Smoking

SEHumphries et al. The Lancet. July (2001) Vol. 357 #9276 p 115.

Links between smoking and coronary disease have been proposed on many occasions. Some of the continuing uncertainty about the proposed links relates to genetic predisposition with or without exposure to tobacco smoke. This paper addresses this uncertainty.

In this instance, genotype for apolipoprotein e was the subject. Apolipoprotein e is believed to be instrumental in the control of the blood levels of lipoproteins (e.g. cholesterol), which have been linked to coronary artery disease.

This was a prospective study of 3052 middle-aged men who were found to be initially free from Coronary Heart Disease (CHD). Smoking habit was ascertained annually.

2303 men were genotyped and 2258 (74% of all those eligible) were followed up to completion.

Outcomes of interest were: acute myocardial infarction (Minf), (fatal or non-fatal), coronary artery (CA) surgery and silent myocardial infarction at follow up.

18836 person years of follow-up.

During the follow-up period 96 of the cohort had had acute Minf, 26 needed CA surgery, 14 had silent Minf.

Using never-smokers, as controls, the relative risk of CA disease in smokers (regardless of genotype) was 1.94 (95% CI = 1.25 to 3.01).

Men who were homozygous for apolipoprotein e3 had the same increased risk whether smoker or ex smoker i.e. RR_{smoker} = 1.74 (95% CI = 1.1 to 2.8) $RR_{exsmoker}$ = 1.68 (95% CI = 1.01 to 2.83) vs. never smoker.

Men with a gene for apolipoprotein E4 who were also smokers: RR = 2.79 (95% CI = 1.59 to 4.91) vs. never smokers. Adjustment had reduced this from 3.17 by correcting for age, Body Mass Index , systolic blood pressure, cholesterol level, triglyceride and fibrinogen in blood.

Comment

Further, statistically significant, evidence of a general association between smoking and heart disease.

For just one of the genotypes studied here (e4), the association is stronger than that required by the test of the balance of probabilities

The e3 homozygous result may show that other factors may have a role to play in the development of CHD.

The highest risk among smokers in this study comes from the e4 allele/smoking combination. In order to assess the relative contributions though we need to know what proportion of the risk is due to e4 in the absence of smoking history.