Big picture genetic scoring approach reliably predicts heart disease

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Specialized risk scores derived from testing that calculates the cumulative effect of an individual's entire DNA sequence, the genome, may reliably predict heart disease in people who have not yet had a heart attack, according to new research in *Circulation: Genomic and Precision Medicine*, an American Heart Association journal.

The study is the latest to use polygenic risk scores (PRSs) based on an individual's entire genome sequence as biomarkers to predict the risk to develop coronary artery disease and heart attack. Several published studies have used PRSs with high accuracy in people of European ancestry. Researchers in this most recent study set out to determine if the results would translate to a different population, in this case French Canadians.

Researchers studied two similar PRSs in 3,639 French Canadian adults with cardiovascular disease and 7,382 adults without heart disease. They found that the PRSs developed and tested in other populations also had the sensitivity and specificity for predicting heart disease in French Canadians.

"PRSs, built using very large data sets of people with and without heart disease, look for genetic changes in the DNA that influence disease risk, whereas individual genes might have only a small effect on disease predisposition," said Guillaume Lettre, Ph.D., lead author of the study and an associate professor at the Montreal Heart Institute and Université de Montréal in Montreal, Quebec, Canada. "The PRS is like having a snapshot of the whole genetic variation found in one's DNA and can more powerfully predict one's disease risk. Using the score, we can better understand whether someone is at higher or lower risk to develop a heart problem."

Early prediction would benefit prevention, optimal management and treatment strategies for heart disease. Because PRSs are simple and relatively inexpensive, their implementation in the clinical setting holds great promises. For heart disease, early detection could lead to simple yet effective therapeutic interventions such as the use of statins, aspirin or other medications.

Results from the study also confirmed original reports showing that the

PRSs can identify about 6% to 7% individuals at high risk for cardiac disease. Lettre said this risk was similar to the high heart disease risk among people with familial hypercholesterolemia, a rare but severe disease that predisposes people to very high levels of low-density lipoprotein (LDL or bad) cholesterol, which puts them at a high risk of heart attack.

"Using the polygenic risk score, even in a normal population, we can find people whose risk is as high as those who have this rare disease," Lettre said.

PRSs, however, did not perform as well in predicting new events in people who had already had heart attacks, possibly because the participants were older and 76% of those them were on statin treatment which could impact PRS performance.

More research needs to be done before PRSs go mainstream for determining individual heart disease risk, according to Lettre.

The next step is to test the genetic scoring systems long term in large clinical studies to determine if managing and treating people based on their risk scores improves individuals' heart health. Researchers should also do studies to better understand how to integrate polygenic risk scores with the other known risk factors, such as blood pressure, diabetes and cholesterol levels, but also to extend these studies to non-European ancestry populations, he said.

The American Heart Association named the use of polygenic risk scores as one of the biggest advances in heart disease and stroke research in 2018.

"Eventually, clinicians could use polygenic risk scores along with family history, cholesterol and blood pressure to determine heart disease risk.

Used early in a person's life it might help clinicians more precisely tailor treatment aimed at preventing a heart attack in later years," said Jennifer Hall, Ph.D., Chief of the American Heart Association's Institute for Precision Medicine. "This type of research is the basis for the work we are doing within the Institute of Precision Medicine."

"There is a lot of interest not only in the science arena but also in the general community about using genetics to capture information about disease risk," Lettre said. "This research is exciting, as genetic testing is becoming more powerful, affordable and it's easy—often requiring only a swab of one's saliva."

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