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Prognostic Value of Dipyridamole Thallium Scintigraphy for Evaluation of Ischemic Heart Disease

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Exercise testing alone or in combination with thallium scintigraphy has significant prognostic value. In contrast, dipyridamole thallium imaging is not dependent on patients achieving adequate levels of exercise, but no long-term prognostic studies have been reported. Accordingly, imaging results of 516 consecutive patients referred for dipyridamole thallium studies were correlated with subsequent cardiac events, death (n = 23) and myocardial infarction (n = 43) over a mean follow-up period of 21 months.

Patients with a history of congestive heart failure, prior myocardial infarction, diabetes mellitus or abnormal scans were significantly more likely to have a cardiac event ($p < 0.03$). With use of logistic regression analysis, an abnormal scan was an independent and significant predictor of subsequent myocardial infarction or cardiac death and increased the relative risk of any event more than threefold. The presence of redistribution on thallium scanning further increased the risk of a cardiac event. Survival analysis demonstrated a significant difference between patients with an abnormal or normal thallium scan over a 30 month period.

In conclusion, dipyridamole thallium scintigraphy demonstrates prognostic value in a large unselected population and may be an adequate clinical alternative to physiologic exercise testing in the evaluation of coronary heart disease.
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Coronary artery disease is the leading cause of morbidity and mortality in the United States (1). Clinical evaluation alone is often insufficient for the detection of asymptomatic coronary artery disease and in predicting the risk of a cardiac event in patients with known coronary atherosclerosis. Cardiac catheterization provides accurate detection and assessment of the severity of coronary artery disease. However, this invasive technique has potential risks and substantial costs that diminish its utility as a screening procedure for the general population. Additionally, even if coronary artery disease is detected by catheterization, the indications for revascularization in asymptomatic patients or those with stable angina pectoris are unclear.

Exercise testing either alone or with radionuclide imaging provides many diagnostic and prognostic data (2–15) and important physiologic or functional information regarding the presence of ischemia. Frequently, however, elderly patients or those with concurrent medical problems such as peripheral vascular disease are unable to attain an adequate level of exercise.

Coronary artery disease is detected by myocardial thallium imaging when a disparity in regional blood flow is demonstrated as a result of coronary hyperemia produced by either exercise-induced or pharmacologic vasodilation. A persistent defect on serial thallium scans suggests nonviable myocardium or scar. However, redistribution on thallium scintigraphy is a marker of potentially ischemic myocardium (16). Thallium imaging after the administration of the coronary vasodilator dipyridamole has been demonstrated to detect coronary artery disease (17–22) and is diagnostically equivalent to perfusion studies performed after maximal exercise (21–23). This technique has also been used to evaluate cardiac risk in patients undergoing elective vascular surgery (24–29) and to predict future cardiac events after myocardial infarction (30).

In contrast to exercise stress testing, dipyridamole thallium scintigraphy is not dependent on the level of exertion achieved, patient motivation or concurrent antianginal medications (18, 19). It is widely applicable for the detection and assessment of coronary artery disease; however, its utility in the general population is unknown. The aim of this study

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was to evaluate the potential clinical utility of dipyridamole thallium imaging in a large unselected patient population. Our hypothesis is that an abnormal thallium scan carries an increased risk of subsequent major cardiac events (myocardial infarction or cardiac death) and that the presence of redistribution on thallium scintigraphy further increases the relative risk of a cardiac event.

Methods

Study patients. All 516 patients referred to the University of Massachusetts Medical Center for the performance of dipyridamole thallium scintigraphy during the 3 year period between January 1, 1983 and December 31, 1985 were analyzed in a retrospective fashion. Reasons for the dipyridamole thallium scanning included preoperative evaluation in patients undergoing vascular surgery, medical evaluation of chest pain or other symptoms possibly related to ischemic heart disease, as well as the assessment of myocardial revascularization. A history of prior myocardial infarction was reported when diagnostic abnormalities (i.e., Q waves) were present on the electrocardiogram (ECG).

Dipyridamole thallium scintigraphy. Dipyridamole thallium imaging was performed according to a previously described protocol (26). Briefly, all patients were studied in the fasting state with all theophylline-containing medications being withheld for ≥36 h. Under continuous ECG monitoring and with frequent blood pressure assessment, the patient was given intravenous dipyridamole (Boehringer-Ingelheim, Inc.) at a rate of 0.56 mg/kg body weight over 4 min. Thallium-201 (1.5 to 2.5 mCi) was administered 3 to 4 min after the infusion of dipyridamole. The occurrence of symptoms was noted during and after the dipyridamole infusion and parenteral aminophylline was available for the reversal of any adverse effects.

Images were acquired in the anterior and 45° and 70° left anterior oblique views for 7 min per view on a standard gamma camera equipped with a high resolution collimator in a 128 × 128 matrix. Similar views were repeated 2.5 to 4 h later. Each scan was qualitatively analyzed by one of three staff nuclear cardiologists. The scans were divided into nine segments (three segments per view) and were read as normal or abnormal; abnormal scans were further classified as demonstrating persistent or transient defects, or both, as previously described (19). Transient defects were further subdivided into those with single segment redistribution or multiple segment redistribution.

Follow-up. Follow-up information was obtained in 504 (98%) of the 516 patients by telephone contact with the patient or family member. Medical records, as well as information obtained from the referring physician, were used for patients who were not personally contacted. Follow-up was considered complete if ≥10 months of information was obtained or the patient died. Clinical follow-up end points of the study included: 1) death classified as cardiac or noncardiac on the basis of medical records and death certificates; 2) myocardial infarction, confirmed by review of ECGs and serum enzyme criteria obtained from medical records; 3) continued chest pain; 4) cardiac catheterization; 5) coronary artery bypass graft surgery; and 6) percutaneous transluminal coronary angioplasty. Only the major end points of cardiac death or myocardial infarction were considered for logistic regression analysis.

Statistical analysis. Fisher's exact *t* test was used to correlate and compare variables from the patient population to determine the significance of differences in the rates of cardiac events. Final results are expressed as mean values ± SD. A nonlinear stepwise logistic regression analysis (BMDPLR Health Sciences Computing Facility, University of California, Los Angeles) was used to determine the statistical value for the prediction of cardiac death or myocardial infarction, or both, by the various clinical and scintigraphic variables. Product limit survival analysis of cardiac events for groups with abnormal and normal scans was also performed.

Results

Patient characteristics. Complete follow-up information was available for 504 (98%) of the 516 patients who underwent dipyridamole thallium scintigraphy during the 3 year study period. The average follow-up interval was 21 ± 8 months. A total of 52 patients (10%) experienced a major cardiac event, defined as either myocardial infarction or cardiac death. There were 43 cases of myocardial infarction during this period and 23 deaths of cardiac origin.

Table 1 shows the clinical data for all 504 patients, as well as the distribution of clinical variables among those who had a cardiac event (n = 52) and those who did not (n = 452). The mean age for all patients was 64 ± 11 years; those who had a cardiac event during the follow-up period were significantly older. The presence of diabetes mellitus and a history of congestive heart failure or myocardial infarction were noted more frequently in patients who experienced a cardiac event than in those who did not. A large percentage of the subjects had a history of hypertension (52%), angina pectoris (63%) or peripheral vascular disease (34%). However, these factors as well as the incidence of valvular heart disease were not significantly distributed among patients based on future events. The use of various medications and the reasons for referral were not significantly different between the groups with and without a cardiac event.

Dipyridamole thallium scintigraphy. Figure 1 illustrates the classification of dipyridamole thallium scans as either normal or abnormal in the 504 patients. Of the 332 abnormal scans, 249 (75%) demonstrated redistribution and 83 (25%) demonstrated only persistent abnormalities. The scans with transient abnormalities were further subdivided into whether

Table 1. Clinical Characteristics of 504 Patients

	Cardiac Event (n = 52)	No Cardiac Event (n = 452)	p Value
Age (yr ± SD)	67 ± 10	64 ± 11	0.0216
Male	33 (63)	230 (51)	0.0859
Reason for referral			
Preoperative assessment	21 (40)	188 (42)	0.8697
Medical evaluation	31 (60)	272 (61)	0.8186
Past medical history			
Diabetes mellitus	22 (42)	84 (19)	0.0001
Hypertension	31 (60)	230 (51)	0.2336
Angina pectoris	31 (60)	287 (64)	0.5036
Congestive heart failure	7 (14)	19 (4)	0.0042
Valvular disease	2 (4)	9 (2)	0.5061
Peripheral vascular disease	21 (40)	151 (33)	0.3376
Previous infarction	26 (50)	154 (34)	0.0232
Medications			
Digoxin	7 (14)	48 (11)	0.5714
Diuretic	20 (39)	137 (30)	0.2302
Beta-adrenergic blocking agent	17 (33)	145 (32)	0.9205
Nitrates	23 (44)	163 (36)	0.2683
Calcium channel blocking agent	14 (27)	106 (24)	0.5965
Antiarrhythmic agent	5 (10)	23 (5)	0.1778

Figures in parentheses indicate percent of patients

or not they had more than one segment of redistribution. More extensive redistribution was noted in 175 (70%) of the 249 scans; the remaining studies had only one segment with a transient abnormality.

Table 2 summarizes the clinical follow-up data and their distribution among patients with and without a normal dipyridamole thallium scan. Myocardial infarction occurred in 43 patients (9%) during the follow-up period, with significantly more patients (n = 38) having an abnormal than a normal scan (n = 5). In addition, there were 14 fatal myocardial infarctions. Overall, death with a cardiac etiology occurred in 23 patients (5%), the great majority of whom (91%) had an abnormal scan. As anticipated, angina pectoris, the performance of cardiac catheterization and coronary

Figure 1. Results of dipyridamole thallium scintigraphy in 516 patients over a 3 year period (1983 to 1985).

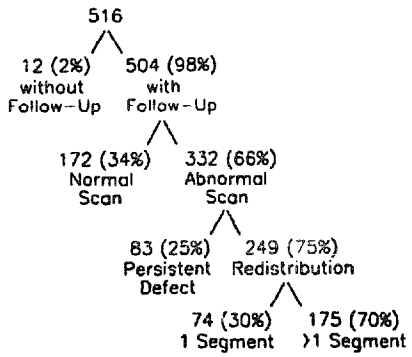


Table 2. Follow-Up Clinical Data in 504 Patients

	Abnormal Scan (n = 332)	Normal Scan (n = 172)	p Value
Myocardial infarction	38 (12)	5 (3)	0.0011
Cardiac death	21 (6)	2 (1)	0.0084
Angina pectoris	195 (59)	83 (48)	0.0079
Cardiac catheterization	53 (16)	13 (8)	0.0071
Coronary surgery	25 (8)	3 (2)	0.0249
Coronary angioplasty	4 (1)	2 (1)	0.9670
Noncardiac death	18 (5)	11 (6)	0.6651

Figures in parentheses indicate percent of patients.

artery bypass graft surgery were also significantly more frequent in the group with an abnormal scan. Noncardiac death and coronary angioplasty were infrequent and not significantly distributed in patients with an abnormal dipyridamole thallium scintigram.

The results of dipyridamole thallium scintigraphy are displayed in Table 3. A normal thallium scan was almost three times more frequent in patients without subsequent myocardial infarction or cardiac death (37% versus 14%). An abnormal scan was noted more frequently in the group with late cardiac events (87%) than in those with normal scan results (64%). In patients with an abnormal scan, the presence of more than one segment demonstrating redistribution, as well as persistent abnormalities, occurred more often in the group that experienced cardiac events.

Adverse reactions. These developed in 35% of all patients undergoing dipyridamole thallium scintigraphy. Chest pain occurred in 88 patients (18%), and 37 (7%) were noted to have ischemic type ST segment depression on the ECG. Other reactions, such as nausea or dizziness, occurred in 120 patients (24%). Intravenous aminophylline was given to 87 patients (17%). No serious complications or long-term sequelae occurred as a result of dipyridamole thallium testing. There was no difference in the rate of occurrence of adverse

Table 3. Results of Dipyridamole Thallium Scintigraphy

	Cardiac Event (n = 52)	No Cardiac Event (n = 452)	p Value
Normal scan	7 (14)	165 (37)	0.0009
Abnormal scan	45 (87)	287 (64)	0.0009
Redistribution >1 seg	30 (58)	145 (32)	0.0002
Redistribution = 1 seg	4 (8)	70 (16)	0.1331
Persistent	37 (71)	202 (45)	0.0003
Total adverse effects	17 (33)	161 (36)	0.6748
Chest pain	7 (14)	81 (18)	0.3860
Ischemic ECG changes	6 (12)	31 (7)	0.2212
Other	12 (23)	108 (24)	0.8961
Aminophylline required	12 (23)	75 (17)	0.2422

Figures in parentheses indicate percent of patients. ECG = electrocardiographic; seg = segment.

Table 4. Predictive Value of Various Clinical Variables

Variable	All Cardiac Events		Myocardial Infarction		Cardiac Death	
	p Value*	Relative Risk†	p Value*	Relative Risk†	p Value*	Relative Risk†
Abnormal scan	0.0004	3.1	0.0004	3.6	0.0034	3.9
Congestive heart failure	0.0137	3.0	0.0776	—	0.0044	5.4
Diabetes mellitus	0.0002	2.8	0.0000	4.1	0.6540	—
Gender	0.0834	—	0.2535	—	0.0081	0.4
Prior myocardial infarction	0.0254	—	0.1283	—	0.0991	—
Peripheral vascular disease	0.3204	—	0.2701	—	0.3413	—

*p values reflect values from step 0 of regression analysis; †relative risk refers to odds ratio after completion of regression model.

reactions between those patients who did and did not experience a cardiac event during the follow-up period.

Prognostic value. Three separate stepwise nonlinear regression analyses were performed to evaluate the prognostic significance of several clinical (Table 1) and scintigraphic (Table 3) variables and their value in the prediction of late myocardial infarction or death. At each step, the variable with the highest chi-square value was entered into the model until no variable had a p value <0.10. Six variables (diabetes mellitus, abnormal dipyridamole thallium scan, history of congestive heart failure, prior myocardial infarction, gender and peripheral vascular disease) were chosen for analysis of their predictive value, based on the two-tailed *t* test, as well as after a preliminary, low precision logistic regression analysis that evaluated all potential predictors.

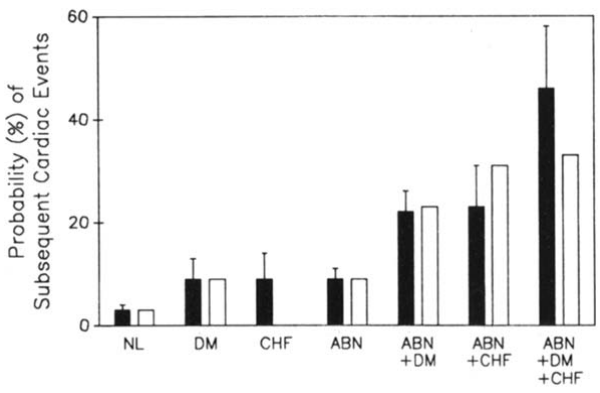
The results of regression analysis are summarized in Table 4. An abnormal scan, history of congestive heart failure, diabetes mellitus and previous myocardial infarction were independent predictors of a late cardiac event ($p < 0.05$), the first three variables having approximately equal significance in the predicting model. In another regression analysis evaluating the variables for cardiac death alone, the best predictors were a history of congestive heart failure and an abnormal thallium scan; male gender added minimal statistical improvement to the model beyond the first two variables alone. In the third analysis, diabetes mellitus and an abnormal scan were the only two predictors included in the model for predicting future myocardial infarction.

From these regression analyses (Fig. 2), the predicted probability of a cardiac event in patients with a normal dipyridamole thallium scan was determined to be 3 ± 1%. An abnormal scan raised the predicted probability to 9 ± 2% and the addition of diabetes mellitus or congestive heart failure raised it to 22 ± 4% or 23 ± 8%, respectively. The combination of diabetes mellitus, congestive heart failure and an abnormal dipyridamole thallium study resulted in the highest predicted probability of having a myocardial infarction or cardiac death (46 ± 12%), and raised the relative risk of a cardiac event more than 26-fold.

Because the finding of an abnormal scan was an important predictor of subsequent events in this population, an additional regression analysis was performed to determine whether any scintigraphic variables were of further prognostic utility in patients with an abnormal scan. The presence of more than one segment demonstrating redistribution on dipyridamole thallium scintigrams was a significant independent predictor of total cardiac events. The relative risk for a late cardiac event of patients with an abnormal scan and presence of redistribution was increased an additional 2.4-fold and the predicted probability for a cardiac event was 10 ± 3% in this group. Persistent perfusion abnormalities on the scan also added an additional significant improvement to the model by increasing the predicted probability to 22 ± 4% in patients with both transient and persistent abnormalities. When the scintigraphic variables in all patients were examined with logistic regression analysis, the presence of redistribution was an independent predictor of a cardiac event ($p = 0.0002$) and more than doubled the risk of a myocardial infarction or cardiac death.

As assessed by product limit analysis (Fig. 3), an abnormal scan confers a statistically significant decrease in event-free survival (without myocardial infraction or cardiac

Figure 2. Comparison of predicted (**solid bar**, with 1 SD) and observed (**open bar**) probabilities of experiencing a myocardial infarction or cardiac death based on the presence of various factors. ABN = abnormal thallium scan; CHF = history of congestive heart failure; DM = diabetes mellitus; NL = normal thallium scan. There were no observed cardiac events in patients having only a history of congestive heart failure (0%).



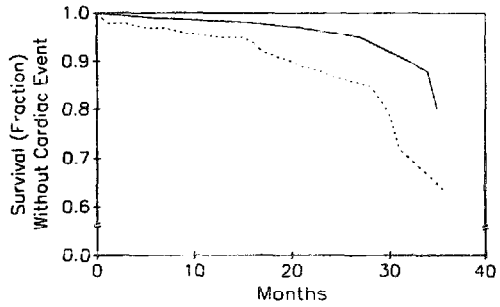


Figure 3. Life table analysis comparing the event-free survival of 172 patients with a normal dipyridamole thallium scan (solid line) with that of 332 patients with an abnormal scan (dashed line). Cardiac death or myocardial infarction occurred more frequently in patients with an abnormal dipyridamole thallium scintigram ($p < 0.005$).

death) as compared with that in patients with a normal scan. The increased incidence of a post-test event for patients with an abnormal scan was significant at 6 months and remained so for up to 36 months. In patients with an abnormal scan, the presence of redistribution did not add appreciably to this survival analysis ($p = 0.12$).

Discussion

The results of this study demonstrate that thallium scintigraphy after dipyridamole infusion has significant prognostic utility and that an abnormal scan markedly increases the risk for the development of subsequent myocardial infarction or cardiac-related death. The presence of multiple transient thallium defects additionally elevates the relative risk of a major cardiac event.

Critique of methodology. An abnormal scan is associated with an increased incidence of myocardial infarction, cardiac death and combined events, as well as of recurrent angina, the performance of cardiac catheterization or coronary artery bypass graft surgery. Although recurrent angina may be a marker of ischemia, the subjective nature of this symptom, as well as influence by medication usage and other factors, makes this a potentially unreliable end point of prognostic testing. Furthermore, the decision to perform coronary arteriography and subsequently coronary artery bypass graft surgery is frequently influenced by individual physicians' biases and may also be affected by the presence of abnormal findings on dipyridamole thallium scintigraphy. Therefore, only the "hard" end points of a cardiac-related death or myocardial infarction were considered in the assessment of the predictive value of dipyridamole thallium imaging.

The factors selected for logistic regression analysis were based on the preliminary statistical findings as well as on known clinically important variables. Additionally, regression analysis including all clinical and scintigraphic variables failed to reveal any new variables that achieved statistical significance. The perfusion studies were grouped as abnormal or normal, so as not to confound analysis by examining a subset of scans such as those with redistribution and comparing them with normal images. We believed that after analyzing the prognostic value of an abnormal scan alone, further evaluation for possible independent predictors in the subgroups with an abnormal study had a more accurate statistical and clinical value. However, even when analyzing the individual scintigraphic variables in the entire population, the presence of redistribution was of significant prognostic value.

Prognostic value. An abnormal dipyridamole scan was found to have independent predictive value for cardiac events overall and for both cardiac death and myocardial infarction independently as demonstrated by regression analysis. The relative risk for these events was increased three to fourfold, independent of other risk factors. The finding that a history of congestive heart failure was predictive for a cardiac event is not surprising because left ventricular dysfunction is a well recognized factor in premature death (31). Diabetes mellitus is a major risk factor for atherosclerosis in coronary artery disease and has long been associated with an increased incidence of myocardial infarction and cardiac death (32). However, the present study demonstrates that this risk is compounded by an abnormal dipyridamole thallium scan, as has been shown with exercise thallium scintigraphy (9).

In contrast to logistic regression analysis, survival analysis incorporates a temporal function into the prediction of cardiac events. This analysis demonstrated a significant difference between patients with an abnormal scan and those with a normal dipyridamole thallium study. In addition, a statistically important difference between the two groups occurred as early as 6 months and was maintained throughout the follow-up period of 3 years.

Among patients with an abnormal scan, the presence of more than one segment of thallium redistribution had independent predictive value for myocardial infarction and for total cardiac events. Multiple transient thallium abnormalities were noted in 35% of the study population and was the scintigraphic variable that placed these patients at the highest risk for a subsequent cardiac event. Although the presence of persistent abnormalities added to the predicted accuracy of the model, this variable was not of independent significance. Interestingly, the presence of only one segment of redistribution appeared to be associated with an event-free follow-up. This may reflect an interpretation artifact caused by a relatively low threshold for abnormal segments by the observers. Therefore, small segmental scan "abnormalities" that are typically subtle and hard to classify appear to have little predictive value for subsequent cardiac events.

A normal dipyridamole thallium scan conferred a good prognosis and identified 34% of the subgroup population who were at a low risk for myocardial infarction or cardiac-related death. These results are consistent with previous

reports (24–30) regarding the prognostic utility of dipyridamole thallium imaging in specifically defined populations. However, our study was not limited by reasons of referral and was performed in essentially an unselected population. An additional advantage over these earlier studies, especially those in patients undergoing vascular surgery, was that extended follow-up information was available.

Comparison with exercise imaging. Perfusion imaging in conjunction with exercise testing has shown good results in detecting coronary artery disease and has excellent prognostic utility (2–13,33). Data from these studies may add to and, in many cases, supplant cardiac catheterization data (2–4,33). It has been shown that patients with a normal thallium scintigram have an excellent prognosis and an annual incidence of myocardial infarction or cardiac death of <1% (11,12). Even in the presence of diabetes mellitus, a normal scan was a predictor of significantly fewer events (9).

Abnormal results of thallium exercise scintigraphy portend a poor prognosis and a significantly increased risk of further cardiac events (5–9). Additionally, the presence, location or amount of thallium redistribution during exercise imaging has been shown to be the scintigraphic variable with the most prognostic utility in relation to future myocardial infarction (3–5,33); it also has significant predictive power for all cardiac events (2,3,10,33). Exercise testing, however, is often limited by the inability of patients to achieve a sufficient level of exertion.

In contrast, dipyridamole thallium scintigraphy is unaffected by patient motivation or medications and can be performed in patients who are otherwise not able to undergo maximal exercise testing because of limitations imposed by peripheral vascular disease, pulmonary disorders or musculoskeletal abnormalities. Dipyridamole thallium imaging also does not require a substantial increase in myocardial oxygen consumption, and the effects of coronary hyperemia, unlike those of exercise, may be quickly and completely reversed (18,21).

Safety and side effects. Aminophylline was required in 17% of the patients undergoing dipyridamole thallium testing in the present setting, all of whom had no lasting sequelae. In other studies, the safety of dipyridamole thallium testing in this type of population is suggested by the fact that only one death has been reported (34) and serious adverse reactions are exceedingly rare (19–21,35,36). The frequency of side effects in our study was similar to that reported in these other studies; the majority consisted of headache, nausea or dizziness. No life-threatening reactions occurred in our patients in more than 500 procedures. Chest pain occurred in 18% of patients during the procedure (this incidence rate was at the low end of the reported range [18% to 43%]) and demonstrated no prognostic value, confirming similar observations noted in smaller study groups (37). ST segment depression, recorded infrequently in our subjects (7%), was also not of predictive utility, a finding consistent with previous studies (19,27,30).

Clinical implications. In an earlier study (30), dipyridamole thallium scanning was demonstrated to be predictive of cardiac events after acute myocardial infarction. The presence of redistribution markedly increased the risk of a late (19 months) cardiac event, a finding that was confirmed by our present study. The majority of prior reports (24–29) demonstrating the prognostic value of dipyridamole thallium imaging have been collected in patients undergoing preoperative assessment before vascular surgery. When these short-term studies are pooled, 29% of patients with transient perfusion abnormalities after dipyridamole administration had a perioperative myocardial infarction or cardiac-related death, as compared with 1% of patients without thallium redistribution. The present study is in agreement with these conclusions and further demonstrates that an abnormal scan increases the risk that a patient will experience subsequent myocardial infarction or death. The independent predictive value of this imaging procedure is further enhanced by the presence of thallium redistribution.

Limitations. Our study has several limitations. Although it does not allow direct comparison between dipyridamole thallium imaging and thallium scanning after exercise, previous studies of dipyridamole thallium scintigraphy have shown similar diagnostic accuracy for this procedure (21,22). Because angiographic information is not available, our study does not permit assessment of the specificity and sensitivity of dipyridamole thallium perfusion imaging or comparison of cardiac catheterization with thallium scintigraphic findings. An additional problem is the lack of quantification of thallium scintigraphic findings. Such quantification may yield additional prognostic information (3,4,7,10,13). Although qualitative interpretation of the thallium scans has been shown to be of high diagnostic (19,21,22) and prognostic (27–30) utility, quantitative analysis of the thallium scintigrams may enhance their usefulness (38). Single photon emission computed tomography may also improve resolution and further increase the diagnostic value of dipyridamole thallium perfusion studies (39,40).

Conclusions. Dipyridamole thallium imaging has long-term prognostic utility in evaluating patients suspected of having coronary artery disease as well as those undergoing an elective surgical procedure. This technique may be used as an initial procedure to screen for the presence of significant coronary artery disease, regardless of the patient's symptoms. Those with an abnormal scan may well be advised to undergo additional evaluation. As in the present study, it would be possible to classify the majority of patients as being at either high or low risk for myocardial infarction or cardiac death. Overall, perfusion imaging after dipyridamole infusion appears to be an effective way to determine prognosis without the use of physiologic exercise and may be an acceptable alternative procedure in many

patients with known or suspected ischemic heart disease who cannot be adequately evaluated by exercise testing (with or without thallium imaging). Further clinical investigations for long-term prognosis are clearly warranted.

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