Coronary Calcium Tells a Tale

Diabetes *from page 1*

were free of cardiovascular disease at baseline. Most of the participants also underwent a coronary CT examination and had a complete risk factor assessment at baseline.

The new analysis focused on 881 people in MESA diagnosed with diabetes at baseline based on a fasting glucose level of 126 mg/dL or higher; 1,686 people diagnosed with metabolic syndrome at baseline based on the criteria of the National Heart, Lung, and Blood Institute; and 4,036 people with neither diagnosis. All 6,603 of these people underwent a baseline coronary CT examination to produce a CAC score. Follow-up tracked their incidence of coronary heart disease events over an average of 4.6 years. The mean age was 62 years; slightly more than half were women. About 40% were white and 28% were African American.

Baseline CAC scores showed that among the people with diabetes, 39% had no coronary calcium, 27% had mild coronary disease (CAC score of 1-99), 14% had moderate disease (CAC score of 100-399), and 21% had significant disease (CAC score of at least 400).

Among the individuals with metabolic syndrome and the people who had neither diagnosis, the percentages with no coronary calcium were higher, and the percentages with significant coronary disease were lower, but in general the CAC scores were similar in all three subgroups, Dr. Malik reported.

During follow-up, coronary events occurred in 33 people in the diabetes group, 43 in the metabolic syndrome group, and 52 in the people without either diagnosis. Calculation of the 10-year event rate within each of these three subgroups showed roughly similar rates within each CAC score category, especially among those with a CAC score of zero. (See box.)

"Many people with metabolic syndrome or diabetes have as low a risk as people without these conditions when their CAC score is minimal or absent," Dr. Malik said.

She called for confirmation of these findings in people followed for longer periods of time. ■

VITALS

Major finding: On CT examination, coronary artery calcium scores appeared similar in patients with diabetes, metabolic syndrome, and neither disease.

Source of data: The findings are based on a new analysis of data from the Multi-Ethnic Study of Atherosclerosis (MESA), which enrolled more than 6,800 people aged 45-84 who were free of cardiovascular disease at baseline. The new analysis focused on coronary CT exams involving those people with diabetes, metabolic syndrome, or neither disease at baseline.

Disclosures: Dr. Malik had no financial disclosures. One of her coauthors is a consultant for GE, and another associate is on the speakers bureau for Takeda.

Coronary Calcium Stratifies Coronary Event Risk

Baseline coronary calcium score	With diabetes (n = 881)		With metabolic syndrome (n = 1,686)		With neither diabetes nor metabolic syndrome (n = 4,036)	
	Patients with CAC score	10-year CER	Patients with CAC score	10-year CER	Patients with CAC score	10-year CER
0	39%	2.0%	46%	0.8%	56%	0.6%
1-99	27%	8.8%	28%	5.5%	24%	3.5%
100-399	14%	14.5%	13%	12.5%	10%	6.3%
400 or more	21%	16.9%	13%	15.8%	10%	11.3%

Note: Data from average 4.6-year follow-up of patients in the Multi-Ethnic Study of Atherosclerosis.
Source: Dr. Malik

ADVANCE Yields More Data on Heart Risk in Diabetes

BY MIRIAM E. TUCKER

MONTREAL — The largest-ever clinical trial in patients with type 2 diabetes is continuing to yield data that are expected to lead to improved prediction of cardiovascular risk in people with diabetes, as well as a better understanding of the relationship between intensive metabolic control and cardiovascular outcomes.

In a symposium lecture at the World Diabetes Congress, Dr. John P. Chalmers summarized data from published and unpublished substudies of the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) study, a randomized, placebo-controlled trial that examined the effect of both intensive blood glucose and blood pressure control on micro- and macrovascular complications. The trial included a multiethnic cohort of 11,140 patients with type 2 diabetes from 215 centers in 20 countries.

The glucose-lowering arm of ADVANCE, funded by grants from the French pharmaceutical company Servier and the National Health and Medical Research Council of Australia, used modified-release gliclazide along with other glucose-lowering drugs to target a hemoglobin A_{1c} of 6.5%.

The intensive-treatment group achieved a mean HbA_{1c} of 6.5%, compared with 7.3% in the standard-treatment group. At a median of 5 years, the intensive group had a 10% relative reduction in the combined outcome of major macro- and microvascular events compared with standard care, primarily as a consequence of a 21% relative reduction in nephropathy. There was a positive trend toward reduction of major cardiovascular events (N. Engl. J. Med. 2008; 358:2560-72).

There was no excess mortality, weight gain, or severe hypoglycemic episodes in the intensive group, said Dr. Chalmers, co–principal investigator for ADVANCE.

In the blood pressure control arm, routine administration of a fixed combination of perindopril and indapamide to patients with type 2 diabetes was associated with a 9% reduction in the relative risk of a major macro- or microvascular event (Lancet 2007; 370:829-40).

In a new, not-yet-published subgroup analysis of the glucose-lowering arm, the results held true regardless of age, duration of diabetes, sex, body mass index, HbA_{1c} at study entry, urinary albumin excretion, glomerular filtration rate, or initial glucose-lowering treatment, said Dr. Chalmers, senior director of the George Institute for International Health, Sydney, and emeritus professor of medicine at the University of Sydney and Flinders University, Adelaide, Australia.

Cognitive function, however, was an independent predictor of cardiovascular risk. Both mild and severe cognitive dysfunction, as measured at baseline by the Mini Mental State Examination, increased the risk for major cardiovascular events with hazard ratios of 1.27 and 1.42, respectively. Cardiovascular death was increased by hazard ratios of 1.41 and 1.56 for mild and severe cognitive dysfunction, respectively, and all-cause death by 1.33 and 1.50 (Diabetologia 2009;52:2328-36).

Another new and unpublished analysis showed that the risk for microvascular complications had a strong linear relationship with HbA_{1c} values all the way down to 6.0%, with each percentage point reduction reducing the risk by 22%. For macrovascular events, cardiovascular death, and all-cause death, the risk reduction was linear down to an HbA_{1c} of 7.0%, then leveled off between 7% and 6%.

A substudy of 647 participants showed no significant associations between cardiovascular risk and body mass index, but there was a relationship with waist-hip ratio, a better index of visceral fat. Urinary albumin excretion also predicted risk: For every 10-fold increase, there was a 2-fold increase in macrovascular events. Similarly, a halving of glomerular filtration rate was associated with a twofold increased risk for cardiovascular events, Dr. Chalmers said.

Using ADVANCE data regarding predictors of cardiovascular risk, the investigators are working to develop a risk engine that is specific for people with diabetes. Data from two other studies presented at the congress showed that neither Framingham score nor the risk engine derived from the 1998 United Kingdom Prospective Diabetes Study (UKPDS) is an accurate risk predictor for patients receiving modern treatments for glucose, blood pressure, and lipid levels.

Dr. Andre Pascal Kengne, also of the George Institute, presented one of these studies, which found that major cardiovascular risk among 7,502 ADVANCE participants was overestimated by 170% and 202% using two different Framingham equations. Another study, from Greek investigators, also found that Framingham and UKPDS scores overestimated the cardiovascular risk in type 2 diabetes patients receiving modern treatment.

Dr. Kengne also presented a separate paper on the predictive value of a risk engine using the independent predictors age at diagnosis, known duration of diabetes, sex, pulse pressure, treated hypertension, atrial fibrillation, retinopathy, HbA_{1c}, albumin/creatinine ratio, and non-HDL cholesterol level at baseline. Based on a cutoff for a 4-year predicted risk of 8% and above (equivalent to 10-year predicted risk of 20% and above), it was possible to reliably identify the 21% of 473 ADVANCE participants in whom 46% of all major cardiovascular disease was recorded during the follow-up period.

External validation will be needed to demonstrate the tool's potential for widespread clinical use, Dr. Kengne said.

Dr. Chalmers also discussed those findings in his presentation. "We have a plan in which an individual clinician can plug in the data and get a risk prediction score. This is potentially very useful. The next step is to validate the data in populations other than ADVANCE. We have plans to do that in two or three populations in different parts of the world."

The ADVANCE investigators are now embarking on the ADVANCE-ON trial, in which the study participants will be observed for 5 years post study in their usual care settings. Primary outcomes will be death from any cause and major macrovascular events.

Dr. Chalmers is on the advisory board for Servier. Dr. Kengne stated that he had no conflicts of interest. ■