Stents versus CABG for Left Main Coronary Artery Disease

TO THE EDITOR: In their report on a noninferiority trial involving patients with left main coronary artery disease, Park et al. (May 5 issue)[1] conclude that percutaneous coronary intervention (PCI) was noninferior to coronary-artery bypass grafting (CABG). However, the authors recognize that a lower-than-expected incidence of the primary end point at 1 year provided insufficient statistical power. Therefore, a 2-year analysis was reported, with a cumulative incidence of the primary end point of 12.2% for PCI and 8.1% for CABG. At this point, the authors shifted the statistical approach to a superiority analysis and reported a P value of 0.12, indicating no significant difference between the two groups.

Taking the number of events listed in Table 2 of the article, we calculated the 95% confidence interval for the 2-year incidence of events as 9 to 16% for PCI and 5 to 12% for CABG. Considering these limits, we estimated the 95% confidence interval for the difference between the treatments as −3 to 11%, which encompasses the predefined noninferiority margin of 7%. Therefore, if the authors had used the initial approach of noninferiority analysis in analyzing the 2-year data, the conclusion would be that PCI did not meet the noninferiority criterion, as compared with CABG.

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No potential conflict of interest relevant to this letter was reported.

1. Park S-J, Kim Y-H, Park D-W, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med 2011;364:1718-27.

TO THE EDITOR: Park et al. suggest that in patients with unprotected left main coronary stenosis, PCI with sirolimus-eluting stents was noninferior to CABG. In consideration of the potential clinical implications, addressing some methodologic issues would be of interest.

First, of the four components of the primary end point, only the rate of ischemia-driven target-vessel revascularization was higher in the PCI group than in the CABG group (9.0% vs. 4.2%). However, systematic late angiography was performed only after PCI. Despite attempts to avoid the consequences of the urge to repair any visualized narrowing (by considering as events only ischemic-driven revascularization), this uneven diagnostic strategy introduced a fundamental design bias. The lack of anatomic assessment might have prevented additional revascularization attempts in surgical patients with mild symptoms or ischemia.

Second, the authors suggest that the systematic use of intravascular ultrasonography (in 91.2% of patients) might have contributed to the favorable PCI outcome. Therefore, additional information on the approach used to guide PCI with this imaging technique would be of critical practical value.[1,2] Undoubtedly, these results will help to further inform clinical decisions in patients with left main coronary stenosis.

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THE AUTHORS REPLY: In response to Correia's concern about the use of noninferiority analysis in evaluating our 2-year data: it should be noted that the prespecified primary trial analysis was a noninferiority analysis at 1 year. This implies that both the power calculation and the noninferiority margin were determined on the basis of the expected 1-year event rates in the control and experimental groups. Our analyses for the 2-year event rates were post hoc exploratory analyses to help readers understand the outcome with longer follow-up because of the unexpectedly low event rates at 1 year. For these analyses, the use of conventional superiority testing was considered most appropriate. Had we chosen to prespecify a noninferiority analysis at 2 years, we would probably have chosen a larger margin, given the longer follow-up. As Correia notes, the 2-year results showed an increasing tendency toward a higher revascularization rate in the PCI group than in the CABG group, with a similar incidence of death, myocardial infarction, and stroke. A larger randomized

study with greater statistical power will be required to confirm these results.

We agree with the criticism of Alfonso et al. with respect to the surveillance strategy that was used in our study. In accordance with previous practice guidelines,[1] we recommended routine angiographic surveillance for patients receiving coronary stents but ischemia-oriented surveillance for patients undergoing bypass surgery. Therefore, in spite of rigorous adjudication of events, the revascularization rate that we report was undoubtedly inflated in the PCI group, as compared with the CABG group. It is interesting that the difference in revascularization rates was reduced between the two groups when only procedures that were performed on the basis of clinical judgment were considered. A further study applying the same surveillance protocol to both populations is required to avoid this bias.

We have previously reported on the potential benefit of intravascular ultrasonography in left main coronary stenting.[2] Practical information on its use during the stenting procedure has also been reported.[3] In brief, intravascular ultrasonography provided information on the extent of disease and vascular morphology before the procedure, which was helpful in determining the treatment strategy. During the stenting procedure, intravascular ultrasonography was used to confirm optimal stenting, including demonstration of sufficient luminal area and complete stent apposition. We believe that intravascular ultrasonographic guidance is responsible for our ability to obtain successful periprocedural and long-term outcomes in left main coronary-artery stenting.

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Since publication of their article, the authors report no further potential conflict of interest.

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Pioglitazone for Diabetes Prevention

TO THE EDITOR: DeFronzo and colleagues (March 24 issue) [1] reported that pioglitazone reduced the conversion from a condition of impaired glucose tolerance to type 2 diabetes. However, the results showed only that pioglitazone reduced patients' blood glucose levels during a glucose-tolerance test while they were taking the active drug. The cost of pioglitazone treatment was substantial weight gain and fluid retention. The potential disease-modifying effects of insulin-sensitizing agents have been investigated previously in studies involving metformin[2] and troglitazone.[3,4] Prevention of diabetes with these drugs can be attributed largely to their short-term pharmacologic effects, with progression to diabetes occurring in a large percentage of the study participants after the drug has been discontinued. In the study by DeFronzo et al., the critical question is whether pioglitazone might have a disease-modifying effect: as part of the primary analysis, the rate at which diabetes developed after the drug washout period should have been determined. The parallel rise in HbA_{1c} levels in both the placebo and the pioglitazone groups that followed the initial decline in these levels in the pioglitazone group suggests that this drug has only a short-term pharmacologic effect. If so, an end point that is more relevant than the effect of pioglitazone on glucose levels should be pursued.

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No potential conflict of interest relevant to this letter was reported.

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