

Testing for a lipoprotein linked to heart risk is as effective as blood work

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Elevated levels of a little-known lipoprotein in the blood that may put people at high risk of cardiovascular disease can be as accurately detected by genetic testing as by conventional laboratory measurement, researchers at Massachusetts General Hospital (MGH) have found. In a study published in JAMA Cardiology, the team reported that genetic risk scoring of the low-density lipoprotein (LDL)-like lipoprotein—known as lipoprotein(a)—may have clinical utility in helping physicians identify candidates for treatment, such as a statin, or for ongoing clinical trials of new medicines. The findings are particularly important in light of the millions of people who use direct-to-consumer genetic testing kits, and for expanding genetic research biobanks.

"Our work demonstrates that genetic risk scoring of lipoprotein(a) offers risk prediction of atherosclerotic cardiovascular disease that's comparable to directly measured lipoprotein(a)," says Pradeep Natarajan, MD, investigator in the Division of Cardiology and Cardiovascular Research Center at MGH and senior author of the

study. "We learned that genetic determinants of elevated lipoprotein(a) may help identify the most effective medication regimen for cardiovascular disease prevention."

Lipoprotein(a) contains a molecule known as apolipoprotein(a) that has been linked by studies to atherosclerotic cardiovascular disease (ASCVD). Genetic variation is believed to account for 75 to 95 percent of lipoprotein(a) level variation in the population. Because nongenetic factors, such as diet and physical activity, do not substantially influence lipoprotein(a) concentrations, a genetic test is well positioned to identify high concentrations. Lipoprotein(a) levels greater than 50 milligrams per deciliter (mg/dL) are associated with a 30 to 50 percent greater risk of ASCVD. Individuals with extremely high levels, greater than 200 mg/dL, could face a three to four times greater risk of ASCVD.

Unlike LDL and HDL cholesterol and other lipoprotein particles that are universally known, lipoprotein(a) is rarely measured and largely underrecognized by physicians. Through their observational study, the MGH researchers sought to determine if the 43 known genetic variants of lipoprotein(a) could predict future disease risk. To that end, they drew upon the UK Biobank's approximately 500,000 adults ages 40 to 69.

"Our results showed that if someone already had their lipoprotein(a) measured, then the incremental predictive benefit of a genetic test is negligible," notes Mark Trinder, with the University of British Columbia, lead author of the study. "Where both findings can be useful, though, is in the case of physicians who are undecided about putting a patient with elevated lipoprotein(a) levels on medication."

Natarajan is encouraged about the potential impact of his team's work on the broader realm of genetic testing. "Using genetic factors enhances our ability



to identify at-risk individuals for cardiovascular disease who could benefit from earlier preventive strategies," he says. "At the same time, genetic testing could help identify candidates for clinical trials who are critical to discovering innovative new therapies to address conditions like elevated lipoprotein(a) and related cardiovascular disease risks."

More information: Mark Trinder et al, Clinical Utility of Lipoprotein(a) and LPA Genetic Risk Score in Risk Prediction of Incident Atherosclerotic Cardiovascular Disease, *JAMA Cardiology* (2020). DOI: 10.1001/jamacardio.2020.5398

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