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Titel des Beitrags:
Genetic markers enhance coronary risk prediction in men: the MORGAM prospective cohorts.

Abstract:
More accurate coronary heart disease (CHD) prediction, specifically in middle-aged men, is needed to reduce the burden of disease more effectively. We hypothesised that a multilocus genetic risk score could refine CHD prediction beyond classic risk scores and obtain more precise risk estimates using a prospective cohort design. Using data from nine prospective European cohorts, including 26,221 men, we selected in a case-cohort setting 4,818 healthy men at baseline, and used Cox proportional hazards models to examine associations between CHD and risk scores based on genetic variants representing 13 genomic regions. Over follow-up (range: 5-18 years), 1,736 incident CHD events occurred. Genetic risk scores were validated in men with at least 10 years of follow-up (632 cases, 1361 non-cases). Genetic risk score 1 (GRS1) combined 11 SNPs and two haplotypes, with effect estimates from previous genome-wide association studies. GRS2 combined 11 SNPs plus 4 SNPs from the haplotypes with coefficients estimated from these prospective cohorts using 10-fold cross-validation. Scores were added to a model adjusted for classic risk
factors comprising the Framingham risk score and 10-year risks were derived. Both scores improved net reclassification (NRI) over the Framingham score (7.5%, \( p = 0.017 \) for GRS1, 6.5%, \( p = 0.044 \) for GRS2) but GRS2 also improved discrimination (c-index improvement 1.11%, \( p = 0.048 \)). Subgroup analysis on men aged 50-59 (436 cases, 603 non-cases) improved net reclassification for GRS1 (13.8%) and GRS2 (12.5%). Net reclassification improvement remained significant for both scores when family history of CHD was added to the baseline model for this male subgroup improving prediction of early onset CHD events. Genetic risk scores add precision to risk estimates for CHD and improve prediction beyond classic risk factors, particularly for middle aged men.