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## CABG or PCI? A CARDIOTHORACIC SURGEON'S PERSPECTIVE

# The devil (or truth) is in the details

**S**HOULD PERCUTANEOUS or surgical intervention be the preferred invasive treatment for patients with multivessel coronary artery disease?

For most physicians who treat coronary artery disease, this question has been answered—percutaneous coronary intervention (PCI) is the preferred therapy. All one has to do to reach this conclusion is to compare the rapid growth of PCI with the steady decline of surgical coronary artery bypass grafting (CABG). Today, for every CABG procedure performed, there are three PCIs. Is this predilection to treat multivessel coronary artery disease preferentially with PCI justified?

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Despite multiple studies comparing the outcomes of surgical and percutaneous coronary treatment, the question remains controversial. Many randomized trials comparing them have shown equivalent survival rates, whereas several observational studies have shown a survival advantage for surgical revascularization. To make sense of these different findings and decide ultimately which intervention is most appropriate for prolonging life, it is necessary to understand the details of the different studies.

### ■ RANDOMIZED TRIALS: THE DETAILS

Fifteen randomized trials have compared outcomes of initial CABG vs PCI, nine comparing CABG vs PCI *without* stenting and six comparing CABG vs PCI *with* stenting.<sup>1–14</sup>

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In each of the nine studies of CABG vs PCI without stenting, 127 to 1,829 low-risk patients were enrolled.<sup>1–9</sup> They had no serious comorbidities, normal ventricular function, and mostly two-vessel coronary artery disease amenable to both procedures. Follow-up was from 1 to 8 years, although in most of the trials it was 3 years or less. In eight of the nine studies, survival was similar in patients treated either way. The only study showing a survival advantage with CABG was the Bypass Angioplasty Revascularization Investigation (BARI).<sup>2</sup> However, this advantage appeared to occur in patients with medically treated diabetes who had internal thoracic artery grafting of the left anterior descending (LAD) coronary artery. A consistent and important observation in these nine trials was that more patients who underwent CABG remained free of angina than those who underwent PCI without stenting, resulting in a rate of repeat revascularization four to 10 times higher after PCI than after CABG.

Similar conclusions were reached in the six randomized trials of CABG vs PCI with stenting.<sup>1,10–14</sup> Except for the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) study,<sup>13</sup> these trials each enrolled from 121 to 1,205 low-risk patients, most with normal ventricular function and two-vessel coronary artery disease amenable to both interventions. At 5 years, rates of survival were similar with both therapies. Just as in the earlier trials comparing CABG and PCI without stenting, a consistent finding was a greater need for repeat revascularization after PCI with stenting than after CABG. However, stenting reduced by half the need for coronary reintervention compared with the earlier PCI procedures without stenting.<sup>15</sup>

**The preference for treating multivessel coronary disease with PCI is not justified**

Randomized trials are often thought of as the gold standard and are quoted as showing survival equivalence after surgical and percutaneous revascularization for multivessel coronary artery disease. However, the devil is in the details, and these trials have shortcomings that call their conclusions into question.

First, for these studies to fairly determine whether CABG is better than PCI in prolonging survival, only patient subgroups in which CABG has been shown to be superior to *medical therapy* in prolonging survival (those with left ventricular dysfunction, three-vessel disease, or proximal stenosis of the LAD artery) should have been compared. But these patient subgroups were usually not included in the trials. Instead, the trials enrolled mostly low-risk patients for whom CABG does not prolong survival compared with medical therapy. Therefore, the only way CABG could have been found to prolong survival was if PCI decreased survival compared with medical therapy!

Second, the trials were underpowered to detect survival differences. To compare survival adequately, 2,000 to 4,000 patients would need to have been included in each treatment group of the individual studies.<sup>1</sup> (Interestingly, a meta-analysis of 7,964 patients from 13 of the randomized trials showed a survival advantage in patients who underwent CABG.<sup>15</sup>)

Third, for findings of these trials to be generalizable, they would need to include patients who are similar to the general population of patients with coronary artery disease undergoing invasive therapy. However, entry criteria excluded many patient subgroups, limiting the generalizability of the findings. In addition, the trials included only a small minority of patients eligible for enrollment (eg, only 5% of patients screened with multivessel disease were eventually enrolled).<sup>7,8</sup>

Fourth, to detect a survival difference, follow-up should be at least 5 years; most of the trials did not run that long.

#### ■ OBSERVATIONAL STUDIES: THE DETAILS

In contrast to these randomized trials, several observational studies have shown a survival advantage of CABG in multivessel coronary

artery disease.<sup>16–18</sup> Two large New York State registry studies have identified angiographic subgroups of patients who live longer after CABG than after PCI.<sup>16,17</sup>

Before coronary stenting became widespread, a study using New York State's Percutaneous Coronary Intervention Reporting System (PCIRS) and Cardiac Surgery Reporting System (CSRS) compared outcomes of 30,000 patients undergoing PCI with those of 30,000 patients undergoing CABG from 1993 to 1995.<sup>16</sup> Patients with prior revascularization, left main coronary artery disease, or recent myocardial infarction were excluded. Patients with one-vessel and two-vessel disease that included the LAD artery and those with three-vessel coronary artery disease irrespective of whether the LAD artery was involved had a survival advantage with CABG. A survival advantage was, however, identified in patients with non-LAD single-vessel disease who underwent PCI.

The second observational study using New York State's PCIRS and CSRS registries compared outcomes of patients with multivessel coronary artery disease who underwent either CABG (N = 37,212) or PCI with stenting (N = 22,102) from 1997 through 2000.<sup>17</sup> As in the previous study, patients with left main stenosis, recent myocardial infarction, or prior revascularization were excluded. To adjust for differences in risk profiles of surgical and percutaneous therapy patients, a propensity score was used. After adjustment, all patients with two-vessel and three-vessel disease derived a survival benefit within 3 years with CABG.

A recent Duke University study reported similar findings.<sup>19</sup> The investigators compared survival in 18,481 patients with coronary artery disease treated with medical therapy (6,862), PCI (6,292), or CABG (5,327) from 1986 to 2000. In patients with severe coronary artery disease (mostly three-vessel), CABG resulted in better survival than PCI, and the survival advantage was sustained in the era of PCI with stenting.

But the devil is still in the details. Whereas randomized studies are biased at the point of entry, observational studies are biased at the point of treatment.

An important consideration in determin-

**The randomized trials were too small, too short, and compared mostly low-risk patients**

ing whether a patient should be treated percutaneously or surgically is the diffuseness of the disease. Patients with focal, discrete obstructions are more likely to be treated with PCI, those with diffuse disease with CABG. This treatment bias would be expected to lower long-term survival rates after CABG, and this bias against surgery makes the survival advantage of CABG found in observational studies even more impressive.

Another important factor influencing treatment selection is recent myocardial infarction. To eliminate “rescue” PCI from confounding the results, patients with recent myocardial infarction were excluded from analysis in these observational studies.

The strengths of these observational studies are that the large number of patients and events powers them to detect differences in the two revascularization strategies, and that they compare the way coronary revascularization is actually practiced.

### ■ DRUG-ELUTING STENTS: THE DETAILS

Will drug-eluting stents eliminate the survival advantage of CABG observed in patients with multivessel coronary artery disease? These stents have reduced the risk of restenosis and the need for repeat intervention after PCI. But will this translate into improved patient survival?

Randomized and observational studies suggest it will not.<sup>16,17,20</sup> In a meta-analysis of 11 randomized trials that compared outcomes of 5,103 patients who received either drug-eluting or bare metal stents, there was no difference in survival or myocardial infarction rates despite a significantly lower rate of restenosis in the drug-eluting stent group.<sup>20</sup>

Further evidence that restenosis does not affect survival comes from New York State observational studies.<sup>16,17</sup> If lower rates of restenosis improve survival, the PCI patients treated in the second study with stents should


have had better adjusted survival rates than those treated in the first study with PCI without stents. This was not observed: adjusted survival was similar. For patients with three-vessel disease including the LAD artery, the adjusted 3-year survival rate was 86% after PCI without stenting and 84% after PCI with stenting.

These findings are consistent with an observational study from Emory University that did not find a difference in survival of patients with or without restenosis after PCI.<sup>21</sup>

Others have suggested that even if target-vessel restenosis is eliminated, PCI will still not be as effective as CABG.<sup>22</sup> This is due to the difference in how PCI and CABG treat coronary artery disease. PCI treats only the stenosis present at the time of intervention; CABG treats both the stenosis present at the time of surgery and any additional stenoses developing in the future proximal to the bypass graft.

### ■ THE TRUTH (DEVIL) IS IN THE DETAILS

In summary, the preference for treating multivessel coronary artery disease with PCI is not justified. Although several randomized trials have suggested that PCI results in survival rates equivalent to those with CABG, these studies were underpowered, lacked sufficient follow-up, and compared mostly low-risk patients who would not be expected to derive a survival benefit from CABG. Risk-adjusted, large observational studies convincingly show that CABG results in better survival compared with PCI, particularly when the LAD artery is involved. Patients with these high-risk angiographic characteristics should be treated with CABG. Despite improvements in PCI and drug-eluting stents that have decreased restenosis, the evidence does not suggest that this will improve survival.

The truth is in the details. 

**Observational studies show that CABG results in better survival than PCI**

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