Stents or Surgery?
New Data on the Comparative Outcomes of Percutaneous Coronary Intervention and Coronary Artery Bypass Graft Surgery

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Coronary angioplasty and coronary bypass surgery are mechanical approaches to atherosclerotic obstructions that impede coronary blood flow. In bypass surgery, arterial and venous conduits are placed beyond the proximal obstructions. By contrast, in angioplasty, the area of narrowing is expanded and now usually buttressed with a stent. Neither mechanical approach addresses the fundamental disease process, however, which needs to be treated with medications and lifestyle changes.

The perennial question is whether angioplasty or surgery yields better clinical outcomes. Even without randomized clinical trials, it is obvious that angioplasty is a less invasive procedure and that patients recover more quickly. Individual randomized trials have been large enough to show that bypass surgery generally reduces angina and repeat interventions to a greater extent than angioplasty does. But for the most important clinical outcome, mortality, single randomized clinical trials have not been large enough to provide definitive results. Because mortality is infrequent after contemporary coronary revascularization, lengthy follow-up is required to provide an adequate comparison of surgery and angioplasty. Large numbers of patients are required to ensure sufficient statistical power to detect clinically meaningful differences in mortality. Trials of the needed size and duration are difficult to organize and highly expensive. The results of every such trial are important pieces of the puzzle.

The Stent or Surgery (SoS) trial is one of the largest randomized comparisons of coronary angioplasty and bypass surgery. Investigators at 53 study centers in 11 countries between 1996 and 1999 randomized 988 patients with multivessel coronary disease to undergo either conventional coronary bypass surgery or angioplasty with a bare-metal stent. The initial report of the SoS trial1 was based on a median of 2 years of follow-up, after which 22 patients assigned to angioplasty had died compared with 8 patients assigned to surgery (hazard ratio 2.9, \( P=0.01 \)). This result was unexpected, because most other randomized trials of angioplasty and surgery had not shown a significant difference in mortality. The extended follow-up of SoS has been eagerly awaited, because more events from this key trial would provide a clearer picture of the overall balance in outcomes between angioplasty and surgery.

The SoS investigators now report mortality at a median 6 years of follow-up.2 Vital status at 5 years was unknown in 9 angioplasty patients and 15 surgery patients, or 2.4% of the 988 patients randomized. The excess number of deaths in the angioplasty group compared with the surgery group grew from 14 at 2 years to 19 at 6 years (53 deaths in the angioplasty group versus 34 deaths in the surgery group). Although the angioplasty-surgery hazard ratio declined to 1.66 (confidence limits 1.08 to 2.55), it was still statistically significant \( (P=0.02) \). Surprisingly, 20 deaths were attributed to cancer among the patients assigned to angioplasty compared with 8 cancer deaths among patients assigned to surgery, but it is important to note that the cause of death was determined by the investigators rather than by an events committee blinded to treatment assignment.

The long-term outcomes of the SoS trial are important data yet difficult to interpret for several reasons. The difference in mortality is small enough that if even a few of the patients lost to follow-up had died, the results would no longer be statistically significant. More than 40% of the 87 deaths in the SoS trial were judged to be noncardiovascular; even though noncardiac death would be expected to occur equally after angioplasty or surgery, more such deaths occurred in the angioplasty group. This result seems more likely due to the play of chance rather than to an adverse effect of angioplasty on noncardiac death. Nevertheless, the trial’s overall results for mortality are the best evidence, and SoS showed significantly more deaths after random assignment to angioplasty rather than to surgery, the only large trial to have such a finding.

SoS Results in Context
The results of SoS need to be interpreted in the context of the totality of evidence provided by all the randomized trials of bypass surgery and angioplasty. We recently published a quantitative review of the 23 completed clinical trials, which randomized a total of 9963 patients.3 Overall, no significant difference in survival could be found between angioplasty and surgery, and the result was the same in the subset of trials that enrolled patients with multivessel coronary disease. Furthermore, no difference in survival was found in the 4 trials that used stents in patients with multivessel disease. We have updated this analysis to include the long-term follow-up.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(Circulation. 2008;118:325-327.)

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Circulation is available at http://circ.ahajournals.org
DOI: 10.1161/CIRCULATIONAHA.108.788489
from SoS (Figure). In the combined results of the Arterial Revascularization Therapies Study (ARTS), Angina With Extremely Serious Operative Mortality Evaluation (AWESOME), Argentine Randomized Study (ERACI II), Medicine, Angioplasty, or Surgery Study for multivessel CAD (MASS II), and SoS trials, 139 deaths occurred among the 1537 angioplasty-assigned patients (9.0%) and 132 deaths among the 1532 surgery-assigned patients (8.6%), which yields a risk ratio of 0.991 (confidence limits 0.69 to 1.42, \( P=0.96 \)) and a risk difference of −0.001 (confidence limits −0.034 to 0.032, \( P=0.96 \)). The comparative mortality after angioplasty or surgery in patients with multivessel coronary disease in the trials that used bare-metal stents was not materially different from the results of the earlier trials that used balloon angioplasty (Figure). The totality of the evidence suggests that in patients with multivessel disease suitable for either angioplasty or surgery, little difference exists in long-term mortality.

Our earlier overview of all trials of angioplasty and surgery clearly demonstrated several other mortality differences in clinical outcomes that are important to patients.\(^3\) The procedural risk is higher with surgery than with angioplasty, especially for stroke. Relief of angina was more complete for 5 years after bypass surgery, and patients were much less likely to undergo a repeat revascularization procedure, even if stents were used for the angioplasty. A well-informed patient might choose one procedure over the other based on the relative weight he or she gives to these various outcomes. It is important that cardiologists who advise patients on coronary revascularization provide balanced information about the alternatives and not unduly favor angioplasty just because they perform the procedure.

**Patients With Diabetes Mellitus**

The potential for variation in the comparative outcomes of coronary angioplasty and bypass surgery in key patient subgroups has been controversial ever since the Bypass Angioplasty Revascularization Investigation (BARI) reported significantly better survival among patients with diabetes mellitus randomly assigned to bypass surgery.\(^4\) Outcomes in subgroups rarely differ from the overall trial results, in part because treatments generally have consistent effects in patients deemed eligible for randomization and in part because the statistical power is quite low to demonstrate differences in outcome between subgroups. The statistical power in key subgroups might be improved by the performance of a meta-analysis of all trials, but outcomes in subgroups are not reported consistently.

In our earlier overview, only 6 of 23 randomized trials of bypass surgery and angioplasty reported outcomes separately among patients with diabetes, and the combined results showed no significant difference in mortality between angioplasty and surgery.\(^3\) With newer data from the SoS and ARTS trials, we have updated our meta-analysis, but the conclusion remains that little difference can be found between the procedures. Overall, there have been 55 deaths among the 436 patients with diabetes assigned to surgery (12.6%) compared with 67 deaths among the 413 patients with diabetes assigned to CABG (16.2%), which yields a risk ratio of 1.23 (confidence limits 0.80 to 1.9, \( P=0.35 \)) and a risk difference of 0.049 (confidence limits 0.002 to 0.0095, \( P=0.04 \)). Interpretation of the evidence available from these 8 randomized trials is difficult, because one method of analyzing the combined data suggests a small but statistically significant difference, whereas the other methods do not. The evidence about the comparative outcomes of angioplasty and surgery patients with diabetes should be clearer after the ongoing CARDia (Coronary Artery Revascularization in Diabetes), FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals with Diabetes), and VA CARDS (Veterans Affairs Coronary Artery Revascularization in Diabetes) randomized clinical
trials have been completed. For other subgroups of interest, not enough published evidence is available to assess variations in the comparative efficacy of surgery and angioplasty according to baseline characteristics. This question would be best answered by pooling individual patient data from all trials to provide maximal statistical power and to provide a complete picture from all available patients.

**Technological Change**

Angioplasty in 2008 is different than it was in 1998, but surgery has also changed over the past 10 years. Although some might argue that technological advances make the results of the SoS trial obsolete, we contend that evidence from earlier trials remains pertinent today. Bare-metal stents clearly reduced the rate of repeat revascularization procedures after angioplasty, yet randomized trials showed no difference in mortality or myocardial infarction between patients who had a stent rather than a balloon angioplasty. In light of this equivalence in hard end points, it is perhaps not surprising that the results of trials comparing angioplasty with bypass surgery had similar results whether balloons or stents were used in the angioplasty procedure.

Drug-eluting stents have become standard in angioplasty today, even with concerns about late stent thrombosis. Head-to-head trials of drug-eluting stents and bare-metal stents have also shown no difference in mortality or myocardial infarction, despite the significant reduction in repeat procedures with the use of drug-eluting stents. On the basis of these considerations, we expect the ongoing trials of bypass surgery versus angioplasty using drug-coated stents will also end in a draw, at least with respect to hard end points. But if history has taught us anything, it is that the results of clinical trials cannot be reliably predicted. So, stay tuned for the results of the next round between coronary angioplasty and bypass surgery.

**Source of Funding**

This work was funded by Contract No. 290-02-0017 from the Agency for Healthcare Research and Quality, Rockville, Md.

**Disclosures**

None.

**References**


**Key Words:*** Editorials ■ angioplasty ■ coronary artery disease ■ revascularization ■ stents ■ surgery ■ trials
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Circulation. 2008;118:325-327
doi: 10.1161/CIRCULATIONAHA.108.788489
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/118/4/325

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