Surgical Revascularization Is Associated With Improved Long-Term Outcomes Compared With Percutaneous Stenting in Most Subgroups of Patients With Multivessel Coronary Artery Disease

Results From the Intermountain Heart Registry

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Background—Coronary artery bypass surgery (CABG) and percutaneous coronary intervention with stenting (PCI-S) are both safe and effective approaches for revascularization in patients with multivessel coronary artery disease. However, conflicting information exists when comparing the efficacy of the two methods. In this study, we examined the outcomes of major adverse cardiovascular events and death for subgroups of typical “real-world” patients undergoing coronary revascularization in the modern era.

Methods and Results—Patients were included if they were revascularized by CABG or PCI-S, had ≥5 years of follow-up, and had ≥2-vessel disease. Patients were followed for an average of 7.0±3.2 years for incidence of death and major adverse cardiovascular events (death, myocardial infarction, or repeat revascularization). Multivariate regression models were used to correct for standard cardiac risk factors including age, sex, hyperlipidemia, diabetes mellitus, family history of coronary artery disease, smoking, hypertension, heart failure, and renal failure. Subgroup analyses were also performed, stratified by age, sex, diabetes, ejection fraction, and history of PCI-S, CABG, or myocardial infarction. A total of 6369 patients (CABG 4581; PCI-S 1788) were included. Age averaged 66±10.9 years, 76% were male, and 26% were diabetic. Multivariate risk favored CABG over PCI-S for both death (hazard ratio 0.85; \( P = 0.001 \)) and major adverse cardiovascular events (hazard ratio 0.51; \( P < 0.0001 \)). A similar advantage with CABG was also found in most substrata, including diabetes.

Conclusions—In this large observational study of patients undergoing revascularization for multivessel coronary artery disease, a long-term benefit was found, in relationship to both death and major adverse cardiovascular events, for CABG over PCI-S regardless of diabetic status or other stratifications. (Circulation. 2007;116[suppl I]:I-226–I-231.)

Key Words: CABG ■ stents ■ coronary artery disease ■ clinical outcomes ■ mortality

Coronary artery bypass surgery (CABG) and percutaneous coronary intervention with stenting (PCI-S) are both safe and effective approaches for revascularization in patients with coronary artery disease (CAD). PCI-S is the most common revascularization strategy for patients with single vessel CAD; however, the question remains which is a better strategy for patients with multivessel CAD.

Several randomized clinic trials have compared CABG with PCI-S and CABG with PCI-S. The Bypass Angioplasty Revascularization Investigation (BARI) trial comparing CABG with balloon angioplasty found no significant difference in the outcome of death or myocardial infarction (MI) at five years in patients with multivessel CAD. The Stent or Surgery (SOS) trial comparing CABG with PCI-S found that CABG was associated with a lower risk of all-cause mortality at 1 year, but neither the ERACI II trial nor the Arterial Revascularization Therapies Study (ARTS) trial found a difference in risk of mortality at 5 years. Recently, a significant survival advantage was reported among patients with multivessel disease undergoing CABG, which included PCI-S. Other studies have confirmed such findings, yet PCI-S is still used for many patients with multivessel CAD.

With these conflicting data, it seems possible that some groups of patients may benefit more from CABG than others. Thus, we examined the long-term outcomes of death and
major adverse cardiovascular events (MACE) among all patients with multivessel CAD undergoing revascularization at a single institution in the modern PCI-S era looking at a variety of substrata.

Methods

Study Patients
All consecutive patients (n=6369) with ≥2-vessel CAD who underwent CABG (n = 4581) or PCI-S (n = 1788) and had ≥5 years of follow-up were studied. PCI-S study patients were drawn from the cardiac catheterization registry of the Intermountain Heart Collaborative Study. CABG patients came from the Intermountain Society of Thoracic Surgery (STS) registry. Details regarding data collection methods and results for the Intermountain Heart Collaborative Study database have been described previously.12 All patients had their procedures performed between 1992 and 2000 at LDS Hospital in Salt Lake City, Utah. Patients were from a 6-state region (Arizona, Colorado, Idaho, Nevada, Utah, and Wyoming), the demographics of which are similar to the overall US white population with respect to socioeconomic factors and ethnicity. This study was approved by the hospital institutional review board.

Angiographic Assessments
CAD was defined as stenosis ≥60% by coronary artery angiography. Assessment of CAD was made by review of angiograms by the patient’s cardiologist, and results were entered into the computer database in a format modified after the coronary artery surgery study protocol. No comparisons were made between drug-eluting stents and bare-metal stents because no patients who received a drug-eluting stent had ≥5 years of follow-up.

Other Risk Factor, Demographic, and Clinical Assessments
In addition to age and gender, patient information collected included diabetes status (diabetes mellitus: fasting blood glucose >125 mg/dL, clinical diagnosis of diabetes mellitus, or antidiabetic medication use; insulin resistance: fasting glucose between 110 and 125 mg/dL, clinical diagnosis of diabetes mellitus, or antidiabetic medication use; insulin resistance: fasting glucose between 110 and 125 mg/dL, and normal: fasting glucose <110 mg/dL), hypertension (systolic blood pressure ≥140 mm Hg, diastolic ≥90 mm Hg, or antihypertensive use), renal failure (glomerular filtration rate ≥90 mL/min, 60 to 89 mL/min, 30 to 59 mL/min, 15 to 29 mL/min, and <15 mL/min), diabetes status, smoking history, family history of CAD, heart failure, and renal failure. Models entered variables using forced variable entry; final models entered significant and confounding covariables. Two-tailed P values are presented with 0.05 designated as nominally significant.

Statistical Analysis
The χ2 test and Student t test were used to examine univariate associations with CABG and PCI-S. To confirm the associations determined by univariate analysis, multivariate Cox regression analysis (SPSS, version 13.0) was performed to determine hazard ratios (HRs) corrected for confounding factors. Kaplan–Meier survival estimates and the log rank tests were used to determine initial association with longitudinal end points. Available baseline risk factors used in the modeling included age, gender, hypertension, hyperlipidemia, diabetes status, smoking history, family history of CAD, heart failure, and renal failure. Models entered variables using forced variable entry; final models entered significant and confounding covariables. Two-tailed P values are presented with 0.05 designated as nominally significant.

As a second method of adjustment, a propensity score was calculated by logistic regression, representing the probability of the patient undergoing CABG (versus PCI-S) given the patient’s other measured variables. The propensity score was used to evaluate the death outcome, both as a covariate along with CABG/PCI-S status in a Cox model and as a stratification tool for univariable evaluation of CABG/PCI-S status within propensity score quintiles. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results
A total of 6369 patients underwent multivessel revascularization (CABG n = 4581; PCI-S n = 1788). Average length of

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n=6369)</th>
<th>CABG (n=4581)</th>
<th>PCI-S (n=1788)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>66.0</td>
<td>66.6</td>
<td>64.5</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>76.1%</td>
<td>76.5%</td>
<td>74.9%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>54.4%</td>
<td>52.5%</td>
<td>59.2%</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>60.7%</td>
<td>60.5%</td>
<td>61.0%</td>
</tr>
<tr>
<td>Smoking*</td>
<td>37.8%</td>
<td>42.9%</td>
<td>24.7%</td>
</tr>
<tr>
<td>Family history of CAD*</td>
<td>46.5%</td>
<td>50.9%</td>
<td>35.3%</td>
</tr>
<tr>
<td>Congestive heart failure*</td>
<td>14.7%</td>
<td>16.2%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Renal failure*</td>
<td>3.3%</td>
<td>4.0%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

*P<0.05.

Figure 1. Five-year event frequencies and differences (P values) among patients undergoing CABG or PCI-S.
follow-up was 6.8±2.9 years for PCI-S and 7.3±3.4 years for CABG. The CABG patients tended to be older and sicker with higher rates of diabetes, smoking, family history of CAD, heart failure, and renal failure (Table 1). Of those who had an ejection fraction (EF) measurement (n=4073; 64%), a significant (P=0.02) but clinically minimal difference was also found between PCI-S (EF 57.5±8.0%) and CABG (EF 56.2±15.6%) patients. PCI-S patients were implanted with an average of 1.66 stents, and CABG patients received 1.35 arterial grafts on average.

Unadjusted Frequency of Outcomes
PCI-S patients experienced a significantly higher percentage of follow-up revascularization (CABG or PCI) and MACE (Figure 1). However, fewer PCI-S patients died, although this difference was not significant (Figures 1 and 2). Table 2 describes univariable results among each outcome.

Adjusted Primary End Points of Death and MACE
After multivariable adjustment for baseline characteristics, a significant mortality advantage for long-term follow-up among patients undergoing CABG became apparent (HR 0.85; P=0.001; Figure 3). However, at 1 year, there was no significant difference in risk of mortality among PCI-S and CABG patients (HR 1.01; P=0.87). Similar results for death were obtained after propensity score adjustment (HR 0.87; P=0.008). The unadjusted long-term event-free survival advantage for MACE persisted after adjustment among the CABG patients (multivariable HR 0.51; P<0.0001).

Table 2. HRs; 95% CIs; and P Values for Univariable and Multivariable Results of Long-Term Outcomes

<table>
<thead>
<tr>
<th>Outcome (outcome frequency)</th>
<th>Univariable (HR; 95% CI; P Value)</th>
<th>Multivariable (HR; 95% CI; P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (n=2118)</td>
<td>1.09; 0.99–1.21; 0.08</td>
<td>0.85; 0.76–0.94; 0.001</td>
</tr>
<tr>
<td>MI (n=940)</td>
<td>0.52; 0.45–0.59; &lt;0.0001</td>
<td>0.46; 0.40–0.53; &lt;0.0001</td>
</tr>
<tr>
<td>Revascularization (n=1056)</td>
<td>0.26; 0.23–0.30; &lt;0.0001</td>
<td>0.25; 0.22–0.28; &lt;0.0001</td>
</tr>
<tr>
<td>MACE (n=3278)*</td>
<td>0.59; 0.55–0.64; &lt;0.0001</td>
<td>0.51; 0.47–0.55; &lt;0.0001</td>
</tr>
</tbody>
</table>

*MACE is the composite point of death, MI, and repeat revascularization.

Stratification by Subgroups
In a subanalysis, several subgroups were evaluated for a survival advantage among the 2 procedures (Figure 4). The survival advantage for CABG was attenuated or nonexistent for some groups, including patients <65 years of age, females, patients with a history of MI, and those with EF ≤40%. Patients with a history of PCI did better with PCI-S (adjusted HR 1.35; P=0.05; Figure 5), and a trend toward superiority for PCI-S was found for patients with a history of CABG (adjusted HR 1.14; P=0.24; Figure 6). When stratified by diabetes, both diabetics (adjusted HR 0.81; P=0.03) and nondiabetics (adjusted HR 0.87; P=0.02) maintained a survival advantage with CABG (Figure 7) with no differential effect.

Discussion
In this observational study of patients with multivessel disease and ≥5 years of follow-up, CABG was found to have a significant survival advantage over patients undergoing PCI-S. This advantage was maintained among most subgroups, including males, those ≥65 years of age, patients without a history of PCI, CABG, or MI, nondiabetics, diabetics, patients with an EF ≥40%, patients with either 2- or 3-vessel disease, and for both complete and incomplete PCI. Indeed, the only subgroups in which the survival advantage trended toward PCI-S were those with a previous history of coronary revascularization (either previous CABG or PCI). CABG patients also experienced fewer repeat revascularizations (CABG or PCI) and MI and 41% fewer events for the composite end point of MACE. Such results are consistent with the reports of other observational studies.9,11
However, at 1 year, as in the SOS trial, there was no significant difference in the outcome of mortality.

In addition to observational studies, numerous randomized clinical trials have also compared survival outcomes between patients undergoing CABG versus PCI (balloon angioplasty and stenting). Most of these report similar 5-year mortality rates for both CABG and PCI, and this has been confirmed by a recent meta-analysis. Why the results differ between the observational studies of patients seen in typical clinical practice and these randomized trials is not known. However, patient selection could possibly explain the differing results. Typically, clinical trial participants are required to meet strict entry criteria and must be considered good candidates for either revascularization approach. Thus, they often have fewer comorbidities and may not represent the average patient presenting for a coronary intervention. Another possible explanation for the nonsignificant difference in mortality between the treatments may be the limited to insufficient power of these trials. Nonetheless, the recently completed SOS trial did find lower mortality rates during long-term follow-up among patients randomized to CABG compared with PCI-S. Other randomized trials, such as the BARI Study, also have found a survival advantage for CABG among certain subgroups of patients such as diabetics, although our study did not find a differential outcome based on diabetes.

In determining a treatment strategy for a patient with multivessel disease, there are a variety of considerations that need to be made when selecting the appropriate treatment. Unfavorable anatomy is a predominant determinant of such a
of $20,468.16. At 5 years, an average cost difference of $63,896 for PCI and $84,364 for CABG patients, a difference after 3 years of follow-up, the average total costs were reduced procedural cost compared with CABG patients. For PCI having a nonsignificant survival advantage at both intervals, such that PCI was determined to be less costly and at least as effective for revascularization over 5 years. However, there continues to be dispute regarding which treatment confers the greatest survival advantage. This study, along with others, found a significant survival advantage for CABG among patients treated in everyday clinical practice. Whether the purported cost savings with PCI-S justify its choice remains to be determined.

Limitations
This study shares the limitations of all nonrandomized, observational studies, including the possibility of selection bias and unadjusted confounding. Although patient treatment selection was not randomized but was chosen by the physician, we attempted to minimize such selection biases through multivariable adjustments as well as propensity analysis. However, certain other characteristics may be unaccounted for in this study. This study does have the advantage of a large sample size and prospective patient observation and data entry among the entire cross-section of patients treated in a large United States cardiovascular hospital.

Not all patients had a documented EF within our system. Many patients had their EF measured at other facilities. The CABG registry is missing some data elements on some patients (e.g., history of MI, history of CABG, and number of arterial grafts).

There are fewer PCI-S patients than CABG patients because the Intermountain STS registry was started about a year before the cardiac catheterization registry of the Intermountain Heart Collaborative Study and because a higher percentage of patients with multivessel CAD were treated with CABG than with PCI-S. Finally, in some cases, the power of our subgroup analyses is limited because of small numbers.

Conclusion
In this large real-world observational study of patients undergoing revascularization for multivessel CAD, a long-term benefit was found in relationship to both death and MACE, for CABG over PCI-S regardless of diabetic status, number of diseased vessels, or completeness of revascularization. Most other subgroups analyzed showed at least a trend toward superiority for CABG. The 1 group of patients in which a survival trend favored PCI-S was those who had received previous coronary revascularization with either PCI or CABG. These data emphasize the fact that CABG remains an excellent and often superior long-term form of revascularization in most groups of patients with multivessel CAD. However, in the subgroup of patients with a history of previous coronary revascularization, a randomized clinical trial appears to be warranted.

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Disclosures
None.

References


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