LETTERS TO THE EDITOR

Platelet Reactivity Is Preferred Over Genotyping in Monitoring Efficacy of Antiplatelet Therapy

We read with great interest the report by Viviani Anselmi et al. (1) on the predictability of platelet reactivity as compared with gene polymorphism in patients undergoing elective percutaneous coronary intervention (PCI). The authors conclude that CYP2C19 metabolizer status independently predicts major adverse cardiac events, whereas platelet reactivity is only an independent predictor in high-risk patients.

Notwithstanding the well-performed and large study (1), we are puzzled by these results. Because the underlying hypothesis of the present study is that an inferior response to thienopyridines is associated with (recurrent) ischemic events, the question is whether genotyping or phenotyping is preferred in identifying patients at risk. Phenotyping (platelet reactivity as assessed by the VerifyNow test) has been explored in a large number of observational studies as well as in the pharmacodynamics analyses of several randomized clinical trials. In contrast to the findings of the present study, the bulk of these data support the supposition that among patients undergoing PCI treated with clopidogrel or prasugrel, higher values of platelet reactivity units are associated with ischemic events (2,3). In addition, platelet reactivity as assessed by the VerifyNow test is correlated with the active metabolite of clopidogrel (4). Furthermore, in the POPular (Do Platelet Function Assays Predict Clinical Outcomes in clopidogrel pretreated patients undergoing elective PCI) (the POPular Study) (2), a significant correlation between (high) on-treatment platelet reactivity and CYP2C19 metabolizer status has been established (5). This is in line with a large meta-analysis on CYP2C19 genotyping and outcome in clopidogrel-treated patients, which demonstrated an association between CYP2C19 genotype and on-treatment platelet reactivity but lacked proof of a significant association of genotype with cardiovascular events (6). An argument in favor of genotyping is that it is stable over time, whereas platelet reactivity is not, because it is influenced by multiple clinical determinants as well as laboratory parameters and comedication (7). As a result of variable baseline platelet reactivity, a response that is stable over time and equal among individuals can result in a broad range of on-treatment platelet reactivity levels (8). Therefore, we consider monitoring platelet reactivity a more appropriate approach of monitoring antiplatelet therapy.

The results of the current study point precisely in the opposite direction, and we are curious how the authors explain these differences and what their findings imply for daily clinical practice.

Nicoline J. Breet, MD, PhD
*Jurrien M. ten Berg, MD, PhD
*Department of Cardiology
St. Antonius Hospital

P.O. Box 2500
3435 CM Nieuwegein
the Netherlands
E-mail: j.ten.berg@antoniusziekenhuis.nl

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References


Reply

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We thank Drs. Breet and ten Berg for their interest in our paper (1). When we designed our study, we aimed to confirm and expand previous observations demonstrating the clinical usefulness of clopidogrel-pathway genotyping and on-treatment platelet residual (OTR) testing in predicting major adverse cardiac events (MACE) in patients with stable coronary artery disease (CAD) receiving drug-eluting stents (DES) and under dual antiplatelet (clopidogrel plus aspirin) therapy. Our results confirmed that CYP2C19 metabolizer status is an independent predictor of MACE after DES implantation and can be used for prognostication in all stable CAD patients. In contrast, high OTR, as assessed with the

*Corresponding author.