EDITORIAL COMMENT

Toward Better Stratification of Patients With Left Main Disease

Value of Clinical and Angiographic-Derived Risk Scores*

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Predicting who will benefit from coronary revascularization and whether percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) would be most beneficial has been the subject of long-standing interest. The American College of Cardiology/American Heart Association coronary artery lesion classification was developed to help identify high-risk lesions in patients undergoing balloon angioplasty, at a time when balloon angioplasty was indicated for discrete single lesions (1). Since that time, PCI therapy has evolved, and the choice of PCI or CABG in patients with more advanced coronary artery disease (CAD) is more challenging. Although the original American College of Cardiology/American Heart Association lesion classification was useful in guiding PCI therapy, its use in the stent era and in more complex CAD has been problematic. Moreover, PCI and CABG have been compared in clinical trials with ever-increasing complexity of CAD; however, patients with left main CAD were excluded from almost all the contemporary comparative trials of CABG and PCI.

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The SYNTAX (Synergy between Percutaneous Coronary intervention with TAXUS and Cardiac Surgery) trial was the first randomized clinical trial to compare clinical outcomes in patients with multivessel and left main CAD (2). In the SYNTAX study, the SYNTAX score (based on 10 angiographic characteristics) provided powerful discrimination of clinical outcomes in all patients undergoing revascularization (3). This score represents the most comprehensive anatomic characterization of CAD to date and has become the subject of intense clinical investigation. Patients with a low SYNTAX score had low rates of nonfatal myocardial infarction or death during study follow-up; and patients with the highest tertile of SYNTAX score had the worst clinical outcomes at study end. A post hoc evaluation of the SYNTAX trial by the study investigators revealed that the SYNTAX score was as predictive or had a more predictive value than the EuroSCORE (European System for Cardiac Operative Risk Evaluation), a risk scoring system based on baseline clinical characteristics (4). That a risk score based on angiographic characteristics alone was more predictive of clinical outcomes than one based on well-established clinical characteristics has surprised many and spurred interest in evaluating the SYNTAX score in populations beyond the SYNTAX trial itself (4,5).

In this issue of *JACC: Cardiovascular Interventions*, Capodanno et al. (6) provide the results of a retrospective evaluation of the SYNTAX score combined with clinical variables to predict mortality and major adverse cardiac events at 2 years, in a registry of patients undergoing PCI or CABG of unprotected left main lesions. These investigators assessed 2 risk scores combining both angiographic and clinical characteristics: the global risk classification, using both the SYNTAX and EuroSCORE to create tertiles of low- to high-risk; (7) and the clinical SYNTAX score, derived by multiplying the SYNTAX score by the age, creatinine, ejection fraction (ACEF) score [(age/ejection fraction) + 1, if for serum creatinine >2.0 mg/dl] (8). These scores as well as the individual angiographic and clinical scores were compared for performance with 2 metrics: calibration and discrimination. Calibration is the degree of correlation between the estimated probability of an outcome as determined by the score model and the actual outcomes, measured by the Hosmer-Lemeshow test. Discrimination is the probability that the score will assign a higher probability of risk to patients who have events than those who do not, measured by the area under the receiver-operator curve. Distilling multiple results and comparisons from this registry, the authors concluded that the global risk classification score had the overall best calibration and discrimination of the various scores in the PCI patients, whereas the ACEF score provided the best overall performance in the CABG patients. Interestingly, only a high SYNTAX score (>32) was able to identify a better outcome with 1 revascularization strategy compared with the other (in this case CABG vs. PCI) among all the scores evaluated.

The findings by Capodanno et al. (6) contribute to the rapidly growing evidence base evaluating risk models in patients undergoing revascularization with either PCI or CABG for patients with extensive CAD. There are only limited validations of risk scores in the population of patients with left main and 3-vessel CAD. Moreover, the SYNTAX score itself was proposed without validation (although based on thoughtful combination of existing risk

models at the time) (3). Thus, these kinds of data are much needed. The use of this information for guiding patient care in patients with complex CAD, however, might be challenging for several reasons. First, the observations from this study rest on the clinical outcomes of interventionalists and surgeons performing PCI and CABG at 2 institutions. The mortality and major adverse cardiac event rates after these procedures constitute an integral element in the calibration and discrimination values determined in their study. Thus, they would be broadly applicable to other practices only if the PCI and CABG outcomes achieved were similar to those obtained in this study. Second, most physicians performing PCI and CABG are not accustomed to routinely evaluating risk scores such as reported by Capodanno et al. (6) before their procedures. Moreover, use of metrics such as calibration and discrimination in assessing the performance of risk models is not intuitive or widely understood by clinicians. Clinicians will need extensive education in both the derivation of these more complex risk models as well as the ability to thoughtfully distinguish the most useful of these models in tailoring therapy. Finally, there are no studies prospectively comparing clinical outcomes after PCI versus CABG in patients selected solely on a risk score. Ironically, use of a risk score as an inclusion criterion in a randomized clinical trial or to guide choice of PCI versus CABG in practice might ultimately weaken the predictive value of the risk score if both PCI and CABG are truly comparable therapies for that specific risk group.

In the end, it seems clear that we are moving into an era where a more sophisticated evaluation of the benefits and risks of revascularization with PCI and CABG is going to be expected before these procedures are performed. Patients are becoming more sophisticated and expect the "best" outcome as well as that their physicians are current with practice standards. The use of appropriateness criteria for revascularization procedures (9) will be gaining tremendous momentum with recent allegations of use of PCI (stents) in patients without severe CAD. Finally, scorecarding of outcomes is proliferating and is being widely used by health care systems to tout their skills and abilities. As physicians are drawn into this type of discussion, it is clear that inappropriate risk stratification is the number one issue raised in defense of less-than-optimal results. For all of these reasons, we will be using more sophisticated risk score systems in our practice. The challenge is to make them more user-friendly and hope that they continue to enhance rather than delay appropriate treatment.

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