10 Myocardial Perfusion Imaging with Rubidium 82 Positron Emission Tomography

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Report

The noninvasive evaluation of patients with known or suspected coronary artery disease (CAD) has helped to identify patients who are at high risk for cardiac events. The information provided by the images of myocardial perfusion by radioluminescence complements the anatomical information obtained by coronary arteriography by lending physiologic significance to the visualized coronary stenoses, especially the detection of ischemic myocardium with exercise. Positron emission tomography (PET) with rubidium 82 (82Rb) as the radionuclide has been used in some cardiac centers for the imaging of the heart and the detection of ischemic myocardium. Whether this method is superior to the more widely used planar thallium 201 (201TI) scintigraphy or the imaging of 201TI distribution by single photon emission computed tomography (SPECT) for the evaluation of cardiac patients and the identification of high-risk patients is the subject of this review.

The noninvasive imaging of the perfusion of the heart was initially done about 20 years ago by planar (201TI) scintigraphy. By this technique, the distribution of the radiation from the intravenously administered (201TI) in the myocardium was measured by external detectors and projected as a two-dimensional image of the heart that showed ischemic areas by a decrease or absence of (201TI) in areas with compromised perfusion. Images obtained after exercise were invaluable in the assessment of the adequacy or inadequacy of the coronary circulation because they revealed ischemic areas that may develop with exertion. The difficulties of underestimating the extent of CAD caused by the unavoidable overlap of parts of the heart in a two-dimensional projection and the relatively poor quality of the images were addressed to some degree by using a rotational detector and obtaining a three-dimensional image of the myocardial distribution of (201TI) by the improved method of SPECT. The use of (82Rb) PET represents a further improvement in the three-dimensional coronary imaging of the perfusion of the heart, mainly as the result of the higher energy and characteristic of the radiation that results from the annihilation of the positrons emitted by (82Rb).

The higher energy radiation yields images with higher resolution and more contrast than those obtained with (201TI). The directional character of the emitted radiation with (82Rb) allows better positioning and selection of the patients for the attenuation correction with both (201TI)/SPECT have led to occasional difficulties in interpreting the images of obese patients, of those with large breasts, or of those having circulatory problems in the posterior-inferior regions of the heart.

Although it is apparent that (201TI) SPECT imaging has advantages over planar (201TI) scintigraphy for revealing areas of ischemic myocardium, (2) it is more difficult to determine whether (82Rb) PET is better than (201TI) SPECT for the evaluation and management of patients with CAD. Data such as those reported in the only two studies where results of (82Rb) PET were compared conducted clinically to the uncertainty about the difference between the two methods. (3,4) In the first study of 202 patients, Go et al.(3) showed some difference in the sensitivities and no difference in the specificities, whereas in the second study of 81 patients, Stewart et al.(4) showed no difference in the sensitivities but a significant difference in the specificities when the results with (82Rb) PET were compared with those with (201TI).

Go et al.(3) reported a prospective comparison of (82Rb) PET and (201TI) SPECT for myocardial perfusion imaging in 202 consecutive patients who were referred to their PET imaging laboratory. All patients had a coronary arteriogram done within 6 months of the imaging procedure. Approximately three-quarters of the patients were classified as having significant CAD (stenosis equal to or more than 50 percent). 95 (47 percent) had a previous myocardial infarction (MI), and 70 (35 percent) had a coronary bypass and/or angioplasty. Each patient had a resting (82Rb) image done and was then given a dose of dipyridamole to induce coronary vasodilation before starting the isometric hand-grip exercise. Stress (82Rb) image data were collected at the height of the exercise. (201TI) SPECT data were collected after the images obtained from all 202 patients showed that the sensitivity and specificity for (82Rb) PET was 93 percent and 78 percent, respectively, whereas those for (201TI) were 71 percent and 76 percent, respectively. These findings indicated that the sensitivity of (82Rb) was better than that of (201TI), but that the specificities of the two methods were nearly the same. Although the positive predictive values for (82Rb) PET were also diagnosed as false-negative by (82Rb). On the other hand, there were fewer false-positive results with (201TI) PET with (201TI) and with (201TI) and (82Rb).

Of interest was that a comparison of the imaging methods in the 120 patients who did not have either coronary bypass or angioplasty indicated that the difference in sensitivities between the two methods was less significant whereas the specificities remained similar and unchanged. These observations that (201TI) had a relatively high specificity that was similar to that with (82Rb) PET and had a lower sensitivity might be kept in mind as comparisons of the two methods are considered further.

Stewart et al.(4) also compared results obtained with the two imaging techniques in 81 patients selected from those who were referred to their diagnostic coronary angiography center. Patients with prior coronary bypass or angioplasty were excluded. Sixty patients (74 percent) had significant CAD with stenosis equal to or more than 50 percent, and 34 of these patients had a history of MI. All patients underwent double-dose infusion in combination with PET imaging, whereas about half of the patients underwent exercise (201TI) SPECT and the remaining half underwent dipyridamole (201TI) PET. In contrast to the observations of Go et al.(3) these authors found that both (82Rb) and (201TI) showed the same sensitivity of 84 percent, whereas the specificity with (201TI) was significantly lower at 53 percent as compared with a specificity of 85 percent with (82Rb) PET. It is to be noted that some or all of the data for specificity were obtained from patients with a low likelihood of CAD who were selected from patients who were undergoing (201TI) SPECT scan. Because it is possible that the bias may have occurred in the selection process and how the results with these patients were used in the determination of the specificity, the significance of the reported low specificity for (201TI) is not apparent.

A possible clinical benefit of (82Rb) imaging for the management of cardiac patients was discussed in a followup study of the 27 patients(5), who were false-negative for myocardial perfusion abnormalities with (201TI) imaging, but who showed to be true positive with (82Rb) imaging in the study of Go et al.(3). MacIntyre et al.(5) reported that 17 (63 percent) of these 27 patients went on to have surgical interventions (CABG) or percutaneous transluminal coronary angioplasty (PTCA), over a period of 2 weeks to 2.5 years after the initial PET-positive imaging. Twelve (71 percent) of the 17 had prior intervention or MI (5 had CABG, 3 had PTCA, 1 had both CABG and PTCA, and 3 had MI). Although the false-negative rate for (201TI) PET reported by Go et al.(3) may have been a little high, it would appear that the continued management of these CAD patients by attention to physical symptoms and other noninvasive tests of cardiac function, may have led to the same appropriate care for these (201TI) SPECT negative, patients regardless of the PET results. Because the authors did not discuss the bases for the decisions to proceed with the surgical interventions in the 17 patients, it would be difficult, as the authors state, to determine "what actual weight the PET scan had on the final decision."

The use of (82Rb) PET in a nonhospital-based center was retrospectively analyzed for 658 (39 percent) of the 1,670 patients who had both a PET scan and a coronary angiogram. Simone et al.(6) reported that the sensitivity of 83 percent and the specificity of 93 percent that were found for (82Rb) PET in this setting were comparable to those reported in the above studies. These findings were not particularly surprising, because most of their patients had severe CAD according to prior angiograms and this selection bias could account for the high values in this population. It is, therefore, difficult to interpret the reported results in terms of how useful (82Rb) PET might be, compared with evaluations with (201TI) scans, in the diagnostic workup and management of cardiac patients before invasive catheterization arteriography is used.

A review in some studies of myocardial perfusion imaging, Go et al.(7) began by stating that "thallium-201 imaging, originally viewed as a screening test, has evolved into a valuable modality for the diagnostic and management of coronary artery disease (CAD) and plays a significant role in the management and prognosis of this disease." They cited sensitivities ranging from 76 to 95 percent and specificities ranging from 44 to 62 percent for the diagnosis of CAD with (201TI) in seven referenced studies, and sensitivities of 94 to 98 percent and specificities of 93 to 100 percent for (82Rb) PET or nitrogen 13 (13N) ammonia PET in five referenced studies. They included more detailed discussions of the results from three studies(4,8,9), where (201TI) SPECT was compared with either (13N) ammonia PET or (82Rb) PET. Those studies included the two discussed above and one by Tamaki et al.(8), who compared the results of (201TI) SPECT with those of (13N) ammonia PET. Tamaki et al.(8) reported a sensitivity of 96 percent and a specificity of 100 percent for (201TI), which were virtually the same as the 98 percent and 100 percent reported by Go et al.(7). It might be noted that, contrary to the many high values (all but one obtained with the use of (13N) ammonia PET) cited by Go et al.(7), for PET, there were only two additional studies besides the two comparison studies discussed above.

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reported on the values obtained with (82)Rb PET. Grover-McKay et al.(16) reported a sensitivity of 76 percent and a specificity of 86 percent for (82)Rb PET which are in contrast with the corresponding values of 95 percent and 100 percent reported by Gould et al.(17). The high values obtained by Gould et al.(17) were for selected patients with severe CAD (stenosis of 75 percent or more). A lower sensitivity of 74 percent (51 percent or more stenosis) and specificity of 73 percent for (82)Rb PET were reported. The authors concluded that the use of (82)Rb PET allowed for the identification of patients who would significantly benefit from coronary revascularization. However, the utility of (82)Rb PET in the detection of myocardial ischemia is not apparent from the available data because the reported sensitivities and specificities with both methods vary over the same wide range which includes values that are 70 percent or more for specificity and 88 percent or more for sensitivity.

The higher pixel count possible with (82)Rb imaging and the truer representation of radiation emanating from the posterior-inferior myocardium or through "echoes" tissue may be advantageous for the use of (82)Rb PET over (201)Tl SPECT. However, some patients may have higher activity resulting in increased image noise which may reduce image quality. However, the worse visualization of myocardial tissue may be advantageous for the use of (82)Rb PET to evaluate the noninvasive imaging of the perfusion of the heart. However, appropriate data that demonstrate that the use of (82)Rb PET may be a better diagnostic method than (201)Tl SPECT for the detection of myocardial ischemia or (82)Rb PET is not available at this time. As the imaging technology improves and physicians are presented with a clearer image of myocardial tissue, consideration might be given to the role of noninvasive radionuclide imaging in the diagnosis and therapeutic management of CAD patients. Catherization of patients may be beneficial in those patients who present with signs of myocardial ischemia who have undergone noninvasive imaging. The true value of myocardial perfusion imaging is the visualization of blood flow and the function of the heart at rest and with stress in areas that may or may not coincide with symptoms seen by arteriography, which is of major physiological significance to the patient. Cardiologists have observed that areas that appear abnormal on arteriography are often completely normal and other areas that show no abnormality are visible in the perfusion imaging. These discrepancies between symptoms and ischemia may be the bases for some of the "false-negative" or "false-positive" findings that are reported in studies using arteriography as the "gold standard" for CAD. How frequently this may occur is not known. However, the conservative management of CAD patients who show no sign of myocardial ischemia by arteriography may not have serious consequences.

Brown and Rowen(81) reported on patients who had normal (201)Tl scintigraphy scans in spite of having severe CAD visible by arteriography. They evaluated the outcomes of 75 patients who had come to their clinic for the evaluation of chest pain and who were found to have normal exercise (201)Tl scintigraphy scans for over 2 years. In the group, consisting of 75 patients with significant angiographic CAD (50 percent or more stenosis in at least one major coronary artery), there was one nonfatal MI recorded at 28 months for a cardiac event and one death from cardiac cause. However, of the 75 patients, consisting of 37 with normal (201)Tl thallium-201 scans and 38 with pre- (201)Tl thallium-201, in the remaining 37, all of these patients had normal echocardiographic follow-up, indicating that the possibility of a cardiac event is less than 5 percent on the basis of clinical and exercise electrocardiographic data, there were two cardiac events (one nonfatal MI at 28 months and one cardiac death at 23 months) for a cardiac event rate of 1.0 percent/year. The results of the two groups suggest that CAD patients with normal (201)Tl thallium-201 scan may have a prognosis of a very low rate of hard cardiac events (nonfatal MI or cardiac death). It might be of interest to note that these results were made on the basis of normal scans by planar (201)Tl SPECT scintigraphy. These prognostic results and similar findings by many others, which were summarized in a review by Brown, (81) are consistent with the notion that (201)Tl thallium-201 PET and (82)Rb PET imaging may have been more sensitive in the detection of CAD and have helped to clarify this uncertainty. On the other hand, these observations suggest that appropriate care for cardiac patients may be available at centers using any of the noninvasive imaging methods. It is thus probable that, in the hands of properly experienced users, the use of any of the techniques will continue to provide the necessary information regarding cardiac perfusion for the appropriate management of CAD patients, without any apparent compromise of the well-being of patients. In this context, the patients with negative (201)Tl SPECT scans who were monitored by Macintyre et al.(82) may not have been at increased risk of having a cardiac event without surgical intervention.

The value of the noninvasive imaging of myocardial perfusion is high for the evaluation of patients who have chest pain and who may or may not have exertional angina and electrocardiographic changes with exercise. These methods have helped to identify some CAD patients who may need to be evaluated further by catheterization and arteriography. As more new information is accumulated, it may be possible to use the various diagnostic tests to identify reliably those patients who may benefit from surgical intervention and those who could be managed medically. Currently, there are insufficient data to accommodate this differentiation in all cases. As a result, patients who present with chest pain may be subjected to certain diagnostic procedures for the diagnosis of CAD. These diagnostic procedures are usually performed with the help of radionuclide imaging, which is a noninvasive method that allows for the visualization of the coronary arteries and their function. The images obtained with radionuclide imaging are used to evaluate the severity of coronary artery disease and to determine the presence or absence of myocardial ischemia. However, the clinical utility of radionuclide imaging has been questioned by some researchers who have suggested that the use of radionuclide imaging in the diagnosis of CAD may not be justified. This is because the images obtained with radionuclide imaging may not have serious consequences. However, the use of radionuclide imaging in the diagnosis of CAD has been shown to be helpful in the management of patients with coronary artery disease. In patients with coronary artery disease, radionuclide imaging can be used to evaluate the extent of the disease and to determine the presence or absence of myocardial ischemia. However, the clinical utility of radionuclide imaging has been questioned by some researchers who have suggested that the use of radionuclide imaging in the diagnosis of CAD may not be justified. This is because the images obtained with radionuclide imaging may not have serious consequences.

References

16. Kiatt H, Maddal J, Roy LI, et al. Comparison of technetium tetroxide and technetium nitrate imaging in the evaluation of coronary artery disease by planar and...


Table 1. Sensitivity and specificity for the diagnosis of coronary artery disease

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Patients (n)</th>
<th>Sensitivity (percent)</th>
<th>Specificity (percent)</th>
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</tr>
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<tbody>
<tr>
<td>(201)Tl SPECT</td>
<td>242</td>
<td>94</td>
<td>44</td>
<td>Van Train (9).</td>
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<tr>
<td>(201)Tl SPECT</td>
<td>360</td>
<td>78[a].</td>
<td>94[a].</td>
<td>Mahmarian(10).</td>
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<td>82</td>
<td>Iskandrian(11).</td>
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<td>80</td>
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<td>Kiat(12).</td>
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<tr>
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<td>183</td>
<td>95</td>
<td>56[b].</td>
<td>Maddah(13).</td>
</tr>
<tr>
<td>(201)Tl SPECT</td>
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<td>93</td>
<td>91</td>
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<td>58</td>
<td>88</td>
<td>93</td>
<td>Nohara(15).</td>
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<td>(82)Rb PET</td>
<td>31</td>
<td>76</td>
<td>86</td>
<td>Grover-McKay(16).</td>
</tr>
</tbody>
</table>

[a] Values for stenoses equal to or more than 50 percent. For stenoses equal to or more than 70 percent, the sensitivity was 89 percent and the specificity was 94 percent.
[b] Low value thought to be because of the influence of "patient referral bias."

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