Editorial

Percutaneous Catheter Interventions Followed by Coronary Artery Bypass Grafting

Primum Non Nocere

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The results of the SYNTAX trial (The Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery),[1] the FREEDOM trial (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease),[2] and other studies are providing clarity and even growing consensus among cardiologists and surgeons about the relative roles of percutaneous catheter interventions (PCI) versus coronary artery bypass grafting (CABG) for coronary revascularization. However, there remains a concern, especially among cardiac surgeons, that some patients with prior PCI may be at increased risk of poor outcomes when undergoing subsequent CABG surgery.[3,4] In a report in this issue of *Circulation: Cardiovascular Interventions* from the E-CABG (European Multicenter Study on Coronary Artery Bypass Grafting), Mariscalco et al[5] acknowledge that the clinical impact of prior PCI in patients who subsequently require CABG remains unsettled. The authors queried the recently established voluntary registry of CABG procedures undertaken at 16 European centers, designated as E-CABG, hoping to answer this persisting concern about possible risks associated with prior PCI at subsequent CABG operations. In addition, they undertook a meta-analysis of publications reporting on outcomes after CABG in patients with prior PCI.

See Article by Mariscalco et al

This E-CABG registry was posted on ClinicalTrials.gov site in December 2014 (URL: http://www.clinicaltrials.gov. Unique identifier: NCT02319083), and the study protocol was described by Biancari et al[6] in 2015. The 16 participating centers represent university and community hospitals in 6 European countries. E-CABG processes are described as involving thorough prospective data collection on all patients with CABG including presenting clinical status and immediate postoperative adverse events. This current report seems to be the first published analysis of CABG outcomes based on a review of more than 3700 patients in the E-CABG registry who had surgery between January 2015 and March 2016.

The E-CABG study group should be commended for undertaking this prospective registry. The Society of Thoracic Surgeons Adult Cardiac Surgery Database, begun in 1989, although much larger, is used principally to promote quality improvement and patient safety among surgeons. The E-CABG registry describes a detailed data collection process which is audited for accuracy and completeness, making this a focused and reliable research instrument. The extent and precision of patient-related and early CABG outcomes data described in the present report validates the goals of the E-CABG collaborators.

This being acknowledged, however, there are limitations to this specific analysis that may weaken their conclusion that prior PCI was not associated with an increased risk of mortality or other adverse outcomes in patients with CABG. As described in Table VI in the Data Supplement, there were 120 patients with PCI(14.9% of the 805 total patients with prior PCI) undergoing CABG who were excluded from this analysis in order to control for any acute PCI-related complication.[5] In fact, these patients, representing 3.17% of E-CABG registry, patients had a mortality rate of 3.3%, twice the rate for patients having PCI 1 month or longer before the CABG procedure. Those patients undergoing CABG within 30 days after PCI also required more postoperative re-exploration for bleeding as well as mechanical support for presumed cardiac failure than those PCI patients with later CABG. It is more precise, then, to conclude that CABG risks are not increased for PCI patients who did not require CABG surgery early after PCI. However, CABG within the first month after PCI, presumably for failure of the PCI or for PCI-related complications, results in worse surgery-related outcomes. Although the relatively high percentage of prior-PCI patients needing early CABG seems alarming, we do not know how many patients were treated successfully with PCI and never needed CABG.

Another question about this analysis concerns the appropriateness of propensity matching PCI patients with those coming to CABG without prior PCI. In fact, when comparing the entire CABG cohort to the 19% of patients with prior PCI, and excluding 120 patients who had early CABG, these non-PCI patients were older, had marginally more compelling presentations in terms of unstable angina and myocardial infarctions, and tended to require more emergency operations. In some practices, these characteristics might drive initial use of PCI rather than CABG, but there seems to have been variability in the approach to these less stable patients. In addition, there were more patients with diabetes mellitus among the patients having CABG surgery without prior PCI. The PCI

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patients, as might be expected, were more likely to be taking antiplatelet medications. Despite this, there was no increase in re-exploration for bleeding in the patients with PCI.

Propensity score weighing by matching CABG only patients with prior-PCI patients simply eliminated some of the actual clinical differences that are seen in the 2 comparator groups. Added propensity matching does reinforce the authors' conclusion that prior PCI is not a specific risk factor for patients with CABG. However, actual clinical differences observed between the entire unweighted cohort and the prior-PCI patients may reflect the influence that prior PCI had on the decision to proceed with CABG surgery. PCI therapy may well be followed by a recommendation for CABG, rather than more PCI, if percutaneous treatment fails. Propensity matching, even when based on multiple clinical characteristics, cannot eliminate fully the biasing effect that prior PCI had on the decision to undertake CABG for recurrent ischemia.

The meta-analysis reported by the authors confirmed, on balance, a higher odds ratio for early CABG mortality in patients with prior PCI. However, there are conflicting reports in the literature, with several published studies failing to demonstrate a negative effect of prior PCI on patients with CABG. Although the present report, based primarily on the E-CABG registry analysis, attempts to demonstrate that prior PCI does not adversely affect CABG mortality and other postoperative outcomes, it is a conclusion that must be viewed as conditional, likely influenced largely by how soon and under what circumstances after PCI the CABG procedure must be undertaken.

Another acknowledged limitation in this analysis of the E-CABG data is the absence of longer follow-up information about the course of these patients. We do not know how the CABG procedures may have been altered by the presence of 1 or more stents. And although we know that left main disease was distributed equally in the 2 groups at the time of CABG, we cannot exclude the possibility that some patients found to have subcritical left main disease refused surgery initially (we do know that 5% of post-PCI CABG patients had been treated with a left main stent) and agreed to it only after a failed attempt to manage their disease less invasively. Despite such limitations, there are important findings in this report. Once out of the 30-day PCI-procedural time frame, there was little indication that a prior PCI adversely affected CABG outcomes. In fact, in this group of E-CABG registry patients, the prior-PCI group seemed to have presented for CABG with fewer or less severe risk factors than the general population of patients with CABG. In addition, there were no postoperative outcomes differences between the 2 comparator groups, including no increase in re-exploration for bleeding after surgery in the patients with PCI, despite the use of antiplatelet medications by many patients with PCI.

It is interesting to note the reasons for referral for CABG among these contemporary PCI-to-CABG patients. Nine out of 10 post-PCI patients were referred for CABG because of coronary artery disease progression. In-stent stenosis was seen in 40%, with just 5% reported to have had stent occlusion. These observations indicate that both failure of stents to maintain patency and failure of medical therapies to slow atherosclerosis progression contribute to the need for subsequent CABG surgery. Perhaps, medical therapies and lifestyle management programs after PCI were not pursued vigorously in these patients. Absence of detail about the type, number, and intensity of medical therapies before CABG is a relative weakness of this study.

To the extent that this large multinational experience from the E-CABG study group is reflective of general practice, we can expect that ≈1 in 5 patients referred for CABG today will have had prior PCI within roughly the prior 3 to 4 years. These former patients with PCI will be referred for CABG because of disease progression or stent failure. It is reassuring that this contemporary real-world experience supports some earlier reports that successfully deployed stents do not add significant risk to patients when subsequently undergoing CABG. Despite this positive finding, it is important to acknowledge that PCI procedures that do necessitate early CABG within the first month may adversely affect CABG outcomes.

Disclosures

None.

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