P2Y12 reaction units

VerifyNow PRU values that correspond to platelet hyporesponsive or hyper-response to dual antiplatelet therapy are associated with a higher risk of thrombotic and hemorrhagic events, respectively. Thus, the PRU value may offer some predictive value for these events.

PRU is a useful tool as a predictor of peri-procedural TE or HE on neurointervention. PRU has a threshold effect of cut-off value to predict the peri-procedural TE. Modified DAPT or TAPT to prevent TE in clopidogrel hypo-responders could not reduce the incidence of TE. We should investigate the further research about modification of regiment on neurointervention [1)].

Kim et al. from the Asan Medical Center retrospectively analyzed the data of 427 patients with unruptured intracranial aneurysms who underwent endovascular treatment between July 2011 and June 2014. When clopidogrel resistance was confirmed via platelet reactivity unit (PRU) assay after dual antiplatelet therapy (aspirin plus clopidogrel) administration for 5 days, triple antiplatelet therapy with cilostazol was administered (Group I, 274 patients). The other group was placed on standard dual antiplatelet therapy (Group II, 153 patients). All patients underwent magnetic resonance diffusion-weighted imaging within 2 days after endovascular coiling.

No significant associations with the occurrence of a thromboembolic event and microembolic event were found between the groups. The occurrence of thromboembolic and microembolic events showed no statistical difference between groups I and II ($p = 0.725$ for thromboembolic events and $p = 0.109$ for microembolic events). Also, the PRU value and the occurrence of microembolic events, using a PRU cutoff value of 240, showed no statistical difference ($p = 0.114$ in group I and 0.064 in group II). There was significant increase in microembolic events after the use of a stent-assisted endovascular procedure. As the PRU value increased, there was a trend toward an increase in the mean number of microembolic lesions without statistical significance.

Even though there is a presumed anti-thromboembolic effect for clopidogrel resistance in other literature, the clinical efficacy of adjustment of additional cilostazol for endovascular coiling of unruptured aneurysms may be limited due to the unspecified cutoff value of the PRU assay for evaluating the resistance [2)].

In patients undergoing percutaneous coronary intervention (PCI) with a stent, high on-treatment platelet reactivity may be associated with an increased risk of stroke. This post hoc analysis of the PENDULUM registry compared the risk of post-PCI stroke according to on-treatment P2Y12 reaction unit (PRU) values. Patients aged ≥ 20 years who underwent PCI were stratified by baseline PRU (at 12 and 48 h post-PCI) as either high (HPR, > 208), optimal (OPR, > 85 to ≤ 208), or low on-treatment platelet reactivity (LPR, ≤ 85). The incidences of non-fatal ischemic and non-ischemic stroke through to 12 months post-PCI were recorded. Almost all enrolled patients (6102/6267 [97.4%]) had a risk factor for ischemic stroke, and most were receiving dual antiplatelet therapy. Of the 5906 patients with PRU data (HPR, n = 2227; OPR, n = 3002; LPR, n = 677), 47 had a non-fatal stroke post-PCI (cumulative incidence: 0.68%, ischemic; 0.18%, non-ischemic stroke). Patients with a non-fatal ischemic stroke event had statistically significantly higher post-PCI PRU values versus those without an event ($P = 0.037$). The incidence of non-fatal non-ischemic stroke was not related to PRU value. When the patients were stratified by PRU ≤ 153 versus > 153 at 12-48 h post-PCI, a significant

difference was observed in the cumulative incidence of non-fatal stroke at 12 months (P = 0.044). We found that patients with ischemic stroke tended to have higher PRU values at 12-48 h after PCI versus those without ischemic stroke.Clinical trial registration:UMIN000020332 [3].

---

findings from a study suggest that the safe PRU range for patients receiving ticagrelor should be shifted to 0-100, which is lower than that of clopidogrel, thought to be 60-210. Further validation of the optimal PRU range for patients receiving ticagrelor is necessary [4].

1)
Kim HJ, Oh JS, Park SQ, Yoon SM, Ahn HS, Kim BT. The Efficacy of P2Y12 Reactive Unit to Predict the Periprocedural Thromboembolic and Hemorrhagic Complications According to Clopidogrel Responsiveness and Safety of Modification of Dual Antiplatelet Therapy : A Meta-Analysis. J Korean Neurosurg Soc. 2020 Sep;63(5):539-549. doi: 10.3340/jkns.2019.0082. Epub 2019 Oct 30. PMID: 31661948; PMCID: PMC7477146.
2)
Kim GJ, Heo Y, Moon EJ, Park W, Ahn JS, Lee DH, Park JC. Thromboembolic events during endovascular coiling for unruptured intracranial aneurysms: Clinical significance of platelet reactivity unit and adjunctive cilostazol. Clin Neurol Neurosurg. 2022 Jan 15;213:107133. doi: 10.1016/j.clineuro.2022.107133. Epub ahead of print. PMID: 35065532.
3)
Matsumaru Y, Kitazono T, Kadota K, Nakao K, Nakagawa Y, Shite J, Yokoi H, Kozuma K, Tanabe K, Akasaka T, Shinke T, Ueno T, Hirayama A, Uemura S, Kuroda T, Takita A, Harada A, Iijima R, Murakami Y, Saito S, Nakamura M. Relationship between platelet aggregation and stroke risk after percutaneous coronary intervention: a PENDULUM analysis. Heart Vessels. 2022 Jan 1. doi: 10.1007/s00380-021-02003-w. Epub ahead of print. PMID: 34973085.
4)
Bohan CO, Wirtz MM, Hendrix P, Goren O, Schirmer CM, Islak C, Grassi DM, Dalal S, Weiner G, Griessenauer CJ. Utility of P2Y12 Reactive Unit Assessment on Ticagrelor in Cerebral Aneurysms Treated with Intracranial Stenting and Flow Diversion: Cohort Study and Case Report From Two Neurovascular Centers. World Neurosurg. 2020 Oct;142:e445-e452. doi: 10.1016/j.wneu.2020.07.052. Epub 2020 Jul 17. PMID: 32688033.