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Bleeding and stent thrombosis with $P2Y_{12}$-inhibitors: a collaborative analysis on the role of platelet reactivity for risk stratification after PCI

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Aims: Balancing bleeding events and thrombotic complications are crucial in patients undergoing PCI and receiving dual antiplatelet therapy. The potential role of platelet function testing in risk stratification after PCI is unknown. We sought to determine the prognostic value of low (LPR), optimal (OPR), or high platelet reactivity (HPR) during $P2Y_{12}$-inhibitor treatment by applying standardised cutoff criteria for recommended platelet function assays (VerifyNOW, Multiplate and VASP) in patients undergoing PCI.

Methods and results: Authors of studies published before December 2014, reporting associations between platelet reactivity, ST and major bleeding were contacted for a collaborative analysis using *a priori* defined, uniform cutoff values for standardised platelet function assays. Based on recommendations of prior consensus documents and the best evidence available (exploratory studies), LPR-OPR-HPR categories were defined as <95, 95-208 and >208 PRU for VerifyNow, <19, 19-46, and >46 U for the Multiplate analyser and <16, 16-50 and >50% for VASP assay, respectively. Seventeen studies including 20,841 patients were pooled for the analysis; 97% were treated with clopidogrel and 3% with prasugrel. Patients with HPR had a significantly higher risk for ST (RR: 2.73, 95% CI: 2.03-3.69, p<0.00001) yet a slightly lower risk for bleeding (RR: 0.84, 95% CI: 0.71-0.99, p=0.04) compared to those with OPR. In contrast, patients with LPR had a significantly higher risk for bleeding (RR: 1.74, 95% CI: 1.47-2.06, p<0.0001), but identical risk for ST (RR: 1.06 95% CI: 0.68-1.05, p=0.85) as those with OPR. Mortality was significantly higher in patients with HPR (RR: 1.54 95% CI: 1.22-1.94, p<0.0002), but was similar between LPR and OPR patients (RR: 1.03 95% CI: 0.76-1.40 p=0.85). Validation cohorts confirmed the results suggested by exploratory studies.

Conclusions: Assessing platelet reactivity during $P2Y_{12}$-inhibitor treatment with the herein-validated cutoff values may help stratifying PCI-treated patients to higher risk for mortality and ST (HPR) or an elevated risk for bleeding (LPR).