^{123}I-IPPA SPECT for the Prediction of Enhanced Left Ventricular Function After Coronary Bypass Graft Surgery

Mario S. Verani, Raymond Taillefer, Ami E. Iskandrian, John J. Mahmarian, Zuo-Xiang He, and Cesare Orlandi for the Multicenter IPPA Viability Trial Investigators

Section of Cardiology, Baylor College of Medicine and Methodist Hospital, Houston, Texas; Hospital Hotel-Dieu De Montreal, Montreal, Quebec, Canada; Section of Cardiology, University of Alabama at Birmingham, Birmingham, Alabama; Medco Research, Inc., Research Triangle Park, North Carolina

Fatty acids are the prime metabolic substrate for myocardial energy production. Hence, fatty acid imaging may be useful in the assessment of myocardial hibernation. The goal of this prospective, multicenter trial was to assess the use of a fatty acid, ^{123}I-iodophenylpentadecanoic acid (IPPA), to identify viable, hibernating myocardium. **Methods:** Patients (n = 119) with abnormal left ventricular wall motion and a left ventricular ejection fraction (LVEF) < 40% who were already scheduled to undergo coronary artery bypass grafting (CABG) underwent IPPA tomography (rest and 30-min redistribution) and blood-pool radionuclide angiography within 3 d of the scheduled operation. Radionuclide angiography was repeated 6–8 wk after CABG. The study endpoint was a ≥10% increase in LVEF after CABG. The number of IPPA-viable abnormally contracting segments necessary to predict a positive LVEF outcome was determined by receiver operating characteristic (ROC) curves and was included in a logistic regression analysis, together with selected clinical variables. **Results:** Before CABG, abnormal IPPA tomography findings were seen in 113 of 119 patients (95%), of whom 71 (60%) had redistribution in the 30-min images. The LVEF increased modestly after CABG (from 32% ± 12% to 36% ± 8%, $P < 0.001$). A ≥10% increase in LVEF after CABG occurred in 27 of 119 patients (23%). By ROC curves, the best predictor of a ≥10% increase in LVEF was the presence of ≥7 IPPA-viable segments (accuracy, 72%; confidence interval, 64%–80%). Among clinical and scintigraphic variables, the single most important predictor also was the number of IPPA-viable segments ($P = 0.008$). The number of IPPA-viable segments added significant incremental value to the best clinical predictor model. **Conclusion:** A substantial increase in LVEF occurs after CABG in only a minority of patients (23%) with depressed preoperative function. The number of IPPA-viable segments is useful in predicting a clinically meaningful increase in LVEF.

Key Words: fatty acids; myocardial hibernation; myocardial viability; myocardial metabolism

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Severe left ventricular dysfunction secondary to coronary artery disease (CAD) is the principal cause of congestive heart failure in the United States, accounting for more than 70% of cases in some series, and carries a dismal prognosis, with a 3-y mortality of nearly 40% with medical therapy alone (*1*). Despite the many recent advances in the treatment of heart failure, including angiotensin-converting enzyme inhibitors (*1–3*), angiotensin-II receptor blockers (*4*), potent inotropic agents (*5*), antiarrhythmic agents (*6*), and β-blockers (*7*), the prognosis remains poor and most patients continue to deteriorate and will either require cardiac transplantation or die within a few years. A generally accepted view is that patients with a depressed left ventricular ejection fraction (LVEF) and multivessel CAD may have improved survival and better clinical outcomes (*8*) with coronary artery bypass grafting (CABG), in comparison with medical management. This potential benefit, however, must be weighed against an increased surgical morbidity and mortality (*9*). Moreover, the prognosis of these patients remains guarded even after CABG, with a 3-y mortality of 23% (*8*). Heart failure remains, in fact, the single most frequent cause of death after CABG (*10*).

Identification of patients in whom ventricular function is most likely to improve after CABG is pivotal to the proper selection of candidates for surgery. PET with FDG, to the extent that it identifies metabolically active myocytes, is one of the best techniques to characterize viable myocardium that will exhibit enhanced contraction after CABG (*11,12*). Because single-chain fatty acids are the predominant metabolic substrate in the myocardium, imaging the myocardial distribution of fatty acid analogs, such as ^{123}I-iodophenylpentadecanoic acid (IPPA), may provide insights into the characterization of viable, hibernating myocardium (*13–21*) and hence assist in identifying the best candidates for CABG. In this multicenter, prospective trial we investigated the potential usefulness of IPPA in predicting enhancement of left ventricular function after CABG.

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For correspondence or reprints contact: Mario S. Verani, MD, Baylor College of Medicine and Methodist Hospital, 6550 Fannin, SM 677, Houston, TX 77030.

MATERIALS AND METHODS

We prospectively recruited patients with abnormal left ventricular wall motion and a preoperative LVEF < 40%, as measured by contrast angiography, radionuclide angiography (RNA), or 2-dimensional echocardiography at their local institutions, and who had already been accepted and scheduled for CABG. Patients were recruited from institutions with a long-standing track record of successful CABG programs, including experience in operating on patients with depressed LVEF. Patients with a recent myocardial infarction (within 6 wk preceding the operation), concomitant valve surgery, or aneurysmectomy and a history of allergy to iodine were excluded. Before CABG, 60% of patients were receiving nitrates, 61% were receiving angiotensin-converting enzyme inhibitors, 58% were receiving diuretics, 46% were receiving digitalis, 42% were receiving β-blockers, and 41% were receiving calcium channel blockers.

Study Protocol

Within 3 d of the scheduled operation, patients underwent IPPA SPECT and blood-pool RNA. The latter was repeated 6–8 wk after the operation for all patients.

Scintigraphic Procedures

^{123}I-IPPA was produced by Nordion International, Inc. (Vancouver, British Columbia, Canada), and shipped to the recruiting institutions. The labeling of IPPA consisted of a precursory step during which trifluoroacetic acid was added to thallic trifluoroacetate, and the resulting solution was added to phenylpentadecanoic acid. This mixture was sealed and left from 1 to 4 h at room temperature. ^{123}I was then added to this mixture, and the vial was heated at 90°C for 25 min. The final product was stable and, because of the relatively long half-life of ^{123}I (13.2 h), could be shipped to sites distant from the production center. Radiopharmaceutical purity was assessed using high-performance liquid chromatography. Only products with labeling efficiency > 90% were accepted for injection.

The patients received an intravenous injection of 157 ± 17 MBq IPPA at rest in the fasting state. Two sets of SPECT images were obtained, the first commencing at 4.0 ± 3.0 min and the second at 30.0 ± 2.5 min after tracer administration. Single- or multiple-head gamma cameras were used to acquire 32 frames per study, on a matrix of 64 × 64 bytes, over a 180° anterior arc, using a low-energy, general-purpose collimator. Each frame was acquired for 20 s during the first acquisition and for 30 s during the second acquisition. Images were stored on magnetic disks or magnetic tapes and were sent in duplicate to 2 core laboratories (Baylor College of Medicine, Houston, TX, and Hospital-Hotel Dieu De Montreal, Montreal, Quebec, Canada) for processing.

A standard filtered backprojection technique with a Butterworth filter (cutoff frequency, 0.45 Nyquist; order, 10) was used to reconstruct transaxial slices, which were then reoriented in the short, horizontal, and vertical long axes. Slices of 1-pixel thickness, spanning the left ventricle from the apex to the base, were recorded on high-resolution photographic paper, both in color and in black and white. Polar maps of the tracer myocardial distribution were constructed using commercially available software (in-house software; Baylor College of Medicine, Houston, TX). To quantitate the extent of abnormality on the IPPA images, as well as the severity of reduction in tracer activity and the reversibility of the abnormalities from the first to the second set of images, the raw polar maps were statistically compared with a composite normal data bank obtained from 30 healthy volunteers (18 men, 12 women; age range, 25–72 y; mean age, 47.7 y), using previously reported software (*22*).

Blood-pool RNA used an in vivo labeling technique with 740–1110 MBq ^{99m}Tc pertechnetate (*23*). Images were acquired for 16–32 frames per cardiac cycle, for a total acquisition time of 5–8 min per view. Standard anterior, 40° left anterior oblique, and 70° left anterior oblique views were acquired with the patients supine. All images were stored on magnetic disks and sent to the core laboratories at Baylor College of Medicine for uniform processing and semiautomatic LVEF computation (*23,24*).

Image Interpretation

All images were analyzed during prescheduled interpretation sessions in which 3 experienced nuclear cardiologists individually and blindly interpreted the images and filled out a standardized interpretation form. Each interpreter coded the images for technical quality (excellent, good, fair, or poor) and tracer uptake, which was scaled from 4 (normal) to 0 (no uptake) and categorized as 1 (severe reduction of uptake), 2 (moderate reduction), or 3 (mild reduction). Ten segments reflecting the vascular territories of the left anterior descending, right coronary, and left circumflex coronary arteries were analyzed (Fig. 1). Agreement among readers was determined for all available images.

For RNA interpretations, images in the 3 standard views were transferred to high-resolution videotapes and simultaneously displayed on large (88.9-cm [35-in.]) and small (35.6-cm [14-in.]) monitors. Images were displayed randomly, without identification of patient names or timing of the study in relation to the operation. The 3 readers individually and blindly interpreted the technical quality of the images and recorded a wall motion score, which ranged from 4 (normal) to 0 (akinesis), with additional scores of 1 (severe hypokinesis), 2 (moderate hypokinesis), 3 (mild hypokinesis), and −1 (dyskinesis). Ten segments reflecting the vascular territories of the left anterior descending, right coronary, and left circumflex arteries were analyzed (Fig. 1). A summed wall motion score was obtained for each patient by adding the individual segmental scores.

Definition of Myocardial Viability

For data analysis, myocardial viability was defined as the presence of normal IPPA activity (score of 4) or an improved

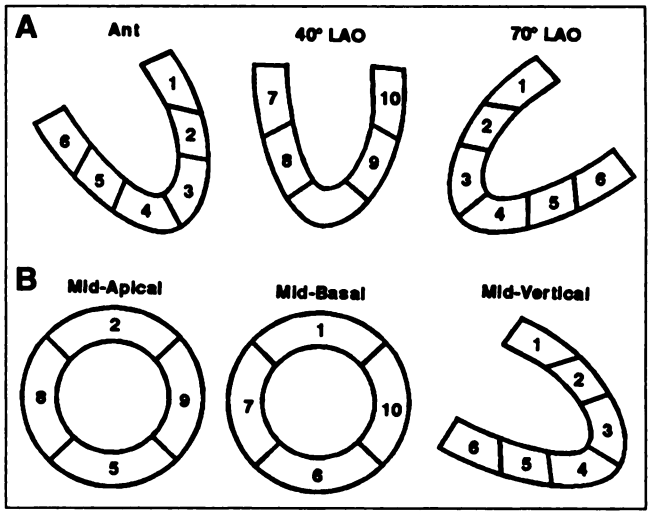

FIGURE 1. Diagram shows left ventricular segments analyzed during RNA (A) and perfusion tomography (B). Ant = anterior; LAO = left anterior oblique.

score from the first to the second set of images, in the segments with dys-synergy. The averaged scores from the 3 readers were used throughout the study.

Study Outcome

The pre-established primary outcome of the study was an increase of LVEF ≥10% after CABG. This level of increase in LVEF was considered clinically meaningful. Other endpoints, such as survival, wall motion, and quality-of-life improvement, will be reported separately.

Statistical Analysis

On the basis of previous publications (*25,26*), we anticipated that the number of viable myocardial segments would be related to an increase in LVEF after CABG. Accordingly, we explored the minimal number of IPPA-viable abnormally contracting left ventricular segments to predict a positive LVEF outcome (≥10% increase). The number of left ventricular segments varied from 5 to 9, and the resulting levels of agreement were graphically depicted using receiver operating characteristic (ROC) curves.

Logistic regression analysis was used to characterize the relationship between IPPA viability and a positive LVEF outcome. All historical, clinical, angiographic, and scintigraphic variables that were available for all patients were initially explored for inclusion in a statistical model. Variables that were related to a positive LVEF outcome with a minimal α of 0.3 were selected. The following 10 variables were eligible for inclusion in this analysis: age, sex, angina, history of myocardial infarction, diabetes mellitus, history of hypertension, preoperative LVEF, presence of a left anterior descending artery stenosis, presence of 3-vessel CAD, and number of IPPA-viable segments. The predicted probabilities of a positive outcome generated by the logistic models were calculated for different levels of expected probability. The resulting range of sensitivity and specificity values was plotted as an ROC curve and superimposed on the curve fit for the agreement between the number of IPPA-viable dyssynergic segments and the LVEF outcome. The extent to which the ROC curve for the predicted model was higher than the observed curve fit indicated the greater predictive value of the model. The incremental value of the IPPA viability criterion, beyond that of the other 9 variables tested, was assessed using incremental χ^2 statistics. Changes in the extent of abnormality of myocardial IPPA uptake and in LVEF associated with CABG were assessed using 2-tailed paired *t* tests. The data are presented as mean ± SD. Whenever pertinent, confidence limits are also reported. $P < 0.05$ was considered statistically significant.

RESULTS

Patient Cohort Characteristics

A total of 188 patients were enrolled, of whom 185 underwent CABG and 138 completed the protocol. The reasons for inability to complete the protocol were perioperative death in 9 patients, administrative or personal reasons in 10, loss to follow-up in 6, protocol violation in 2, and miscellaneous reasons in 20. The patient characteristics are summarized in Table 1. Most patients were men with a high frequency of prior myocardial infarction and of coronary risk factors.

TABLE 1
Patient Characteristics

Characteristic	Finding
No. of patients	119
No. of men	105 (88%)
Mean age ± SD (y)	62.7 ± 9.8
Age range (y)	38–84
Hypertension	73 (61%)
Smoking history	73 (61%)
Family history	73 (61%)
Hyperlipidemia	58 (49%)
Diabetes mellitus	51 (43%)
Typical angina	69 (58%)
Atypical angina	15 (13%)
Nonanginal pain	7 (6%)
No symptoms	27 (23%)
Prior myocardial infarction	86 (72%)
Q-wave infarct	62 (52%)
Prior coronary angioplasty	15 (13%)
Prior CABG	10 (8%)

Coronary Anatomy, Baseline Ejection Fraction, and Bypass Grafting

Preoperative coronary angiography showed 40% of the patients to have 3-vessel CAD, 48% to have 2-vessel CAD, and 12% to have 1-vessel CAD. Overall, 82% of the patients had significant stenosis (≥75% of the luminal diameter) of the left anterior descending artery; 78%, of the right coronary artery; and 65%, of the left circumflex artery. Bypass grafting was performed for most coronary stenoses (98% of stenoses of the left anterior descending artery, 91% of those of the left circumflex artery, and 83% of those of the right coronary artery). Baseline (prebypass) LVEF was ≤30% in 54% of patients, 31%–40% in 24%, 41%–50% in 15%, and ≥50% in 7%.

^{123}I-IPPA Imaging

Among the 138 subjects who successfully completed the protocol, 119 (86%) had preoperative images that were technically interpretable and were thus included in the final analysis. The IPPA images were considered to be of good or excellent quality in 68% of patients, of fair quality in 30%, and of poor quality in 2%. Before CABG, abnormal IPPA findings were seen in 113 of the final 119 patients (95%), of whom 71 (60%) had evidence of redistribution in the 30-min images. The IPPA score in the preoperative study improved from 2.54 ± 0.79 in the initial images to 2.77 ± 0.70 in the 30-min images ($P = 0.0001$). The IPPA defect size in the resting images averaged 33.9% ± 17.9%, of which 11.3% ± 8.6% was reversible in the 30-min images.

LVEF Before and After Revascularization

The RNA images were considered to be of good or excellent quality in 88% of the patients and of fair quality in 12% of the patients, both before and after CABG. The LVEF increased significantly ($P < 0.001$), albeit modestly, after CABG (Fig. 2). Patients with a baseline LVEF < 40% had a significant increase in this parameter after CABG (from

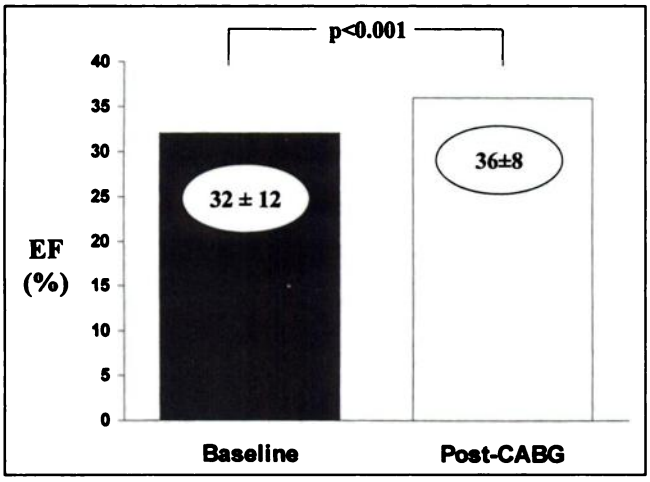

FIGURE 2. Bar graph shows change in LVEF after coronary bypass grafting. EF = ejection fraction.

28% ± 7% to 32% ± 10%, $P < 0.001$), whereas patients with a baseline LVEF ≥ 40% did not have a statistically significant change in LVEF (from 51% ± 12% to 52% ± 10%). The changes in LVEF are summarized in Table 2. An increase in LVEF by ≥10% after CABG (the primary study outcome) occurred in 27 of the 119 patients (22.7%). The changes in LVEF relative to the number of IPPA-viable segments are summarized in Table 3.

By ROC analysis, the best predictor of a ≥10% increase in LVEF was the presence of ≥7 IPPA-viable segments (Table 3). Using this number of segments as the threshold of viability, 32 patients were considered viable. The interobserver agreement with respect to categorizing patients as viable or nonviable on the basis of ≥7 IPPA-viable segments ranged from 75% to 83%.

The mean LVEF at baseline was significantly lower in the IPPA-viable patients than in the IPPA-nonviable patients (27% versus 34%, $P = 0.013$). Patients who had ≥7 IPPA-viable abnormally contracting left ventricular segments had a more substantial increase in LVEF than those with <7 IPPA-viable segments (Fig. 3). Likewise, for a higher threshold, that is, ≥8 IPPA-viable segments, the increase in LVEF was more substantial in patients with ≥8 viable segments than in those with <8 viable segments. Using this number of segments as the threshold of viability, only 18 patients were considered viable. The overall accuracy of ≥7 IPPA-viable segments for detecting a ≥10% LVEF increase was 73% (confidence interval, 64%–80%). The accuracy for ≥8 IPPA-viable segments was 77% (confidence interval, 69%–85%), but this criterion decreased the sensitivity for correct prediction of the change in LVEF from 50% to 36% and increased the specificity from 80% to 93%.

TABLE 2
Changes in LVEF After Coronary Revascularization

Change	No. of patients	%
>5% decrease	7	5.9
No change (−5% to 4%)	66	55.5
5%–9% increase	19	16.0
≥10% increase	27	22.7

Wall Motion Before and After Revascularization

The summed baseline (pre-CABG) wall motion score was lower in the 32 patients with ≥7 IPPA-viable segments than in the remaining patients, who had <7 IPPA-viable segments (15.4 ± 6.5 versus 22 ± 10.1, $P = 0.008$). The change in summed wall motion score after CABG was higher in the patients with ≥7 IPPA-viable segments than in the remaining patients (4.8 ± 8.3 versus 1.3 ± 6.1, $P = 0.052$).

Figure 4 illustrates a patient with improved LVEF after CABG, with the corresponding IPPA images. Figure 5 illustrates a patient with no improvement in LVEF after CABG.

Logistic Regression Analysis for Prediction of a ≥10% Ejection Fraction Increment

The best predictive model by stepwise logistic regression analysis included the number of IPPA-viable segments per patient, a history of diabetes mellitus or of myocardial infarction, and the presence of stenosis of the left anterior descending artery. The accuracy of this model for prediction of a ≥10% LVEF increase was 73% (Table 4). The single most important predictor of a ≥10% LVEF increase was the number of IPPA-viable segments ($P = 0.008$).

Incremental Value of IPPA

The incremental value of the number of IPPA-viable segments for predicting a ≥10% postoperative increase in LVEF is shown in Table 5. The incorporation of a history of diabetes mellitus into the baseline model (which contained age, sex, the baseline LVEF, and a history of angina or hypertension) was of borderline incremental value. The incorporation of a history of myocardial infarction and the number of IPPA-viable segments into the baseline model had a significant incremental value.

DISCUSSION

The principal finding of our study is that a relatively large extent of IPPA-viable myocardium (7/10 segments) must be present in the abnormally contracting ventricular segments before one can see a substantial increase in LVEF after CABG. Interestingly, Pagley et al. (*26*) recently reported that patients for whom ^{201}Tl scintigraphy shows a greater extent of myocardial viability (at least two thirds of the left ventricle) have improved outcome after CABG, in comparison with patients with lesser amounts of viable myocardium. ROC curves showed that ≥7 IPPA-viable segments afforded the best overall accuracy for prediction of LVEF improvement. However, a continuum existed between the number of IPPA-viable segments and the change in LVEF. Requiring fewer abnormally contracting segments to be IPPA-viable would increase the sensitivity for detecting an increase in LVEF but would also decrease the specificity, with an

TABLE 3
Change in LVEF Relative to Number of IPPA-Viable Segments

Segment count threshold	IPPA assessment	Ejection fraction improvement			Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
		Yes	No	Total					
5	Viable	17	48	65	63	48	26	81	51
	Nonviable	10	44	54	(45, 81)	(38, 58)	(15, 37)	(71, 91)	(42, 60)
	Total	27	92	119					
6	Viable	15	30	45	56	67	33	84	65
	Nonviable	12	62	74	(37, 75)	(57, 77)	(19, 47)	(76, 92)	(56, 74)
	Total	27	92	119					
7	Viable	13	19	32	48	79	41	84	72
	Nonviable	14	73	87	(29, 67)	(71, 87)	(24, 58)	(76, 92)	(64, 80)
	Total	27	92	119					
8	Viable	9	9	18	33	90	50	82	77
	Nonviable	18	83	101	(15, 51)	(84, 96)	(27, 73)	(75, 89)	(69, 85)
	Total	27	92	119					
9	Viable	5	4	9	19	96	56	80	78
	Nonviable	22	88	110	(4, 34)	(92, 100)	(24, 88)	(73, 87)	(71, 85)
	Total	27	92	119					

Patient was assessed as IPPA-viable if number of IPPA-viable segments equaled or exceeded segment count threshold. Patient with fewer segments was assessed as nonviable. Numbers in parentheses are 95% confidence intervals.

opposite effect produced by a larger number of IPPA-viable segments. By stepwise regression analysis, the number of IPPA-viable segments was the single most important variable associated with the postoperative increase in LVEF. Clinical variables, such as the resting LVEF and the presence of angina pectoris, were not significant predictors. Moreover, the number of IPPA-viable segments had a substantial incremental value over the best possible model, which included clinical, angiographic, and demographic variables.

In this study, IPPA was used to assess the probability of improvement in left ventricular function after CABG. After an intravenous injection, IPPA undergoes rapid myocardial extraction (half-time blood clearance of 2.5 min) followed by a biexponential myocardial clearance, with a fast component (half-time, 3.5 min) and a slow component (half-time, 130 min) (*27*). The fast component is attributed to β-oxidation, whereas the slow component results from incorporation into the triglyceride pool. The uptake and metabolism of IPPA are not unlike those of ^{14}C-palmitic acid, a favorite myocardial substrate, except that the cardiac uptake of IPPA is higher than that of palmitic acid (4.4% versus 2.8% of the administered dose, respectively) (*14–16*). Thus, the use of IPPA to assess myocardial viability has a good rationale on the basis of its physiologic properties. In dogs with experimental coronary occlusion for 90–120 min, the uptake and washout of IPPA are decreased in the infarct areas (*13*). Using an experimental canine model of low-flow ischemia, Shi et al. (*28*) suggested that the myocardial retention of IPPA tracked well with the accumulation of FDG. Likewise, Yang et al. (*29*), in a similar canine model of low-flow ischemia, concluded that IPPA was superior to ^{201}Tl for the assessment of myocardial viability.

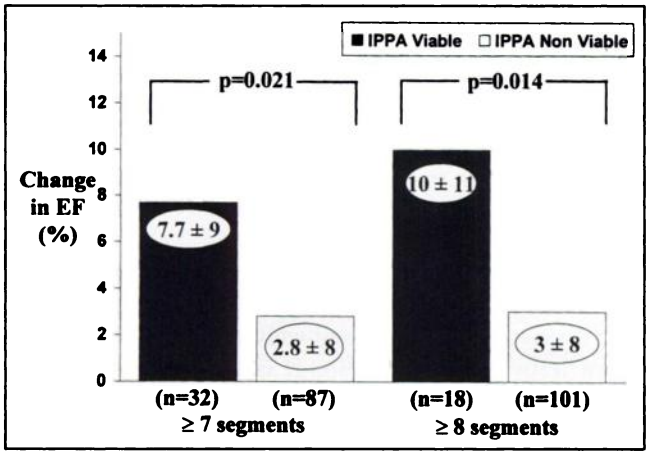

FIGURE 3. Bar graph shows change in LVEF with coronary bypass grafting relative to number of viable myocardial segments. EF = ejection fraction.

Murray et al. (*19*), in a study of 15 patients with CAD and an LVEF < 35%, reported a reduced IPPA clearance of 17.8% ± 2.3% in biopsy-viable segments and 13.4% ± 2.4% in biopsy-nonviable segments. In healthy volunteers, the IPPA clearance was 21.2% ± 5.0%. After CABG, systolic wall motion at rest or during exercise improved in 75% of the IPPA-viable segments and failed to improve in 67% of IPPA-nonviable segments.

To our knowledge, this is the largest prospective study assessing the effects of CABG on the LVEF. We elected to use a ≥10% increase in LVEF as a clinically useful endpoint for the study. The accepted reproducibility of RNA-determined LVEF is within 5% at rest (*30*). In the core

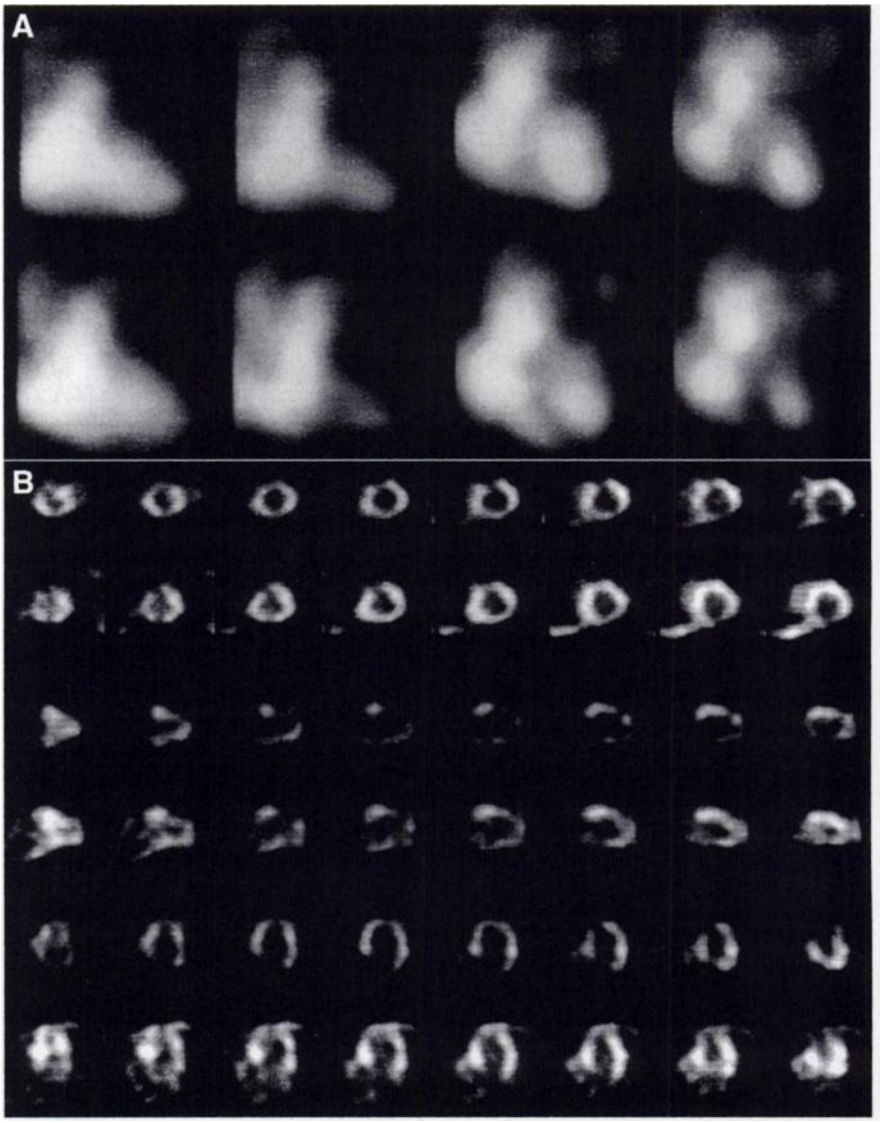

FIGURE 4. (A) Radionuclide angiograms before (top row) and after (bottom row) coronary bypass grafting. Substantial improvement occurred in this patient, with ejection fraction increasing from 32% (preoperative) to 53% (postoperative). For each pair, image on left was taken at end-diastole, and image on right was taken at end-systole. The 4 images on left are anterior view, and the 4 on right are 40° left anterior oblique view. (B) Corresponding preoperative IPPA images are shown, with 2 top rows denoting short-axis slices, middle 2 rows denoting vertical long-axis slices, and bottom 2 rows denoting horizontal long-axis slices. Early images are shown in top row of each pair, and 30-min redistribution images are shown in bottom row of each pair. Decreased uptake was evident in rest image, with redistribution present in 30-min images.

laboratory where the current RNA studies were processed, a ≥7% change in RNA-determined LVEF on 2 sequential studies interspaced by 6 wk is outside the 95% confidence limits and thus can be ascribed to a true change (*24*). Because in the present trial the interval between the 2 studies was 6–8 wk, we elected to expand slightly the minimal level beyond which a given change in LVEF might indicate a true change.

Although regional left ventricular function may improve after revascularization, without necessarily changing the LVEF, we considered that a substantial increase in LVEF (≥10%) would be a clinically meaningful improvement in ventricular function. A sustained improvement in LVEF achieved through an enhancement in myocardial perfusion may indeed have a long-term benefit on prognosis. However, enhanced survival may also result from other forms of therapy, such as administration of angiotensin-converting enzyme inhibitors to patients who have depressed LVEF without a corresponding change in LVEF (*1*). Moreover, certain medications that can induce an increase in LVEF, such as inotropic (*31*), calcium channel–blocking (*32*), and antiarrhythmic (*6*) therapy, may not enhance survival. We suggest that the increase in LVEF in these diverse clinical scenarios may reflect fundamentally different mechanisms. An enhanced LVEF after myocardial revascularization would denote a persistent correction of an intrinsic abnormality (i.e., myocardial hypoperfusion). However, a drug-induced improvement in LVEF is a dose-related phenomenon, secondary to a decrease in afterload or enhanced inotropic state, and hence would not reflect a fundamental correction of the underlying abnormality.

Our data show that a substantial, clinically meaningful increase in LVEF can indeed occur after CABG in patients with depressed LVEF preoperatively, albeit in only a minority of such patients (22.7%). If one could prospectively identify which patients are most likely to exhibit such an enhanced LVEF after revascularization, then one could preferentially target them for CABG. Obviously, other factors are and will continue to be important in the selection of patients with decreased LVEF for CABG, such as

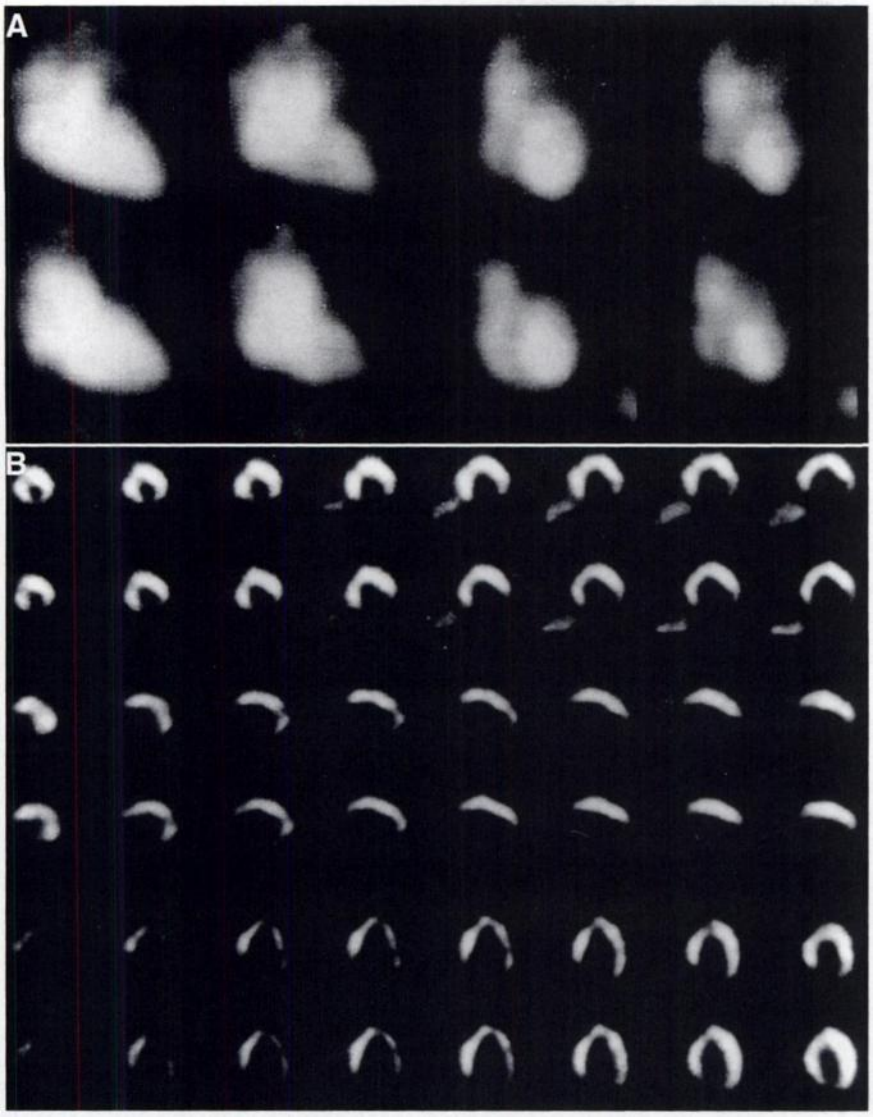

FIGURE 5. (A) Radionuclide angiograms before (top row) and after (bottom row) coronary bypass grafting. LVEF was 24% before and after coronary bypass grafting. For each pair, image on left was taken at end-diastole, and image on right was taken at end-systole. The 4 images on left are anterior view, and the 4 on right are 40° left anterior oblique view. (B) Corresponding IPPA images show severe decrease in inferoposterior apical uptake, with no improvement in 30-min images. Top 2 rows display short-axis slices, middle 2 rows display vertical long-axis slices, and bottom 2 rows display horizontal long-axis slices.

presence of angina, age, overall clinical status, technical considerations, and severity of congestive heart failure symptoms. However, since the CASS investigators showed that patients with multivessel disease and depressed LVEF have improved survival with CABG (*8,10*), the combination of appropriate coronary anatomy and a decrease in LVEF has often become a major, if not the principal, indication for CABG in such patients. Revascularization is most likely to improve myocardial perfusion, LVEF, and prognosis in patients with hibernating (hypoperfused) but structurally and metabolically preserved myocardium. Conversely, revascularization is unlikely to produce any of these sustained benefits in patients with little or no evidence of myocardial viability in regions with abnormal contraction. Ragosta et al. (*25*) showed that only patients in whom rest–redistribution thallium imaging shows substantial viability (≥7/15 myocar-

TABLE 4
Stepwise Logistic Regression Analysis

Parameters accepted into model	χ^2 *P*
Number of IPPA-viable segments	0.007
History of diabetes	0.034
History of myocardial infarction	0.066
Left anterior descending artery stenosis	0.168

TABLE 5
Incremental Value of Number of IPPA-Viable Segments

Parameters added to cumulative model	Goodness of fit (−2 log L)	Incremental goodness of fit (χ^2)	*P*
Diabetes mellitus	125.491	3.710	0.54
Left anterior descending artery stenosis	125.039	0.452	0.501
Three-vessel coronary disease	123.842	1.197	0.274
History of myocardial infarction	115.664	8.178	0.004
Number of IPPA-viable segments	108.572	7.092	0.008

dial segments) derive a substantial LVEF improvement after CABG. A recent study from the same institution by Pagley et al. (*26*) showed that patients with a greater extent of viability have improved survival after CABG compared with patients with a lesser extent of viability.

Although IPPA was the best predictor of enhanced LVEF after CABG among the variables we analyzed, the accuracy of the best statistical model was only 73%. Moreover, the sensitivity and specificity of the best IPPA criterion of viability (≥7 ventricular segments) when used alone, as opposed to part of a multifactorial statistical model, were only 48% and 79%, respectively. We do not know how these values would compare in our patient cohort with values from alternative techniques to assess myocardial viability, such as ^{201}Tl imaging (*25,26,33–36*), ^{99m}Tc-sestamibi (*35,37,38*), nitroglycerin-augmented ^{201}Tl or ^{99m}Tc-sestamibi imaging (*39*), dobutamine echocardiography (*12*), or PET (*11,12,40*). The accuracy of these techniques has been defined relative to an improvement in regional, not global, ventricular function. The weighted mean overall accuracies of rest–redistribution thallium imaging (74%), ^{99m}Tc-sestamibi (71%), FDG (80%), and dobutamine echocardiography (83%) for detection of improved wall motion after revascularization (*40*) are similar to one another and to the current results. None of the previous studies defined the accuracy of these alternatives for predicting a clinically useful increase in LVEF, and none has been tested in a multicenter trial. The ability of these techniques would likely be lower to predict a ≥10% increase in LVEF than to predict improved regional function.

Determination of the ability of IPPA to predict improved regional function after CABG was not the goal of this study. Phase I and II investigations of this agent in 22 patients who underwent revascularization showed a sensitivity of 73% and a specificity of 72% for predicting improvement in wall motion. In the same patients, ^{201}Tl and IPPA had similar accuracies for identifying viable myocardium (Medco Research, Inc., Research Triangle Park, NC, unpublished data, January 1995).

IPPA in this trial produced SPECT images of good or excellent quality in only 68% of our patients, and the images were of only fair quality in 30%. This finding may be because of the fast washout of IPPA, which is substantial by 30 min after administration, requiring rapid imaging during the initial acquisition and an increase in the acquisition time in the 30-min images. Conceivably, an acquisition faster than ours, with multiple-head detectors, may further improve imaging with IPPA.

CONCLUSION

In this prospective, multicenter trial of patients with severe impairment of left ventricular function, IPPA imaging was useful for assessing myocardial viability and for predicting a clinically substantial augmentation of LVEF after CABG. Further studies with this metabolic fatty acid appear warranted, especially a comparison with more readily available tracers such as ^{201}Tl and with the ^{99m}Tc-labeled agents. Follow-up data may add important clues about the ultimate clinical usefulness of this new tracer.

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