

Strong Relationship Found Between Retinopathy, Coronary Atherosclerosis

Patients enrolled in the Veterans Affairs Diabetes Trial were evaluated.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

Although atherosclerosis and retinopathy are generally considered unrelated conditions, increasing evidence suggests that there may be shared risk factors and/or mechanisms contributing to both complications, according to Peter D. Reaven, MD.¹

"Few studies have been able to directly compare the extent of atherosclerosis with categories of retinopathy," he said during a presentation at the American Diabetes Association's 67th Scientific Sessions in Chicago. Dr. Reaven is Associate Professor of Clinical Medicine at the University of Arizona College of Medicine and Director, Diabetes Program at the Carl T. Hayden VA Medical Center in Phoenix.

To compare the extent of atherosclerosis with categories of retinopathy, Dr. Reaven and colleagues assessed the cross-sectional association between retinopathy and atherosclerosis as measured by computed tomography (CT)-detectable coronary artery calcium (CAC) in a subgroup of patients with type 2 diabetes. The patients were enrolled in the Veterans Affairs Diabetes Trial (VADT) (see *VADT at a Glance*). Retinopathy was assessed by seven-field stereo fundus photography, and the photos were centrally read at the University of Wisconsin.

A total of 211 patients (95% of whom were male), with a mean age of 62.1 ±9.2 years, a mean type 2 diabetes duration of 12.5 ±8.5 years, and A1C levels 9.2 ±1.4% were included.

VADT AT A GLANCE

- The VADT is a multisite long-term study examining the effect of glucose control on cardiovascular complications in older patients with established, poorly controlled type 2 diabetes.
- The main objective of the 20-site, 1,792-patient study is to ascertain whether intensive glucose control can reduce major cardiovascular events in patients with difficult-to-control type 2 diabetes. The VADT cohort includes about 20% Hispanics and 20% African Americans.
- The study design consists of a standard treatment arm and an intensive treatment arm, with a goal of 1.5% difference in A1C values between the two groups. The trial is now in its sixth year, with completion expected in May 2008.
- The current results of the trial show that excellent control of glucose and cardiovascular risk factors can be achieved and maintained in this population. The results of these interventions on cardiovascular outcomes will ultimately have important implications for the clinical care of older patients with advanced type 2 diabetes.

Source: *Endocr Pract.* 2006 Jan-Feb;12 Suppl 1:85-88.

CAC AND AGATSTON SCORE

The amount of CAC is usually expressed as an Agatston score, which is based on the area and the density of the calcified plaques.

A test is considered to be positive if calcification is detected within the coronary arteries. Absolute Agatston scores of <10, 11 to 99, 100 to 400, and >400 have been proposed to categorize individuals into groups having minimal, moderate, increased, or extensive amounts of calcification, respectively. The amount of calcification can give, to some extent, an indication of the overall amount of atherosclerosis.

It is well established that individuals with Agatston scores >400 have an increased occurrence of coronary procedures within 2 to 5 years after the test. Individuals with very high Agatston scores (>1,000) have a 20% chance of suffering a myocardial infarction or cardiac death within 1 year.

A test is considered to be negative if no calcifications are detectable within the coronary arteries. Although this does not absolutely exclude the presence of atherosclerotic deposits within the coronary arteries, it does indicate that there is nothing more than minimal atherosclerosis, and the risk of a coronary event over the next 2 to 5 years is very low. The likelihood that a significant coronary artery narrowing is present is also very low.

Although there is little controversy that Agatston scores can provide information on the risk of future events, there is considerable debate as to whether the Agatston score provides predictive information beyond that obtained from traditional risk factors.

The American Heart Association and the American College of Cardiology provide guidelines for testing for CAC that are updated yearly and are available online at www.ahajournals.org/misc/sci-stmts_topindex.shtml. These guidelines currently suggest that screening for calcification may be of value for an individual who is considered to be at intermediate 10-year risk, which is defined as a 10% to 20% likelihood of a cardiac event within the next 10 years.

Source: <http://circ.ahajournals.org/cgi/content/full/108/8/e50>.

The investigators found that retinopathy correlated with CAC—both by absolute score ($r=0.18$, $P=.008$) and by categories of retinopathy. “The median CAC, measured by Agatston score, increased across retinopathy categories,” Dr. Reaven said (see *CAC and Agatston Score*).

Among patients with no retinopathy, the median CAC score was 197; for patients with microaneurisms only, it was 262; for those with mild nonproliferative diabetic retinopathy (NPDR), 364; for moderate-to-severe NPDR, 300; and for patients with proliferative retinopathy (PDR), 981.

The authors found a 3.2-fold increase in coronary artery calcification if proliferative diabetic retinopathy was present.

According to the abstract, investigators performed a multivariable linear regression analysis with forward and backward elimination to find a parsimonious subset of risk factors to include with PDR in predicting CAC. Dr. Reaven and his colleagues found that after adjustment for age, HDL cholesterol, insulin use, prior cardiovascular event, prior coronary revascularization, and ethnicity-race, PDR was significantly ($P=.04$) associated with the \log_{10} of CAC+1. This

indicated a 3.2-fold increase in CAC if PDR was present.

Although hypertension history, baseline blood pressure, A1C, diabetes duration were also candidate variables in the multivariable modeling, they were not significant, the investigators found. “Moreover, using logistic regression, individuals with PDR were approximately sixfold more likely to have CAC >400—a clinically relevant high-risk group—compared with those with no PDR,” Dr. Reaven said. “This was even after adjustment for other cardiovascular disease [CVD] risk factors.”

These data indicate a “surprisingly strong” relationship between retinopathy and the extent of coronary atherosclerosis as indicated by CAC, he added. “The data suggest (1) that identifying type 2 diabetes patients with PDR may predict those who are at uniquely high risk for clinical CVD, and (2) the potential to identify and treat shared risk factors for these common micro- and macrovascular complications.” ■

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1. Reaven PD, Moritz T, Emanuele N, et al. Proliferative diabetic retinopathy is strongly related to coronary artery calcium in the Veterans Affairs Diabetes Trial (VADT). #0268. Presented at the American Diabetes Association's 67th Scientific Sessions. June 22-26, 2007. Chicago.