Propensity Analysis of Long-Term Survival After Surgical or Percutaneous Revascularization in Patients With Multivessel Coronary Artery Disease and High-Risk Features

Sorin J. Brener, MD; Bruce W. Lytle, MD; Ivan P. Casserly, MD; Jakob P. Schneider, RN; Eric J. Topol, MD; Michael S. Lauer, MD

Background—Although most randomized clinical trials have suggested that long-term survival rates after percutaneous coronary intervention (PCI) or surgical multivessel coronary revascularization (CABG) are equivalent, some post hoc analyses in high-risk groups and adjustment for severity of coronary disease have suggested higher mortality after PCI. Methods and Results—We studied 6033 consecutive patients who underwent revascularization in the late 1990s. PCI was performed in 872 patients; 5161 underwent CABG. Half the patients had significant left ventricular dysfunction or diabetes. Propensity analysis to predict the probability of undergoing PCI according to 22 variables and their interactions was used. The C-statistic for this model was 0.90, indicating excellent discrimination between treatments. There were 931 deaths during 5 years of follow-up. The 1- and 5-year unadjusted mortality rates were 5% and 16% for PCI and 4% and 14% for CABG (unadjusted hazard ratio, 1.13; 95% CI, 1.0 to 1.4; \( P = 0.07 \)). PCI was associated with an increased risk of death (propensity-adjusted hazard ratio, 2.3; 95% CI, 1.9 to 2.9; \( P < 0.0001 \)). This difference was observed across all categories of propensity for PCI and in patients with diabetes or left ventricular dysfunction. Other independent predictors of mortality (\( P = 0.01 \) for all) were renal dysfunction, age, diabetes mellitus, chronic lung disease, peripheral vascular disease, left main trunk stenosis, and extent of coronary disease (Duke angiographic score).

Conclusions—In patients with multivessel coronary artery disease and many high-risk characteristics, CABG was associated with better survival than PCI after adjustment for risk profile. (Circulation. 2004;109:2290-2295.)

Key Words: angioplasty ■ bypass surgery ■ coronary disease ■ survival

Randomized clinical trials (RCTs) from a decade ago comparing percutaneous coronary intervention (PCI; mainly balloon angioplasty) and CABG in patients with multivessel coronary artery disease showed that all-cause mortality is comparable.\(^1\)\(^-\)\(^7\) More recent trials comparing coronary stenting with CABG showed similar results.\(^8\)\(^-\)\(^12\) Nevertheless, post hoc analyses in diabetic patients\(^13\) and modeling to account for severity of coronary artery disease (CAD)\(^14\) have suggested improved survival after CABG. Thus, it was not clear how contemporary PCI (frequently incorporating stents and glycoprotein [GP] IIb/IIIa inhibitors) compares with CABG in patients with a more advanced risk profile than in RCTs.

Methods

We considered consecutive patients with multivessel CAD revascularized between January 1, 1995, and December 31, 1999. Patients were excluded if they had prior CABG or also required valve surgery, if a cardiac surgeon had refused them because of severe comorbidity or lack of appropriate target vessels, if they died during the procedure (2 patients), if they were undergoing primary PCI for an acute myocardial infarction (MI), or if they did not have a valid US Social Security number. The Cleveland Clinic Institutional Review Board approved research based on ongoing clinical registries of patients undergoing CABG and PCI and waived the requirement for informed consent.

Clinical Data

Since the early 1970s, clinical data on patients undergoing revascularization have been systematically abstracted and recorded in the cardiovascular information registry. Angiographic data obtained before revascularization were quantitatively described with the Duke Prognostic Weight Index.\(^15\)\(^-\)\(^17\)

End Points

The primary end point was all-cause mortality.\(^18\)\(^-\)\(^21\) The Social Security Death Index was used to determine timing of death.\(^22\) In-hospital post-procedural MI was defined as Q-wave MI (QMI; new pathological Q waves) or non-QMI (peak creatine kinase-MB \(\geq 30\) ng/mL or \(\sim 4\) times the upper limit of normal, PCI cohort only).

Statistical Analyses

Baseline variables were compared by use of the Wilcoxon rank-sum test or the \(\chi^2\) test as appropriate. Survival was compared with Kaplan-Meier curves\(^23\) and multivariable Cox proportional-hazards regression,\(^24\) confirmed by testing of weighted Schoenfeld residuals.\(^25\) A propensity analysis was carried out\(^26\)\(^,\)\(^27\) by use of a nonparsimonious logistic regression model\(^28\) for treatment with PCI versus CABG. All the
variables listed in Table 1 were included in this model, along with significant interactions. The score was then incorporated into subsequent proportional-hazards models as a covariate; it also was used to divide the population according to deciles of propensity score. All analyses were performed with the SAS 8.2 system.

Results
Characteristics of subjects according to revascularization procedure are shown in Table 1. CABG patients had a significantly higher risk profile than PCI patients. Of 6033 patients, 872 (14%) underwent PCI (stents, 70%; GP IIb/IIIa inhibitors, 51%) and 5161 (86%) underwent CABG (mammary artery grafting in 89%). Ninety-six percent of PCI patients had 4 lesions treated, and 84% of CABG patients had 4 distal anastomoses. Complete revascularization was achieved in 645 PCI patients (74%) and in 4212 CABG patients (82%; P<0.0001).

Treatment Strategy and Outcome
The incidence of periprocedural QMI was 0.1% and 0.8% for PCI and CABG, respectively (P<0.0001). In the PCI group, 49 patients (5.6%) suffered a periprocedural non-QMI. By 30 days, death occurred in 11 (1.3%) and 59 (1.1%), respectively (P=0.73). The surgical mortality was roughly one third that reported by the Society of Thoracic Surgery for the same period.29 The median follow-up among survivors was 5.2 years (range, 2.6 to 7.6 years). There were 931 deaths: 148 PCI and 783 CABG patients. The Kaplan-Meier 1- and 5-year mortality risks were 5% and 16% for PCI and 4% and 14% for CABG (unadjusted hazard ratio, 1.13; 95% CI, 1.0 to 1.4; P=0.07; Figure 1). After risk adjustment (Table 1), treatment with PCI was associated with an increased risk of death (adjusted hazard ratio, 2.1; 95% CI, 1.7 to 2.6; P<0.0001). The other significant predictors of mortality are listed in Table 2.

Propensity Analyses
In PCI patients, the median propensity score (0=CABG, 1=PCI) was 0.52 (interquartile range, 0.20 to 0.79); in CABG patients, the median score was 0.03 (interquartile range, 0.01 to 0.11). The C-statistic for the propensity score model was 0.90, indicating excellent discrimination. Predictors of choice of revascularization are listed in Table 3.
mortality across cohort deciles is shown in Figure 2. The
adjusted hazard ratios for mortality range from 1.5 to 3.3,
consistently (but not always statistically significantly) favoring
CABG. As expected from the demographics, the absolute
mortality rate decreases as the propensity score increases,
consistent with the lower risk of PCI patients. Table 2 details
the statistically significant independent predictors of mortality in
the various analyses. PCI was associated with a hazard ratio of 2.3
(95% CI, 1.9 to 2.9) after the propensity score was introduced
into the model. There was no significant interaction between
treatment and any of the patient characteristics, including angiog-
graphic severity of CAD, with regard to mortality risk.

**Selected High-Risk Patient Subsets**

In ~50% of patients, high-risk features such as diabetes
mellitus or left ventricular dysfunction (consistently excluded
from all comparative trials) were present.13,30 There were
2319 patients (265 PCI, 2054 CABG) with diabetes. Among
the 1504 non–insulin-treated diabetics, there were 270 deaths
(18%), and PCI was associated with an increased risk (21% versus 17%; adjusted hazard ratio, 1.7; 95% CI, 1.2 to 2.5;

$P<0.008$). Among the 815 insulin-treated diabetics, there
were 198 deaths (24%), and PCI again was associated with an
increased risk of death (31% versus 23%; adjusted hazard
ratio, 2.6; 95% CI, 1.7 to 3.9; $P<0.0001$).

Among 627 patients with an ejection fraction ≤30%, there
were 183 deaths (29%). The 5-year death rate tended to be
higher for PCI (37% versus 28%; adjusted hazard ratio, 1.6;
95% CI, 0.9 to 2.7; $P=0.09$).

**Coronary Stenting**

Coronary stenting was performed in 609 patients, of whom 88
(14%) died, which was not substantially different from other
PCI patients. In a proportional-hazards model that compared
patients who had stenting to those referred for CABG, that
considered the covariates listed in Table 1, and that incorpo-
rated a new propensity score for stenting versus CABG,
stenting was associated with a higher death risk (adjusted
hazard ratio, 2.2; 95% CI, 1.7 to 2.9; $P<0.0001$).

**Discussion**

This registry of contemporary multivessel revascularization at a
tertiary referral institution is substantially larger than any of the
individual comparative RCTs and includes more CABG patients
than all trials combined. Concern about an observational data-
base notwithstanding, the principal findings are that (1) the
choice of revascularization is driven primarily by the clinical
presentation and presence of high-risk features; (2) long-term

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**Figure 1.** Cumulative unadjusted survival in PCI and CABG cohorts.

**Table 2. Predictors of Mortality: Results of Proportional-Hazards Analyses**

<table>
<thead>
<tr>
<th>Model/Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>1.13 (0.99–1.40)</td>
<td>0.07</td>
</tr>
<tr>
<td>Covariate adjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>3.72 (3.12–4.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age in years</td>
<td>1.53 (1.42–1.64)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCI</td>
<td>2.12 (1.74–2.58)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Insulin-treated diabetes</td>
<td>1.72 (1.45–2.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>1.61 (1.38–1.88)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1.54 (1.34–1.78)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>1.22 (1.11–1.34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(10% decrease)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non–insulin-treated diabetes</td>
<td>1.35 (1.16–1.57)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Angiographic score (10% increase)</td>
<td>1.05 (1.01–1.08)</td>
<td>0.007</td>
</tr>
<tr>
<td>Left main disease</td>
<td>1.23 (1.05–1.44)</td>
<td>0.01</td>
</tr>
<tr>
<td>Propensity adjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>2.30 (1.85–2.86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Propensity score (0.1 increase)</td>
<td>0.83 (0.79–0.87)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

For the covariate-adjusted model, variables are presented in the order of
Wald $\chi^2$ value from highest to lowest. Only those variables with $P<0.01$ are
shown. For the covariate-adjusted model, all the variables listed in Table 1
were candidates for model entry. For the propensity-adjusted model, all the
variables listed in Table 1, along with pertinent interactions, were used to
derive the propensity score from a nonparsimonious logistic regression model.
survival is better for the CABG cohort, which is confirmed and strengthened by propensity analyses; and (3) the frequent use of stents and GP IIb/IIIa during PCI was not sufficient to alter the survival advantage of the CABG-treated patients, in whom internal mammary artery use was very high and perioperative mortality was exceptionally low.

### Registry Versus RCT Data

Although RCTs of PCI versus CABG enroll a small proportion of patients screened, this study reports on most of the patients revascularized at our institution. Nevertheless, the vast majority of these patients (86%) were treated with CABG according to their physicians’ and their own preference.

### Table 3. Predictors of Selection for PCI: Results of Nonparsimonious Logistic Regression Modeling Used to Develop the Propensity Score

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>$\chi^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular ejection fraction (10% increase)</td>
<td>1.22 (1.19–1.25)</td>
<td>320</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total occlusion</td>
<td>0.26 (0.31–0.33)</td>
<td>124</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left main disease</td>
<td>0.06 (0.03–0.09)</td>
<td>119</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.38 (0.30–0.49)</td>
<td>57</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proximal left anterior descending artery disease</td>
<td>0.45 (0.36–0.55)</td>
<td>57</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Angiographic score</td>
<td>0.98 (0.98–0.99)</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>0.38 (0.28–0.53)</td>
<td>33</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior MI</td>
<td>15.4 (4.6–52.1)</td>
<td>19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction and unstable angina interaction</td>
<td>0.96 (0.94–0.98)</td>
<td>15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non–insulin-treated diabetes mellitus</td>
<td>0.62 (0.49–0.79)</td>
<td>15</td>
<td>0.0001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction and prior MI interaction</td>
<td>0.96 (0.94–0.98)</td>
<td>13</td>
<td>0.0003</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.68 (0.55–0.84)</td>
<td>12</td>
<td>0.0003</td>
</tr>
<tr>
<td>Unstable angina and prior MI interaction</td>
<td>0.55 (0.37–0.83)</td>
<td>8</td>
<td>0.0037</td>
</tr>
<tr>
<td>Median family income ($10 000 increase)</td>
<td>0.91 (0.83–0.99)</td>
<td>5</td>
<td>0.025</td>
</tr>
<tr>
<td>Body mass index in kg/m²</td>
<td>1.02 (1.00–1.04)</td>
<td>3</td>
<td>0.07</td>
</tr>
<tr>
<td>Age in years</td>
<td>1.01 (1.00–1.02)</td>
<td>3</td>
<td>0.09</td>
</tr>
<tr>
<td>Ejection fraction data missing</td>
<td>0.71 (0.45–1.11)</td>
<td>2</td>
<td>0.13</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.90 (0.72–1.11)</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>Days of procedure after January 1, 1995</td>
<td>1.00 (1.00–1.01)</td>
<td>&lt;1</td>
<td>0.40</td>
</tr>
<tr>
<td>Black race</td>
<td>1.17 (0.79–1.74)</td>
<td>&lt;1</td>
<td>0.43</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.93 (0.76–1.13)</td>
<td>&lt;1</td>
<td>0.44</td>
</tr>
<tr>
<td>Insulin-treated diabetes mellitus</td>
<td>1.12 (0.83–1.49)</td>
<td>&lt;1</td>
<td>0.46</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.84 (0.52–1.37)</td>
<td>&lt;1</td>
<td>0.49</td>
</tr>
</tbody>
</table>

Variables are shown in descending order of Wald $\chi^2$ values.
Meta-analysis of 8 RCTs comparing PCI with CABG demonstrated among 3371 patients a similar mortality at nearly 3 years (relative risk, 1.08; 95% CI, 0.79 to 1.50). Compared with the Bypass Angioplasty Revascularization Investigation (BARI), our patients were 3 to 5 years older and significantly more often had diabetes and lower ejection fraction. Although early mortality was similar, the 5-year survival after CABG and PCI was lower in our cohort, 86% versus 89% and 84% versus 86%, respectively, in concordance with higher-risk baseline characteristics. Compared with the more recent 1200 patients Arterial Revascularization Therapies Study (ARTS), 1-year mortality in our registry was also higher for both groups, 4% versus 2.8% for CABG and 5% versus 2.5% for PCI. These differences reflect older age, a doubling of the incidence of diabetes, and an absolute 5% lower ejection fraction. Similar to our data, in the Stent or Surgery (SoS) trial, there were fewer deaths in the CABG group than in the PCI group at 2 years of follow-up (2% versus 5%; hazard ratio, 2.91; P = 0.01).

Among registry data, the Duke series is the largest with 2924 PCI and 3890 CABG patients treated between 1984 and 1990 and followed up for an average of 5 years. Among the 4 anatomic subsets of high-risk 2- and 3-vessel CAD, the adjusted mortality for CABG is 25% to 60% lower than for PCI.

**Diabetic Patients**

The subset of diabetic patients in this study was very large compared with RCTs. As demonstrated by Niles et al., most series demonstrated excess mortality with PCI compared with CABG after 5 to 6 years. The difference was most pronounced in the BARI randomized patients. The BARI registry confirmed that after adjustment for baseline differences, there was an ≈25% increase in mortality in PCI patients, which was not inconsistent with the randomized trial data. The Northern New England Cardiovascular Study Group found results very similar to ours in 2766 BARI-like patients, showing a 50% excess mortality in diabetics treated with PCI between 1992 and 1996. This excess doubled in patients with 3-vessel CAD (adjusted hazard ratio, 2.01; 95% CI, 1.04 to 3.91; P = 0.0038). In contrast, Barsness et al. found no difference in 5-year survival among diabetics treated between 1984 and 1990 with either CABG (74%) or PCI (76%; adjusted P = 0.91). Similar data were generated from the Coronary Angioplasty Versus Bypass Revascularisation Investigation (CABRI) and Angina With Extremely Serious Operative Mortality Evaluation (AWESOME).

The challenge in the interpretation of these results is to understand the mechanisms responsible for the worse outcome associated with PCI. Although the difference in unadjusted mortality between the 2 cohorts is of only borderline significance, “equalization” of the risk profile by statistical adjustment reveals both a much more profound difference in outcome and the effectiveness of triage to either revascularization method in clinical practice.

Post hoc analyses from BARI showed that diabetics with subsequent QMs fare better after CABG than after PCI and that progression of CAD is significantly more ominous in PCI than in CABG patients, in whom proximal extension of CAD is less critical as long as complete revascularization was performed and bypasses remain patent. Although internal mammary artery and vein graft patency appeared to be similar in diabetics and nondiabetics, restenosis is markedly higher in diabetics.

**Left Ventricular Dysfunction**

Most RCTs excluded patients with very low ejection fraction. These data present the outcome of >600 patients with severe impairment of the left ventricle and demonstrate the important and independent role of prevascularization systolic dysfunction in long-term prognosis.

**Study Limitations**

It is nearly impossible to capture all the differences between patients and the thought processes involved in the choice of revascularization, and it was difficult to ensure that patients in both groups were suitable for both procedures, as in RCTs. Although propensity analyses are powerful, they are inherently limited by the number and accuracy of the variables evaluated. There have been substantial changes in the routine management of patients undergoing PCI since this cohort was analyzed. The introduction of drug-coated stents in 2003 and the evidence for the routine use of more potent antiplatelet therapy for 1 year after the procedure are 2 innovations that were not part of the therapy for the patients analyzed and may well have affected the results. Furthermore, the extremely low perioperative mortality at this institution posits an important limitation with regard to applicability of these data. Finally, because our follow-up was only 5 years, the long-term life expectancy implications of our findings are not yet entirely clear.

**Conclusion**

Effective comparison of CABG and PCI in RCTs and registries is affected by patient and procedure selection bias, the duration of follow-up, and the type of events studied. Thus, analysis at an interval of 5 years favors, to a certain extent, CABG patients because it precedes the development of severe graft disease while capturing most events in the PCI cohort.

Despite these limitations, we conclude that at a large tertiary institution with particularly low surgical mortality, patients with multivessel CAD and many high-risk features appear to have a better 5-year survival when treated with CABG than with PCI. Further research is needed to determine whether drug-eluting stents and improved medical management will close the mortality gap in these patients.

**References**


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