes used in clinical practice, and ^{201}Tl SPECT is considered specific for myocardial viability and infarct detection. Although not all SPECT studies were performed with gated technique, limiting the usefulness of information on LV wall contractility, cardiac MRI function was not used for MI detection. Moreover, most infarcts were small and had little or no effect on regional contractility. Finally, that subendocardial areas of myocardial delayed enhancement are not completely specific for MI and nonischemic diseases may infrequently manifest themselves as subendocardial enhanced areas is a limitation of this study that cannot be definitively solved with current technology. Unfortunately, the myocardial delayed enhancement technique cannot be used in an ESRD patient population because of the safety issue of NSF associated with gadolinium. We have found no cases of NSF in our patient group after a mean follow-up period of 3 years.

We conclude that cardiac MRI with myocardial delayed enhancement can identify unrecognized MI in patients with ESRD. The sensitivities of ECG and SPECT were low in the detection of MI owing to their reduced usefulness in identification of small areas of MI. Our data suggest that myocardial infarct size and LV mass significantly influence the detection utility of these methods.

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