# 血管形成術後の抗血小板薬3剤併用は有効である

## HOST-ASSURE:血管形成術後の血栓予防において抗血小板薬3剤併用は倍用量の2剤併用と同等に有効である

## HOST-ASSURE: Three-drug regimen equal to double-dose two-drug approach in preventing clots after angioplasty

血管形成術後血栓予防薬の比較において、アジアで好まれる3剤併用療法は欧米諸国の高リスク患者に対し一般的に使用される倍用量2剤併用療法と同等に安全で有効であることが示されたとの研究結果が第61回American College of Cardiology学会で発表された。アスピリンと倍用量（150mg）クロピドグレルを用いた倍用量2剤併用療法（DDAT）は有望な抗血小板療法である。アジアにおける高リスク患者に対する3剤併用抗血小板療法（TAT）では、2剤併用抗血小板療法（DAT:アスピリンとクロピドグレル75mgの併用）にシロスタゾールを併用する。HOST-ASSUREスタディでは患者をTAT（1,879人）またはDDAT（1,876人）に無作為に割り付けた。一次エンドポイントは、血管形成術後1ヵ月以内の心血管関連死、非致死性心発作、脳卒中および重大な出血のイベント発現であった。これらのイベントの合計がTAT群では23例（1.2%）、DDAT群では27人（1.4%）であり、倍用量2剤併用療法に対する3剤併用療法の非劣性が示された。心筋梗塞はTAT群の方が少なかった（1例対5例）。副作用はDDATの方が少なかった（8例）が、TAT群の34例のうち生命を脅かしたり重篤な有害反応を来したりするものはなかった。

## Full Text

In a comparison of drugs to prevent blood clots after angioplasty, a three-drug regimen favored in Asia to increase anti-clotting effect was found to be as safe and effective as a double-dose two-drug treatment commonly used in high-risk patients in Western countries, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Angioplasty comes with a known risk of blood clots. For that reason, treatment with anti-platelet drugs such as clopidogrel is standard after angioplasty. Double-dose dual anti-platelet therapy (DDAT), using aspirin and double-dose (150 mg) clopidogrel, is a potent anti-platelet regimen for high-risk patients undergoing angioplasty. In Asia, cilostazol is added to dual anti-platelet therapy (DAT: aspirin and 75 mg of clopidogrel) in a regimen of triple anti-platelet therapy (TAT) in high-risk patients. Several studies have demonstrated that cilostazol does more than prevent platelet clumping; it also shows activity in preventing restenosis, vasodilation, protecting kidneys, and improving blood levels of cholesterol and triglycerides.

"TAT is widely used in Korea and Japan because we experienced the benefit of cilostazol in terms of major adverse cardiovascular events (MACE) after angioplasty," said Hyo-Soo Kim, MD, PhD, director of cardiac catheterization and coronary intervention at Seoul National University Hospital, Republic of Korea, and the study's principal investigator. "In the numerous clinical studies about angioplasty, we have an impression that the MACE rate is lower in Korean studies than in Western ones."

Although previous studies support the addition of cilostazol to conventional dual anti-platelet therapy, cilostazol is not familiar to many Western physicians because it was developed by a Japanese company that has neither marketed it widely outside Asia nor sponsored a large clinical trial of the drug. "Most clinical evidence supporting cilostazol's benefit comes from investigator-initiated trials like ours," Dr. Kim said. "HOST-ASSURE is the first large-scale randomized trial to directly compare the two treatment strategies and confirm the non-inferiority of TAT compared with DDAT."

The 2 x 2 factorial trial was designed to compare the two anti-platelet regimens and two types of drug-releasing stents (data to be reported in the future). Patients were randomly assigned to TAT (1,879 patients) or to DDAT (1,876 patients). All patients received 300−600 mg of clopidogrel plus 300 mg of aspirin before angioplasty with (TAT) or without (DDAT) a loading dose of 200 mg of cilostazol. In the TAT group, 100 mg of cilostazol twice daily was added to DAT for a month after the procedure; in the DDAT group, the maintenance regimen was 150 mg of clopidogrel with aspirin.

The primary endpoint was the occurrence of events including cardiovascular-related death, non-fatal heart attack, stroke and major bleeding at one month after angioplasty. That total was 23 patients (1.2 percent) in the TAT group and 27 patients (1.4 percent) in the DDAT group, demonstrating non-inferiority of the three-drug regimen compared with the double-dose two-drug treatment. The TAT group had fewer heart attacks (one patient vs. five). The DDAT group had fewer side effects (eight patients), but none of the 34 patients in the TAT group who had side effects developed life-threatening or severe adverse reactions. The most frequent side effects of cilostazol are headache and gastrointestinal trouble, and most of the side effects are reversible, Dr. Kim noted. Patients will be followed for three years.

"This study provides evidence for the already popular adjunctive use of cilostazol in clinical practice in Asia – in particular in Korea and Japan," Dr. Kim said. "If TAT is equivalent to a potent regimen such as DDAT that is used for high-risk patients, TAT would be preferred because it has additional vascular biologic benefit on top of its anti-platelet effect."

HOST-ASSURE was sponsored by the Ministry of Health and Welfare, Republic of Korea, and supported by a grant from the Innovative Research Institute for Cell Therapy, Seoul National University Hospital, and an unrestricted grant from Boston Scientific Korea. The funding sources had no role in study design, data collection or analysis. Dr. Kim has no conflict of interest with the sponsor or funders.

## ACC2012特集