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Acute Coronary Syndromes

NO ASSOCIATION OF PARAOXONASE-1 Q192R AND THROMBOTIC EVENTS DURING DUAL ANTI-PLATELET THERAPY IN PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION

ACC Oral Contributions

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Background: Platelet inhibition during clopidogrel treatment is known to be influenced by genetic variation, especially by reduced function alleles of cytochrome P450 (CYP) 2C19. However, recent data suggests that paraoxonase-1 (PON1) Q192R, and not CYP2C19, is the major contributor to the variability in treatment response. The aim of this study was to assess the influence of PON1 Q192R on thrombotic events in patients treated with dual antiplatelet therapy after primary percutaneous coronary intervention (PCI).

Methods: Patients with acute myocardial infarction (AMI) presenting in the Leiden University Medical Center between 2004 and 2010 were treated according to the standardized guideline-based MISSION protocol. All patients (n=1,245) underwent a primary PCI and received dual antiplatelet therapy with aspirin and clopidogrel. Thrombotic events (AMI, stent thrombosis and cardiac death) were recorded during the first year after the index event. PON1 Q192R (rs662) was genotyped using a TaqMan assay (Applied Biosystems). CYP2C19*2 (rs4244285) was genotyped using MassArray platform (Sequenom). Associations were tested with Cox regression analysis.

Results: During follow up, 55 patients (4.4%) suffered from a recurrent thrombotic event during dual antiplatelet therapy. PON1 Q192R genotype was not associated with the combined endpoint, hazard ratio 0.74 (95% CI 0.47-1.16), $p=0.19$. Also with the separate endpoints no association was found. In contrast, CYP2C19*2 genotype was a strong predictor of outcome, especially in a recessive model, hazard ratio 2.2 (95% CI 1.43-3.33), $p<0.001$.

Conclusions: PON1 Q192R genotype was not associated with recurrent thrombotic events in patients with AMI infarction undergoing primary PCI and treated with dual antiplatelet therapy, whereas CYP2C19*2*2 carriers did have an increased risk of antiplatelet treatment failure.