Coronary Artery Disease

Low Yield of Stress Imaging in a Population-Based Study of Asymptomatic Patients After Percutaneous Coronary Intervention

Tyler Peterson, MD; J. Wells Askew, MD; Malcolm Bell, MBBS; Daniel Crusan, BS; David Hodge, MS; Raymond J. Gibbons, MD

Background—Little is known about the clinical value of stress imaging studies in asymptomatic patients after percutaneous coronary intervention (PCI).

Methods and Results—Residents of Olmsted County, MN, who underwent PCI were followed up for the occurrence of stress imaging (stress nuclear or stress echocardiography), coronary angiography, or coronary artery bypass grafting (without angiography) as initial procedures after PCI. Patients whose first follow-up procedure was a stress imaging test were evaluated for their symptom status at the time of the study and whether they underwent angiography or revascularization (PCI or coronary artery bypass grafting) within 90 days. Of 1848 patients who underwent PCI during the study period, 710 (38%) had stress imaging as their initial procedure after PCI, and 241 (13% of the entire cohort) were asymptomatic at the time of testing. The majority (86%) of these 241 patients underwent PCI for acute myocardial infarction or unstable angina. Within 90 days of stress imaging, 16 of the 241 asymptomatic patients underwent angiography, and 2 patients were revascularized. Stratified by timing after PCI, none of 138 asymptomatic patients tested within 2 years of PCI underwent revascularization. Two of 103 asymptomatic patients tested after 2 years from PCI underwent revascularization. Compared with patients who were asymptomatic at the time of stress imaging, patients who did not undergo any follow-up procedures (stress imaging, angiography, or coronary artery bypass grafting) after the index PCI were older, were more likely to have comorbidities, and had significantly greater all-cause mortality (P<0.001).

Conclusions—In a population-based sample of patients undergoing PCI primarily for acute coronary syndromes, 1 in 8 had subsequent stress imaging when they were asymptomatic. These stress imaging tests resulted in further revascularization in <1% of patients. The low rate of downstream revascularization suggests that stress imaging in asymptomatic patients after PCI has low value. (Circ Cardiovasc Imaging. 2014;7:438-445.)

Key Words: cardiac imaging techniques ■ percutaneous coronary intervention

Rapid advances in cardiac imaging techniques have given physicians exciting tools to diagnose and treat disease. However, these advances have also brought a marked increase in the use of imaging procedures and concerns over inappropriate use and escalating costs.1,2 Appropriateness use criteria (AUC) have been developed to help guide physicians on cardiac imaging utilization. However, individual AUC are based on expert consensus opinion when there are gaps in the published evidence.

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In asymptomatic individuals, the AUC for cardiac radionuclide imaging and the AUC for stress echocardiography categorize repeat stress imaging <2 years after PCI as inappropriate and stress imaging ≥2 years after PCI as uncertain.3,4 There is little evidence on the frequency and impact on repeat revascularization of after-PCI stress imaging in asymptomatic patients. This longitudinal cohort study was designed to assess the frequency of after-PCI stress nuclear or stress echocardiography in patients residing in Olmsted County, MN, and the rate of referral for coronary angiography and revascularization after stress imaging in asymptomatic patients. Our hypothesis was that stress imaging studies are common in patients after PCI but only infrequently lead to repeat PCI or coronary artery bypass grafting (CABG) in asymptomatic patients.

Methods

The study was approved by the Mayo Clinic Institutional Review Board. Patients having undergone PCI between January 1, 1995, and June 30, 2008, were identified using the coronary catheterization database (n=15201). Patients were included if they were residents of Olmsted County, MN, and underwent PCI during this time (n=2424). Patients with a history of CABG (n=325), in-hospital death (n=41), stress imaging within 60 days post PCI (n=93), or those who failed to grant

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research authorization were excluded (n=117). Patients with prior PCI were not excluded. The final study group consisted of 1848 patients (Figure 1).

After PCI, we determined the first follow-up procedure as stress imaging (stress nuclear or stress echocardiography), coronary angiography, or CABG (without angiography). Patients whose first follow-up procedure was a stress imaging test were evaluated for their symptom status at the time of the study and whether they underwent angiography or revascularization (PCI or CABG) within 90 days of the stress test. Asymptomatic patients were defined as patients who did not have chest pain or an anginal equivalent at the time of their follow-up stress imaging. A 60-day black-out period after PCI was applied to asymptomatic patients with stress imaging as their first procedure to exclude diagnostic tests completed for the purposes of cardiac rehabilitation, staging of procedures, or assessment of functional capacity.

Olmsted County offers a unique advantage for population-based studies. Mayo Clinic is the only medical center within the county (population: 106,470 in 1990 and 144,248 in 2010) that offers stress single photon emission computed tomography, stress echocardiography, angiography, PCI, or CABG during the study period.

Stress Imaging

**Single Photon Emission Computed Tomography**
These methods have been described previously. Patients assigned to exercise stress underwent symptom-limited treadmill studies with the Bruce, modified Bruce, or Naughton protocol. Pharmacological stress studies used intravenous adenosine 140 μg/kg per minute for 6 minutes, dipyridamole 0.56 mg/kg for 4 minutes, or intravenous dobutamine starting at 10 μg/kg per minute and increasing every 3 minutes to a maximum of 50 μg/kg per minute. Radioisotope (either thallium 201 or technetium 99m sestamibi) was administered near peak exercise or at peak drug effect.

**Echocardiography**
These methods have also been described previously. Patients who were referred for exercise underwent a symptom-limited treadmill study using the Bruce, modified Bruce, or Naughton protocol. Pharmacological studies used dobutamine titrated to a peak dose of 40 μg/kg per minute with the option for atropine ≤2 mg if 85% of the age-predicted maximal heart rate was not achieved. Standard end points were used for test termination.

**Image Interpretation and Analysis**
Single photon emission computed tomography image interpretation was performed by consensus of 2 experienced readers. Rest and stress images were reviewed in 3 planes (short axis, horizontal axis, and vertical long axis) and scored for a 17-segment model. A 5-point scoring system was used to assess each segment (0=absent, 1=severely diminished, 2=moderately diminished, 3=mildly diminished, and 4=normal). An abnormal study had perfusion defects at rest or with stress. The study was considered positive for ischemia if there were new perfusion defects with stress. The summed difference scores (SDSs) and summed stress scores (SSSs) were determined. Using previously published criteria, the summed scores were divided into low risk (0–4), intermediate risk (5–7), and high risk (>7) for the SDS and low risk (0–3), intermediate risk (4–8), and high risk (>8) for the SSS. Based on the patient’s sex and body habitus as well as the extent and severity of the lesions, mild fixed defects were considered normal by the consensus of 2 readers because the majority have been found to represent soft tissue attenuation. Studies with mild fixed defects were reported to referring physicians as normal and analyzed as normal in the data set.

![Diagram](http://circimaging.ahajournals.org/)

**Figure 1.** Of the 241 patients who were asymptomatic at the time of stress imaging, only 2 proceeded to subsequent revascularization within 90 days. *We excluded 117 patients who did not grant research authorization, 41 patients who had in-hospital death during their index procedure, 93 patients who underwent stress imaging within 60 days of percutaneous coronary intervention (PCI), and 325 patients because of prior coronary artery bypass grafting (CABG).
Stress echocardiography interpretation was reviewed in a digitized quad-screen format in standard views. The left ventricular ejection fraction was determined by visual assessment or by the modified Quinones method. \(^1^0\) Regional wall motion was assessed on a scale of 1 to 5 at rest and peak stress in each of 16 segments. \(^1^1\) Patients with normal stress echocardiograms had normal left ventricular regional and global systolic function at baseline and no stress-induced wall motion abnormalities. Patients with abnormal stress echocardiograms had baseline regional wall motion abnormalities (fixed), stress-induced regional wall motion abnormalities (ischemic), or both (mixed). The overall change in left ventricular end-systolic size was assessed visually by comparing side-by-side rest and stress digitized images. The left ventricular end-systolic size response was considered abnormal if it did not change appreciably or if it increased in response to stress. The population was also stratified according to the severity of the stress echocardiographic results. Using previously published criteria, the number of abnormal and ischemic segments at peak stress was reported. \(^1^2\)

### Patient Follow-up
All-cause mortality was determined with Accurint and Mayo Clinic records.

### Statistical Analysis
Continuous variables are presented as mean±SD. Discrete variables are summarized using group percentages. For all analyses, a \( P \) value of <0.05 was considered statistically significant. Survival was estimated using the Kaplan–Meier method with the log-rank test determining statistical significance; the proportionality assumption was met for both groups of patients. Cox proportional hazard models were used to estimate the hazard ratios for all-cause mortality. Multivariable models were constructed using the variables of interest in the analysis. Given the number of events, the study had the flexibility to investigate the models without concern about overfitting. The proportional hazard assumption was met for the variables included in the models. Models were constructed using an initial stepwise selection process, which included clinical judgment. Variables included had univariate significance at the 0.15 level and were complete in 90% of the patients in the study.

### Results

#### Patient Characteristics
Baseline clinic characteristics of the 1848 study patients at the time of PCI are summarized in Table 1. A majority of the group had a prior myocardial infarction, and 86% presented with an acute myocardial infarction or unstable angina. More than half of the patients received a stent in their native left anterior descending coronary artery with 63% having multivessel disease. Almost two thirds of the patients received bare-metal stents. The mean follow-up after PCI was 8.4±4.3 years (median, 8.2 years; 25th percentile, 5.4 years; 75th percentile, 11.7 years). The vast majority of the patient follow-up was accomplished through Mayo Clinic records. Accurint was helpful in identifying 3 deaths not previously known from Mayo Clinic records.

#### First Follow-Up Procedures
Of the 1848 patients enrolled after index PCI, 710 (38%) underwent stress echocardiography or stress nuclear as their first procedure (mean time to stress imaging, 2.2±2.5 years), 577 (31%) underwent angiography as their first procedure (mean time to angiography, 1.5±2.5 years), 14 (<1%) underwent CABG as their first procedure, and 547 (30%) had no follow-up procedures (stress imaging, angiography, or CABG) during the follow-up period (Figure 1). Of the 710 who underwent stress imaging as their first procedure, 241 (34%) were asymptomatic at the time of the procedure (mean time to stress imaging in asymptomatic group, 2.6±2.5 years). These 241 asymptomatic patients comprised 13% of the total group of 1848 who underwent PCI and were the focus of this study.

Baseline clinical characteristics at the time of PCI comparing patients who were asymptomatic at the time of follow-up stress imaging and patients with no follow-up procedures (stress imaging, angiography, or revascularization) are compared in Table 2. Patients with no follow-up procedures were significantly more likely (\( P \leq 0.05 \) for all) to be older and have a history of congestive heart failure, hypertension, and prior cerebral vascular accident or transient ischemic attack.

### Timing of Stress Imaging and Stress Imaging

#### Results in Asymptomatic Patients
In the 241 asymptomatic patients with stress imaging as their first procedure, 138 (57%) of the stress tests occurred during
the first 2 years after PCI, and 103 (43%) occurred >2 years after PCI (Figures 1 and 2).

Of the 241 stress tests in asymptomatic patients, 137 were stress nuclear (Table 3) and 104 were stress echo (Table 4). Of the stress nuclear studies, 54 (39%) were abnormal, 5 (4%) of these studies were high risk by SDS (SDS>7), and 16 (12%) of the studies were high risk by SSS (SSS>8). Of the stress echo studies, 66 (63%) were abnormal, 12 (12%) had ≥5 ischemic segments at peak stress, and 32 (31%) had ≥5 abnormal segments at peak stress.

**Subsequent Coronary Angiography and Revascularization**

Within 90 days of stress imaging in the asymptomatic patients, 16 underwent angiography and 2 underwent revascularization (both PCI). Five of the angiograms occurred within 2 years of PCI, and 11 of the angiograms occurred 2 years after PCI. None of the 138 asymptomatic patients who tested within 2 years of PCI underwent revascularization. Two of the 103 asymptomatic patients tested 2 years after PCI underwent revascularization (Figure 1).

Of the 2 patients who did undergo revascularization within 90 days, 1 patient had a stress nuclear study 4 years after the index PCI while asymptomatic. The stress nuclear study showed extensive inferior ischemia (SDS=8). The patient underwent PCI 2 days after stress imaging, with stents placed in a 90% posterior lateral artery stenosis and a 70% mid-left anterior descending artery stenosis. The second patient underwent stress echocardiography 9 years after the index PCI while asymptomatic. The stress echocardiogram showed 5 segments of ischemia inferiorly at peak stress. PCI was completed 30 days after stress imaging, with 1 stent placed in a 90% proximal right coronary artery lesion.

**Subsequent Angiography and Revascularization in Patients With Markedly Abnormal Stress Imaging Results**

There were 16 patients with high-risk nuclear results (SSS>8 or SDS>7); 3 of these underwent angiography within 90 days, and 1 was revascularized. There were 32 patients who had stress echocardiograms, with ≥5 abnormal or ischemic segments at peak stress. Of these 32 patients, 10 underwent angiography within 90 days, and 1 was revascularized.

**All-Cause Mortality**

All-cause mortality was significantly less in asymptomatic patients who received stress imaging as their first procedure compared with patients who were free from all procedures (Figure 3). However, even after adjustment for differences in baseline clinical characteristics using Cox proportional hazard

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### Table 2. Baseline Clinical Characteristics Comparing Patients Who Were Asymptomatic With Stress Imaging as First Procedure and Patients With No Follow-Up Procedures

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic Patients With Stress Test as First Procedure (n=241)</th>
<th>Patients With No Follow-Up Procedures (n=547)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>62.9 (11.4)</td>
<td>66.9 (14.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of CHF, n (%)</td>
<td>18 (7.7)</td>
<td>77 (14.9)</td>
<td>0.006</td>
</tr>
<tr>
<td>History of hypertension, n (%)</td>
<td>137 (59.8)</td>
<td>350 (67.3)</td>
<td>0.048</td>
</tr>
<tr>
<td>Prior CVA/TIA, n (%)</td>
<td>16 (6.8)</td>
<td>67 (12.4)</td>
<td>0.020</td>
</tr>
<tr>
<td>Mod/severe renal disease, n (%)</td>
<td>3 (1.3)</td>
<td>16 (3.0)</td>
<td>0.15</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>16 (6.8)</td>
<td>58 (11.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death (post PCI), n (%)</td>
<td>2 (0.8)</td>
<td>2 (0.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All variables had <5% of the data missing, except for hypertension, which had 5.6% missing. CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; PCI, percutaneous coronary intervention; and TIA, transient ischemic attack.

*Not including patients who died in hospital at the time of their index PCI. Death rates are cumulative from survival curves.

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**Figure 2.** Histogram detailing the timing of stress imaging after percutaneous coronary intervention (PCI) in 241 patients who were asymptomatic at the time of the stress test. A total of 138 (57%) patients were tested within 2 years of PCI, and 103 (43%) were tested ≥2 years after PCI.
models (Table 5), a statistically significant lower hazard ratio for stress testing remained.

Discussion

Our study has 6 main findings. First, even after the exclusion of 93 patients during the 60-day black-out period, stress imaging was still the most common first procedure after PCI (38%).

Second, stress imaging in asymptomatic patients is relatively common; 1 in 8 patients in the entire cohort underwent stress imaging while asymptomatic as their first procedure after PCI.

Third, our study describes the timing of stress imaging after PCI in asymptomatic patients, permitting comparison with current AUC. Of the asymptomatic patients who underwent stress imaging after PCI, 57% had testing within 2 years of the index PCI, which is inappropriate according to current AUC. This finding is in agreement with work by Habr et al., who found that of asymptomatic patients undergoing stress echocardiography after PCI, the majority were tested within 2 years.

Fourth, despite markedly abnormal stress imaging results in 48 patients, only 16 total patients went on to angiography within 90 days. The relatively low rate of markedly abnormal stress tests (48 of 241) may help explain the low overall referral rate to angiography. However, the finding is also consistent with previous studies, which have demonstrated that there is a surprisingly modest rate of referral to angiography among patients with the most abnormal test results. Mudrick et al. suggested that a similar paradox may exist in cardiac imaging after PCI and reported similar findings.

Of PCI underwent revascularization. Two of the 101 asymptomatic patients tested 2 years after PCI underwent revascularization. The rate of revascularization directly related to stress imaging in asymptomatic patients after PCI in our cohort is 0% in patients tested within 2 years, 2% in patients studied after 2 years, and <1% overall. This finding supports the current AUC for stress testing asymptomatic patients <2 years after PCI and suggests that stress imaging asymptomatic patients >2 years after PCI is also of low yield.

Previous administrative database studies have found higher yields for stress testing after PCI. Shah et al. reviewed the use of stress testing after revascularization (PCI or CABG) from administrative billing records and found that the yield of stress testing for subsequent revascularization was 5%. Mudrick et al. found a yield of stress testing for revascularization of 7% in a Medicare population who had undergone PCI. However, these studies did not have information about patient symptoms at the time of stress imaging. Our analysis is the first to concentrate on asymptomatic patients at the time of stress testing, which may at least partially explain the considerably lower yield.

Finally, our study demonstrates that, paradoxically, patients who never underwent stress imaging, angiography, or CABG had higher risk features at baseline. The acute coronary syndrome literature has documented a risk-treatment paradox. Previous studies have demonstrated that there is a paradox of stress testing for subsequent revascularization and a paradox of stress imaging absence of stress testing.
of increasing age and comorbidities in patients who did not undergo any testing after PCI. After adjustment for baseline clinical characteristics using Cox proportional hazard models, stress imaging in asymptomatic patients remained protective with a hazard ratio of 0.5 (95% confidence interval, 0.3–0.7; Table 5). Given its low rate, revascularization after stress imaging cannot explain the difference in outcome. Unmeasured comorbidities, such as medical noncompliance, general frailty, and obstructive sleep apnea, could contribute. The absence of ejection fraction data on many patients in our study did not permit adjustment for this important variable.

Limitations
The study population consisted of residents of Olmsted County, a relatively homogenous population, with all patients treated at a large academic center in the Midwestern United States. The study also spans a relatively long time frame, which encompasses changes in cardiovascular practice, notably the introduction of drug-eluting stents.

Although all patients were residents of Olmsted County and Mayo Clinic was the only center performing stress SPECT, stress echocardiography, angiography, PCI, and CABG within the county, we cannot account for patients who may have left the county and received care elsewhere. This may underestimate follow-up events. However, work by Jabre et al. found that 92% of patients after a myocardial infarction continued to live in or near Olmsted County and receive care in the county, with the result that complete follow-up was available through the medical record.

Although few of the positive stress tests resulted in referral for angiography within 90 days of the stress test, we were unable to account for changes in medical therapy after follow-up scans or for the impact of scan findings on later decisions to proceed with revascularization. A previously published multicenter prospective registry has documented only limited changes in medical therapy after moderate to severely abnormal stress imaging results.15

Our cohort was dominated by patients who had PCI for acute coronary syndromes. Only a small subset (14%) underwent PCI for nonacute indications, which may limit the applicability of our study results to patients with stable CAD. Other studies have found higher rates of PCI for nonacute indications.23 A previous Mayo Clinic publication reviewing all PCIs (including patients who live outside Olmsted County) between March 2003 and September 2004 found the percentage of PCIs done for elective reasons to be 32%.24 We think that the higher percentage of patients treated for acute indications in our study data is reflective of our population-based cohort because almost all Olmsted County residents with acute coronary syndromes are treated at Mayo. Patients from elsewhere who undergo PCI are more likely to have stable CAD.

Our results do not apply to studies performed within 2 months of PCI on asymptomatic patients for purposes of cardiac rehabilitation, staging of procedures, or assessment of functional capacity.

Data on anti-ischemic medications were not available at the time of stress imaging.

Conclusions
In a population-based sample of patients undergoing PCI primarily for acute coronary syndromes, we found stress imaging to be relatively common in asymptomatic patients after PCI. The results of the tests often show ischemia but rarely result in

Table 5. Hazard Ratios for All-Cause Mortality in Asymptomatic Patients With Stress Testing as First Procedure vs Patients With No Follow-Up Procedures

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 y)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>History of CHF</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>COPD</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Moderate to severe renal disease</td>
<td>0.0003</td>
</tr>
<tr>
<td>Stress testing as first procedure</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; CHF, congestive heart failure; and COPD, chronic obstructive pulmonary disease.
further revascularization. The low rate of downstream revascularization found in our study suggests that stress testing asymptomatic patients after PCI has low value either before or after 2 years.

Acknowledgments
We would like to thank Dr Robert McCully for review of and assistance with the stress echocardiography sections of the article.

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Disclosures
Dr Gibbons is a consultant for Lantheus Medical Group and a speaker for AstraZeneca. Dr Peterson had full access to all of the data in the study and takes responsibility for the accuracy of the data and data analysis. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

This population-based study of Olmsted County, MN, residents who underwent percutaneous coronary intervention (PCI) was designed to assess the frequency of stress imaging after PCI and the rate of referral for angiography and revascularization after stress imaging in asymptomatic patients. Currently, the appropriate use criteria for cardiac radionuclide imaging and stress echocardiography categorize repeat stress imaging <2 years after PCI as inappropriate and stress imaging ≥2 years after PCI as uncertain. Of 1848 Olmsted County, MN, residents who underwent PCI between 1995 and 2008, 241 (13%) were asymptomatic at the time of stress imaging performed after PCI. The rate of revascularization within 90 days of stress imaging was 0% in the 138 asymptomatic patients tested within 2 years, 2% in the 103 patients studied after 2 years, and <1% overall. These data affirm the current appropriate use criteria for stress testing asymptomatic patients <2 years after PCI and suggest that stress imaging in asymptomatic patients ≥2 years after PCI is also of low yield.
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