Cessation of smoking after myocardial infarction
Effects on mortality after 10 years

ANDERS ÅBERG, ROBERT BERGSTRAND, SAGA JOHANSSON, GÖRAN ULVENSTAM, ANDERS VEDIN, HANS WEDEL, CLAES WILHELMSSON, LARS WILHELMSEN

From Section of Preventive Cardiology, Department of Medicine, Östra Hospital, Göteborg, Sweden

SUMMARY Ten annual cohorts of men suffering from their first myocardial infarction have been followed up to a maximum period of 10·5 years. One thousand and twenty-three male patients of 1306 were smokers. Three months after the infarction 55% had stopped smoking and 45% continued smoking. These two groups were then compared and followed with regard to non-fatal reinfarctions and deaths.

Preinfarction characteristics were shown to be similar for the two groups. The prognostic comparability of the two groups was tested using two multiple logistic models. Those who stopped smoking had a slightly higher predicted two year mortality after the infarction. In different age groups it is shown with life table technique that those who stopped smoking had a considerably higher survival rate and lower cumulative frequency of reinfarction.

The present study shows a reversion of the expected prognosis after myocardial infarction caused by changing the smoking habit.

Cigarette smoking is one of the major risk factors for the development of coronary heart disease.[1-3] In a previous report we have shown the beneficial effects of stopping smoking after myocardial infarction. Those who stopped smoking had only half the cardiovascular mortality rate and only half the rate of non-fatal recurrences compared with those who continued to smoke.[4] An increased death rate among those who continue to smoke has also been shown by others.[5-7]

The aim of the present study was to investigate whether our early findings were stable or even enhanced during a prolonged follow-up, and if the proposed effect of changing the smoking habit differed in certain age-groups.

Patients and methods

As from 1 January 1968, all cases of myocardial infarction occurring in Göteborg have been registered by the MI Register.[8] The present study comprised men who suffered their first myocardial infarction and whose ages were as follows: for the two years 1968 to 1969 all patients aged 55 years and below; for the two years 1970 to 1971 all patients aged 67 years and below (with the exception of a random 30% sample for those aged 57 to 59 who formed a reference group); for 1972 every other patient below 65 years; from 1973 up to and including 31 December 1977 all patients aged 59 years and below, making a total of 1306 male patients who survived their stay in hospital.

All patients were followed from discharge up to a maximum period of 10·5 years at a special post-myocardial infarction clinic. Control examinations took place immediately after discharge (one to three weeks), and three, 12, 24, 60, and 120 months after the infarction, as well as at stages indicated by the clinical situation. The treatment of patients after discharge from hospital was completely standardised and uniform rules were established by means of regular meetings of members of this clinic. All patients were informed about the relation between smoking and coronary heart disease, and smokers were advised to stop smoking. Printed information was given in the form of special brochures. For all interviews, physical examinations, and laboratory investigations, identical questionnaires and laboratory methods were used by the same group of investigators. In order to ascertain a uniform collection of data, special forms were pre-

pared. The form for the period of hospital stay contained vital statistics, information on previous diseases, cardiovascular and respiratory symptoms, smoking habits, physical activity at work and during leisure time, conditions at onset of the disease, during hospital care, and at discharge. The form used for follow-up examinations included the occurrence of cardiovascular and respiratory symptoms, smoking habit, complications, certain diseases, physical status, and laboratory data.[9]

Patients who smoked at least one cigarette, or the equivalent amount of tobacco each day, or who had stopped smoking less than three months before the myocardial infarction, were classified as smokers. Patients who had never smoked or who had smoked continuously for less than one month were defined as non-smokers. Other patients were regarded as ex-smokers. The patients who stopped smoking after myocardial infarction and were still non-smokers three months after the myocardial infarction were regarded as having stopped smoking.

For recording dyspnoea and chest pain on exertion the questions published by Rose and Blackburn[10] were used. All subjects who had dyspnoea or chest pain when walking up a small hill or walking rapidly on level ground, or upon lesser exertion, were recorded as having dyspnoea or chest pain upon exertion. Previously known hypertension and diabetes were recorded if present. With regard to chest pain and dyspnoea at the onset of myocardial infarction, the patient's statement at the first interview was used. Left ventricular failure during the hospital stay was considered to exist when more than occasional basal pulmonary râles or increased prominence of pulmonary vessels on x-ray film were noted in the patient's records. Other conditions, such as atrial fibrillation, were considered to have occurred if they had been recorded at any time during the period of stay in hospital. Also recorded were disturbances of consciousness, hypotension, or leucocytosis, maximum temperature during the first three days in hospital, the number of days in hospital, and treatment when in hospital and when discharged. Blood samples for transaminase determinations (AST and ALT) were taken on three consecutive days according to a special standardised schedule.

The occurrence of deaths and reinfarction was established by the MI register.[8] The same criteria of diagnosis for non-fatal reinfarction were applied as were used for acute myocardial infarction at the beginning of the study. For new, non-fatal reinfarction to be registered, two of the following three criteria had to be fulfilled: central chest pain suspected to be caused by myocardial infarction, transaminase rises according to a special pattern, or typical electrocardiographic abnormalities of recent onset.[8]

The reinfarction was considered non-fatal if the patient was discharged alive from hospital or survived reinfarction for more than 28 days. The diagnosis "death caused by coronary heart disease" was based in 80% of the cases on necropsy and in 20% of the cases on typical course of the fatal episode. Death certificates and necropsy records were available for all patients who died. Deaths were divided into those caused by coronary heart disease and other deaths. In the present investigation other causes of death comprised stroke, pulmonary embolism, cancer, sepsis, and suicide.[11]

The present report deals with the effect of stopping smoking by comparing those who smoked before myocardial infarction and later stopped, with those who continued to smoke after the infarction.

Statistical analyses

The Mantel-Haenszel test was used to get a crude test of the difference between the two survival curves. The Cox proportional hazard model was used.[12][13] This model assumes proportional hazards, that is the effect of stopping smoking should be proportional to the mortality rate (hazard). Early after the myocardial infarction there is an extremely high mortality rate but the effect of stopping smoking is probably low in this period. In this study the patients are included after three months. A plot of the different hazard functions showed that the Cox model was well suited for this observation period. The probability of cardiovascular death during the initial follow-up was calculated using multiple logistic models.[13] There is no ideal model to adjust for prognostic factors. Therefore, two models were used. In model I age, peak enzyme level, and the occurrence of left ventricular failure were used in a Cox analysis. In model II Cox analysis included age and a logistic severity index[14] using previous hypertension and variables listed in Tables 1 and 2.

For analyses of the fourfold table Fisher's exact test was used. Differences of continuous variables were tested by t test. P values based on a two sided test are given.

Table 1 *Variables recorded during hospital stay in relation to smoking status three months after myocardial infarction*

Risk factor	Stopped (n=542)	Continued (n=441)	p
Dyspnoea on infarction (%)	25·0	23·9	<0·20
Left ventricular failure (%)	25·1	16·4	>0·001
Atrial flutter/ fibrillation	3·5	5·2	0·19

Table 2   *Variables recorded during hospital stay in relation to smoking status three months after myocardial infarction*

Risk factor	Stopped (n=542) X̄ SD	Continued (n=441) X̄ SD	p
Mean peak AST (ukat/l)	3·1±2·3	2·7±2·5	<0·01
Relative heart volume (ml/m² BSA)	470±91	467±92	>0·20

Table 3   *Numbers of men with first myocardial infarction and different smoking habits discharged alive from hospital 1968 to 1977*

Age (y)	Non-smokers	Ex-smokers	Smokers	Total
–39	4	2	33	39
40–44	4	3	76	83
45–49	13	13	170	196
50–54	37	33	303	373
55–59	45	53	320	418
60–	28	42	121	191
Total	131	146	1023	1300

Table 4   *Numbers of men with first myocardial infarction in relation to smoking status at three months*

Age (y)	Stopped		Continued		Total	
	No.	%	No.	%	No.	%
–39	13	43	17	57	30	3·1
40–44	30	40	45	60	75	7·6
45–49	88	54	76	46	164	16·7
50–54	163	56	129	44	292	29·7
55–59	181	58	129	42	310	31·5
60–	67	60	45	40	112	11·3
Total	542	55	441	45	983	

Results

Smoking habits and age distributions of the patients are presented in Table 3; 1023 patients were smokers (78%), 131 non-smokers (10%), and 146 ex-smokers (11%). For six patients the smoking status before myocardial infarction could not be established. Three months after infarction, 542 (55%) patients had stopped smoking while 441 (45%) continued to smoke. Between discharge and the establishment of the post-myocardial infarction smoking habit at three months after infarction 11 patients had died and in an additional 29 patients the smoking habit could not be established because the patients were alcoholics, mental hospital patients, or had moved from the area. Thus, 983 patients were followed.

The percentage of patients who stopped smoking in the different age groups is presented in Table 4 and was unchanged for the different annual cohorts throughout the study. There was a difference in mean age, those who stopped smoking being older than those who continued (53·2 vs 52·0; p<0·01). Of the patients who claimed to have stopped smoking three months after myocardial infarction, 90% were still not smoking at the 12 month control. Carboxy-haemoglobin was tested in 100 patients in 1973. These patients were at various stages in the follow-up from three months up to five years after myocardial infarction. One patient had a carboxyhaemoglobin over the normal value.

The prognostic comparability of the two groups in the present study was assessed. Some preinfarction characteristics are presented in Table 5. The fre-

Table 5   *Preinfarction characteristics in relation to smoking status at three months after myocardial infarction*

Characteristic	Stopped (n=542) %	Continued (n=441) %	p
Angina pectoris	33·9	39·9	>0·20
Hypertension	17·7	22·5	0·076
Diabetes	5·2	4·6	>0·20
Digitalis therapy	3·1	4·8	>0·20

Table 6 Number of deaths during up to 10·5 years follow-up in relation to smoking status three months after myocardial infarction

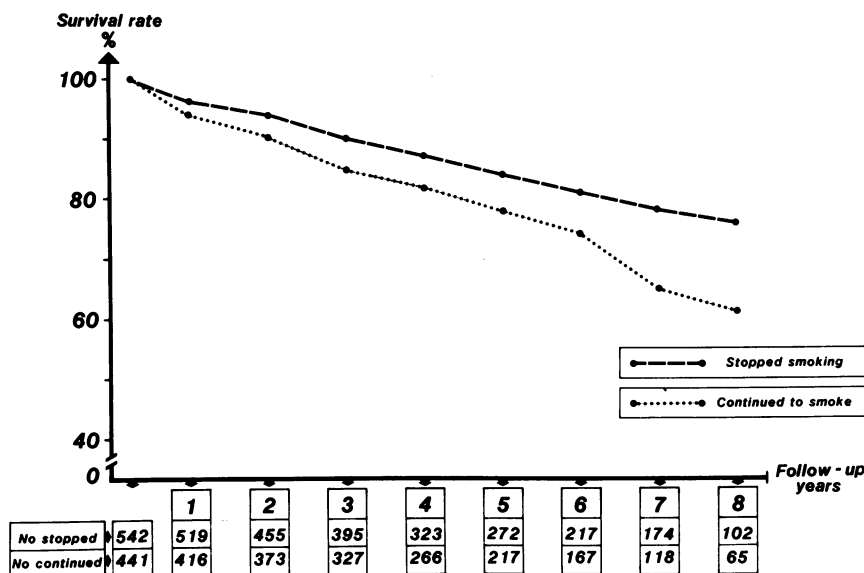| Age (y)	Stopped smoking				Continued to smoke			
	No.	Cause of death			No.	Cause of death		
		CHD	Other	Total		CHD	Other	Total
≤50 (n=269)	131	10	3	13 (10%)	138	20	10	30 (22%)
>50 (n=714)	411	70	14	84 (20%)	303	74	22	96 (32%)
Total (n=983)	542	80	17	97 (18%)	441	94	32	126 (29%)

CHD, coronary heart disease.

Fig. 1 Survival curves for all patients in relation to smoking status at three months. (The period after eight years is not shown because of the small number of patients involved.)

quency of hypertension tended to be slightly higher in the group who continued to smoke.

Prognostic variables, defined above, differed in the two groups (Table 1 and 2) in respect of left ventricular failure and mean peak enzyme change. According to prognostic model I there was a 9·3% higher expected mortality after two years in the group that stopped smoking. According to prognostic model II this difference in expected mortality was slightly less, but still the group that stopped smoking was biased to a 8·1% higher expected mortality for two years of follow-up (p<0·01). This difference was small, however; the expected two year mortality for the group who continued to smoke was 8·3% and 9·0% for those who stopped smoking.

Other variables after discharge from hospital have been studied. During the follow-up period there were no differences between the groups in the frequency of angina pectoris, diabetes, or hypertension. The blood pressure levels three, 12, and 24 months after infarction did not differ between the groups. The cholesterol and triglyceride values at the same controls were also comparable. Treatment with lipid lowering drugs was never more frequent than 8% in the highest cholesterol quintile and was the same in both groups. The mean weight tended to be higher one year after the myocardial infarction for those who stopped smoking (p=0·084). The frequency of beta blocking treatment increased during the study period, but was comparable in the two groups.

There were altogether 223 deaths during up to 10·5 years of follow-up and these were related to smoking habits three months after myocardial infarction (Table 6). In the group who stopped smoking the cumulative survival rate was 84% after five years and in the group who continued to smoke the five year survival rate was 78% (Fig. 1). The Mantel test gave a significant difference between the survival curves
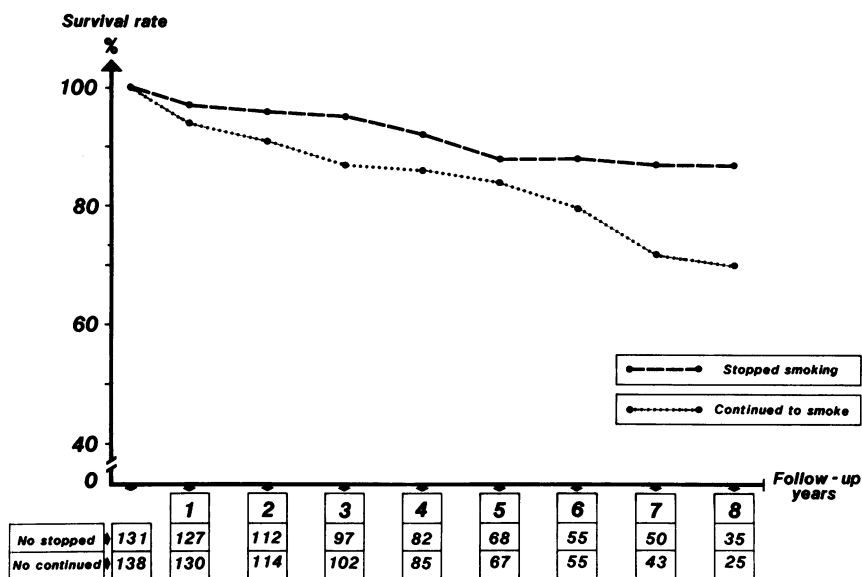
Survival rate %

| No stopped | 131 | 127 | 112 | 97 | 82 | 68 | 55 | 50 | 35 |
| No continued | 138 | 130 | 114 | 102 | 85 | 67 | 55 | 43 | 25 |

Fig. 2   *Survival curves for patients below 50 years of age in relation to smoking status at three months. (The period after eight years is not shown because of the small number of patients involved.)*
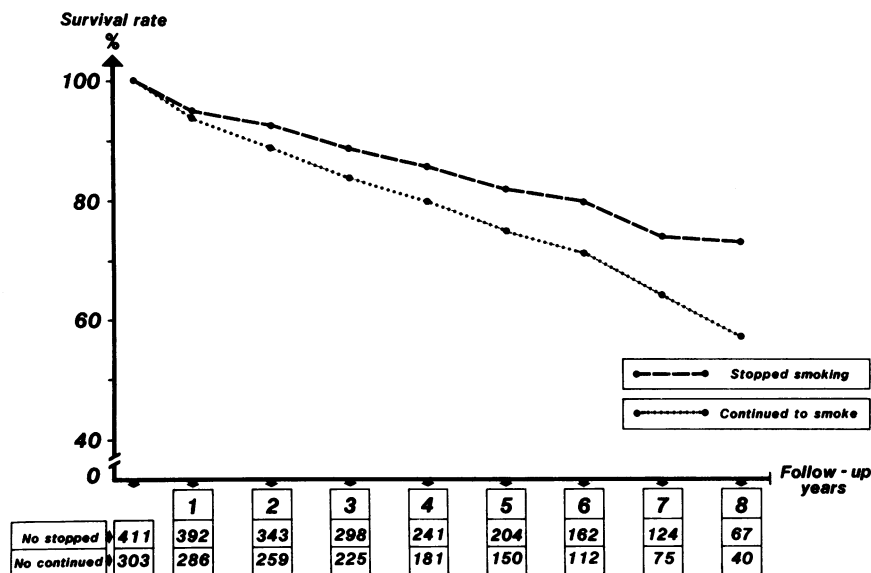
Survival rate %

| No stopped | 411 | 392 | 343 | 298 | 241 | 204 | 162 | 124 | 67 |
| No continued | 303 | 286 | 259 | 225 | 181 | 150 | 112 | 75 | 40 |

Fig. 3   *Survival curves for patients above 50 years of age in relation to smoking status at three months. (The period after eight years is not shown because of the small number of patients involved.)*

(p<0·0001). The Cox analysis of survival curves showed a difference (p<0·001) after adjusting for age and the prognostic index. Seventy-five per cent survival was reached after 71 months for those who continued to smoke and was not reached after 115 months for those who stopped smoking.

Below 50 years of age, those who stopped smoking had a five year survival rate of 88% and those who continued had 84% survival after 5 years (Fig. 2; p<0·02). Above 50 years of age, those who stopped smoking had a survival rate of 82% after five years and those who continued a 75% survival rate (Fig. 3; p<0·001).

Among the 983 patients there were 231 non-fatal

Table 7 *Number of non-fatal reinfarctions during up to 10·5 years follow-up in relation to smoking status three months after myocardial infarction*

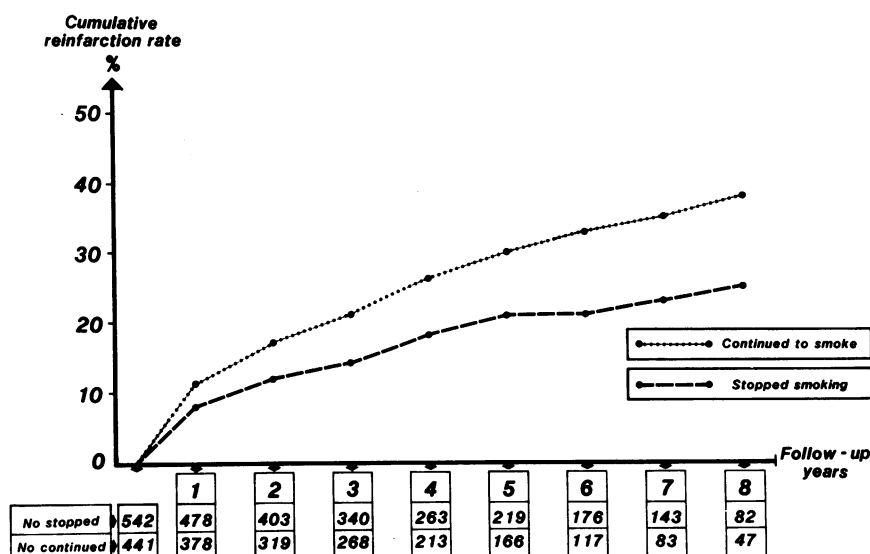| Age (y)	Stopped smoking		Continued to smoke	
	No.	Reinfarction	No.	Reinfarction
≤50 (n=269)	131	23 (18%)	138	38 (28%)
>50 (n=714)	411	81 (20%)	303	89 (29%)
Total (n=983)	542	104 (19%)	441	127 (29%)

Fig. 4 *Cumulative reinfarction rate for all patients in relation to smoking status at three months. (The period after eight years is not shown because of the small number of patients involved.)*

recurrences during up to 10·5 years follow-up (Table 7). The difference between the two groups was not strongly related to age above and below 50.

The cumulative reinfarction rate after five years was 21% for those who stopped smoking and 30% for those who continued to smoke (Fig. 4; p<0·0001).

Below 50 years of age, those who stopped smoking had a five year reinfarction rate of 20% and those who continued to smoke had a rate of 27% (p=0·06). Above 50 years of age those who stopped smoking had a reinfarction rate of 21% and those who continued a rate of 31% (p<0·01).

Discussion

The patients studied were unselected and the methods used were standardised and unchanged throughout the period of follow-up.[8][9] The number of patients who could not be followed up was negligible. The two groups studied were previously shown to have had an equal tobacco consumption before the onset of myocardial infarction.[4] Patients who stopped smok-

ing after infarction seldom resumed smoking.[15] This was in contrast to experience of antismoking campaigns in the general population.[16] The validity of the reported tobacco consumption after myocardial infarction was tested in a separate study, blood levels of carboxyhaemoglobin being correlated with the reported tobacco consumption. The correlation was good and ex-smokers had blood levels in the normal range (C Wilhelmsson, unpublished observations).

The completeness and quality of endpoints (death and non-fatal reinfarction) have been tested and discussed previously,[8][11] as have the methods used during the follow-up period.[9] The two groups studied were comparable regarding variables recorded before the infarction except for a slight but not significant difference in the frequency of hypertension before myocardial infarction. When other variables of more pronounced prognostic importance after myocardial infarction were analysed the prognostic index was worse in the group who stopped smoking and this group had a slightly higher predicted two year mortality than the group that continued to smoke. Thus, the

patients who stopped smoking had a more severe risk of myocardial infarction. The survival rate in this group was, however, considerably higher, reflecting an inversion of the expected prognosis. The difference in group survival rate was shown in the totality of patients as well as among men under 50 years of age, and in the former the lack of difference between the two groups in mortality after one year supports an early effect of the cessation of smoking, since a higher mortality was predicted among those who stopped.[14] In the lower age groups the difference was evident within three years after the myocardial infarction. This rapid beneficial effect of withdrawal from cigarette smoking suggests improvement of factors with relatively short time constants, such as a decrease in lethal arrhythmias, or a change of platelet adhesiveness or of myocardial metabolism, rather than effects mediated via progressive changes in the coronary arteries.

The observed reduction of mortality was supported by our previous finding[4] and by other investigators.[5-7,17] The findings were further supported by the observed reduction of non-fatal reinfarctions.

The present study shows a reversion of the expected prognosis after myocardial infarction caused by changing the smoking habit. Tobacco smoking is a major risk factor both for the initial occurrence of clinical coronary heart disease and for the prediction of subsequent episodes. The finding of this study suggests that it is highly plausible that tobacco smoking among survivors of myocardial infarction makes a causal contribution to reinfarction and coronary death.

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Requests for reprints to Dr Göran Ulvenstam, Section of Preventive Cardiology, Department of Medicine, Östra Hospital, S-416 85 Göteborg, Sweden.