MedicalXpress

# Genetic variant identified that may increase heart disease risk among people with type 2 diabetes

August 27 2013

A newly discovered genetic variant may increase the risk of heart disease in people with type 2 diabetes by more than a third, according to a study led by researchers at Harvard School of Public Health (HSPH) and Joslin Diabetes Center. It is the first genome-wide association study (GWAS) to identify a novel genetic variant associated with coronary heart disease (CHD) in people with type 2 diabetes, who have a two- to four-fold higher risk of heart disease compared with those without diabetes. The finding could lead to new interventions aimed at preventing or treating CHD among patients with type 2 diabetes.

"This is a very intriguing finding because this variant was not found in previous genome-wide association studies in the general population," said lead author Lu Qi, assistant professor in the HSPH Department of Nutrition and assistant professor at the Channing Division of Network Medicine, Brigham and Women's Hospital. "This means that the genetic risk factors for cardiovascular disease may be different among those with and without diabetes."

"The identification of this genetic variant opens up the possibility of developing treatments that are specifically aimed at breaking the links between diabetes and CHD," said co-lead author Alessandro Doria, associate professor in the Department of Epidemiology at HSPH and a researcher at Joslin Diabetes Center.

The study appears online August 27 and will appear in the August 28, 2013 issue of *JAMA* (*Journal of the American Medical Association*).

More than 370 million people worldwide have type 2 diabetes and CHD is the leading cause of death among diabetic patients. Overall CHD-related mortality has been declining in the United States and other industrialized countries over the past few decades. But CHD deaths that are diabetes-related are on the rise because of the increasing prevalence of the latter ailment. Although prior genome-wide studies have found many genetic variants for CHD in people in the general population, no such study had examined genetic determinants for CHD specifically in those with type 2 diabetes.

For their analysis, the researchers used data from several long-term studies: the Nurses' Health Study, the Health Professionals Follow-up Study, the Joslin Heart Study, and two Italian studies—the Gargano Heart Study and the Catanzaro Study. They looked at 4,188 diabetic patients, including 1,517 with CHD and 2,671 without CHD as a control group.

Testing more than 2.5 million genetic variants, the researchers found that a variant near the GLUL gene, a gene that encodes a key enzyme regulating the conversion of glutamic acid to glutamine, was consistently associated with a 36% increased risk of CHD in people with diabetes. There was no association between this variant and CHD risk in study participants without diabetes.

They also found that the variant may interfere with the expression of a gene that regulates blood levels of amino acids involved in insulin secretion and glucose metabolism—key functions that go awry in those with type 2 diabetes.

Since these amino acids are nutrients affected by food intake, it's

possible that changes in diet may help reduce increased CHD risk among people with diabetes. The finding may also provide scientists with other targets for therapies to help prevent or treat CHD in diabetic patients.

**More information:** "Association between a genetic variant related to glutamic acid metabolism and coronary heart disease in type 2 diabetes," Lu Qi, Qibin Qi, Sabrina Prudente, Christine Mendonca, Francesco Andreozzi, Natalia di Pietro, Mariella Sturma, Valeria Novelli, Gaia Chiara Mannino, Gloria Formoso, Ernest V. Gervino, Thomas H. Hauser, Jochen D. Muehlschlegel, Monika A. Niewczas, Andrzej S. Krolewski, Gianni Biolo, Assunta Pandolfi, Eric Rimm, Giorgio Sesti, Vincenzo Trischitta, Frank Hu, and Alessandro Doria, *JAMA*, online August 27, 2013.

Provided by Harvard School of Public Health