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CLOPIDOGREL RESPONSE VARIABILITY AND ITS CORRELATION WITH RECURRENT CARDIOVASCULAR EVENTS IN CHINESE PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Objective The present study was designed to explore response variability and its correlation with recurrent cardiovascular events in Chinese patients undergoing Percutaneous coronary intervention (PCI).

Methods Platelet aggregation (5 and 20 μmol/l, ADP) and the expression of CD 62p (P- selectin) and CD 42b (GP Ib) were measured at baseline, at 12 h, and at 36 h after clopidogrel loading dose in 111 consecutive Chinese patients undergoing PCI. Clopidogrel responsiveness was defined according to the degree of inhibition of platelet function (platelet aggregation and P-selectin expression) after clopidogrel administration compared with the baseline values (before clopidogrel), IPA<10% (clopidogrel non-responders), 10% ≤30% (responders). Patients were followed up in 1, 3, 6, 12 months after PCI. The study end points was defined recurrent cardiovascular events (recurrent CV: cardiovascular death, stent thrombosis, ischaemic stroke, ACS), readmission, bleeding events.

Results There was marked interindividual variability in drug response, as measured by platelet aggregation and P-selectin expression. The ratios of the non-responders at 12 and 36 h were 32% (35/109) and 19% (21/109), respectively, by 5 μmol/l ADP; 38% (41/109) and 28% (31/109)by 20 μmol/l ADP; and 27% (29/109) and 17% (19/109) by P-selectin expression. The maximal aggregation rates stimulated by 5 μmol/l ADP of non-responders were significantly higher compared with those of the responders (57.53±14.24% vs 33.91±10.79, p<0.0001) at 12 h and at 36 h (48.65±15.46 vs 30.31±16.04, p<0.0001). During the 12-month follow-up, 21(19.63%) patients recurrent cavascular events occurred: 5 deaths (6.47%), 2 ischaemic stroke (1.87%), 14(19.63%)ACS. Cumulative recurrent CV in non-responders was significantly higher than responders in 3 months (p=0.005), 6 months (p=0.002), 12 months (p<0.0001). Multivariable Cox regression analysis, including pertinent covariables, confirmed individual responsiveness variability to clopidogrel as a significant independent predictor of 12-month recurrent CV. Non-responders carried a 24.28-fold risk (95% CI 3.05 to 193.41, p=0.003) compared with responders. Low responders carried 11.95-fold risk (95% CI 3.08 to 178.46, p=0.002) compared with responders. During the 12-month follow-up, 61(57.01%) patients occurred readmission, non-responders had a higher incidence of readmission (p=0.01) than responders. The bleeding scores in responders were significantly higher than non-responders during 3 (p=0.026), 6 (p=0.040), 12 (p=0.031) months follow-up by Bleed Score classification.

Conclusion The antiplatelet effectiveness of clopidogrel has a wide interindividual variation among Chinese patients undergoing PCI. Non-responders' IPA after clopidogrel is higher than that of responders. Individual responsiveness variability to clopidogrel is a significant independent predictor to recurrent cardiovascular events, non-responders and low responders to clopidogrel have higher risk for recurrent cardiovascular events than responders.