

Impact of high on-treatment platelet reactivity on long-term clinical events in AMI patients: a fact or mirage?

Accumulating evidences have indicated the cut-offs for high on-treatment platelet reactivity (HPR) and low on-treatment platelet reactivity (LPR) that can be used in future trials for personalized antiplatelet therapy to balance clinical efficacy and safety (1, 2). However, recent prospective randomized trials using the current platelet function testing (PFT) did not demonstrate any clinical benefit (3–5). Consequently, it is unclear whether PFT-based treatment modification influences the outcomes of the therapy.

Compared with patients with stable angina, platelet activation can be more closely related with thrombotic events among those with acute myocardial infarction (AMI) in the thrombogenic milieu (6). Furthermore, Jakl et al. (7) reported another evidence to show the impact of HPR on clinical events in AMI patients. This report may be of importance because it reveals the impact of HPR on longest-term (e.g., 5-year) adverse events in AMI patients using the readily available Multiplate® analyzer (8).

There would be a long and rough journey before personalized antiplatelet therapy can be regarded as a standard therapy to maximize clinical benefit (1, 2). When considering the results of Jakl et al. from a critical point of view, several issues need to be considered. First, there are limited concordances between the criteria of HPR (and LPR) and PFTs (1, 9, 10). Although point-of-care PFT systems (e.g., VerifyNow assay and Multiplate® analyzer) are much better for clinical simplicity than other PFT systems (e.g., light transmittance aggregometry and VASP assay), a few evidences to support their superiority pertaining to clinical reliability exist (1, 2). In addition, whether ADP- vs. multiple agonist-mediated PFT assay can more precisely predict the risk of ischemia and bleeding events might be another issue (11). Jakl et al. (7) suggested that HPR to arachidonic acid only was more predictive for ischemic events than HPR to both ADP and arachidonic acid. Second, the level of platelet reactivity may be variable according to the disease activity or phase. In particular, platelet reactivity can be much changeful during the early period among AMI patients (loading vs. maintenance dose and acute vs. subacute phase), which implicate the potential of change for the criteria of HPR (and LPR) over time (1, 2). Jakl et al. (7) measured Multiplate® analyzer mostly before discharge. Whether HPR (to ADP or arachidonic acid) measured during dual antiplatelet therapy can be a consistent risk factor even after discontinuation of P2Y12 receptor inhibitor (or aspi-

rin) can be another issue. Jakl et al. (7) did not show any data for adherence to the antiplatelet regimen. Third, the cut-off of HPR (and LPR) can be different according to the cohort characteristics (12) because its contribution toward thrombus formation may vary according to its level of interaction with other thrombogenic components (e.g., inflammation, coagulation activity, shear stress, and endothelial dysfunction). Compared with the western population, East Asian population has a higher level of HPR (and LPR) cutoffs among AMI patients (13, 14); East Asians may have a low tendency toward developing thrombophilia and a higher risk of bleeding. Without performing the receiver operating characteristic curve analysis, Jakl et al. (7) evaluated the clinical impact of predefined HPR cutoff on ischemic events. Finally, only platelet reactivity cannot explain the whole spectrum of the occurrence of thrombotic events. Conditions predisposing to thrombus formation may include abnormal vessel wall (vulnerable plaque), abnormal blood flow, and abnormal blood constituents (vulnerable blood). Jakl et al. (7) did not suggest detailed data regarding the lesion characteristics, stent profile, and important biochemical measurements. Risk prediction models or scoring systems, including important clinical or laboratory variables, can be more reliable for predicting clinical events and consequently help in the early introduction of personalized therapy.

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