Rest and Exercise Potassium-43 Myocardial Perfusion Imaging for the Noninvasive Evaluation of Aortocoronary Bypass Surgery


SUMMARY

Sixteen patients undergoing aortocoronary bypass surgery were evaluated with rest and exercise potassium-43 (43K) myocardial imaging and contrast angiography an average of 5.5 months postoperatively. The results of 43K imaging allowed the division of these patients into two groups. Group I consisted of patients in whom there was either normalization or significant improvement in postoperative images when compared to abnormal preoperative studies (five patients), or patients in whom preoperative imaging was not accomplished but whose postoperative images both at rest and exercise showed a normal homogeneous pattern of 43K distribution (four patients). All patients in this group had at least one patent bypass graft, and 13 of 16 total grafts were patent. Group 2 consisted of seven patients in whom postoperative rest and exercise 43K studies were either not significantly different from preoperative evaluation, or had worsened. Of these patients, three experienced intraoperative infarction, two demonstrated significant distal native coronary disease, and one had a single occluded graft. In both groups there was good correlation between the anatomic sites of graft patency or occlusion and the location of either increased perfusion or lack thereof on the 43K image. Perfusion abnormalities occurring in the presence of occluded grafts, or improvement in perfusion occurring in the presence of patent grafts were best appreciated by comparison of exercise images. Abnormalities occurring in the presence of infarction were detected at rest as well. Thus, in this initial group of patients, 43K rest and exercise myocardial imaging appeared to offer a sensitive noninvasive means of evaluating the results of aortocoronary bypass surgery.

Additional Indexing Words:
Exercise testing Heart scan Myocardial revascularization Radioisotope techniques Rectilinear scanner

The introduction of aortocoronary bypass surgery has greatly altered the therapeutic approach toward patients with angina pectoris. However, the symptomatic improve-

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nature and inherent risks of catheterization prohibit the use of this procedure for long term sequential evaluation. We have recently described a noninvasive method for evaluating regional myocardial perfusion and detecting myocardial ischemia. The technique is that of precordial imaging following the intravenous injection of potassium-43 ($^{43}$K) at rest and during treadmill exercise. This report describes our initial experience with this technique in assessing the results of aortocoronary bypass surgery.

Methods

Patient Selection

The 16 postoperative patients comprising this study group were selected from among 60 patients from our institution in whom aortocoronary bypass surgery was undertaken for the treatment of angina pectoris refractory to nitrite and propranolol therapy. These 16 patients do not represent a consecutive series and were selected without regard to postoperative symptoms by the following criteria: (1) absence of a major documented transmural myocardial infarction preoperatively (defined by Q waves of at least 0.04 sec in at least two leads); (2) absence of associated valvular or congenital disease, or significant left ventricular dysfunction, that required an additional cardiac surgical procedure; and (3) willingness to undergo postoperative cardiac catheterization and angiographic evaluation, and exercise testing. Sequential pre and postoperative $^{43}$K myocardial imaging studies both at rest and exercise were obtained in 12 of the patients. Four patients in whom the postoperative rest and exercise $^{43}$K study was normal, but who were not imaged preoperatively, completed the group. Patients with abnormal postoperative $^{43}$K studies in whom preoperative imaging data were unavailable were not included, since there was no means of assessing or inferring change in the image.

The 16 patients in this study received 24 bypass grafts. Ten received single grafts, four double grafts, and two triple grafts. Eleven grafts were to the left anterior descending coronary artery, nine to the right coronary artery, and four to the circumflex coronary artery. Three of the left anterior descending grafts were internal mammary to coronary artery anastomoses; the remaining grafts were all of the saphenous vein type. Postoperative evaluation was undertaken an average of 5.5 months following surgery (range 1-16 months).

Cardiac Catheterization and Angiography

Preoperative laboratory evaluation included right and retrograde left heart catheterization, selective right and left coronary cineangiography on 35 mm film in multiple projections, and biplane left ventricular cineangiography. The postoperative study included selective opacification of individual grafts which, if patent, allowed visualization as well of the native circulation distal to the site of anastomosis. If selective injection of a graft was not possible, an assessment as to graft patency or occlusion was made from an aortic root angiogram with the catheter positioned just above the aortic valve. Selective catheterization of the native circulation was accomplished in 10 of 16 patients, including all patients in whom a bypass graft was occluded. Postoperative left ventriculograms were performed in 10 of 16 patients.

Angiographic studies were independently interpreted by two of the authors. Arterial stenosis was considered hemodynamically significant if greater than 70% of the luminal diameter was compromised. Left ventriculograms were evaluated for the presence of dyssynergy by both qualitative assessment and superimposition of traced outlines of end systolic and end diastolic cavity silhouettes.

Potassium-43 Myocardial Imaging

Potassium-43 myocardial imaging studies consisted of two parts: a resting study, with $^{43}$K injected intravenously and distributed within the left ventricular myocardium with the patient in a resting state; and an exercise study in which the radioactive tracer was injected during maximal treadmill exercise. Abnormalities present in myocardial images obtained in the resting state can be related to the presence, location and extent of myocardial infarction. Abnormalities present only in the myocardial image obtained following maximal exercise can be related to the presence, site and extent of regional perfusion abnormalities associated with stress induced angina pectoris. Although further experimental validation is required, data obtained in this manner have been shown to correlate well with coronary arteriographic and left ventriculographic abnormalities in man. The procedure has been associated with a low incidence of false-negative results and no false-positive results to date.

In view of the 22.4 hour physical half-life of the tracer, rest and exercise studies were separated by at least four days. This minimized residual activity present from the initial study. The radioisotope dose used for each study was approximately one mCi. For the resting study, $^{43}$K was injected intravenously with the patient upright after a 12-24 hour fast. In this manner splanchic blood flow and resultant subdiaphragmatic radionuclide accumulation are reduced.

For the exercise study, maximal graded exercise stress testing was performed in a standard fashion on a motorized treadmill. Increments in rate and incline occurred at three minute intervals. The initial rate was 1.7 mph at a grade of 10% with stepwise increases to a potential maximum of 6.0 mph at 20% grade during the sixth and final stage. ECG monitoring was constant, employing a four lead system with positioning of unipolar recording electrodes at standard positions $V_1$ and $V_4$, over the xyphoid, and at the suprasternal notch. Patients were exercised to the point of severe fatigue or angina pectoris. At this time $^{43}$K was injected intravenously. Exercise was then continued for an additional 30-45 sec, allowing for essentially complete intracellular distribution of the radioactive tracer during exercise. The patient was then immediately transported to the adjacent scanning laboratory where myocardial imaging was accomplished.
Imaging was performed with a rectilinear scanner (Picker Magnascanner 500) with a five inch crystal and a 31 hole Picker Model 2122 collimator. A 0.34-0.70 MeV window was employed. Scanning was accomplished at a count density of 1000 with contrast enhancement (40% count rate differential). Duplicate images were obtained in both anterior and 40-50° left anterior oblique positions.

Images were interpreted by two of the authors who were not present at the time of the exercise procedure, and who were not aware of the clinical diagnosis or arteriographic findings if such were already available. In 13 of 16 patients, postoperative 43K studies were performed and interpreted prior to angiographic evaluation. A qualitative assessment of the images was made as to whether 43K activity within the visualized myocardium was homogenous (normal), or whether "cold" regions of relatively decreased tracer activity were present (abnormal).

Results

Clinical and Angiographic Evaluation

Postoperatively, 11 of 16 patients noted either a marked decrease in frequency and severity of angina pectoris or were entirely asymptomatic. In two patients there was a mild but definite clinical improvement, and three patients were unimproved. A clinical diagnosis of postoperative myocardial infarction was made in three patients on the basis of the development of Q waves of greater than 0.04 seconds duration in at least two leads. In another patient myocardial infarction was suspected on the basis of loss of R wave voltage in the right precordial leads.

Eighteen of 24 bypass grafts were angiographically patent at the time of postoperative evaluation. Patency with respect to individual vessels was as follows: left anterior descending, 8 of 11; right coronary, 7 of 9; and circumflex coronary artery, 3 of 4. Thirty of 16 patients had at least one patent graft. Three of 10 patients with single grafts had graft occlusion, and two of these three patients were asymptomatic. Both of these two asymptomatic patients sustained an intraoperative infarction. In two patients, patient grafts were associated with significant obstructive distal coronary disease and poor "runoff"; neither was symptomatically improved postoperatively. Left ventriculography demonstrated significant segmental akinesis in four patients, confirming the suspicion of myocardial infarction, and was otherwise unchanged in the remaining patients studied.

Potassium-43 Imaging

On the basis of the results of postoperative 43K imaging, patients could be divided into two groups (table 1). Group 1 consisted of patients in whom preoperative imaging was not accomplished but whose postoperative myocardial images both at rest and exercise showed a normal homogenous pattern of 43K distribution (four patients); or patients in whom there was either normalization or significant improvement in postoperative exercise images when compared to their abnormal preoperative perfusion scans (five patients; figs. 1, 2). In the latter five patients, preoperative resting images were normal, and abnormalities were apparent only in exercise images. One patient in this group postoperatively demonstrated evidence of intercurrent anteroseptal infarction on his resting image, but nevertheless showed improvement in the postoperative exercise image. Of this total group of 9 patients, four had patent single grafts, two had patent double grafts, one patient had one of two grafts patent, and two patients had two of three grafts patent. There was good correlation between the anatomic location of initial coronary artery stenoses and preoperative exercise 43K image abnormalities, and also between angiographically demonstrable graft patency and the anatomic site of increased perfusion postoperatively. All patients in this group were clinically improved.

Group 2 consisted of seven patients in whom postoperative rest and exercise 43K studies were either not significantly different from preoperative evaluation, or had worsened. Of these patients, three experienced intraoperative myocardial infarction (two patients with occluded single grafts, and one with a patent single graft; figs. 3, 4). All three of these patients with postoperative infarction noted significant symptomatic improvement, as well as increased exercise tolerance. Two of the remaining four patients had patent grafts with poor distal runoff or new occlusive native coronary disease distal to the site of saphenous vein anastomosis. In both patients, exercise 43K images were unchanged postoperatively and both were unimproved clinically (fig. 5). One patient had a single occluded graft without infarction. This patient demonstrated persistence of exercise scan abnormalities (fig. 6), and was not improved clinically. The final patient in this group had a single patent right coronary artery graft into a region which was the best perfused preoperatively, as well as inoperable occlusive disease of the left anterior descending and circumflex coronary arteries. Exercise images in this patient were also unchanged postoperatively in the presence of mild symptomatic improvement. In group 2 there was also good anatomic correlation between sites of abnormal perfusion and coronary
Table 1

Postoperative Clinical Status, Angiographic and Myocardial Imaging Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Postoperative angiogram</th>
<th>Postoperative 43K</th>
<th>Clinical status</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Patent single RCA graft. LV normal.</td>
<td>Normal</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>5</td>
<td>Patent single LAD graft. LV normal.</td>
<td>Normal</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>8</td>
<td>Patent LAD graft. Ocluded RCA graft. CIRC obstructed.</td>
<td>Less abnormality; improved in LAD distribution</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>9</td>
<td>Patent single LAD graft. LV normal.</td>
<td>Normal</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>11</td>
<td>Patent single LAD graft. LV normal.</td>
<td>Normal</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>12</td>
<td>Patent RCA and CIRC grafts. Stenotic LAD graft. LV shows ASMI.</td>
<td>Markedly improved; small ASMI present on resting image</td>
<td>Marked improvement</td>
</tr>
<tr>
<td>13</td>
<td>Patent LAD and RCA grafts. Ocluded CIRC graft. LV normal.</td>
<td>Markedly improved</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>15</td>
<td>Patent LAD and CIRC grafts. RCA inoperable and occluded.</td>
<td>Markedly improved</td>
<td>Marked improvement</td>
</tr>
<tr>
<td>16</td>
<td>Patent RCA and CIRC grafts. LV normal.</td>
<td>Normal</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>1</td>
<td>Patent RCA graft. LAD, CIRC inoperable. LV normal.</td>
<td>Abnormal</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>3</td>
<td>Patent RCA graft with new distal RCA disease. LAD inoperable. LV unchanged.</td>
<td>Abnormal</td>
<td>Unimproved</td>
</tr>
<tr>
<td>4</td>
<td>Ocluded LAD graft. CIRC inoperable. LV unchanged.</td>
<td>Abnormal</td>
<td>Unimproved</td>
</tr>
<tr>
<td>6</td>
<td>Patent LAD, RCA grafts with poor &quot;runoff.&quot; LV unchanged.</td>
<td>Abnormal</td>
<td>Unimproved</td>
</tr>
<tr>
<td>7</td>
<td>Ocluded LAD graft. LV shows new ASMI.</td>
<td>Abnormal, unchanged at exercise. ASMI present at rest</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>10</td>
<td>Ocluded RCA graft. LV shows IMI.</td>
<td>Abnormal, unchanged; IMI at rest</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>14</td>
<td>Patent LAD graft. LV shows ASMI.</td>
<td>Abnormal, ASMI at rest.</td>
<td>Marked improvement</td>
</tr>
</tbody>
</table>

Abbreviations: RCA = right coronary artery; LAD = left anterior descending coronary artery; CIRC = circumflex coronary artery; LV = left ventricular cineangiogram; ASMI = anteroseptal myocardial infarction; IMI = inferior myocardial infarction.

arterial stenoses. It should be emphasized that in the absence of infarction, abnormalities present in patients with either occluded grafts or distal native vessel disease could only be appreciated in exercise images.

Exercise Testing

Preoperative exercise tests (usually performed in conjunction with 43K imaging) were available in 13 of 16 patients (10 improved and three unimproved patients; table 2). Postoperative exercise studies were available in all 16 patients. Postoperative exercise tests were electrocardiographically positive (defined by at least 1 mm of persistent flat or downsloping ST segment depression for at least 0.08 seconds in a lead with an isoelectric ST segment and upright T wave in the control tracing), or produced ischemic chest pain in only two of 13...
Preoperative (left) and postoperative (right) exercise ⁴¹⁳I images in the anterior view on a patient (§12) with widely patent right and circumflex grafts and an anterior descending graft which had a 50-70% stenosis at the site of distal anastomosis. Note the significant increase in anterolateral wall radiomucide accumulation due to increased perfusion postoperatively.

clinically improved patients. This is in contrast to findings preoperatively where all 10 patients so studied demonstrated either chest pain or ischemic ST segment changes, or both with exercise. When pre and postoperative exercise tests were compared in these patients, mean heart rate significantly increased following surgery (135 beats/min versus 145 beats/min, \( P < 0.05 \)), while mean duration of exercise was unchanged (six versus seven minutes). The three unimproved patients all demonstrated typical chest pain and abnormal ST segment changes postoperatively and had no significant change in duration of exercise or achieved heart rate.

No complications were encountered when, in accordance with the ⁴¹⁳I protocol, exercise was continued 30-45 seconds after the onset of chest pain or fatigue. Likewise, in a series of 55 patients with coronary heart disease similarly studied, no complication occurred during exercise testing.

Discussion

Although initial results of aortocoronary bypass surgery indicate that the majority of revascularized patients experience improved quality of life and

Postoperative left ventriculogram in the same patient (§14), whose myocardial images were shown in figure 3. An end diastolic frame is shown on the left, end systolic frame in the middle, and superimposed outlines of both on the right. Note the anteroapical region of akinesis corresponding to the intraoperative myocardial infarction. The infarction could not be definitively diagnosed by electrocardiographic changes.
Figure 5

Preoperative rest and exercise anterior view 43K images shown on the left and postoperative exercise image shown on the right in patient #3 with a patent right bypass graft and progression of distal native right coronary disease. Note the absence of improvement in the postoperative exercise image.

diminution of symptoms, several more years of observation and detailed evaluation will be necessary in order to establish the incidence of complications and long term prognosis associated with this surgical procedure. Repeated sequential postoperative evaluations in the catheterization laboratory require repeated hospitalization at considerable cost, are not without risk, and are particularly difficult to justify in the asymptomatic patient. If comparable data could be obtained by a noninvasive technique, it would be of considerable value, both for performing sequential long term studies and for selection of individual postoperative patients for further catheterization evaluation. This report demonstrates the feasibility of rest and exercise 43K myocardial imaging as such a noninvasive technique for evaluating postoperative aortocoronary bypass patients.

The results of 43K myocardial imaging generally correlate with clinical evaluation and exercise testing of patients who have had coronary artery bypass procedures. However, this technique also adds another dimension: an assessment of regional muscular viability by localizing that which is transiently ischemic and distinguishing it from muscle which has been infarcted and is fibrotic. As noted in three patients in this series, abnormal images could be demonstrated in the face of decreased or absent symptoms and increased exercise tolerance, resulting not from increased blood flow, but rather from infarction in the presence of either occluded or patent grafts. Similarly, abnormal images were recorded in patients with patent grafts but persistent myocardial ischemia due to distal obstructive lesions in the

Table 2

Exercise Data in 16 Postoperative Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Preoperative exercise test</th>
<th>Postoperative exercise test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duration (min)</td>
<td>Maximum heart rate</td>
</tr>
<tr>
<td>2</td>
<td>N.D.</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>N.D.</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>110</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>143</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>125</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
<td>111</td>
</tr>
<tr>
<td>13</td>
<td>6</td>
<td>115</td>
</tr>
<tr>
<td>15</td>
<td>7</td>
<td>158</td>
</tr>
<tr>
<td>16</td>
<td>N.D.</td>
<td>5</td>
</tr>
</tbody>
</table>

Group 1

| 1       | 4               | 140              | Yes         | Yes         | 6              | 150         | Yes         | Yes          |
| 3       | 7               | 125              | Yes         | Yes         | 6              | 125         | Yes         | Yes          |
| 4       | 4               | 150              | Yes         | Yes         | 5              | 150         | Yes         | Yes          |
| 6       | 7               | 165              | Yes         | Yes         | 5              | 177         | Yes         | Yes          |
| 7       | 7               | 150              | Yes         | Yes         | 7              | 167         | No          | No          |
| 10      | 6               | 150              | Yes         | RBBB        | 7              | 158         | No          | RBBB         |
| 14      | 9               | 143              | Yes         | Yes         | 9              | 158         | No          | No          |

Group 2

Abbreviations: N.D. = Not done; RBBB = rate related right bundle branch block.

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native coronary arteries. On the other hand, no patient with a patent graft and normal distal coronary vessels demonstrated an abnormality in the distribution of the graft; and no patient with graft occlusion demonstrated normal perfusion in the corresponding myocardial region.

The correlation between $^{43}$K myocardial imaging at rest and exercise and contrast angiography presented in this group of patients is comparable to that reported previously in patients with coronary heart disease and angina pectoris, where in 55 patients there was only one false-negative and one equivocal exercise $^{43}$K image. A similar correlation has been noted in patients with false-positive exercise tests and normal coronary angiograms, in whom all exercise $^{43}$K images have been normal. The reproducibility of this technique has been previously demonstrated. The potential difficulties of concealment of ischemic zones by overlying normal myocardial activity, and of distinguishing the normal central cavitary zone of decreased activity from ischemic zones, have been minimized when careful attention to technique has been followed and imaging in multiple views has been employed.

Resolution is not as yet ideal, but has been sufficient for visualization of abnormalities in major coronary vascular beds. Future advances in both instrumentation design and collimation, together with computer analysis of data, will probably lead to improved resolution, and should also allow the acquisition of quantitative dynamic measurements.

Our results are in contrast to those presented by Bennett et al. who have claimed to distinguish increased $^{43}$K perfusion in patients at rest following aortocoronary bypass graft surgery. In our experience abnormalities in resting radioisotope myocardial images have been associated with myocardial infarction rather than transient ischemia. Transiently ischemic left ventricular regions, to which bypass grafts are made, can best be identified only when the tracer has been distributed during stress related hypoperfusion sufficient to induce clinical angina pectoris. Blood flow to these regions is normal or near normal at rest, and is relatively decreased with resultant inadequate myocardial oxygenation only when such a stress is imposed. This concept is supported by experimental data in the dog obtained by Gould et al., as well as by the demonstration of normal perfusion patterns at rest in patients with coronary heart disease and no infarction in whom the intracoronary injection of tracers have been made.

Although our results appear promising, it must be emphasized that as yet only a small number of patients from a markedly heterogeneous group have been studied. A larger volume of data will be required to establish the imaging patterns and reliability of this technique in the various situations resulting from combinations of individual patent and occluded grafts, alone and in combination with associated myocardial infarction and progressive or new native coronary arterial disease. The results of this study, however, do demonstrate the potential value of this method for sequentially studying the results of aortocoronary bypass surgery in a totally noninvasive manner. Present practical limitations of the technique center about the current relative high cost of the cyclotron produced radionuclide, and the need for a closely coordinated effort between the clinical cardiologist and the specialist in nuclear medicine. The radioactive tracer can, however, be obtained commercially for investigational use, the equipment employed is simple, and most importantly, the procedure is safe.

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References

7. Strauss HW, Zaret BL, Martin ND, Wells HP Jr, Flamm MD Jr: Noninvasive evaluation of regional
9. ZARET BL, MARTIN ND, FLAMM MD Jr: Myocardial imaging for the noninvasive evaluation of regional perfusion at rest and following exercise. In Nuclear Cardiology, edited by STRAUSS HW, PIT B, JAMES AE. St. Louis, CV Mosby, In press
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