Cytochrome 2C19*17 allelic variant, platelet aggregation, bleeding events, and stent thrombosis in clopidogrel-treated patients with coronary stent placement.

BACKGROUND: The cytochrome P450 (CYP) 2C19 isoenzyme plays an important role in clopidogrel metabolism. A recently explored CYP2C19*17 allelic variant has been linked to increased transcriptional activity, resulting in extensive metabolization of CYP2C19 substrates, which may lead to an enhanced platelet response to clopidogrel treatment. The aim of this study was to assess the impact of CYP2C19*17 on ADP-induced platelet aggregation, the risk of bleeding, and stent thrombosis in clopidogrel-treated patients undergoing percutaneous coronary intervention. METHODS AND RESULTS: The study population included 1524 patients undergoing percutaneous coronary intervention after pretreatment with 600 mg clopidogrel. Genotypes were determined with a TaqMan assay. ADP-induced platelet aggregation was assessed on a Multiplate analyzer. The primary clinical safety end point was the 30-day incidence of bleeding defined according to Thrombolysis in Myocardial Infarction criteria, and the primary clinical efficacy end point was the 30-day incidence of stent thrombosis. For both heterozygous (*wt/*17; n=546) and homozygous (*17/*17; n=76) allele carriers, significantly lower ADP-induced platelet aggregation values were found compared with wild-type
homozygotes (*wt/*wt; n=902; P=0.039 and P=0.008, respectively). CYP2C19*17 allele carriage was significantly associated with an increased risk of bleeding; the highest risk was observed for CYP2C19*17 homozygous patients (P=0.01, chi(2) test for trend). Multivariate analysis confirmed the independent association of CYP2C19*17 allele carriage with platelet aggregation values (P<0.001) and the occurrence of bleeding (P=0.006). No significant influence of CYP2C19*17 on the occurrence of stent thrombosis was found (P=0.79). CONCLUSIONS: CYP2C19*17 carrier status is significantly associated with enhanced response to clopidogrel and an increased risk of bleeding.