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EDITORIAL COMMENT

Left Anterior Descending Coronary Artery Revascularization

Patient-Tailored Therapy?*

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Coronary revascularization continues to be a useful therapeutic tool in the management of selected patients with symptoms or significant myocardium at ischemic jeopardy. The Remote Medical versus the 10-year CABG (Coronary Artery Bypass Surgery) trials emphasized the greater survival benefit in patients with worse anatomic and ischemic risk (1). Patients with the greatest myocardial ischemia, poorest left ventricular function, and most anatomic coronary disease tended to receive the greatest benefit (2). With the advent of percutaneous coronary intervention (PCI), there was a general belief that, in patients with less severe disease, PCI was a reasonable alternative strategy to coronary artery bypass grafting (CABG), even in the initial balloon era. Conversely, for patients with more complex disease, CABG generally was considered more likely to provide the best outcomes. This approach has continued into the present.

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However, because of recognized additional risk for the left anterior descending artery (LAD), the single-vessel PCI algorithm has been challenged frequently regarding the best strategy for this specific vessel. Remarkably, these conceptual strategies are based on a paucity of trial data covering nearly 30 years. Furthermore, the technology for CABG, PCI, and even the quality of medical therapeutics has continued to evolve, often at a pace that tends to make multicenter randomized trials of debatable impact by the time long-term follow-up is completed.

One popular way to address relatively small trial data encompassing a changing field is to perform a meta-analysis. In this issue of the *Journal*, Kapoor et al. (3) describe the results of such an analysis, examining comparative outcomes for PCI versus CABG in patients with isolated LAD disease. In their analysis of 9 randomized control trials (RCTs) including 1,210 patients with isolated single-vessel LAD disease, treatment strategies varied greatly for PCI from balloon angioplasty to stents (although only one small trial included drug-eluting stents [DES]) as well as for CABG, which included standard on-pump surgery to limited thoracotomy using off-pump techniques.

Nevertheless, the accurate statistical analysis performed by the authors showed a virtual lack of heterogeneity among the different trials, suggesting that the overall balance between CABG and PCI has remained stable over the years despite significant changes in both fields. Indeed on analysis, there was no difference in rates of mortality for either revascularization strategy at 30 days, 1 year, and 5 years. Specific, adverse procedure-related events were not different between revascularization strategies, including the incidence of myocardial infarction and stroke. The use of CABG appeared to have a greater incidence of procedure-associated arrhythmias, whereas bleeding risks were not different between treatments, although for these latter 2 events, there were only a small number of studies reporting these events.

Not surprisingly, those patients undergoing CABG had longer hospital stays by >3 days, but angina relief was significantly better, favoring CABG at years 1 and 5, whereas the need for repeat revascularization was significantly less for CABG compared with PCI at the same time intervals. No data are given on the composite risk of major adverse coronary and cerebral events for this analysis, but one could speculate that, based on the difference in repeat revascularization, a combined-risk end point might have favored the use of CABG as the lower-risk procedure.

The impact of these findings no doubt will be debated. The most confident conclusions are equivalent death rates and greater need for revascularization in the PCI group. In general, this is what we have learned to expect. Added to these findings, the recognized greater acute morbidity for CABG supported in this study by an increased hospital stay, the therapies may be considered equal, or perhaps favoring PCI acutely and CABG late. But much is missing for clinical decision-making. The population tended to be young, with few patients who were 75 years or older, a low incidence of reduced ejection fractions, significantly fewer women, and only 1 study in which DES was used. There also was great variation in the incidence of unstable angina in the studies. Thus, although we can be comforted by similar mortality in the analysis, this only applies to the population studied. Contemporary revascularization confronts many more complex clinical and anatomic subsets.

Although RCTs give reassurance of patient equivalency, the requirement to randomize may include patients eligible for either therapy but not ideal for one or the other

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treatment based often on coronary anatomy or perhaps less often on patient characteristics such as diabetes. These subtle variations which are not quantified in RCTs always raise concern regarding the applicability of the trial results to clinical practice. An example is the Emory EAST (Emory Angioplasty versus Surgery Trial) registry (4), in which patients who were eligible for randomization but who were not randomized and were ultimately treated based on individualized physician decisions had better overall outcomes than did the randomized patients. This result suggests that individualized patient decisions can make a difference because ideal decisions rest on far more factors than just "eligibility" for either revascularization strategy. The best therapeutic intervention for a 45-year-old airline pilot with single-vessel LAD disease may be significantly different than for a 78-year-old woman with global left ventricular dysfunction, diabetes, and renal insufficiency, even though both revascularization strategies are theoretically acceptable for each patient from a strictly randomization standpoint. Likewise, specific anatomic findings, such as a small distal LAD for grafting or an ostial LAD lesion with left main disease involvement, when considering PCI may make each case more ideally amenable to the opposite therapy, even though each circumstance is potentially treatable by an assigned strategy.

None of these examples is meant to negate the value of RCTs or the meta-analysis reported by Kapoor et al. (3). The examples do, however, emphasize that although the meta-analysis gives reassurance in terms of equivalent survival in a general population, considerable physician input remains necessary to best manage patients with isolated LAD disease. Conversely, registry data are likewise often flawed by greater-risk or older patients selected for PCI who are perhaps not ideal, either to avoid being turned down or already having been turned down for a presumed higher-risk CABG procedure. There are no asterisks in these databases for such circumstances.

The issue of patient composition affecting registry outcome data has been recently highlighted by the SYNTAX PCI Registry (5). The PCI registry was populated with high-risk patients turned down for CABG. The resultant "palliative" PCI was associated with, not unexpectedly, poor outcomes because of patients with multiple, high-risk comorbidities. In contrast, the CABG registry of PCI turndowns was comprised of lower-risk patients turned down predominantly for unfavorable anatomy for PCI, not for adverse systemic abnormalities. Successful stenting of a symptomatically culprit lesion, unresponsive to medical treatment may improve a patient's quality of life (a worthwhile clinical accomplishment) despite a significant risk for subsequent morbid events. Thus, caution must be exercised in interpreting outcomes of comparative registries unless one is certain of the distribution of patient profiles and the goals of therapy.

During the coming years, the ultimate additional benefit of DES is yet to be realized. To the extent that late thrombosis is limited and less restenosis leads to better late outcomes (lower rates of late revascularization will potentially lead to lower late event rates secondary to less repeat procedures) (6), DES may have a significant impact on improving PCI outcomes in isolated LAD disease. But again, these results will need to be modulated by more varied patient and anatomic populations to be able to accurately predict the best strategy for individual patient circumstances.

Conclusions

Considering the equivalent survival with CABG and PCI, isolated LAD revascularization should be dictated by anatomic and patient characteristics and preferences. Individualizing strategies has the greatest opportunity to provide optimal patient outcomes.

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Key Words: revascularization ■ percutaneous coronary intervention ■ coronary artery disease ■ coronary artery bypass grafting ■ meta-analysis.