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Titel des Beitrags: Lack of replication in polymorphisms reported to be associated with atrial fibrillation.

Abstract: Atrial fibrillation (AF) is the most common sustained arrhythmia and has a substantial heritable component. Numerous associations between single nucleotide polymorphisms (SNPs) and AF have been described, but few have been replicated. We sought to systematically replicate SNPs that are reported to be associated with AF in two large study samples of European descent. We searched PubMed for studies reporting associations between SNPs and AF published before July 1, 2007. SNPs were genotyped in two independent case-control samples from Germany and the United States. Associations between SNPs and AF were assessed using logistic regression models adjusting for age, sex, and hypertension. A meta-analysis of the results from the two studies was performed. We identified 21 SNPs and the angiotensin-converting enzyme insertion/deletion polymorphism that were reported to be associated with AF in the literature. Nine of these genetic variants were not represented on common genome-wide SNP arrays. We successfully genotyped 21 of these 22 variants in 2,145 cases with AF from the German Competence Network for Atrial Fibrillation and 4,073 controls from the KORA S4 study and 16 variants in 790 cases.
and 1,330 controls from the Massachusetts General Hospital. None of the SNPs replicated in independent populations with AF. Our results suggest that previously reported associations to AF were likely false positives and highlight the need for systematic replication of genetic associations in large, independent cohorts to accurately detect variants associated with disease.