To bypass or stent? The changing rules of an advancing game

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Coronary artery bypass grafting surgery (CABG) and percutaneous coronary intervention (PCI) are among the most common medical procedures performed in the United States.¹ Although in the past decade, significant advances have been made in both of these procedures, and numerous studies published about them, the question of whether, and which one of these modes of coronary revascularization should be offered to any individual patient, and diabetic patients in particular, remains a matter of ongoing debate.² The relative benefit of CABG versus PCI in diabetics was first identified in the Bypass Angioplasty Revascularization Investigation (BARI) study, which showed that CABG was associated with improved 10-year survival compared with balloon angioplasty.³ In the past few years, however, many landmark studies have been published,^{4,5} prompting a 2014 update⁶ of the 2012 revascularization guidelines.⁷

The 2 major updates (Table 4 of the update article⁶) regarding PCI and CABG are: (1) the change to Class I, Level B evidence, rather than the previous Class IIa, Level B evidence, for recommendation of CABG to improve survival in patients with diabetes mellitus and multivessel disease; and (2) a new recommendation for a heart-team approach for patients with complex multivessel disease and diabetes mellitus (Class I, Level C).⁶

The major driving forces for the guideline updates are the subsequent publications of the FREEDOM (Future REvascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial, in 2012,⁴ along with the 5-year results of the SYNTAX (Synergy Between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery), trial in 2013,⁵ stratified according to diabetic status.⁸ SYNTAX, the large (n = 1800; 85 centers) trial, was the first to randomize CABG and PCI in advanced coronary disease.⁵ In addition to introducing

the SYNTAX score, that study demonstrated the important influence of coronary anatomy objectively, through comparative quantified analysis. The 5-year diabetic substudy of SYNTAX showed that CABG, relative to PCI, was associated with significantly lower major adverse cardiac and cerebrovascular events.⁸

The FREEDOM trial⁴ is the largest (n = 1900: 140 centers) randomized trial to date comparing CABG to PCI in diabetics with multivessel disease. Reported results from that study were that CABG is superior to PCI with respect to the primary outcome of all-cause mortality, non-fatal myocardial infarctions, or non-fatal stroke at 5 years, across all levels of the SYNTAX score; however, CABG was associated with a higher proportion of strokes. A recent meta-analysis showed that CABG was associated with a one-third reduction in all-cause mortality, compared with PCI in diabetics with multivessel disease.⁹

We performed a cumulative analysis (Figure 1) of the included studies in that meta-analysis^{4,8,10-15}; all-cause mortality at the longest available follow-up strongly and statistically favored CABG following the publication of FREEDOM (before FREEDOM: cumulative odds ratio [OR] 0.63, 95% confidence interval [CI], 0.35-1.12, $P = .12$; after FREEDOM: cumulative OR 0.69, 95% CI, 0.53-0.89, $P = .005$). After inclusion of the SYNTAX, United States Department of Veterans Affairs (VA),¹⁴ and MASS II (Medicine, Angioplasty, or Surgery Study) trial¹⁵ data, the revised point estimate was 0.62, with a similar CI but greater statistical significance ($Z = -3.27$, $P = .001$).

Data Supplement 6 of the 2014 update⁶ provides a table that identifies the trials that the Writing Committee considered when revising the guidelines; the table does not include the recently published VA randomized trial¹⁴ of PCI versus CABG in diabetes. A point to note is that the BARI 2D trial, which is included, is an indirect, nonrandomized comparison of PCI and CABG.¹⁶

No updates have been made with respect to unprotected left main disease.⁶ The current 2012 American guidelines⁷ recommend CABG (Class I, Level B) to improve survival. PCI is a reasonable alternative option (Class IIa, Level B) if the coronary anatomy is low risk (SYNTAX score ≤ 22) or is an ostial or trunk lesion and the risk of surgery is high. In the subanalysis of the unprotected left main disease cohort in the SYNTAX study, no differences were found in major adverse cardiac and cerebrovascular events between CABG and PCI for low and intermediate SYNTAX scores at 5 years.⁵

A recent Bayesian meta-analysis of 12 studies comparing CABG with PCI in patients with unprotected left main

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Cumulative Meta-analysis of Randomized Trials Comparing CABG versus PCI (Bare-metal and Drug-eluting stents)

FIGURE 1. Cumulative meta-analysis of all-cause mortality at the longest reported follow-up. Studies used were the Arterial Revascularization Therapies Study (ARTS I),¹⁰ the Argentine Randomized Study: Coronary Angioplasty with Stenting Versus Coronary Bypass Surgery in Patients with Multiple-Vessel Disease (ERACI II),¹¹ Stent or Surgery (SOS),¹² Coronary Artery Revascularization in Diabetes (CARDia),¹³ Future REvascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multi-vessel Disease (FREEDOM),⁴ SYnergy Between Percutaneous Coronary Intervention With TAXus and Cardiac Surgery (SYNTAX),⁸ United States Department of Veterans Affairs (VA),¹⁴ and the Medicine, Angioplasty, or Surgery Study II (MASS II).¹⁵ CABG, Coronary artery bypass grafting surgery; PCI, percutaneous coronary intervention; CI, confidence interval.

disease reported that at 1 year, mortality rates were similar following CABG and PCI¹⁷; in addition, Data Supplement 4 of the 2014 update⁶ shows a large number of studies with equivalent survival after CABG and PCI. One of the current limitations of the comparative unprotected left main disease revascularization investigations is that only a small number of studies assess long-term outcomes; current trials are underway, including the EXCEL (Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial, to assess longitudinal 5-year outcomes in unprotected left main disease patients.¹⁸

Finally, one of the main messages from the SYNTAX study is that the severity of coronary disease is an important factor in PCI, whereas patient comorbidities may be more relevant for CABG.^{5,19} Incorporation of clinical and anatomic risk scores, along with patient preference, is essential in the therapeutic decision making for any individual patient.^{2,20} Therefore, having a heart team consisting of at least one general cardiologist, an interventional cardiologist, and a cardiac surgeon is essential to provide the very best, patient-centered, evidence-based recommendation.^{2,20} These updates reflect the dynamic paradigm of coronary revascularization techniques and highlight the importance and influence of robust scientific studies.

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