

Study disproves link between genetic variant, risk of coronary artery disease

October 7 2010

A genetic marker touted as a predictor of coronary artery disease is no such thing, according to a study led by researchers at the Stanford University School of Medicine.

The massive international study, published online Oct. 7 in the *Journal of the American College of Cardiology*, assessed the predictive value of a leading genetic assay for risk of atherosclerosis.

The study analyzed the data from more than 17,000 patients with cardiovascular disease and 40,000 others to assess whether carrying a particular variant of the KIF6 gene indicated a greater risk for coronary artery disease — a disease characterized by a buildup of cholesterol plaque in the walls of the arteries of the heart. The disease can lead to chest pain as well as heart attacks, which are often fatal.

The study found essentially no association between the gene variant and the risk of coronary disease. "This study puts the nail in the coffin," said Tom Quertermous, MD, the William G. Irwin Professor in Cardiovascular Medicine at Stanford and the study's senior author. "This is such a big study — if there was a significant association between this variant and coronary disease, we would have found it."

Celera Corp., which pioneered the mapping of the human genome, owns the assay and currently performs the majority of the testing services. In June, as part of its effort to make the assay more widely available, Celera announced it had received approval from the European Union to

market a test kit for the variant that would make it easier for physicians to collect patients' samples. The company said it would also submit an application to the U.S. Food and Drug Administration this year for approval of the test kit.

Previous studies of the variant were less conclusive because they were based on fewer patients with [coronary artery disease](#), said the new study's leader, assistant professor of medicine Themistocles Assimes, MD, PhD. These earlier studies had suggested a 22-55 percent greater risk for those who had the variant. "We are showing that the additional risk is almost certainly nil in subjects of European ancestry. If it is not nil, it is at most 2 percent," Assimes said.

The study pulled together data from research groups around the world that have genetically fingerprinted individuals with known coronary disease as well as subjects with no known disease. Most of the data were from people of European descent, but a lack of association was also noted in smaller number of subjects of non-European ancestry. The Stanford researchers' co-authors include more than 130 scientists, clinicians and administrators at over 70 research organizations in Europe and North America.

The study offers good news to patients whose KIF6 test result had indicated they were at risk for heart attacks. "They don't need to worry so much," Quertermous said. "If they are on medications strictly because of their KIF6 test result, they should ask their doctor to reconsider the need for these medications."

Because of the study's design, it could not directly confirm or refute the marker's ability to identify the subjects' response to statins, which are drugs that lower cholesterol levels. However, Assimes cautioned that the original observation, which found the KIF6 variant indicated a good response to the medication, assumed that carriers of the variant not on

statins were at significantly increased risk of coronary disease compared to non-carriers.

"In light of our findings, the marker's ability to identify statin responders is also in doubt," said Assimes. "Until very large-scale studies are performed to directly test the marker's ability to identify statin responders, I would not withhold statins from patients just because their KIF6 test was negative."

The finding's larger message is that more caution is warranted when using genetic markers to guide health care. There's understandably great desire to use the information about human genetics that's been amassing since the sequencing of the human genome 10 years ago, said Quertermous, who has worked in the field for more than 20 years. "It's something I've been waiting for, for a long time."

That's because the well-known risk factors for atherosclerosis, such as high cholesterol, smoking, diabetes and high blood pressure, appear to account for only about half the variation of rates of coronary disease observed in human populations. The balance of variation is likely explained by a combination of inherited variants in or near genes that are important in the pathogenesis of disease in addition to other unrecognized, adverse environmental exposures.

"Using genetics to help improve our ability to predict coronary disease is particularly important because we have several different classes of drugs at our disposal that can substantially reduce the risk of heart attacks" said Assimes. "But we still need to be careful about what we put into practice and not get carried away too quickly. We know from previous experience that a positive association between a genetic variant and a common disease, such as coronary disease, needs to be consistently observed in many human population studies before it can be believed."

In fact, Quertermous points out that even for the roughly one dozen genetic markers that have been successfully validated to date, evidence to support their use in clinical practice is lacking. However, this situation will likely change in the near future as researchers reliably identify more genetic markers.

The data collections used in this study were supported by more than 30 institutions including government and nonprofit agencies and the following companies: Astra Zeneca, Berlin Chemie, Boots Healthcare, deCODE genetics, Glaxo-Smith-Kline, McNeil Pharma (former Woelm Pharma), MSD Sharp & Dohme and Pfizer.

Provided by Stanford University Medical Center

Citation: Study disproves link between genetic variant, risk of coronary artery disease (2010, October 7) retrieved 8 May 2024 from <https://medicalxpress.com/news/2010-10-link-genetic-variant-coronary-artery.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--