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Individualized intensified antiplatelet therapy based on platelet reactivity testing reduces the incidence of cardiovascular events in patients undergoing percutaneous coronary intervention

To the Editor,

We read with great interest the article by Jeong et al. (1) titled "Impact of high on-treatment platelet reactivity on long-term clinical events in AMI patients: a fact or mirage?" published in *Anatol J Cardiol* 2016 Nov 16. Epub ahead of print. The authors stated that it is unclear whether platelet function testing (PFT)-based treatment modification influences the outcomes of the antiplatelet therapy. They mentioned that recent prospective randomized trials using the current PFT did not demonstrate any clinical benefit (1). However, is this true?

We performed a thorough search of the literature that revealed a substantial number of recent studies demonstrating the safety and efficacy of PFT guidance in patients undergoing percutaneous coronary intervention (PCI) (2-5). A recent meta-analysis that included 13 clinical studies and a total of 7290 patients concluded that the PFT-based intensified protocol is associated with a significant reduction in major adverse cardiovascular events, stent thrombosis, cardiovascular death, and target vessel revascularization without increasing the risk of major bleeding (2).

The authors claimed that there is little evidence to support the VerifyNow assay and Multiplate Analyzer as clinical, reliable PFT systems (1). A study involving 671 myocardial infarction patients treated with PCI in the TRANSLATE-ACS Registry who had undergone VerifyNow PFT concluded that intensification of the antiplatelet therapy is associated with low risk of ischemic events at 1 year among patients with high platelet reactivity (3). Aradi et al. (4) in their study involving 741 patients verified the clinical impact of treatment with prasugrel in patients with acute coronary syndromes who have high platelet reactivity using PFT with the Multiplate Analyzer.

Furthermore, current European Society of Cardiology (ESC) guidelines have clearly stated that PFT should be considered in specific high-risk situations (compliance issue, history of stent thrombosis, suspicion of resistance, and high bleeding risk) and has a Class IIb indication (5). In the Assessment of Dual Anti-Platelet Therapy with Drug-Eluting Stents trial, the largest observational PFT study conducted to date, approximately 50% of 30-day post-PCI stent thrombosis is attributable to high platelet reactivity (5). Based on the currently available evidence, the ESC guidelines recommend the Verify Now assay, the Multiplate Analyzer, and the VASP assay for monitoring platelet inhibition during P2Y12 inhibitors administration (5).

The authors refer to studies that have methodological flaws, such as the periprocedural use of glycoprotein IIb/IIIa receptor inhibitors and the use of high-dose clopidogrel instead of potent P2Y12 inhibitors, such as prasugrel and ticagrelor, to intensify platelet inhibition; these studies do not include patients at high risk of stent thrombosis.

Several prospective observational studies involving large patient populations have demonstrated that high platelet reactivity is an independent and strong predictor of post-PCI ischemic events. In patients with high platelet reactivity who are undergoing PCI, the intensification of dual antiplatelet therapy using PFT reduces the incidence of ischemic events without increasing the risk of major bleeding.

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Author's Reply

To the Editor,

We thank Zhou et al. (1) for their interest in our previous editorial entitled "Impact of high on-treatment platelet reactivity on long-term clinical events in AMI patients: a fact or mirage?" published in *Anatol J Cardiol* 2016 Nov 16. Epub ahead of print.

Based on their recent meta-analysis (2), Zhou et al. (1) have pointed clinical usefulness of phenotype (platelet function test)-guided antiplatelet therapy to maximize clinical efficacy and safety following percutaneous coronary intervention (PCI). Understandably, our group generally agrees with the concept of therapeutic window between high and low platelet reactivity (HPR and LPR, respectively) during P2Y12 inhibitor administration. For the past 10 years, we also have performed numerous clinical studies to reveal strategies against the imminent risks related with platelet reactivity.

In 2012, Jeong et al. (3) firstly suggested the concept of "East Asian Paradox." Despite low response to clopidogrel in East Asians (mainly due to high prevalence of the cytochrome P450 2C19 loss-of-function allele), East Asian patients have a similar or lower rate of ischemic events after PCI compared with that in Caucasian patients, suggesting the different therapeutic window of platelet reactivity in East Asian patients. More importantly, active metabolite concentration during potent P2Y12 inhibitor (e.g., ticagrelor and prasugrel) appeared greater in East Asian vs. Caucasian population (~40%) (4), suggesting that their reduced-dose regimen could be more optimal for East Asian patients. Therefore, we need to be cautious in applying the clinical data and guideline originated from Western patients for East Asian subjects.

How can we understand this mystery? Maybe the concept of platelet reactivity itself could not explain the whole spectrum of this unique phenomenon. Our group has confidence in the concept of "vulnerable blood," including the whole blood components related to thrombogenicity. Although we believe that platelets are the main factors for arterial thrombosis, there is much evidence to support clinical importance of other blood components (e.g., cholesterol, hormone, inflammation, coagulation, and fibrinolytic system). Inflammation and thrombin cascades may

play crucial roles in the development of atherosclerosis and thrombosis. Intriguingly, the levels of these biomarkers in East Asian population seem lower than those in Caucasian population (5). When a patient has less corrupt "vulnerable blood," the impact of HPR may be limited and the hazard of LPR would be prominent after PCI.

Life is beautiful because it is not an open book. In the same manner, in vivo blood is mostly safe because it is very complicated and interactive. Although the concept of platelet reactivity was a big step forward, we now need to have more prudent and comprehensive approach to cover the real aspect of "vulnerable blood."

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Usefulness of left atrial speckle-tracking echocardiography in patients with atrial fibrillation

To the Editor,

We read the article entitled "Association between left atrial function assessed by speckle-tracking echocardiography and the presence of left atrial appendage thrombus in patients with