Gene linked with death after coronary bypass surgery

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Duke University Medical Center researchers have found a genetic variant that seems to be associated with lower five-year survival after a coronary artery bypass.

The scientists found the same gene was associated with mortality in two different sets of patients, with about 1,000 patients in each group (1,018 and 930 patients, respectively).

"After the second analysis, we were ecstatic to see this was validated," said senior author Mihai Podgoreanu, assistant professor of anesthesiology at Duke. "This is the first study I know about in the field of perioperative medicine to show increased genetic susceptibility for long-term mortality while replicating the genetic association in an independent cohort."

The study was published in the Sept. 12 issue of *Circulation*.

The team found common variants in the thrombomodulin (THBD) gene, involved in regulation of blood coagulation and inflammation, to be independently associated with increased long-term mortality risk following a coronary artery bypass graft (CABG) procedure, after accounting for currently known risk factors.

"In any biomarker association study, current wisdom is that there are a lot of false positive findings, so we used specimens from a different, independent cohort of patients to increase our confidence that the initial

results were not spurious," Podgoreanu said.

"This finding has the potential to significantly improve the classification ability of traditional mortality-prediction models after a patient's open heart surgery," Podgoreanu said.

He said the findings open up the field for more work, but it is too soon to say how this genetic finding should be used to benefit individual cardiac surgical patients and extend their survival. It's also too soon for great numbers of people to have their genomes sequenced and learn whether they carry this particular gene variant.

That said, Podgoreanu does see ways in which the finding might help patients.

"We need to work to find uses for any sort of biomarker," he explained. "There are possibilities that we could apply this information someday to a patient's prognosis, and for careful monitoring or increased surveillance if a person has a 2.5 times higher risk of dying, instead of letting them go their way after a CABG surgery."

Treatment outcomes also need to be tested according to a "personalized" susceptibility profile. The Duke Clinical Research Institute is known for its work with patients who have cardiac/coronary disease and testing when it is best to employ one of three therapeutic options: 1) medication only, 2) opening a clotted vessel with angioplasty and a stent, or 3) bypassing the clotted vessel with a graft from another vessel, as in CABG procedures, Podgoreanu said. "But at no point has genetic or biomarker information been superimposed on this care-improvement testing process, so the results of this preliminary study will provide ammo for more studies with a genetically stratified trial," he said.

The findings also may benefit patients someday, because genetic results

are unchanging. "If we take saliva or blood from patients before surgery and find they carry this gene variant, we can be more sure about their risk profile, as opposed to simply measuring values of the protein product of that gene in their blood profiles that are subject to change, for example, in response to the stress of surgery or medications," Podgoreanu said.

Provided by Duke University Medical Center