Using the Risk of Restenosis as a Guide to Triaging Patients Between Surgical and Percutaneous Coronary Revascularization

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Background—Coronary artery bypass graft (CABG) and percutaneous coronary revascularization (PCI) are strategies for treating coronary disease. Because the principal limitation of PCI is restenosis, CABG might be favored for those at high risk for restenosis. Using a clinical risk score for predicting restenosis, we examined whether patients with higher risks for restenosis were preferentially referred for CABG.

Methods and Results—A procedural registry of 2320 revascularization patients from whom data on procedure type, demographics, comorbid conditions, health status, vessel anatomy, and outcomes were taken was analyzed. Patients were classified and scored into 3 categories of restenosis risk ranging from 11% to 44%, as defined by 8 preprocedural characteristics. The objective of this study was to describe referral patterns between PCI and CABG in each category of risk. 2060 patients underwent nonemergent revascularization. 1404 of the patients underwent PCI and 656 were treated with CABG. Among the patients at low and intermediate risk for restenosis, twice as many were referred to PCI. Among those at the highest risk, 3-times as many were referred to PCI, resulting in a significant trend for those with the higher risks of restenosis to be preferentially referred to PCI ($P < 0.015$). Similar results were seen when the analysis was restricted to only those with multivessel disease.

Conclusions—Patients at higher risk for restenosis were being preferentially treated with PCI as opposed to CABG. These results may have implications for reevaluating current patterns of triaging patients between PCI and CABG, and for the use of drug-eluting stents within PCI patients. (Circulation. 2004;110[suppl II]:II-50–II-54.)

Key Words: bypass • angioplasty • restenosis • atherosclerosis

Substantial investigative efforts and rapid technical innovations have created 2 viable revascularization strategies for treating patients with occlusive coronary disease: percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG). Throughout the past 2 decades, clinical trials have directly compared these 2 strategies.

Short-term and long-term results of multiple studies, including the Randomized Intervention Trial of Angina,1,2 the Bypass Angioplasty Revascularization Investigation,3 the Emory Angioplasty versus Surgery Trial,4 and the recent Arterial Revascularization Therapies Study,5 have all demonstrated equivalent survival and nonfatal myocardial infarction rates, although a greater prevalence of post-treatment angina has been repeatedly shown after PCI. Long-term costs have also been similar, with the early savings from PCI being eroded over time by the need for repeat procedures. Only the recent Stent or Surgery trial6 has demonstrated an early survival advantage from CABG, although a recent meta-analysis of 13 trials and 7964 patients also suggested a 5-year survival advantage from CABG.7 Current strategies for triaging patients between these 2 treatments is highly variable, with individual clinicians having to weigh the benefits of a less invasive PCI strategy against the greater potential need for a repeat procedure and the higher likelihood of residual symptoms.

Because the need for repeat procedures after PCI is the primary limitation of this technique, it seems clinically intuitive that referring patients at higher risk for restenosis to surgery would be an effective strategy for optimizing patients’ outcomes. In fact, the significantly higher health status (symptoms, function, and quality of life) observed in the CABG group of the Stent or Surgery trial and a recent observational registry were almost completely accounted for by the lower health status in PCI patients requiring repeat procedures.8,9 To implement such a triage strategy, however, requires creating a system to rapidly assess patients’ risk for restenosis and prospectively implementing a practice of preferentially referring higher-risk patients to surgery. We recently developed a simple clinical risk score that classifies patients into low-risk (15%), intermediate-risk (23%), or high-risk (44%) groups for requiring a repeat PCI after an initially successful procedure.10 For this tool to be clinically...
useful, however, it would need to improve on current clinical decision-making. Because it is possible that clinicians intuitively incorporate patients' risks for restenosis when recommending a revascularization treatment, the opportunity to improve current care is not known.

The objective of this study was to describe current referral patterns of patients needing coronary revascularization to PCI or CABG as a function of the underlying risk for restenosis. Finding that patients at higher risk for restenosis are not being referred more often for CABG may identify an important opportunity to improve the efficiency of triage and, potentially, the outcomes of patients needing coronary revascularization.

Methods

Patient Population
This study used a well-developed procedural registry that quantified the health status of patients before and 1 year after coronary revascularization. The process of patient recruitment, success, and possible selection biases have been previously described.30,11 From February 1999 to August 2000, 689 patients undergoing CABG at the Mid America Heart Institute (MAHI), an urban tertiary care center, and 1631 patients undergoing PCI participated in this study. All consenting patients were administered a series of health status questionnaires at baseline and during follow-up. These health status data were used to supplement an existing procedural database. Approval from the Saint Luke's Hospital Institutional Review Board was obtained before the conduct of this study.

Clinical and Procedural Assessments of Disease Severity
MAHI has maintained a procedural database for patients undergoing coronary interventions since 1982. This database provides a detailed description of the coronary anatomy, the type of revascularization performed, procedural results, and postprocedure complications. Definitions compatible with the national registries of the American College of Cardiology and the Society of Thoracic Surgeons are used.

MAHI Restenosis Risk Model
To examine the association between current referral patterns of patients requiring coronary revascularization and the risk of restenosis, we used a recently developed Restenosis Risk Model.14 This model is generated from 8 clinical characteristics that group PCI patients into 3 categories of risk for 1-year target vessel revascularization. The risk of restenosis is calculated by assigning a point value for each of the following 8 clinical characteristics: the presence of diabetes and acute myocardial infarction (AMI) are each assigned 4 points; age older than 55 and daily angina as assessed by a Seattle Angina Questionnaire15 (SAQ Angina Frequency score 30) with 3 points each; previous history of PCI, male gender, and weekly/monthly angina (SAQ Angina Frequency Score 31 to 90) with 2 points each; and multivessel coronary disease is assigned 1 point. Restenosis risk scores range from 0 to 19. Patients with a score of between 0 and 4 have a 15% rate of restenosis within 1 year and are categorized as low risk. A moderate risk of restenosis (23%) is observed with a cumulative score of 5 to 8 points. Patients with a cumulative score of 9 to 19 points have a 44% risk of restenosis during the year after their procedure and are categorized as high risk. Because AMI patients were excluded from the analysis, the range of scores in the current study is 0 to 15.

The success of this model in identifying patients with restenosis is comparable to other more invasive and complex techniques. Receiver operating curves, confirmed by bootstrap validation, were created to evaluate model performance. The c-index of this model is 0.65. This is a substantial improvement over previous studies of clinical predictors of restenosis (c=0.51) and is comparable to predictors with angiographic data (c=0.63 to 0.73).16–18

Definition of Target Vessel Revascularization
All patients were followed-up for at least 1 year. Restenosis was defined as a repeat target vessel revascularization between 30 days and 1 year. A 30-day “blanking” period was created to exclude patients undergoing staged procedures.

Statistical Analyses
For descriptive purposes, categorical data are reported as frequencies and differences between groups were compared with χ² or Fisher exact test when the frequency in any given cell was <5. Continuous data are reported as the mean±SD, and differences between groups were tested using an analysis of variance.

The restenosis risk model was applied to all patients in the procedural database to estimate their risk of restenosis. Because the purpose of this study was to describe current triage patterns for coronary revascularization in the context of patients’ risk for target vessel revascularization were they to be treated with PCI, it was important for the clinical circumstances to be such that either PCI or CABG would be a reasonable treatment option. Because PCI is clearly the preferred revascularization strategy in the setting of AMI,19–24 these patients were excluded from the current analysis.

The primary analysis is a description of the ratio of PCI to CABG within each category of preprocedural restenosis risk. This allowed validation of the concept that patients with a higher risk of restenosis might experience significantly fewer repeat procedures had they been treated with CABG. The secondary sensitivity analysis was designed to exclude the possibility that there might be a greater mortality risk from CABG in the group with a higher risk of restenosis that could have offset the potential gains of preferentially referring these patients to CABG. Because we considered that patients at high risk for mortality from CABG might preferentially be referred for PCI, we calculated the expected operative mortality of all patients for CABG. We used the risk scoring system of the Northern New England Cardiovascular Disease Study Group, which includes 8 variables and stratifies the risk of mortality from 0.4% to ≥28.3%. The c-index of this model is 0.74 to 0.76.12 Such models are well-established tools for assessing operative risk.13 Because this model generates 14 categories of risk, we collapsed the categories into low risk, medium risk, and high risk (<1%, 1% to 3.9% and >4%). A χ² test was then used to assess whether any significant differences between the expected perioperative risk of PCI and CABG patients were present within each category of restenosis risk. The value for declaring statistical significance was P<0.05, and all analyses were conducted using SAS version 8.2.

Results

Baseline Characteristics
Of the 2320 consecutive patients undergoing revascularization and participating in this registry, 101 were excluded because they presented with AMI. An additional 159 patients were excluded because of insufficient baseline data to generate a risk score. Thus, a total of 2060 (93%) patients, 1404 PCI and 656 CABG patients, were available for these analyses. Baseline characteristics are provided in the Table.

Patients undergoing PCI were more likely to be younger (65.3±11.5 versus 66.9±10.5, P=0.002), to smoke (20.2% versus 15.9%, P=0.02), to be normotensive (31.8% versus...
Baseline Characteristics of PCI and CABG Groups

<table>
<thead>
<tr>
<th>Demographics</th>
<th>PCI, n=1404 (%)</th>
<th>CABG, n=656 (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>65.3±11.5</td>
<td>66.9±10.5</td>
<td>0.002</td>
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<tr>
<td>Male</td>
<td>1000 (71.2)</td>
<td>466 (71.0)</td>
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</tr>
<tr>
<td>White</td>
<td>1311 (95.2)</td>
<td>622 (95.7)</td>
<td>0.63</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>711 (50.6)</td>
<td>195 (29.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoker</td>
<td>277 (20.3)</td>
<td>101 (15.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>958 (68.2)</td>
<td>527 (80.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>Diabetes</td>
<td>352 (25.0)</td>
<td>179 (27.3)</td>
<td>0.28</td>
</tr>
<tr>
<td>BMI</td>
<td>32±5.2</td>
<td>28.3±5.2</td>
<td>0.36</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>112 (8.0)</td>
<td>27 (4.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Peripheral vascular ds</td>
<td>182 (13.0)</td>
<td>94 (14.3)</td>
<td>0.340</td>
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<tr>
<td>Cerebral vascular ds</td>
<td>220 (15.7)</td>
<td>79 (12.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>COPD</td>
<td>142 (10.1)</td>
<td>67 (10.2)</td>
<td>0.94</td>
</tr>
<tr>
<td>EF &lt;40</td>
<td>176 (12.4)</td>
<td>145 (22.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Coronary ds</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main</td>
<td>37 (2.6)</td>
<td>154 (23.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 vessel</td>
<td>489 (34.8)</td>
<td>52 (8.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>2 vessel</td>
<td>421 (30.0)</td>
<td>134 (20.6)</td>
<td></td>
</tr>
<tr>
<td>3 vessel</td>
<td>494 (35.2)</td>
<td>463 (71.2)</td>
<td></td>
</tr>
<tr>
<td>Aspirin use</td>
<td>811 (92.0)</td>
<td>256 (92.7)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

PCI indicates percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; BMI, body mass index; ds, disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction.

19.6%, P<0.001), and to have renal insufficiency (8% versus 4.1%, P=0.001), an ejection fraction >40% (84.1% versus 77.3%, P<0.001), and less extensive coronary disease. More patients underwent PCI if they had had a previous revascularization procedure (50.6% versus 29.7%, P<0.001). No differences in race, gender, body mass index, chronic obstructive pulmonary disease, or peripheral vascular disease were detected. Most notably, no difference in the prevalence of diabetes was observed between those undergoing PCI and CABG.

Procedures by Risk Score
The primary objective of this study was to describe the ratio of PCI versus CABG procedures among different categories of risk for restenosis. This is shown graphically in Figure 1.

Had the risk of restenosis been an important factor in triaging patients between PCI and CABG, then proportionately fewer PCI procedures would be expected among higher categories of preprocedural risk. In contrast, the highest PCI-to-CABG ratio was seen in the group with the highest risk of restenosis.

Among the 765 patients in the lowest risk group, 67% were treated with PCI and the PCI-to-CABG ratio was 2.05. Among the 964 patients with an intermediate risk of restenosis, 66.6% of patients underwent PCI and the PCI-to-CABG ratio was 2.0. Of the 331 patients at high risk for restenosis, 75% underwent PCI and the PCI-to-CABG ratio was 3.0. A statistical difference in the proportion of patients undergoing PCI or CABG was observed across the different categories of restenosis risk (P=0.015). Paradoxically, those with the highest risk of target vessel revascularization were most likely to be triaged to PCI.

Differences in Need for Target Vessel Revascularization
To confirm the logic that target vessel revascularization procedures could be averted by preferentially referring those at greatest risk to CABG, we examined the difference in target vessel revascularization rates within each category to restenosis risk. Among the 514 PCI patients in the lowest restenosis risk group, 77 (14.9%) required a target vessel revascularization procedure over the next year as compared with 2 of the 249 CABG patients (0.8%; absolute risk reduction [ARR]=14.1%). In the moderate-risk group, 144 of 642 PCI patients required a repeat procedure (22.4%) as compared with 4 of 318 CABG patients (1.3%; ARR=21.1%). In the highest restenosis risk group, 106 of the 248 PCI patients at the highest risk for restenosis required target vessel revascularization (42.7%) as compared with 3 of the 80 CABG patients (3.8%; ARR=38.9%). Thus, for every 2.6 patients at high risk for restenosis referred to CABG rather than PCI, 1 patient would be expected to avoid a repeat revascularization procedure.

Relationship of CABG Mortality Risk and Procedure Use
To address the possibility that an excess procedural mortality for undergoing CABG might support the triage of patients at high risk for restenosis to PCI, we compared the expected mortality risk for all patients using the Northern New England Models. Figure 2 shows the expected mortality risks for the PCI and CABG patients by each category of restenosis risk. No significant differences were observed, suggesting that the lack of association between risk of restenosis and the use of PCI is not explained by this potential factor (Cochran-Mantel-Haenszel P=0.32).

Discussion
This is the first study to our knowledge to examine the association between the risk for restenosis and the triage of patients between CABG and PCI. Given that one of the principal advantages of CABG over PCI is its ability to avoid repeat procedures, we expected that those patients at the highest risk for restenosis would preferentially be referred for surgical revascularization. This was not the case. In fact, the
opposite was observed in that the proportion of patients undergoing PCI increased as the risk of restenosis increased. This suggests that current practice has not identified an important opportunity to improve the triage of patients and more rationally apply expensive medical technologies to the treatment of occlusive coronary artery disease.

Several potential insights may explain these findings. First, at MAHI, there is no process for formally establishing the risk of restenosis at the time patients are considered for PCI. Although variables for single-vessel disease, asymptomatic patients, and comorbidities such as diabetes are incorporated into our risk stratification model, extenuating clinical circumstances may have warranted additional weight on some of these characteristics in selecting therapy and have outweighed the mean values incorporated in our model. Although the interventional cardiologists informally estimate the risk for restenosis when triaging their patients, the absence of a formal statistical process makes systematic approaches to improved decision-making difficult, and there is certain to be variability in the estimates of individual practitioners. For example, Lee et al have demonstrated that statistical models of outcome prediction after CABG were more accurate than estimates of senior clinicians and that clinicians had substantial variability in their estimates.22

Finding a paradoxically higher rate of PCI use in the patients at highest risk suggests that the use of our restenosis risk model may improve the efficiency and efficacy of current triage strategies.

An additional explanation may be that angiographic characteristics, not included in the current model, may explain the greater use of PCI in patients with a higher risk of restenosis. However, models with more detailed angiographic variables have similar discriminatory ability, and it is unlikely that substantial differences in the categorization of individual patients’ risk for restenosis would have occurred. More importantly, the use of a model that is easily acquired avoids significant interoperator variability in generating the predictor variables and is effective at predicting risk suggests that it could be readily applicable in multiple settings. Most importantly, the variables in this model can be collected before the selection of a mode of revascularization, in contrast to minimal luminal diameter, which is only known after PCI is performed, and can therefore be used to guide initial decision-making.

A final consideration is that patient or physician preferences for a less invasive revascularization strategy, despite knowing that a high risk of a repeat procedure was being undertaken, may have been responsible for our findings. Our database did not capture patient preferences for mode of revascularization, yet it would be surprising to find that patients with the highest preprocedural risk for restenosis would have a greater preference for PCI than patients at lower risk. Similarly, although physician preferences may have significantly influenced the selection of revascularization strategy, we believe that the seeming preference to preferentially select those with least likelihood of a durable result for PCI is illogical. Plans are being made at MAHI to routinely acquire and present the risk of restenosis at the time of angiography so that clinicians can more readily incorporate this information when they recommend a strategy for revascularization.

In summary, we found that patients with higher preprocedural risks of restenosis were preferentially being treated with PCI as opposed to CABG, despite recent data suggesting that the better health status outcomes from CABG are largely because of the lower gains acquired by PCI patients experiencing restenosis.8,9 We found that among the 16% of patients at the highest risk for restenosis, patients were 3-fold more likely to be treated with PCI rather than CABG, and that for every 2.6 of these patients referred to CABG, 1 would have avoided a repeat procedure over the subsequent year. These results may have implications not only for the future triage of patients between PCI and CABG but also for the use of drug-eluting stents within patients being treated percutaneously.

Acknowledgments
Dr Spertus owns the copyright to the Seattle Angina Questionnaire.
References


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_Circulation_. 2004;110:II-50-II-54
doi: 10.1161/01.CIR.0000143121.71433.05
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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