Medical Costs and Quality of Life 10 to 12 Years After Randomization to Angioplasty or Bypass Surgery for Multivessel Coronary Artery Disease

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Background—Coronary bypass surgery (CABG) and angioplasty (PTCA) have been compared in several randomized trials, but data about long-term economic and quality-of-life outcomes are limited.

Methods and Results—Cost and quality-of-life data were collected prospectively from 934 patients who were randomized in the Bypass Angioplasty Revascularization Investigation (BARI) and followed up for 10 to 12 years. CABG had 53% higher costs initially, but the gap closed to <5% during the first 2 years; after 12 years, the mean cumulative cost of CABG patients was $123 000 versus $120 750 for PTCA, yielding a cost-effectiveness ratio of $14 300/life-year added. CABG patients experienced significantly greater improvement in their physical functioning for the first 3 years but not in later follow-up. Recurrent angina substantially reduced all quality-of-life measures throughout follow-up. Cumulative costs were significantly higher among patients with diabetes, heart failure, and comorbid conditions and among women; costs also were increased by angina, by the number of revascularization procedures, and among patients who died.

Conclusion—Early differences between CABG and PTCA in costs and quality of life were no longer significant at 10 to 12 years of follow-up. CABG was cost-effective as compared with PTCA for multivessel disease. (Circulation. 2004;110:1960-1966.)

Key Words: cost-benefit analysis • follow-up studies • angioplasty • surgery • coronary disease

Coronary artery revascularization with either angioplasty (PTCA) or bypass surgery (CABG) is one of the most common major surgical procedures performed in the United States. Randomized trials comparing the outcomes of CABG with PTCA among patients with multivessel coronary disease have shown little difference between the procedures in the rates of mortality and nonfatal myocardial infarction.1–4 Because serious cardiac events are roughly equivalent, costs, quality of life, and functional status become the most important considerations in choosing between CABG and PTCA.

Long-term follow-up of patients after coronary revascularization is important because outcomes may be affected by deterioration of saphenous vein grafts and progression of atherosclerosis in native vessels.5 Consequently, the Bypass Angioplasty Revascularization Investigation (BARI) extended the follow-up of patients randomized to CABG or PTCA, and here we report their long-term economic and quality-of-life outcomes.
contact information released to Stanford University were withdrawn from the study at that point.

Medical costs were measured as the sum of hospital costs, physician fees, outpatient procedure costs, and the cost of prescription drugs. A copy of the hospital bill was obtained for each admission. We converted hospital charges to costs using the departmental cost-to-charge ratios contained in the admitting hospital’s Medicare Cost Report. For the 12% of admissions for which billing data were not available (640 Veterans Affairs hospital admissions and 131 of 5827 non–Veterans Affairs hospital admissions), we considered the Medicare payment for the diagnosis-related group to be the cost of admission. Data on physicians’ fees were collected for admissions to the hospitals of the 7 participating sites. Unavailable data on physicians’ fees for coronary revascularization were imputed as the mean of measured values; for other inpatient, outpatient, and rehabilitation services, we used the Medicare fee schedule. Prescription drug costs were defined as the median wholesale price as listed in the 2002 Drug Topics Red Book for the most common dosage of each medication taken by the SEQOL patients. We did not include the monetary costs of informal care supplied by family members or of time lost from work. Cumulative medical costs were calculated with a modification of the actuarial method of Etzioni and coworkers after conversion to 2002 US dollars. Multivariable analyses were performed on the logarithm of 10-year cumulative costs. We analyzed serial quality-of-life scores using linear mixed-effects models with random intercepts (SAS PROC MIXED).

Cost-Effectiveness
We assessed the cost-effectiveness of CABG as compared with PTCA on the basis of data collected during trial follow-up. We also projected lifetime cost-effectiveness using the method described below.

Cost-effectiveness ratios were calculated by the general formula

$$ CE(t) = \frac{[Cost(t)_{cabg} - Cost(t)_{ptca}]}{[Life-Years(t)_{cabg} - Life-Years(t)_{ptca}]} $$

where Cost(t) indicates the mean cumulative cost up to time “t,” and Life-Years(t) indicates the mean life-years of survival up to time “t.” Costs and life-years were both discounted at a 3% rate after the date of randomization according to standard principles for cost-effectiveness studies. We also estimated quality-adjusted life-years (QALYs) during follow-up by mapping quality-of-life scores to patient utility using a method described in detail elsewhere. The derived utility scores at baseline and each year of follow-up were then used to quality-adjust each life-year of survival. For the 5.6% of annual follow-up contacts in which a utility score could not be derived because of missing quality-of-life data, we imputed the utility score as the average of the previous year’s and subsequent year’s values.

Long-term cost-effectiveness was projected in a 2-step procedure. We compared the observed mortality rate in SEQOL patients between the 5th and 10th year of follow-up with the expected age-, sex-, and race-specific mortality rates from the US Life Tables and assumed the relationship between observed and expected mortality rates would continue to apply to the remaining SEQOL patients. Future life expectancy for each patient still alive at last follow-up contact was estimated by Monte Carlo simulation, based on the adjusted US Life Tables. We assumed that the medical costs for surviving patients would continue to accrue at the same rate as that observed between the 5th and 10th years of follow-up. To account for higher expenditures at the end of life, medical costs were estimated separately for the last quarter of life, the remainder of the last year of life, the year preceding the last year of life, and the remaining years of life. We used the means of 250 simulations of both future survival and costs for each surviving patient to project lifetime cost-effectiveness.

Results
A total of 1829 patients were randomized in BARI; 952 at 1 year, 485 at 5 years (15% versus 16%) or 10 years (18% versus 19%). The percentage of patients who were employed full-time or part-time declined steadily during follow-up. No significant difference was observed between the treatment groups in the employment rates at any point. At baseline, 45% of the CABG patients were employed versus 40% of the PTCA patients; at 1 year, 34% versus 31%, at 5 years 24% versus 26%, and at 10 years 19% versus 21% were employed.

Cost and Cost-Effectiveness
The initial cost of revascularization was significantly lower for the PTCA patients (Figure 2) than it was for the CABG patients, but this advantage steadily narrowed during the next 3 years. In the extended follow-up, the mean cumulative costs in the PTCA group remained between $1000 and $4000 lower than those of the CABG group. After 12 years of follow-up, the mean cumulative medical cost in the PTCA patients was $120 750 compared with $123 000 among the CABG patients (P=0.55). CABG patients had higher costs for hospital care, physicians’ services, and nursing facility care, whereas PTCA patients had higher costs for cardiac drugs and outpatient tests (Table 1). PTCA patients had significantly more coronary revascularization procedures (Table 1) than did CABG patients.

Quality of Life
More CABG patients rated their health as improved as compared with baseline for the first 3 years of follow-up (Figure 1). The percentage of patients who rated their health as improved after the initial revascularization procedure declined steadily during the subsequent 10 years.

Physical function, as assessed by DASI, improved after initial coronary revascularization and declined steadily during the subsequent 10 years (Figure 1). The initial improvement in physical function was significantly greater among the CABG patients than among the PTCA patients (Figure 1). This advantage narrowed during the subsequent 10 years.

Mental health, as measured by the RAND Mental Health Inventory 5 scale, improved after the initial revascularization procedure and remained relatively unchanged for the next 6 years of follow-up; it improved in the later follow-up (Figure 1). No significant differences were noted between the PTCA and CABG patients in mental health scores at any point in the follow-up.

Patient utility scores improved significantly after the initial revascularization procedure. Utility scores were significantly higher among CABG patients for the first year of follow-up (Figure 1) and were roughly equivalent thereafter. CABG patients had a lower prevalence of angina than did PTCA patients at 1 year of follow-up (10% versus 24%), but not at 5 years (15% versus 16%) or 10 years (18% versus 19%).

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The actuarial survival rates at 5, 7, 10, and 12 years of follow-up were 86.2%, 80.3%, 69.3%, and 61.2% for SEQOL PTCA patients as compared with survival rates of 89.2%, 82.3%, 69.3%, and 61.3% for SEQOL CABG patients. During the 12 years of observation, PTCA patients accrued a mean of 8.42 life-years of survival (discounted), whereas CABG patients accrued a mean of 8.58 life-years of survival (discounted). The cost-effectiveness of CABG as compared with PTCA was $14 300/life-year added at 12 years. CABG patients had a cost-effectiveness ratio $100 000/life-year added in 77% of 1000 bootstrap replications and $50 000 in 71%, and they had lower costs and better survival in 28% of replications. The cost-effectiveness ratio for CABG became more favorable over time, especially between 1 and 3 years of follow-up (Figure 3).

The mortality rate of patients in this study during years 5 through 10 of follow-up was 1.75%/year higher than expected for the US population matched on age, sex, and race. Assuming that this pattern of mortality would continue, the projected mean life expectancy for the entire cohort of CABG patients was 12.36 years and their projected lifetime cost was $164 000. For PTCA patients, the projected life expectancy was 12.12 years and their projected lifetime cost was $160 000. The projected lifetime cost-effectiveness ratio was $13 300/life-year added for CABG as compared with PTCA.

Sensitivity Analysis
To assess whether our results were sensitive to discount rate, we varied the rate from the baseline value of 3% to 0% and 6%/year. At a 0% discount rate, the 12-year cumulative cost of PTCA was $136 700 versus $138 700 for CABG (P=0.76), whereas at a 6% discount rate, the cumulative cost was $108 300 versus $110 800 (P=0.36).

To assess whether the cost-effectiveness ratio was sensitive to quality-of-life measures, we estimated utility scores. PTCA patients accrued 6.45 QALYs during 10 years of observation as compared with 6.58 QALYs among CABG patients, yielding a cost-effectiveness ratio for CABG of $11 300/QALY.
To assess the sensitivity of the economic analysis to outliers, we trimmed an equal number of the highest and lowest cost observations from both the PTCA and CABG groups. After removing 2 observations from each extreme of the cost distribution, mean cumulative 12-year costs were trimmed to $118,000 for PTCA and $121,900 for CABG, yielding a cost-effectiveness ratio of $23,500/life-year added by CABG. After removing 4 patients from each extreme, mean cumulative costs were trimmed to $117,100 for PTCA and $121,000 for CABG, yielding a cost-effectiveness ratio of $25,100/life-year added by CABG.

## Patients With Diabetes

The 92 PTCA patients with diabetes had higher costs and lower survival rates than did the 114 CABG patients. After 12 years, the cumulative costs for patients with diabetes were $150,100 for PTCA versus $151,100 for CABG, and mean survival time was 6.40 years for PTCA versus 8.00 years for CABG. Outcomes were better among patients without diabetes. Twelve-year cumulative costs for patients without diabetes were $113,200 for PTCA versus $114,400 for CABG, and survival times were 8.92 years for PTCA versus 8.76 years for CABG.

## Correlates of Outcome

Angina exerted a substantial negative effect on quality of life throughout the study. Patients with angina had lower DASI, RAND Mental Health Inventory 5 scores, health ratings, and utility scores at every time point (Figure 4). Patients with chronic exertional angina at entry to the study experienced greater improvements in quality-of-life scores at 1 year than did patients without preceding effort angina; DASI improved by 8.3 points versus 2.7 points (P < 0.0001), RAND Mental Health Inventory 5 scores improved by 2.6 points versus 0.9 points (P = 0.15), utility improved by 0.24 versus 0.03 points (P = 0.005), and self-rated health improved for 39% versus 32% (P = 0.03) of patients with and without chronic effort angina at baseline, respectively.

In a multivariable analysis, 10-year costs were significantly higher in patients who had diabetes, heart failure, or comorbid conditions, as well as among women (Table 2). When follow-up data were added to the model, the number of coronary revascularization procedures was a highly significant predictor of costs, as was presence of angina in follow-up (Table 2). Patients who died during follow-up had considerably higher costs, especially in view of the reduced time available to accrue costs (Table 2). Initial randomization assignment to either CABG or PTCA was not a significant predictor of 10-year costs.

## Discussion

In the 5-year follow-up of this randomized trial, CABG patients experienced significantly greater improvements in physical function and better relief from angina, whereas PTCA patients returned to work earlier. The cost of the
initial revascularization procedure was 35% lower among PTCA patients, but this difference had narrowed to 5% by 5 years of follow-up, mostly as a result of the greater need for additional revascularization procedures among PTCA patients. In this extended follow-up study, we found that 10 years after randomization, these early differences between PTCA and CABG in the economic and quality-of-life outcomes were no longer significant. The trend toward similar outcomes over the long term emphasizes the chronic and progressive nature of coronary atherosclerosis. Nevertheless, each revascularization procedure had distinct advantages that persisted for several years.

**Figure 3.** Cost-effectiveness (CE) ratio of CABG relative to PTCA (vertical axis) expressed as dollars/life-year added, calculated from cumulative cost and survival data at various follow-up intervals (horizontal axis). ○ indicates projected lifetime cost-effectiveness ratio. Data point at 1-year follow-up is off the scale at $597 000/life-year added.

**Figure 4.** Quality-of-life scores (vertical axis) in patients with angina (●) and free of angina (○) at 1, 5, and 10 years' follow-up (horizontal axis). A, Mean DASI scores. B, Mean RAND Mental Health Inventory V (MHI5) scores. C, Percentage of patients reporting excellent or very good health (Ex/VG). D, Mean time trade-off utility scores. Error bars indicate ± 2 SE.
Although differences between the procedures narrowed over time, the cost-effectiveness of CABG relative to PTCA for multivessel coronary disease remained favorable (Figure 3). The cost-effectiveness ratio of $14 300/life-year added after 12 years’ follow-up is well within the range of acceptable medical therapies.16 The cost-effectiveness ratio for CABG calculated from observed data was unacceptably high when follow-up was limited to 1 year (> $500 000/life-year added), but it became increasingly favorable during further follow-up. The improvement in the cost-effectiveness ratio over time was largely because of the narrowing of the cost differential between the 2 procedures, with the remainder resulting from a small survival advantage among CABG patients. These observations underscore the importance of a long-term perspective in economic evaluation, as an initially costly procedure may prove cost-effective over the long term if it either provides extended clinical benefits or the initially higher cost can be offset by preventing subsequent hospitalizations.

The distribution of medical care costs in this study followed the pattern seen in almost all health economic evaluations: A small percentage of patients consume a disproportionate amount of medical resources and thereby generate high costs. The departure of costs from a normal distribution required that we use statistical methods that are appropriate for skewed data in hypothesis testing (nonparametric procedures) and regression analysis (log transformation of costs). The costs incurred in the highest tail of the distribution are high costs. The departure of costs from a normal distribution has been affected by these patient withdrawals. Patients in the present study were enrolled before the introduction of coronary stents and other improvements in coronary revascularization. Interpretation of the results of any clinical trial may be affected by subsequent innovations, yet the therapeutic principles that are derived from carefully performed studies are likely to remain established. Newer developments have tended to reduce the cost of CABG and to increase the cost of PTCA.19,20 Although the rate of repeat revascularization procedures after PTCA has been considerably reduced by stents, it is still significantly greater than it is after CABG. This observation suggests that differences in initial costs between contemporary PTCA and CABG also will narrow over time, as they have in recent randomized trials with coronary stents.4

One of the striking findings of this study was the substantial negative impact that angina exerted on quality of life. Patients with chronic effort angina upon entering the study experienced improved quality of life 1 year after initial revascularization. Patients with angina in follow-up experienced significantly lower functional status, emotional health, and utility (Figure 4). Patients with angina also had 8.2% higher medical costs (Table 2), even after controlling for the differential between the 2 procedures, with the remainder resulting from a small survival advantage among CABG patients. These observations underscore the deleterious effect of angina on patient well-being and suggest that therapies that relieve angina may be cost-effective even though they do not reduce mortality.

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A limitation of this study is that 80 subjects (9%) either withdrew or were lost to follow-up, despite the great effort made to study all patients for at least 10 years. Most of these losses occurred after 5 years, when most differences in outcome between randomized groups had narrowed. Consequently, the major conclusions of this study are unlikely to have been affected by these patient withdrawals.

In conclusion, a long-term perspective on coronary revascularization suggests that the choice of procedure affects outcomes in the medium term (2 to 3 years), with little change

| TABLE 2. Effect of Baseline Factors and Follow-Up Events on Cumulative 10-Year Costs |
|---------------------------------|---------------------------------|------------------|
| **Factor**                      | **Percentage Increase in Cost (95% CLs)** |
|                                | **Baseline Only** | **Baseline + Follow-Up** |
| Diabetes                        | 9.9 (5.6–14.4) | 8.5 (4.9, 12.1) |
| Heart failure                   | 6.1 (0.5–12.1) | 9.6 (4.9, 14.6) |
| Abnormal LV function            | 4.1 (0.03–8.2) | ... |
| Comorbidity                     | 3.3 (1.0–5.5) | 2.3 (0.5, 4.2) |
| Female gender                   | 6.1 (2.3–10.0) | 4.1 (1.0, 7.3) |
| Age (at 10 y)                   | ... | 2.6 (1.1, 4.1) |
| Death                           | ... | 24.5 (18.9, 30.4) |
| CABG procedures                 | ... | 22.2 (18.8, 25.7) |
| PTCA procedures                 | ... | 7.6 (6.3, 8.8) |
| Angina in follow-up             | ... | 8.2 (5.2, 11.2) |
| Years of follow-up < 10         | ... | −3.7 (−4.5, −2.9) |
| Resulting from death            | ... | −1.5 (−2.6, −0.5) |
| Resulting from withdrawal       | ... | ... |
| Model $R^2$                     | 0.06 | 0.40 |
subsequently. The relatively small additional cost of CABG is cost-effective by current standards because of its initial advantage in clinical outcomes and relatively small increase in long-term cost.

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References
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