De-escalation of dual antiplatelet therapy appears safe and effective

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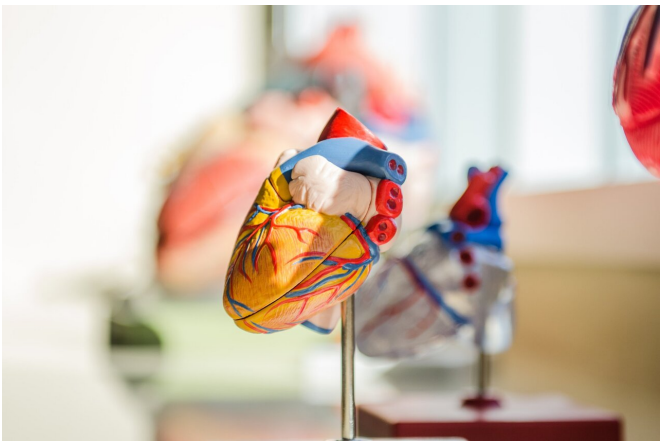

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Among patients who had a cardiac stent inserted after a heart attack, switching to less-potent dual antiplatelet therapy (DAPT) after 30 days was safer and more effective in preventing adverse events a year later than continuing on a high-potency DAPT regimen, according to data presented at the American College of Cardiology's 70th Annual Scientific Session.

"We have shown that, in patients who have had a heart attack and who've been treated with newer-generation stents and guideline-recommended medical therapy, de-escalation of DAPT by switching from ticagrelor to clopidogrel is completely safe and more effective than continuing to treat patients with ticagrelor," said Kiyuk Chang, MD, professor of Cardiology, Division of Internal Medicine at the Catholic University of Korea in Seoul and lead author of the study.

The study's primary endpoint, a composite of death due to a heart attack or stroke, a nonfatal heart attack or stroke, or bleeding requiring medical intervention at any time from one to 12 months after the stenting procedure, was met.

Stenting, also known as coronary angioplasty or percutaneous coronary intervention (PCI), is a minimally invasive procedure in which a flexible tube (catheter) is threaded through an artery under local anesthesia. At the site of an arterial blockage, a tiny balloon at the tip of the catheter is inflated to unblock the artery, and a stent—a tiny mesh tube coated with medication—is inserted to prop it open.

Current treatment guidelines recommend that after the insertion of a cardiac stent, patients should receive DAPT, which includes aspirin and a P2Y12 inhibitor like clopidogrel or ticagrelor, for six to 12 months. P2Y12 is a receptor on the surface of platelets—blood cells that help the blood to clot. P2Y12 inhibitors reduce clotting by partially blocking the action of the P2Y12 receptors. Ticagrelor is a newer agent that, compared with clopidogrel, is more potent, faster acting and has a more predictable antiplatelet effect, but also poses a higher risk of bleeding. Switching between P2Y12-inhibiting medications can increase (escalate) or decrease (de-escalate) the level of P2Y12 receptor inhibition.

Previous studies have shown that patients are at the highest risk for another heart attack during the first 30 days after stent insertion. Bleeding risk, by contrast, remains high during the maintenance phase of treatment (after the first 30 days). This trial, known as TALOS-AMI, is the largest study to date to test the safety and efficacy of a DAPT de-escalation strategy in minimizing the risk of both another heart attack and a bleeding episode, Chang said.

The trial enrolled 2,697 patients from East Asia (80% male, median age 60 years) 30 days after they had undergone stenting following a heart attack. During the month after their procedure, all patients had received DAPT with ticagrelor plus aspirin and had experienced no serious adverse events such as another heart attack, stroke or major bleeding. Patients were randomly assigned

either to continue taking ticagrelor plus aspirin daily for a year or to switch after 30 days to clopidogrel, a less-potent P2Y12 inhibitor, plus aspirin.

At one year, the adverse events defined in the primary endpoint (death due to a heart attack or stroke, a nonfatal heart attack or stroke, or bleeding requiring medical intervention) occurred in 59 patients in the clopidogrel group (4.6%) compared with 104 in the ticagrelor group (8.2%), a statistically significant difference. Three percent of patients in the clopidogrel group experienced bleeding that required medical intervention, compared with 5.6% in the ticagrelor group, also a statistically significant difference. Outcomes for arterial blockages (ischemia) were similar in the two groups.

"We found that the higher-potency DAPT regimen with ticagrelor was needed only during the first 30 days after a heart attack, when the risks of another heart attack or arterial blockage are highest, and that this regimen may be harmful once this early phase has passed," Chang said. "Many cardiologists are already using DAPT de-escalation in patient treatment, and the results of this study provide scientific evidence to justify this practice."

The study findings have limitations, Chang said. The trial was not blinded, meaning that both patients and their doctors knew who was receiving which drug. Secondly, the trial was conducted only in South Korea. A genetic variant that reduces the effectiveness of clopidogrel occurs significantly more frequently in people of East Asian ethnicity than in other ethnic groups, he said.

"However, we showed the clinical safety and efficacy of switching from ticagrelor to clopidogrel in an East Asian population, which suggests that this de-escalation strategy could be safely applied to clinically similar patients of other ethnicities," he said.

Another limitation is that the overall incidence of primary endpoint events in the trial was lower than the researchers had initially estimated, Chang said. In both groups, fewer patients than expected experienced arterial blockages during the study period. This finding may be explained in part by the fact that patients were randomly assigned to treatment 30 days after undergoing PCI, rather than at the time of PCI, and that all patients enrolled in the trial had received the most technologically advanced cardiac stents, which may pose a lower risk for adverse events than older devices. Additionally, a relatively large difference in the number of expected versus actual bleeding events was seen in the clopidogrel group, while in the ticagrelor group the gap between expected and observed bleeding events was smaller.

Chang and his colleagues are now planning to conduct a follow-up study that will examine differences in outcomes between patients similar to those enrolled in the TALOS-AMI trial who are or are not treated with the DAPT de-escalation strategy in the "real world" outside of a clinical trial setting.

Provided by American College of Cardiology