No association of paraoxonase-1 Q192R genotypes with platelet response to clopidogrel and risk of stent thrombosis after coronary stenting.

In clopidogrel-treated patients undergoing coronary stenting, high on-treatment platelet reactivity was linked to a higher risk of stent thrombosis (ST). Platelet response to clopidogrel is significantly influenced by genetic factors. Recently published findings showed a highly significant impact of a common polymorphism (Q192R) within the paraoxonase-1 (PON1) gene on clopidogrel treatment efficacy but no influence of the CYP2C19*2 genetic variant as previously demonstrated. The aim of this study was to assess the impact of the PON1 Q192R genotype in parallel to that of CYP2C19*2 on the antiplatelet effect of clopidogrel and the risk of ST in clopidogrel-treated patients. In 1524 patients undergoing percutaneous coronary intervention, ADP-induced platelet aggregation was assessed in relation to PON1 Q192R and CYP2C19*2 genotypes. The clinical impact of genetic variants was investigated by comparing genotype frequencies of both genetic variants in a registry of 127 cases with early ST vs. an early ST-free control cohort (n = 1439). For PON1 Q192R genotypes, platelet aggregation values were similar across all genotype groups (P = 0.65). For CYP2C19*2 genotypes, significantly higher aggregation values were found in CYP2C19 wt/*2 and *2/*2 patients when compared with wt/wt allele carriers (P< 0.0001).
Comparing genotype frequencies between ST cases and controls, no differences were observed for PON1 Q192R genotype distributions (P = 0.23), whereas the genotype distribution differed for CYP2C19*2 genotypes (P = 0.019). The PON1 Q192R genotype did not influence platelet response to clopidogrel or the risk of ST in clopidogrel-treated patients, whereas the CYP2C19*2 genotype impacted on both antiplatelet effect of clopidogrel and risk of coronary ST.