MedicalXpress

Study verifies that cholesterol-associated gene variants can predict cardiovascular events

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A study appearing in this week's New England Journal of Medicine confirms that a combination of gene variants previously associated with cholesterol levels does reflect patients' cholesterol levels and can signify increased risk of heart attack, stroke or sudden cardiac death. Led by researchers from the Massachusetts General Hospital Cardiology Division, the study's findings are a first step towards the ability to identify individuals who might benefit from earlier use of cholesterol-lowering medications and other measures to combat elevated risk.

"The prospect of personalized medicine has received much hype, but until recently, there has been little hard evidence to support the promise," says Sekar Kathiresan, MD, MGH Director of Preventive Cardiology, the paper's lead author. "We feel that our data provides two insights. First, we provide a foundation for the possibility that a panel of gene variants will eventually be useful in preventive cardiac care. Second, we show that the combination of multiple variants related to cholesterol importantly contribute to the genetic risk for heart attack."

It is estimated that about half the variation in high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol levels is inherited, rather than being caused by lifestyle factors such as diet and exercise. While studies have associated several gene variants with cholesterol levels, exactly how those variants impact the risk of cardiovascular disease is unclear. The current study was designed to explore the

influence of those variants on the risk of cardiovascular events -- heart attack, stroke or sudden cardiac death -- and whether measuring such variants could help predict risk better than simply measuring HDL and LDL levels.

Since the effects of individual gene variants appears slight, the research team looked at a combination of 9 single-nucleotide polymorphisms (SNPs) previously associated with cholesterol levels. They analyzed data from 5,414 Swedish adults who participated in a major prospective epidemiological study and correlated data -- including standard measurements of HDL and LDL cholesterol and the presence of the 9 gene variants -- with information on the participants' subsequent medical histories available from a registry of information collected on all Swedish citizens. After the initial genotyping of participants not receiving lipid-lowering therapy, participants were assigned a genotype score ranging from 0 to 18, based on how many copies of the unfavorable SNPs they carried. Of the participants who had no cardiovascular events before enrolling in the study, 238 suffered a heart attack, stroke or cardiac death during the subsequent 10.6 years.

Higher genotype scores did reflect higher LDL ("bad") cholesterol and lower HDL ("good") cholesterol levels. Importantly, those with genotype scores of 11 or higher had a 63 percent greater risk of a cardiovascular event than did those with scores of 9 or lower. Although testing for the panel of 9 SNPs was not better than standard risk factors for predicting cardiac events in the overall population, among participants classified at intermediate risk by standard measures, adding the 9-SNP panel significantly improved the ability to distinguish truly elevated or reduced risk levels.

"A current clinical dilemma is how early to start patients on cholesterol-lowering medications like statins that can reduce the risk of heart attack. Our data suggest that those individuals classified as higher risk based on

a genetic test may deserve more intense pharmacological and lifestyle treatments," says Kathiresan. "But before we can move from our pilot data to information that can impact the care of patients with or at risk for cardiovascular disease, we need to discover all the risk-related variants -- and there will probably be 50 to 100 -- and then conduct clinical studies confirming that this information can reliably guide patient care." Earlier this year Kathiresan, an instructor in Medicine at Harvard Medical School, and colleagues from the Broad Institute of Massachusetts Institute of Technology and Harvard University began this gene-discovery process and identified six new cholesterol-associated gene variants in a separate study published in Nature Genetics.

Source: Massachusetts General Hospital