Thallium-201 Myocardial Perfusion Scintigrams in the Evaluation of Aorto-Coronary Saphenous Bypass Surgery

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The effect of aorto-coronary bypass graft surgery (CBG) upon regional myocardial perfusion (RMP) was studied in 23 patients using thallium-201 myocardial perfusing imaging after exercise. We compared the changes in RMP with the clinical status and ECG's during graded treadmill exercise (GTX) before and after CBG.

After CBG, the New York Heart Association's "functional class" improved from 3.2 ± 0.1 (mean ± SE) to 1.2 ± 0.2, p < 0.005. The GTX performance of the patients was also significantly improved postoperatively as judged by the total exercise time (11.7 ± 0.6 min postop, compared with 7.2 ± 0.5 min preop; p < 0.005).

Postoperative improved Tl-201 scintigrams were observed in 19 patients, but in only nine patients did the perfusion distribution return to normal. Thus, Tl-201 exercise scintigrams following CBG demonstrate improved RMP in most patients. Failure of regional myocardial perfusion to improve postoperatively, however, does not preclude marked alleviation of angina and improved exercise tolerance.

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In recent years, aorto-coronary bypass has been widely used in the treatment of angina pectoris (*1–5*). Postoperative evaluation of these patients has usually included a history, physical examination, and resting and stress ECG tests. Definitive objective assessment of graft patency, however, requires postoperative cardiac catheterization with selective visualization of the grafts. This technique is not without morbidity and considerable cost, and obviously cannot be recommended for all patients. In addition, angiography cannot assess the functional contribution of a patent bypass graft to overall myocardial perfusion.

Myocardial perfusion scintigrams have recently been used for the noninvasive evaluation of patients with coronary artery disease (*6–8*). Limited experience with potassium-43 and rubidium-81 suggests that exercise perfusion scintigrams are useful in evaluating the results of aortocoronary bypass surgery (*9,10*). Thallium-201 is a better myocardial perfusion imaging agent than potassium-43, because of its half-life (73 hr), low radiation energy, low total-body radiation dose, and other favorable physical and biologic properties (*11,12*). Recent investigations have described the sensitivity and specificity (*7*), as well as the limitations, of cardiac imaging with Tl-201 for the diagnosis of coronary artery disease (*13*). The purposes of the present investigation

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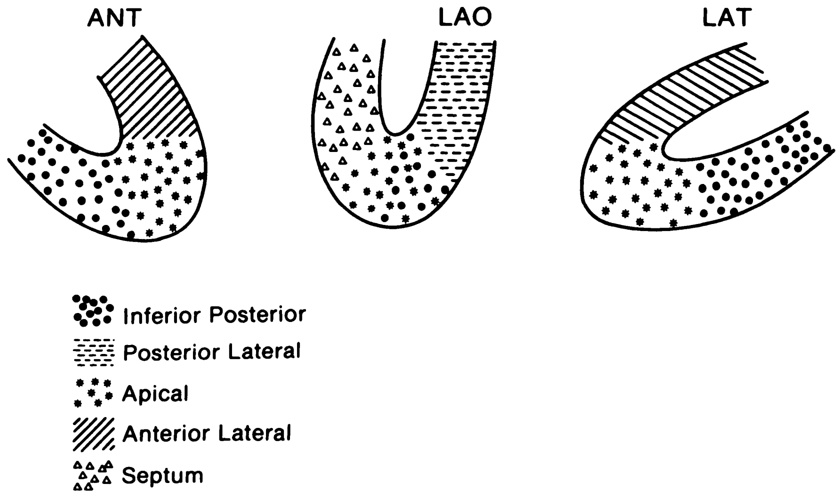

FIG. 1. Myocardial segments analyzed in Tl-201 scintigrams. ANT = anterior view, LAO = left anterior oblique view, LAT = left lateral view.

were to study the effect of aorto-coronary bypass graft surgery on regional myocardial perfusion assessed with exercise Tl-201 scintigrams, and to correlate these changes in perfusion with the clinical results of the operation and with the graded treadmill exercise tolerance test (GTX).

METHODS

Twenty-three patients who were recommended for coronary bypass surgery at the University of Iowa Hospitals were randomly selected to participate in this study. Twenty were male and three female. They ranged in age from 40 to 64 yr (mean = 54). Patients with unstable angina or significant valvular lesions were excluded. Informed consent was obtained from all patients before the studies, and the research protocol was approved by the Human Use Committee.

All patients underwent cinecoronary arteriography, performed by the method of Judkins. Left ventriculograms were performed in the 30° right anterior oblique view after injection of 30–50 cc of sodium meglumine diatrizoate (Renographin-76) into the left-ventricular cavity. All patients had 50% or greater obstructions of two or more coronary arteries. Fourteen had three-vessel disease and nine had two-vessel disease. Since significant distal lesions were not present, independent surgical opinion considered the vessels graftable. All vessels with greater than 50% lesions were bypassed. Patients were classified as having previous myocardial infarction on the basis of diagnostic Q waves on ECG, or subendocardial infarction documented by typical enzyme, ECG and clinical history.

Exercise electrocardiogram (GTX). A GTX protocol as described by Sheffield (*14*) was used. The exercise test was considered positive if 1 mm or more of flat or downsloping ST depression persisted 0.08 sec after the J joint in three consecutive cycles, during or immediately after the exercise. The occurrence of exercise-induced pain characteristic of angina pectoris was noted. In addition, the following parameters were assessed during the GTX: maximal heart rate, peak systolic arterial pressure, total exercise time, maximal ST depression, and any rhythm disturbances. All the GTX tests were interpreted by one of the observers (M.S.V.) without knowledge of the coronary arteriograms or the results of the myocardial perfusion imaging (MPI). A negative test required that at least 85% of the maximum predicted rate be achieved with less than 1 mm of ST depression on ECG. Tests were designated nondiagnostic if less than 1 mm ST depression occurred but 85% of maximum predicted rate was not achieved. One patient preoperatively, and five patients postoperatively, were receiving digitalis and developed 2–3 mm of ST depression during the GTX; these GTX findings were also considered nondiagnostic. Nitrates were not given to any of the patients in the 2 hr preceding the test.

Thallium-201 myocardial perfusion imaging and its evaluation. The preoperative Tl-201 scintigrams under exercise were performed within 72 hr before the scheduled operation. Postoperative studies were performed 8–12 wk postoperatively.

Thallium-201 (1.5 to 2.0 mCi) was rapidly injected i.v. during the peak of GTX through a previously placed cannula in the upper extremity, and then flushed with 5 cc of saline. The exercise was continued for an additional 1 min following the injection. Peak exercise was determined by any of the following: 2 mm or more of ST depression; increasing chest pain associated with at least 1 mm of ST depression; incapacitating fatigue or dyspnea; or achievement of target heart rate (85% of maximum predicted).

Myocardial perfusion images were obtained from 10 to 15 min following the injection of Tl-201, using a gamma camera with a low-energy general-purpose collimator. Counting was done with the dual-channel analyzer windows centered at 75 and 167 keV, and window widths of 20% each. Count density in the region of the myocardium was from 1,500 to 2,000 counts/sq. cm. Each study included an anterior view, a 45° left anterior oblique view, and a left lateral view. The scanning time for each of the views ranged from 8 to 15 min.

The MPIs were interpreted independently by three of the authors, from scintigraphic films. The postoperative and preoperative scintigrams were compared without knowledge of the patient's clinical course. Total agreement of interpretation occurred in 82% of the cases. In cases of disagreement, the interpretation of the two observers in agreement was used. Each scintigram was divided into five segments (Fig. 1): septal, apical, antero-lateral, inferoposterior, and postero-lateral. The perfusion of each segment was graded from 1 (normal perfusion to 4 (minimal perfusion). Examples of different classes of perfusion are shown in Figs. 2 and 3. Thus, for each patient a "total perfusion index" could be calculated with a score of 5 indicating normal regional perfusion. Improvement in any segment by at least one class was considered significant, and the overall MPI was considered improved when the total postoperative score was less than the preoperative score.

Statistical analysis of the data used the paired t test and the Fisher executive test (*15*). Results are expressed as the mean ± 1 s.e.

RESULTS

Table 1 presents the clinical, arteriographic, GTX, and Tl-201 scintigraphic findings.

Preoperative and postoperative clinical evaluation. Preoperatively, 22 of the 23 patients had significant angina pectoris. The twenty-third patient, who had Type II hyperlipidemia and a strongly positive GTX, was asymptomatic. In this patient catheterization demonstrated severe three-vessel disease and a 60% main left coronary artery lesion. Twenty patients were in functional Class 3 or 4, and the remaining two patients were in functional Class 2. Postoperatively, the mean functional class of the patients was significantly improved to 1.2 ± 0.2 (Fig. 4), compared with the preoperative functional class (3.2 ± 0.1, $p < 0.005$).

GTX test. Comparison of pre- and postoperative GTX tests indicated that as a group the patients experienced substantial improvement in exercise tolerance following the coronary bypass procedure (Fig. 5).

Thallium-201 myocardial scintigrams. Of the 23

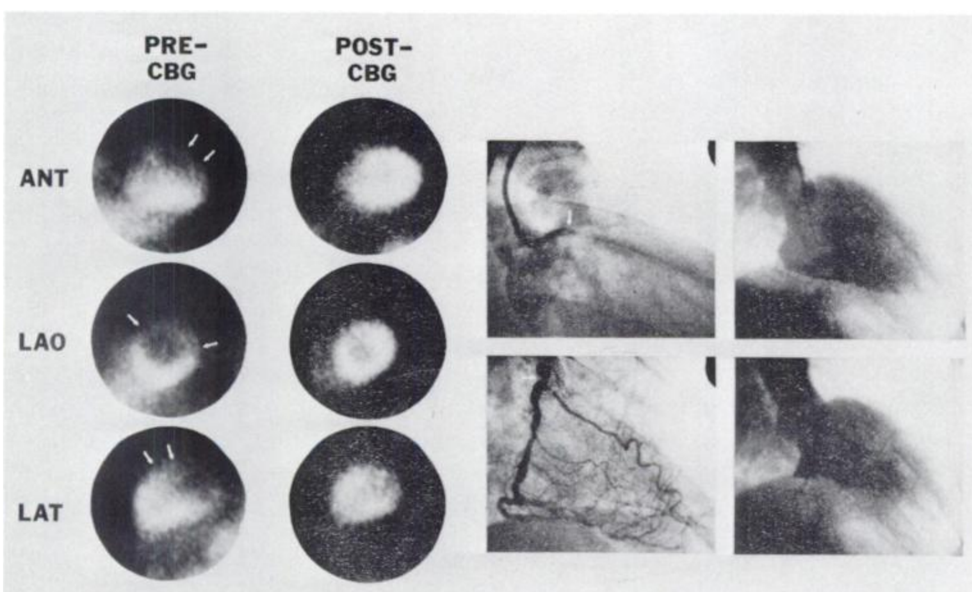

FIG. 2. Improvement of Tl-201 scintigrams following coronary bypass graft. Preoperatively patient was in NYHA Class 4 and had total occlusion of main left coronary (arrow) and severe lesions in right coronary (arrow). Left ventriculogram shows marked anterior wall hypokinesis. Preoperative scintigrams (pre-CBG) showed marked decrease in perfusion—Class 4—of anterolateral wall (arrows in top and bottom frames), upper interventricular septum and posterior lateral wall (arrows in middle frame). Postoperative scintigrams (post-CBG) are normal following three coronary bypass grafts. Patient became asymptomatic postoperatively.

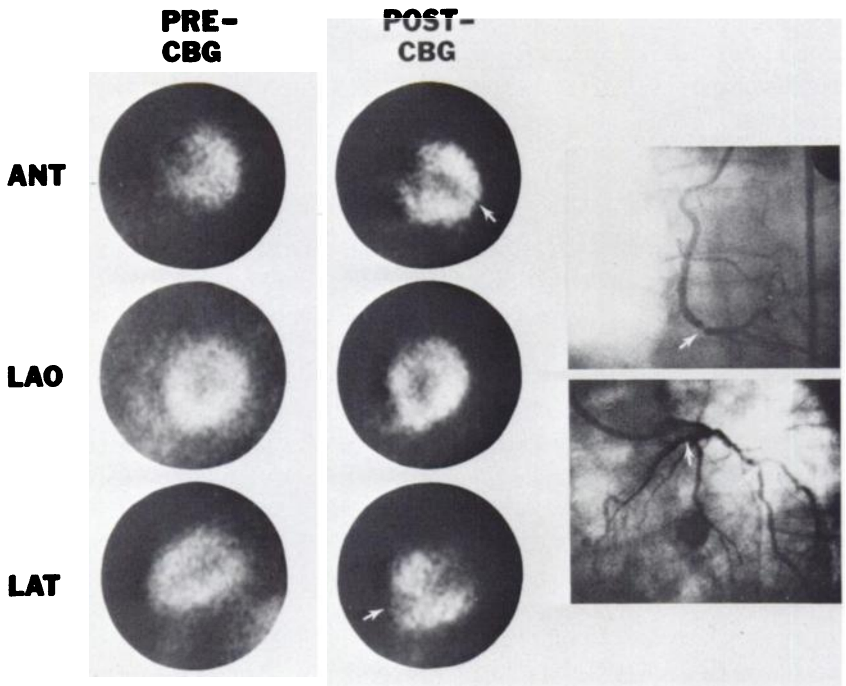

FIG. 3. Example of worsened Tl-201 scintigrams following CBG. Preoperative (pre CBG) scintigrams are normal, although patient had three-vessel coronary disease (arrows) and severe angina. Following implant of three grafts the scintigrams show moderate decrease in perfusion (Class 3) at apex, best seen in lateral view (arrow, bottom panel) but patient became asymptomatic (see text). In addition, there is a modest decrease in perfusion of upper portion of septum in LAO projection.

patients, 22 had abnormal MPIs preoperatively. A total of 115 myocardial segments were studied. Preoperatively, 64 of these segments were abnormally perfused. In all cases, the vessels corresponding to the abnormally perfused segments were bypassed. Postoperatively, 39 of the segments became normal, six improved, 14 did not change, and five became worse (Fig. 6A). Of 51 segments normal preoperatively, 47 remained normal and four became abnormal (Fig. 6B). The total perfusion index improved from 9.4 ± 0.4 preoperatively to 6.7 ± 0.4 postoperatively ($p < 0.01$) (Table 1).

Correlations between the pre- and postoperative Tl-201 scintigrams, functional class, and GTX. Nineteen patients with improved postoperative regional myocardial perfusion (nine of whom became normal) changed from NYHA functional Class 3 or 4 to functional Class 1 and had improved exercise tolerance (Table 1). The incidence of residual perfusion defects was not different in the patients with a positive postoperative GTX (seven of nine patients), compared with those with a negative postoperative GTX (five of nine patients). The perfusion index appeared slightly better in the patients with a negative postoperative GTX when compared with the patients with a postive postoperative GTX, but the difference was not statistically significant (6.3 ± 0.5 against 7.3 ± 0.7, respectively, $p > 0.05$). None of our patients had evidence of transmural myocardial infarction perioperatively, as shown by abnormal Q waves. Twelve patients with a previously documented myocardial infarction seemed to have a slightly worse perfusion postoperatively when compared with those without myocardial infarction, but again the difference did not reach statistical significance (perfusion indices of 7.1 ± 0.7 and 6.0 ± 0.3, respectively, $p > 0.05$). Since the patients with previous myocardial infarction, as a group had a worse preoperative perfusion index than those without infarction (10 ± 0.6 against 8.5 ± 0.6, $p < 0.05$), the actual improvement in perfusion was comparable in both groups. An example of improved MPI is shown in Fig. 2.

Three patients in this series demonstrated worsened MPI, even though none of them had ECG or other clinical evidence of perioperative myocardial infarction. One patient had a normal preoperative perfusion index that became abnormal postoperatively, with the new perfusion defect in the apex (Fig. 3). This patient had three-vessel disease, and all three vessels were bypassed. In this case it is possible that the postoperative abnormal MPI reflected partially enhanced perfusion of previously diffusely ischemic myocardium. The patient went from functional Class 3 to Class 1, and his exercise tolerance improved markedly. The second patient with worsened MPI had a previous antero-septal infarction and three-vessel coronary disease. Preoperatively there was a mild perfusion defect in the anterolateral wall and a marked perfusion defect in the infero-posterior wall. Postoperatively these defects persisted and a moderate perfusion defect was noted in the posterolateral wall; in addition there was a mild perfusion defect in the septum. Nevertheless, the

TABLE 1. CLINICAL, GTX, ARTERIOGRAPHIC, AND MPI FINDINGS

Case			Angina (NYHA Class)		GTX				Coronary arteriograms (1% obstruction)				Pre-op	Exercise Tl-201 scintigrams										"Total perfusion" index	
					DP (× 10³)		ST Dep							Septum		Apical		Ant Lat		Inf Post		Post Lat			
No.	Sex	Age	Pre	Post	Pre	Post	Pre	Post	RCA	LAD	CX	DIAG	infarction	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	M	53	I	I	22.7	32.3	+	ND*	100	60	60	50	—	I	I	II	I	I	I	I	I	I	I	6	5
2	M	40	II	I	13.2	27.2	+	+	—	90	90	—	—	III	I	II	I	III	I	I	I	I	I	10	5
3	M	46	IV	I	19.5	24.0	+	ND*	100	—	90	—	—	I	I	III	I	I	I	III	I	III	I	11	5
4	M	49	IV	I	22.5	21.0	+	+	80	—	90	—	—	I	I	II	III	I	I	III	I	III	I	10	7
5	M	46	II	I	20.5	26.3	+	+	80	90	40	90	—	I	I	III	I	I	I	II	II	I	I	8	6
6	M	48	III	II	13.7	16.0	+	+	95	100	95	—	—	III	I	III	III	I	I	III	I	I	I	10	7
7	M	47	III	I	20.4	27.2	ND	—	30	60	50	—	—	I	I	III	II	I	I	III	II	II	I	10	7
8	M	59	III	I	14.3	29.5	+	—	100	100	75	—	+ SE	III	I	III	I	I	I	III	I	I	I	11	5
9	M	62	III	I	15.0	30.2	+	ND*	100	75	100	75	+ INF	III	I	II	I	III	III	III	I	II	II	13	8
10	M	58	IV	I	14.9	24.5	ND	+	70	50	80	—	—	I	II	I	III	I	I	I	I	I	I	5	8
11	F	58	III	I	11.2	26.3	+	—	100	90	90	—	+ AS	I	II	I	I	II	II	III	III	I	II	8	10
12	F	63	III	I	16.5	22.1	+	—	90	100	90	—	—	I	I	I	I	I	I	III	II	I	I	7	6
13	M	48	III	IV	20.3	19.6	+	+	100	100	100	—	+ INF, AS	II	II	II	II	II	II	II	III	II	III	10	12
14	M	61	IV	I	16.5	29.5	+	+	—	90	90	90	+ AS	II	I	II	I	I	I	II	I	II	I	9	5
15	M	64	III	I	14.3	25.6	+	+	100	90	100	—	+ INF, POST	I	I	III	II	I	I	III	II	IV	IV	12	10
16	M	56	IV	I	NA	25.6	NA	—	80	100	100	100	+ SE	IV	I	IV	I	IV	I	I	I	I	I	14	5
17	F	59	III	I	18.0	NA	+	—	—	100	80	—	—	II	I	II	I	III	I	I	I	I	I	9	5
18	M	61	IV	I	22.9	30.4	+	+	50	—	40	90	—	I	I	II	II	I	I	II	I	II	I	8	6
19	F	41	IV	I	22.8	36.4	—	—	90	—	40	80	+ INF	I	I	II	I	I	I	III	II	II	I	9	6
20	M	64	IV	I	15.6	30.4	+	—	100	95	80	—	+ INF	II	I	I	I	I	I	III	I	III	I	10	5
21	M	59	III	II	13.7	13.5	ND*	—	100	100	100	—	+ AS	I	I	III	II	I	I	III	I	I	I	9	6
22	M	55	III	I	NA	24.7	+	ND*	—	95	95	—	+ ANT	I	I	II	I	I	I	II	I	I	I	7	5
23	M	61	IV	I	18.9	33.0	+	ND*	100	—	70	—	+ SE	I	I	II	II	II	I	III	III	I	II	9	9
Mean ± SE					17.4 ±0.8	26.1 ±1.3																		9.4 ±0.4	6.7 ±0.4
					$p < 0.005$																			$p < 0.01$	

ANT = anterior; Ant Lat = anterolateral; AS = anteroseptal; CX = circumflex artery; DIAG = diagonal branch; DP = peak double product (systolic pressure × heart rate); F = female; GTX = graded treadmill exercise ECG; INF = inferior; Inf Post = inferoposterior; LAD = left anterior descending artery; M = male; ND = nondiagnostic; NYHA = New York Heart Association; Post = postoperative; Post Lat = posterolateral; Pre = preoperative; RCA = right coronary artery; SE = subendocardial; ST Dep = >1 mm depression of ST segment; * = patients using digitalis; + = positive result; — = negative result. Perfusion of each segment was graded between 1 (normal perfusion) and 4 (minimal perfusion). Total perfusion index is sum of scores for each of five myocardial segments evaluated. Normal perfusion scintigram would have a score of 5. The worst perfusion index encountered in this series was 14. Thus, a decrease in total perfusion index implies improved regional myocardial perfusion.

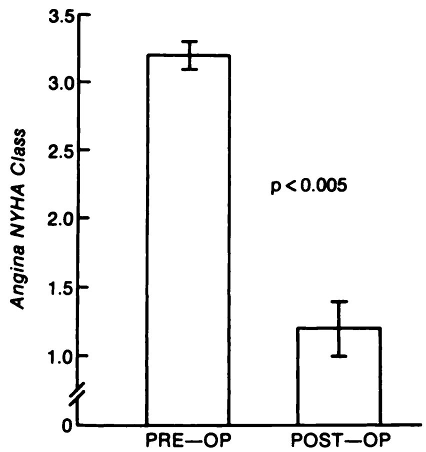

FIG. 4. New York Functional Class before and after coronary bypass graft. Columns indicate mean ± s.e.

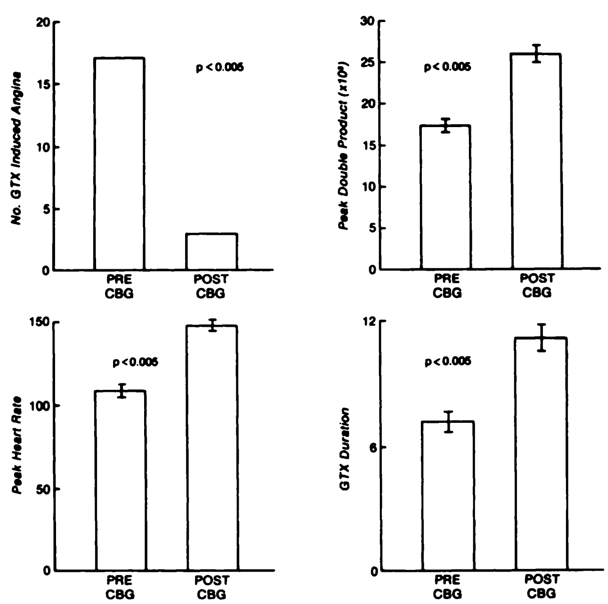

FIG. 5. Results of graded treadmill exercise before and after coronary bypass graft. GTX duration (bottom right) is expressed in minutes. Results are expressed as mean ± 1 s.e.

patient's functional class improved from 3 to 1 postoperatively and his exercise tolerance also improved markedly. We have no explanation for the scintigram findings in this patient. Thus, in two patients with substantial clinical improvement, there was deterioration in the postoperative thallium perfusion scintigrams. The third patient with worsened postoperative MPI had previously undergone triple-vessel coronary bypass graft but continued to have angina. His thallium MPI showed decreased perfusion in the posterior wall. Graft opacification showed patent LAD and RCA grafts with poor distal runoff and narrowing of the anastomotic site in the circumflex graft. He underwent surgical correction of the latter but the symptoms and the MPI worsened after the second operation and he went from functional Class 3 to Class 4. The observed perfusion defect in the posterior wall was more extensive postoperatively.

DISCUSSION

The most significant findings in this investigation are: first, we have demonstrated, using Tl-201 stress myocardial perfusion imaging, that 70% of the preoperative underperfused myocardial segments showed improved perfusion postoperatively, and that 85% of the patients who submitted to saphenous bypass grafts had demonstrable improvement in regional myocardial perfusion; second, some residual perfusion abnormalities can be seen postoperatively in 60% of the patients submitted to coronary bypass grafts, even in the patients without a previous myocardial infarction; and third, improved, although still abnormal, myocardial scintigrams are usually associated with a striking clinical improvement.

The improvement of regional myocardial perfusion following coronary bypass graft will depend on the increase in regional myocardial flow afforded by a patent saphenous graft, as well as on the potential reversibility of the perfusion defect. Obviously one would not expect fibrotic, scarred muscle to increase its Tl-201 uptake postoperatively. Thus, as expected, we found that patients with previous myocardial infarction had a slightly higher prevalence of postoperative residual abnormalities in their perfusion scintigrams.

There are three areas in this study that require some discussion: a) resting myocardial perfusion scintigrams were not done, b) postoperative cardiac

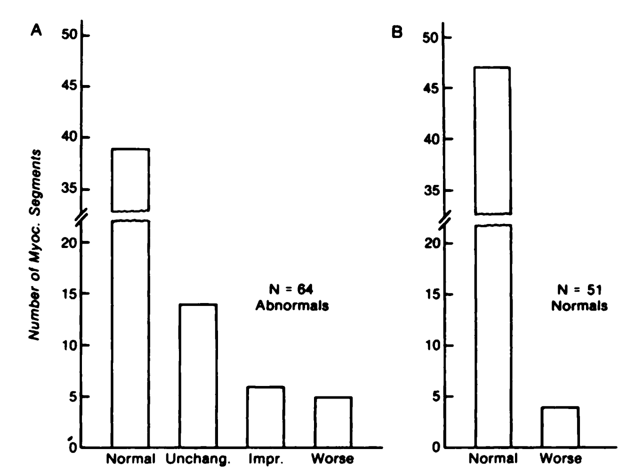

FIG. 6. Changes of Tl-201 scintigrams following coronary bypass graft. In 6A, all segments had abnormal preoperative perfusion. In 6B, all segments had normal preoperative perfusion.

catheterization was not done, and c) inherent problems with Tl-201 perfusion scintigrams.

Resting myocardial perfusion scintigrams probably would have helped us to separate ischemic from infarcted myocardial segments. Even without this information, however, we were able to classify our patients into those with and without a previous myocardial infarction using other criteria. Surprisingly, we found that even in patients with a previous myocardial infarction, postoperative myocardial perfusion images were occasionally completely normal. Thus, in this series, two of three patients with subendocardial infarction, and three of nine patients with transmural infarction, had normal postoperative myocardial perfusion scintigrams. Postoperative cardiac catheterization would have permitted us to correlate our functional assessment of myocardial perfusion with anatomic graft patency. Although this information would have been of interest, one cannot estimate flow rates in patent grafts with conventional angiographic methods and, furthermore, one patent graft may perfuse a variably sized region of the myocardium via anastomosing channels, some of which may not be visualized by angiography. A direct assessment of flow rates in the grafts in the late postoperative period would have been of considerable interest, but the methods of making such measurements are not available in our institution *(16,17)*.

Although the thallium perfusion scintigram does provide an index of regional myocardial perfusion, several studies have demonstrated that the sensitivity of this procedure does have significant limitations *(7,13)*. For example, only about ⅔ of patients with angiographically documented coronary disease have abnormal exercise thallium perfusion scintigrams. In addition, experimental studies suggest that a sizable perfusion deficit must be present before the abnormality is detectable with a perfusion scintigram *(13)*. Furthermore, the myocardial perfusion image assesses only relative rather than absolute changes in perfusion. Lastly, the level of exercise can affect the MPI, more intense exercise tending to accentuate perfusion differences. It has been reported that there is a 10% nonreproducibility between the Tl-201 exercise scintigrams performed at different times in the same patients *(18)*. Since postoperatively our patients were able to exercise more strenuously, one would expect to find more pronounced perfusion abnormalities in the absence of patent bypass grafts. This study has demonstrated that increases in myocardial perfusion following coronary bypass procedures are of sufficient magnitude to be easily detectable with thallium perfusion scintigrams.

Previous studies using potassium-43 *(9)* and rubidium-81 *(10)* also noted improved regional myocardial perfusion in most patients following coronary bypass graft. The present study confirms this experience using Tl-201—an imaging agent that is probably superior to either potassium-43 or rubidium-81.

In summary, regional myocardial perfusion improves in most patients following coronary bypass grafting. Furthermore, striking clinical improvement occurs even though postoperative myocardial perfusion images are still abnormal—although improved—in most patients.

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Stomach Artifact in Bone Scintigraphy (Letter to the Editor). Accepted 2/7/78.
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The Ventilation Study: Before and After the Perfusion Lung Scan? (Letter to the Editor) Accepted 2/7/78.
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Misuse of Statistics—Correlation Coefficient (r) Thy Heart is Treacherous. (Letter to the Editor). Accepted 3/1/78.
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Prominent Motion of a Meckel's Diverticulum (Letter to the Editor). Accepted 3/5/78.
Frederick N. Hegge

Rating of the Radiopharmaceuticals for Brain Imaging (Letter to the Editor). Accepted 3/7/78.
Ramesh Chandra

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Thomas P. Haynie and Howard J. Glenn

Effect of Phenobarbital on Liver Uptake of Ga-67 (Letter to the Editor). Accepted 3/7/78.
Todd W. Hubbard, Steven M. Larson and David R. Allen

Possible Tumor Localization of Tc-99m-Labeled Liposomes: Effects of Lipid Composition, Charge, and Liposome Size. Accepted 3/7/78.
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A Model for the Radionuclide Measurement of Ascitic Fluid Volumes. Accepted 4/13/78.
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The Specificity of Pyrophosphate Myocardial Scintigrams in Patients with Prior Myocardial Infarction (Concise Communication). Accepted 4/19/78.
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