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EDITORIAL COMMENT

Prasugrel Only May Be Enough After Percutaneous Coronary Intervention for Chronic Coronary Syndrome Patients*

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For more than 2 decades, dual antiplatelet therapy (DAPT), combining aspirin and a $P2Y_{12}$ receptor inhibitor, has been the cornerstone post-percutaneous coronary intervention (PCI) treatment for patients with acute coronary syndrome (ACS) as well as for those with chronic coronary syndrome (CCS), effectively reducing thrombotic risks. However, the associated bleeding risks, primarily caused by aspirin, have always been a concern, often representing a double-edged sword in clinical practice. Furthermore, the dogma of 12-month DAPT from previous randomized controlled trials (RCTs) may need to be applied differently in the current clinical setting. For example, in the past, optimal medical therapy (ie, statins) was not widely available, stents were not used, or older stent platforms were used, procedures were often performed late after diagnosis of ACS, patients with high bleeding risk were typically excluded from early RCTs, and operators were inexperienced.[1,2] In the era of first-generation drug-eluting stents (DES), the problems of restenosis and repeated target-lesion revascularization (TLR) were largely solved, but the problem of very late stent thrombosis emerged. Therefore, DAPT for 12 months or more was the standard of care after DES implantation and remained so for more than a decade.[3,4] Because of the low risk of atherothrombotic events in patients with CCS, it has been recommended in recent guidelines that DAPT can be attenuated and that a shorter duration can be maintained as opposed to guidelines for ACS. Recent guidelines recommend single-antiplatelet therapy (SAPT) following 6 months of DAPT for usual patients with CCS undergoing PCI, and even 1 month of DAPT is acceptable for patients with very high risk of life-threatening bleeding. DAPT containing potent $P2Y_{12}$ inhibitors, such as prasugrel or ticagrelor, may be considered, at least as initial therapy in patients with complex stented lesions with high risk of stent thrombosis, and even monotherapy may be useful in case of aspirin intolerance.[5,6]

Minimizing post-PCI bleeding is crucial because of its significant association with all-cause mortality and major adverse cardiovascular events. Beyond mortality linked to bleeding, cessation of antiplatelet treatment because of hemorrhagic complications can raise the risk of thrombotic incidents. In addition, anemia causes poor clinical outcomes by reducing oxygen delivery, augmenting oxygen demand through neuroendocrine stimulation, and requiring blood transfusions that lead to depletion of 2,3-diphosphoglyceric acid and nitric oxide, resulting in low tissue oxygen and vasoconstriction, which enhance platelets aggregation.[7] To reduce the bleeding risk, there have been ongoing efforts to de-escalate DAPT in many ways.[8]

Aspirin prevents ischemic events by antiplatelet effect while increasing gastrointestinal (GI) bleeding by local effects with mucosal injury by reduced mucus and bicarbonate secretion and systemic effects of prostaglandin depletion and platelet inactivation, which may be synergistic. Therefore, aspirin is less attractive when considering SAPT for de-escalation because of its less effective antithrombotic effect and significant GI bleeding risk.

Prasugrel demonstrates a faster, more consistent, and generally stronger antiplatelet action than

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clopidogrel. It remains unaffected by drug interactions or the impact of CYP2C19 loss-of-function variants,[9] so if SAPT is considered immediately after PCI, prasugrel may be an appropriate candidate.

In this issue of *JACC: Asia*, Masuda et al[10] reported the comparative analysis of the ASET (Acetyl Salicylic Elimination Trial) pilot studies. These studies were conducted separately in Brazil (ASET Brazil) and Japan (ASET Japan). ASET Brazil was conducted in 201 patients, and ASET Japan was conducted in 206 Japanese patients with CCS. They all started prasugrel monotherapy after implantation of a biodegradable-polymer platinum-chromium everolimus-eluting stent (EES), with a maintenance dose of 10 mg per day in ASET Brazil and 3.75 mg per day in ASET Japan. They summarized clinical outcomes and assessed geographic and ethnic differences in baseline demographics and procedures and concluded that prasugrel monotherapy following PCI was safe and feasible in selected low-risk patients with CCS after PCI, regardless of the ethnic and geographic differences in baseline demographic, procedures, and prasugrel dosage.

Recently, the results of STOPDAPT-3 (Short and Optimal Duration of Dual Antiplatelet Therapy After Everolimus-Eluting Cobalt-Chromium Stent-3) were presented that prasugrel monotherapy (3.75 mg per day in Japanese) after PCI with DES was not superior to DAPT for major bleeding but was noninferior for cardiovascular events in patients with ACS or high bleeding risk. However, there was an excess of any coronary revascularization (1.05% vs 0.57%; $P < 0.05$) and subacute definite or probable stent thrombosis (0.58% vs 0.17%; $P < 0.05$) in the prasugrel monotherapy group compared with the DAPT group, indicating that a strategy of de-escalation immediately post-PCI could be harmful among ACS patients.[11] In a subgroup analysis stratified by ACS and non-ACS, the no-aspirin group had a higher risk of cardiovascular events than the DAPT group in patients with ACS but not in those without ACS.

In these contexts, this report by Masuda et al[10] raises the prospect that starting with prasugrel monotherapy after PCI in patients with CCS may be a safe and effective antithrombotic strategy. We look forward to seeing this proven in future large-scale RCTs.

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