Risk of Restenosis and Health Status Outcomes for Patients Undergoing Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft Surgery

John A. Spertus, MD, MPH; Ravi Nerella, MD; Richard Kettlekamp, MD; John House, MS; Steve Marso, MD; A. Michael Borkon, MD; John S. Rumsfeld, MD, PhD

Background—Previous comparisons of percutaneous coronary interventions (PCIs) and coronary artery bypass graft (CABG) surgery have demonstrated similar survival but have also generally found better health status outcomes (symptoms, function, and quality of life) with CABG. The principal limitation of PCI has been the occurrence of restenosis. No previous studies comparing the health status outcomes of PCI and CABG have examined differences in these outcomes as a function of patients’ preprocedural risk for restenosis.

Methods and Results—We examined the health status outcomes, using the Seattle Angina Questionnaire (SAQ), among 1459 consecutive patients (1027 treated with PCI and 432, with CABG), stratified by their risk for restenosis. In multivariable-adjusted, linear regression analyses, no differences in 1-year angina or quality of life were observed among the 37.4% of patients at low risk for restenosis. However, among the 46.7% at intermediate risk for restenosis, 1-year health status scores were moderately better after CABG surgery compared with PCI (difference in SAQ angina frequency scores favoring CABG: 6.1 ± 1.7 points, P = 0.0003; difference in SAQ quality of life = 5.8 ± 1.6 points, P = 0.0004). Even larger differences in 1-year outcomes favoring CABG surgery were observed in patients at high risk for restenosis (SAQ angina frequency difference = 10.8 ± 4.2, P = 0.01; SAQ quality of life difference = 10.8 ± 3.9, P = 0.006).

Conclusions—The relative health status benefits of CABG surgery compared with PCI increase as the risk of restenosis increases. Although selecting CABG or PCI is complex, preprocedural restenosis risk should be considered. It should also be tested as a means for considering drug-eluting as opposed to bare metal stents in PCI. (Circulation. 2005;111:768-773.)

Key Words: angioplasty • bypass • restenosis • quality of life

Numerous studies have compared the outcomes of coronary revascularization between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery. Although most studies have found no differences in survival or nonfatal myocardial infarction, they have consistently shown that patients who undergo PCI are more likely to have recurrent angina and to require repeat procedures.1–5 Also, because the elimination of angina is more complete with surgery, patients may derive a greater quality-of-life benefit with CABG compared with PCI.6–8 The principal reason for recurrent angina and repeat procedures after PCI appears to be the development of restenosis. For example, in the recent Stent or Surgery trial, 6-month angina frequency scores were significantly better among patients treated with CABG surgery overall, but no difference was seen in the subset of PCI patients who did not have a repeat procedure.9 Similarly, an observational registry identified that patients who underwent surgical revascularization had better symptom control and quality of life and that most of this difference was attributable to PCI patients who required a repeat procedure.10

If the health status (ie, angina and quality of life) benefits of CABG surgery are most evident in those PCI patients who develop clinical restenosis, then it is reasonable to consider preferential referral of patients at high risk of restenosis to CABG surgery. Currently, however, no data demonstrate that preprocedural risk for restenosis is associated with differences in outcomes between CABG surgery and PCI.

We examined the differences in health status outcomes between CABG surgery and PCI among a prospective cohort of consecutive patients undergoing coronary revascularization. Using a previously reported clinical risk score to stratify patients into categories of low, intermediate, and high risk for restenosis,11 we examined the differences in 1-year health status among those treated surgically and those treated with PCI. Establishing clinically meaningful differences in patient...
outcomes among patients at higher risk for restenosis could support more efficient treatment selection in such patients.

**Methods**

**Study Sample**

Data were prospectively collected from a consecutive series of patients undergoing coronary revascularization at the Mid America Heart Institute in Kansas City, Mo. The purpose of this study was to describe the health status of patients before and 1 year after coronary revascularization. The details of patient recruitment have been previously described. In brief, from February 1999 to August 2000, all patients undergoing coronary revascularization were approached to participate in the study. Among all 3669 patients who underwent PCI or CABG during the time period, 29 (0.8%) were urgent cases and died during the procedure, 78 (2%) were non–English speaking, 40% (17% versus 21%, \( P = 0.01 \)) had chronic obstructive pulmonary disease, 101 (25%) had previous PCI, and 127 (29%) had an ejection fraction <40% (17% versus 21%, \( P = 0.01 \)). No differences in restenosis risk score (5.5 ± 3 versus 5.4 ± 3, \( P = 0.4 \)) or any of the other variables listed in Table 1 were present.

Because the intent of this study was to provide a tool for the triage of patients between PCI and CABG, we thought it important to focus on patients potentially eligible for both procedures. Because PCI is clearly preferable for primary reperfusion in the setting of acute myocardial infarction,13,14 these patients were excluded from the current analysis, giving a final analytic cohort of 1459 patients. 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**

The Mid America Heart Institute has maintained a procedural database for patients undergoing coronary interventions since 1982. This database provides a comprehensive description of coronary anatomy, technique of revascularization, procedural results, and complications. It is compatible with American College of Cardiology and Society of Thoracic Surgeons data definitions.

**Outcome Assessment**

Angina frequency and quality of life were measured with the Seattle Angina Questionnaire (SAQ), a 19-item, disease-specific measure for patients with coronary artery disease. Each SAQ domain has been independently demonstrated to be valid, reproducible, sensitive to

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**TABLE 1. Baseline Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>PCI (n=1027)</th>
<th>CABG (n=432)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>66.1 ± 11.1</td>
<td>66.0 ± 10.6</td>
<td>0.92</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>717 (70)</td>
<td>319 (74)</td>
<td>0.12</td>
</tr>
<tr>
<td>Race (white)</td>
<td>966 (95)</td>
<td>408 (95)</td>
<td>0.92</td>
</tr>
<tr>
<td>Body mass index</td>
<td>29.2 ± 5.8</td>
<td>28.5 ± 5.1</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior revascularization</td>
<td>528 (51)</td>
<td>127 (29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>176 (18)</td>
<td>67 (16)</td>
<td>0.39</td>
</tr>
<tr>
<td>Hypertension</td>
<td>706 (69)</td>
<td>350 (81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>164 (16)</td>
<td>48 (11)</td>
<td>0.02</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>314 (31)</td>
<td>210 (50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine &gt; 2.0</td>
<td>21 (2)</td>
<td>26 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left main CAD</td>
<td>26 (3)</td>
<td>107 (25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>88 (9)</td>
<td>32 (7)</td>
<td>0.46</td>
</tr>
<tr>
<td>Diabetes</td>
<td>257 (25)</td>
<td>122 (28)</td>
<td>0.20</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%</td>
<td>121 (15)</td>
<td>87 (21)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Preprocedural restenosis risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (score &lt;4)</td>
<td>393 (38)</td>
<td>153 (35)</td>
<td></td>
</tr>
<tr>
<td>Intermediate (score 4–8)</td>
<td>453 (44)</td>
<td>225 (52)</td>
<td></td>
</tr>
<tr>
<td>High (score &gt;8)</td>
<td>181 (18)</td>
<td>54 (13)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline health status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAQ angina frequency</td>
<td>35.5 ± 27.8</td>
<td>33.1 ± 25.6</td>
<td>0.14</td>
</tr>
<tr>
<td>SAQ quality of life</td>
<td>56.0 ± 23.9</td>
<td>56.1 ± 23.2</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>1-Year health status characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAQ angina frequency</td>
<td>91.3 ± 18.9</td>
<td>96.0 ± 12.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SAQ quality of life</td>
<td>85.7 ± 18.6</td>
<td>90.6 ± 14.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are n (%) or mean ± SD. CAD indicates coronary artery disease.
TABLE 2. Clinical Restenosis Risk Model

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Risk Points Assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction (STEMI patients)</td>
<td>4</td>
</tr>
<tr>
<td>undergoing primary PCI</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>4</td>
</tr>
<tr>
<td>Daily angina (SAQ angina frequency score ≤30)</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt;55 y</td>
<td>3</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>2</td>
</tr>
<tr>
<td>Weekly/monthly angina (SAQ angina frequency score 31–90)</td>
<td>2</td>
</tr>
<tr>
<td>Male sex</td>
<td>2</td>
</tr>
<tr>
<td>Multivessel coronary artery disease</td>
<td>1</td>
</tr>
</tbody>
</table>

Restenosis Risk Model

A recently developed restenosis risk model was used to categorize each patient’s risk for clinical restenosis, defined as a repeat procedure within the next year to the target vessel of the original procedure. The goal in creating the restenosis risk model was to use clinical data that could be readily obtained before PCI and therefore used to inform risk stratification before the procedure. Using logistic regression, with the development of clinical restenosis as the dependent variable, we applied a univariate screen to a wide array of candidate demographic, cardiac, and noncardiac predictor variables. Variables with a univariate probability value <0.10 were considered in the multivariable model. The final risk model was developed by forward stepwise regression, with retention of those predictors that were independently associated with restenosis (P<0.05). Its c statistic was 0.65, and the model had good calibration (Hosmer-Lameshow P=1.0), suggesting no significant differences across the range of predicted restenosis rates.

To facilitate clinical application, each predictor was given an approximately linear score weighted by its individual β coefficient in the logistic model. Those predictor variables with β coefficients >0.6 were assigned 4 points, those with coefficients of 0.5 to 0.6 were assigned 3 points, those with coefficients of 0.3 to 0.5 were assigned 2 points, and significant predictors with coefficients <0.3 were given 1 point. The final model included 8 clinical characteristics (Table 2) and assigned 4 points for the presence of diabetes (insulin or non-insulin dependent) and acute myocardial infarction within 24 hours of the procedure; 3 points for age <55 and daily angina (as assessed by SAQ angina frequency scores ≤30); 2 points for a prior history of PCI, male sex, and weekly/monthly angina (SAQ angina frequency score=31 to 90); and 1 point for the presence of multivessel coronary disease. On the basis of these preprocedural characteristics, patients can be divided into 3 groups of restenosis risk. Patients categorized as being at low risk have a score of 0 to 3 and a 5% risk of restenosis; those at intermediate risk have a score of 4 to 7 and a 12% risk of restenosis; and those at high risk have a score >8 and a 44% risk of restenosis.

Statistical Analysis

For descriptive purposes, categorical data are reported as frequencies, and differences between groups were compared with a χ² or Fisher’s 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 by ANOVA. Least-squares means±SEs were calculated for all multivariable-adjusted analyses.

The primary analysis compared the difference in 1-year health status (SAQ angina frequency and quality-of-life scores) between patients treated with CABBG surgery and those treated with PCI within each category of preprocedural restenosis risk (low, intermediate, high). Patients were stratified by their risk for restenosis, and multivariable models were used to control for baseline differences between treatment groups (CABBG versus PCI). To create the multivariable models, we first identified sociodemographic and clinical characteristics that differed between patients undergoing CABBG and PCI (Table 1). We then constructed multivariable linear regression models that included those variables that differed by applied treatment (P<0.10). In the final model, age, sex, body mass index, hypertension, family history of heart disease, creatinine >2.0 mg/dL, history of cerebrovascular disease, history of prior coronary revascularization, presentation with unstable angina, the presence of left main coronary artery disease, and an ejection fraction <40% remained as independent variables. Because some may believe that PCI is the only appropriate treatment for single-vessel coronary disease (eg, isolated, proximal disease of the left anterior descending artery), we conducted a sensitivity analysis in which only those with multivessel disease were included. For all analyses, statistical significance was assumed when the probability value was <0.05.

To establish whether patients lost to follow-up may have biased these results, we conducted a propensity analysis by using a multivariable logistic regression model including all univariate predictors (P<0.10) for missing the follow-up assessment. This propensity score was then calculated for all patients in the study. Primary analyses were repeated with addition of an indicator for quintile of risk to have not participated in follow-up. In none of the models was the propensity quintile statistically significant, suggesting minimal observable bias in our analyses. Analyses were conducted with SAS version 8.2.

Results

Baseline Characteristics

Baseline characteristics of patients undergoing PCI and CABBG are compared in Table 1. Despite similar sociodemographic characteristics, patients undergoing CABBG were more likely to have a history of hypertension, family history of coronary artery disease, renal dysfunction, left main coronary artery disease, and an ejection fraction <40%. They were less likely to have had a prior revascularization procedure or cerebrovascular disease. No differences in baseline SAQ angina frequency or quality-of-life scores were observed. Coronary stents were used in 83% of the PCI procedures.

After 1-year of follow-up, significantly more patients treated with PCI required a repeat revascularization procedure (26% versus 2%, P<0.0001). Overall, at 1 year, CABBG surgery patients had significantly less angina compared with PCI patients (1-year SAQ angina frequency scores of 96±12.9 versus 91.3±18.9, P<0.001). Similarly, 1-year quality-of-life scores were significantly better for patients treated with CABBG surgery as opposed to PCI for the overall study population (90.6±14.2 versus 85.7±18.6, P<0.001).

Univariate 1-Year Health Status by Procedure, Stratified by Preprocedural Restenosis Risk

Angina frequency and quality-of-life scores at 1 year were compared in patients who received CABBG surgery versus PCI within each stratum of preprocedural restenosis risk. Overall, 37.4% of the patients were classified as being at low risk, 46.7% at intermediate risk, and 16.1% at high risk for restenosis. Among those at low risk for restenosis, no significant differences in 1-year angina frequency (96.5±1 versus 95.5±0.5, P=0.38) or quality-of-life (91.3±1.1 versus 90.3±0.7, P=0.40) scores were found between those treated with CABBG surgery and those treated with PCI.
Multiple randomized trials have demonstrated equivalent mortality after CABG surgery and PCI,12,4,5,20 while one has suggested a survival advantage for surgery.3 Because mortality outcomes are fairly similar, it is important to examine other patient outcomes, particularly patient-reported health status outcomes with CABG surgery and that it may be reasonable to preferentially consider surgical revascularization for these patients.

**Discussion**

This study found a significant relationship between the preprocedural risk of restenosis and the relative benefits of CABG surgery compared with PCI with respect to patients’ 1-year health status (angina frequency and quality of life) outcomes. We found no difference between CABG surgery and PCI for 1-year angina frequency or quality of life among patients at low risk for restenosis. However, in patients at intermediate risk for restenosis, CABG surgery was associated with significantly less angina and better quality of life. Among the patients at highest risk for restenosis, even larger differences in outcome were seen in favor of the CABG-treated patients. In this group, the angina frequency score was 94.4±10.2 for patients treated with CABG surgery compared with 83.4±10.5 for those who received PCI (P=0.01). The 1-year quality-of-life scores were 86.4±9.5 and 76.3±9.8, respectively (P=0.01).

Among patients in the intermediate restenosis risk group, however, greater angina relief was achieved for those patients undergoing CABG surgery compared with those treated with PCI (96.5±1.1 versus 90.3±0.8, P<0.001). One-year quality of life was also better among intermediate-risk patients treated with CABG surgery (90.7±1.1 versus 84.9±0.8, P<0.001). Finally, in the group at highest risk for restenosis, both angina relief (92.8±3.3 versus 84.6±1.8, P=0.03) and quality of life (87.8±3.1 versus 77.9±1.7, P=0.006) were significantly better after CABG surgery as opposed to PCI. The magnitudes of these differences in the high-risk group were substantially larger than those observed in the intermediate-risk patients.

**Restricted Analyses in Those With Multivessel Coronary Disease**

Because patients with single-vessel disease may not be ideal candidates for CABG surgery, we repeated the analyses only in those with multivessel coronary disease. Among the 676 PCI patients and 410 CABG patients with multivessel disease, similar results were found when comparing 1-year health status outcomes by stratum of restenosis risk. Among the patients at the lowest risk of restenosis, no differences in angina frequency (100±3.7 versus 100±3.9, P=0.92) or quality-of-life (86.6±4.5 versus 87.5±4.8, P=0.60) outcomes were observed. In the intermediate-risk group, patients who underwent CABG surgery had significantly more angina relief (angina frequency score of 97.1±8.9 versus 91.4±9.1, P=0.001) and better quality of life (92.1±8.6 versus 87.3±8.7; P=0.004) than did PCI-treated patients. Among the patients at highest risk for restenosis, even larger differences in outcome were seen in favor of the CABG-treated patients. In this group, the angina frequency score was 94.4±10.2 for patients treated with CABG surgery compared with 83.4±10.5 for those who received PCI (P=0.01). The 1-year quality-of-life scores were 86.4±9.5 and 76.3±9.8, respectively (P=0.01).

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Multiple randomized trials have demonstrated equivalent mortality after CABG surgery and PCI,12,4,5,20 while one has suggested a survival advantage for surgery.3 Because mortality outcomes are fairly similar, it is important to examine other patient outcomes, particularly patient-reported health...
status (symptom burden and quality of life), because differences in these outcomes may help guide the choice of therapy. Although it has been shown that both CABG surgery and PCI can improve health status outcomes, there have been few head-to-head comparisons, and the results have been inconsistent. Previous studies either have found equivalent health status outcomes or have favored CAGB surgery, linked to less angina and fewer repeat procedures. Interestingly, although restenosis is the proposed mechanism for the potential differences in health status outcomes, to our knowledge, no one has previously evaluated health status outcomes after CAGB surgery versus PCI stratified by restenosis risk. These are the first data to demonstrate that a relatively simple risk stratification tool can identify patients who may preferentially benefit from CAGB surgery compared with PCI. In particular, although we found no difference in the 1-year health status outcomes among those with the lowest risk of restenosis, CAGB surgery provided better average health status among patients with moderate and high preprocedural risks of restenosis.

The availability of drug-eluting stents is an important consideration in the interpretation of these data. At the time of this registry, only bare metal stents were available. Several recent clinical trials have demonstrated the superiority of drug-eluting stents in preventing restenosis compared with bare metal stents. For example, in the RAVEL trial (RAandomized study with the sirolimus-eluting Bx VElocity balloon-expandable stent), no episodes of significant restenosis occurred among patients treated with a sirolimus-eluting stent compared with a restenosis rate of 28.8% in the bare metal stent group. In the SIRIUS trial (SIRolImUS-coated stent in patients with de novo coronary artery lesions), rates of 4.1% versus 16.6% were observed. The costs of drug-eluting stents are substantially higher than those of bare metal stents, however. If one presumes that the differences in outcomes observed in this study are due to restenosis after PCI and that the use of drug-eluting stents would produce outcomes as good as those observed after CAGB surgery, then these results suggest that little clinical benefit would be obtained with the use of drug-eluting stents in the population of patients at low risk for restenosis. Conversely, among those at high restenosis risk, substantial benefit would likely be observed. As providers seek to develop a rational strategy for the adoption of expensive new technologies like drug-eluting stents, risk-stratification approaches such as the one supported by the results of this study may form the foundation for the cost-effective allocation of such therapies.

Several potential limitations of this study are worth noting. First, the population used to develop the restenosis risk model was the same population in which we conducted these analyses. Furthermore, the discriminative ability of our restenosis risk model was only modest. Predicting restenosis in patients undergoing PCI has been a subject of great investigative interest. The most recently published model, using a more complex set of preprocedural variables from 1312 patients in the Prevention of Restenosis With Tranilast and Its Outcomes (PRESTO) database, reported a c statistic of only 0.63. Our model was slightly better, is easier to implement, and was derived from a larger dataset. Although better models to predict restenosis are needed, we would expect inaccuracies in predicting restenosis to bias our results to the null hypothesis. Finding clinically significant outcomes differences by using an imperfect model underscores the potential of risk stratification, based on risk of restenosis, to select a patient’s revascularization strategy. Future investigators should validate this model in different populations and determine whether the clinically significant differences in outcomes that we observed are present. Second, we did not collect data about the costs of therapy. Because the implications of our findings about the triage of therapy have direct implications for the costs of care, quantifying this important outcome is critical for future work. A third limitation is our loss to follow-up. Although we found no selection bias by propensity scores for missing data, we cannot completely exclude this possibility. Finally, this is an observational study, so it is possible that unmeasured clinical factors may account for the differences in observed outcomes between CAGB and PCI. In this regard, multivariable models were used to address confounding due to measured factors, and multivariable results were consistent with the unadjusted analyses.

In conclusion, we have documented a significant relationship between the preprocedural risk of restenosis and both the control of angina and patients’ quality of life 1 year after revascularization. Selecting an optimal mode of coronary revascularization is a complex process that needs to incorporate a number of clinical factors, technical considerations, and patient preferences. However, using health status outcomes as part of clinical decision making is an important step forward in tailoring treatment recommendations to how such treatments will affect patients’ lives. By using a simple scoring algorithm that can be generated at the time of coronary angiogram, without the need for complex angiographic measurements, treatment recommendations tailored to individual patient’s likelihood of durable procedural success can be made. Future testing of this approach for the triage of CAGB surgery versus PCI and/or drug-eluting versus bare metal stents is warranted.

Acknowledgment
Dr Rumsfeld is supported by a VA Health Services Research Advanced Research Career Development Award (98341-2).

References


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Circulation. 2005;111:768-773; originally published online February 7, 2005;
doi: 10.1161/01.CIR.0000155242.70417.60
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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