CLINICAL STUDIES

Prognostic Value of Dipyridamole Thallium-201 Imaging in Elderly Patients

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The prognostic value of intravenous dipyridamole myocardial perfusion imaging has not been studied in a large series of elderly patients. Patients aged 70 years of age and older with known or suspected coronary artery disease were evaluated to determine the predictive value of intravenous dipyridamole thallium-201 imaging for subsequent cardiac death or nonfatal myocardial infarction. Of the 348 patients, 207 were asymptomatic and 141 were asymptomatic; 52% of the asymptomatic group had documented coronary artery disease. During 23 ± 15 months of follow-up, there were 52 cardiac deaths, 24 nonfatal myocardial infarctions and 42 revascularization procedures (percutaneous transluminal coronary angioplasty in 20; coronary artery bypass surgery in 22). Clinical univariate predictors of a cardiac event included previous myocardial infarction, congestive heart failure symptoms, hypercholesterolemia and diabetes (all p < 0.05).

The presence of a fixed, reversible or combined thallium-201 defect was significantly associated with the occurrence of cardiac death or myocardial infarction during follow-up (p < 0.05).

Cardiac death or nonfatal myocardial infarction occurred in only 7 (5%) of 150 patients with a normal dipyridamole thallium-201 study (p < 0.001). Stepwise logistic regression analysis of clinical and radionuclide variables revealed that an abnormal (reversible or fixed) dipyridamole thallium-201 study was the single best predictor of cardiac events (relative risk 7.2, p < 0.001). As has been demonstrated in younger patients, previous myocardial infarction (relative risk 1.8, p < 0.001) and symptoms of congestive heart failure at presentation (relative risk 1.6, p = 0.02) were also significant independent clinical predictors of cardiac death or myocardial infarction.

Dipyridamole thallium-201 myocardial imaging is a powerful independent noninvasive technique for prognosis in the elderly, a group with limited exercise capacity, the potential for advanced coronary artery disease, and a high risk for cardiac events.

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In this century, the average life expectancy has increased from a mean of 47 years to nearly 75 years (1). Clinical management strategies in elderly patients have become increasingly more aggressive, with the goals of improving quality of life and functional capacity and decreasing cardiac morbidity and mortality (2-6). Coronary artery disease remains the leading cause of morbidity and fatal events in this age group (7-10). Evaluation of the elderly patient must consider the risk of adverse cardiac events initiated by aggressive diagnostic evaluation and subsequent therapy.

Historically, exercise thallium-201 myocardial imaging has demonstrated prognostic value in the assessment of known or suspected coronary artery disease in patients of various ages (11-22). Abnormal findings on an exercise electrocardiogram (ECG), exercise-induced thallium-201 perfusion defects, a blunted or diminished hemodynamic response and impaired cardiac reserve have significant prognostic value in various patient subsets (15,17-19,21).

Pharmacologic stress has emerged as an effective strategy for the evaluation of subjects with known or suspected coronary artery disease (23-31). Combined analysis of dipyridamole test results and clinical data has been useful in identifying high risk patient subsets (23-31). The utility of clinical and scintigraphic risk stratification in patients >65 years of age has received limited attention (13,20).

Although elderly patients are commonly referred for evaluation of known or suspected coronary artery disease and are frequently limited in their capacity to perform exercise stress, no previous reports have specifically focused on the assessment of these older (≥70 years) patients with dipyridamole thallium-201 imaging. This investigation attempted to determine the prognostic significance of dipyridamole thallium-201 testing in this elderly patient subset and to establish guidelines for the application of drug stress myocardial imaging in the clinical management of elderly patients.

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Methods

Study patients. Consecutively tested patients ≥70 years of age referred to the Saint Louis University Medical Center for intravenous dipyridamole thallium-201 imaging from August 1, 1984 to June 1, 1989 were retrospectively evaluated. Of the 354 patients identified, clinical follow-up information was available in 348 patients (95%). A total of 93 patients (26%) have been included in previous reports from this institution (31,32).

Procedure and Design

Dipyridamole infusion protocol. All dipyridamole infusions were performed in the morning with the patient fasting. Preinfusion heart rate, 12-lead ECG and blood pressure measurements were obtained with the patient in the supine and sitting positions. After baseline measurements were recorded, dipyridamole was infused at a rate of 0.56 mg/kg body weight over 4 min through an indwelling intravenous catheter (30,31). The 12-lead ECG, heart rate and blood pressure were monitored every minute for a total of 10 min from the start of infusion. After dipyridamole infusion, the patient assumed the sitting position and began active leg swinging for 4 min. Thereafter, 2 mCi of thallium-201 was injected intravenously through the indwelling catheter. Active leg-swinging exercise was continued for an additional 2 min. Patients were continuously monitored for any cardiac and noncardiac side effects, including chest pain, nausea, flushing, light-headedness, headache and dizziness. Short-acting sublingual nitroglycerin and parenteral aminophylline were available to reverse persistent side effects. Cardiac medications were not interrupted before the dipyridamole infusion. Methylxanthines were withheld for 48 h before the study. We previously found (32) no significant increase in the incidence of noncardiac or cardiac side effects among elderly patients undergoing dipyridamole thallium imaging at our institution. In the current study of patients ≥70 years of age, the same observation held true. A total of 39 patients (11%) required aminophylline for reversal of symptoms or signs of myocardial ischemia. However, there were no prolonged episodes of ischemia and no myocardial infarction. Severe hypotension or death.

Thallium-201 imaging and analysis. Planar thallium-201 imaging was performed within 5 min after injection by using a small field of view gamma camera (APEX model 215M, Elscint Corporation) equipped with a low energy, high resolution, parallel hole collimator. Sequential images were obtained in the anterior, 45° left anterior oblique and left lateral views. Images were acquired at the 80-keV photo-peak with 20% window and stored on a 256 × 256-byte computer matrix. Approximately 500,000 counts were acquired during each 10-min image (30,31). Redistribution images were obtained in the same views 4 h after infusion. Images were analyzed by two observers without prior knowledge of the patients’ clinical history or angiographic results. Discordant results were adjudicated by consensus opinion and evaluation of quantitatively determined thallium activity washout curves (22). Thallium images of the left ventricle were divided into five approximate regions for each view (33). Each segment was scored as normal or as having a reversible or fixed thallium defect. Thallium scans with a reversible, fixed or combined (reversible and fixed) defect were classified as abnormal for subsequent statistical analysis of their prognostic value. The number of abnormal thallium segments was classified as 0 to 2, 3 to 5 and >5 segments for each set of radionuclide images for cardiac risk assessment.

Follow-up procedure. Clinical follow-up information was obtained through a telephone interview or a medical clinic visit. The protocol was approved by the Institutional Review Board of the university and written informed consent was obtained before each procedure. During each patient or family member contact, the following clinical events were ascertained: the occurrence of cardiac death, noncardiac death, nonfatal myocardial infarction or a revascularization procedure (percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery) ≤3 months (early) or >3 months (late) after the dipyridamole test date. Interventionsal strategies performed within 3 months of the dipyridamole test date were considered to be potentially influenced by the index test results and are classified as distinct from those occurring outside the 3-month period (22). The cardiac event rate was defined as the occurrence of confirmed cardiac death or nonfatal myocardial infarction. The initial cardiac event was considered the significant clinical end point for subsequent data analysis in all cases. Documentation of cardiac death, noncardiac death, nonfatal myocardial infarction or a revascularization procedure was confirmed in all cases by subsequent medical chart review or telephone contact with the referring physician.

Statistical analysis. Multivariate and stepwise logistic regression analyses were performed by using clinical and radionuclide variables to detect significant differences in event rates (Table 1) (34). Relative risk ratios were calculated for those variables found to be statistically significant in the stepwise regression analysis (34). Actuarial event-free rates were analyzed by using Mantel-Breslow survival analysis (34). Confidence intervals for binomial proportions were calculated yearly for each of the survival analysis groups (34). Differences in event rates were calculated by using the log-rank statistic over the duration of the follow-up period (36). Frequencies were compared with chi-square analysis. The number of abnormal thallium-201 segments was compared with the incidence of cardiac death or nonfatal myocardial infarction by a one-way analysis of variance. A p value < 0.05 was considered statistically significant. For repeat regression analysis modeling, a p value of 0.05 divided by the number of independent comparisons was used as the level for statistical rejection.
Follow-up data. The overall cardiac event rate in the 348 patients was 22% over the 23 ± 15-month follow-up period: 52 cardiac deaths, 24 nonfatal myocardial infarctions and 24 early and 18 late revascularization procedures. The 18 late procedures comprised coronary angioplasty performed in 7 patients and coronary bypass surgery performed in 11 patients ≥3 months after testing.

Comparative clinical and radionuclide imaging characteristics of patients with cardiac death or nonfatal myocardial infarction during the follow-up period are presented in Table 1. The 2-year cardiac event rate was greater in patients with than in those without a prior myocardial infarction (27% vs. 12%, p = 0.02) (Fig. 1). Symptoms of congestive heart failure at presentation increased the risk of cardiac death and nonfatal myocardial infarction (35% vs. 15% at 2 years, p = 0.001) (Fig. 2). The incidence of cardiac death and nonfatal myocardial infarction was greater in patients receiving digi- talis therapy (27% vs. 14% at 2 years, p = 0.05).

Dipyridamole Thallium-201 Imaging

ST segment depression ≥1 mm after dipyridamole infusion occurred in 26 patients (7.5%), with no significant differences recorded in the cardiac event rates between those with or without ischemic ECG changes (Table 2). Dipyridamole-induced chest discomfort was documented in 52 patients (15%). Cardiac event rates were significantly greater in patients with dipyridamole-induced chest pain than in those without such symptoms (Table 2).

Normal versus abnormal dipyridamole thallium-201 scan results. Of the 149 patients with normal findings on a dipyridamole thallium-201 scan, only 3 (2%) had a fatal cardiac event compared with 48 (24%) of 199 patients with an abnormal scan result (p < 0.001). The overall cardiac event rate (cardiac death or nonfatal myocardial infarction) was 5% (7 of 149) for patients with a normal scan result versus 35% (69 of 199) for patients with an abnormal result (p < 0.001). Of the seven patients who had a cardiac event, five had documented atherosclerotic disease in the carotid, renal or peripheral vessels. The other two patients had symptoms of congestive heart failure at presentation: one patient had a diagnosis of hypertrophic cardiomyopathy and one had echocardiographically documented mitral regurgitation.

Fixed versus reversible thallium defect. Of the 199 patients with an abnormal thallium-201 scan result, 71 (20%) and 69 (20%) patients, respectively, had fixed only, reversible only or a combined (fixed and reversible) thallium-201 defect (Table 2). The event-free survival rate was significantly lower in patients with an abnormal than in those with a normal thallium scan result (p < 0.001) (Fig. 3). When event-free survival rates are compared according to type of defect, patients with a combined defect had the lowest event-free survival rate (p < 0.001) (Fig. 4). Patients with a fixed or reversible defect had an intermediate event-free survival rate, with some overlap in confidence intervals between the two groups (p < 0.001).
Figure 2. The actuarial event-free survival rate was significantly better for the 303 patients without symptoms of congestive heart failure (CHF) at presentation than for the 45 patients with such symptoms. The p values represent significance levels for differences in cardiac event rates over the total duration of the follow-up study. C.I. = confidence interval.

To assess the prognostic impact of the extent of defect, the cardiac event rate was compared with the number of abnormal thallium-201 segments. Patients with <2, 3 to 5 and >5 abnormal myocardial segments had, respectively, an event rate of 13%, 48%, and 40% at 2 years. (p < 0.001) (Fig 5).

Coronary revascularization. A total of 112 patients underwent coronary angiography within 6 months of the index test date; 42 of these underwent a coronary revascularization procedure, including 3 with normal and 39 with abnormal thallium-201 scan. Among the latter 39 patients, 24 underwent their revascularization procedure within 3 months of the intravenous dipyridamole scan.

Coronary surgery. Of the 42 patients receiving surgical therapy, 71% had a reversible or combined thallium-201 defect and 21% had a fixed defect only. The mean number of abnormal thallium defects was significantly greater in the 17 patients receiving late revascularization than in the 306 patients who did not undergo a surgical procedure (4.4 ± 3.4 vs. 2.3 ± 2.5, respectively, p < 0.001). The 30-day operative mortality rate was 7% (3 of 42). One patient died of renal failure and sepsis after coronary bypass surgery. A fatal myocardial infarction and death secondary to congestive heart failure were recorded in the other two patients.

Univariate and Multivariate Analyses

Univariate analysis. Before statistical modeling was initiated, univariate regression analysis was utilized to determine significant predictors of cardiac events (Table 3). Significant variables included an abnormal thallium-201 defect (combined, fixed or reversible), prior myocardial infarction, symptoms of congestive heart failure, number of abnormal segments on thallium testing, presence of atypical chest pain, digitalis therapy, hypercholesterolemia and a history of diabetes mellitus.

Multivariate logistic regression analyses. All significant univariate predictors were then entered into the regression model to detect independent predictors of cardiac death or
nonfatal myocardial infarction. Results from multivariate stepwise logistic regression analysis of clinical and radionuclide imaging variables revealed three variables that were significant predictors of a cardiac event. An abnormal thallium-201 scan result was the single best predictor of a cardiac event (p < 0.001). Patients with an abnormal scan result were 7.2 times more likely than patients with a normal result to have a cardiac event. Symptoms of congestive heart failure at presentation (odds ratio 2.1, p = 0.01) and a history of myocardial infarction (odds ratio 2.2, p < 0.001) were independently associated with a greater risk of a cardiac event than that of patients without this clinical history.

On the basis of results from univariate and stepwise analysis, various multivariate models for prediction of cardiac events were used to simulate a clinical spectrum of patient characteristics (Table 4). Symptoms of congestive heart failure alone predicted only 23.7% of the cardiac events (p = 0.001) compared with prior myocardial infarction, which predicted 47% of cardiac events (p < 0.001). By type of thallium-201 defect, the predictive power of thallium imaging was 33% in patients with a combined thallium defect (odds ratio 2.3, p < 0.001), 29.7% for those with only a reversible defect (odds ratio 1.6, p = 0.02) and 29.3% for patients with only a fixed defect (odds ratio 1.6, p = 0.03).

When combined variables were examined, evidence of reversible myocardial hypoperfusion, as documented by a reversible or combined thallium-201 defect, predicted 60.5% of cardiac events (p < 0.001). The cumulative power for prediction of a cardiac event was greatest in the presence of any abnormal thallium defect alone (90.7%, p < 0.001), an abnormal thallium defect plus the presence of congestive heart failure (92%, p < 0.001), or a prior myocardial infarction (92%, p < 0.001).

Discussion

Previous studies. Although the diagnostic utility of dipyridamole thallium-201 myocardial imaging has been investigated in many patient subsets, previous studies (23-31) have not specifically focused on the prognostic value of this noninvasive test in the elderly. We previously reported (32) that intravenous dipyridamole thallium imaging is safe in the elderly patient, with sensitivity and specificity values comparable to those in younger patients. Prognostic thallium-201 imaging data in older age groups have almost exclusively focused on older patients, using 65 years as the cut point and exercise as the stress (13,20).

Investigations (23-31) of the prognostic significance of dipyridamole thallium-201 imaging in patients with inadequate exercise tolerance have isolated various clinical and radionuclide imaging variables associated with a worse outcome. Age has been reported (29,31) to be a significant univariate predictor for cardiac events, including cardiac death, nonfatal myocardial infarction or revascularization procedure. Multivariate analysis of clinical and intravenous dipyridamole thallium-201 imaging data in patients undergoing...
Table 3. Univariate Predictors of Cardiac Death or Nonfatal Myocardial Infarction in 348 Patients ≥70 Years of Age

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Chi-Square</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous MI</td>
<td>16.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHF symptoms</td>
<td>10.84</td>
<td>0.001</td>
</tr>
<tr>
<td>Atypical chest pain</td>
<td>7.54</td>
<td>0.006</td>
</tr>
<tr>
<td>Digitalis therapy</td>
<td>7.25</td>
<td>0.007</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>5.37</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.12</td>
<td>0.05</td>
</tr>
<tr>
<td>Typical chest pain</td>
<td>2.56</td>
<td>0.11</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>2.11</td>
<td>0.15</td>
</tr>
<tr>
<td>Gender</td>
<td>1.44</td>
<td>0.23</td>
</tr>
<tr>
<td>Beta-blocker therapy</td>
<td>1.09</td>
<td>0.29</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0.75</td>
<td>0.39</td>
</tr>
<tr>
<td>History of cigarette smoking</td>
<td>0.35</td>
<td>0.49</td>
</tr>
<tr>
<td>Age</td>
<td>0.20</td>
<td>0.63</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.02</td>
<td>0.97</td>
</tr>
<tr>
<td>Family history</td>
<td>0.01</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Table 4. Incremental Value of Clinical and Radionuclide Variables for the Prediction of Cardiac Death or Nonfatal Myocardial Infarction in the 348 Patients ≥70 Years of Age

<table>
<thead>
<tr>
<th>Variables</th>
<th>No.</th>
<th>% Predicted</th>
<th>Relative Risk</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF symptoms</td>
<td>45</td>
<td>23.7</td>
<td>2.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Fixed defect</td>
<td>71</td>
<td>29.3</td>
<td>1.6</td>
<td>0.03</td>
</tr>
<tr>
<td>RV defect</td>
<td>70</td>
<td>29.4</td>
<td>1.6</td>
<td>0.02</td>
</tr>
<tr>
<td>CM defect</td>
<td>58</td>
<td>32.0</td>
<td>2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous MI</td>
<td>102</td>
<td>47.0</td>
<td>2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV defect + CHF</td>
<td>102</td>
<td>42.0</td>
<td>1.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Fixed defect + CHF</td>
<td>104</td>
<td>46.0</td>
<td>2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CM defect + CHF</td>
<td>96</td>
<td>50.0</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CM defect + prior MI</td>
<td>131</td>
<td>59.2</td>
<td>2.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RV or CM defect + CHF</td>
<td>126</td>
<td>60.5</td>
<td>2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fixed defect + prior MI</td>
<td>146</td>
<td>61.8</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV or CM defect + CHF</td>
<td>150</td>
<td>64.5</td>
<td>3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV defect + prior MI</td>
<td>151</td>
<td>63.5</td>
<td>2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV or CM defect + prior MI</td>
<td>176</td>
<td>66.7</td>
<td>2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal defect</td>
<td>199</td>
<td>90.7</td>
<td>7.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal defect + CHF</td>
<td>212</td>
<td>92.0</td>
<td>7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal defect + prior MI</td>
<td>223</td>
<td>92.0</td>
<td>6.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abnormal = abnormal thallium-201 perfusion defect; CM = combined fixed and reversible thallium-201 perfusion defects; RV = reversible thallium-201 perfusion defect; other abbreviations as in Table 1.
Cardiac event rate was significantly greater in patients with myocardial perfusion scan was defined as a defect involving events. In our large series of elderly patients, a low risk of any thallium-201 defect was predictive of a lower survival rate. Several investigators (25,27,38) have identified patients with thallium-201 defect (any type) as a predictor of survival rate. When additional clinical variables were considered, the presence of any thallium-201 perfusion abnormality had a greater predictive accuracy than did clinical characteristics or the type of perfusion defect. Slightly >90% of cardiac deaths or nonfatal myocardial infarctions occurred in patients with a thallium-201 defect (any type). The incremental increase in the prediction of cardiac events after the addition of clinical variables was small. However, the power of clinical variables may have been underestimated because clinicians pre-selected patients for intravenous dipyridamole thallium-201 testing who were considered to be at increased clinical risk, thus increasing the probability of subsequent abnormal test results and cardiac events.

In our elderly patients with a normal thallium-201 perfusion study result, only 5% had a cardiac death or a nonfatal myocardial infarction during a 23 ± 15 month follow-up period. When additional clinical variables were considered, a higher risk subset of patients with normal thallium-201 imaging could be identified by the association of symptoms of congestive heart failure or concomitant atherosclerotic disease. Yousif et al. (31) reported a similarly low incidence of cardiac death or nonfatal myocardial infarction in asymptomatic patients (average age 63 ± 12 years) with previously documented coronary artery disease referred for intravenous dipyridamole thallium imaging; some of these patients are included in the present series. In this earlier study of younger patients (31), no deaths or myocardial infarctions occurred during the 14 ± 10 months of follow-up in patients with a normal thallium scan result.

Actuarial survival analysis revealed that the extent of the thallium-201 defect was predictive of a lower survival rate. Several investigators (25,27,38) have identified patients with 0 to 1 abnormal myocardial segments on thallium testing as a low risk cohort not associated with a high rate of cardiac events. In our large series of elderly patients, a low risk myocardial perfusion scan was defined as a defect involving <3 abnormal myocardial segments on thallium testing. The cardiac event rate was significantly greater in patients with ≥3 abnormal myocardial segments.

Limitations of the study. When study entry is limited to a retrospectively identified series of patients, a causal relation between abnormal test results and the incidence of cardiac events is difficult to infer without significant attention to influential covariates. Because study entry was limited only by age, numerous clinical variables that could have affected the study results may not have been accounted for in the statistical analyses.

Repeat statistical analyses were utilized to determine important patient and radionuclide characteristics associated with an adverse event. Repeat analysis holding the level of significance at the 0.05 level increases the probability of a type I error. For repeat regression analysis modeling, a p value of 0.05 divided by the number of independent comparisons was used as the level for statistical rejection.

Data collection from a single institution is influenced by patient referral patterns and limits the general applicability of study results to varied institutions. The generalizability of study findings may be slightly different if patient entry criteria differ significantly from those of the patients included in this study. The supply of intravenous dipyridamole was limited before the use of this drug was approved by the Food and Drug Administration. Despite this, our data were collected from a large and heterogeneous group of patients, and the results should be applicable to an unselected group of elderly patients.

Five percent of patients were unavailable for follow-up study. Although inclusion of results from this missing group could affect overall study results, the clinical and radionuclide characteristics of those patients lost to follow-up were typical of the current study group. Quantitative imaging might have increased the sensitivity for detection of the subtle redistribution over that achieved by qualitative interpretation alone.

Relation to previous studies. The study group comprised patients referred for evaluation of known or suspected coronary artery disease on the basis of presence of symptoms (atypical chest pain 19%, typical angina 27%), prior history of myocardial infarction (29%) or coronary revascularization (9%) and previous coronary angiographic results. This group represented a spectrum of patients, including those undergoing preoperative evaluation and postinfarction risk stratification. As such, the data cannot be directly compared with those of previous studies limited to either the preoperative or the postinfarction use of dipyridamole thallium-201 imaging for risk stratification.

With one exception (39), this and previous observational studies (23-28,30) have demonstrated a significantly increased risk for cardiac events in association with the presence of dipyridamole-induced thallium-201 redistribution. Despite the high negative predictive value of dipyridamole thallium stress imaging for subsequent cardiac events (82% to 100% in preoperative screening), the positive predictive value of thallium-201 redistribution for subsequent events is much lower (27% to 58%) (39).

The prognostic value of dipyridamole thallium-201 imaging is influenced by several factors: the patient group, method of perfusion scan interpretation, access of clinicians to test data, the definition of cardiac events utilized and interventions (if any) to reduce risk based on the results of the test. Studies performed in tertiary referral centers may not be applicable in medical facilities with a different referral base, scan interpretation method or clinical intervention strategy. The initial report (23) of preoperative cardiac risk defined by dipyridamole thallium imaging and the most recent comparable study (39) evaluated a similar number of
patients (48 vs. 60) but derived significantly different outcomes despite a comparable occurrence of dipyridamole-induced thallium redistribution (33% vs. 37%). In the 6-year period between the publication of these two important studies, significant evolution has occurred in patient selection and referral patterns for dipyridamole thallium-201 imaging and in the management of patients based on the results of this preoperative screening procedure.

Our elderly study group comprised a consecutive series of patients and was larger than that in most previous reports; it provided data on the value of dipyridamole thallium-201 stress imaging derived from a wide referral base (inpatients and outpatients) studied over several years with a spectrum of presenting clinical syndromes. Consistency of scan interpretation technique by the use of the same expert observers should theoretically have minimized technical and observer-based variability in our study. The results of dipyridamole thallium data were made available to clinicians and were integrated into the decision to perform subsequent coronary revascularization in 42 patients (12%), despite the advanced age of this group. Although the study was not performed in a blinded fashion and modifications were made, as anticipated, in medical and surgical management on the basis of study results, 52 cardiac deaths and 24 nonfatal myocardial infarctions were observed after a mean follow-up period of 2 years. This "hard" cardiac event rate (11%/year) is comparable to previous event rates in preoperative dipyridamole thallium-201 studies (44 [9.4%] of 575) (40) and after myocardial infarction (22 [15.6%] of 141) (26,28,41). The hard cardiac event rate in one recent "negative" study (39) was 5% (3 of 60 patients), highlighting the potentially confounding effect of differences among study groups.

The current study identified the presence of any fixed or reversible dipyridamole thallium-201 defect as a powerful predictor of subsequent cardiac events (relative risk 7.2). The previously documented (42) risk of recent myocardial infarction and coexisting congestive heart failure was confirmed in this study, but added little to the relative risk above that associated with a perfusion defect alone. The presence of a fixed or combined (fixed and reversible) perfusion defect was found to be at least as predictive of subsequent cardiac death or myocardial infarction as was a reversible perfusion defect, an observation similar to that in previous reports (39,43). Clearly, fixed defects with the potential for late (>4 h) redistribution may also contribute to the risk of subsequent adverse ischemic cardiac events, although this finding was not evaluated in the current study.

Clinical versus scintigraphic risk stratification. It is clear from this and previous studies (25) that a combined clinical and perfusion imaging assessment optimizes risk stratification, regardless of the clinical setting. The most cost-effective approach to preoperative risk stratification may be initial clinical classification into high, moderate and low risk categories, with subsequent angiography frequently required in clinically high risk patients and no further evaluation needed in low risk patients (44). In this algorithm, the presence of prior myocardial infarction and congestive heart failure (two factors identified in the current study), diabetes mellitus and angina pectoris was a clinical high risk marker. One additional clinical risk marker, age ≥70 years, was utilized to define our study group. As such, all patients in the current study would have at least one clinical high risk variable (44) and would be in a moderate risk category in which the presence or absence of thallium-201 redistribution defines the likelihood of subsequent cardiac events. By applying this clinical-scintigraphic approach, dipyridamole thallium redistribution has been associated with a 10-fold increase in the risk of perioperative cardiac events (29.6% vs. 3.2%) (25,44).

It is reasonable to conclude that elderly (≥70 years) patients are at least a moderate risk patient group, even in the absence of prior myocardial infarction or congestive heart failure. The prognosis of these patients can be defined further with dipyridamole thallium-201 imaging. Prospective studies are required to determine whether subsequent management modifications based on this assessment will modify outcome in elderly patients with coronary heart disease.

Conclusions. Advanced age has been correlated with an increased risk of cardiac events. The purpose of this study was to investigate the prognostic utility of intravenous dipyridamole thallium-201 myocardial imaging in patients ≥70 years of age. Our study indicates that intravenous dipyridamole thallium myocardial imaging results are highly predictive of cardiac events in the elderly. In particular, the subsets of elderly patients with an abnormal thallium scan result and a previous myocardial infarction or a prior history of congestive heart failure were at greatest risk for cardiac death or nonfatal myocardial infarction. A normal dipyridamole thallium study result, irrespective of a previous history of myocardial infarction, was associated with a highly favorable survival rate, particularly in the absence of concomitant noncardiac atherosclerotic disease, or congestive heart failure. The data extend the results of dipyridamole and exercise stress thallium-201 studies in younger age groups to the growing number of elderly patients who are frequently unable to exercise maximally but remain at significant risk for cardiac events.

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