The optimal threshold of high post-treatment platelet reactivity could be defined by a point-of-care VerifyNow P2Y12 assay

We read with great interest the study by Price et al.1 which verifies that high post-treatment platelet reactivity (HPPR) measured with a point-of-care VerifyNow assay (Accumetrics Inc., San Diego, CA, USA) is associated with post-discharge events after percutaneous coronary intervention (PCI) with drug-eluting stent (DES), including stent thrombosis. To the best of our knowledge, this is the first study to identify a threshold of HPPR of VerifyNow based on the clinical outcomes.

Recently, a number of studies have demonstrated that clopidogrel non-responsiveness proven in the laboratory testing, i.e. HPPR, has been associated with an increased risk for cardiovascular events.2 Light transmittance aggregometry (LTA) is the gold standard test to determine the clopidogrel responsiveness. However, the abundant demands of LTA make it difficult to utilize in daily practice. VerifyNow was developed as a point-of-care assay on the day of PCI. It might suggest a subclinical coronary intervention: is the current antiplatelet therapy adequate? J Am Coll Cardiol 2007;49:657–666.


References


Responsiveness with VerifyNow assay—Impact on Safety (GRAVITAS) trial (Clinicaltrials.gov NCT00645918) reports a '%' inhibition by comparing the ratio of ADP-induced reactivity with iso-TRAP-induced reactivity, this was not available because the assay device used in a portion of our study did not contain the iso-TRAP channel required for this calculation (but did have the same ADP-channel). However, from a pathophysiologic standpoint, we believe that post-treatment reactivity is a better measure of risk. Indeed, the ‘response’ toclopidogrel as measured by percent inhibition may overestimate the risk of stent thrombosis in non-responders and underestimate the risk of stent thrombosis in responders. This is because patients with low pre-treatment reactivity who demonstrate only a small percentage inhibition may be categorized as ‘non-responders’ despite persistent low reactivity. Conversely, patients with very high pre-treatment reactivity who have a large percentage inhibition may be categorized as ‘responders’ but continue to have high post-treatment reactivity.2

Dr Jeong and colleagues provide important data regarding the relationship between platelet reactivity measured by the VerifyNow device and light transmittance aggregometry (LTA). They demonstrate that our ‘optimal’ cut-off for high HPPR with the VerifyNow P2Y12 assay that we identified using the receiver—operator characteristic curve analysis is consistent with previous, operational definitions of HPPR proposed by investigators using LTA. Despite the growing body of data that support the clinical significance of inter-individual response variability, the clinical implication of any definition of HPPR, including our own, must be verified in much larger, prospective studies. Moreover, the appropriate management of patients with HPPR is unknown. The Gauging Responsiveness with A VerifyNow assay: Impact on Thrombosis And Safety (GRAVITAS) trial (Clinicaltrials.gov identifier NCT00645918)—a randomized, placebo-controlled study which is examining whether an increased clopidogrel maintenance dose in patients with HPPR reduces thrombotic events in patients undergoing drug-eluting stent implantation—may help answer this question.

References

Matthew J. Price
Division of Cardiovascular Diseases
Scripps Clinic,
10666 North Torrey Pines Road
Maildrop 51056
La Jolla CA 92037
USA
Tel: +1 858 554 5032
Fax: +1 858 554 6883
Email: price.matthew@scrippshealth.org