Look Deeper to Find Impact of Family History

Stroke in the family also increases an individual's risk of coronary heart disease, a study shows.

BY LINDA LITTLE
Contributing Writer

GRAPEVINE, TEX. — A strong family history of heart disease can increase an individual's future risk for coronary heart disease fourfold, and even a moderate family history can lead to a twofold increase in risk, a population-based study has shown.

"Most clinicians limit family history assessment to the presence of early-onset disease in a first-degree relative," Maren Scheuner, M.D., said at a meeting sponsored by the American College of Medical Genetics. "However, familial risk is influenced by the number of affected relatives, their degree of relationship and lineage, and age at diagnosis."

By analyzing data on 4,035 respondents to a national mail survey called HealthStyles, the researchers found that even a moderate history of coronary heart disease (CHD) increased the risk of CHD. Additionally, a strong family history of stroke also increased the CHD risk.

"If you have a family history of CHD, we know that it increases the risk," said Dr. Scheuner of the department of health services at the University of California School of Public Health, Los Angeles. "We have shown that a family history of stroke also influences the risk of CHD."

The researchers stratified respondents' family history of CHD and stroke as weak, moderate, or strong. Those with a strong family history had one or more family members with onset of heart disease or stroke at or before age 60. Those with a moderate family history had one or two family members with heart disease or stroke at a later age. Those with a weak family history had no relatives with heart disease or stroke or only one or two affected second-degree relatives. The survey also obtained self-reported information on risk factors such as diabetes, hypertension, high cholesterol, and obesity.

Individuals with strong family histories of CHD were four times as likely to have the disease, compared with those with a weak history. If three or four risk factors are present—such as diabetes, high blood pressure, high cholesterol, and obesity—the risk is increased 27 times given a strong familial CHD risk, compared with those with a weak family history of heart disease and no risk factors. If only two risk factors are present, then the risk is increased 19 times, and if no risk factors are present, then the risk for CHD associated with strong familial CHD is increased only twofold.

Turning to the risk of stroke, a person with a strong family history of CHD has 2.5 times the risk of stroke as a person with a weak family history of CHD. And an individual with a strong family history of stroke has a threefold increase in the risk of a stroke and a twofold increase in the risk of CHD, she reported.

A strong family history of CHD was also associated with a 1.5-fold increased risk of diabetes, high cholesterol, high blood pressure, and obesity. A strong family history of stroke was associated with a twofold increase in diabetes and a 1.5-fold increase in high blood pressure and obesity, respectively.

Moderate family histories of CHD resulted in a twofold increase in CHD, but not an increased risk for stroke, diabetes, high cholesterol, high blood pressure, or obesity. If there was a moderate family history of stroke, the risk of stroke was increased, but the risk for the other conditions was not increased.

Survey respondents were 60% female and 72% white, with a mean age of 48 years. Overall, 6.4% had a personal history of CHD, 4.2% had a personal history of stroke, and 12.3% had a personal history of diabetes. More than 15% of the respondents reported a family history of all three conditions. Almost one-third of respondents reported a strong family history of CHD; about 15% reported a strong family history of stroke.

The findings show that familial risk algorithms for CHD and stroke that incorporate characteristics such as age at diagnosis, number of affected relatives, and their degree of relationship and lineage, can stratify cardiovascular risk as moderate (about a 1.5- to 2.5-fold increase) or strong (about a 2.5- to 5-fold increase) Dr. Scheuner said.

Modifiable cardiovascular risk factors such as diabetes, high cholesterol, hypertension, and obesity are associated with strong familial CHD and stroke risk, and when present they substantially increase the cardiovascular risk.

The absence of risk factors diminishes the association between familial risk and CHD or stroke, she said. ■

Four Biomarkers Predict Cardiovascular Events in Women

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — The presence of inflammatory markers, a low hemoglobin, or both is superior to traditional cardiovascular risk factors for predicting adverse cardiovascular outcomes in women under evaluation for suspected myocardial ischemia, Christopher B. Arant, M.D., said at the annual meeting of the American College of Cardiology.

The standard cardiovascular risk factors appear to considerably underestimate the true risk of cardiovascular events in women presenting with chest pain, added Dr. Arant, a cardiologist at the University of Florida, Gainesville.

He reported on 595 women, mean age 58 years, who underwent coronary angiography as part of an evaluation for suspected myocardial ischemia in the National Heart, Lung, and Blood Institute–sponsored Women and Ischemia Syndrome Evaluation (WISE).

Standard CV risk factors appear to underestimate the true risk of CV events in women presenting with chest pain.

DR. ARANT

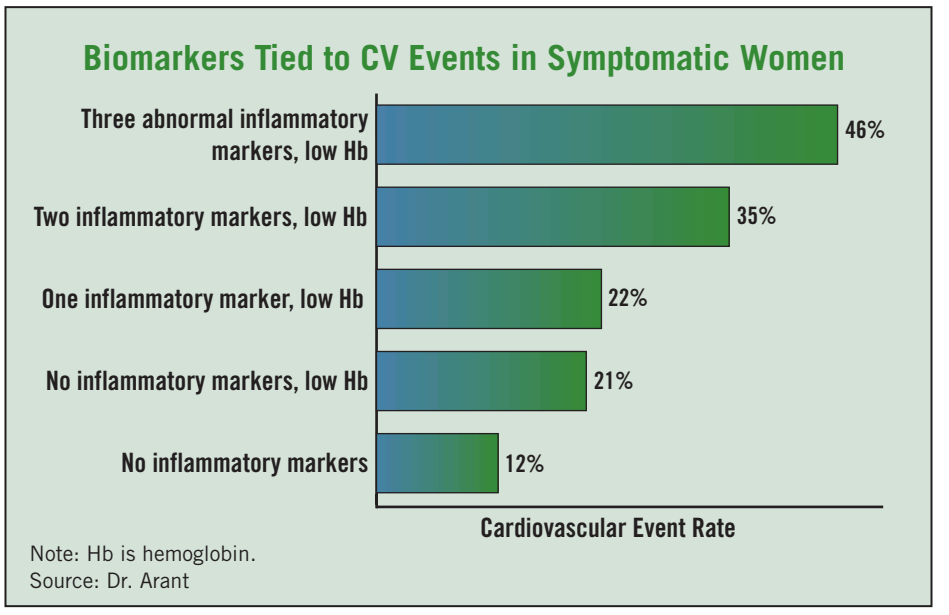
During a mean 3.6 years of follow-up, all-cause mortality among the women was 7%, and the rate of an MI, heart failure, stroke, another vascular event, or death was 20%. Yet the predicted 10-year risk of a cardiovascular event in WISE participants based upon their Framingham Risk Score was a mere 4.6%. This underestimate emphasizes the need to develop better methods of recognizing women at high risk, which is the mission of WISE.

Inflammation plays a key role in atherosclerosis and its related complications, perhaps even more so in women than in men. Dr. Arant and his coinvestigators previously examined the predictive power of three inflammatory markers—C-reactive protein, interleukin-6, and serum amyloid A—and demonstrated that they were strong predictors of cardiovascular risk in the WISE cohort. They also separately established that hemoglobin level was an independent predictor of adverse cardiovascular outcomes.

In their new study, they showed that adding a hemoglobin concentration below 12 g/dL to the three inflammatory markers created a four-biomarker combination that incrementally and independently predicted cardiovascular events in the WISE study women. (See chart.)

In a Cox multivariate regression analysis, the only traditional risk factors that predicted cardiovascular events were diabetes (79% increase in risk), and obstructive coronary artery disease on angiography (65% increased risk).

In contrast, the presence of any one of the four biomarkers was associated with a 90% increased risk of cardiovascular events during follow-up. Two positive biomarkers conferred a 192% increased risk. Women with three had a 368% increased risk, and those with four abnormal biomarkers had a 550% increased risk.



The mean hemoglobin in the WISE cohort was 12.9 g/dL. Why a modest reduction to below 12 g/dL was predictive of cardiovascular events in the WISE population remains speculative. Hemoglobin is not an obvious marker of inflammation. Yet physicians have known for some time that low hemoglobin is an independent predictor of cardiovascular events in heart failure patients.

One possibility is that mild anemia may reflect bone marrow underproduction of red blood cells due to systemic inflammation. Thus, in that sense, a low hemoglobin may indeed be a surrogate marker for inflammation. However, the observation that adding hemoglobin to the three inflammatory markers yielded an incremental increase in event risk in WISE suggests a low hemoglobin may be acting directly to increase risk.

Studies of sickle cell anemia patients suggest that hemoglobin may be important in the transport of nitric oxide, known to play a key role in endothelial function. Nearly two-thirds of women in WISE did not have obstructive coronary artery disease, and instead presumably had what is often described as microvascular disease. Thus inadequate nitric oxide could exacerbate their endothelial dysfunction, which might explain the link between low hemoglobin and increased cardiovascular events, Dr. Arant hypothesized.

A pearl from the WISE chest pain registry is that women with cardiac ischemia have a high prevalence of atypical angina. "Any pain above the waist in women who have risk factors requires a good history and physical exam and needs to be considered as an anginal equivalent," he said. ■