Management of Secondary Risk Factors in Patients with Intermittent Claudication

K. Cassar, R. Coull, P. Bachoo, E. Macaulay and J. Brittenden*

Vascular Unit, Ward 36, Aberdeen Royal Infirmary, University of Aberdeen, UK

Objectives: the first line management of patients with intermittent claudication is "best medical therapy" i.e., smoking cessation, exercise, antiplatelet therapy and risk factors modification. The aim of this study was to assess the current management of risk factors in primary care and to compare General Practitioner (GP) attitudes and actual management. Design and Methods: postal questionnaire of all 336 GPs in the referral area (Grampian, Scotland). Questionnaire and measurement of serum cholesterol, blood glucose and HbA_{1c} of new clinic patients (n = 104) with claudication referred by general practitioners.

Results: a 73% GP response rate was obtained. Ninety-five percent of GPs would treat risk factors. The vast majority would prescribe aspirin, yet 28% of patients were on no anti-platelet therapy. Eighty-nine percent of GPs would advise an increase in exercise but only 14% of patients recalled being told to do so. One in seven of the GPs would not check serum cholesterol, 18% considered cholesterol lowering therapy to be primary prevention and 41% would only treat levels above 5.5 mmol/l. Eighty-five percent of patients were on a statin or had a cholesterol above 5 mmol/L. Seventy-seven percent of GPs would check glucose levels, and 14% of patients were found to be previously undiagnosed diabetics. **Conclusions:** risk factors in claudicants are suboptimally managed. Urgent guidelines for the specific management of

claudicants by general practitioners, as well as strategies to ensure their implementation, are required.

Key Words: Intermittent claudication; Risk factors; Cholesterol; Smoking; Antiplatelet therapy; Exercise.

Introduction

Intermittent claudication affects between 1.7¹ and $7.1\%^2$ of the population over 55 years of age. In terms of the limb, the condition is relatively benign with less than 10% of claudicants requiring intervention to prevent limb loss and less than 1% per year requiring amputation.^{3,4} However, cardiovascular mortality in patients with intermittent claudication is twice to three times increased compared to an age and sex matched population.⁴ In the Edinburgh Artery study almost 20% of patients with intermittent claudication were dead within 5 years,² 13.7% from cardiovascular causes. The major risk factors for both cardiovascular disease and peripheral vascular disease – cigarette smoking, hypercholesterolemia, hypertension and diabetes – are well recognised. The Joint British recommendations on prevention of coronary heart disease in clinical practice state that patients with peripheral arterial disease should be managed in the same way as those with established coronary heart disease.⁵

The Scottish Intercollegiate Guidelines Network published a national clinical guideline on "Drug Therapy for Peripheral Vascular Disease" in July 1998.6 This guideline recommends that all claudicants should be prescribed aspirin. Although risk factors are acknowledged it was felt that specific recommendations for their modification was out with the remit of the guideline. Currently, no clear guidelines are available for the management of individual risk factors in patients with intermittent claudication.

It has been estimated that 55% of claudicants have hypertension, 14% are diabetic and 56% have abnormalities of lipid metabolism.⁷ It is unclear what proportion of patients with these risk factors are diagnosed and treated in primary care prior to attending a specialist clinic. However, a previous study of patients with peripheral vascular disease admitted to a regional vascular unit, revealed that 80% of hypercholesterolaemic patients were undiagnosed at the time of hospital admission.⁸

The aim of this study was to determine the attitudes of General Practitioners (GPs) to referral, risk factor management and treatment in patients presenting with life-style limiting claudication. This involved a postal survey questionnaire of all GPs within the

^{*} Please address all correspondence to: J. Brittenden, Ward 36, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, UK.

referral area of a regional vascular unit. Questions were asked about the following: antiplatelet therapy, diabetes, cholesterol, smoking and exercise. The extent of treatment of these risk factors was also assessed in new patients attending the vascular out-patient clinic in order to compare GP atittudes with actual treatment of risk factors.

Materials and Methods

GP questionnaire

A Postal survey questionnaire was sent to all 336 GPs within the referral area of a regional vascular unit (Grampian, Scotland) in September 2001 (see Appendix A). The questionnaire was developed in conjunction with the Health service research unit and department of general practice in the University of Aberdeen. The general practitioners were asked about whether they would treat risk factors in patients with intermittent claudication. Further specific questions were asked about the following risk factors: antiplatelet therapy, exercise, diabetes, cholesterol and smoking. The questionnaire was anonymous and no reminders were sent out.

Patient survey

One hundred and four consecutive patients presenting with claudication to the Grampian Vascular Out-Patients clinic at Aberdeen Royal Infirmary were asked to complete a questionnaire regarding risk factor management. All patients surveyed were referred by GPs before the GP questionnaires were sent out. Questionnaires were completed by the patient before they were seen by a doctor and only those from patients in whom the diagnosis of intermittent claudication was correct were analyzed. A further 21 patients were referred by the GP with a diagnosis of intermittent claudication which was not confirmed on clinical grounds and have, therefore, not been included in this analysis. The patients were referred by 100 of the GPs included in the postal survey. Patients were asked about whether they had undergone any blood investigations, what treatment they were on and what advice they had been given by their general practitioner. The responses of the patients were cross-checked with the information provided by the GP in the referral letter. Blood glucose, HbA_{1c}, and serum cholesterol levels were measured at the clinic. Ethical approval was sought but was deemed unnecessary by local ethical committee.

Results

A 73% response rate was received from the GP postal questionnaire. The first question asked GPs how they would manage patients with intermittent claudication at initial presentation (Fig. 1). The vast majority of GPs recognized the importance of risk factor management with 50% stating that they would undergo a period of risk factor management and reassess prior to referral, and 45% would treat risk factors and refer directly to the vascular OP clinic. The management of individual risk factors will be discussed below and compared to the findings in clinic patients. No significant differences in risk factor management were noted between male and female patients attending the clinic.

Patients

One hundred and four consecutive new patients with intermittent claudication completed the patient questionnaire. There were 57 males and 47 females (F:M ratio = 1:1.2), with a median age of 70 years (range 41–85) (Table 1). The mean (standard deviation) estimated



Fig. 1. GP management at initial patient presentation.

Table 1. Level of cholesterol at which GPs initiate treatment.

What level of cholesterol would you treat?	п	%
<5 mmol/l	11	5
>5 mmol/l	85	36
>5.5 mmol/l	42	18
>6 mmol/l	54	23
Depends on risk factor profile	43	18
Depends on HDL/cholesterol ratio	6	3
Total	235	100

walking distance was 228 metres (283 m), and the mean (standard deviation) ankle-brachial pressure index was 0.67 (0.19). The patients had significant cardiac co-morbidity with 32% having a history of angina or myocardial infarction, 12% had coronary artery by-pass grafting and 43% were on anti-hypertensive therapy.

Risk factors

Aspirin

Ninety percent of the GPs stated that they would prescribe aspirin routinely to patients with intermittent claudication and 71% would prescribe clopidogrel if the patient had a contra-indication to aspirin. Amongst the patients surveyed 59% were prescribed aspirin and 7% self-medicated. One percent was taking clopidogrel and 5% were on warfarin. In total 72% of the 104 patients with claudication were on antiplatelet or anti-coagulant medication. Of the remaining patients, 8% complained of side effects to aspirin and thus 20% were not an aspirin and had no contraindication to the drug.

Physical exercise

Eighty-nine percent of GPs stated that they advise claudicants to increase their level of activity. Only 15 (14%) patients could recall being given advice to increase their level of physical activity. Only five (5%) of the GP letters had any reference to advice about exercise.

Diabetes and HbA_{1c} measurement

When asked if they would measure blood glucose levels, 77% of GPs stated that this was their normal practice. Only 29% of the 104 patients attending the clinic could recall having their blood glucose checked and another 30% were unsure. Only in 12 of these patients did the GP referral letter mention the patient's blood glucose level. There were 16% known diabetics and of the remaining 86 patients 12 (14%) were found to have a HbA_{1c} level greater than 6.5 which is indicative of diabetes.⁹

Cholesterol measurement and treatment

Eighty-five percent of GPs would routinely check serum cholesterol levels in patients with claudication. Only 53 (51%) of the patients could recall having their serum cholesterol checked and 26 (25%) were unsure. The levels of cholesterol that GPs would treat are shown in Table 1. It is of note that 18% of GPs stated that they would not treat cholesterol in claudicants unless other risk factors were present. First line management consisted of dietary advice in 70% and statin and diet in 30%. Eighteen percent of GPs stated that they exercised an age limit to commencing lipid-lowering therapy. The age limits were as follows: 70 years, n = 4 (2%); 75 years, n = 20 (8%); 80 years, n = 17 (7%) and two (1%) would not treat patients over 85 years of age. Eighty-five percent of patient were on a statin or had a cholesterol above 5 mmol/l. Thirty-nine patients were on a statin, of these 18 (46%) still had a cholesterol level over 5 mmol/l and eight (21%) had a cholesterol level above 5.5 mmol/l. Of the 65 patients not on a statin the cholesterol levels were as follows: <5 mmol/l, n = 16; 5–5.4 mmol/l, n = 7; 5.5–5.9 mmol/l, n = 14; and >6 mmol/l n = 28.

Cigarette smoking

Nearly all (99%) of GPs stated that they would advise patients to stop smoking and had access to a smoking cessation clinic. Eighty-seven percent would prescribe nicotine replacement therapy. Thirty-nine percent of patients admitted to smoking, and 44% claimed to have stopped smoking, 15% within the previous year. Seventeen percent had never smoked. In the GP referral letter, there was no mention of the smoking status in 32 cases (31%). Only 34 (85%) of the smokers could recall being advised to stop smoking and 31 (78%) had been given an explanation of the effects of smoking on their condition. Only seven (18%) of the 39 smokers had been given any further help to stop smoking.

Discussion

It is generally accepted that the first line management of patients with intermittent claudication is "best medical therapy" aimed at reducing risk factors and advice to exercise regularly. Housley, in a 1988 leading article summarized the treatment of claudication as "Stop smoking and keep walking".¹⁰ In 1988, the Scottish Intercollegiate guideline network recommended that in addition all claudicants should be prescribed aspirin. Also in 1998, the Joint British recommendations on prevention of coronary heart disease in clinical practice stated that patients with peripheral vascular disease were "just as likely to die from a heart attack as many patients who have survived there first myocardial infarction" and recommended that they should be managed in the same way as those with established coronary heart disease.⁶ This includes the detection and treatment of diabetes and lipid abnormalities.

In this survey we have revealed deficiencies in the management of each of the following risk factors: antiplatelet therapy, exercise, diabetes, cholesterol, and smoking. Firstly with regards to anti-platelet therapy, although the majority of the GPs questioned stated that they would prescribe aspirin to claudicants this does not appear to occur in practice as over a quarter of the patients surveyed were on no anti-platelet or anti-coagulant medication. Antiplatelet therapy protects against non-fatal myocardial infarction, non-fatal stroke and vascular death in patients with intermittent claudication.¹¹ It is surprising that despite the unequivocal evidence for the use of aspirin and the presence of national guidelines that it is still not standard practice for all claudicants to be prescribed an antiplatelet agent.

Exercise has been clearly shown to be of benefit, not only in terms of secondary prevention but also in its ability to increase patients' walking distance in structured programmes.¹² Most GPs in this survey stated that they would advise claudicants to increase their level of physical activity but only a small minority of patients (14%) could recall being advised to do so. Patient recall may be inaccurate, but clearly there is a huge discrepancy here on what is one of the most fundamental and basic treatment options available.

Diabetes has long been recognised as a major risk factor for peripheral vascular disease. In the Framingham Trial, the age-adjusted risk ratio for intermittent claudication in diabetic patients compared to controls was five times greater for men and four times greater for women.¹³ All patients with intermittent claudication should have blood glucose measured in order to identify patients with diabetes. Surprisingly only 77% of the GPs questioned stated that they would measure blood glucose in this group of patients. Furthermore, 12 of the 104 patients were found to be previously undiagnosed diabetics.

To date, there have been three published major randomised controlled secondary prevention trials involving statins – the Scandinavian simvastatin survival study (4S),¹⁴ the cholesterol and recurrent events trial (CARE)¹⁵ and the long term intervention with pravastatin in ischaemic disease study (LIPID).¹⁶ These have totaled over 17 000 patients and have shown that total mortality and major coronary events can be significantly reduced by lowering cholesterol with statin therapy in patients with a history of cardiac disease.

Until recently the effect of lipid reduction in patients with isolated peripheral vascular disease has not been studied. However, the Joint British Recommendations on prevention of coronary heart disease⁵ has stated that what evidence there is available supports the treatment of claudicants with statins with the aim of reducing the serum cholesterol to less than 5 mmol/l. In our study, 1 in 7 of the GPs questioned

would not even check serum cholesterol level in claudicants. Furthermore, 18% of GPs consider cholesterol lowering therapy to be primary rather than secondary prevention and thus would not start statin therapy in claudicants irrespective of the cholesterol level unless they had other risk factors. Furthermore, despite the recommendations to reduce cholesterol levels to less than 5 mmol/l, 41% of GPs in our survey would only treat levels above 5.5 mmol/l. Of the 65 patients not on statin therapy, 49 (75%) had a cholesterol level greater than 5 mmol/l and 42 (65%) of these had a level greater than 5.5 mmol/l. Nearly half the patients on a statin had a cholesterol greater than 5 mmol/l suggesting suboptimal therapy. In total, 85% of patient were on a statin or had a cholesterol above 5 mmol/l, illustrating how common lipid abnormalities are in claudicants.

Recently the Heart Protection Study¹⁷ has shown that treatment with simvastatin 40 mg results in a 40% reduction in total mortality, vascular mortality, coronary heart disease events, strokes and noncoronary revascularisations in patients with peripheral vascular disease. The Heart Protection Study has shown that statin therapy should be provided to all patients with intermittent claudication providing their cholesterol is greater than 3.5 mmol/l. This represents a considerable change in current practice, which may be difficult to achieve given that our current guidelines are not being met.

Smoking cessation reduces the risk of mortality in patients with coronary heart disease and benefits are observed within one year of stopping smoking.¹⁸ Encouraging patients to stop smoking, reinforced at several visits has been shown to double the smoking cessation rate.¹⁹ Similarly nicotine replacement therapy increases quit rate by approximately two-fold.²⁰ Antidepressants (bupropion and nortriptyline) have also been found useful in helping patients to stop smoking.²¹ Practically all the GPs in our study stated that they would advise their patients to stop smoking and a significant proportion (>85%) would prescribe nicotine replacement therapy. However only a small proportion (10%) of smokers in our patient group had been prescribed nicotine replacement therapy. Thus with regards to smoking claudicants again appear to be receiving suboptimal therapy.

In this study we have shown that risk factors are common in claudicants and are clearly being managed suboptimally. While general practitioners claim that they would treat risk factors in claudicants, a significant proportion would not test for major risk factors and would not treat risk factors optimally. This may in part be due to the paucity of guidelines for the management of specific risk factors in patients with claudication rather than cardiovascular disease. Clearly, the basic message even with regards to aspirin and exercise is not being conveyed into clinical practice. Furthermore this is not a problem unique to this area as other health regions have highlighted deficiencies in risk factor management in vascular patients.²² It may be that GPs wish the diagnosis of IC to be confirmed prior to initiating treatment of risk factors. Indeed in this patient survey almost one fifth of patients referred with a diagnosis of intermittent claudication by the GPs were not found to have peripheral vascular disease. However, 50% of GPs stated that they would undergo a period of risk factor management and reassess prior to referral and 45% would treat risk factors and refer directly. We of course are unable to comment on the practices of the 27% of GPs who did not respond to the questionnaire. It does, however provide a unique insight into GPs' attitudes and management of patients with intermittent claudication. What is unclear is how well vascular surgeons manage these risk factors or whether they assume that they are being investigated and treated in primary care. We are currently performing a survey of the members of the vascular surgeons of Great Britain and Ireland to evaluate this.

In conclusion, risk factors in claudicants are being suboptimally investigated and treated in the community. Urgent guidelines for general; practitioners on the specific management of patients with intermittent claudication, as well as strategies to ensure their implementation, are required.

Acknowledgements

We would like to thank Sanofi-Synthelabo for sponsoring our audit nurse Rona Coull who performed this audit. We would also like to thank Professor Philip Hannaford, of the University Department of General practice and Dr Ruth Thomas from the Health Service Research Unit for their help with the Project.

References

- CRIQUI MH, FRONEK A, BARRETT-CONNOR E, KLAUBER MR, GABRIEL S, GOODMAN D. The prevalence of peripheral arterial disease in a defined population. *Circulation* 1985; 71: 510–515.
- 2 LENG GC, LEE AJ, Fowkes FGR *et al.* Incidence, Natural history and cardiovascular events in symptomatic and asymptomatic peripheral arterial disease in the general population. *Int J Epid* 1996; **25**: 1172–1181.

- 3 FOWKES FGR. Epidemiology of atherosclerotic arterial disease in the lower limbs. *Eur J Vasc Surg* 1988; **2**: 293–291.
- 4 JELNES R, GAARDSTING O, HOUGAARD JENSEN K, BAEKGAARD N, TONNESEN KH, SCHROEDER T. Fate in intermittent claudication: outcome and risk factors. *Br Med J* 1986; **293**: 1137–1140.
- 5 WOOD D, DURRINGTON P, POULTER N, MCINNES G, REES A, WRAY R. Joint British Recommendations on prevention of coronary heart disease in clinical practice. *Heart* 1998; **80**: S1–S29.
- 6 INTERCOLLEGIATE GUIDELINES NETWORK (SIGN). Drug therapy for peripheral vascualr disease, publication number 27, July 1998.
- 7 VRAY M, CHWALOW J, CHARANSONNEY O et al. National study of obliterative disease of the lower limbs involving general practitionaires in France: Attemio study. J Cardiovasc Pharmacol 1995; 25: S51–S57.
- 8 EVANS SM, TWONEY P, HAGGART PC *et al.* Prevalence and treatment of hypercholesterolaemia in patients with peripheral vascular disease. *Br J Surg* 2000; **87**: 491 (abstract).
- 9 MACAULAY EM, SHAW JM, SIGURDSSON HH, SIMPSON WG, CROSS KS. Plasma glucose should not be used for screening in patients with vascular disease (abstract). *Br J Surg* 1999; Suppl. 1: 26.
- 10 HOUSLEY E. Treating claudication in 5 words. *BMJ* 1988; **296**: 1483–1484.
- 11 ANTITHROMBOTIC TRIALISTS' COLLABORATION. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; **324**: 71–86.
- 12 LENG GC, FOWLER B, ERNST E. Exercise for intermittent claudication (Cochrane Review). In: The Cochrane Library. Issue 1, 2002. Oxford: Update Software.
- 13 KANNEL WB, McGEE DL. Update on some epidemiologic features of intermittent claudication: The Framingham study. J Am Geriatr Soc 1985; 33: 13–18.
- 14 PEDERSEN TF, KJEKSUS J, BERG K *et al* for the Scandinavian Simvastatin Survival Study Group. Baseline serum cholesterol and treatment effect in the Scandinavian simvastatin survival study. *Lancet* 1995; **345**: 1274–1275.
- 15 SACKS FM, PFEFFER MA, MOYE LA *et al*. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med* 1996; **335**: 1001–1009.
- 16 THE LONG-TERM INTERVENTION WITH PRAVASTATIN IN ISCHAEMIC DISEASE (LIPID) STUDY GROUP. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* 1998; **339**: 1349–1357.
- 17 COLLINS R, PETO R, ARMITAGE J. The MRC/BHF Heart Protection Study: preliminary results. Int J Clin Prac 2002; 56: 53–56.
- 18 DALY LE, MULCAHY R, GRAHAM IM, HICKEY N. Long term effect on mortality of stopping smoking after unstable angina and myocardial infarction. *BMJ* 1983; 287: 324–326.
- 19 Law M, TANG JL. An analysis of the effectiveness of interventions intended to help people stop smoking. *Arch Intern Med* 1995; 155: 1933–1941.
- 20 SILAGY C, LANCASTER T, STEAD L, MANT D, FOWLER G. Nicotine replacement therapy for smoking cessation (Cochrane Review). In: The Cochrane Library. Issue 1, 2002. Oxford: Update Software.
- 21 HUGHES JR, STEAD LF, LANCASTER T. Antidepressants for smoking cessation (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2002. Oxford: Update Software.
- 22 HARRISON E, HOLDSWORTH RJ. Should all claudicants be on a statin? Abstract presented at The Annual Scientific Meeting of the Vascular Surgical Society November 2001. In print: BJS.

Accepted 5 November 2002