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Editorial Comment

Assessing Prognosis by Means of Radionuclide Perfusion Imaging: What Technique and Which Variables Should Be Used?*

GEORGE A. BELLER, MD, FACC

Charlottesville, Virginia

The prognostic value of exercise and pharmacologic stress myocardial perfusion imaging has been established in thousands of patients evaluated in multiple clinical studies (1–5). The major prognostic variables on stress perfusion images predictive of future cardiac events are a large defect size (>25% of the left ventricle), defects in more than one coronary vascular supply region suggestive of multivessel coronary artery disease (CAD), defect reversibility reflective of inducible ischemia in multiple myocardial scan segments, a large number of nonreversible defects, transient or persistent left ventricular (LV) cavity dilation from stress to rest images, increased lung thallium-201 (Tl-201) uptake and a rest LV ejection fraction measured on gated single-photon emission computed tomography (SPECT) <40% (6–16). Data from a multicenter registry (17) comprising 8,408 symptomatic patients showed that the number of coronary vascular territories with ischemia (chi-square 40.1, $p < 0.0001$) and the number of territories with infarction (chi-square 55, $p < 0.0001$) were independent predictors of cardiac death at a mean follow-up of 2.6 years, even after adjusting for pretest risk. In that analysis, patients with three ischemic territories had a 5.2% mortality rate compared with 2.3% in patients with one ischemic vascular territory identified. Perhaps the most predictive nonimaging variable for future cardiac events is failure to attain a workload >6 metabolic equivalents (METS) (18). Other high exercise electrocardiographic (ECG) stress test variables are failure to attain ≥85% of maximal predicted heart rate for age, >2.0-mm horizontal or downsloping ST segment depression in multiple ECG leads and an inadequate blood pressure rise during exercise (1).

Incremental prognostic value of imaging variables. Numerous studies (19–24) have shown that incremental prognostic information is obtained when variables from stress myocardial perfusion imaging are added to information obtained solely from clinical and ECG stress test variables. Hachamovitch et al. (23) evaluated the incremental prognostic value of technetium-99m (Tc-99m) sestamibi SPECT imaging in 2,200 consecutive patients. When a stepwise Cox proportional hazards model and receiver operating characteristic curve analysis was used, nuclear testing added incremental prognostic value after inclusion of the most predictive clinical and exercise variables (global chi-square 12 for clinical variables, 31 for clinical plus exercise test variables and 169 for clinical plus exercise plus nuclear test variables). Some studies (15) have shown that when clinical, ECG stress test and scintigraphic variables are known, there is little additional prognostic information yielded by addition of coronary angiographic variables, such as the number of vessels with significant stenoses. Furthermore, recent data (23,25,26) have indicated that the extent of inducible hypoperfusion on post-stress SPECT perfusion images provides superior stratification of patients with stable chest pain attributed to known or suspected CAD into low and high risk groups than the Duke treadmill score. Hachamovitch et al. (23) found that in their study of 2,200 patients, 834 of 1,187 with an intermediate risk treadmill score had a normal Tc-99m sestamibi SPECT scan that was associated with a 0.4% rate of death or infarction during follow-up. Of the remaining patients with intermediate risk scores, the event rate was 6.4% and 8.9%, respectively, in patients with mild or severe SPECT defects. Approximately 50% of patients are classified in an intermediate risk category when the Duke treadmill score alone is used for prognostication, leaving the clinician with perhaps greater indecision regarding management strategy than before treadmill test referral (25).

Perhaps the most valuable contribution of exercise or pharmacologic stress imaging is its excellent negative predictive value for predicting a low event rate in patients with a normal scan on symptom-limited exercise testing or with vasodilator stress imaging (1,4,27–30). Patients with normal perfusion scans have a <1.0 cardiac death or nonfatal infarction rate per year, even if angiographic CAD has been demonstrated (31,32).

Tl-201 reinjection and defect reversibility. The identification of defect reversibility on stress and 4-h redistribution imaging can be enhanced by either quantitative scan analysis or reinjection of a second dose of Tl-201 at rest after acquisition of the delayed redistribution images (33–39). Application of "reinjection" Tl-201 imaging in the clinical setting has been directed toward improving the detection of viable myocardium in defects that appear to be persistent, suggesting myocardial scar, on stress and redistribution imaging. Dilsizian et al. (34) reported that 87% of myocardial regions showing reversibility after Tl-201 reinjection showed improved regional perfusion and function after coronary angioplasty. Bonow et al. (40) found an 88% concordancy rate between viability assessed on Tl-201 reinjection imaging and positron emission tomographic–fluorine-18 fluorodeoxyglucose evidence for viability in the same patients.

To date, scant data exist concerning the value of Tl-201

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From the Cardiovascular Division, Department of Medicine, University of Virginia Health Sciences Center, Charlottesville, Virginia.

Address for correspondence: Dr. George A. Beller, Cardiovascular Division, Box 158, University of Virginia Health Sciences Center, Charlottesville, Virginia 22908. E-mail: gbeller@virginia.edu.

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Abbreviations and Acronyms

ACME = Angioplasty Compared to Medicine (study)
CAD = coronary artery disease
ECG = electrocardiogram, electrocardiographic
LV = left ventricular
SPECT = single-photon emission computed tomography (tomographic)
Tc-99m = technetium-99m
Tl-201 = thallium-201

reinjection imaging to improve the prognostic value of conventional stress/redistribution perfusion imaging. The rationale for reinjection imaging for risk stratification is that the better the identification of defect reversibility, the greater should be separation of low and high risk subsets of patients with chronic CAD. This is because the number of reversible defects is directly related as a continuous variable to an increased incidence of subsequent cardiac events in patients treated medically (1–3).

Tl-201 reinjection to enhance prognostic value of stress perfusion imaging. In this issue of the Journal, Zafrir et al. (41) sought to retrospectively evaluate the prognostic utility of Tl-201 reinjection versus Tl-201 stress/redistribution imaging in the prediction of future cardiac events in 366 consecutive patients with chronic CAD who underwent either exercise or dipyridamole stress. Surprisingly, they found that Tl-201 reinjection did not contribute independent prognostic information for cardiac events when compared with stress/redistribution imaging, even though 107 patients showed defect reversibility only on reinjection images. There were 159 patients showing defect reversibility on delayed redistribution images, whereas 100 had only nonreversible defects. The death or nonfatal infarction rate was 12% in patients showing reversible defects by reinjection only and 12.6% in patients with reversible defects on redistribution images, values not significantly different than the 15% event rate in patients with solely nonreversible defects. Furthermore, in contrast to previously published observations, the number of reversible defects on either the redistribution or the reinjection images was not predictive of future cardiac events. There were only 0.8 reversible defects compared with 3.8 nonreversible defects/patient in the event group on stress/redistribution imaging. There were only 1.1 reversible defects/patient on reinjection images in the event group, whereas 2.7 defects/patient remained nonreversible. Thus, the majority of the overall defect size still comprised presumed scar after reinjection. Interestingly, the number of nonreversible defects/patient was significantly greater in the event group than the nonevent group on both redistribution and reinjection images. Total size of the post-stress defect (reversible and nonreversible), presence of LV cavity dilation and an increased lung/heart Tl-201 ratio (on exercise imaging) were also significant predictors of events. However, with respect to defect size, the breakpoint between high and low risk subsets only occurred at six or more defects (using a nine-segment model). The event rate in the 73 patients with five defects (>50% of the left ventricle) was no different than the event rate in the 53 patients with two defects (see Fig. 3, Zafrir et al. [41]). Thus, overall defect size was only discriminating when ≥60% of the left ventricle exhibited hypoperfusion on post-stress scintigrams.

Number of reversible Tl-201 defects and subsequent cardiac events. There are several possible explanations why defect reversibility and extent of reversible defects were not significant prognostic variables in the study of Zafrir et al. (41): First, 40 of the 48 events were cardiac death; 8 were nonfatal infarction. Late revascularization, an "ischemic" end point often used in prognostic studies, was not included in the criteria for future events. Cardiac death is more likely to be predicted by extent of myocardial scar, increased lung Tl-201 uptake and persistent LV cavity dilation, variables reflective of extent of myocardial damage and poor LV function, than by variables reflective of ischemia, such as defect reversibility and inducible ST segment depression. In fact, of the 48 patients who had an event in the study by Zafrir et al. (41), 29 had LV cavity dilation. The findings of the present study are consistent with those of Travin et al. (42) who reported that occurrence of nonfatal myocardial infarction during follow-up after exercise Tl-201 scintigraphy was most closely associated with the extent and severity of scintigraphic ischemia, whereas cardiac death was significantly associated with abnormal Tl-201 lung uptake and a low exercise workload. It should be stated that in the study by Zafrir et al. (41), the number of patients in event or nonevent groups with a previous myocardial infarction is not stated, but only 171 (47%) of the 366 patients had angina before stress testing, and <50% in the exercise group had inducible ST segment depression. Hence, this group of patients with CAD may have had a lower propensity for stress-related ischemia. This supposition is supported by the fact that only patients with some "fixed" perfusion defects on stress/redistribution imaging were included in the retrospective analysis. In contrast, in a different group of patients with one- or two-vessel disease entered into the Angioplasty Compared to Medicine (ACME) study (43), 6 (10%) of 59 patients with nonreversible defects and 26 (18%) of 146 patients with reversible defects died during follow-up. The mortality rate was 20% in patients with three or more reversible defects. Thus, the ACME patient group had a greater prevalence of subsequent cardiac deaths associated with ischemia than with extensive areas of scar.

Some methodologic issues may have contributed to the finding that the presence and extent of reversible defects were not predictive of death and nonfatal infarction in the study by Zafrir et al. (41). Planar and not SPECT imaging was used, and visual assessment and not quantitation was utilized for analysis of scans. Quantitative SPECT imaging is the most sensitive technique for identifying multiple zones of hypoperfusion and ischemia in the distribution of the three major coronary arteries and their branches (44). Quantitation of defect severity in the study by Zafrir et al. (41) might also have yielded information on whether the presence of mild to moderate

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nonreversible defects (>50% Tl-201 uptake vs. peak uptake) was more predictive of future events than severe nonreversible defects, which are more indicative of nonviability. Several studies (45–49) have suggested that patients with extensive areas of hibernation composed of viable myocardium have a high cardiac event rate with medical therapy during follow-up.

Normal patients or patients with a <5% pretest likelihood of CAD were not included in the study of Zafrir et al. (41); therefore the investigators interpreting the images knew that all images were acquired in patients with CAD and may have been unintentionally biased and overinterpreted reversibility on redistribution and reinjection images. This overinterpretation may be why as many as 266 patients were designated as showing "reversibility." Also, by not including low risk patients with a <5% likelihood of CAD or angiographically normal coronary arteries and normal scan results, the extent of ischemia or reversible defect size is more difficult to relate to subsequent events as a continuous variable. Most previous studies showing the prognostic value of the number of reversible defects included patients with normal scans and a very low event rate. In the study by Hachamovitch et al. (23), the event group had 3.9 reversible defects/patient versus 0.7 for the no-event group. Another possible explanation for lack of predictive power of defect reversibility in the study by Zafrir et al. (41) is that many patients were receiving anti-ischemic medications, such as beta-blockers, calcium antagonists and nitrates, at the time of testing. These drugs can diminish defect size on stress images and perhaps reduce the prevalence of defect reversibility.

One possible explanation for the lack of prognostic value of Tl-201 reinjection in the study of Zafrir et al. (41) is that majority of nonreversible defects seen on stress/redistribution imaging, in fact, did not show a substantial amount of reversibility after reinjection. In this study, reinjection of another rest dose of Tl-201 only reduced the average number of nonreversible defects from 3.8 to 2.7 in the event group and from 3.0 to 2.1 in the nonevent group, when the reinjection images were compared with the redistribution images. Thus, the amount of "new reversibility" identified by reinjection was modest. Reinjection may add most to the appreciation of defect reversibility in the visual assessment of SPECT images, where background suppression is usually used by the computer or imaging device to "clean up" the images and produce the clear high contrast defects that readers prefer for interpretation (50). This background suppression can obscure the visual detection of significant residual Tl-201 uptake in a defect area and can obscure the visual appreciation of subtle redistribution. With reinjection, the additional Tl-201 activity may be sufficient to bring the defect over the cutoff threshold of the imaging system so that residual activity becomes visible in the images. Zafrir et al. (41) used planar imaging with no background suppression, thus optimizing the visual appreciation of redistribution on delayed images. No more was gained with reinjection imaging.

Finally, in the study of Zafrir et al. (41), 109 patients underwent coronary artery bypass graft surgery, and 68 underwent coronary angioplasty before or during follow-up. This high rate of revascularization in the study cohort may have contributed to the low prevalence of reversible defects in the event and nonevent groups and the low prevalence of subsequent nonfatal infarction for the overall group (2%). The highest risk patients with left main or three-vessel CAD may have already undergone revascularization, reducing the ischemic burden associated with extensive angiographic disease. Machecourt et al. (11) and Stratmann et al. (13) found a higher mortality rate in patients with nonreversible or mixed defects than in those with reversible defects, which may have been due to revascularization of patients who manifested extensive areas of ischemia on testing or who had high risk coronary anatomy at coronary angiography.

The findings of the study by Zafrir et al. (41) are consistent with other recent studies that also sought to determine the prognostic value of Tl-201 reinjection. Tisselli et al. (51) found that the scintigraphic variable that was the strongest predictor of hard events was the presence of more than three nonreversible defects that remained fixed after reinjection. As in the study by Zafrir et al. (41), the presence of reversible Tl-201 defects did not predict subsequent death or infarction. In fact, even more than two nonreversible defects showing reversibility after reinjection did not predict hard events. The number of reversible defects on stress/redistribution and after reinjection was not significantly different in the event and nonevent groups, similar to that observed in the study of Zafrir et al. (41). Petretta et al. (52) showed that in postinfarction patients, Tl-201 reinjection imaging provided incremental prognostic information to clinical, exercise and Tl-201 stress/redistribution data, but only the *sum* of abnormal segments that were reversible and moderately irreversible after reinjection was more predictive of hard events at follow-up. The extent of reversibility as a prognostic variable alone was not improved by reinjection Tl-201 imaging.

What can we learn from the study of Zafrir et al. (41) and other studies assessing the prognostic value of stress perfusion imaging?

1. Results and conclusions of prognostic studies that seek to identify perfusion scan variables indicative of high risk can differ greatly depending on the criteria for patient selection, the number of patients included with a previous infarction and LV dysfunction, whether planar or SPECT imaging is used, whether visual or quantitative scan analysis is undertaken, whether only "hard" events or "hard" and "soft" events are considered as end points, whether a high incidence of coronary revascularization is performed either soon after scintigraphy or during follow-up and how many low risk patients without CAD are included.

2. It is clear from virtually all published studies that the extent of hypoperfusion (defect size, number of segmental defects or a summed stress score) on post-stress images is a powerful predictor of outcome. A defect size >20% to 25% of the left ventricle identifies a higher risk group. The extent of defect reversibility becomes a strong predictor of outcome in patients with a high prevalence of multivessel CAD, in which nonfatal cardiac events (e.g., revascularization, myocardial

infarction, hospital admission for angina) are included in the prognostic model and where early revascularization is not undertaken as a result of scintigraphic findings. The extent of nonreversible defects emerges as a strong predictor of cardiac death in patients with a previous myocardial infarction and poor LV function but little evidence for residual ischemia.

3. Increased lung Tl-201 uptake and transient or persistent LV cavity dilation provide supplementary prognostic information as to defect size and extent of defect reversibility.

4. Although reinjection Tl-201 imaging enhances the detection of viability in patients with chronic CAD and LV dysfunction and improves the prediction of functional improvement after revascularization, it does not appear to provide supplemental prognostic information over variables derived from stress/redistribution Tl-201 imaging for predicting subsequent cardiac death or infarction, at least when planar imaging is utilized. Whether consideration of the number of mild to moderate nonreversible defects on stress/redistribution or stress/reinjection images as a prognostic variable improves the prognostic value of stress perfusion imaging is unknown. However, it does improve identification of myocardial viability.

Which patients benefit most from use of stress perfusion imaging? Controversy still exists concerning when it is cost-effective to add the more expensive radionuclide perfusion imaging procedures to standard exercise ECG testing in the evaluation of patients with suspected or known CAD. Certainly, with respect to patients who present with an unstable chest pain syndrome of new onset associated with a high likelihood of CAD, direct referral to cardiac catheterization may be the most cost-effective approach. Such patients often have ischemic ECG changes when the ECG is acquired during or soon after resolution of pain. Also, patients with known CAD, with or without a previous infarction, and refractory symptoms on maximal medical therapy can be directly referred for coronary angiography if it is the judgment that medical therapy has failed and revascularization is indicated.

Exercise ECG stress testing alone can be the first test of choice in patients with a <15% likelihood of CAD on the basis of age, gender, type of chest pain presentation, number of CAD risk factors and ECG findings at rest. If these patients achieve >85% of the maximal predicted heart rate for age with a normal ECG response, no further testing appears warranted. However, if such patients demonstrate an ischemic ST segment response that might possibly represent a false positive test outcome, or have no inducible ST segment depression at <85% of maximal predicted heart rate, then repeat testing with SPECT perfusion imaging would be indicated. Ideally, quantitative gated SPECT with a Tc-99m–labeled agent should be utilized. If normal perfusion and normal systolic thickening are seen on the gated SPECT study, then no further testing is necessary. However, these patients should be evaluated with additional diagnostic testing to determine the etiology of the chest pain syndrome.

Patients who benefit the most from a combined ECG stress test and a SPECT perfusion scan at the outset are those with a 15% to 90% or intermediate pretest likelihood of CAD. Not only are the sensitivity and specificity of CAD detection enhanced by radionuclide imaging, but additional prognostic information is acquired from analysis of both the treadmill stress test results and perfusion imaging variables, as described earlier. If Tl-201 is used as the imaging agent, as it was in the study of Zafrir et al. (41), then quantitative scan analysis and measurement of the lung/heart Tl-201 ratio should be performed. Acquisition of a second set of "reinjection" images in this instance appears not to be very useful because most of the prognostic information required for risk assessment is derived from analysis of stress and delayed redistribution studies. Patients with normal scan results, particularly at >70% of maximal predicted heart rate, can be assured of a good prognosis. In contrast, high risk patients with scintigraphic abnormalities will most likely benefit from early coronary angiography and revascularization strategies.

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References

1. Beller GA. Clinical Nuclear Cardiology. Philadelphia: WB Saunders, 1995: 137–68.
2. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging: a diagnostic tool comes of age. Circulation 1991;83:363–81.
3. Brown KA. Prognostic value of myocardial perfusion imaging: state of the art and new developments. J Nucl Cardiol 1996;3:516–37.
4. Berman DS, Hachamovitch R. Risk assessment in patients with stable coronary artery disease: incremental value of nuclear imaging. J Nucl Cardiol 1996;3 Suppl:S41–9.
5. Gibbons RJ. Role of nuclear cardiology for determining management of patients with stable coronary artery disease. J Nucl Cardiol 1995;1 Suppl: S118–30.
6. Nygaard TW, Gibson RS, Ryan JM, Gascho JA, Watson DD, Beller GA. Prevalence of high-risk thallium-201 scintigraphic findings in left main coronary artery stenosis: comparison with patients with multiple- and single-vessel coronary artery disease. Am J Cardiol 1984;53:462–9.
7. Iskandrian AS, Heo J, Lemlek J, Ogilby JD. Identification of high-risk patients with left main and three-vessel coronary artery disease using stepwise discriminant analysis of clinical, exercise, and tomographic thallium data. Am Heart J 1993;125:221–5.
8. Ladenheim ML, Pollock BH, Rozanski A, et al. Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. J Am Coll Cardiol 1986;7:464–71.
9. Gill JB, Ruddy TD, Newell JB, Finkelstein DM, Strauss HW, Boucher CA. Prognostic importance of thallium uptake by the lungs during exercise in coronary artery disease. N Engl J Med 1987;317:1486–9.
10. Homma S, Kaul S, Boucher CA. Correlates of lung/heart ratio of thallium-201 in coronary artery disease. J Nucl Med 1987;28:1531–5.
11. Machecourt J, Longere P, Fagret D, et al. Prognostic value of thallium-201 single-photon emission computed tomographic myocardial perfusion imaging according to extent of myocardial defect: study in 1,926 patients with follow-up at 33 months. J Am Coll Cardiol 1994;23:1090–106.
12. Marie PY, Danchin N, Durand JF, et al. Long-term prediction of major ischemic events by exercise thallium-201 single-photon emission computed tomography: incremental prognostic value compared with clinical, exercise testing, catheterization and radionuclide angiographic data. J Am Coll Cardiol 1995;26:879–86.
13. Stratmann HG, Williams GA, Wittry MD, Chaitman BR, Miller DD. Exercise technetium-99m sestamibi tomography for cardiac risk stratification of patients with stable chest pain. Circulation 1994;89:615–22.
14. Kaul S, Lilly DR, Gascho JA, et al. Prognostic utility of the exercise thallium-201 test in ambulatory patients with chest pain: comparison with cardiac catheterization. Circulation 1988;77:745–58.

15. Kaul S, Finkelstein DM, Homma S, Leavitt M, Okada RD, Boucher CA. Superiority of quantitative exercise thallium-201 variables in determining long-term prognosis in ambulatory patients with chest pain: a comparison with cardiac catheterization. J Am Coll Cardiol 1988;12:25–34.
16. Boyne TS, Koplan BA, Parsons WJ, Smith WH, Watson DD, Beller GA. Predicting adverse outcome with exercise SPECT technetium-99m sestamibi imaging in patients with suspected or known coronary artery disease. Am J Cardiol 1997;79:270–4.
17. Shaw LJ, Kesler KL, Marwick TH, et al. Development of a stress myocardial perfusion imaging model to predict cardiac death [abstract]. Circulation 1996;94 Suppl I:I-20.
18. Snader CE, Marwick TH, Pashkow FJ, Harvey SA, Thomas JD, Lauer MS. Importance of estimated functional capacity as a predictor of all-cause mortality among patients referred for exercise thallium single-photon emission computed tomography: report of 3,400 patients from a single center. J Am Coll Cardiol 1997;30:641–8.
19. Pollock SG, Abbott RD, Boucher CA, Beller GA, Kaul S. Independent and incremental prognostic value of tests performed in hierarchical order to evaluate patients with suspected coronary artery disease: validation of models based on these tests. Circulation 1992;85:237–48.
20. Iskandrian AS, Chae SC, Heo J, Stanberry CD, Wasserleben V, Cave V. Independent and incremental prognostic value of exercise single-photon emission computed tomographic (SPECT) thallium imaging in coronary artery disease. J Am Coll Cardiol 1993;22:665–70.
21. Pancholy SB, Abdel Fattah A, Kamal AM, Ghods M, Heo J, Iskandrian AS. Independent and incremental prognostic value of exercise thallium single-photon emission computed tomographic imaging in women. J Nucl Cardiol 1995;2:110–6.
22. Berman DS, Hachamovitch R, Kiat H, et al. Incremental value of prognostic testing in patients with known or suspected ischemic heart disease: a basis for optimal utilization of exercise technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography [published erratum appears in J Am Coll Cardiol 1996;27:756]. J Am Coll Cardiol 1995;26:639–47.
23. Hachamovitch R, Berman DS, Kiat H, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. Circulation 1996;93:905–14.
24. Hachamovitch R, Berman DS, Kiat H, et al. Effective risk stratification using exercise myocardial perfusion SPECT in women: gender-related differences in prognostic nuclear testing. J Am Coll Cardiol 1996;28:34–44.
25. Shaw LJ, Hachamovitch R, Iskandrian AE. Treadmill test scores: attributes and limitations. J Nucl Cardiol 1997;4:74–8.
26. Iskandrian AS, Johnson J, Le TT, Wasserleben V, Cave V, Heo J. Comparison of the treadmill exercise score and single-photon emission computed tomographic thallium imaging in risk assessment. J Nucl Cardiol 1994;1:144–9.
27. Wackers FJ, Russo DJ, Russo D, Clements JP. Prognostic significance of normal quantitative planar thallium-201 stress scintigraphy in patients with chest pain. J Am Coll Cardiol 1985;6:27–30.
28. Staniloff HM, Forrester JS, Berman DS, Swan HJ. Prediction of death, myocardial infarction, and worsening chest pain using thallium scintigraphy and exercise electrocardiography. J Nucl Med 1986;27:1842–8.
29. Pamelia FX, Gibson RS, Watson DD, Craddock GB, Sirowatka J, Beller GA. Prognosis with chest pain and normal thallium-201 exercise scintigrams. Am J Cardiol 1985;55:920–6.
30. Steinberg EH, Koss JH, Lee M, Grunwald AM, Bodenheimer MM. Prognostic significance from 10-year follow-up of a qualitatively normal planar exercise thallium test in suspected coronary artery disease. Am J Cardiol 1993;71:1270–3.
31. Brown KA, Rowen M. Prognostic value of a normal exercise myocardial perfusion imaging study in patients with angiographically significant coronary artery disease. Am J Cardiol 1993;71:865–7.
32. Abdel Fattah A, Kamal AM, Pancholy S, et al. Prognostic implications of normal exercise tomographic thallium images in patients with angiographic evidence of significant coronary artery disease. Am J Cardiol 1994;74:769–71.
33. Ohtani H, Tamaki N, Yonekura Y, et al. Value of thallium-201 reinjection after delayed SPECT imaging for predicting reversible ischemia after coronary artery bypass grafting. Am J Cardiol 1990;66:394–9.
34. Dilsizian V, Rocco TP, Freedman NM, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. N Engl J Med 1990;323:141–6.
35. Rocco TP, Dilsizian V, Strauss HW, Boucher CA. Technetium-99m isonitrile myocardial uptake at rest. II. Relation to clinical markers of potential viability. J Am Coll Cardiol 1989;14:1678–84.
36. Tamaki N, Ohtani H, Yonekura Y, et al. Significance of fill-in after thallium-201 reinjection following delayed imaging: comparison with regional wall motion and angiographic findings. J Nucl Med 1990;31:1617–23.
37. Dilsizian V, Smeltzer WR, Freedman NMT, Dextras R, Bonow RO. Thallium reinjection after stress-redistribution imaging: does 24-hour delayed imaging after reinjection enhance detection of viable myocardium? Circulation 1991;83:1247–55.
38. Inglese E, Brambilla M, Dondi M, et al. Assessment of myocardial viability after thallium-201 reinjection or rest-redistribution imaging: a multicenter study: the Italian Group of Nuclear Cardiology. J Nucl Med 1995;36:555–63.
39. Dilsizian V, Freedman NM, Bacharach SL, Perrone-Filardi P, Bonow RO. Regional thallium uptake in irreversible defects: magnitude of change in thallium activity after reinjection distinguishes viable from nonviable myocardium. Circulation 1992;85:627–34.
40. Bonow RO, Dilsizian V, Cuocolo A, Bacharach SL. Identification of viable myocardium in patients with chronic coronary artery disease and left ventricular dysfunction: comparison of thallium scintigraphy with reinjection and PET imaging with ^{18}F-fluorodeoxyglucose. Circulation 1991;83:26–37.
41. Zafrir N, Leppo JA, Reinhardt CP, Dahlberg ST. Thallium reinjection versus standard stress-redistribution imaging for prediction of cardiac events. J Am Coll Cardiol 1998;31:1280–5.
42. Travin MI, Boucher CA, Newell JB, LaRaia PJ, Flores AR, Eagle KA. Variables associated with a poor prognosis in patients with an ischemic thallium-201 exercise test. Am Heart J 1993;125:335–44.
43. Parisi AF, Hartigan PM, Folland ED, for the ACME Investigators. Evaluation of exercise thallium scintigraphy versus exercise electrocardiography in predicting survival outcomes and morbid cardiac events in patients with single- and double-vessel disease: findings from the Angioplasty Compared to Medicine (ACME) study. J Am Coll Cardiol 1997;30:1256–63.
44. Mahmarian JJ, Boyce TM, Goldberg RK, Cocanougher MK, Roberts R, Verani MS. Quantitative exercise thallium-201 single photon emission computed tomography for the enhanced diagnosis of ischemic heart disease. J Am Coll Cardiol 1990;15:318–29.
45. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution ^{201}Tl imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. Circulation 1993;87:1630–41.
46. Di Carli MF, Davidson M, Little R, et al. Value of metabolic imaging with positron emission tomography for evaluating prognosis in patients with coronary artery disease and left ventricular dysfunction. Am J Cardiol 1994;73:527–33.
47. Eitzman D, al-Aouar Z, Kanter HL, et al. Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. J Am Coll Cardiol 1992;20:559–65.
48. Lee KS, Marwick TH, Cook SA, et al. Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction. Relative efficacy of medical therapy and revascularization. Circulation 1994;90:2687–94.
49. Gioia G, Powers J, Heo J, Iskandrian AS. Prognostic value of rest-redistribution tomographic thallium-201 imaging in ischemic cardiomyopathy. Am J Cardiol 1995;75:759–62.
50. Watson DD. Thallium-201 reinjection: truth or artifact? J Nucl Biol Med 1992;36 Suppl 2:15–21.
51. Tisselli A, Pieri P, Moscatelli G, et al. Prognostic value of persistent thallium-201 defects that become reversible after reinjection in patients with chronic myocardial infarction. J Nucl Cardiol 1997;4:195–201.
52. Petretta M, Cuocolo A, Bonaduce D, Nicolai E, Vicario ML, Salvatore M. Prognostic value of coronary angiography in patients with chronic ischemic left ventricular dysfunction and evidence of viable myocardium on thallium reinjection imaging. J Nucl Cardiol 1997;4:387–95.