Correlations of Tc-99m Pyrophosphate Myocardial Scintigraphy and the Results of Coronary-Artery Bypass Surgery

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This study indicates that abnormal myocardial scintigrams with Tc-99m pyrophosphate tend to improve after coronary-artery bypass surgery, frequently changing from positive to normal. The significance of this change is uncertain. It does not correlate well with the clinical state but may simply reflect the natural course of myocardial scintigraphy in response to hospitalization, medical management, and presumably improved myocardial oxygenation. Postoperative myocardial scintigrams are useful in detecting perioperative infarction. ECG interpretation may be difficult in the immediate postoperative period and, in three cases, there were scintigraphic criteria of perioperative infarction without diagnostic changes on ECG. Patients with positive preoperative scintigrams, especially in association with Functional Class IV angina, are at increased risk during coronary-artery bypass surgery.

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Technetium-99m PPi myocardial scintigraphy may be positive in coronary-artery disease in the absence of acute myocardial infarction (*1,2*). The incidence of positivity is greater in patients with unstable angina, and the rate is further increased in the presence of congestive heart failure (*2*). It has been reported that scintigrams change after coronary-artery bypass (CAB) surgery with a decrease and often a disappearance of the myocardial activity seen preoperatively (*3,4*). The significance of this change is unknown. Additionally, it is not known whether the postoperative improvement in the scintigram parallels the clinical improvement.

The presence of unstable angina or acute myocardial infarction increases the risk of coronary-artery bypass surgery (*5,6*). For patients with unstable angina who have not had a recent infarction, other criteria may portend a higher surgical mortality. These include continued anginal pain after hospitalization, hypertension, and triple-vessel disease (*7*). Myocardial scintigraphy, as a sensitive indicator of cellular injury and death, might also be

a useful parameter in the evaluation of patients with unstable angina undergoing CAB surgery.

A recognized complication of surgery for coronary-artery disease is the occurrence of perioperative acute myocardial infarction (AMI). The incidence of infarction has been reported to range from 5–30% (*8,9*). Intraoperative infarction may account for up to 60% of the operative deaths (*10,11*). The incidence of perioperative AMI may be even higher than usually reported if parameters other than just ECG changes are taken into consideration. CPK-MB isoenzyme elevation and positive pyrophosphate myocardial scintigrams may increase the yield for the detection of AMI and nontransmural insults (*3,12*).

The present study was designed to determine the natural course of myocardial scintigrams in bypass

surgery, the predictive value of positive against that of normal scintigrams for the clinical outcome, the sensitivity for the diagnosis of perioperative infarction, and the correlation of preoperative studies and surgical death. Scintigrams were performed on a series of patients just before surgery, in the early postoperative period, and at later followup.

METHODS

A total of 92 patients were studied. Patients scheduled for surgery were included in the study when their surgical date coincided with our routine myocardial imaging schedule. All 92 patients had a preoperative scintigram. Seventy had a repeat scintigram in the immediate postoperative period and 28 had a third study later. The average time between surgery and the early postoperative study was 7.4 days, with a range of 3–21 days. Late followup scintigrams were obtained in 28 patients at an average of 20.5 wk after surgery. Sixty-eight patients were more than 2 mo postoperative and were reevaluated clinically for history of chest pain, exercise tolerance, or congestive heart failure and were assigned a functional class according to the New York Heart Association. The average followup interval was 23.8 wk, with a range of 8–55 wk.

All patients were injected intravenously with 20 mCi of Tc-99m stannous pyrophosphate containing less than 0.15 mg of tin. The radiopharmaceutical was chromatographed before each injection. Strips of ITLC-SG, 7 × 0.5 cm, were developed with acetone to detect free Tc-99m, and with saline to separate reduced hydrolyzed forms as described previously (13). Two hours after the injection, images

FIG. 1. Grading system. No cardiac activity = 0; activity less than ribs = 1+; equal to or greater than ribs = 2+; equal to or greater than sternum = 3+.

were obtained by gamma camera in the anterior, 45° left anterior oblique, and left lateral projections, with a 15,000-hole, high-resolution collimator. A 20% window was used over the 140-keV photopeak, and 400,000 counts were obtained for each view.

The scintiphotos were interpreted independently by two observers. Pre- and postoperative studies were randomly mixed, identification withheld, and the clinical information was not known to either physician at the time of his interpretation. Interpretation was based on a system wherein myocardial activity was graded from zero to 3+: zero for no myocardial activity; 1+ when activity in the region of the heart was above background but less than that in the ribs; 2+ when equal to or greater than rib activity; and 3+ when myocardial activity equaled or exceeded sternal activity (Fig. 1). Myocardial activity of 2+ and 3+ was considered positive.

The criterion used for the diagnosis of perioperative infarction was the appearance of new Q waves on the postoperative ECG. ST-T wave changes alone, or enzyme changes alone, were not considered adequate for the diagnosis of AMI.
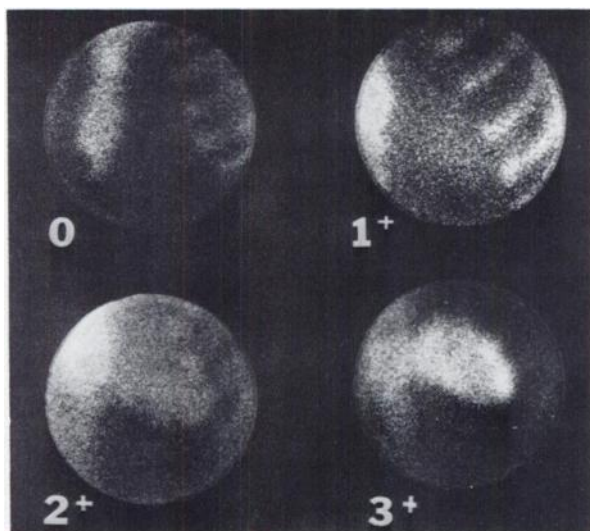
Deaths occurring in the operating room and during the first 4 postoperative wk were considered surgical deaths.

RESULTS

Preoperative scintigram. Of the 92 preoperative scintigrams, 37 were positive, giving a preoperative positivity rate of 40%. All were 2+ in intensity. Preoperatively, 50 patients had Functional Class (FC) IV angina—that is, pain at rest—of which 24 had positive scans (48%). In the FC III group, there were 13 positive studies among the 41 subjects (32%). There was one patient with left main coronary-artery diesase and congestive heart failure who did not have chest pain.

Followup clinical data were available for 68 patients. Of the remaining 24 patients, eight were excluded because they were less than 2 mo postoperative, 15 had died, and one patient was lost to followup. Sixty-five of the 68 survivors showed clinical improvement, and 46 had improved to FC I (68%). In the FC IV group, 24 of 40 patients (60%) improved to FC I, and seven more had improved to FC II. In the FC III group, 17 of 28 patients (61%) improved to FC I and nine to FC II.

Correlation of the preoperative scintigrams with the clinical results on the 68 long-term followup patients, plus the 15 deaths, showed that 29 of 50 patients (58%) with normal preoperative scintigrams improved symptomatically from FC III or IV to FC I following CAB surgery. Similarly, 17 of 33 patients (52%) with positive studies also im-

proved. Excluding the ten operative and five late deaths, the improvement rates for the positive and normal groups were 68% and 67%, respectively, compared with the overall survivors' improvement rate of 68% (Table 1).

Postoperative. Postoperative scintigrams were obtained on 70 patients. Fifty-two of the 70 had normal postoperative myocardial scintigrams (74%). Nineteen of these were in patients with positive preoperative studies, giving a conversion rate of 63% (Fig. 2).

Followup information was available on 60 patients with postoperative scintigrams. Thirty of 43 patients with normal scintigrams had improved to FC I (70%). Eleven of 17 patients with positive postoperative scintigrams were also FC I at late followup (65%).

Late followup. Of the 28 late followup scintigrams, 23 were normal (82%). In two of the six patients with positive late scintigrams, the early postoperative study was normal. Both had a favorable clinical response to surgery. Fourteen of 16 (88%) of the patients who were clinically FC I had normal scintigrams. Nine of 12 (75%) of those who were FC II and III likewise had normal scintigrams.

Perioperative infarction. Ten patients had ECG criteria of perioperative infarction. In eight, the infarct was seen on scintigraphy. The two instances in which the scintigram failed to show the infarct were both nine days after surgery, whereas the average time on the six positive studies was six days postoperative. Additionally, postoperative scintigraphy on three other patients showed a new localized hot spot, without diagnostic changes on the ECG (Fig. 3).

Surgical mortality. There were ten surgical deaths among the 92 patients, giving a mortality rate of 11%. Thirty-seven of the 92 preoperative scintigrams were positive. Seven of the ten deaths were in this group, for a mortality rate of 19%, compared with 5.5% in the patients with a normal preoperative study (Table 2).

In the Functional Class III group, the operative mortality was higher in the patients with a positive scintigram, with two of 13 (15%) deaths against one death among 29 (3.5%) patients with a normal scintigram. In the Functional Class IV group, five deaths occurred in those 24 patients with positive preoperative scintigrams, for a surgical mortality rate of 20%. One death occurred among 25 patients with normal preoperative scintigrams (4%) (Table 3).

DISCUSSION

Hot-spot myocardial scintigraphy with Tc-99m

TABLE 1. CORRELATION OF PRE- AND POST-OPERATIVE SCINTIGRAPHY AND IMPROVEMENT TO FC I AT LATE FOLLOWUP

	Scintigram result	Clinically improved	
Preoperative	50 neg	29	58%
	33 pos	17	52%
			p = NS
Postoperative	43 neg	30	70%
	17 pos	11	65%
			p = NS

pyrophosphate is a sensitive indicator of cellular injury and death. Once a cell enters anaerobic metabolism, calcium diffuses into the cell and attaches to the mitochondria (14). Technetium-labeled phosphates are also free to enter the cell and either are deposited along with the calcium or displace other anions previously laid down with the calcium (15). It is not surprising, therefore, that pyrophosphate myocardial scintigrams are frequently positive in unstable coronary-artery disease in direct relationship to the severity of the clinical state (16,17).

In the present study, the incidence of positivity in unstable angina was similar to that found by other workers, and the scintigrams generally became normal following coronary-artery bypass surgery (16,18). The significance of this change is not known, and in this group of patients did not appear related to the change in symptoms following surgery.

Except when the left main coronary artery is diseased, there is no evidence that coronary-artery bypass surgery prolongs life (19–21). The procedure does alleviate symptoms, however, and those patients who survive surgery are generally improved (22). The most common indication, therefore, for coronary-artery bypass surgery is uncontrollable angina. Improvement of both symptoms and scintigraphic findings occurred with a high degree of regularity, but the scintigram tended to become normal with the same frequency in those patients who improved to
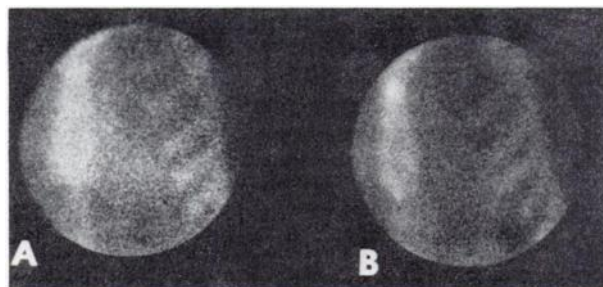

FIG. 2. (A) Positive preoperative scintigram (grade 2+); (B) normal postoperative study.
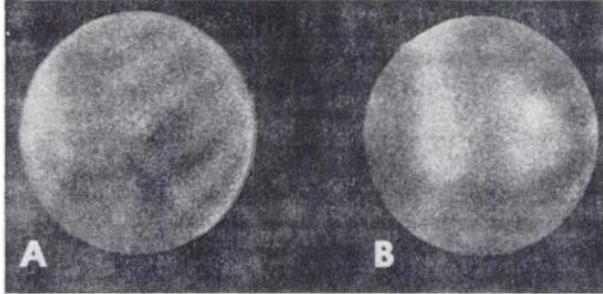
FIG. 3. (A) Preoperative image; (B) new lesion postoperatively.

Functional Class I as in those who realized little improvement following surgery and were still left with significant chest pain.

The late-followup scintigrams also failed to correlate with the long-term clinical results of coronary-artery bypass surgery. Seventy-five percent of those patients who had only minor improvement and were still experiencing chest pain with exertion continued to have normal myocardial scintigrams. This finding does not differ significantly from that in the group of patients who were essentially asymptomatic at late followup. The improvement in the appearance of myocardial scintigraphy following coronary-artery bypass surgery therefore continued into the late followup period irrespective of the clinical state.

The reason why myocardial scintigraphy tends to normalize with coronary-artery bypass surgery, but still does not parallel the clinical state, may be that symptomatic improvement is not a sufficient objective parameter by which to judge the results of bypass surgery. It has been well demonstrated that sham operation is effective for the relief of anginal

pain that appears to be of cardiac origin (23). The surgery itself may cause infarction of the ischemic segment, which would relieve the pain but result in an abnormal postoperative scintigram. Patients who are relieved of angina but have a persistently positive postoperative scintigram may be experiencing myocardial injury and continued cellular death with a placebo effect from the surgery. It is hoped that a longer followup period will shed more light on the true nature of a persistently positive scintigram. If the concentration of phosphates in myocardial cells is a marker of continuing cellular death, one would expect that those patients with persistently positive scintigraphy after bypass surgery would have a higher morbidity and myocardial dysfunction, with varying degrees of dyskinesis and pump failure.

Although postoperative ECG changes and elevated cardiac enzymes may be unreliable, myocardial scintigraphy is a sensitive indicator of perioperative infarction, and successfully detected six of the eight infarctions seen on ECG (28–30). The two instances where the study was normal were both done 9 days following surgery, against 6 days for the positive studies. These might not be true false-negatives. In three cases where scintigraphy showed a new focal lesion following surgery in the absence of ECG changes, there could well have been a perioperative infarction that was undetectable by ECG. It is doubtful whether cardioversion caused the pyrophosphate uptake in these cases (26). Pericardial inflammation can lead to pyrophosphate concentration, but the pattern is diffuse rather than focal, except in the postmyocardial infarction syndrome (27).

The most striking finding of this study was the association of operative mortality and positive preoperative scintigraphy. The seemingly homogeneous group of unstable angina may be divided into two subgroups with the same symptom complex. In the subgroup with positive pyrophosphate myocardial scintigram, the surgical mortality was substantially greater. This would be in keeping with the observation that the incidence of phosphate concentration in the myocardium is a measure of the severity of the myocardial insult. Patients with FC IV angina had a higher positivity rate on the preoperative scintigram than those with FC III.

The overall mortality rate in our series was high. A number of factors may account for this, including the high proportion of FC IV patients. Only those patients with pain at rest were classified as FC IV, and our patient population may not be directly comparable with those of other series. This higher mortality rate did afford us the opportunity to evaluate the preoperative scintigram as an indicator of surgical risk. The surgical mortality of those patients

TABLE 2. PREOPERATIVE SCINTIGRAMS AND SURGICAL MORTALITY

Scintigram result	Deaths	
37 pos	7	19%
55 normal	3	5.5%
		$p < 0.05$

TABLE 3. PREOPERATIVE FC AND SCINTIGRAMS CORRELATED WITH SURGICAL MORTALITY

	Scintigram result	Deaths	
FC III	13 pos	2	15%
	29 normal	1	3.5%
			$p = NS$
FC IV	24 pos	5	20%
	25 normal	1	4%
			$p < 0.05$

with a normal preoperative study was 5.5%, which is similar to those of other series. It is primarily those patients with a positive scintigram who have an unusually high surgical mortality rate. This held true for both FC III and FC IV patients, although it was more pronounced in the FC IV group.

ACKNOWLEDGMENTS

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