Screening for Asymptomatic Coronary Artery Disease With Myocardial Perfusion Imaging Does Not Reduce Cardiovascular Events in Middle-Aged and Older Patients With Diabetes

Reviewed by Michael Pignone, MD, MPH

STUDY

Young LH, Wackers FJ, Chyun DA, Davey JA, Barrett EJ, Taillefer R, Heller GV, Iskandrian AE, Wittlin SD, Filipchuk N, Ratner RE, Inzucchi SE; DIAD Investigators: Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized, controlled trial. *JAMA* 301:1547–1555, 2009

SUMMARY

Design. A multicenter, randomized trial.

Subjects. The study included 1,123 adults ages 50–75 years with type 2 diabetes and no history of symptomatic coronary heart disease (CHD). Mean age was 60 years, 23% were of self-reported non-white race, and just over half were men. The mean LDL cholesterol level was 114 mg/dl and mean systolic blood pressure was 132 mmHg, and 10% of subjects were current smokers. Just fewer than half of participants were taking lipid-lowering medication, a similar proportion were taking aspirin, and just more than 20% were using insulin.

Methods. Eligible participants were randomly assigned to either receive screening with adenosine-stress radionuclide myocardial perfusion imaging (MPI) or receive no screening. The stress MPI tests were reviewed locally by nuclear cardiologists, and their results were provided to the participants and their physicians. MPI tests were also evaluated separately by an independent expert panel, with quantification of the size of the perfusion abnormality and identification of nonperfusion abnormalities. Further testing and treatment decisions were made by the participants' physicians and were not dictated by trial protocol. The primary endpoint was the incidence of nonfatal myocardial infarction (MI) and cardiac death. Analysis was on an intention-to-treat basis.

Results. During a mean of 4.8 years of follow-up, the cumulative incidence of nonfatal MI and cardiac death was 2.7% in the screening group and 3.0% in the control group (hazard ratio [HR] 0.88, 95% CI 0.44–1.88) Among those in the screened group, incidence was lower for those with no (n = 400) or small (n = 50) perfusion defects compared with the 33 participants with moderate or large defects (2 vs. 12.1%, HR 6.3, 95% CI 1.9–20.1). Utilization of effective treatments such as statins and antihypertensive medications increased during the trial but did not differ between screening and no-screening groups. Similarly, use of cardiac catheterization or revascularization, although initially higher in the screened group, did not differ between groups during the entire study.

Conclusions. Screening with MPI did not reduce CHD events in this population of patients with diabetes, but the relatively low-risk nature of the trial participants limits definitive conclusions about its effects.

COMMENTARY

CHD is an important cause of morbidity and mortality in adults, particularly those with diabetes. CHD events, including angina, MI, and sudden cardiac death, can be predicted with multivariate risk equations that incorporate age, sex, blood pressure, lipid levels, smoking status, and the presence of diabetes or glucose levels. These risk predictions can be used to guide decisions about preventive therapies.

The most common risk prediction equations for U.S. populations are derived from the Framingham Heart Study and have been shown to have relatively good accuracy overall, although their performance in patients with diabetes is somewhat limited by their use of a crude measure (presence or absence of diabetes) and the relatively small number of people with diabetes included in the cohort from which these risk equations were derived.[1,2]

Because middle-aged and older patients with diabetes generally have high risks of CHD events, some

experts have suggested that all adults with diabetes be considered at high risk and treated accordingly.[3] Some have suggested that more aggressive screening is warranted in diabetes to better detect high-risk patients and treat them even more aggressively.[4] Potential additional screening tests include computed tomography scanning for coronary calcium, exercise or pharmacological stress imaging, and carotid ultrasound examination. Such tests have been shown to be associated with higher event rates, even after controlling for standard risk factors, but their effect on treatment decision making and actual CHD outcomes has not been well studied, and more recent recommendations have called for more research.[5]

In that context, the Detection of Ischemia in Asymptomatic Diabetics (DIAD) trial was designed to examine the effects of routine screening with MPI for adults with diabetes ages 50–75 years and no history of symptomatic coronary disease. The design of the trial was well suited to address whether routine screening itself would change outcomes. There was little loss to follow-up, and a high proportion of participants in the screening arm received the MPI test. During the course of the study, a relatively large proportion (30%) of control group members received a similar type of test, but this should not be considered a flaw because it reflects the correct comparison (routine screening vs. testing as clinically warranted).

The observed CHD event rate among participants was quite a bit lower than anticipated in the design of the trial (0.6% per year, compared with an expected rate of 1–2% per year). As a result, the main estimate of effect in the trial had a very wide confidence interval (0.44–1.88) that did not allow for a conclusion with confidence that the intervention produced net benefit, net harm, or no net effect.

The 12% of participants with moderate or large perfusion defects had higher event rates (2.4% per year) compared with participants with small or no defects, who had low event rates (0.4% per year). Whether the stratification of risk achieved with stress MPI produces sufficient benefit to justify its costs depends on how the information is used for treatment decision making and whether the differences in treatment produce more benefit than harm.

Several factors make it difficult to demonstrate benefit from screening. First, the threshold for prescribing many effective therapies, including statins and antihypertensive medication, is being pushed lower as better information emerges about treatment efficacy and safety and costs decrease with availability of generic versions of key medications.[6] In that sense, further stratification of risk will not change the decision about treatment because it is warranted even in quite low-risk (0.5% per year) patients. Second, it is unclear whether further testing with cardiac catheterization and revascularization produces any benefit among those found to have abnormal screening tests. Although this question has not been definitively answered, available evidence suggests that large benefits are unlikely. Finally, the results of DIAD suggest that, in practice, providers and patients do not make substantially different decisions about treatment in the face of MPI results compared to when no such screening tests are available.

Given these factors and the high cost of MPI screening, it is unlikely that routine use of such tests represents a good allocation of resources and effort for CHD prevention. Working to improve treatment and adherence to proven effective therapies for patients at moderate or high risk based on standard risk assessment should remain the primary focus for CHD prevention efforts at this time.

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