

## EDITORIAL



## Treatment of Left Main Coronary Artery Disease

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When coronary arteriography was developed in the early 1960s, the very high risk associated with obstructive left main coronary artery disease became evident; this risk was related to the large volume of myocardium supplied by this vessel. Among patients receiving the medical therapy available at the time, the 5-year mortality approached 60%, and the survivors usually had severe symptoms, including angina, heart failure, or both.<sup>1</sup> Several years later, after coronary-artery bypass grafting (CABG) became available, two multicenter, randomized trials that compared medical treatment with surgical treatment showed that surgical treatment was strikingly superior.<sup>2,3</sup> Since then, there has been general agreement that, in the absence of contraindications, patients with left main coronary artery disease should undergo prompt revascularization. However, the specific revascularization techniques have undergone considerable evolution.

In 1979, Andreas Grüntzig reported that percutaneous transluminal coronary angioplasty, the technique that he had described just a year earlier, was not suitable for the treatment of this condition.<sup>4</sup> Others agreed and commented on the high risk of this procedure,<sup>5</sup> and for the next two decades, unprotected left main coronary artery disease, in which the coronary circulation is not protected by a bypass graft, was managed almost exclusively by means of CABG. When bare metal coronary stents became available, a few intrepid interventional cardiologists attempted this approach in patients who were not candidates for surgical treatment; the results were mixed.<sup>5</sup> The complications included procedure-induced occlusion and, later, restenosis, both of which are especially serious in patients with unprotected

left main coronary artery disease. These problems were largely overcome by technical improvements in stent placement and the development of drug-eluting stents. These advances led to greater use of percutaneous coronary intervention (PCI) and to multiple comparisons between the two competing revascularization strategies (i.e., CABG and PCI with drug-eluting stents). These strategies have been compared in multicenter, randomized trials as well as in studies that used registry data.<sup>6,7</sup>

The two strategies generally provided similar results with respect to the composite end point of death, myocardial infarction, stroke, or unplanned ischemia-driven revascularization. Stroke occurred more frequently in the CABG group than in the PCI group (i.e., PCI with drug-eluting stents), whereas the need for repeat revascularization was greater in the PCI group than in the CABG group.<sup>7,8</sup> As a consequence, PCI with drug-eluting stents is being used with increasing frequency, currently exceeding the frequency of CABG in many centers.<sup>7,9</sup> Despite the thousands of patients involved in these comparisons, a degree of uncertainty about the findings has persisted, because they have been based on inadequately sized, hypothesis-generating trials and meta-analyses, many of which involved a mixture of trials and studies based on registry data.

It is in this context that the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial, now published in the *Journal*, should be viewed.<sup>10</sup> EXCEL is a large, multinational, multicenter trial that randomly assigned 1905 patients with unprotected left main coronary artery disease, who were considered to be suitable for either strategy of revascularization by a

“heart team” that included an interventional cardiologist and a cardiac surgeon. The goal of both strategies was to achieve complete anatomical revascularization. The status of the patients ranged from low to high risk, as assessed at an angiographic core laboratory; more than half the patients had multivessel coronary artery disease as well. The EXCEL investigators used a contemporary second-generation fluoropolymer-based cobalt–chromium everolimus-eluting stent, which has shown a very low incidence of stent thrombosis and restenosis, and they frequently used intravascular ultrasonography to facilitate more effective stent placement. Contemporary surgical techniques were used in the arterial revascularization procedures — aortic and transesophageal ultrasonography was used frequently, and off-pump CABG was performed in many patients.

EXCEL was a well-designed and rigorously conducted trial; the heart teams were skilled, and at 30 days, all-cause mortality was 1% in both treatment groups. The incidence of the primary composite end point (death, stroke, or large myocardial infarction at 3 years) was also essentially identical in the two strategies, with a hazard ratio of 1.00. Although the rate of all-cause death was numerically higher in the PCI group than in the CABG group, this was related in part to a trend of an increased incidence of deaths from noncardiovascular causes. With respect to the 3-year end points, the rate of stroke was numerically higher in the CABG group than in the PCI group, and the rate of ischemia-driven revascularizations was significantly higher in the PCI group than in the CABG group.

The take-home message from the EXCEL trial is that the majority of patients with unprotected left main coronary artery disease, which was a very serious, life-shortening, and disabling condition early in my professional lifetime, can now be managed equally well by means of two strategies of revascularization if carried out by expert, experienced teams such as those participating in the EXCEL trial. The outcomes of shorter hospital stay, greater early safety benefit, and more rapid recovery and return to normal activity favor

PCI over CABG. However, despite the similar results with respect to the primary end point of death, stroke, or myocardial infarction at 3 years, it should be noted that the PCI group exhibited a greater increase in these events between 30 days and 3 years than did the CABG group (11.5% vs. 7.9%,  $P=0.02$ ). Therefore, it is reassuring that the EXCEL investigators plan further follow-up of these patients.

Disclosure forms provided by the author are available with the full text of this editorial at [NEJM.org](http://NEJM.org).

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