Lack of Association Between the Trp719Arg Polymorphism in Kinesin-Like Protein-6 and Coronary Artery Disease in 19 Case-Control Studies.


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OBJECTIVES: We sought to replicate the association between the kinesin-like protein 6 (KIF6) Trp719Arg polymorphism (rs20455), and clinical coronary artery disease (CAD).

BACKGROUND: Recent prospective studies suggest that carriers of the 719Arg allele in KIF6 are at increased risk of clinical CAD compared with noncarriers.

METHODS: The KIF6 Trp719Arg polymorphism (rs20455) was genotyped in 19 case-control studies of nonfatal CAD either as part of a genome-wide association study or in a formal attempt to replicate the initial positive reports.

RESULTS: A total of 17,000 cases and 39,369 controls of European descent as well as a modest number of South Asians, African Americans, Hispanics, East Asians, and admixed cases and controls were successfully genotyped. None of the 19 studies demonstrated an increased risk of CAD in carriers of the 719Arg allele compared with noncarriers. Regression analyses and fixed-effects meta-analyses ruled out with high degree of confidence an increase of ≥2% in the risk of CAD among European 719Arg carriers. We also observed no increase in the risk of CAD among 719Arg carriers in the subset of Europeans with early-onset disease (younger than 50 years of age for men and younger than 60 years of age for women) compared with similarly aged controls as well as all non-European subgroups.

CONCLUSIONS: The KIF6 Trp719Arg polymorphism was not associated with the risk of clinical CAD in this large replication study.

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