Myocardial Perfusion Scintigraphy: Effect on Diagnostic and Clinical Management Algorithms

Nathan Better, J. Anthony Parker, Thomas P. Rocco, Michael Simons and Ernesto V. Gervino
Departments of Nuclear Medicine and Cardiology, Beth Israel Hospital; Department of Cardiology, West Roxbury Department of Veterans Affairs Medical Center; and Harvard Medical School, Boston, Massachusetts

Research has demonstrated that myocardial perfusion imaging increases the sensitivity and specificity of stress electrocardiography. However, the additional effect of the perfusion component of a stress study on clinical management algorithms remains poorly defined. **Methods:** We prospectively assessed the decision-making process in 518 patients, from 191 clinicians, undergoing stress myocardial perfusion imaging in our departments. Each clinician was asked, by telephone interview, to define the probability of reversible myocardial ischemia and their management plan (i.e., no antianginal treatment, medical therapy or an invasive intervention) in three stages: pretest, after the stress data was made available and after completion of the perfusion study. **Results:** The results of the stress data alone influenced the estimate of the probability of reversible ischemia in 149 of 518 patients, and management strategy in 50 of 518 patients. The data from the perfusion component in isolation changed probability of reversible disease in 219 of 518 patients and altered clinical management in 77 of 518 patients. Of 103 patients in whom an invasive procedure was planned after the stress data, the availability of the perfusion data led to deferral of catheterization in 48 cases (46.6%). Conversely, of the 415 patients triaged to a noninvasive plan after stress data, only 29 (7.0%) were changed to an invasive strategy. Of note, only 2.3% of women changed from a conservative strategy as a consequence of the perfusion data, compared to 9.1% of men. **Conclusion:** The perfusion component of a stress study has a significant effect on both estimation of clinical probability and the definition of patient management strategy. Myocardial perfusion imaging reduced the number of catheterizations in patients initially triaged to an invasive management strategy. Conversely, the effect of stress and perfusion data in patients triaged to conservative management on clinical grounds, especially women, remains less well defined.

Key Words: myocardial perfusion imaging; management; probability of reversible myocardial ischemia

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The role of myocardial perfusion is well established in the evaluation of patients with coronary artery disease. Perfusion tracers increase the sensitivity and specificity of stress electrocardiography (*1*) and alter the clinical assessment of probabilities of coronary disease especially when pretest probability is intermediate (*2,3*). The value of perfusion imaging is also well established in assessing prognosis, peri-operative risk (*4–11*) and extent of coronary disease. While scintigraphic imaging has been shown to be more sensitive than conventional electrocardiography in detecting coronary disease, limited information is available regarding the incremental effect of perfusion imaging on clinical patient management. Significant changes in management have been attributed to nuclear stress imaging (*12,13*), but such alterations attendant specifically to the perfusion component remain unexplored. The present study was designed to study this issue.

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For correspondence or reprints contact: M. Simons, MD, Cardiovascular Division, Beth Israel Hospital, 330 Brookline Ave., Boston, MA 02215.

We attempted to assess clinician's diagnostic decision making and assessment of probabilities of disease at three different stages in perfusion stress testing: before the stress test, after completion of the exercise electrocardiographic portion of the test and after completion of the perfusion part of the test. This approach allows one to evaluate the clinical effect of each component of stress testing separately and to assess their utility in terms of clinical decision making in groups of patients with different prior probabilities (as assessed by referring clinicians) of coronary disease. In addition, we studied the incremental effect of perfusion imaging on the use of other testing modalities (e.g., coronary angiography).

MATERIALS AND METHODS

Patient Selection

The study population consisted of 518 prospectively recruited patients referred for clinically indicated stress ^{201}Tl or ^{99m}Tc-sestamibi myocardial perfusion scintigraphy at Boston's Beth Israel Hospital and the West Roxbury Department of Veterans Affairs Medical Center. Recruitment occurred between March and October 1993. Patients were excluded if the referring physician could not be contacted or had received results of any component of the test before interview.

Study Design

The study evaluated referring clinicians' clinical decision making and assessment of probabilities of disease before the initiation of the stress test, after conclusion of the ECG portion, and after conclusion of the perfusion part of the study. During the stress protocol, hemodynamic parameters were recorded, as was the presence and character of chest pain (anginal, atypical or none). Patients were exercised according to a standard or modified Bruce protocol as appropriate. If an exercise study could not be performed, the patient underwent a standard infusion of intravenous adenosine (a 6-min infusion at 70–140 ug/kg/min), dipyridamole (0.142 mg/kg/min over 4 min) or dobutamine (up to 40 ug/kg/min). The ECG data were recorded as either positive (>1 mm of ST depression 0.08 sec after the J point), equivocal (0.5 to 1 mm ST depression 0.08 sec after the J point), negative or uninterpretable (baseline ECG changes such as left bundle branch block, left ventricular hypertrophy with strain pattern or the clinical use of digitalis). The clinician was also informed of the details of ST depression, including the severity of change and the recovery period.

Myocardial perfusion imaging was performed as either planar (three standard views) or as SPECT acquisition. The initial stress imaging was commenced 10 min after the intravenous injection of ^{201}Tl (1.6–3.0 mCi) at peak stress. At the Beth Israel Hospital, another 0.8–1.4 mCi of ^{201}Tl was injected 10 min before the acquisition of the delayed images, 3–24 hr following stress; at the West Roxbury DVAMC, standard redistribution images were performed, followed by ^{201}Tl reinjection or 24-hr imaging if fixed perfusion defects were identified. Alternatively, at the West Roxbury DVAMC, ^{99m}Tc-sestamibi was used in a standard two-day

TABLE 1
Patient and Stress Test Characteristics

No. of patients	518
Patient age (years ± s.d.)	62.8 ± 11.4
Sex (men:women)	368:150
Pretest indication (diagnosis:prognosis)	210:308
Stress (exercise:pharmacological)	476:42
Persantine	26
Adenosine	15
Dobutamine	1
Heart rate (bpm):	
Rest (± s.d.)	66 ± 12
Peak exercise (± s.d.)	132 ± 28
Peak pharmacological (± s.d.)	79 ± 15
Blood pressure (mmHg):	
Rest (± s.d.)	138 ± 21/81 ± 9
Peak exercise (± s.d.)	187 ± 33/86 ± 12
Peak pharmacological (± s.d.)	134 ± 27/76 ± 16
Imaging (planar:SPECT)	161:357
Radiopharmaceutical (^{201}Tl; ^{99m}Tc-sestamibi)	443:75
Stress test within previous 6 mo (yes:no)	103:415

stress-rest protocol (20 mCi per injection), with imaging commenced at 1 hr postinjection (n = 75).

The indications for stress testing were categorized in binary fashion either as diagnostic (tests done for the diagnosis of coronary artery disease) or prognostic (including patients with prior myocardial infarction, disease at cardiac catheterization and those patients referred for cardiac risk stratification before noncardiac surgery). Patients in the diagnostic group had no known history of coronary artery disease.

After the scintigraphic study was completed, the referring clinicians were contacted by telephone and the following questions were asked:

1. What is your estimate of the probability of reversible myocardial ischemia in this patient?
2. If you were not allowed to perform any additional testing, what would your management be?

The clinician was instructed to assume that no stress test of any kind would be performed. In reply to the first question, possible answers were either low, moderate or high probability. To the second question, choices included either no antianginal treatment, antianginal medical therapy, cardiac catheterization or an invasive intervention. After the answers were recorded, the results of the stress component of the study were reported to the clinician. This included test duration, symptoms, hemodynamic changes and electrocardiographic findings. The above questions were then repeated; clinicians were instructed to assume that the perfusion information would not become available. Finally, the results of myocardial perfusion scintigraphy were provided, including comparisons to prior studies, and the above questions repeated a third time. If the clinician was aware of the result of any component of the myocardial perfusion stress study before the telephone interview, the patient was immediately excluded from the trial.

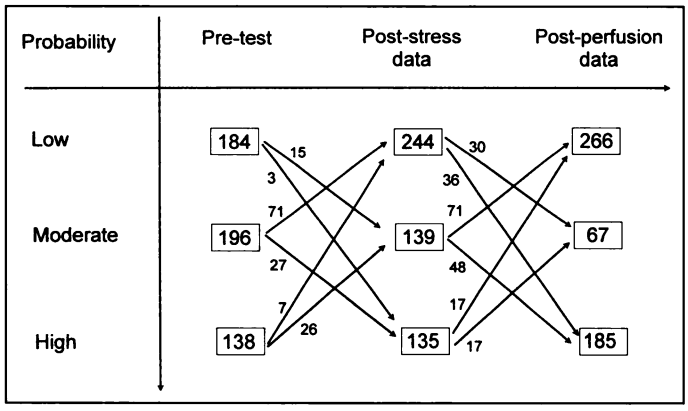

FIGURE 1. Changes in probability of reversible myocardial ischemia according to the referring physician. Of note, 149 patients changed clinical probability with the stress data and 219 changed with the perfusion component.

Statistical Analysis

Results were analyzed for a change in probability of ischemia and for a change in management strategy from pretest to post-ECG to postperfusion data. To analyze management changes, "no antianginal treatment" and "medical therapy" were considered as "noninvasive" management; "catheterization" and "intervention" were considered as "invasive" management. Comparisons were made using chi square analysis. Demographic differences between groups of patients was assessed with chi square analysis for binary variables and with the Student's t-test for continuous variables.

RESULTS

Patient and stress test characteristics are recorded in Table 1. Of the 518 patients, 210 were evaluated for diagnosis of coronary artery disease, while 308 had studies performed for prognostic indications. The referral base consisted of 191 physicians. All clinicians interviewed were the primary decision makers in determining further management of the individual patient; most were cardiologists, with less than 20% being internists or house staff. No one physician contributed more than 7% of the study population.

Probability of Reversible Myocardial Ischemia

The changes in probability of ischemia are recorded in Figure 1. With the stress component, the clinical assessment of the pretest probability of reversible ischemia was changed in 149 patients (increased in 45 patients, decreased in 104 patients); probability assessment was unaltered in 369. The perfusion component altered the assessment of probability in 219 patients (increased in 114 patients, decreased in 105 patients); probability assessment was unchanged in 299 patients ($p < 0.001$). Of note, 37 of the 219 patients (16.9%) who changed status with the perfusion data, did so to their original pretest probability. The changes in clinical probability were most striking in those patients with a moderate pretest probability. With the stress data, 98 of 196 patients (50%) with a moderate probability of disease changed category; with perfusion data, 119 of 139 patients (86%) changed. When compared to pretest probability, 52 of 184 (28.2%), 115 of 196 (58.6%) and 52 of 138 (38%) of patients who had low, moderate or high probability respectively changed clinical probability as a result of the perfusion component.

Management Plan

Changes in physician management strategy are detailed in Figure 2. With stress data, management strategy was changed in 50 of 518 patients ($p < 0.001$ versus pretest). Of note, only 17 of 399 patients (4.2%) changed from a noninvasive to an invasive strategy with the stress information. In contrast, 33 of 119 patients (27.7%) changed from cardiac catheterization/intervention to conservative management.

The data from the perfusion component altered the management strategy in 77 of 518 patients ($p < 0.001$). Again, only 29 of 415 (7.0%) changed from medical management to an invasive strategy, while 48 of 103 (46.6%) had cardiac catheterization or an intervention deferred. Ten patients of these 77

(13.0%) changed back to their original management strategy after the perfusion data.

We then assessed whether perfusion imaging was equally important in the evaluation of male and female patients. Of 368 men, 40 (10.9%) and 61 (16.6%) had management strategy changed by the stress and perfusion data, respectively. Similarly, of the 150 women, 10 (6.7%) and 16 (10.7%), had management altered by the stress and perfusion components, respectively. However, it is the direction of these changes that is of interest. As seen in Table 2, women rarely changed from a conservative to an invasive strategy (1.6% and 2.3%) with the stress and perfusion components of the study, respectively. Conversely, 5.4% and 9.1% of men in this study population changed to an invasive strategy as a consequence of the two components. On the other hand, both sexes had similar numbers of changes away from an invasive to a noninvasive management strategy.

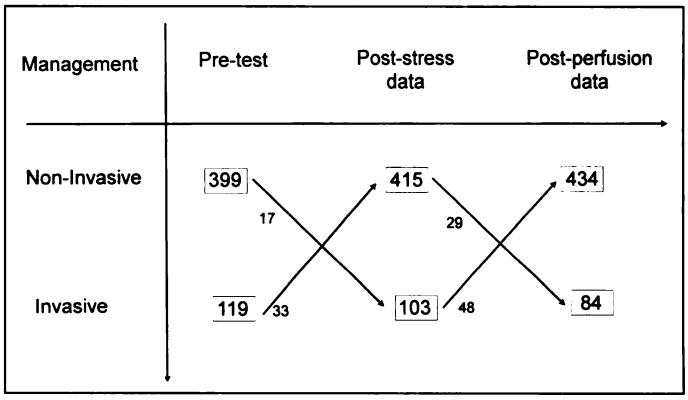

FIGURE 2. Changes in management strategy of referring physicians. While 46.6% had cardiac catheterization deferred due to the perfusion information, only 7.0% of patients had a conservative approach altered by the perfusion data.

DISCUSSION

The increased diagnostic sensitivity and specificity provided by perfusion imaging in addition to ECG stress testing is well established (*1,2*). To further assess the effect of diagnostic accuracy on clinical practice, we prospectively evaluated 518 perfusion stress tests and analyzed the effect of information from different components of the test on clinical practice. We collected and analyzed referring physician's assessment of probability of ischemic coronary disease and their patient management strategy before the stress test, after the ECG-stress component and after the perfusion component. We deliberately did not impose any numerical scale on the clinicians to judge probabilities of disease: each was free to use their own judgment and clinical guidelines. To assess how these changes in clinicians' estimates of disease probabilities altered their patient management strategies, we asked the referring physicians to indicate their plan of clinical treatment at the three stages of the test.

Changes in Management Strategy

The major findings of the present study include the demonstration of the incremental value of the perfusion component of a stress test study with respect to clinical management. In the 518 subjects enrolled, the stress data resulted in 50 changes in management. The data from the perfusion component resulted in 77 changes in management strategy. Of these 77 patients, 10 had their management altered by the perfusion data back to their original pretest management. Interestingly, perfusion imaging much more frequently resulted in the change from invasive to noninvasive strategy than vice versa (46.6% versus 7.0%; $p < 0.001$).

The present data suggest that the greatest effect of stress myocardial perfusion imaging is seen in patients in whom cardiac catheterization would otherwise have been performed. This effect is seen with both the stress and perfusion components of the study. Of equal interest is the observation that myocardial perfusion imaging has little clinical effect upon patients in whom pretest management was noninvasive: only 29 of 415 (7.0%) of these patients changed to an invasive procedure after the perfusion component. This lack of effect is particularly noted in women; only 2.3% had a change in management to an invasive strategy subsequent to the perfusion component, as compared to 9.1% for men. This gender difference has been noted in previous work, and our findings agree (*12,14*). Thus, it can be reasonably argued that noninvasive testing may be overused, particularly in women who are initially triaged to conservative pretest management. The present data confirm the findings of Bobbio et al. (*15*) regarding exercise electrocardiography, but also demonstrate the incremental value of perfusion imaging.

Of note, Bobbio et al. (*15*) also address alterations in medical regimens as well as catheterization that are attendant to the exercise electrocardiogram. In the present study, we found that 14 patients (2.7%) changed from a conservative regime to no antianginal treatment with the stress component, while an additional 34 patients (6.6%) made this change to no antianginal treatment after perfusion imaging. However, alterations in therapeutic regime, or even the reassurance value of a negative study are not reflected in the present study and may also represent significant management changes. From a cost effectiveness standpoint, avoiding many years of drug therapy in such patients would translate, as does deferring cardiac catheterization, into many dollars saved.

A recent article by Oosterhuis et al. (*16*) demonstrated the incremental diagnostic value of ^{201}Tl, but did not show an influence on the decision to treat a patient noninvasively compared with invasively. Although our data appear contradictory to this study, it should be emphasized that coronary angiography was performed in all patients enrolled in the Oosterhuis study, thereby precluding a direct comparison. In fact, deferral of cardiac catheterization was an endpoint in the present study.

Limitations

Several limitations of the present study merit comment. First, in the present study, referring physicians changed the probability of reversible myocardial ischemia in 149 of 518 patients on the basis of the stress data and in 219 patients as a consequence of the perfusion imaging. As expected, as test results became available, fewer patients were classified as having a moderate probability of reversible myocardial ischemia. The true significance of perfusion imaging alone in patients with a moderate

TABLE 2
Effect of Changes in Management with Stress and Perfusion Components of the Test According to Gender

	Noninvasive to invasive	Invasive to noninvasive
Stress component		
Men	5.4%	27.4%
Women	1.6%	28.5%
Perfusion component		
Men	9.1%	43.2%
Women	2.3%	59.1%

probability of disease may be underestimated. Although the definition of probability varies between physicians, the large number of changes in the moderate group is consistent with previous reports (*2,17,18*). Second, our probability definitions were not independently assigned but were made by the individual clinician. This was done so that changes in probability could be more easily addressed as each component became available.

Previous studies have attempted to define the utility of nuclear stress studies in reducing the need for cardiac catheterization (*12,13*). However, it is difficult to specifically identify the incremental value of the radiopharmaceutical component. To overcome this problem in the present study, management strategy was assessed by a telephone interview, rather than a questionnaire. The referring physician was required to commit to a management strategy immediately after the ECG-stress data were made available, and again after the availability of scintigraphic data. Although this technique was designed to separate the two components of a stress myocardial perfusion study, referring physician bias cannot be fully excluded. Although physicians were asked to assume that the perfusion data would not become available, it is possible that a conservative approach was maintained until complete test results were available. Since the telephone interview was commenced before the clinician was aware of the test results, the answers could thus not be tested for reproducability.

The ultimate outcome of patients within the present study group has not been assessed. The present data cannot assess the correctness of the changes in diagnostic thinking and management algorithms attendant to the exercise electrocardiogram and radiopharmaceutical data. Future studies will be required to assess this important issue. Similarly, our endpoint of a final management strategy was determined by telephone interview soon after completion of the test. It is possible that management may differ over ensuing weeks, particularly after the clinician has discussed the results with the patient. This too requires further study.

Finally, it should be noted that all the patients in the group initially were referred for a nuclear stress study. This therefore only represents a small subset of the total cardiological population, a group in whom the expectations of the referring clinicians were high, regarding the incremental benefit of the nuclear component. Once again, clinician bias may still be present, but the study was aimed to assess whether the ordering of this test actually translated into incremental management alterations.

CONCLUSION

The present study documents the clinical utility of the radiopharmaceutical component of the stress myocardial perfusion study in altering both the diagnostic and clinical management strategies. These data confirm the role of such noninvasive testing in reducing the number of cardiac catheterizations performed by as much as 46.6%. Further, the present data demonstrate that stress myocardial perfusion imaging has relatively less signficance, particularly in women, when the pretest management strategy was to be noninvasive.

The present data suggest that the greatest effect of stress myocardial perfusion imaging is seen in patients in whom cardiac catheterization would otherwise have been performed. This effect is seen in both the stress and perfusion components of conventional studies.

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