Tagged MRI and PET in severe CAD: discrepancy between preoperative inotropic reserve and intramyocardial functional outcome after revascularization

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Mazzadi, Alejandro N., Marc F. Janier, Benjamin Brossier, Xavier André-Fouët, Didier Revel, and Pierre Croisille. Tagged MRI and PET in severe CAD: discrepancy between preoperative inotropic reserve and intramyocardial functional outcome after revascularization. Am J Physiol Heart Circ Physiol 287: H2226–H2233, 2004.—In severe coronary artery disease (CAD), it has been shown that intramyocardial inotropic reserve as assessed with tagged magnetic resonance imaging (MRI) is uniformly distributed among positron emission tomography (PET) patterns reflecting normal or concomitant reductions in perfusion and glucose metabolism. This preliminary study aimed to delineate the relationship between preoperative values of intramyocardial inotropic reserve (in different PET patterns of perfusion and glucose uptake) and intramyocardial functional outcome after surgical revascularization in severe CAD. Twelve patients underwent preoperative tagged MRI (baseline, 10 μg·kg−1·min−1 of dobutamine, H215O[18F]fluorodeoxyglucose PET imaging, and postoperative resting tagged MRI. Regional midmyocardial circumferential shortening (Ecc, in %) and PET patterns (normal, match viable, mismatch viable, and infarcted) were assessed in three tagged MRI/PET short-axis slices. Ecc at baseline ranged from 12 ± 6 to 8 ± 5 and 4 ± 4% in normal, match-viable, and infarcted regions, respectively (P < 0.05) and was 8 ± 5% in mismatch-viable regions. Of the 429 regions studied, 187 showed preoperative inotropic reserve with dobutamine, but 238 showed postoperative functional improvement. Postoperative functional improvement was less common in infarcted regions (41 vs. ~60% in the other PET patterns), but the extent of improvement was similar among PET patterns (~6%). Postoperative functional improvement occurred in 53% of all (normal, match viable, and mismatch viable) regions without inotropic reserve. In severe CAD, revascularization affords greater intramyocardial functional benefit than expected from the evaluation of intramyocardial inotropic reserve with low-dose dobutamine. Postoperative functional improvement in PET-viable regions without inotropic reserve suggests that factors other than regionally enhanced perfusion contribute to such functional improvement.

magnetic resonance imaging; positron emission tomography; dobutamine; myocardial viability

THE IDENTIFICATION OF VIABLE myocardium in patients with coronary artery disease (CAD) is a critical factor in guiding decisions regarding revascularization. Positron emission tomography (PET) was the first method used to predict functional outcome after revascularization in CAD, and it is generally based on the assessment of glucose metabolism and perfusion (19). In recent years, several studies have focused on dobutamine stress testing for the detection of viability in CAD. Such studies are based on the principle that dobutamine can induce a sustainable functional improvement if myocardium is viable (i.e., able to increase regional perfusion with stimulation; Ref. 14). These studies were mainly performed by measuring systolic wall-thickening changes with dobutamine using echocardiography (27, 29) or magnetic resonance (MR) imaging (MRI; Refs. 10, 33). Nevertheless, the thickening of the full wall provides a general indication of regional contractility performance and does not inform about intramyocardial behavior at different transmural sites (28, 35). Because intramyocardial deformation can be quantified by measuring transmural strains with tagged MRI (7, 8, 37), the relationship between the tagged MRI values of intramyocardial strains after low-dose dobutamine and the corresponding PET patterns of perfusion and glucose uptake was recently evaluated in severe CAD patients (20). It was found that the presence of inotropic reserve, evaluated by midmyocardial change after dobutamine administration, did not correlate with resting myocardial perfusion as assessed with PET. Indeed, although some dobutamine echocardiography studies in conjunction with either PET (21, 25) or single photon emission computed tomography (SPECT; Ref. 23) suggested that a positive inotropic response is more likely to occur in regions with preserved rather than reduced perfusion, the above-mentioned tagged MRI study (20) indicated that the proportion of dobutamine-responsive regions does not differ between regions with normal or concomitant reductions in perfusion and glucose uptake. This suggests a discrepancy between inotropic reserve as measured by the systolic thickening of the full wall and that computed by intramyocardial strain during dobutamine infusion. Moreover, the presence of intramyocardial inotropic reserve does not correlate with resting myocardial perfusion as assessed with PET, which highlights the fact that more viability is present in severely injured regions than expected by PET and there exists a profound discordance between the dobutamine tagged MRI and PET criteria of myocardial viability.

The present study sought to delineate the relationship between preoperative values of intramyocardial inotropic reserve (for different PET patterns of perfusion and glucose uptake) and intramyocardial functional outcome after surgical revascu-
artery. Therefore, we evaluated intramyocardial inotropic reserve by tagged MRI with low-dose dobutamine and functional outcome after revascularization in relation to myocardial PET patterns in severe CAD.

METHODS

Study design. Patients were studied with institutional review board approval and with their written informed consent. We studied 12 patients with angiographically documented atherosclerosis (>70% diameter stenosis) in two or three coronary arteries and left ventricular dysfunction [left ventricular ejection fraction (LVEF) < 50%; Table 1]. Between 10 and 20 days before revascularization, all patients underwent tagged MRI (at baseline and after administration of 10 μg·kg⁻¹·min⁻¹ dobutamine) and PET (perfusion and glucose uptake evaluation) on consecutive days. All patients underwent tagged MRI at rest 20 ± 5 mo after revascularization (Table 1). The preoperative tagged MRI and PET parameters were correlated with the results of resting tagged MRI on followup study.

Magnetic resonance imaging. Patients were examined on a 1.5-T MR unit (Vision; Siemens Medical Systems; Erlangen, Germany) with gradient amplitude of 25 mT/m and a phased-array chest coil. After we located the long axis of the left ventricle using an ungated cine MRI acquisition using a 7-mm tag-line separation. Each breathhold segmented k-space gradient-echo sequence. Imaging parameters were as follows: field of view, 28 cm; slice thickness, 8 mm; slice spacing, 8 mm; repetition time, 80 ms; echo time, 4.8 ms; flip angle, 20°; segmentation, 5–7 lines; image matrix, 256 × 140 interpolated to 256 × 256 for display; and one signal was acquired using echo sharing.

Tagged MR acquisitions were obtained from three short-axis locations: basal, midventricular, and apical (Fig. 1A). These locations were selected on an end-diastolic, two-chamber, long-axis cine view. Tagged MR images at rest (Fig. 1B) were obtained using an ungated multplane localizer image set, we first obtained short-axis cine views to assess overall cardiac function parameters at rest. Cine MRI acquisitions were obtained using an end-inspiratory breathhold segmented k-space gradient-echo sequence. Imaging parameters were as follows: field of view, 28 cm; slice thickness, 8 mm; slice spacing, 8 mm; repetition time, 80 ms; echo time, 4.8 ms; flip angle, 20°; segmentation, 5–7 lines; image matrix, 256 × 140 interpolated to 256 × 256 for display; and one signal was acquired using echo sharing.

Tagged MR acquisitions were obtained from three short-axis locations: basal, midventricular, and apical (Fig. 1A). These locations were selected on an end-diastolic, two-chamber, long-axis cine view. Tagged MR images at rest (Fig. 1B) were obtained using a breathhold segmented k-space tagged turboshell sequence with a grid-tagging pattern. Imaging parameters were the same as for cine MRI acquisition using a 7-mm tag-line separation. Each breathhold acquisition took 16–25 heartbeats. Then after a 10–15-min dobutamine infusion (10 μg·kg⁻¹·min⁻¹), cine MRI and tagged MRI (Fig. 1C) were repeated using the same imaging protocol. Single-lead ECG, blood pressure, and pulse oxymetry values were monitored during the study. MRI studies lasted 45 min.

Postoperative tagged MRI was performed using the same protocol at rest only (Fig. 1D).

Table 1. Characteristics of study population

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Means ± SD are shown. %DR, diameter reduction; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery.

PET imaging. PET studies were performed using Siemens/ECAT EXACT HR+ 63 slice whole body tomography (6).

Perfusion assessment. H215O (185 MBq iv) was injected over 10 s. Acquisition lasted 5 min, and emission scans were reconstructed in a 128 × 128 matrix using a Hanning filter with a cutoff frequency of 0.15 mm⁻¹. The scan sequence consisted of 22 frames: 10 images × 4 s, 2 images × 10 s, 6 images × 20 s, and 4 images × 30 s.

Glucose uptake assessment. The [18F]fluorodeoxyglucose (18FDG) studies were performed using a hyperinsulinemic euglycemic clamp (9). One hour after the H215O studies, 18FDG (2 MBq/kg iv) was administered as a bolus. The 18FDG emission scans were reconstructed in a 128 × 128 matrix using a Hanning filter (cutoff frequency, 0.18 mm⁻¹). Transaxial resolution was 8 mm at the center of the field of view. The 18FDG reconstruction provided a dynamic series: 6 images × 10 s, 12 images × 30 s, 13 images × 60 s, and 20 images × 120 s. Static 18FDG images were reconstructed from 45- to 60-min slices (Fig. 2A).

Image analysis. Tagged images (see Fig. 1) were processed using FindTags software on a Silicon Graphics workstation.

We reported strain change between the reference state (end diastole) and the deformed state (end systole) as the percentage change in circumferential length for normal strain (Evc, circumferential shortening). A positive value indicates compression between two material points (shortening), whereas a negative value reflects strain elongation (stretching). A midmyocardial transmural location was chosen to evaluate systolic function at each of the three predefined short-axis locations (apical, midventricular, and basal: see Fig. 1A).

Factor analysis of medical image sequences (FAMIS; Ref. 11) was applied to the H215O PET dynamic series to obtain myocardial factor images representing relative perfusion (see Fig. 2B; Refs. 2, 16). FAMIS computation was performed on H215O short-axis slices resulting from the addition of three 2.5-mm slices. To apply FAMIS to the resulting slices, aggregates were generated as 2 × 2-pixel square clusters. Three-factor images were systematically extracted that corresponded to the right and left ventricle cavities and the left myocardium (Fig. 2B).

Image registration. Baseline and followup short-axis MR slices were matched by use of anatomic landmarks such as right ventricle insertion sites, papillary muscle location, and relative apex-to-base location as determined on a long-axis localization map (Fig. 1A).
Twelve regions per short-axis slice were drawn on the corresponding static 18FDG image (Fig. 2A) using an automated sectorization procedure. These regions were then superimposed on the corresponding myocardial factor image (Fig. 2B).

$E_{cc}$ at the midmyocardial transmural location was evaluated at baseline, after dobutamine administration, and at followup in the 12 corresponding PET regions at each of the three short-axis locations.

To compute the relative perfusion ($%H_{2}^{15}O$) and the relative glucose uptake ($%18FDG$), two or three regions per patient were selected as controls using the information from angiography, $E_{cc}$, and perfusion. Selection of control regions was restricted to basal and midventricular slices, and only territories with no angiographic stenosis in the supplying artery were considered. Among all regions studied in a given patient, those selected as controls had to belong to the group of the seven regions with the best $E_{cc}$ and perfusion values. Moreover, perfusion normality was checked in the preselected control regions by computing absolute myocardial blood flow using a one-compartment kinetic model (3).

Regions were classed according to previously described classic PET patterns (4, 19, 34) as follows: normal ($%18FDG \geq 90$ and $%18FDG + %H_{2}^{15}O \leq 1.2$), match viable (55 $%18FDG < 90$ and $%18FDG + %H_{2}^{15}O \leq 1.2$), infarcted ($%18FDG < 55$ and $%18FDG + %H_{2}^{15}O \leq 1.2$), and mismatch viable ($%18FDG + %H_{2}^{15}O > 1.2$).

The percentage of variability (4) between two tagged MRI repeated measures of $E_{cc}$ in myocardial regions from healthy volunteers ($n = 4$) ranged between 4 and 10%. A threshold of twice the $E_{cc}$ represented by the percentage of variability (i.e., 2% changes in $E_{cc}$) was used to define the presence of inotropic reserve with dobutamine administration ($E_{cc}$ dobutamine $- E_{cc}$ baseline $> 2%$) or the presence of a significant functional improvement after revascularization ($E_{cc}$ followup $- E_{cc}$ baseline $> 2%$).

**Fig. 1.** A: long-axis localizer view in a patient. Three tag lines at baseline were chosen at three ventricular levels (basal, midventricular, and apical) for matched correlation with positron emission tomography (PET) slices. Basal tag line (dotted line) was taken into account in this image. B–D: localizer views also helped to match tagged magnetic resonance imaging (MRI) short-axis images before revascularization (dotted line; B) and with 10 $\mu$g·kg$^{-1}$·min$^{-1}$ dobutamine infusion (C) and tagged MRI images at rest after revascularization (D). Tagged MRI and PET images were divided into 12 regions of interest. E: plot constructed from B–D represents circumferential shortening ($E_{cc}$) in the 12 regions of interest. Despite almost normal regional perfusion, the contractile performance at baseline was found to be depressed. This finding can probably be explained by the presence of mismatch-viable regions (i.e., hibernating myocardium) and the effect of the presence of a lateral ischemic boundary (tethering effect).

$H_{2}^{15}O$ and static 18FDG PET volumes were realigned to generate short-axis slices suitable for matched correlation with the three baseline short-axis MR images.

Registration was performed on PET slices resulting from the addition of three 2.5-mm slices. Circumferential registration (in-plane registration) between MR strain slices (8 mm) and PET slices (7.5 mm) was carefully conducted while taking into account relative apex-to-base locations (from the long-axis localizer views) and matching landmark locations.

**Data analysis and interpretation.** The preoperative analysis was performed on four sets of images: tagged MR images at baseline and after dobutamine administration (for functional analysis), myocardial factor images, and static 18FDG images (for perfusion and glucose uptake).

On followup, tagged MRI images at rest were acquired. Therefore, we obtained for each patient a regional plot of function (at baseline, after dobutamine administration, and on followup; see Fig. 1E) as well as of perfusion and glucose uptake (see Fig. 2C) at the three short-axis locations (see Fig. 1A).
Statistical analysis. Linear regressions were fitted by the least-squares method. Paired t-test was used to compare LVEF values. Normal distribution of data and standard deviations were tested using the Kolmogorov-Smirnov test and the equal variance test, respectively. ANOVA and a subsequent Tukey’s test for multiple comparisons were performed to compare mean values. If the normality test failed on comparison of mean values, a Kruskal-Wallis ANOVA on ranks was performed. In this case, the median of the groups is shown instead of the mean.

Proportions were analyzed using a χ² goodness-of-fit test.

Data are displayed as means ± SD. *P < 0.05 was interpreted as statistically significant.

RESULTS

Population. Twelve patients were studied before and after surgical revascularization (see Table 1). Seven patients had two-vessel CAD and five had three-vessel CAD. Seven patients had diabetes, four had hypertension, and four had hypercholesterolemia. During revascularization, the 12 patients received 26 grafts (20 arterial and 6 vein grafts); 7 of 11 patients received only arterial grafts (patients 1, 4, and 7–11). No clinical evidence of myocardial ischemia was observed between preoperative and followup imaging studies.

Preoperative LVEF was 28 ± 11% at baseline (vs. 39 ± 13% after a 10 μg·kg⁻¹·min⁻¹ infusion of dobutamine; *P < 0.01). At baseline, the rate-pressure product at the initiation of the tagged MRI study (9,944 ± 1,481 mmHg/min) differed significantly from that recorded 10 min after the beginning of dobutamine infusion (11,681 ± 1,643 mmHg/min; *P < 0.01).

At followup, LVEF was 38 ± 12% (*P < 0.01 vs. baseline) and had increased in all patients by a mean of 10 ± 4% (Table 1). A significant linear correlation (*r = 0.82; *P < 0.01; Fig. 3) was found between the changes in LVEF at rest, after infusion of dobutamine before revascularization (LVEF_dobutamine − LVEF_baseline), and the changes in LVEF at rest, between baseline (before revascularization) and followup (LVEF_followup − LVEF_baseline).

Ecc at baseline and PET patterns. Of 432 regions (36 per patient), 429 had data suitable for comparative tagged MRI and PET analysis at the three predefined set points (baseline, dobutamine, and followup).

Based on H²¹⁵O and ¹⁸FDG PET images, 143 regions were defined as normal, 112 as match viable, 78 as mismatch viable, and 96 as infarcted. In the 28 normal regions selected as controls, absolute perfusion at baseline averaged 0.95 ± 0.22 ml·g⁻¹·min⁻¹. In these control regions, Ecc at baseline was 16 ± 4% and did not change significantly with dobutamine administration (17 ± 5%) or at followup (16 ± 4%; *P = not significant).

Among normal, match-viable, and infarcted regions, a positive linear correlation was found between regional values of Ecc at baseline and both perfusion (*r = 0.43; *P < 0.01) and glucose uptake (*r = 0.53; *P < 0.01).

At baseline, Ecc ranged from 12 ± 6 to 8 ± 5% in normal and match-viable regions, respectively (*P < 0.05) and was 4 ± 4% in infarcted regions (*P < 0.05 vs. normal and match viable). Ecc for mismatch-viable regions (8 ± 5%) differed significantly from both normal and infarcted regions (*P < 0.05).

Inotropic reserve and functional improvement on followup. As previously described (20), the proportion of regions with inotropic reserve (Ecc increase with dobutamine administration of ≥2% from baseline) differed significantly as a function of PET patterns (χ² = 11.2; degrees of freedom = 3; *P = 0.01); the highest proportion was observed in mismatch-viable regions (60%), whereas the proportion did not differ significantly between normal (41%), match-viable (44%), and infarcted (42%) regions (Fig. 4).

The proportion of regions showing functional improvement at followup (Ecc increased by >2% from preoperative baseline values) also varied according to PET patterns (χ² = 11.5; degrees of freedom = 3; *P < 0.01); a lower proportion (41%) was found in infarcted regions, whereas the proportions were similar for normal (58%), match-viable (60%), and mismatch-viable (63%) regions.

The number of regions with preoperative inotropic reserve was smaller than the number that showed postoperative functional improvement: 187 of the 429 regions studied showed inotropic reserve, but 238 showed functional improvement. This trend was observed in 8 patients, whereas in 2 patients the number of dobutamine-responsive regions was higher than the number of regions that improved on followup, and in the remaining 2 patients, an equal number of both kinds of regions was found.

Of 187 regions with inotropic reserve (Fig. 4A), 124 showed postoperative functional improvement. A significant correlation was found between Ecc with dobutamine administration and Ecc at followup among regions with inotropic reserve (Fig. 5A). In these 187 regions, the mean extent of the functional change at followup (Ecc followup − Ecc baseline) did not differ between regions graded viable by PET (normal, match viable, and mismatch viable) but was slightly lower in infarcted regions (*P < 0.05 vs. mismatch viable; see Fig. 4). The extent of Ecc change at followup in regions that showed both inotropic reserve and postoperative improvement (n = 124), however, was not less marked in infarcted regions: 6 ± 3 (n = 24) vs. 6 ± 3% for normal (n = 34) and match-viable (n = 31) and 7 ± 3% (n = 35) for mismatch-viable regions (*P = not significant).

Of the 242 regions without inotropic reserve (see Figs. 4B and 5B), 114 (47%) showed postoperative functional improve-
ment. Of these 114 regions, 99 (87%) were graded viable by PET (Table 2). Accordingly, in PET-viable regions without inotropic reserve, the mean postoperative Ecc change was positive (see Fig. 4B). In contrast, the proportion of infarcted regions without inotropic reserve but showing functional improvement at followup was lower (27%; Table 2), and the mean Ecc change at followup for all of the 56 infarcted regions without inotropic reserve was negative (\(P < 0.05\) vs. mismatch viable; see Fig. 4B). The extent of change at followup for regions without inotropic reserve but with postoperative functional improvement (\(n = 114\)) was 5 ± 3, 5 ± 2, 4 ± 2, and 7 ± 3% for normal, match-viable, infarcted, and mismatch-viable regions, respectively (\(P < 0.05\) infarcted vs. mismatch viable).

The disagreement between preoperative inotropic reserve and postoperative functional outcome was very marked among regions classed as viable on PET. Normal, match-viable, and mismatch-viable regions accounted for the 87% of the regions.

**DISCUSSION**

The major findings of this preliminary study are that revascularization affords an intramyocardial functional benefit that is greater than would be expected from the evaluation of intramyocardial inotropic reserve in severe chronic CAD. Postoperative functional improvement in PET-viable regions without inotropic reserve suggests that factors other than regionally enhanced perfusion contribute to this functional improvement.

The patients enrolled in this study presented with multivessel CAD, severe left ventricular dysfunction, and risk factors. In all patients, the LVEF improved significantly after revascularization, and as described elsewhere (26), a significant correlation was found between LVEF change with dobutamine administration before revascularization and changes in LVEF associated with revascularization. Moreover, PET yielded predictive values for functional outcome at followup in the range previously published (24, 27), and mismatch-viable regions, which are a reliable sign of viability on PET, behaved as expected regarding functional impairment at rest, the number of regions with inotropic reserve, and postoperative functional improvement (21, 24, 29). In such a population of patients, we found a poor concordance between regions with preoperative inotropic reserve and those showing postoperative intramyocardial functional improvement.

The disagreement between preoperative inotropic reserve and postoperative functional outcome was very marked among regions classed as viable on PET. Normal, match-viable, and mismatch-viable regions accounted for the 87% of the regions.

**Fig. 4.** Ecc changes with dobutamine (gray bars; Ecc with dobutamine – Ecc baseline) and at followup (black bars; Ecc followup – Ecc baseline) in regions with \(A\) or without \(B\) inotropic reserve for different PET patterns. Average (±SE) intramyocardial functional improvement after revascularization in regions without preoperative inotropic reserve \(B\) was positive in regions classed as viable on PET, *\(P < 0.05\) vs. infarcted regions.

**Fig. 5.** Despite the considerable scatter, a significant correlation \((P < 0.01)\) was found between Ecc (in %) with dobutamine and after revascularization. A: Ecc with dobutamine treatment. B: Ecc without dobutamine treatment. In line with the functional improvement on followup registered in a number of regions without inotropic reserve \((c)\), such a correlation was weaker in such a region than in regions with inotropic reserve \((\bullet)\).
uptake that showed different with normal or moderately reduced perfusion and glucose that did not respond to dobutamine (13). We found that regions increased significantly at followup in dysfunctional regions effect an inability to increase blood regions probably re. of inotropic reserve. Because dobutamine-unresponsive re- at-rest functioning after revascularization despite the absence of inotropic reserve that showed postoperative functional improvement (23). In this regard, it was previously reported that \( E_{cc} \) on tagged MRI increased significantly at followup in dysfunctional regions that did not respond to dobutamine (13). We found that regions with normal or moderately reduced perfusion and glucose uptake that showed different \( E_{cc} \) levels were able to improve at-rest functioning after revascularization despite the absence of inotropic reserve. Because dobutamine-unresponsive regions probably reflect an inability to increase blood flow with stimulation (12), the postoperative functional improvement in these regions suggests that factors other than regionally enhanced perfusion after revascularization could play a role in such functional improvement. For instance, improvement may well be related to postvascular changes in mechanical factors that affect systolic function such as total or partial normalization of wall stress, improvement in left ventricular diastolic compliance (22), or a diminished tethering effect (15). In fact, our study shows that revascularization affords a functional benefit greater than would be expected from dobutamine tagged MRI testing, which suggests that factors other than the postoperative regional improvement in perfusion contribute to this functional benefit.

The proportion of infarcted regions with postoperative functional improvement was less than for the other PET patterns but was in general higher than the previously reported ventriculographic or echocardiographic values (23, 27, 34). Moreover, in infarcted regions that showed intramyocardial functional improvement on followup, the degree of functional improvement was not less marked than for the other PET patterns. The ability to retain cellular integrity even in severely hypoperfused regions was anticipated in a tagged MRI study in first anterior infarction patients: Bogaert et al. (4) studied \( E_{cc} \) after reperfusion in two transmural levels defined as subendocardial and subepicardial. One week after reperfusion, they observed a large recovery in subepicardial layers of severely injured match regions (blood flow < 50% on PET; Ref. 4). Kramer et al. (18) evaluated microvascular integrity (by contrast-enhanced MRI) and inotropic reserve (by tagged MRI) in patients with recent myocardial infarction after reperfusion. They observed that both regions with normal gadoteridol first-pass enhancement (associated with viable myocardium) and those with hypoencancement (myocardial damage) showed improved \( E_{cc} \) on followup (60 and 47% of regions, respectively; \( P = \text{not significant} \)) regardless of significant functional differences at baseline. Moreover, the extent of functional improvement was similar for both groups of regions (18). These data are consistent with our findings of postoperative functional improvement in infarcted PET regions. Neverthless, in our study, the proportion of infarcted regions with postoperative functional improvement was significantly lower than in PET-viable regions. This discrepancy with the findings of Kramer et al. (18) could be related to the fact that regions showing hypoencancement during contrast-enhanced MRI represent a mixture of viable and nonviable tissues, whereas infarcted PET regions more strictly characterize severe myocardial injury. In fact, our study, like other tagged MRI work (4, 18), suggests the presence of viable tissue even in regions with a high degree of transmural infarction, which is not detectable by PET, in which substantial postoperative functional improvement could occur.

The present study, like the previous above-referenced study from our laboratory (20), presents two significant differences with respect to the majority of reports on myocardial viability, as follows: 1) inotropic reserve and functional improvement after revascularization were computed by means of intramyocardial change instead of systolic wall-thickening change; and 2) the analysis focused on relatively small regions covering the entire functional spectrum (see below). Despite these differences, in our studies, PET and dobutamine tagged MRI matched the well-known trend in myocardial viability studies: in general, radionuclide imaging has a higher sensitivity, whereas inotropic reserve imaging has a higher specificity (32).
In turn, both imaging techniques showed a similar, modest predictive value that is in line with some previous PET (24, 27, 34), dobutamine echocardiography (24, 27), and dobutamine MRI (13, 31) reports on myocardial viability of dysfunctional myocardium (agreement range, 53–75%). It is noteworthy that in patients with single-vessel CAD and recently reperfused myocardial infarction, Geskin et al. (13) evaluated the ability of low-dose dobutamine tagged MRI to predict functional recovery (8 wk after infarction) and reported 63% agreement in dysfunctional regions, which is near our 59% over all regions. Thus the clinical use of dobutamine tagged MRI for predicting postoperative functional outcome seems unclear so far. The reasons for such imperfect prediction warrant closer scrutiny especially by coupling tagged MRI with high-resolution imaging techniques to enable assessment of infarction transmurality. In this regard, the results of a recent MRI study (36) suggest that the accuracy of the dobutamine test does not depend on the transmurality of the scar (assessed with delayed enhancement). Although the transmurality of the scar was not detectable by PET, such a finding seems to be in disagreement with our results, indicating a disparate test accuracy for different PET patterns. Despite protocol differences (thickening of the full wall measurements, quantitative analysis, and large segmentation in Wellnhofer’s study), such a difference from our findings could also be ascribed to the investigation of different pathophysiological processes by contrast-enhanced MRI and PET (30). Nevertheless, dobutamine-tagged MRI in conjunction with PET appears in our studies (20) to be of physiological and clinical interest other than prediction of viability. For instance, our results indicate a relatively high proportion of infarcted regions with both inotropic reserve and postoperative functional improvement. This finding suggests that more viability than usually expected could be present in severely injured regions. In these regions, an increasing amount of evidence is pointing to the beneficial effects of late myocardial reperfusion (1). Although such benefits have never been associated with functional improvement, it is conceivable that the evaluation of intramyocardial change with a highly sensitive technique (i.e., tagged MRI) could highlight some functional improvement after reperfusion in regions classed nonviable by PET.

Technical considerations and limitations. A few authors (13, 17) have examined the use of dobutamine tagged MRI in nonsevere CAD. In contrast to our study, their analysis was centered on at-rest dysfunctional regions; moreover, they defined myocardial viability as a postoperative return to normal function (13). In our study, the analysis was related to preoperative regional PET patterns independent of regional functional status, and we assessed functional improvement after revascularization as opposed to reestablishment of normal function. Thus our analysis design was intended to address the entire PET spectrum and to overcome the difficulty of a consistent definition of “normal function” in CAD. In addition, from the clinical point of view, the evaluation of postoperative functional improvement is a more useful endpoint, as some (e.g., infarcted) myocardial regions are very unlikely to actually recover normal function after revascularization.

Because of the relatively small number of patients, the present study must be considered preliminary. Our results confirm a postoperative functional benefit greater than would be expected from the evaluation of inotropic reserve, but additional studies are necessary to reliably determine the exact predictive value of dobutamine tagged MRI for functional outcome after revascularization.

In the present study, the time between revascularization and postoperative assessment of function was 20 ± 5 mo. Consequently, although there was no clinical evidence of myocardial ischemia during that period in our patient population, graft occlusion and progression of native and graft disease could theoretically occur. Because postoperative angiography in patients without angina symptoms is ethically unacceptable, graft patency and disease progression in the native coronary arteries was not evaluated. However, all patients underwent surgical revascularization without percutaneous angioplasty, and most of them had coronary grafts with the internal mammary artery (graft closure incidence at 10 yr, 10%).

The \( E_{cc} \) was chosen to evaluate systolic function because 1) it is the most widely used tagged MRI parameter and has less variability than other parameters, and 2) it makes the largest contribution to the LVEF (5).

\( E_{cc} \) was computed from tagged images at the midmyocardial layer location, which helped enable robust measurement by avoiding the segmentation errors than can occur near the endocardial and epicardial interfaces. In addition, this location was chosen so as to ensure correct matching between MRI and PET data.

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GRANTS

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REFERENCES


