Multilocus Heterozygosity and Coronary Heart Disease: Nested Case-Control Studies in Men and Women

Background: Generalized allelic heterozygosity has been proposed to improve reproductive fitness and has been associated with higher blood pressure, but its association with chronic disease is not well characterized.

Methods: Using the Affymetrix Genome-Wide Human 6.0 array, we performed whole genome scans in parallel case-control studies of coronary heart disease (CHD) nested in the Health Professionals Follow-up Study and Nurses’ Health Study. We examined ~700,000 single nucleotide polymorphisms (SNPs) in 435 men with incident CHD and 878 matched controls and 435 women with incident CHD with 931 matched controls. We examined the relationship of genome-wide heterozygosity with risk of incident of CHD and with baseline levels of cardiovascular risk factors.

Results: In both cohorts, approximately 227650 (SD 2000) SNPs were heterozygous. The number of heterozygous SNPs was not related to risk of CHD in either men or women (adjusted odds ratios per 2000 heterozygous SNPs 1.01 [95% confidence interval, 0.91-1.13] in women and 0.94 [0.84-1.06] in men). We also found no consistent associations of genome-wide heterozygosity with levels of lipids, inflammatory markers, adhesion molecules, homocysteine, adiponectin, or body-mass index.

Conclusions: In these parallel nested case-control studies, we found no relationship of multilocus heterozygosity with risk of CHD or its major risk factors. Studies in other populations are needed to rule out associations with lower levels of heterozygosity.

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