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Thallium-201 imaging in assessment of aortocoronary artery bypass graft patency[1]

JAMES A. SBARBARO[2], HARISCHANDRA KARUNARATNE, SEMA CANTEZ, PAUL V. HARPER, AND LEON RESNEKOV

From the Departments of Medicine (Section of Cardiology), Radiology (Section of Nuclear Medicine and Surgery), University of Chicago, Pritzker School of Medicine, Chicago, Illinois, USA

SUMMARY Fifteen patients with significant coronary artery disease confirmed by cardiac catheterisation were studied before and after aortocoronary artery bypass graft surgery by rest and exercise ^{201}Tl myocardial scintigraphy in an attempt to predict graft status non-invasively. Segmental myocardial perfusion comparisons in pre- and postoperative exercise images allowed correct predictions of high ($\geq$67%) or low ($\leq$50%) graft patency rates in 10 of 15 patients, while similar comparisons in postoperative rest and exercise images yielded 13 of 15 correct predictions. Furthermore, 20 of 21 myocardial segments with increased postoperative perfusion when compared with corresponding segments in preoperative exercise studies were supplied by patent grafts. Regional graft occlusion, however, was difficult to predict. It was also difficult to predict graft status when myocardial segments were shown to have unchanged perfusion postoperatively as compared with the preoperative segmental assessment. Despite these limitations, the non-invasive technique of ^{201}Tl imaging can provide useful information regarding coronary artery bypass graft patency.

Thallium-201 has previously been shown to be a useful agent for non-invasive cardiac imaging (Bradley-Moore *et al.*, 1975; Lebowitz *et al.*, 1975). Its myocardial cell uptake depends on adequate myocardial blood flow as well as integrity of the cell membrane NA-K ATPase activity, but, nevertheless, several studies have demonstrated that ^{201}Tl distribution in the heart is proportional to local perfusion over a clinically relevant range of coronary blood flows (Strauss *et al.*, 1975; Mueller *et al.*, 1976; Strauss and Pitt, 1977; Pohost *et al.*, 1977; Weich *et al.*, 1977), suggesting a particular role for perfusion imaging in assessing patients with ischaemic heart disease. Thus, Bailey *et al.* (1977), Ritchie *et al.* (1977b), and Botvinick *et al.* (1978) have shown that comparison of rest and exercise myocardial scans with a perfusion marker such as ^{201}Tl yields useful information about both the presence and location of important occlusive lesions of the coronary arteries.

Controversy still exists about the role of aortocoronary artery bypass graft surgery in the management of ischaemic heart disease (Braunwald, 1977; Murphy *et al.*, 1977; McIntosh and Garcia, 1978). Knowledge of postoperative graft patency is necessary for evaluating the benefit of surgery in relieving cardiac pain, improving ventricular function, protecting against further myocardial infarction, and increasing longevity.

Graft patency has usually been evaluated by cardiac catheterisation, which neither lends itself to serial studies, nor is entirely free of risk. Recent studies have attempted to assess surgical results by comparing myocardial perfusion imaging using K-43 (Zaret *et al.*, 1974), Rb-81 (Lurie *et al.*, 1975), and ^{201}Tl (Ormand *et al.*, 1977; Ritchie *et al.*, 1977a; Greenberg *et al.*, 1978), with graft patency demonstrated at cardiac catheterisation.

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[2] Present address: Cardiopulmonary Unit, Medical Center Hospital of Vermont, Burlington, Vermont 05401, USA.

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In this study we have investigated the potential role of ^{201}Tl imaging in the non-invasive assessment of aortocoronary bypass surgery graft patency by studying patients at rest and on exercise before and after surgery and comparing the results with pre- and postoperative coronary arteriograms and left ventriculograms.

Methods

I: PATIENTS AND PROCEDURES

Fifteen male patients, ages 42 to 64 years (mean 52), with coronary arteriograms showing greater than 75 per cent reduction in cross-sectional area in at least two coronary arteries were studied. All underwent multistage exercise treadmill testing using the Bruce procedure (Bruce *et al.*, 1973) within three months before cardiac surgery. ^{201}Tl, 2 mCi, was injected intravenously at the point of angina, $\geqslant$2 mm ST depression, maximum fatigue, or when 90 per cent of the maximum predicted heart rate was achieved. Thereafter exercise was continued for an additional 45 to 60 seconds, after which the patient was moved to an immediately adjacent room where imaging started 10 minutes after the injection, using a Searle Pho-Gamma IV scintillation camera equipped with a low-energy, high-resolution collimator and interfaced to an Ohio-Nuclear 160 data acquisition system. AP, LAO 30°, LAO 60°, and RAO 30° views were obtained in this sequence in all patients, with collection over 10 to 15 minutes of 300 000 counts per image. In 12 of the 15 patients rest images were similarly obtained, separated by at least one week from the exercise study. In the three remaining patients, four hour postexercise delayed images were taken to approximate the rest state.

Three to six months after myocardial revascularisation surgery, all patients underwent repeat cardiac catheterisation, as well as rest and exercise ^{201}Tl scans, using procedures identical to the preoperative studies (Fig. 1).

Selective coronary arteriography, biplane left ventriculography, and selective contrast injection of

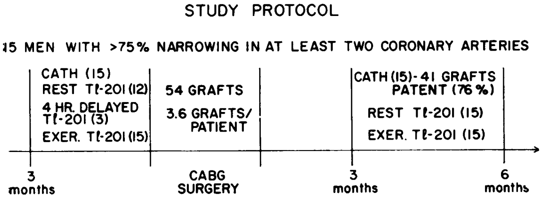

Fig. 1 *Study procedure.*

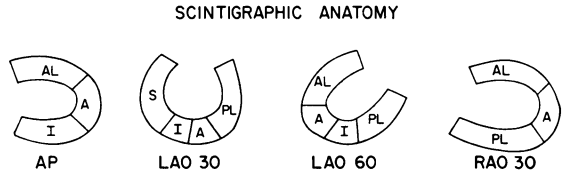

Fig. 2 *Scintigraphic anatomy in four views. A, anterior; PL, posterolateral; AL, anterolateral; S, septal; I, inferior.*

the grafts were performed by the Judkins technique (Judkins, 1967), and filmed in multiple projections. Arteriograms were interpreted by two experienced observers unaware of the scintigraphic data. No graft was considered occluded until attempts at both selective (in most cases utilising marker rings as guides) and non-selective (using aortograms and ventriculograms) opacification failed to show patency.

II: DATA ANALYSIS

Digital and analogue images were analysed in the unprocessed state by two experienced observers unaware of the clinical or catheterisation findings. Inter-observer disagreement was rare, and was resolved by a third experienced observer. RAO views were found to provide little diagnostic information and were, therefore, excluded from further analysis. The heart was divided into septal, inferior, apical, anterior, and posterolateral segments for scintigraphic analysis, as shown in Fig. 2. A segment was graded zero if no defect was present, 1+ if a defect occupying less than 50 per cent of that segment was present, and 2+ if the defect occupied 50 per cent or more of that segment.

New or larger postoperative exercise induced defects were identified and compared with degrees of graft patency in individual patients. Pre- and postoperative rest scans were also compared.

In addition, pre- and postoperative exercise scans, and postoperative rest and exercise scans were compared as possible predictors of the extent of postoperative myocardial revascularisation, in the following manner:

(1) Scan A was considered to show 'increased' perfusion when compared with scan B if either a net reduction in the size or the number or in both size and number of segmental perfusion defects were noted in scan A when compared with scan B.

(2) Scan A was considered to show 'decreased' perfusion when compared with scan B if either

a new increase in the size or the number or in both size and number of segmental perfusion defects were noted in scan A when compared with scan B.

(3) Scan A and scan B were felt to show 'similar' perfusion when either no change in the size or the number or in both size and number of segmental perfusion defects were noted when the two scans were compared.

Corresponding pre- and postoperative exercise scintigraphic segments were compared as possible predictors of regional graft patency. For these analyses, the blood supply of the septal segment was assumed to be from left anterior descending grafts, and apical and anterior blood supply from left anterior descending or diagonal or from both grafts. Inferior segments were felt to be supplied by right coronary artery or dominant left circumflex grafts, and posterolateral segments from left circumflex or dominant right coronary artery grafts or from both.

Perioperative myocardial infarction was diagnosed from an analysis of serial electrocardiograms and cardiac enzymes (CK) and isoenzymes (CK MB) as well as from results of pre- and postoperative technetium-99m pyrophosphate scans (Walsh *et al.*, 1977).

Table *Summary of patient data*

Case no.	*Age (y)*	*Percentage graft patency*	*Multiple-stage exercise testing (MSET)*	*Maximum[c] pressure—rate product*	*Graft patency rate predicted by MSET*	*New or larger perfusion defects (PD) with exercise*	*New or larger postop rest PD*	*Absent or smaller postop rest PD*	*Periop MI*
1*	54	100 (3/3)							
Preop			I	18 200		Yes			
Postop			+	26 720		No	Yes		
2	42	75 (3/4)							
Preop			+	17 040		Yes			
Postop			+	26 720		No	Yes	Yes (2)	
3	58	100 (3/3)							Inferior
Preop			I	21 000		No			
Postop			–	28 525		Yes	Yes	Yes (2)	
4	54	75 (3/4)							
Preop			+	23 200		Yes			
Postop			I	26 600		No	Yes		
5	64	33 (1/3)			Yes				
Preop			+	12 000		Yes			
Postop			+	25 575		No	Yes		
6	49	100 (5/5)			Yes				
Preop			+	22 080		Yes			
Postop			–	30 060		No			
7	62	100 (3/3)							
Preop			+	9 900		Yes			
Postop			+	19 500		Yes	Yes	Yes	
8	52	50 (2/4)							
Preop			+	21 000		Yes			
Postop			I	21 000		Yes			
9	56	100 (3/3)							
Preop			+	18 850		Yes			
Postop			I	23 200		Yes	Yes (2)	Yes	
10	54	100 (4/4)							
(P) Preop			+	21 000		Yes			
Postop			+	30 060		Yes			
11†	44	33 (1/3)							
Preop			+	20 480		Yes			
Postop			+	22 545		Yes			
12	49	75 (3/4)			Yes				
Preop			+	21 710		Yes			
Postop			–	30 060		No			
13	47	67 (2/3)			Yes				
Preop			+	20 300		Yes			
Postop			–	28 390		No	Yes		
14	53	33 (1/3)							
(P) Preop			I	10 500		Yes			Inferior
(P) Postop			I	15 000		Yes			
15	46	80 (4/5)							Anteroseptal
Preop			+	8 500		Yes			
Postop			+	23 200		No	Yes (2)	Yes	

*, Patent right coronary graft to posterior descending with 95 per cent occlusion; †, unbypassed critical LAD lesion; (P), taking propranolol; +, positive; –, negative; I, inconclusive; [c], mean of peak blood pressure in mmHg × maximum achieved heart rate/min.

Results

(A) SURGICAL RESULTS

Fifty-four grafts were placed at surgery in the 15 patients (average = 3·6 grafts/patient), of whom eight had three, five had four, and two had five grafts positioned. Fifty-two were saphenous vein, and two internal mammary bypass grafts. At repeat catheterisation three to six months after operation 41, or 76 per cent were patent. All patients had at least one, and 12 of the 15 had two or more grafts patent at the time of restudy. Angina was much improved or absent in 14 of the 15 patients after operation.

(B) MULTIPLE-STAGE EXERCISE TESTING

Using $\geqslant$1·0 mm of horizontal or downsloping ST segment depression measured 80 ms after the J point of the electrocardiogram as the criterion for a positive response, reversion of a preoperative positive to a postoperative negative multistage exercise test predicted graft patency rates of $\geqslant$67 per cent in three patients, while a newly positive postoperative multiple stage exercise testing indicated $\leqslant$50 per cent graft patency in one patient. In the remaining 11 patients, however, exercise testing failed to provide any clear indication of graft status (Table).

The level of exercise performed, as shown by pressure-rate products (peak systolic blood pressure in mmHg × maximum achieved heart rate/minute), increased significantly in 14 of the 15 patients in postoperative tests. Preoperatively, pressure-rate products ranged from 8500 to 23 200, with a mean of 17 717, rising postoperatively to a range of 15 000 to 30 060, and a mean of 25 143.

Two patients were exercised while taking propranolol before surgery, and one of these remained on this drug at the time of postoperative exercise testing; no patient was exercised while on digoxin (Table).

(C) NEW OR LARGER EXERCISE-INDUCED ^{201}TL PERFUSION DEFECTS

New or larger perfusion defects were noted in 14 of 15 patients in preoperative exercise and 7 of 15 patients in postoperative exercise ^{201}Tl scans when compared with corresponding images in the rest state. Three of these seven patients who developed such defects with exercise postoperatively had $\leqslant$50 per cent graft patency, compared with one patient with $\leqslant$50 per cent graft patency among those eight patients without new or larger exercise-induced postoperative perfusion defects.

(D) COMPARISON OF PRE- AND POSTOPERATIVE ^{201}TL REST SCANS

Analysis of the postoperative rest ^{201}Tl scans revealed 11 segments in nine patients with new or larger perfusion defects when compared with corresponding segments in the preoperative rest scans. Perioperative myocardial infarction in the distribution of these particular segments was documented in two of these nine patients (Table); 10 of 11 segments were supplied by patent grafts.

In contrast, seven segments in five patients showed smaller or absent postoperative rest ^{201}Tl defects when compared with preoperative studies. None of these patients developed perioperative myocardial infarctions nor were graft occlusions in the distribution of these segments shown in any (Table).

Fifty-seven segments were unchanged in postoperative rest scans when compared with corresponding preoperative rest studies.

(E) COMPARISON OF PRE- AND POSTOPERATIVE EXERCISE ^{201}TL AS PREDICTOR OF EXTENT OF MYOCARDIAL REVASCULARISATION

Fig. 3 depicts the relation between a comparison of pre- and postoperative exercise scans and percentage graft patency. All eight patients in whom postoperative exercise scans showed 'increased' perfusion when compared with the preoperative exercise study had high graft patency rates ($\geqslant$67%). Five patients with 'similar' perfusion in pre- and postoperative exercise scans had graft patency rates ranging from 33 to 100 per cent, whereas both patients with 'decreased' perfusion postoperatively had low graft patency rates ($\leqslant$50%).

Fig. 4 shows pre- and postoperative exercise ^{201}Tl scans from a patient with 75 per cent graft patency. Postoperative perfusion was judged to be 'improved', since a large inferior defect noted preoperatively is now smaller, and large apical and posterolateral defects are no longer present in the postoperative exercise scan as compared with the preoperative study.

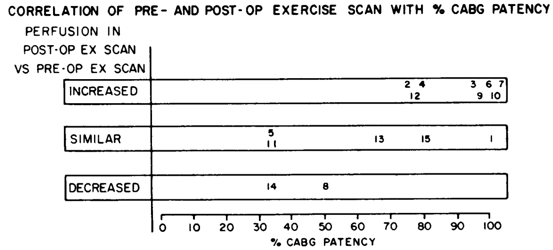

Fig. 3 *Correlation of pre- and postoperative exercise scans with percentage graft patency.*

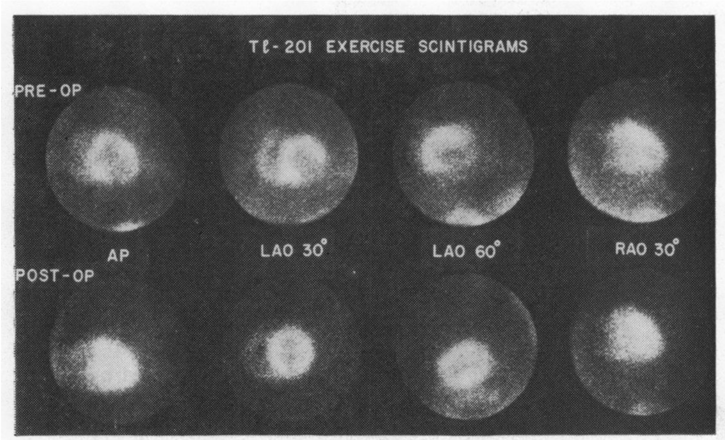

Fig. 4 *^{201}Tl pre- and postoperative exercise myocardial scintigrams from a patient in whom three of four grafts were patent showing improved uptake in the inferior, apical, and posterolateral regions.*

(F) COMPARISON OF POSTOPERATIVE REST AND EXERCISE ^{201}TL AS PREDICTOR OF EXTENT OF MYOCARDIAL REVASCULARISATION

Fig. 5 depicts the relation between a comparison of postoperative rest and exercise scans and percentage graft patency. In 11 patients with 'increased' or 'similar' perfusion in postoperative exercise scans when compared with postoperative rest studies, 10 had two-thirds or more of their grafts patent (1 to 67%, 3 to 75%, 1 to 80%, 5 to 100%); in four patients with 'decreased' postoperative exercise perfusion when compared with the resting state, three had one-half or less of their grafts patent (2 to 33%, 1 to 50%).

Fig. 6 shows identical postoperative rest and exercise scans and, therefore, 'similar' perfusion in a patient with 100 per cent graft patency. An apical defect present at rest is unchanged after exercise; no new exercise-induced defects are noted.

Since each patient is designated by the same number in all Figures and in the Table, it should be noted that the degree of graft patency, which could not be judged by pre- and postoperative exercise scan comparison in five patients (cases 1, 5, 11, 13, 15), was correctly predicted in four of this group (cases 1, 11, 13, 15) by comparing the postoperative exercise scan with the postoperative rest study. One patient (case 10) had graft patency correctly pre-

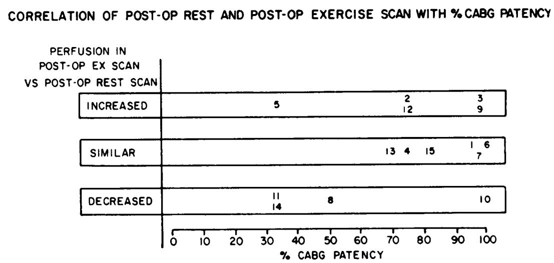

Fig. 5 *Correlation of postoperative rest and exercise scans with percentage of graft patency.*

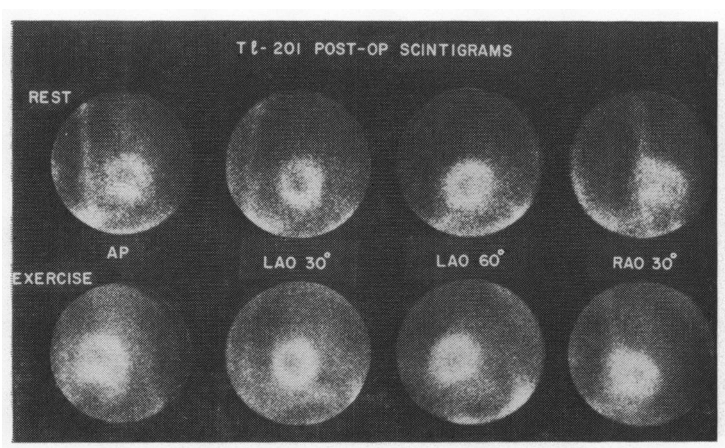

Fig. 6 *^{201}Tl postoperative rest and exercise myocardial scintigrams—all grafts patent.* Note—*the apical defect present at rest remains unchanged on exercise.*

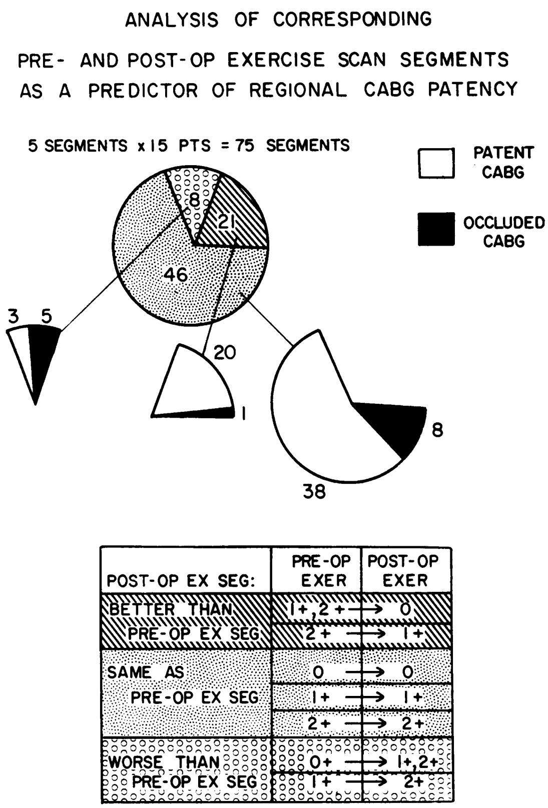

Fig. 7 *Value of corresponding pre- and postoperative myocardial scintigraphic segments as predictors of graft patency.*

dicted by pre- and postoperative exercise scan comparison and not by postoperative rest-exercise analysis. In nine patients (cases 2, 3, 4, 6, 7, 8, 9, 12, 14), graft patency was correctly predicted by both methods.

(G) COMPARISON OF PRE- AND POSTOPERATIVE EXERCISE SEGMENTS AND REGIONAL GRAFT PATENCY

Fig. 7 shows the relation between a comparison of corresponding pre- and postoperative exercise segments and patency in grafts defined as supplying those specific segments (see Methods). Of 21 postoperative segments having a grading better than the corresponding preoperative exercise segment, 20 were supplied by patent grafts. Of eight postoperative segments having a worse grading than the corresponding preoperative exercise segment, five were supplied by occluded grafts; 38 of 46 segments unchanged postoperatively were supplied by patent grafts.

In Fig. 8 large apical and inferior preoperative exercise-induced defects, respectively, are smaller and absent in the postoperative exercise scan. Both segments were supplied by patent grafts.

Discussion

This study confirms the useful role of myocardial perfusion imaging in the non-invasive assessment of coronary artery bypass graft patency. High ($\geqslant$67%) or low ($\leqslant$50%) graft patency rates were correctly predicted in 13 of 15 patients (87%) from postoperative rest-exercise scan analysis. This compared with only four of 15 (27%) correct predictions using pre- and postoperative multistage exercise electrocardiographic data.

Initially, we had expected that new or larger postoperative exercise-induced defects would closely correlate with significant graft occlusion, as has been shown by other investigators (Ritchie *et al.*, 1977a; Greenberg *et al.*, 1978). However, we found only a weak association (3/7 with significant graft occlusion if such defects were present *vs.* 1/8 if they were not) between these variables. Occlusive lesions

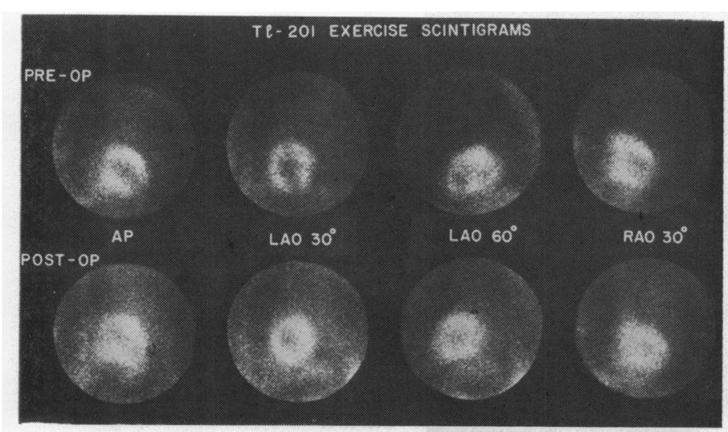

Fig. 8 *^{201}Tl pre- and postoperative exercise myocardial scintigrams. Apical and inferior uptake defects before operation are respectively smaller or absent after surgery. Both segments were supplied by patent grafts.*

in coronary arteries which were not bypassed or patent grafts to coronary arteries with significant occlusions distal to the sites of anastomoses, both uncommon in our study (Table), have been suggested as possible explanations for new postoperative exercise-induced defects in patients with patent grafts (Ritchie *et al.,* 1977a). Four of seven patients with such defects did not have significant graft occlusion; in fact, we were surprised to note that in all four patency of all the grafts positioned was found at the postoperative catheterisation studies. This suggests that despite patent grafts, certain patients may still develop new or larger perfusion defects on exercise possibly as a result of regional maldistribution of blood flow at high myocardial work loads. As already noted, 14 of 15 patients were able to perform greater amounts of exercise in the postoperative as compared with preoperative multistage exercise treadmill testing studies.

A further unexpected finding was 11 new or larger segmental postoperative rest defects in nine patients. Only two of these developed perioperative myocardial infarction in the distribution of the segment in question, and 10 of 11 of these segments were supplied by patent grafts. One explanation for this phenomenon is that the increased ^{201}Tl uptake in the adjacent myocardium as a result of enhanced blood flow via patent grafts may have caused small or difficult to recognise preoperative resting defects easier to recognise postoperatively because of the greater relative difference in counts between the two areas which followed aortocoronary artery bypass graft surgery. On the other hand, Bulkley and Hutchins (1977), who studied the hearts of patients dying soon after surgery, noted areas of myocardial damage in the distribution of patent grafts suggesting the possibility of reperfusion necrosis occurring in segments of the myocardium subjected to a sudden new blood flow through the graft at the end of cardiopulmonary bypass. It is possible, therefore, that intraoperative myocardial injury, not recognisable by infarct detection techniques currently in use, may be responsible for some of these new or larger postoperative rest defects; cardiac imaging, therefore, may have an important additional role in assessing techniques for the preservation of myocardial integrity during surgery.

In contrast, we presume that the seven segments in the five patients with smaller or absent postoperative rest defects when compared with preoperative rest studies represent regions of the myocardium with improved postperative resting flow. No perioperative myocardial infarction occurred in these patients, and all the segments were supplied by patent grafts.

Eight patients had 'increased' perfusion in the postoperative exercise scans. All had high graft patency rates, and all were able to achieve a higher exercise load postoperatively. In contrast, the two patients with 'decreased' perfusion had low graft patency rates. No clear pattern of graft patency emerged in the five patients with 'similar' perfusion in pre- and postoperative exercise scans (Fig. 3).

When postoperative rest and exercise scans were compared, 10 of 11 patients with 'similar' (six patients) or 'increased' (five patients) perfusion had high graft patency rates (1 to 67%, 3 to 75%, 1 to 80%, 5 to 100%); three of four with 'decreased' perfusion had a low patency rate (2 to 33%, 1 to 50%) (Fig. 5). The phenomenon of smaller or absent perfusion defects with exercise, which may be secondary to increased postoperative perfusion through patent grafts or via collaterals, has been noted previously (Strauss and Pitt, 1977). Whatever the mechanism, our results support the assumption that patients showing this phenomenon, as well as those who have no decrease in perfusion in postoperative rest and exercise scan comparisons, probably have patent grafts. Those whose postoperative studies show diminished perfusion with exercise are likely to have occluded or poorly functioning grafts.

Recognising that our assigning blood flow from specific coronary bypass grafts to scintigraphic segments is arbitrary, nevertheless, no fewer than 20 of 21 segments with smaller or absent perfusion defects in postoperative exercise segments were actually supplied by patent grafts. Prediction of occluded grafts was, however, unreliable, being present in five of eight segments with larger postoperative exercise defects when compared with preoperative exercise studies. No predictions could be made regarding graft patency in the 46 segments demonstrating no change in perfusion in pre- and postoperative exercise scans (Fig. 7).

Several limitations of our approach to the non-invasive predictions of graft patency should be recognised. First the selection of $\geqslant$67 per cent as high and $\leqslant$50 per cent as low graft patency is clearly arbitrary, and may have little clinical meaning for the individual patient with postoperative chest pain. As can be seen from Fig. 3 and 5, however, these criteria do represent a natural division in our data, and may be useful for group analysis. In addition, though the results of this study are in general agreement with previously published reports (Ormand *et al.,* 1977; Ritchie *et al.,* 1977a; Greenberg *et al.,* 1978), the number of patients in all of these studies, including our own, is small, indicating the need for further comparative studies. The cost of ^{201}Tl myocardial scintigraphy is not trivial, and a high degree of sensitivity and specificity will have to be shown before this or similar isotopic imaging techniques can be accepted as a standard diagnostic procedure. Finally, the ability of imaging to predict regional graft patency was limited to 21 of 75 segments and the technique failed to predict graft occlusion reliably. In 46 of 75 segments imaging could not indicate graft status.

Despite these problems we were able in this study to predict high and low degrees of graft patency in 10 of 15 patients by comparing pre- and post-operative exercise ^{201}Tl scans, and in 13 of 15 patients by postoperative rest and exercise scan comparisons. As noted above, while regional graft patency could be assessed by the finding of a smaller or absent segmental postoperative exercise defect compared with the corresponding preoperative exercise segment, regional graft occlusion could not be reliably predicted. New or larger perfusion defects occurring in postoperative exercise scans were not by themselves sufficient to predict graft status.

Thus at present it appears that high rates of graft patency can now be separated from low patency rates by ^{201}Tl imaging. The development of further refinements in imaging techniques should permit this type of investigation to provide the clinician with a reliable method of evaluating the results of aortocoronary bypass graft surgery in a non-invasive fashion.

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Requests for reprints to Dr Leon Resnekov, Hospital Box 423, University of Chicago Medical Center, 950 East 59th Street, Chicago, Illinois 60637, USA.