

EDITORIAL

Drug-Eluting Stents or Bypass Surgery for Left Main Disease: The Impact of Diabetes Mellitus

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Comparison between percutaneous coronary interventions (PCI) and coronary artery bypass grafting (CABG) for unprotected left main (ULM) disease, particularly in the era of drug-eluting stents (DES), remains controversial. Patients with ULM disease are an important subgroup because of the amount of myocardium supplied and the potential for significant adverse outcomes associated with failure and/or complications of the revascularization strategy. Multiple randomized trials have compared PCI using DES versus CABG in these patients.¹⁻⁴ The primary end points are typically composite; hence, no 1 study was powered to detect differences in mortality alone. Nonetheless, concerns have been raised in recent publications (notably using second-generation contemporary DES), demonstrating statistically significant excess mortality (as a secondary end point) and major adverse events in the PCI arm at 5 years, respectively.^{3,4} A recent pooled analysis of all randomized trials was more reassuring, with no evidence of excess mortality up to 5 years, but with excess repeat revascularization in the PCI arm.⁵

ULM disease. The registry is large, multicenter, including consecutive patients, and extending over more than 2 decades. Since it is nonrandomized, statistical adjustments were made to account for differences in patient characteristics. At 5 years, the adjusted outcomes were no different between the 2 revascularization strategies, except for excess repeat revascularization in the PCI arm.⁶ The 10-year follow-up had the same overall conclusion, but a landmark analysis demonstrated an increase in the risk of death as well as the composite adverse event end point in the PCI arm in the later 5 years.⁷

The impact of diabetes mellitus on outcomes of PCI in patients with complex coronary artery disease has long been recognized.⁸ Even with significant reduction in rates of repeat revascularization with the use of DES, PCI for multivessel disease remained inferior to CABG in diabetic patients with multivessel disease.⁹ In this issue of the *Journal of the American Heart Association (JAHA)*, the MAIN-COMPARE investigators explore the interaction between diabetes mellitus and the revascularization method over the 10 years of follow-up.¹⁰ There was no significant difference in mortality or major adverse cardiac and cerebrovascular events between PCI and CABG in both diabetic and nondiabetic patients. Repeat procedures were lower with CABG than with PCI for both diabetic and nondiabetic cohorts. Interestingly, the authors report a significant interaction between diabetic status and bare metal stent versus CABG revascularization during the early

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The MAIN-COMPARE (MAIN Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization from Multi-Center Registry) has been a significant source of information about PCI versus CABG in patients with

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years of the registry, whereby diabetic patients had significantly lower major adverse cardiac and cerebrovascular events rates and marginally lower mortality with CABG. However, in later years, with use of DES, major adverse cardiac and cerebrovascular events and mortality after CABG or DES PCI were not significantly affected by the diabetic status.

At first glance, this is unexpected given what we know about the interaction between diabetes mellitus and PCI versus CABG outcomes. Interestingly, the observation of lack or weakness of interaction between mortality and ULM revascularization approach in diabetic patients versus nondiabetic patients has been reported in other randomized trials. A patient-level pooled analysis of >11 000 patients from 11 randomized trials comparing CABG to stenting sought to examine an adequately powered sample for 5-year mortality. Overall, with a relative preponderance of complex anatomy and multivessel disease, patients undergoing CABG had lower risk of death than those in the PCI group. However, there was no mortality benefit noted with CABG in nondiabetics with multivessel disease, or in patients with ULM disease regardless of the diabetic status.¹¹ Although the majority of ULM patients have multivessel disease as well, this analysis demonstrated that the equipoise of PCI and CABG was more apparent in those with less complex anatomy, as determined by SYNTAX scores.¹² In the subgroup analysis of the EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial, which compared CABG to DES PCI for ULM disease with low SYNTAX scores, similar observations were made. While diabetic patients met the primary end point more frequently than nondiabetics, the 3-year primary end point was similar after treatment with PCI and CABG in diabetic patients (20.7% versus 19.3%, hazard ratio: 1.03; 95% CI, 0.71–1.50; $P=0.87$).¹³ Importantly, the 10-year results of a 600-patient randomized trial using second-generation DES had similar outcomes: no significant differences in overall mortality or composite major adverse cardiac and cerebrovascular events (except for excess repeat procedures in PCI arm), no difference between PCI and CABG in the diabetic subgroup, and better outcomes of CABG in patients with ULM and multivessel disease.¹⁴

It is difficult to be certain about the plausibility of these findings. Ischemic adverse events following stenting are either related to device failure or progression of disease in other coronary segments. The difference between the interaction of DM and PCI outcomes in the bare metal and DES eras suggests a device-related mechanism. Bare metal stents were associated with considerable restenosis rates, particularly in diabetic patients, and those are more consequential in the left main trunk, given the extent of myocardium at risk. DES are associated with marked reduction in

restenosis, particularly with focal lesions and short stent length, typical of ULM lesions. Additionally, procedural outcomes have improved with intravascular imaging, increasing operator experience, and other improvements in PCI practice. A word of caution concerning interpretation of late follow-up in any study is probably warranted. Late outcomes, particularly mortality, are certainly influenced by the index procedure. However, multiple other identifiable and unidentifiable factors can influence late outcomes as well. Many aspects of clinical care change over years, whether the patient underwent CABG or PCI. For example, improved and extended antiplatelet therapy, high-potency statins, and lower blood pressure targets likely reduced disease progression in nonstented segments. Improved medical therapy and secondary prevention may, at least in part, explain similar outcomes with CABG and PCI in the DES era.

What is the take home message? The majority (\geq two thirds) of patients with ULM disease and diabetes mellitus also have significant multivessel disease, and for these patients the evidence for lower mortality with CABG is clear.^{14–16} However, for the small fraction of ULM disease patients with isolated disease or less complex multivessel disease, the findings of MAIN-COMPARE,¹⁰ and those from the extended follow-up of other randomized trials,^{11,14} indicate that these patients can be considered for DES PCI, regardless of diabetes mellitus status.

ARTICLE INFORMATION

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Disclosures

None.

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