Four Criteria for Assessing CVD Risk Identified

BY MITCHEL L. ZOLER

FROM THE ANNUAL CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY

STOCKHOLM — Four simple clinical conditions play the biggest role in risk-stratifying outpatients with stable atherothrombotic disease, based on a 45,000-patient, international registry followed for 4 years.

Polyvascular disease heads the list of four factors, followed by history of an ischemic event within the past year, history of an ischemic event at any time, and diabetes, Dr. Deepak L. Bhatt said at the congress. The registry results notably showed polyvascular disease to pose the strongest risk for a subsequent ischemic event, and placed diabetes below the risk from a prior ischemic event, a finding that further dislodges diabetes from its perch as a myocardial infarction risk equivalent, said Dr. Bhatt, chief of cardiology at the VA Boston Healthcare System.

"It's an important point, but unfortunately the myth lingers on" that diabetes is a myocardial infarction risk equivalent, he said. It is a myth Dr. Bhatt dates to studies reported more than a decade ago.

In the more contemporary database studied by Dr. Bhatt and his associates, with patients followed from 2003 to 2008, patients with diabetes may have been better managed. "It's not that diabetes is not an important risk factor, but a prior ischemic event trumps diabetes," he said in an interview. The new analysis shows "only a myocardial infarction is a myocardial infarction risk equivalent."

The 4-year results from the Reduction of Atherothrombosis for Continued Health (REACH) registry also added new evidence on the role of polyvascular disease, the study's "most potent predictor of future ischemic events. REACH is the largest and longest registry" to show a strong polyvascular effect, a risk factor that until now has been underappreciated, Dr. Bhatt said.

"A patient with angina and claudication [ischemic disease in two vascular beds] may look stable, but the message from these data is that these patients are at exceedingly high risk for something bad happening over the next 4 years," and so need even tighter medical control of lipids, blood pressure, and other treatable risks.

Dr. Bhatt and his associates are in the final stages of refining a secondary-prevention risk model, a formula to mathematically stratify patients' risk based on the new REACH analysis. While the model isn't ready for release yet, it is based on the four major risk factors he reported. Until now, "there really hasn't been any major attempt to risk-stratify secondary prevention patients, in part because many physicians seem to feel that the risk faced by all secondary-prevention patients is the same. "These data show that's not true. There is a wide range of risk in this population, and risk stratification is called for." Higher-risk patients could receive, for example, intensive case management by a nurse, or may be candidates for expensive, new antiatherosclerotic, anti-inflammatory, or antithrombotic therapies, with some nearing the market. "I don't think we can afford to use [new, expensive treatments] on all patients. This analysis helps identify patients at the highest risk" who make good candidates for efficacy studies.

Polyvascular disease at baseline linked with a twofold increased risk for an ischemic event during follow-up.

DR. BHATT

The REACH registry initially enrolled more than 68,000 people at 5,587 centers in 44 countries during 2003 and 2004. Reports on the baseline and 1-year follow-up data appeared several years ago (JAMA 2006;295:180-9, and JAMA 2007;297:1197-206).The new analysis used data collected after 4 years' follow-up from 45,227 of the participants.

The database included 21,890 patients with a prior ischemic event (myocardial infarction or stroke) at the time of enrollment into the registry. Another 15,264 patients entered based on having symptomatic, stable atherosclerosis but no event history. The final 8,073 participants had no documented disease but at least three risk factors off this list: current treatment for diabetes, diabetic retinopathy, an ankle-brachial index below 0.9, asymptomatic carotid stenosis with at least 70% occlusion, carotid intima media thickness at least twice that at adjacent sites, systolic blood pressure of at least 150 mm Hg, hypercholesterolemia, current smoker, age 65 or older in men, and age 70 or older in women.

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Major Finding: Four-year follow-up of a large, atherothrombotic disease database found four factors that strongly determine risk for new ischemic events: polyvascular disease, ischemic event within the past year, any history of an ischemic event, and current treatment for diabetes.

Data Source: The REACH registry, which enrolled in 44 countries and tracked ischemic events in 45,227 patients with established atherothrombotic disease or multiple risk factors for 4 years during 2003-2008.

Disclosures: REACH is partially sponsored by Sanofi-Aventis and Bristol-Myers Squibb. Dr. Bhatt reported receiving research grants from AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Heartscape, Sanofi-Aventis, and the Medicines Company.

The average age of the enrollees at baseline was 68; two-thirds were men. Nearly half had a prior ischemic event, 44% had a history of diabetes, 28% had an ischemic event during the prior year, and 16% had polyvascular disease, defined as atherosclerotic disease in at least two vascular beds: coronary, cerebrovascular, or peripheral. During follow-up, the participants had 5,481 events—cardiovascular death, myocardial infarction, or stroke.

In a multivariable regression model, polyvascular disease at baseline linked with a twofold increased risk for an ischemic event during follow-up, compared with enrollees with no history of clinical cardiovascular events but with markers that placed them at risk, such as hypertension or hypercholesterolemia. Patients with a history of a recent ischemic event had a 70% higher risk for a follow-up event compared with enrollees without an event history. Patients with diabetes at enrollment had a 44% increased risk for a follow-up event compared with participants without diabetes, which did match the increased risk from an older ischemic event. Heart failure also appeared as a strong risk factor. "Our analysis provides simple criteria for assessing the risk of cardiovascular events in stable outpatients," Dr. Bhatt said. ■

Concurrently with Dr. Bhatt's report, the results were published online (JAMA 2010 Aug. 30 [doi: 10.1001/jama.2010.1322]).

Y-Chromosome Variant May Raise Risk of Heart Disease

BY BRUCE JANCIN

FROM THE ANNUAL CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY

STOCKHOLM — Genetic variation in the Y chromosome constitutes a novel, potent, independent risk factor for coronary artery disease that could help explain the male disadvantage in heart disease.

Among British men, carriage of one of the I-haplogroup variants of the Y chromosome confers a 55% increased risk of coronary heart disease after traditional risk factors, including blood pressure, lipids, and smoking, were controlled for, Dr. Nilesh J. Samani reported at the congress.

That's a whopping contribution to cardiovascular risk. By comparison, each of the standard risk factors confers a risk more in the 10%-20% range, observed Dr. Samani of the University of Leicester (England).

He explained that not all Y chromosomes are the same. Genetic variation evolves far more slowly in the Y chromosome than in other chromosomes because it does not recombine during reproduction. The Y chromosome is passed on from father to son intact.

The I-haplogroup is thought to have been introduced into Europe by the Gravettian culture, which migrated from the Middle East about 25,000 years ago. The I-haplogroup is carried by about 15% of British men. However, the prevalence exceeds 60% among men in parts of Scandinavia and Eastern Europe.

To test the hypothesis that genetic variation in the Y chromosome influences cardiovascular risk, Dr. Samani and his coworkers turned first to the British Heart Foundation Family Heart Study. In a cross-sectional sample that comprised 811 men with CAD and 633 controls, the investigators showed that the I-haplogroup was associated with a 67% increased relative risk of CAD, compared with men whose Y chromosome did not contain the I-haplogroup.

For confirmation, the investigators went to the database of the West of Scotland Primary Coronary Prevention Study (WOSCOPS), one of the landmark early randomized trials of statins for primary prevention. Among 1,542 genotyped male participants followed prospectively for 4.9 years, 484 developed CAD. Men who carried the I-haplogroup on their Y chromosome had a 50% increased risk of CAD during the follow-up period.

Carriage of one of the I-haplogroup variants of the Y chromosome raised coronary heart disease risk by 55%.

DR. SAMANI

When the data from the two studies were combined, results yielded a total of 2,986 men, 1,295 of whom developed CAD. Those in the I-haplotype group had a 55% greater risk of CAD, compared with the others after conventional cardiovascular risk factors were controlled for.

The specific genes involved in the increased CAD risk associated with the I-haplotype have not yet been identified. Dr. Samani and his coworkers are working on that via ongoing studies of gene expression in cells isolated from men with different Y chromosome haplogroups.

Dr. Samani speculated that the varied prevalence of the I-haplogroup across Europe might help account for the widely variable rates of CAD on the continent. The prevalence of the I-haplogroup is much greater in Northern and Eastern than in Southern and Western Europe—as are CAD rates among men.

His Y chromosome study project is funded by the British Heart Foundation. He reported having no financial conflicts. ■