Diabetes in Older Patients: Worse Long-term Outcomes After Coronary Interventions

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Older persons with diabetes mellitus (DM) constitute a very large high-risk subgroup of patients in whom outcomes from percutaneous coronary intervention (PCI) are less favorable than those in most patient subsets. The follow-up risk of death or an ischemic cardiovascular event that requires hospitalization is about 10-fold higher than the risk of hospitalization for major bleeding in patients with DM older than 65 years who have undergone a PCI for the next 3 years of follow-up.

My colleagues and I recently reported on a study of the long-term outcomes of older patients with DM after PCI in the Journal of the American College of Cardiology. All older patients with DM should be considered for aggressive optimization of secondary prevention therapies after PCI because the ischemic event risk remains quite high. Primary care physicians who see an older patient with DM within 3 years post-PCI should consider him or her to have a 30% to 50% absolute risk of another major ischemic event and a 3% to 5% risk of a major bleeding event. However, bleeding often is considered an act of commission from the drug therapy, where ischemic events are just considered the natural history of the disease. Perhaps informing patients who have DM and have had PCI about the relative risks of these outcomes would improve adherence and motivation to have more aggressive dual anti-platelet therapy (DAPT).

A meta-analysis of the pivotal randomized trials for drug-eluting stents (DES) versus bare-metal stents (BMS) suggested very large improvements in restenosis with DES and a trend to fewer myocardial infarctions (MIs) and deaths in the patients with DM randomly assigned to DES.1 There was thought among many cardiologists, including myself, that DES might considerably mitigate the excess hazard of DM for subsequent ischemic cardiovascular events. By leveling the playing field for patients with DM, we hoped—on the basis of the pivotal randomized trials of DES versus BMS—that the outcomes for our patients in routine practice who had DM would become more similar to those for patients who did not. However, these trials included very few older patients with DM. Also, the generalizability of the pivotal trials to an unselected population of real-world patients was not well-characterized. The pivotal trials largely treated patients who had simple lesions and relatively mild disease to keep assessment of additional revascularizations for restenosis with BMS and DES clean and straightforward. Therefore, many real-world patients with DM who had multiple lesions and diffuse disease at high likelihood of requiring multiple procedures were not enrolled.

The longer-term bleeding risk in older patients with DM committed to DAPT after DES implantation has been poorly defined. Although this group was hypothesized to be at substantially increased bleeding risk with DAPT, they also are known to be at increased risk for thrombotic cardiovascular events. The prasugrel and ticagrelor randomized controlled trials confirmed a greater relative benefit of more intensive oral DAPT in patients who had DM than in those who did not. However, the trials included few older patients and those with increased bleeding risk were excluded.2-5 We looked at data from US hospitals that were linked with Medicare inpatient claims data. We found that even with DES, the excess hazards of death, MI, and subsequent revascularizations in patients with DM adjusted for baseline risk remains substantial. The excess hazard conferred by DM, particularly DM that requires insulin treatment, is similar whether BMS or DES is implanted. Other therapies likely need to be developed or fully exploited to mitigate the excess risk of DM in these patients, such as more aggressive antiplatelet therapy for secondary prevention and perhaps, if possible, more aggressive lipid therapy.
Our study suggests that the long-term risk of major bleeding that requires hospitalization is somewhat small compared with that of death and ischemic events. Therefore, the risk-benefit tradeoff between more intensive antiplatelet therapy and bleeding appears favorable. Pending further study, and based on the efficacy and bleeding safety results from the PLATElet inhibition and patient Outcomes (PLATO) and TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitorN with Prasugrel-Thrombolysis In Myocardial Infarction trials in patients with DM, I would strongly consider ticagrelor or prasugrel in patients who have DM with acute coronary syndrome (ACS) undergoing PCI based on the bleeding rates versus ischemic event rates we observed in this unselected, real-world population.

When referring a patient with DM for catheterization, electively or for ACS, the primary care physician should weigh in on his risk of outpatient bleeding, based on the known comorbidities. An acceptable bleeding risk—my definition would be less than 5% risk of a major bleed in 2 years—supports a more aggressive antiplatelet therapy approach at the time of PCI and in at least early follow-up.

Ticagrelor demonstrated a mortality benefit in the PLATO trial. Given the recent results of the randomized Future REvascularization Evaluation in patients with Diabetes mellitus: optimal management of Multivessel disease trial of multivessel DES PCI versus coronary artery bypass graft (CABG) in patients with DM, support of CABG in these patients, when feasible, is encouraged. When CABG is not feasible technically or because of unacceptable comorbidities for surgery, encourage DES in patients who have insulin-dependent DM.

References

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