Use of dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is the key for the prevention of ischemic complications in patients with acute coronary syndromes (ACSs) as well as in those undergoing percutaneous coronary intervention (PCI). However, DAPT also increases the risk of bleeding complications, which have shown a similar prognostic impact compared to that of thrombotic events. Especially, in ACS patients, since current guideline recommends at least 12 months of DAPT duration with potent P2Y12 inhibitors (ticagrelor or prasugrel), the bleeding risk is much higher than in non-ACS patients adopting shorter DAPT duration with clopidogrel. Therefore, finding optimal antiplatelet strategies without increase in bleeding is the cornerstone in the management of DAPT following PCI. The evolved stent performance and drug delivery mechanism of current generation drug-eluting stent (DES) compared to early generation DES, which significantly reduced the rate of ischemic events, provided the stage for investigating various de-escalation antiplatelet strategies, especially in patients at high bleeding risk (HBR).

Various de-escalation approaches of antiplatelet treatment to find an optimal strategy for balancing ischemic and bleeding risks in patients with ACS have been tested, including potent P2Y12 inhibitor monotherapy following short DAPT, dose reduction of a potent P2Y12 inhibitor, and guided or unguided switching from potent P2Y12 inhibitors to clopidogrel. Almost all these de-escalation modalities consistently showed lower bleeding and comparable ischemic event rate compared with standard DAPT with potent P2Y12 inhibitors. In general, approximately 40% of patients undergoing PCI have HBR conditions. However, patients at HBR are usually excluded or under-represented in clinical trials evaluating antiplatelet therapy in PCI. Especially, management of antithrombotic treatment in patients at HBR and high ischemic risk (e.g., ACS, complex PCI etc…) simultaneously, so called ‘bi-risk’, has represented a difficult challenge.

There are some data regarding de-escalation of antiplatelet therapy in patients at bi-risk. Recently published MASTER DAPT study investigated 1 month of DAPT as compared with a longer course of DAPT with respect to clinical outcomes in HBR patients undergoing PCI. The authors have reported that 1 month of DAPT was noninferior to the continuation of therapy for at least 2 additional months with regard to the incidence of net adverse clinical
from the corresponding author(s) upon reasonable request.

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In this issue of the Korean Circulation Journal published the post-hoc analysis of TICO (The Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus-eluting Stent for Acute Coronary Syndrome) trial in patients at HBR. In this HBR subgroup analysis of TICO trial, the overall population (n=2,980) was classified into HBR and non-HBR groups according to the ARC-HBR criteria (HBR patients, n=453 [15.2%]) and PRECISE-DAPT score (≥25) (HBR patients, n=504 [16.9%]). Consistent with the main study results, ticagrelor monotherapy following 3-month DAPT was associated with lower rate of NACE and major bleeding than ticagrelor based 12-month DAPT in both HBR and non-HBR groups. And, similar to the result of TWILIGHT-HBR, HBR patients showed higher rate of NACE, major bleeding and ischemic events than non-HBR patients regardless of two HBR definitions. These findings may provide some clinical evidence of short DAPT followed by potent P2Y12 inhibitor monotherapy in ACS patients at HBR, that is the patients who have ‘bi-risk.’ However, this post-hoc analysis have some limitations. There is an issue of underpower. In the current study, the proportion of HBR patients was only 15–16% of overall population. Moreover, the proportion of HBR patients maintaining ticagrelor monotherapy was just 7%. Thus, due to the small sample size of HBR patients and low incidence of primary endpoint events, it is hard to draw confirmative conclusions on clinical benefit of ticagrelor monotherapy following short DAPT in ACS patients with HBR. This may be partly by the exclusion criteria of TICO trial, which excluded patients with increased risk of bleeding. In general, HBR patients comprise about 40% of PCI population in a real-world setting. Therefore, caution is needed in applying this result into our daily clinical practice and well-designed dedicated trials enrolling patients with both ischemic and bleeding risk simultaneously are essential.

**REMAINING ISSUES**

Regarding potent P2Y12 inhibitor monotherapy following short DAPT in ACS population, while there has been an abundant data using ticagrelor, there is a paucity of data using
prasugrel. However, theoretically, since prasugrel have similar antiplatelet potency to ticagrelor, we may postulate that prasugrel also would be clinically efficacious. Next issues are how long we should continue potent P2Y12 inhibitor monotherapy and how to change potent P2Y12 inhibitors to other agents in ACS population. We have several options switching to low dose of ticagrelor or prasugrel, or clopidogrel or aspirin. In order to decide optimal antithrombotic strategy in ‘bi-risk’ patients, we need a very careful tailored approach considering patient’s comorbidities, lesion and procedure complexity all together.

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