PAPERS AND ORIGINALS

Intermittent claudication: factors determining outcome

W G HUGHSON, J I MANN, D J TIBBS, H F WOODS, I WALTON

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Summary and conclusions

Two groups of patients were followed up for four to eight years after first referral or admission to hospital for intermittent claudication (IC) in a study of the natural history of the disease and of factors determining its outcome. In one series of 60 patients, those who stopped or reduced smoking after referral had a much improved prognosis. Thus even after the diagnosis of IC it is extremely important that patients should be encouraged to stop smoking, since this correctable factor appears to be of greater importance in determining outcome than other medical risk factors for the disease that are less amenable to treatment. In the second study, 160 patients were followed up for eight years after first hospital admission. They had a total of 480 hospital admissions and had spent 11 190 days in hospital; their life expectancy after the age of 60 was about half that of the general population. Age, coronary artery disease, cerebrovascular disease, and diabetes were associated with an adverse outcome.

Introduction

Patients with intermittent claudication (IC) have a life expectancy similar to that of a healthy population 10 years older.[1] Deaths are due chiefly to coronary artery and cerebrovascular disease.[2] Patients with diabetes have a worse prognosis than those without,[3] but data concerning the prognostic importance of other factors such as hypertension are conflicting.[2-5] In studies in which smoking habits were investigated patients who stopped smoking had an improved life expectancy and lower amputation rate compared with those who continued,[3 4] but the smoking habits of the patients before referral and possible confounding by other risk factors were not considered. We carried out two studies to examine in detail the prognostic importance of smoking and other risk factors in IC.

University Department of Social and Community Medicine, Oxford OX13QN

W G HUGHSON, MD, DPHIL, Rhodes scholar

J I MANN, DM, PHD, lecturer

Radcliffe infirmary, Oxford

D J TIBBS, MCH, FRCS, consultant surgeon

H F WOODS, DPHIL, MRCP, clinical pharmacologist (present appointment: professor of clinical pharmacology, University of Sheffield, Sheffield S10 2TN)

I WALTON, MSC, MRCP, lecturer in medicine

Study 1

PATIENTS AND METHODS

During November 1971 to July 1972, 60 consecutive patients (47 men and 13 women) aged 40-79 years were referred to one of us (DJT) because of symptoms of IC. They represented all patients referred to the only peripheral vascular surgical service in the Oxford region at that time. On referral a detailed medical history was obtained, blood pressure was recorded, and limbs and peripheral pulses were examined. A blood sample was taken after a 14-hour overnight fast, and glucose,[6] cholesterol,[7] triglyceride,[8] and urate (Technicon SMA 12/60) concentrations were measured. A 12-lead electrocardiogram was recorded, and patients thought likely to benefit from surgery underwent arteriography.

Follow-up was carried out during July to December 1976, information being obtained on all 60 patients. Sixteen had died, and all but one of the remainder were personally interviewed during this period. Further information was obtained from hospital records and general practitioners. To investigate which factors might predict an unfavourable outcome we defined an "adverse event" as any of the following: (1) death; (2) amputation; (3) onset of IC in a previously asymptomatic leg; (4) onset of rest pain in a limb previously free of rest pain; (5) myocardial infarction or cerebrovascular accident in a patient with no history or evidence of coronary artery or cerebrovascular disease; and (6) operation for deterioration of peripheral vascular disease. (Surgery related to the initial referral, and any subsequent operation for a failed primary procedure, was not included as an adverse event. Subsequent operations were considered to be adverse events, however, when a change in the patient's condition, usually more than a year after referral, had clearly been the indication for surgery.) Adverse events were identified independently by a physician (Dr Diana Gale), who was provided with details of the patient's history after first referral but had no knowledge of the presence or absence of risk factors.

Life tables were calculated, considering the time between referral and the development of the first adverse event.[9 10] Some patients stopped smoking at the time of referral, and to assess the effects of this further life tables were computed using the following time intervals: (1) from three months after referral—that is, after three months without smoking—to the first adverse event, any event occurring in the three months after referral being excluded; (2) from six months after referral to the first adverse event; and (3) from one

year after referral to the first adverse event. Corrections were made in each life table for age and sex. Five patients were excluded from the life-table analyses because of incomplete data (3) or death shortly after referral and unrelated to peripheral vascular disease (2).

RESULTS

The average duration of symptoms before referral was 14 months (range 1 to 72 months). Thirty-four patients (57%) had IC in one limb only, and 9 (15%) complained of rest pain. The median walking distance was 150 yards (137 m). The most common site of pain was the calf, although thigh, buttock, and foot pain were also reported. Eighteen patients (30%) had evidence or a clear history of ischaemic heart disease and 9 (15%) of cerebrovascular disease. Hypertension (at least two recordings of a systolic pressure exceeding 160 mm Hg or diastolic pressure exceeding 90 mm Hg, or established hypotensive drug treatment) was present in 14 (23%), and 9 (15%) had hyperlipidaemia (cholesterol concentration over 6·7 mmol/l (259 mg/100 ml) or triglyceride concentration over 2·15 mmol/l (190 mg/100 ml)). One patient gave a history of gout and had hyperuricaemia. None had diabetes.

The 16 deaths were due to ischaemic heart disease (6), ruptured aortic aneurysm (3), stroke (4), and postoperative complications (3). Several surviving patients had non-fatal ischaemic events, including myocardial infarction (4), stroke (4), onset of angina (2) or congestive heart failure (2), arterial embolism (2), and onset of rest pain (7). Nine patients underwent amputation during the follow-up period, and 80 reconstructive operations were performed.

Patients aged 70-79 years had a particularly poor prognosis, and none of the eight patients in this age group was alive after two years. Patients who had had a stroke before referral also had a poor prognosis when compared with those with no history of cerebrovascular disease (fig 1).

Only one patient had never smoked, all the rest being cigarette smokers on referral. All were strongly urged to discontinue smoking. Eleven stopped completely, and nine reduced their daily cigarette consumption from over 20 to below 10. The remainder did not alter their smoking habits appreciably during the follow-up period. To assess the effect of continued smoking on prognosis several life tables were constructed. The starting point (time zero) of the life table shown in fig 2 is 12 months after referral, since it was considered that any beneficial effect of stopping smoking would probably take at least one year to become evident. The probability of an adverse event was much greater in patients who continued to smoke after referral compared with those who stopped or smoked less. Table I shows the effect of different periods of non-smoking or reduced smoking: as the period increased so did the likelihood of having an improved prognosis. There was no difference in the number of cigarettes smoked between those who stopped or smoked less and those who continued smoking; nor were there differences in age at onset, age at first referral, claudication distance, or prevalence of other risk factors.

Fourteen patients underwent repeat arterial surgery because of worsening symptoms. Nine of these were persistent smokers and five patients who stopped or reduced smoking after referral. The interval between initial and repeat operations was significantly shorter, however, in those who continued to smoke (Mann-Whitney U test, $P < 0.05$).

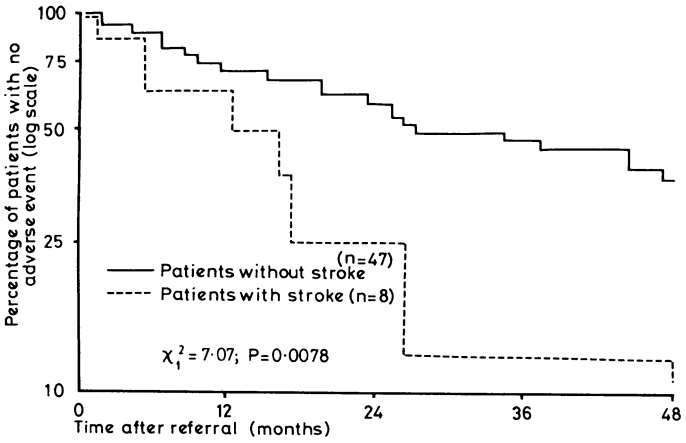

FIG 1—Effect of cerebrovascular disease on prognosis of patients with intermittent claudication.

TABLE I—*Significance of difference in survival between patients who stopped or reduced smoking and those who continued to smoke according to different starting points (date of referral, and 3, 6, and 12 months later) chosen for survival curves*

	Referral	Months after referral		
		3	6	12
Significance ..	$\chi_2^2 = 1.72$; P = 0·4242	$\chi_2^2 = 3.13$; P = 0·1191	$\chi_2^2 = 4.59$; P = 0·1007	$\chi_2^2 = 7.07$; P = 0·0296

In this study the presence of ischaemic heart disease and high lipid and glucose concentrations did not appear to influence prognosis.

Study 2

METHODS

The small number of patients in study 1 necessitated using adverse events as end-points, which could account for our inability to show that ischaemic heart disease, diabetes, hypertension, and hyperlipidaemia were important prognostic factors. To obtain further information on the natural history of IC we used the Oxford Record Linkage Study (ORLS)[11] to identify all the 160 patients discharged from hospital after a first admission for peripheral vascular disease in the Oxford region during 1965-6. This information system also provided data on subsequent hospital admissions, surgical procedures, and deaths up to the end of 1972. Hospital records were examined for information concerning risk factors, and life tables were constructed as described above using death and amputation as end-points.

RESULTS

The patients (99 men and 61 women) were aged 35-90 (mean 68·6), and all were studied for at least five years; 94 died. Table II shows the proportion who survived for five years after their first hospital admission compared with the estimated proportion of people expected to survive in the general population of England and Wales.

TABLE II—*Percentages of patients who survived for five years after first hospital admission for peripheral vascular disease (PVD) compared with estimated five-year survival of general population of England and Wales**

Age (years)	Men		Women	
	PVD	General population	PVD	General population
35-49	60	98	100†	98
50-59	76	92	86	96
60-69	48	80	64	90
70-79	27	59	33	73
80-94‡	14	44	20	51

*Rates for general population of England and Wales calculated from Annual Abstract of Statistics.[13]
†Only six patients at risk.
‡Rates for general population provided only for people aged 80-85, so proportion surviving is overestimate compared with patients with PVD.

The 160 patients had a total of 480 hospital admissions during the follow-up period. The average duration of each admission (excluding convalescent admissions) was 18 days, and if all admissions including those for convalescence and limb fitting are counted 11 190 patient-days were spent in hospital. Forty-eight patients (30%) underwent amputation, 12 (8%) on both legs. Reconstructive surgery was performed on 53 patients (33%) (eight (15%) of whom underwent subsequent amputation) and sympathectomy on 38 (24%). Survival and the likelihood of amputation depended strongly on age.*

Fifty-eight patients (36%) had evidence of ischaemic heart disease, as described above. The death rate was significantly higher among these patients than among those with no evidence of this disease (14 (24%) alive after eight years compared with 49 (48%); $P < 0.0001$).* A similar trend was apparent among patients with cerebrovascular disease.*

* Life tables for study 2 may be obtained from Dr J Mann, University Department of Social and Community Medicine, Oxford.

The diagnosis of diabetes was based on a history of treatment, since glucose concentrations were rarely recorded in the notes. The presence of diabetes thus defined was not associated with increased mortality but was associated with increased risk of amputation. After eight years 20% of the patients without and 56% of those with diabetes had undergone amputations ($P < 0.005$).

Twenty patients (13%) were being treated for hypertension, and their prognosis did not appear to differ from that of patients not receiving treatment; neither did prognosis differ when other arbitrary cut-off points based on the blood-pressure readings recorded in the notes were considered. Smoking habits on first admission were recorded for 117 (73%) of the 160 patients, 105 (90%) of whom were smokers or ex-smokers. Smoking habits after referral were rarely recorded in follow-up hospital notes, however, so that the effect on outcome of stopping or reducing smoking could not be determined.

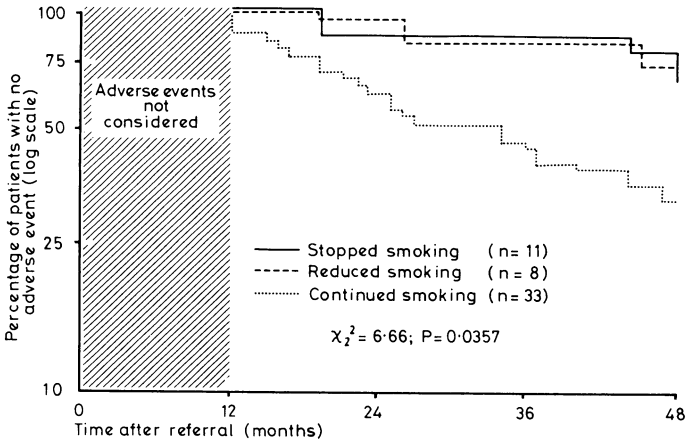

FIG 2—Effect on prognosis of smoking habits after referral.

Discussion

Age, ischaemic heart disease or cerebrovascular disease, and continued smoking were the principal factors associated with an adverse prognosis in patients with IC. Our failure to show the effects of other risk factors on prognosis may have been a consequence of the methods used. Bias, however, is unlikely to have affected the results. The differences observed were highly significant, and probably the factors identified in the two studies are major ones determining patient outcome.

At first our results appear to suggest that there is probably little value in treating hyperlipidaemia or even hypertension, but this may not be so. We considered several non-fatal adverse events in the life-table analyses, and since the risks of coronary artery disease and stroke—the leading causes of death in patients with IC—are increased with raised serum lipid concentrations and blood pressure, it would be unwise to withhold treatment of these disorders on the basis of these data. A further study is now under way to see whether correcting hyperlipidaemia results in an improved prognosis.

The rate of readmission to hospital of patients with IC was greater than that of patients admitted with other conditions, and the average duration of each acute admission (18 days) was twice as long as the average duration of admission to general hospitals in the ORLS area for all causes during the period.[12] Thus IC was associated not only with a significantly reduced life expectancy but also with appreciable morbidity and a considerable drain on health service resources. Smoking was the only correctable risk factor with an appreciable effect on prognosis, and we have found it useful to show patients with IC the life table in fig 2, which illustrates the benefits of stopping smoking. It is extremely important to encourage patients with IC to stop smoking so that the morbidity and mortality associated with the disease may be decreased.

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Intermittent claudication: prevalence and risk factors

W G HUGHSON, J I MANN, A GARROD

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Summary and conclusions

Risk factors for intermittent claudication (IC) were studied in 54 patients—that is, all patients with IC on the lists of two general practices—and 108 controls. Smoking was the factor most strongly associated with the development of IC, but systolic and diastolic blood pressures and concentrations of triglyceride, urate, and fibrinogen were all significantly higher among the patients with IC than the controls. The presence of more than one factor appeared to be associated with a multiplicative increase in risk. Cholesterol, an important risk factor for ischaemic heart disease, was not associated with an increased risk of IC. IC was present in about 2% of the men and 1% of the women, who were aged 45-69 years.

These findings suggest that IC, a common and disabling manifestation of atherosclerosis, may be largely preventable.

Introduction

The aetiology of peripheral vascular disease has been less well investigated than other clinical manifestations of atherosclerosis. Data from the Framingham study[1] suggest that risk factors for peripheral vascular disease may be different from those for ischaemic heart disease and cerebrovascular disease. We studied a group of unselected patients from two Oxfordshire general practices together with controls in an attempt to determine the