# ステント留置後の患者においてDAPTを中止することにより予後が改善する(Abstract 19-LB-19719[STOPDAPT-2] and 19-LB-20276[SMART-CHOICE])

## STOPDAPT-2:より短期間の DAPT 後に P2Y12 阻害薬単剤療法を継続することにより 1 年後の予後が改善する

## STOPDAPT-2: Shorter DAPT followed by P2Y12 inhibitor monotherapy improves outcomes at one year

ステント留置 1 か月後にアスピリン服用を中止したが P2Y12 阻害薬クロピドグレル服用を継続した患者は、併用投与を続けた患者に比べ 1 年後の予後が有意に良好であった、と American College of Cardiology's 68th Annual Scientific Session で発表された。STOPDAPT-2 トライアルでは、アスピリンの早期中止はトライアルの主要評価項目(心血管死、心筋梗塞、ステント血栓症、脳卒中および大出血の複合)の観点から優れていることが示された。また、アスピリン中止により、出血は減少し虚血性イベントは増加しなかった。もう 1 つのトライアル SMART-CHOICE において、ステント留置後 3 か月後にアスピリンを中止し P2Y12 阻害薬服用を継続した患者においても、同様の結果が得られた。

Full Text

Patients who stopped taking aspirin one month after receiving a stent but continued taking the P2Y12 inhibitor clopidogrel fared significantly better after one year compared with those who followed the standard practice of continuing both medications, according to research presented at the American College of Cardiology's 68th Annual Scientific Session. Stopping aspirin early was found to be superior in terms of the trial's primary endpoint, a composite of death from cardiovascular causes, myocardial infarction, clotting near the stent, stroke and major bleeding.

The trial sheds new light on the optimal way to balance the risk of clotting and bleeding in patients who undergo procedures to clear blocked arteries. Giving these patients antiplatelet medications that reduce the body's ability to clot blood can reduce the chance of clot-related problems such as myocardial infarctions and stroke, but these medications can also lead to uncontrolled bleeding.

The newest generation of stents release drugs that prevent new blockages from forming around the stent. While current guidelines recommend patients take aspirin and a P2Y12 inhibitor such as clopidogrel for at least 12 months after receiving a stent, a strategy known as dual antiplatelet therapy (DAPT), doctors have sought to determine whether this is the best combination of drugs to use with newer drug-eluting stents. The new trial assessed whether stopping aspirin after one month but continuing clopidogrel alone for 12 months might be a better approach.

"Standard 12-month DAPT is currently recommended by the guidelines, and one-month DAPT has not yet been implemented in daily clinical practice," said Hirotoshi Watanabe, MD, research associate at Kyoto University Graduate School of Medicine and the study's lead author. "According to our findings, one-month DAPT followed by clopidogrel monotherapy could be a good option after drug-eluting stent implantation with an advantage of fewer bleeding events."

The trial, known as STOPDAPT-2, enrolled 3,009 patients who received a drug-eluting stent at 89 medical centers in Japan. Patients who were taking oral anticoagulants, could not tolerate clopidogrel or had a history of bleeding in the brain were excluded. Half of the patients were randomly assigned to receive standard DAPT. The other half took aspirin plus clopidogrel or prasugrel (another P2Y12 inhibitor) for the first month and took clopidogrel only after that, with patients who took prasugrel initially switching to clopidogrel after the first month.

In the one-month DAPT group, aspirin was stopped at one month in 96 percent of patients, while DAPT was continued up to one year in 88 percent of patients in the standard 12-month DAPT group. Overall, stopping aspirin after one month reduced the risk of adverse events by 36 percent. After one year, 2.4 percent of patients who stopped aspirin after one month experienced the composite primary endpoint compared to 3.7 percent among those following standard DAPT.

An analysis of secondary endpoints revealed stopping aspirin after one month significantly reduced the rate of bleeding. Overall, 0.4 percent of those stopping aspirin experienced major bleeding compared to 1.5 percent among those following standard DAPT. Furthermore, stopping aspirin after one month did not increase the events related to clotting, known as ischemic events, in a secondary endpoint that included a composite of death from cardiovascular causes, heart attack, clotting around the stent or stroke.

"One-month DAPT followed by clopidogrel monotherapy as compared with standard 12-month DAPT reduced the bleeding events and did not increase the ischemic events," Watanabe said. "That lead to a net clinical benefit for both ischemic and bleeding outcomes."

One limitation of the study is that most of the participants were at low or intermediate risk for ischemic events. Watanabe said it is unknown whether the study can be extrapolated to apply in higher-risk patients. To answer this question, the researchers are continuing to enroll patients in the trial who have acute coronary syndrome, a group that is at higher risk for ischemic events.

The study received funding from Abbott Vascular Japan, Co., Ltd.

In another study at the American College of Cardiology's 68th Annual Scientific Session, patients who stopped taking aspirin three months after receiving a stent but continued taking a P2Y12 inhibitor—clopidogrel, prasugrel or ticagrelor—did not experience higher rates of death from any cause, myocardial infarction (MI) or stroke after a year compared with those receiving standard therapy. Furthermore, patients who stopped taking aspirin after three months had a significantly lower rate of bleeding.

The trial, known as SMART-CHOICE, assessed whether stopping aspirin after three months but continuing the P2Y12 inhibitor alone for 12 months would offer better results.

"Our study demonstrated that P2Y12 inhibitor monotherapy after a short duration of DAPT is a novel antiplatelet strategy balancing ischemic and bleeding risk in patients undergoing PCI," said Joo-Yong Hahn, MD, PhD, professor of medicine at Sungkyunkwan University School of Medicine in Seoul, South Korea and the study's lead author. "Even though this treatment strategy needs to be confirmed in other trials, aspirin may be discontinued in most patients receiving current-generation drug-eluting stents, especially in patients with bleeding risk or in those with stable ischemic heart disease."

The trial enrolled 2,993 patients who underwent PCI and received a drug-eluting stent at 33 medical centers in South Korea. Patients were randomly assigned to receive either standard DAPT for a year or aspirin plus a P2Y12 inhibitor for three months and continue with only the P2Y12 inhibitor for nine more months after that.

After one year, 2.9 percent of patients who stopped aspirin early experienced the primary endpoint, a composite of death from any cause, heart attack or stroke, compared to 2.5 percent among those following standard DAPT. Based on thresholds determined before the trial began, these rates indicate that stopping aspirin early was not inferior to DAPT in terms of the trial's primary endpoint.

In addition, stopping aspirin early was found to reduce the risk of bleeding by about 40 percent. Overall, 2 percent of those stopping aspirin experienced major bleeding compared to 3.4 percent among those following standard DAPT. Taken together, the net rate of all adverse clinical events (death from any cause, MI, stroke or bleeding) was not significantly different between the two groups.

A little more than three-quarters of the study participants took clopidogrel, the most common P2Y12 inhibitor, with the rest taking either prasugrel or ticagrelor. Hahn said that the trial's inclusion of different P2Y12 inhibitors distinguishes it from other trials investigating alternatives to DAPT.

"The SMART-CHOICE trial has a unique design to include all kinds of P2Y12 inhibitors, including clopidogrel, prasugrel and ticagrelor," Hahn said. "Therefore, we believe that the SMART-CHOICE trial, compared with several ongoing trials on P2Y12 inhibitor monotherapy after PCI, provides more generalizable answers to the concept of P2Y12 inhibitor monotherapy across a broad spectrum of patients receiving current-generation drug-eluting stents."

One limitation of the study is that a considerable proportion of patients in the group assigned to stop aspirin early in fact received aspirin after three months, although a more detailed analysis suggested this discrepancy did not undermine the overall findings. Another limitation is that the trial allowed patients to know which medications they had been assigned to take, rather than giving some patients a placebo.

The researchers will further analyze the data to determine whether the type of P2Y12 inhibitor used or variables reflecting patients' physiological response to the P2Y12 inhibitor may affect outcomes. In addition, they are investigating whether the risk of ischemic events varied among patients with acute coronary syndrome versus stable ischemic heart disease.

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