GENETICS

**CAD GENETIC RISK
HELPS PREDICT SCD**

Genome-wide association studies (GWAS) have been used to predict the risk of developing coronary artery disease (CAD) and to identify genetic variants that might prove useful in determining the risk of sudden cardiac death (SCD). In a new report published in the *European Heart Journal*, Hernesniemi *et al.* developed a weighted genetic risk score for CAD (GRS_{CAD}) that also predicted SCD risk.

“As CAD is the underlying condition in the majority SCDs, the genetic propensity for CAD is probably linked to a higher proportion of SCD cases than most other factors,” explains Jussi Hernesniemi, the corresponding author of the study. To explore this link, the GRS_{CAD} was calculated using the genetic variants most strongly associated with CAD, as identified by the CARDIoGRAMplusC4D Consortium, which included 153 single-nucleotide polymorphisms with $r^2 < 0.2$. In a meta-analysis of 1,035 autopsies which included 306 SCDs due to CAD, the GRS_{CAD} was associated with the occurrence of SCD due to CAD after adjusting for age, BMI, and sex (OR 1.042 for one allele increase, 95% CI 1.023–1.061, $P = 9.1 \times 10^{-6}$).

This association was replicated in a prospective follow-up study that included 2,321 patients undergoing clinical exercise testing at baseline. GRS_{CAD} was significantly associated with the risk of all-cause SCD (HR 1.045, 95% CI 1.010–1.081, $P = 0.011$) and SCD due to CAD (HR 1.049, 95% CI 1.010–1.090, $P = 0.014$). Addition of the GRS_{CAD} to risk modelling for SCD led to an integrated discrimination improvement of 0.010 units (95% CI 0.002–0.017, $P = 0.010$) and a net reclassification improvement of 18% (95% CI 2.8–33.2, $P = 0.020$). The association between GRS_{CAD} and SCD due to CAD remained significant in autopsy studies and all available clinical data from the Finnish Cardiovascular Study (FINCAVAS) after adjustment for previously developed genetic risk scores (OR 1.045, 95% CI 1.028–1.063, $P = 1.7 \times 10^{-7}$).

These results show that genetic propensity for CAD can be linked to the risk of SCD. “We would like to see if genetic components can provide significant reclassification value to risk modelling among individuals free of CAD at baseline,” adds Hernesniemi.

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Original article Hernesniemi, J. A. *et al.* Predicting sudden cardiac death using common genetic risk variants for coronary artery disease. *Eur. Heart J.* doi:10.1093/eurheartj/ehv106