Cost-Effectiveness of Coronary Artery Bypass Grafts Versus Percutaneous Coronary Intervention for Revascularization of High-Risk Patients

Kevin T. Stroupe, PhD; Douglass A. Morrison, MD, PhD; Mark A. Hlatky, MD; Paul G. Barnett, PhD; Lishan Cao, MS; Christopher Lyttle, MA; Denise M. Hynes, RN, PhD; William G. Henderson, PhD; for the Investigators of Veterans Affairs Cooperative Studies Program #385 (AWESOME: Angina With Extremely Serious Operative Mortality Evaluation)

Background—A Department of Veterans Affairs Cooperative Study randomized high-risk patients with medically refractory myocardial ischemia, a group largely excluded from previous trials, to urgent revascularization with either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). The present study examined the cost-effectiveness of PCI versus CABG for these high-risk patients.

Methods and Results—Of 454 patients at 16 Department of Veterans Affairs medical centers, 445 were available for the economic analysis (218 PCI and 227 CABG patients). Total costs were assessed at 3 and 5 years from the third-party payer’s perspective, and effectiveness was measured by survival. After 3 years, average total costs were $63,896 for PCI versus $84,364 for CABG patients, a difference of $20,468 (95% confidence interval [CI] $13,918 to $27,569). CIs were estimated by bootstrapping. Survival at 3 years was 0.82 for PCI versus 0.79 for CABG patients (P=0.34). Precision of the cost-effectiveness estimates were assessed by bootstrapping. PCI was less costly and more effective at 3 years in 92.6% of the bootstrap replications. After 5 years, average total costs were $81,790 for PCI versus $100,522 for CABG patients, a difference of $18,732 (95% CI $9,873 to $27,831), whereas survival at 5 years was 0.75 for PCI patients versus 0.70 for CABG patients (P=0.21). At 5 years, PCI remained less costly and more effective in 89.4% of the bootstrap replications.

Conclusions—PCI was less costly and at least as effective for the urgent revascularization of medically refractory, high-risk patients over 5 years. (Circulation. 2006;114:1251-1257.)

Key Words: revascularization | bypass | angioplasty | cost-benefit analysis

Coronary revascularization is an expensive technique and among the most frequently performed in the United States; 1,204,000 percutaneous coronary intervention (PCI) procedures and 306,000 coronary artery bypass grafting (CABG) surgeries were performed in 2002.1 Estimates of healthcare costs associated with revascularizations range from $12 to $20 billion each year.2 The Department of Veterans Affairs (VA) through its Cooperative Studies Program conducted a randomized, controlled trial (the Angina With Extremely Serious Operative Mortality Evaluation [AWESOME] trial) to compare PCI with CABG for the urgent revascularization of medically refractory, high-risk myocardial ischemia patients, a group that has largely been excluded from previous clinical trials.3,4

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From the Cooperative Studies Program Coordinating Center (K.T.S.), Hines VA Hospital, Hines, Ill; Midwest Center for Health Services and Policy Research (K.T.S., D.M.H.), Hines VA Hospital, Hines, Ill; Feinberg School of Medicine (K.T.S., L.C., C.L.), Chicago, Ill; VA Information Resource Center (K.T.S., D.M.H.), Hines, Ill; Tucson VA Medical Center (D.A.M.), Tucson, Ariz; University of Arizona (D.A.M.), Tucson, Ariz; Stanford University School of Medicine (M.A.H., P.G.B.), Stanford, Calif; VA Health Economics Resource Center (P.G.B.), Menlo Park, Calif; VA Cooperative Studies Program Coordinating Center (P.G.B.), Palo Alto, Calif; Loyola University Chicago (D.M.H.), Maywood, Ill; and University of Colorado Health Outcomes Program (W.G.H.), Aurora, Col.


Correspondence to Kevin T. Stroupe, PhD, Edward Hines, Jr, VA Hospital, PO Box 5000 (151H), Hines, IL 60141. E-mail Kevin.Stroupe@va.gov

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Methods

Setting and Patients

The multicenter, randomized, controlled AWESOME trial evaluated the survival of high-risk patients who underwent coronary revascularization with either PCI or CABG, as described in detail previously. Briefly, between February 1995 and February 2000, the AWESOME trial enrolled patients with medically refractory myocardial ischemia at high risk for adverse outcomes at 1 of 16 VA medical centers. High risk was defined as 1 or more of the following: prior open heart surgery, age >70 years, left ventricular ejection fraction <0.35, myocardial infarction within 7 days, and intra-aortic balloon pump required.

Patients who met the 3 clinical criteria (myocardial ischemia, medically refractoriness, and high risk) underwent coronary angiography. Patients considered acceptable for either PCI or CABG were invited for randomization. Patients were excluded if they had single-vessel circumflex disease, unprotected (ungrafted) >50% left-main stenosis, no vessels suitable for revascularization, comorbid disease likely to limit life expectancy to <1 year, or angioplasty within the preceding 6 months. Among eligible patients, 454 consented to the study; 222 were randomized to PCI and 232 to CABG. Insufficient information was available to identify 9 patients in national VA databases, which left 445 patients for the cost-effectiveness analysis (218 PCI and 227 CABG patients). Patients who were clinically eligible but not randomized were similar to study patients across a wide range of characteristics. This cost-effectiveness study was approved by the Hines VA Hospital Human Subjects Subcommittee.

Data Sources

The clinical trial database of AWESOME patients was linked to several VA and Medicare databases to obtain information on healthcare utilization and cost. Although the original trial ended in March 2000, data from national databases allowed us to extend follow-up through September 2004. Data on hospital stays and outpatient visits in VA, VA contract care, and medications acquired from VA were obtained from national VA data sources. For Medicare-eligible patients, we obtained information on non-VA healthcare from Medicare claims data. Dates of death were obtained from the VA Beneficiary Identification and Records Locator Subsystem Death File.

Costs of Care

We estimated cumulative costs at 3 and 5 years to ascertain whether short-term differences persisted over the longer run. We estimated costs from a third-party payer’s perspective. We did not include the costs of informal care supplied by family members or time lost from work or usual activities. All costs were adjusted to 2004 US dollars with the Consumer Price Index.

We estimated costs of inpatient care, including inpatient revascularizations, in VA and Medicare-covered facilities based on Medicare reimbursement rates. Medicare reimburses most hospital services at a predetermined rate based on the diagnostic related group (DRG). This DRG price is calculated by multiplying standard dollar amounts for operating and capital expenses found in the Federal Register by a national “weight” associated with the DRG for each hospitalization. Additional payments may be made for providing medical education or serving lower-income populations.

To estimate hospital costs for all short-term hospital stays at a VA facility from 1995 through 2004, we obtained the DRG for each hospitalization from national VA databases and multiplied the DRG weight by the standard dollar amount for large urban areas in 2004. We used the standard amount for other areas as a sensitivity analysis. We adjusted the cost estimates to account for education and service to lower-income populations based on national average adjustment rates. To estimate hospital costs for inpatient admissions at Medicare-covered facilities from 1995 through 2003, we used the DRG price in the Medicare claims data. We estimated the cost of physician services for short-term VA admissions and for Medicare-covered admissions by the average reimbursement provided for inpatient physician services for Medicare patients in each DRG.

We also estimated outpatient costs based on Medicare reimbursement rates. We obtained costs of outpatient care in the VA from 1998 through 2004 from the VA Health Economics Resource Center’s (HERC) national average cost databases, which contain patient-level cost estimates for each outpatient visit based on Medicare reimbursement rates for each current procedural terminology code during that visit. For outpatient costs from the period 1995 through 1997, which predates the HERC databases, we applied an average cost for each type of visit, and we adjusted these cost estimates to approximate Medicare reimbursement rates.

For types of care that occurred less frequently, we used cost estimates from the national VA databases. We obtained costs of rehabilitation, mental health care, and long-term care in VA from the HERC national average cost databases from 1998 through 2004, and we applied HERC costing methods to estimate these costs from 1995 through 1997. We obtained the cost of inpatient and outpatient care paid through contract with the VA from national VA databases. Costs for medications that patients obtained from VA outpatient pharmacies between 1999 and 2004 were available from national VA pharmacy databases. Because pharmacy data were not available for the entire study period, we excluded pharmacy costs from the primary analysis and examined pharmacy costs in a sensitivity analysis (described below).

Effectiveness

Effectiveness was measured in years of survival after randomization. We calculated years of survival as the number of years between randomization and either the date of death or the end of follow-up (September 2004).

Analysis

We compared costs between patients randomized to PCI and CABG on an intention-to-treat basis, regardless of their actual revascularization procedure. We compared healthcare utilization and costs using t tests for continuous variables and χ² tests for dichotomous and categorical variables. We calculated 95% confidence intervals (CIs) around differences in mean costs between patients randomized to PCI or CABG using bias-corrected accelerated bootstrapping to adjust for skewness in the cost data. We estimated survival after

### Table 1. Baseline Characteristics of Patients Randomized to PCI or CABG

<table>
<thead>
<tr>
<th></th>
<th>PCI (n=218)</th>
<th>CABG (n=227)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, y</td>
<td>68±9</td>
<td>67±9</td>
<td>0.81</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>216 (99)</td>
<td>224 (99)</td>
<td>0.69</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>14 (6)</td>
<td>20 (9)</td>
<td>0.34</td>
</tr>
<tr>
<td>VA insurance only, n (%)</td>
<td>97 (45)</td>
<td>90 (40)</td>
<td>0.30</td>
</tr>
<tr>
<td>High-risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;70 y</td>
<td>105 (48)</td>
<td>110 (48)</td>
<td>0.95</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>66 (30)</td>
<td>74 (33)</td>
<td>0.60</td>
</tr>
<tr>
<td>Myocardial infarction &lt;7 days</td>
<td>77 (35)</td>
<td>72 (32)</td>
<td>0.42</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &lt;0.35</td>
<td>40 (18)</td>
<td>52 (23)</td>
<td>0.24</td>
</tr>
<tr>
<td>Intra-aortic balloon pump required</td>
<td>5 (2)</td>
<td>4 (2)</td>
<td>0.75</td>
</tr>
<tr>
<td>Two or more high-risk factors</td>
<td>68 (31)</td>
<td>73 (32)</td>
<td>0.83</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>147 (69)</td>
<td>155 (70)</td>
<td>0.74</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>64 (30)</td>
<td>78 (35)</td>
<td>0.23</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>19 (9)</td>
<td>31 (14)</td>
<td>0.10</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>36 (17)</td>
<td>53 (23)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
randomization as the area under the Kaplan-Meier survival curves and used log-rank tests.

We estimated the cost-effectiveness at 3 and 5 years of follow-up as the difference in mean cost \([\text{cost}(t)_{\text{PCI}} - \text{cost}(t)_{\text{CABG}}]\) and the difference in mean life years of survival \([\text{life-years}(t)_{\text{PCI}} - \text{life-years}(t)_{\text{CABG}}]\), where \text{cost}(t)\) indicates the mean cumulative cost and life-years(t) indicates the mean life-years of survival up to time "t." As is standard in cost-effectiveness analyses, we discounted both costs and life-years at 3% per year starting with the date of randomization.\(^{23}\) When one treatment in a cost-effectiveness analysis is both more effective and less costly, that treatment is considered the "dominant" or preferred treatment. When neither treatment is dominant, the tradeoff between costs and improved survival is compared.\(^{23}\) We first examined whether one treatment was dominant. The precision of the cost-effectiveness estimate was assessed by the bootstrap method, using 1000 resamplings of size 445 with replacement of patients randomized to PCI or CABG.\(^{21}\) We determined the proportion of bootstrap replications that produced a dominant result.

### Sensitivity Analysis

In our primary analysis, VA short-term hospital costs were estimated with 2004 standard dollar amounts for large urban areas\(^{15}\) in the DRG price calculation. As a sensitivity analysis, we also calculated VA short-term hospital costs using standard amounts for other urban areas.\(^{15}\) Additionally, because pharmacy data were not available from the VA from 1995 through 1998, they were excluded from our primary analyses. In sensitivity analyses, we compared pharmacy costs from 1999 through 2004 between patient groups.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

### Results

A total of 218 patients randomized to PCI and 227 patients randomized to CABG were included in the economic analysis. Patients averaged 67 years of age, and 32% had 2 or more factors that indicated a high risk for coronary revascularization (Table 1).

### Costs of Care

The costs of the initial revascularization were lower for patients randomized to PCI ($17,231 for PCI patients versus $17,894 for CABG patients, \(P<0.0001\)). Although more patients randomized to PCI received a subsequent revascularization within 3 years of randomization (37% versus 18%, \(P<0.0001\); Table 2), total costs at 3 years remained significantly higher for patients randomized to CABG. At 3 years, the average total cost for patients randomized to PCI was $63,896 versus $84,364 for patients randomized to CABG, a difference of $20,468 (95% CI $13,918 to $27,569, \(P<0.0001\); Table 3).

Between 3 and 5 years of follow-up, the groups had similar healthcare utilization and similar rates of revascularization (6% of PCI patients versus 4% of CABG patients; \(P=0.24\)). Consequently, follow-up costs of care between 3 and 5 years were similar ($17,894 for PCI patients versus $16,158 for CABG patients, \(P=0.51\); Figure 1). After 5 years of follow-up, mean total costs for PCI patients were $81,790 versus

### Table 2. Healthcare Utilization After 5 Years of Follow-Up

<table>
<thead>
<tr>
<th>Medical Resource Use</th>
<th>PCI (n=218)</th>
<th>CABG (n=227)</th>
<th>Difference (95% CI*)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial revascularization, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>216 (99.1)</td>
<td>18 (7.9)</td>
<td>\ldots</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CABG</td>
<td>3 (1.4)</td>
<td>211 (93.0)</td>
<td>\ldots</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Up to 3 years of follow-up†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subsequent revascularizations, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>63 (28.9)</td>
<td>31 (13.7)</td>
<td>\ldots</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CABG</td>
<td>36 (16.5)</td>
<td>13 (5.7)</td>
<td>\ldots</td>
<td>0.0003</td>
</tr>
<tr>
<td>Nonrevascularizations, mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term hospital stays, n</td>
<td>2.26</td>
<td>2.19</td>
<td>0.07 (−0.88 to 0.87)</td>
<td>0.79</td>
</tr>
<tr>
<td>Rehabilitation, mental health care, and long-term care stays, n</td>
<td>0.2</td>
<td>0.4</td>
<td>−0.2 (−0.38 to 0.20)</td>
<td>0.16</td>
</tr>
<tr>
<td>Outpatient visits, n</td>
<td>57.0</td>
<td>56.8</td>
<td>0.2 (−17.97 to 19.37)</td>
<td>0.98</td>
</tr>
<tr>
<td>Non-VA hospital stays, n</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1 (−0.35 to 0.36)</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>3 to 5 Years of follow-up†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subsequent revascularizations, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>8 (3.7)</td>
<td>9 (4.0)</td>
<td>\ldots</td>
<td>0.87</td>
</tr>
<tr>
<td>CABG</td>
<td>7 (3.2)</td>
<td>0 (0.0)</td>
<td>\ldots</td>
<td>0.07</td>
</tr>
<tr>
<td>Nonrevascularizations, mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term hospital stays, n</td>
<td>0.9</td>
<td>0.8</td>
<td>0.1 (−0.43 to 0.56)</td>
<td>0.39</td>
</tr>
<tr>
<td>Rehabilitation, mental health care, and long-term care stays, n</td>
<td>0.2</td>
<td>0.1</td>
<td>−0.1 (−0.66 to 0.21)</td>
<td>0.07</td>
</tr>
<tr>
<td>Outpatient visits, n</td>
<td>29.4</td>
<td>32.0</td>
<td>−3 (−15 to 12)</td>
<td>0.53</td>
</tr>
<tr>
<td>Non-VA hospital stays, n</td>
<td>0.3</td>
<td>0.3</td>
<td>0.0 (−0.44 to 0.28)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

*CI for the difference PCI minus CABG.
†Subsequent revascularizations include those performed in VA, under contract with VA, or in Medicare-covered facilities. Patients may have had both a PCI and CABG in the followup period. Hospital stays and outpatient visits include care provided in a VA facility or a facility under contract with VA. Non-VA hospital stays include Medicare-covered hospitalizations.
$100,522 for CABG patients, a difference of $18,732 (95% CI $9,873 to $27,831, \( P = 0.0012 \)).

### Survival

At 3 years of follow-up, the probability of survival was 0.82 for PCI patients versus 0.79 for CABG patients (\( P = 0.34 \); Figure 2). After 5 years, the probability of survival was 0.75 for PCI patients versus 0.70 for CABG patients (\( P = 0.21 \)).

### Cost-Effectiveness Analysis

After 5 years of follow-up, life expectancy was 3.97 life-years for PCI patients versus 3.78 life-years for CABG patients (\( P = 0.18 \)). Over the same period, PCI patients incurred $18,932 less of healthcare costs. PCI was the dominant treatment because it was as effective as CABG and resulted in significantly lower costs.

We conducted a bootstrap analysis to characterize the precision of our cost-effectiveness estimate by sampling with replacement 445 observations from the data on trial participants. The differences in costs and life-years of survival between PCI and CABG patients for these 1000 samples are plotted in Figure 3. Points in the lower-right quadrant of the figure indicate replications in which PCI is less costly and more effective (ie, the dominant treatment). PCI was the

![Figure 1. Cumulative mean cost over 5 years of follow-up.](image1)

![Figure 2. Kaplan-Meier survival curves for patients randomized to PCI or CABG at 5 years of follow-up.](image2)
dominant treatment in 92.6% of the bootstrap replications at 3 years (data not shown), and PCI was the dominant treatment in 89.4% of the bootstrap replications at 5 years (Figure 3).

Sensitivity Analysis
In sensitivity analyses, we used the standard dollar amounts for other areas to estimate VA short-term hospital costs. We found that at 3 years after randomization, the average total cost for patients randomized to PCI was $60 740 versus $78 070 for patients randomized to CABG, a difference of $17 555 (95% CI $9003 to $26 376, P<0.0001). The bootstrap analysis indicated that at 3 years, PCI was the dominant treatment in 93.5% of replications. At 5 years, the average total cost for patients randomized to PCI was $78 070 versus $95 625 for patients randomized to CABG, a difference of $17 555 (95% CI $9003 to $26 376, P<0.0001). The bootstrap analysis indicated that at 5 years, PCI was the dominant treatment in 90.3% of replications. To examine whether the exclusion of drug costs from our primary analysis would bias our results, we compared the costs of drugs from the VA outpatient pharmacy during the period that drug data were available (1999 through 2004). During this period, PCI patients’ drug costs were $4848 versus $4442 for CABG patients, a difference of $406 (95% CI $687 to $1499; P=0.46).

Discussion
The AWESOME trial randomized patients with refractory myocardial ischemia who were at high risk for coronary revascularization to PCI or CABG. At 5 years, PCI patients had significantly lower medical costs than CABG patients and survival that was at least as good, which suggests that PCI is the economically “dominant” strategy in high-risk patients. The combination of lower costs and similar outcomes is uncommon but has been reported for other interventions in cardiovascular medicine.24,25

Patients in AWESOME who initially received PCI had more repeat revascularizations in follow-up than patients who initially received CABG. This basic pattern has been seen in all prior studies of PCI,26 including those using balloon angioplasty, bare-metal stents,27–29 and drug-coated stents.30 The difference in costs between the PCI and CABG strategies has varied somewhat among studies, ranging from a 5% gap at 5 years31 to a 45% gap at 3 years.32 The 19% gap in average total costs favoring PCI at 5 years found in AWESOME was somewhat greater than in prior trials.

In contrast to previous studies in which survival was generally slightly better in CABG-assigned patients, PCI-assigned patients had survival that was at least as good as patients assigned to CABG. A formal meta-analysis33 of PCI versus CABG trials reported a 1.9% survival advantage for CABG at 5 years (P<0.02) after all studies were pooled. This meta-analysis excluded the AWESOME trial, however, because its entry criteria, restricted to high-risk subjects, were so different from the other trials that AWESOME was regarded as a unique investigation. The present results may differ from most previous trials because AWESOME included a uniquely ill patient population that has been largely excluded from other trials,5 and many previous trials did not include stenting in the initial procedure.

The high-risk factors in AWESOME were identified from a prior VA surgical-risk study that examined preoperative characteristics and operative mortality (ie, within 30 days of bypass surgery).4 The previous surgical-risk study found that operative mortality was higher for patients with previous cardiac operation (12.5% versus 3.9%), ejection fraction <0.20 (13.8% versus 4.9%), myocardial infarction within 30 days (7.4% versus 4.3%), and the need for an intra-aortic balloon pump (15.8% versus 3.9%).34

Recently, 2 trials of PCI versus CABG that used stents have reported clinical results at 5 years.35,36 In the Arterial Revascularization Therapies Study (ARTS), there was no significant difference in survival.35 In the Argentine Randomized Trial: Coronary Bypass Surgery With Multivessel Disease (ERACI II) trial, there was a trend toward better survival for the PCI patients at 5 years (92.8% versus 88.4%, log-rank test; P=0.1).36 Thus, the survival results in the present study are comparable to other trials involving stents.

The Swiss Trial of Invasive versus Medical management of Elderly patients (TIME) trial, which compared medical therapy with PCI,37–41 is the only other study to enroll severely ill patients at high risk for coronary revascularization. For patients at high risk for coronary revascularization, it is important to consider whether medical therapy, which was not tested in AWESOME, might be the preferred strategy. Because TIME found that for a population similar to that in AWESOME, PCI was economically attractive relative to medical therapy, it implies that the conclusions of the present study would not have been altered had AWESOME included a medical therapy arm.

Owing to data limitations, non-VA costs were limited to hospitalizations covered by Medicare that occurred among the 296 patients (67%) who were Medicare eligible throughout the study and the 67 patients (15%) who became Medicare eligible during the study.

The AWESOME trial was conducted while bare-metal stents were being introduced into practice, with 11% of PCI patients receiving stents in the first year compared with 88% of PCI patients in the final 2 years. Drug-eluting stents were not available at the time of the study. Although stents and
drug-coated stents tend to increase overall costs of PCI by roughly 5%, this differential is small compared with the 19% gap in 5-year costs we found between the PCI- and CABG- assigned patient groups, so our basic conclusions are unlikely to be affected. Additionally, outcomes were expressed in life-years, rather than quality-adjusted life-years. If CABG resulted in a much higher quality of life than PCI, decision makers might be willing to incur the higher costs for the improved quality of life. However, outcomes data from the AWESOME trial, although incomplete, suggest no such advantage of CABG with respect to quality of life.42

In conclusion, the present study suggests that PCI has advantages over CABG among high-risk subjects with refractory angina and coronary disease amenable to revascularization.

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Disclosures
None.

References

CLINICAL PERSPECTIVE

Clinical trials are the optimal method to compare alternative therapies and can be used to assess economic and clinical outcomes. Coronary revascularization procedures (angioplasty and bypass surgery) are quite expensive, and consequently, the value they provide for the money spent is of considerable interest. In patients with medically refractory ischemia, the AWESOME (Angina With Extremely Serious Operative Mortality Evaluation) trial found a lower mortality rate in patients randomly assigned to coronary angioplasty than in those assigned to coronary artery bypass grafting surgery. In the present study from the AWESOME trial investigators, economic analyses are used to show that angioplasty patients incurred significantly lower costs than surgery patients over 5 years of follow-up. Angioplasty was therefore more effective clinically and significantly less costly, which led to a highly favorable cost-effectiveness ratio. The patient population enrolled in AWESOME is unique among randomized trials comparing angioplasty and surgery, so these results apply only to patients with medically refractory ischemia. The AWESOME trial results suggest further that a simpler and less expensive method of coronary revascularization leads to better economic and clinical outcomes in patients with medically refractory angina.
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