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Genetic test may improve post-stent treatment, outcome

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Using genetic testing to inform which blood thinner to use following a procedure to open narrowed blood vessels resulted in significantly fewer complications among patients, according to new research in *Circulation: Genomic and Precision Medicine*, an American Heart Association journal.

In the United States, heart disease is the leading cause of death, and stroke is the fifth-leading cause. A major contributor to these cardiovascular diseases is clogged blood vessels (atherosclerosis), which result from the buildup of fatty deposits or plaque.

Treatment for clogged blood vessels often includes angioplasty. In this procedure, the doctor inserts a small, medical balloon into the damaged blood vessels, and then inflates and removes it. Small tubes, or stents, also may be used to hold open the blood vessels. To prevent further damage from occurring, patients often take multiple blood thinners, such as clopidogrel and aspirin, after stent placement.

Previous research has shown that clopidogrel is less effective in patients with mutations on a specific gene, called CYP2C19, than in patients without the mutations. Whether genetic testing can help guide treatment in clinical practice, however, has remained unclear.

In this study, results showed that genetic testing for CYP2C19 mutations could be used to guide blood-thinner treatment after stent placement. Furthermore, patients with the mutations who received one of two

clopidogrel alternatives compared to clopidogrel were more than three times less likely to die or have a heart attack, stroke or other major complications 12 months after treatment. Specifically, major complications occurred among 27 percent of clopidogel patients with the genetic mutations, compared to 8 percent of patients with the mutations who received the alternative medications.

These findings are similar to those of an earlier, multicenter study that found the risk of a major cardiovascular event more than doubled in patients with the genetic mutations who took clopidogrel.

"Using an algorithm based on genetic testing to guide treatment is sustainable and associated with better clinical outcomes in a real-world clinical practice, although it is difficult to consistently maintain," said Craig R. Lee, Pharm.D., Ph.D., F.A.H.A., associate professor of pharmacy at the University of North Carolina at Chapel Hill Eshelman School of Pharmacy. "Clinicians need to be aware of the increased risk of major adverse cardiovascular events associated with use of clopidogrel in patients receiving stents who carry either one or two copies of the mutation."

Study participants included 1,193 patients at the University of North Carolina Cardiac Catheterization Laboratory who received stent placement between July 1, 2012, and June 30, 2014. Their average age was 63 years and more than two-thirds were male. Most were white, 21 percent were black, and 1 percent was Asian. Patients identified as high risk, due to decreased blood flow to the heart, received the genetic testing. Follow up was 12 months.

The study has several limitations. For one, the investigators collected information after treatment, so they could not definitively say whether blood-thinner choice and the results of genetic testing caused better patient outcomes. Another limitation includes the use of a single

hospital, which may not be applicable to different settings.

"We are using CYP2C19 genetic testing on a daily basis at our institution to help decide in a timely manner which drug to prescribe," said George "Rick" Stouffer, III, M.D., F.A.H.A., chief of cardiology and co-director of the McAllister Heart Institute at UNC.

More information: *Circulation: Genomic and Precision Medicine*, DOI: 10.1161/CIRCGEN.117.002069

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