Some heart patients may respond differently to anti-platelet drugs

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The cause of heart attacks or strokes among some patients treated with anti-platelet drugs may be different than for patients who have undergone surgical procedures to restore blood flow, according to researchers at Duke Medicine.

The finding—reported Nov. 4, 2012, at the American Heart Association 's Scientific Sessions annual meeting and published in the Journal of the American Medical Association – provides new insights into a subset of heart patients with acute coronary syndromes (ACS) whose risk for cardiovascular events remained unchanged despite taking medicine that successfully reduced platelet clotting function.

"Platelet-rich clot formation after artherosclerotic plaque rupture plays a major role in the occurrence of ACS events, including heart attack and stroke," said senior author Matthew T. Roe, M.D., MHS, a cardiologist at Duke and member of the Duke Clinical Research Institute. "It seems intuitive that by reducing the clotting tendency with anti-platelet drugs, we would see a reduction in the risk of cardiovascular events, but our study shows that for some patients, this may be a more complex interaction."

Roe and colleagues analyzed data from the TRILOGY ACS study, a large international trial that compared two platelet inhibitor drugs called P2Y12 blockers—prasugrel and clopidogrel – together with aspirin therapy. Both drugs block an important pathway that leads to the clumping activity of platelets. This pathway is believed to be important

in the occurrence of heart attacks in patients who have been treated with cardiac stents.

The main TRILOGY ACS study enrolled more than 9,000 patients with acute coronary syndrome who were treated with medication only instead of receiving revascularization procedures such as angioplasty or stenting. The rial showed no significant difference in adverse cardiovascular events between the anti-platelet drugs over 30 months.

More than 2,500 TRILOGY ACS participants took part in a platelet function sub-study, providing blood samples that were analyzed at nine different points over 30 months to determine how the patients' platelet function responded to prasugrel vs. clopidogrel. The periodic blood tests identified a condition known as "high on-treatment platelet reactivity," or HPR. HPR has previously been found in up to half of patients treated with clopidogrel and has been linked to a higher risk of adverse outcomes for patients who undergo coronary stent placement.

Researchers found that a blood test measuring platelet aggregation showed prasugrel was more effective than clopidogrel in inhibiting platelet clotting function and that a smaller percentage of patients treated with prasugrel had HPR. But the researchers did not see a significant difference between the incidence of death, heart attacks or strokes among the study participants, regardless of whether they were taking clopidogrel or prasugrel. And the blood tests, which correlate low scores with more potent platelet inhibition, did not independently identify patients at risk for cardiovascular events.

"We could not show that there was a reliable cut point with this blood test for discriminating between patients who are at risk for an event vs. and those who are not at risk based on platelet aggregation measurements," Roe said. "That's interesting, because previous studies with patients undergoing coronary stent placement have shown that the

measurement was independently predictive. It may be that in this population of medically treated ACS patients, the correlation isn't robust and that these patients may respond differently to these types of platelet inhibitors."

Roe said these findings may explain the main outcome of the primary TRILOGY ACS trial, which reported no significant difference between prasugrel and clopidogrel in reducing cardiovascular events, especially during the first 12 months.

"The TRILOGY ACS platelet function study is a landmark for many reasons," said Paul A. Gurbel, M.D., director of the Sinai Center for Thrombosis Research at Sinai Hospital of Baltimore and lead author. "It is the largest study of its kind conducted prospectively in a major clinical trial. Whereas platelet function data from observational studies in over 20,000 patients treated with stents support a strong and independent relation of HPR to risk for ischemic event occurrence, the same was not observed prospectively in this study of medically treated patients. The reasons for this disparity may be related to the stent implantation itself or other unknown factors. This is an area for future research."

Provided by Duke University Medical Center