Not all diabetics are created equal (in cardiovascular risk)

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This editorial refers to ‘Coronary calcium measurement improves prediction of cardiovascular events in asymptomatic patients with type 2 diabetes: the PREDICT study,’1 by R.S. Elkeles et al., on page 2244

Current guidelines continue to recommend all persons with diabetes be considered at high risk and treated accordingly. For example, National Cholesterol Education Panel Guidelines state ‘Persons with type 2 diabetes should be managed as a coronary heart disease (CHD) risk equivalent. Treatment for low density lipoprotein (LDL) cholesterol should follow Adult Treatment Panel III recommendations for persons with established CHD.’2 This remains an important tenet, as up to 80% of persons with diabetes will suffer a cardiovascular event. This has led some to conclude that further risk stratification in persons with diabetes is neither warranted nor useful.

However, persons with diabetes are not all at equal risk. The data from PREDICT,2 as well as previous coronary artery calcium (CAC) studies, demonstrate that persons with diabetes will have widely varied cardiovascular risk. While many persons with diabetes do have increased cardiovascular risk compared with the general population, there is a defined subset who have a very low cardiovascular risk and an equally large subset who are at extremely high risk. These groups cannot be discerned on the basis of HbA1c levels, duration of diabetes, age, gender or cardiovascular risk factors. Clearly, coronary calcium scanning (CCS) is not only becoming widely accepted in intermediate risk patients, such as those with several cardiovascular risk factors3,4 but data continue to accumulate indicating that presumed high-risk patients may actually benefit from further risk stratification. Increasing evidence that lower LDL-cholesterol values are warranted in persons with extremely high cardiovascular risk (with targets proposed as low as 1.8 mmol/L or 70 mg/dL). Despite this, there will be times when clinicians may need evidence to decide which patients warrant the highest doses of lipid-lowering therapy (some require dual or triple cholesterol-lowering therapies) to achieve these targets. Identifying diabetic persons with 10-, 20- or 30-fold increased risk of cardiovascular events will be important to justify these therapies to both the clinician and patient.

Evidence from the study by Elkeles et al.2 demonstrates that a simple, 5-min non-invasive, low-radiation test can potentially identify these patients at markedly increased cardiovascular risk. This study is not unique. It is one of many accumulating studies in this cohort that demonstrate this increased risk with increasing CAC scores (representing increasing atherosclerotic burden). Earlier data from Raggi et al.5 and Anand et al.6 demonstrated that persons with diabetes are up to 58 times more likely to suffer a cardiovascular event with high scores (>1000) than those without coronary calcium detected on a CT scan. This is highly consistent with larger studies including persons with and without diabetes.7 Large prospective studies of CCS are demonstrating marked improvement in cardiovascular risk prediction compared with Framingham or other risk stratification tools. Uniform findings between the study by Elkeles et al.2 (in a diabetic cohort) and Detrano et al.8 (from a 6814-person NIH-sponsored population-based study) support more widespread application of this test in persons at intermediate (and perhaps high) perceived cardiovascular risk. Further data are emerging from prospective cohorts in Germany9 and Rotterdam10 that further clarify the potential use of this test in more diverse, population-based groups.

However, caution must be applied in the widespread application of such testing. Cost–effectiveness algorithms are just starting to be published, and the potential benefit of the increased knowledge provided by the test must be weighed against the radiation dose (albeit small for a calcium score only, unlike CT angiography, where doses can be 10-fold higher). Previous guidelines have suggested that these high-risk groups should not undergo calcium scoring; however, compelling data from these studies are likely to add to the impetus to update these recommendations.

If cost–effectiveness can be established, this would make it appealing to derive LDL targets based upon something more objective, such as a measure of the atherosclerosis burden. When clinical trial data are combined, including the Treating to

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New Targets (TNT) and Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) studies, maximal LDL lowering can be calculated to reduce cardiovascular events by 45–50%. Moreover, epidemiological studies imply that prolonged LDL lowering in primary prevention will reduce the risk even more.11 Overall, the study by Elkeles et al.12 adds important additional information to strengthen their conclusion that ‘Measurement of CACS is a powerful predictor of cardiovascular events in asymptomatic patients with type 2 diabetes and can further enhance prediction provided by established risk models.’

Thus, consideration for testing should be used in at least three diabetic subgroups that have been identified previously as targets for advanced risk stratification with cardiac CT.17 These include patients with type 1 diabetes (up to 50% of whom will be identified as being at low risk based on a negative calcium scan (score = 0)); non-compliant patients (as several studies have demonstrated improved adherence with visualization of CAC)13,14, and younger diabetic patients (choosing a starting age for lipid-lowering and ACE inhibitor therapy is often arbitrary, and some younger patients may benefit from statin therapy). Identification of early plaque should allow better cardiovascular outcomes, as there are now robust therapies to treat patients identified as being at high risk. Furthermore, cost savings related to less pharmaceutical use for those found with no CAC (very low risk of cardiovascular short-term events) should outweigh the cost of testing these populations.

Widespread use of CCS in persons at high risk (including those with diabetes) is not warranted, as widespread use of CCS will increase costs and may identify only a subset of patients who need increased therapies. A basic tenet that applies to all diagnostic testing must be applied to CCS as well: that a test should alter the treatment of the patient. If patients are already being treated aggressively, there is probably little or nothing to be gained by CCS testing. Alternatively, if the patient or physician is reluctant to treat a given diabetic patient maximally, then testing may help clarify the need (or lack thereof) of lipid-lowering therapy. Simply, this test will be useful for those for whom decisions concerning prevention strategies may be altered on the basis of the test results.

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**References**


