Screening, Diagnosis, and Management of CAD in Asymptomatic Diabetic Patients*

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Type 1 and type 2 diabetes mellitus (DM) have been long-recognized coronary atherosclerosis risk factors and independent predictors of myocardial infarction, stroke, and cardiovascular death, as well as a leading cause of retinal disease, nephropathy, and neuropathy. Accordingly DM has been prominently positioned as a “super risk factor” or coronary heart disease risk equivalent in many position papers and guidelines (1). Despite these statements, screening for coronary artery disease (CAD) and the management of asymptomatic disease once it is detected remain controversial (2,3). In this issue of JACC, Zellweger et al. (4) present the main findings of the BARDOT (Basel, Asymptomatic high-Risk Diabetics’ Outcome Trial). Among those with type 2 DM and no prior history of CAD, the yield of screening with stress nuclear scintigraphy was 22%, which is comparable to the screening for chronic kidney disease in the same population (5). Those with initially asymptomatic CAD eventually developed more major adverse cardiac events (MACE) (cardiac death, myocardial infarction [MI], and symptom-driven revascularization), and evidence of permanent myocardial damage (scar) than those without. Importantly, the majority of MACE events were not revascularization procedures, but natural history events including MI and death. Although there was an attempt to randomize patients in a pilot trial identified at screening (n = 82) and explore the benefit of invasive revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery) versus conservative medical therapy, there was insufficient observed power (36%) to detect meaningful differences in MACE between these 2 approaches; however, those treated conservatively had significantly higher rates of new ischemia or evidence of fixed defects on follow-up nuclear scintigraphy that those who underwent revascularization. Thus, these data indicate that there were 2 opportunities to screen and detect disease in BARDOT, at the time of initial enrollment and then in follow-up as depicted in Figure 1. Thus, this type of approach would suggest that intervention could ultimately reduce the risk of new heart failure and downstream complications if broadly applied in the population. In BARDOT, those treated conservatively had considerably lower rates of antiplatelet agents and statins prescribed; hence, there appears to be an opportunity to optimize medical therapy in those with normal nuclear stress tests. What the BARDOT trial has taught us is that in the modern era of multidrug DM treatment and risk factor control in asymptomatic patients, screening for significant CAD has a high yield and those found to have disease have event rates (approximately 10%) similar to those with asymptomatic CAD who would have come to attention for revascularization.

As revascularization outcomes continue to improve and become more durable with improved PCI and surgical techniques, it is conceivable that routine screening and management guidelines will be developed for those with DM (6). Results from BARDOT suggest waiting for symptomatic events will lead to more irreversible myocardial disease (Figure 1) and likely heighten the future risk of complications with revascularization, the development of heart failure, and cardiovascular death. Although optimal medical therapy is powerful in reducing the risk of binary MACE events and slowing the progression of atherosclerosis, multiple drugs

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need to be used in the same patient and high rates of many drug classes are needed in populations to balance the risk-benefit equation (7,8). We believe the door is open for research in patients with DM for the detection and optimal management of asymptomatic CAD, in which mechanical revascularization is likely to have a prominent role even in those with the best medical therapy in reducing irreversible cardiac events.

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