

Coronary Artery Bypass Grafting Among Patients With Prior Percutaneous Coronary Interventions

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The results of multiple studies including the New York State Registry data,¹ the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial,² the FREEDOM (Future Revascularization Evaluation In Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease)³ trial, and the EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization)⁴ trial have aimed to provide an evidence-based role for percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) for coronary revascularization. Each of these studies has primarily addressed the question of an initial revascularization approach, as opposed to outcomes among patients with prior PCI who develop restenosis and/or progression of other coronary artery disease to the extent that surgical bypass becomes necessary. Concern remains that patients with prior PCI may be at increased risk for poor outcomes when undergoing subsequent CABG surgery in the acute/subacute (<30 days since index PCI procedure) and distant (>30 days since index PCI) setting. Given that the number of patients undergoing CABG previously treated with PCI is increasing up from 21% in 2008 to 29% in 2018 per a recent study from the Society of Thoracic Surgeons 2018 Adult Cardiac Surgery Database,⁵ there is renewed interest in the safety and outcomes in this clinically important group of patients.

From a historical perspective, previous retrospective studies of prior PCI in patients requiring CABG are conflicting. In 1996, Jones et al⁶ first documented a negative impact of prior PCI, based on an extensive review that included

172 184 patients undergoing CABG. Similarly, Hassan et al⁷ identified prior PCI as an independent predictor of in-hospital mortality (3.6% versus 2.3%) in a retrospective cohort of 6504 patients undergoing first-time isolated CABG, while Bonaros et al⁸ also reported that prior PCI predicted increased in-hospital mortality (4.4% versus 2.4%) and major adverse cardiac events (7.9% versus 4.3%). However, other studies failed to demonstrate a negative prognostic impact of prior PCI. Metha et al⁹ analyzing a total of 34 316 isolated CABG patients at 16 different statewide institutions observed similar mortality rates between patients with and without prior PCI (2.3% versus 1.9%), although major complications and longer hospitalization were recorded in the PCI group only. In the Massachusetts Adult Cardiac Surgery Database,¹⁰ 12 591 patients with CABG were considered for analysis, and prior PCI (≥ 14 days) did not affect early and late survival.

Based on this background, Mariscalco et al¹¹ and the current study by Biancari et al¹² in this issue of the *Journal of the American Heart Association (JAHA)* analyzed a voluntary registry of CABG procedures undertaken at 16 European centers (E-CABG), representing university and community hospitals in 6 European countries through prospective data collection to gain insight into the potential risk associated with prior PCI and subsequent CABG procedures. The design of this registry allows capture of a more inclusive patient population undergoing CABG with theoretically diverse referral pathways, preoperative selection criteria, and treatment strategies. While both studies examined hospital/30-day death as the primary outcome with secondary outcomes including length of stay in the intensive care unit, stroke, postoperative use of intra-aortic balloon pump and/or extracorporeal membrane oxygenation, acute kidney injury, renal replacement therapy and bleeding, the present study also included 1-year all-cause mortality in secondary outcome analysis and included data on the number of prior PCIs performed as well as location of prior stent placement within the coronary circulation in a patient population with an intermediate SYNTAX score. Both studies demonstrated that prior PCI was not associated with an increased risk of mortality after CABG and did not confer any additional risk in terms of postoperative morbidity, including low cardiac output, blood transfusion requirement, and renal or cardiac

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complications with similar results observed in those patients with diabetes mellitus. Furthermore, the current study showed that while the total number of adverse events was higher in patients undergoing isolated CABG with multiple prior PCIs or in whom PCI was performed in all 3 main coronary arteries, this did not reach statistical significance.

Although these studies were well-conducted registries, there are limitations to the study design and analysis that may weaken the overall conclusions. First, one must consider the strict exclusion criteria of this study. The aforementioned results can only be applied to isolated CABG, as combined CABG with valve repair/replacement or aortic surgery were excluded from analysis. Importantly, PCI performed <30 days before the index procedure was also excluded from analysis. Two-hundred and thirty-five patients (15.4% of patients with prior PCI) underwent CABG within 30 days after PCI and had a risk of in-hospital/30-day death twice that (3.8%) of those with PCI performed >30 days before CABG. Data from Mariscalco et al also showed that those patients undergoing CABG within 30 days after PCI required more postoperative re-exploration for bleeding as well as mechanical support for presumed cardiac failure than those PCI patients with later CABG. Stevens et al¹⁰ found that although hospital mortality post CABG did not differ between patients with a history of remote (≥ 14 days) PCI, CABG after recent (<14 days) PCI was associated with higher hospital mortality and morbidity (4.1% versus 1.9% and 58% versus 43%, respectively). While P2Y12 receptor inhibitor use within 5 days before CABG was included in all adjusted analyses of the current study and did not affect the 30-day and 1-year survival, clopidogrel use was an independent predictor of severe-massive bleeding, acute kidney injury, and a trend toward increased risk of postoperative dialysis.

An additional limitation of this study is the lack of data on the location of anastomoses distal to the stented region, the length of stented region, or the amount/degree of myocardium protected. Longer stented regions imply that more distal bypass grafting was used, involving smaller target vessels with less favorable run-off and potential for reduced long-term graft patency, while the opposite may be true for this study set. Data presented here focused on in-hospital/30-day mortality as primary outcome with 1-year mortality as a secondary outcome. Given the above along with the natural history of saphenous vein grafts, it would be helpful to ascertain outcomes at 3 to 5 years postoperatively with regards to graft patency. Given the mean delay of 3.6 to 6.2 years from the most recent PCI to CABG, we are unable to assess the impact of collateral circulation formation on outcomes post CABG. Conclusions taken from the current data set must be reconciled with the fact that the current study was not powered to detect differences with >1 PCI or PCI in 2 (320 pts) or 3 (106 pts)

coronary arteries. In fact, the rates of adverse events were higher if ≥ 3 prior PCIs were performed before CABG. Moreover, the low overall operative mortality after CABG procedures could explain the lack of difference in mortality between the no PCI and prior PCI groups. Although not presented as an independent predictor of mortality, there was a statistically significant greater use of “off-pump” surgery in the prior PCI cohort.

Of particular note is the reason for referral for CABG in these post PCI patients. Seventy-five percent to eighty percent of patients were referred for coronary artery disease progression with an increasing percentage of total referral from 1 to >3 PCIs cohort referred for in-stent stenosis with 6% to 10% increase in stent thrombosis in the same subgroup. These observations indicate that both failure of stents to maintain patency, 52% in 1 previous PCI group at any drug eluting stent, and failure of medical therapies to slow atherosclerosis progression contribute to the need for subsequent CABG surgery. It is possible that newer stent technologies/iterations, advances in intracoronary imaging and pressure/flow assessment, more aggressive medical therapies including use of intensive statins (not reported), anti-platelet therapy, and lifestyle management programs after PCI may have aided these patients. Furthermore, logistic regression analysis in the current study identified age, female sex, urgency of the procedure, SYNTAX score, left ventricular ejection fraction $\leq 50\%$, critical preoperative state, ST-elevation myocardial infarction, and estimated glomerular filtration rate as independent predictors of hospital/30-day mortality post CABG. While these factors were not specifically addressed in this study, 1 can assume the above variables need to be considered when making decisions about the mode of revascularization among patients with prior PCI and recurrent/progressive CAD.

In our opinion, a patient-centered approach and a practical understanding of the current literature is critical when referring stable patients with prior PCI for CABG. A well-informed patient and their caregiver(s) whom have been informed of the risks and benefits of CABG versus PCI with regards to periprocedural and long-term morbidity and outcome is always a sound initial approach to management. After this discussion, risk calculators including SYNTAX and STS score should be calculated for all patients, with particular attention paid to presence of absence of diabetes mellitus, degree of left ventricular dysfunction, concomitant valvular abnormalities, atrial fibrillation, aortic root dilation or presence of porcelain aorta, and arterial versus venous graft usage that may affect long-term graft patency. For higher-risk patients with complex anatomy or borderline elevated perioperative mortality, referral to a cardiothoracic surgeon or interventional cardiologist with comfort and expertise in periprocedural management of high-risk patients and lesion

subtypes (eg, chronic total occlusions, heavy calcification, bifurcation lesions) increases the likelihood of procedural success. Lastly, one must consider the location of anastomotic sites and the degree/extent of myocardium protected. If the decision is made for CABG in these stable patients, cessation of dual antiplatelet therapy is dependent on time from the most recent PCI. Newer generation stent technology has reduced the need for dual antiplatelet therapy longer than 1 to 3 months post-PCI for most patients, although this remains an active area of investigation. The preference for most cardiothoracic surgeons is discontinuation of dual antiplatelet therapy 5 to 7 days before planned surgery. Finally, medical and cardiopulmonary optimization is key before surgery. Medical optimization for congestive heart failure, moderate glucose control, and prevention of deconditioning improves periprocedural, in-hospital, and 30-day outcomes post CABG and has been extensively studied.

In conclusion, this large CABG cohort with patients from both university and community hospitals and 6 European countries reflects a growing trend in patients referred for CABG with prior PCI (20%) referred because of disease progression despite medical therapy. This study confirms earlier reports that successful prior stenting does not add to significant in-hospital/30-day mortality in patients with an intermediate SYNTAX score when subsequently undergoing isolated CABG after a minimum of 30 days after the most recent PCI. Longer-term follow-up of this and other cohorts will help to further inform future clinical decision making in this increasingly common group of patients.

Disclosures

Dr Armstrong is a consultant to Abbott Vascular, Boston Scientific, Cardiovascular Systems, Medtronic, and Philips. Dr Kahlon has no disclosures to report.

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