Multi-gene test predicts early heart disease risk

January 8 2018

A risk score based on multiple genetic differences, or polygenic risk score, predicted significantly more cases of early-onset heart disease than standard tests for single genetic defects, according to new research in the American Heart Association's journal *Circulation: Genomic and Precision Medicine*.

"Our results provide convincing evidence that the polygenic risk score could be added to the genetic investigation of patients with very early coronary artery disease," said study lead author.

Sébastien Thériault M.D., M.Sc., FRCPc, assistant professor at Laval University in Quebec City, Quebec, Canada, and researcher at the Quebec Heart and Lung Institute.

Heart disease is the leading cause of death, both in the United States and worldwide. The most common form is coronary artery disease, which occurs when the blood vessels to the heart narrow or harden. Most people can decrease their risk by not smoking, being physically active, maintaining a healthy diet and body weight, and controlling cholesterol, blood pressure and blood sugar.

In rare instances, however, high blood levels of the so-called bad cholesterol, LDL, result from a genetic defect called familial hypercholesterolemia (FH). Patients with this genetic defect are at increased risk for early-onset heart disease, defined in the study as before age 40 in men and age 45 in women, so early diagnosis and

treatment are critical. The problem is that many patients with early-onset heart disease do not have this single genetic defect which can be measured by current tests.

Accordingly, this study looked at the relationship between a risk score based on multiple genetic differences and early-onset heart disease. Results showed that the polygenic risk score predicted a high risk for early-onset heart disease in 1 out of 53 individuals at the same level as FH does. The prevalence of FH is 1 in 256 individuals for the single genetic test for FH.

"The increase in genetic risk was independent of other known risk factors, suggesting that testing for multiple genetic differences is clinically useful to evaluate risk and guide management," said senior author Guillaume Paré, M.D. M.Sc. FRCPc, associate professor of medicine at McMaster University and Hamilton Health Sciences in Hamilton, Ontario, Canada, and director of the Genetic and Molecular Epidemiology Laboratory. "Combining polygenic screening with current testing for familial hypercholesterolemia could potentially increase five-fold the number of cases for which a genetic explanation can be found."

The investigators developed the polygenic risk score based on 182 genetic differences related to coronary artery disease. They then compared polygenic risk scores between study participants with and without early-onset heart disease.

Study participants included 30 patients with early-onset heart disease seen in the investigators' clinic from 2014 to 2016. None of the patients in this study with high polygenic risk scores had the single, rare genetic defect for FH. Ninety-six patients with early-onset heart disease enrolled in the UK Biobank study between 2006 and 2010 were also tested. As controls, the study also included 111,283 UK Biobank participants without early-onset heart disease. Forty-seven percent of the UK

Biobank participants were male and their average age was 58 years. The UK Biobank is a large study in the United Kingdom looking at the relationship between genetics, the environment and disease.

All study participants were of European descent, so the results may not apply to other populations. Another limitation is its inclusion of patients with severe early-onset heart disease, which is more likely to have genetic causes than milder disease.

Provided by American Heart Association