No association of ABCB1 C3435T genotype with clopidogrel response or risk of stent thrombosis in patients undergoing coronary stenting.

Abstract:

The prodrug clopidogrel requires intestinal absorption by the efflux pump P-glycoprotein MDR1 (multidrug resistant-1), encoded by the ABCB1 gene. Prior studies suggested that a common and functional genetic variant (C3435T, rs1045642) within ABCB1 influences clopidogrel treatment efficacy; however, existing data are highly inconsistent, because other studies failed to replicate this postulated association. Thus, the aim of this study was to assess the association of ABCB1 C3435T genotypes with the antiplatelet efficacy of clopidogrel and the risk of stent thrombosis (ST) in large cohorts of clopidogrel-treated patients undergoing percutaneous coronary intervention. DNA samples from 1524 clopidogrel-treated patients undergoing percutaneous coronary intervention were genotyped for ABCB1 C3435T, and ADP-induced platelet aggregation was assessed in whole blood on a Multiplate analyzer. The clinical impact of the genetic variant was investigated by comparison of genotype frequencies in a registry of 66 cases with definite drug-eluting stent ST versus an ST-free control cohort (n=1408). Platelet aggregation values were similar across ABCB1 C3435T genotypes (P=0.73). No significant influence of ABCB1 C3435T genotypes on the occurrence of ST was found when ST case subjects...
were compared with control subjects (P=0.89). ABCB1 C3435T genotypes did not influence the antiplatelet response to clopidogrel or the risk of ST in clopidogrel-treated patients undergoing percutaneous coronary intervention. Routine genotyping of ABCB1 C3435T polymorphisms should not be recommended for risk stratification in clopidogrel-treated patients undergoing percutaneous coronary intervention who are similar to those evaluated in the present study.