Intermittent Claudication in Hypertensive Men

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Intermittent claudication is an important cause of morbidity in middle-aged and older members of the community (Hughson et al., 1978a, b). Smoking is the strongest risk factor and is associated with an eightfold chance of developing claudication (Gordon and Kannel, 1972; Hughson et al., 1978a). Raised blood pressure also confers an increased (threefold) risk of developing intermittent claudication (Gordon and Kannel, 1972; Hughson et al., 1978a), which may therefore be regarded as a vascular complication of hypertension. As such it has been overshadowed by life-threatening sequelae such as stroke and myocardial infarction, and has received little attention. This study reports the incidence of intermittent claudication in hypertensive men attending hospital clinics, and examines the associated factors.

Patients and Methods
The Glasgow Blood Pressure Clinic consists of hypertension clinics in four teaching hospitals. Clinical information on all patients is recorded in a standard manner and stored in a computer (Glasgow Blood Pressure Clinic, 1972). At the first attendance intermittent claudication, diagnosed by ordinary clinical methods, is specifically sought and recorded as absent, doubtful, probable, or definite. A computer printout identifying all men with probable or definite claudication at entry to the clinic between 1969-76 was the basis of this study. A control group of hypertensive patients who did not have intermittent claudication was drawn from a list of all patients who had entered the clinic. Each patient with claudication had a single control matched for sex, age (same decade), hospital, and hospital number (providing an approximate match for date of entering the clinic). Clinical data were taken from proformas completed at the first attendance. Smoking habits were recorded in four categories; current cigarette smokers, ex-smokers, pipe or cigar smokers, and those who had never smoked. Alcohol consumption was recorded by a simple scoring system that correlates highly significantly with biochemical evidence of liver dysfunction (Ramsay, 1977). Current antihypertensive treatment was documented fully, but previous treatment was not recorded systematically. However, there was no reason to believe that the available data were biased for the present purpose. The statistical methods used were chi-square, with Yates’s correction when appropriate (Swinscow, 1976), and Student’s unpaired t test.

Results
Of 1,357 hypertensive men, 75 (5.5 per cent) had probable or definite intermittent claudication. The incidence was clearly related to increasing age and to smoking (Table 1). In patients over 40 years of age, cigarette smokers had a relative risk for claudication of 4.6 ($\chi^2 = 15.0, p<0.001$) and ex-smokers a relative risk of 4.5 ($\chi^2 = 9.6, p<0.01$) compared to those who had never smoked. Pipe or cigar smokers had a non-significant increase in risk. The patients with claudication and matched hypertensive controls are compared in Table 2. The relationship with current and previous cigarette smoking was confirmed. More patients with claudication had angina ($p<0.001$) and myocardial infarction, but a history of stroke was equally common in the two groups.

Table 1. Incidence of Intermittent Claudication in Hypertensive Men Related to Age and Smoking Habits. (%).

| Smoking     | 39  | 40-49 | 50-59 | 60- | TOTAL  |
|-------------|-----|-------|-------|-----|--------|
| Never smoked| 1/131 (0.8) | 2/133 (1.5) | 3/135 (2.2) | 2/49 (4.1) | 8/448 (1.8) |
| Pipe or cigar| 0/11 (0.0)  | 0/32 (0.0)  | 3/42 (7.1)  | 1/19 (5.3)  | 4/104 (3.8)  |
| Ex-smokers  | 0/18 (0.0)  | 2/33 (6.1)  | 4/64 (6.3)  | 6/32 (18.8) | 12/147 (8.2) |
| Cigarettes  | 1/121 (0.8) | 9/209 (4.3) | 22/218 (10.1)| 19/110 (17.3)| 51/658 (7.8) |
| TOTAL       | 2/281 (0.7) | 13/407 (3.2) | 32/459 (7.0) | 28/210 (13.3) | 75/1357 (5.5) |

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Table 2. Clinical Features of Hypertensive Men with Intermittent Claudication, and of Control Hypertensive Patients without Claudication matched for sex, age, hospital and hospital number. Mean (and SD) results.

|                  | Intermittent claudication (n = 75) | Control patients (n = 75) |
|------------------|-----------------------------------|--------------------------|
| Age (years)      | 56.6 (8.0)                        | 56.3 (7.9)               |
| Weight (kg)      | 70.9 (11.5)                       | 74.1 (10.8)             |
| Serum cholesterol (mmol/l) | 6.3 (1.2)                        | 6.3 (1.0)               |
| Systolic BP (mmHg) | 187 (29)                         | 186 (30)                |
| Diastolic BP (mmHg) | 109 (17)                         | 109 (16)                |
| Untreated        | 26                                | 30                       |
| Antihypertensive drugs/patient | 1.11                             | 0.85                    |
| Smoking*:        |                                   |                          |
| never            | 8                                 | 22                       |
| pipe or cigar    | 4                                 | 11                       |
| ex-smokers       | 12                                | 7                        |
| cigarettes       | 51                                | 35                       |
| Alcohol:         |                                   |                          |
| nil or occasional| 48                                | 50                       |
| frequent or heavy| 24                                | 23                       |
| Angina**         | 24                                | 5                        |
| Myocardial infarction | 10                             | 5                        |
| Stroke           | 13                                | 12                       |

\*χ² = 14.1, p < 0.01.  **χ² = 15.9, p < 0.001

Blood pressure did not differ between the groups, but patients with claudication were taking slightly (but not significantly) more antihypertensive drugs. However, comparisons of measurements only in untreated patients, and in pairs of patients who were concordant for the number of drugs taken, failed to reveal a significant difference in blood pressure. Patients with claudication and controls did not differ in age (by design), height, weight, alcohol intake, or serum total cholesterol. The drugs taken currently when entering the clinic were not different in the two groups, although more patients with claudication were taking a β-blocker (8 patients versus 2 controls). When previous antihypertensive treatment was included (Table 3) the excess of β-blocker treatment in patients with claudication reached significance (χ² = 4.4, p < 0.05), and remained just significant when patients who had never received any treatment were excluded (χ² = 3.9, p < 0.05). The frequency of treatment with diuretics, central-acting sympathetic blockers or postganglionic adrenergic blockers did not differ significantly. Examination of the twelve matched pairs, which included a patient who had taken a β-blocker, revealed that 9 of the 12 with claudication also had angina, compared to 1 of 12 control patients (p < 0.05, McNemar’s test).

Table 3. Antihypertensive Drugs taken Currently and in the Past by 75 Hypertensive Men with Intermittent Claudication and by matched control patients.

|                  | Intermittent claudication | Control patients |
|------------------|---------------------------|------------------|
| Diuretics        | 33                        | 22               |
| Postganglionic adrenergic blockers | 12                        | 12               |
| Centrally-acting sympathetic blockers | 39                       | 33               |
| β-adrenergic blockers* | 10                       | 2                |

\*χ² = 4.4, p < 0.05

Discussion

Intermittent claudication was present in 6.8 per cent of hypertensive men aged over 40 years at entry to the clinic, compared to the prevalence of 2.2 per cent in men aged 45 to 69 years in the community (Hughson et al., 1978a). Even allowing for possible referral bias (e.g. from vascular clinics) and less stringent diagnostic criteria in the present study, the relationship between claudication and hypertension (Gordon and Kannel, 1972; Hughson et al., 1978a) seems to be confirmed. As in population studies (Gordon and Kannel, 1972; Hughson et al., 1978a; Heliovaara et al., 1978) cigarette smoking was an outstanding risk factor in hypertensive men, and ex-smokers had a similar risk. Pipe and cigar smoking cannot be exonerated by the absence of a significant association in this study, as the number of patients was small, and a significant risk has been shown in a previous study (Heliovaara et al., 1978). In accord with population data (Hughson et al., 1978a), body weight and serum cholesterol were not related to claudication. Intermittent claudication could not be related to the severity of hypertension, although such an association may have been obscured by the use of single blood pressure measurements, or by the heterogeneity of the patients as regards antihypertensive treatment. Nevertheless, claudication was also unrelated to a history of stroke, the complication that reflects most closely the severity of hypertension (Gordon and Kannel, 1972), but was closely associated with ischaemic heart disease, which is less clearly linked to hypertension (Gordon and Kannel, 1972). Sirtori et al. (1974) have shown a higher intake of alcohol and carbohydrate in patients with claudiation than in controls, and speculated that these factors may be responsible for the high triglyceride concentrations observed in claudication (Hughson et al., 1978a; Sirtori et al., 1974). The possibility that alcohol may be a confounding factor in the relationship between smoking and claudication has also been raised (Lithell et al., 1975). This study failed to confirm an increased alcohol consumption by patients with claudiation, and showed that the relationship between smoking and claudication was independent of alcohol.

The influence of antihypertensive treatment on intermittent claudication has not been studied systematically. Cross-sectional studies like the present one can give only limited information on this aspect, since the presence of intermittent claudiation, and its frequent association with angina, would tend to bias the decision whether or not to treat milder degrees of hypertension. However, it was felt that the pattern of drugs used by patients with and without claudiation might be more revealing. In particular, there was anecdotal evidence that β-adrenergic blockers can cause intermittent claudication (George, 1974; Conway, 1975; Rodger et al., 1976), and this, if it was a common problem, would result in an excess of β-blocker treatment among hypertensive patients with claudiation. In fact this was observed, but
there are grounds for doubting whether the statistical association between \( \beta \)-blockers and claudication represents cause and effect. During the period of the study \( \beta \)-blocking drugs were used almost exclusively in hypertensive patients who also had angina. Since angina was closely related to intermittent claudication, a spurious association between \( \beta \)-blockers and claudication was to be expected. Angina is an important confounding factor which needs to be considered in any future study of the relationship between \( \beta \)-blockers and peripheral vascular disease.

It is of interest to consider the management of the patient with intermittent claudication who also has mild hypertension, not requiring treatment in its own right. Should the presence of claudication be considered an indication for antihypertensive treatment? It is not known whether the prognosis of claudication is improved by lowering the blood pressure, but there is some evidence to suggest that the outcome may be disappointing. Claudication showed no relationship to the severity of hypertension in this study; the prognosis of claudication was not influenced by the presence or absence of hypertension in another (Hughson et al., 1978b); and claudication keeps company with ischaemic heart disease (Table 2) which has not so far yielded to antihypertensive treatment. On the other hand, there is good evidence that the prognosis of claudication is greatly improved by stopping or reducing cigarette smoking (Hughson et al., 1978b). The increased risk of claudication in ex-smokers in the present study does not contradict this, as most had quit smoking only shortly before entering the clinic. On the evidence available it would seem that a high priority should be given to inducing these patients to stop smoking.

Conclusions

Intermittent claudication was diagnosed in 5.5 per cent of hypertensive men attending a blood pressure clinic, and was strongly related to increasing age and to current or past cigarette smoking. Co-existent ischaemic heart disease was common, but claudication was not related to the severity of the hypertension or to a history of stroke. There was a statistical relationship between treatment with \( \beta \)-blockers and claudication, but this was probably a spurious association through their common link with angina, and not cause and effect. Claudication was not related to body weight, serum cholesterol or alcohol intake, and the association of smoking and claudication was independent of alcohol. There is at present no evidence that treatment of hypertension will prevent or ameliorate intermittent claudication, whereas a beneficial effect of stopping smoking has been shown.

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Medicine By All

The late Elizabethan Annals of the College are full of disciplinary action against those who, without due qualification, practised physic, and there were some pretty odd characters around who did so. A Mr Beauter gave a boy four pills after inspecting his urine. The boy’s mouth suppurated and streamed with saliva; all his teeth became loose and several fell out. An early case of mercury poisoning? Richard Powell of Grub Street, a dyer of cloth, gave a purgative to a clergyman’s wife because she had a stricture of the bowel. His defence was that the decocation was of senna and made up by an apothecary. The Annals do not relate what happened to the patient; maybe the diagnosis was wrong, or so it is to be hoped. Robert Swaine treated the ulcerated leg of Thomas Jackson, a brown baker, and the medicine he gave threw the baker into six bouts of perspiration.

But it was the women accused who seem to have been more enterprising and more numerous than the men. Catherine Clark of Pickleherring was convicted of illegal practice but what she did is not recorded. Alice Minstrel, a widow, gave a bitter potion of herbs to Mr Leerland, whereupon he had sixty stools. Cecilia Pople was accused by three surgeons of wrong and absurd practice in that she treated a woman by fumigation, the woman dying twelve days later. Then there was a woman called Scarlet who treated a man with an ulcerated knee by applying mercury ointment and giving him antimony in white wine until he became completely paralysed. Lastly there was Chaire, an ale-wife in the Smithfield Bars, who gave purges and burnt bits of cloth for which her charges were high, as she said it took so long to burn the cloth properly. She confessed that she had practised physic ever since Mrs Saunders was hanged. Now who was she and why did she hang? The investigating Fellows never asked.