Genetic-Test Algorithm Is Validated for CAD Assessment

BY MITCHEL L. ZOLER

ORLANDO — A genetic test surpassed conventional risk-factor assessment for predicting the presence of an obstructive coronary lesion, based on results from a prospective study of 525 patients with suspected coronary artery disease.

The results performed better than either the Diamond-Forrester method or the Framingham Risk Score for predicting obstructive coronary artery disease, Dr. William E. Kraus said at the annual scientific sessions of the American Heart Association.

The genetic test examines RNA expression for 23 genes in a peripheral blood sample. The test is marketed in the United States under the name Corus by CardioDx.

The risk algorithm used to interpret the genetic-test results factors the person's age and gender. The genes primarily control immune responses, including neutrophil activation, natural killer cell activation by T cells, and adaptive immunity. The functions of other genes that are part of the test remain unknown, but prior results identified their expression as tracking with coronary disease risk, said Dr. Kraus, a cardiologist at Duke University in Durham, N.C.

The Personalized Risk Evaluation and Diagnosis in the Coronary Tree (PREDICT) study enrolled patients at 43 U.S. sites with suspected coronary disease who were scheduled for coronary catheterization and angiography. The subjects included both symptomatic and asymptomatic individuals. Researchers collected clinical data and a blood specimen from each person prior to their angiography.

Angiography identified a coronary stenosis that obstructed at least 50% of at least one major coronary artery (diameter of at least 1.5 mm) in 192 of the 525 patients (37%).

VITALS

Major Finding: The Corus genetic test bested two standard risk factor assessments for predicting obstructive coronary artery disease.

Source of Data: Prospective comparison of three screening tests in 525 patients.

Disclosures: The study was sponsored by, and Dr. Kraus received research support from, CardioDx, the maker of Corus.

The risk algorithm prospectively divided participants into a low-risk group of 174, a medium-risk group of 177, and a high-risk group of 174. Angiography found a coronary disease prevalence of 17% in the low-risk group, 33% in the medium-risk group, and 60% in the high-risk group.

The gene-test algorithm results accounted for 72% of the coronary artery disease found in the study. In contrast, applying the Diamond-Forrester method for determining coronary disease risk accounted for 66% of the coronary disease (N. Engl. J. Med. 1979;300:1350-8).

A more detailed comparison of the genetic-test algorithm to the Diamond-Forrester method showed that in the study group of 525, Diamond-Forrester identified 150 of the patients (29%) at medium risk for coronary disease, and the overall rate of actual disease in these people was 39%.

Running the genetic-test algorithm on these 150 people identified 32 as actually having a low risk, 65 as having a high risk, and 53 with a medium risk. The actual coronary disease rate found within each of these stratified subgroups confirmed the validity of the gene-test reclassification: In the 32 people categorized as low risk by the genetic test but medium risk by Diamond-Forrester the actual rate of coronary disease was 25%. Among the 53 people rated with a medium risk by the genetic tests the prevalence of actual coronary disease was 30%. And in the 65 patients that the genetic test flagged as having a high disease risk the actual prevalence was 52%.

The genetic-test algorithm has similar success reclassifying the coronary disease risk when the first determinant used was the Framingham Risk Score. ■

PPI/Clopidogrel May Raise Risk After PCI

BY SHERRY BOSCHERT

SAN DIEGO — Prophylactic use of a proton pump inhibitor plus clopidogrel after percutaneous coronary revascularization was associated with significantly greater risk for cardiovascular events, compared with taking clopidogrel alone, a small retrospective study found.

After percutaneous coronary intervention (PCI), 40 (56%) of 72 patients discharged on concomitant clopidogrel and proton pump inhibitor (PPI) therapy developed major adverse coronary events over a mean follow-up of 50 months, compared with 92 (38%) of 243 patients discharged on clopidogrel alone, Dr. Ekta Gupta and her associates reported at the annual meeting of the American College of Gastroenterology.

After researchers adjusted for baseline characteristics including the type of stent, patients in the combination-therapy group had a 95% excess risk for major adverse coronary events, said Dr. Gupta of the University of Arkansas, Little Rock. "Our study suggests that 'routine' use of prophylactic PPIs to prevent gastrointestinal bleeding should be avoided."

The adverse coronary events studied included cardiac or noncardiac death, MI, and target vessel failure (which was defined as a composite of cardiac death, MI, or target vessel revascularization).

Most patients who got a PPI used rabeprazole, with a minority getting omeprazole or lansoprazole. The study excluded patients who received pantoprazole or esomeprazole because previous studies found no association between these two drugs and an impaired response to clopidogrel seen with the other PPIs, suggesting that the adverse PPI-clopidogrel interaction may not apply to the whole class of drugs, she said.

If a PPI needs to be used after PCI, it may be preferable to use esomeprazole or pantoprazole, Dr. Gupta suggested. Alternatively, clinicians may want to consider separating the dosing of clopidogrel and the PPI to avoid potential drug-drug interaction.

Dr. Gupta had no conflicts of interest related to this study. ■

Antihypertensives Cut Events, but Not LVH, in Women

BY BRUCE JANCIN

ORLANDO — Hypertensive women experience significantly less regression of left ventricular hypertrophy than do men in response to equal pharmacologic lowering of blood pressure, yet their resultant reduction in cardiovascular events is just as great.

This new finding in a secondary analysis of the LIFE (Losartan Intervention for End Point Reduction in Hypertension) trial suggests that the optimal degree of left ventricular hypertrophy (LVH) regression for risk reduction in response to antihypertensive therapy is different in men and women, Dr. Peter M. Okin observed at the annual scientific sessions of the American Heart Association.

LIFE involved 9,193 hypertensive patients with ECG evidence of LVH, including 4,963 women. Participants were randomized to losartan- or atenolol-based antihypertensive therapy with as-needed hydrochlorothiazide to a target blood pressure of 140/90 mm Hg or less.

Unadjusted 5-year rates of the three end points and the composite were all lower in women than men, yet women experienced less LVH regression.

The primary results, demonstrating significantly better outcomes in the losartan arm, have previously been reported (Lancet 2002;359:995-1003).

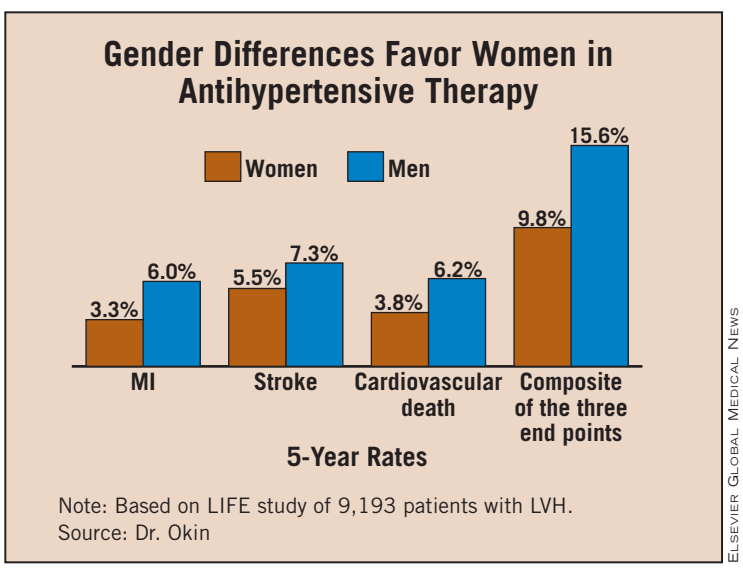
In the new secondary analysis, unadjusted 5-year rates of MI, stroke, cardiovascular death, and a composite of the three end points were all significantly lower in women than men, regardless of treatment arm. (See chart.)

Yet women experienced less LVH regression: a mean 3.0-mm reduction in Sokolow-Lyon voltage from a baseline of 28.2 mm, compared with a 4.8-mm decrease from a baseline of 32.1 mm among men, according to Dr. Okin of Cornell University, New York.

Mean baseline blood pressure was 173/99 mm Hg in men and similar (175/97 mm Hg) in women. The men experienced a mean 30/18–mm Hg reduction in blood pressure with treatment, compared with a 29/17–mm Hg reduction in women.

In multivariate Cox regression analyses, women who experienced significant regression of LVH as reflected in a decrease in Sokolow-Lyon voltage equal to or greater than the median 3.0 mm had an adjusted 40% reduction in the relative risk of the composite of MI, stroke, and cardiovascular death. Men who equaled or exceeded the sex-specific median 4.5-mm decrease had a 32% risk reduction.

The LIFE study was supported by Merck & Co. Dr. Okin reported having no relevant financial conflicts. ■



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