

PAPERS AND SHORT REPORTS

How well can we predict coronary heart disease? Findings in the United Kingdom Heart Disease Prevention Project

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Abstract

The probability of myocardial infarction developing over five years in a group of middle aged men was predicted with knowledge of their ages, blood pressures, cholesterol concentrations, and smoking habits as recorded in an initial screening examination. Although the top 15% of the risk distribution predicted 115 (32%) of the subsequent cases of myocardial infarction, there was a considerable overlap in predicted risk between those subjects who did and those who did not go on to develop a myocardial infarction. Of the subjects in the top 15% of risk, only 72 (7%) of those initially free of coronary heart disease and 43 (22%) of those initially with coronary heart disease actually developed a myocardial infarction over the subsequent five years. Thus, although a group of subjects at high risk can be identified, among whom will be a high proportion of potential victims of heart attack, many subjects will be wrongly classified.

These findings may explain part of the difficulty in persuading patients of the potential benefits of reducing risks and highlight the need for research to improve the prediction of the development of coronary heart disease.

Introduction

Various risk factors are well established as predictors of subsequent coronary heart disease. Although many risk factors have been postulated, those that consistently appear to be the best predictors are age, sex, blood pressure, plasma concentrations of total and high density lipoprotein cholesterol, and smoking habit.¹⁻⁶ Relative weight has usually been found not to be an independent predictor. Some risk factors may be of different importance in men and women⁷ and also in those who are free of coronary heart disease when the factors are measured and those who already show signs of ischaemia, either on electrocardiography or by giving a history of chest pain.⁵ Various statistical procedures have been used to obtain with these predictive variables the best predictions in groups of people. The object of the present study was to see how useful the predictions based on group experience are for single patients who may want to know what sort of a risk they run.

Methods

The subjects of this study were men participating in the United Kingdom Heart Disease Prevention Project, a longitudinal study of the multifactorial prevention of coronary heart disease in middle aged men working in British industries.^{8,9} At the initial screening examination single measurements were made of height, weight, blood pressure (using a London School of Hygiene sphygmomanometer), and plasma cholesterol concentration and subjects were asked to answer a questionnaire that included standardised questions on angina.¹⁰ The men were followed up for both cardiovascular morbidity and mortality, as described previously.⁹ For the present study we considered only the 8147 men on the intervention side of the trial who had been examined at the start of the trial (86% of those eligible) and for whom complete data were available, as only 10% of the control group had been examined initially.^{8,9} Follow up averaged 5.3 years and included reports on morbidity (on which reporting stopped after this period) and mortality. A definite or probable myocardial infarction according to the criteria of the World Health Organisation was the end point for this study. Fatal and non-fatal events were combined, but only one end point was permitted for each man, men dying after having had an earlier heart attack being counted only once.

Age, systolic blood pressure, plasma cholesterol concentration, smoking habit, physical activity, and body mass index (weight/height²) as assessed at the start of the study were entered as predictive variables

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into a logistic regression analysis in which the development of myocardial infarction over the period of the study was the outcome variable.¹¹ Factors found not to have a significant ($p < 0.05$) predictive effect were omitted from the prediction formula. The logistic regression model permitted the estimation of the probability of each subject subsequently developing a myocardial infarction during the study period. The estimation was made with a weighted linear combination of the predictive variables, the weights being the regression coefficients determined in the analysis and the derived score being termed a multiple logistic function. The whole procedure was done separately in those without and those with evidence of ischaemia at the initial examination (codable Q waves, ST-T wave items or left bundle branch block on electrocardiography (Minnesota codes 1:1-3, 4:1-3, 5:1-3, 7:1), or angina or chest pain lasting one hour according to the questionnaire⁸). For the purposes of comparison a multiple logistic function, using weights derived from the European part of the Seven Countries Study,³ was also used to predict the development of myocardial infarction; this was possible only for those initially without coronary heart disease as that study excluded those who initially showed evidence of ischaemia.

Results

Neither physical activity nor body mass index was significantly related to the development of myocardial infarction, and so both were deleted from the final multiple logistic function. The remaining variables—age, systolic blood pressure, plasma cholesterol concentration, and smoking habit—contributed to the prediction of myocardial infarction ($p < 0.001$ overall).

Table I shows the mean probabilities of developing a myocardial infarction according to the derived multiple logistic function formulas for the groups of men who did and did not develop a myocardial infarction. The probabilities for those who developed a myocardial infarction were naturally higher than the probabilities for those who did not, although the actual values were low (the predicted probabilities of developing a myocardial infarction in those who actually did so were only 5% and 14% respectively in those without and with ischaemia initially). Inevitably, a formula derived from its own population is a better predictor than one derived from another population, but table I shows that the formulas derived from this study's population and from the Seven Countries Study had similar abilities to distinguish between those who did and did not subsequently develop a myocardial infarction.

TABLE I—Probabilities (%) of developing myocardial infarction predicted by multiple logistic functions derived from two different studies

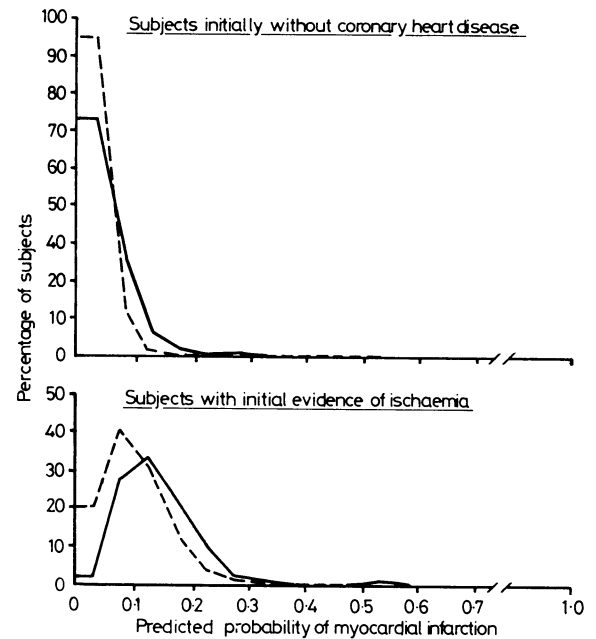
	No of subjects	Mean (range) predicted probability	
		Study 1*	Study 2†
<i>Subjects initially without coronary heart disease</i>			
Developed myocardial infarction	211	5.0 (1-25)	2.4 (0-10)
Did not develop myocardial infarction	6610	3.0 (0-41)	1.5 (0-23)
<i>Subjects initially showing evidence of ischaemia</i>			
Developed myocardial infarction	149	14.1 (4-52)	
Did not develop myocardial infarction	1177	10.8 (2-52)	

*Prediction derived from the best multiple logistic function from the Heart Disease Prevention Project, based on age, systolic blood pressure, plasma cholesterol concentration, and smoking habit.

†Prediction derived from the multiple logistic function from the Seven Countries Study,³ based on age, systolic blood pressure, plasma cholesterol concentration, and smoking habit.

The figure shows the distribution of the initial multiple logistic function prediction among men who developed a myocardial infarction during the follow up period and those who did not. There was an appreciable overlap in the predicted probability of developing a myocardial infarction between those who did and did not actually go on to develop one. To examine the value of using, for example, the top 15% of the distribution of the multiple logistic function prediction, table II gives contingency tables for those with and without initial evidence of ischaemia. Among those initially free of coronary heart disease these top 15% of men in the multiple logistic function distribution included 72 (34%) of those who went on to develop a myocardial infarction; for every 100 men at this high risk, however, only seven actually developed a myocardial infarction. Among those

with initial ischaemia the top 15% of the multiple logistic function distribution included 43 (29%) of the men who went on to develop myocardial infarction, but for every 100 of these men designated as being at high risk only 22 developed a myocardial infarction.



Distributions of predicted probabilities of developing a myocardial infarction in subjects who later developed myocardial infarction (—) and in those who did not (---), according to whether they had initial evidence of ischaemia.

TABLE II—Value of using 85th centile of distribution of initial predicted probability of developing a myocardial infarction as definition of high risk

	Developed myocardial infarction	Did not develop myocardial infarction	Total
<i>Subjects initially without coronary heart disease</i>			
Above 85th centile*	72	951	1023
Below or at 85th centile	139	5659	5798
<i>Subjects initially showing evidence of ischaemia</i>			
Above 85th centile†	43	156	199
Below or at 85th centile	106	1021	1127

*Predictive value of being above 85th centile (that is, in the top 15% of risk) = $72/1023 = 7\%.$ †

†Predictive value of being above 85th centile (that is, in the top 15% of risk) = $43/199 = 22\%.$ ‡

‡Predictive value = probability that those identified as being in the top 15% of risk will actually develop a myocardial infarction during the follow up period.

Discussion

This study confirms others that have shown the predictive value of the measured risk factors age, blood pressure, total cholesterol concentration, and smoking habit. Though our observations were obtained from an intervention study, and the men studied made changes in their risk factors during the course of the study, these changes were small⁸ and we did not find any change in the incidence of coronary heart disease over the course of the study.⁹ In addition, our prediction of later events by the degree of initial risk factors was much in line with results from other purely observational studies. The study started in 1971, and concentrations of high density lipoprotein cholesterol were not measured; if they had been this might have added to the predictive power of the initial screening variables.⁶ By deriving a new multiple logistic function formula from our own data we were able to improve the prediction of those who might develop a myocardial infarction, but despite this a large overlap remained between those who developed myocardial infarction and those who did not.

These risk factors may be used in this way to identify people at high risk so that intervention may be directed towards them. In population terms this may be a profitable approach as the top 15% of the risk distribution may provide 32% of the cases of myocardial infarction over the subsequent five years. For individual people, however, the accuracy of the prediction is low: among those without initial evidence of coronary heart disease only 7% characterised as being at high risk will actually develop a myocardial infarction in the subsequent five years. Prevention has been suggested to be more effective in those with initial ischaemia.^{12 13} Even in this group, however, only one fifth of those characterised as being at high risk will develop a myocardial infarction in the subsequent five years. This discrepancy between the importance to the population as a whole and that to a single patient may explain some of the difficulties of persuading people of the potential benefits of reducing risks.⁸

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Analysis and management of renal failure in fourth MRC myelomatosis trial

MRC WORKING PARTY ON LEUKAEMIA IN ADULTS

Abstract

During March 1980 to February 1982, 73 out of 80 patients in renal failure admitted to the fourth MRC myelomatosis trial were managed by a planned policy of high fluid intake (≥ 3 l/24 h) in addition to receiving one of the two chemotherapeutic regimens being tested in the main trial. Patients were also randomised to receive either sodium bicarbonate to render their urine neutral or no supplement. Follow up continued till death or to April 1983.

Of 49 patients who survived more than 100 days, 39

achieved reversal of their renal failure (18 complete, 21 partial). Recovery of renal function, as assessed by a fall in the serum creatinine concentration, was achieved even when light chain proteinuria persisted. Partial recovery of renal function was associated with prolonged useful life in several patients. In only 14 of the 80 patients studied was death directly attributable to renal failure. Survival of patients in the study was appreciably better than in equivalent groups of patients in other MRC trials in which less stringent policies of fluid intake were used. Patients randomised to receive alkali fared marginally better than the others, but the difference was not significant.

These results show that in many cases patients with myelomatosis who develop renal failure may have this complication reversed by taking a high fluid intake. Furthermore, though light chain is an essential component of renal disease in these patients, other factors are also important and are accessible to treatment.

Introduction

Several reports have emphasised the poor clinical outlook for patients with myelomatosis who develop renal failure.¹⁻⁸ It is not clear, however, that this is due entirely to death from renal failure itself. The incidence of renal failure is considerably higher than the death rate attributable to this cause.⁷

The single factor most commonly implicated in the induction of renal lesions in myelomatosis is free light chain.^{9 10} Nevertheless, only a proportion of patients with light chain proteinuria develop renal failure. This has led to the widely held concept of

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