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Exercise Training Versus Angioplasty for Stable Claudication. Long and Medium Term Results of a Prospective, Randomised Trial*

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Objectives: *To compare percutaneous transluminal angioplsty (PTA) against exercise training in the treatment of stable claudication.*
Design: *Prospective, randomised trial.*
Materials: *Fifty-six patients with unilateral, stable, lower limb claudication assessed prior to randomisation, at 3 monthly intervals for 15 months, and at approximately 6 years follow-up. Thirty-seven patients were available for long term review.*
Outcome measures: *Ankle/brachial pressure index (ABPI), treadmill claudication and maximum walking distances, percentage fall in ankle systolic pressure after exercise.*
Results: *Significant increases were seen in ABPI in the patients treated with PTA at all assessment to 15 months. However in terms of improved walking performance, the most significant changes in claudication and maximum walking distance were seen in the exercise training group. At long term follow-up, there was no significant difference between the groups. Subgroup analysis by angiographic site of disease showed greater functional improvement in those patients with disease confined to the superficial femoral artery treated by exercise training. The overall prognosis for the whole group of patients was benign, with only two (4%) undergoing amputation.*
Conclusions: *Exercise training confers a greater improvement in claudication and maximum walking distance than PTA, especially in patients with disease confined to the superficial femoral artery.*

Key Words: Intermittent claudication; Percutaneous transluminal angioplasty; Exercise therapy; Randomised controlled trial.

Introduction

Percutaneous transluminal angioplasty (PTA) is an established treatment option for patients with lower limb intermittent claudication. It has low complication rates[1] and 5 year patency rates of 80% for aortoiliac and 60% for femoropopliteal disease.[1] Exercise therapy is an alternative, non-invasive treatment for claudication that has been shown to improve patients' walking performance,[2–4] but its effectiveness compared to PTA has not been fully established. A randomised, prospective trial was established to compare these two treatment options, and preliminary results showed a greater improvement in the medium term following exercise therapy than after PTA.[5] This paper reports the final results of the study, including the long-term follow-up of patients 5 years after randomisation.

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Patients and Methods

Between July 1987 and September 1990, 56 patients with stable unilateral claudication were randomised to receive either PTA (30 patients) or to enter a supervised exercise programme (26 patients). The entry criteria for the trial were as follows: (1) stable unilateral claudication with a failure of conservative management for 3 months prior to randomisation; (2) a lesion(s) on angiography suitable for angioplasty, as agreed by surgeons and radiologists; (3) a maximum walking distance of less than 375 m, to allow patients to double their treadmill maximum walking distance within the study protocol. Patients were assessed prior to randomisation, at 3 monthly intervals for 15

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Table 1. **Angiographic site of lesion(s) in each group**

Site of Lesion	PTA (n=30)	Exercise (n=26)
Superficial Femoral Artery (SFA)	15	13
Iliac Artery/Iliac and Superficial Femoral Artery (IA)	15	13

months, and finally at almost 6 years after treatment. At each assessment, resting ankle/brachial pressure indices (ABPI) were measured and the patients exercised on a treadmill at 3 km/h up a 10 degree incline. Claudication and maximum walking distances were recorded up to a maximum of 750 m (equivalent to 15 min walking). Within 45 s of stopping exercise, the ankle systolic pressure was re measured and expressed as a percentage of the resting ankle systolic pressure (% fall in ankle pressure).

In May and June 1994 those patients who were still available for review were re-evaluated to assess their long-term progress. Thirty-seven patients (22 PTA; 15 Exercise) were re-tested, 10 patients had died (4 PTA; 6 Exercise) and the remaining patients were either uncontactable, too ill for review or had undergone amputation. Excluding patients who had died, 80% of patients who were available were re-evaluated.

Subgroups of patients divided according to the angiographic site of disease are shown in Table 1. Half of the patients in each treatment group had disease confined to the superficial femoral artery, and in other half a proximal iliac artery lesion was present. The number of patent run-off vessels below the knee did not differ significantly between groups.

PTA was performed using a conventional guidewire and balloon catheter technique. The lumen was overdilated by 10% above normal, and the balloon inflated for two periods of 45 seconds using the manufacturer's recommended inflation pressures. Heparin cover of 3000–5000 units was given intraarterially during the procedure. Post-procedure angiograms were taken to confirm the success of the angioplasty.

Patients randomised to the exercise training group were invited to attend supervised exercise classes twice a week for the first 6 months. After this, attendance was required on a regular basis according to the patient's progress. Each class lasted 30 min. Dynamic leg exercises were performed, with the intensity of exercise increasing as the patient's exercise tolerance improved. Patients were also encouraged to perform the same exercises at home on a regular basis.

Statistical analysis

Comparison of proportions between groups was made using either the Chi-square test with Yates correction or Fisher's exact probability test as appropriate. The non-parametric data of claudication distance, maximum walking distance and % fall in ankle pressure were analysed as paired data sets with the pre-treatment values using the Wilcoxon matched pairs signed rank sum test (Wilcoxon paired test).

Results

Mean age and proportions of male to female were not significantly different between groups for the patients reviewed. The follow-up time for the PTA group was median 74 months (range 48–83) and for the exercise group was median 70 months (range 45–83). Pre-treatment values for ABPI, claudication distance, maximum walking distance and % fall in ankle pressure were similar for both groups.

In the intervening time since randomisation four patients in the PTA group and 4 patients in the exercise group had undergone angioplasty of the ipsilateral leg. Of the PTA patients undergoing repeat ipsilateral angioplasty, three had the original disease site re-angioplastied, and one patient had a further angioplasty in a different arterial segment. In the contralateral leg, three PTA patients and three exercise patients had received further angioplasty. Two patients had undergone reconstructive surgery; one in the PTA group had an aortobifemoral graft, and one in the exercise group had a femoro-femoral cross-over graft donating to the ipsilateral leg. Overall in the entire randomised group of 56 patients, only two (4%) had undergone amputation.

The profile of the changes of ABPI, maximum walking distance and % fall in ankle pressure with time are shown in Figs. 1–3. In the interests of clarity, the data at long term follow-up have been presented at the median follow-up time of 70 months, although it should be stressed that the range of long term follow-up lies between 45 and 83 months. Claudication distance was significantly greater than pre-treatment values in the exercise group at 6 months ($p = 0.005$), 9 months ($p = 0.001$), 12 months ($p = 0.001$) and 15 months ($p = 0.0001$) in contrast to the PTA group which showed no significant improvement at any of these time intervals.

Patients' performance was analysed further by subgroups according to the different patterns of disease, as shown in Table 1. The improvement in

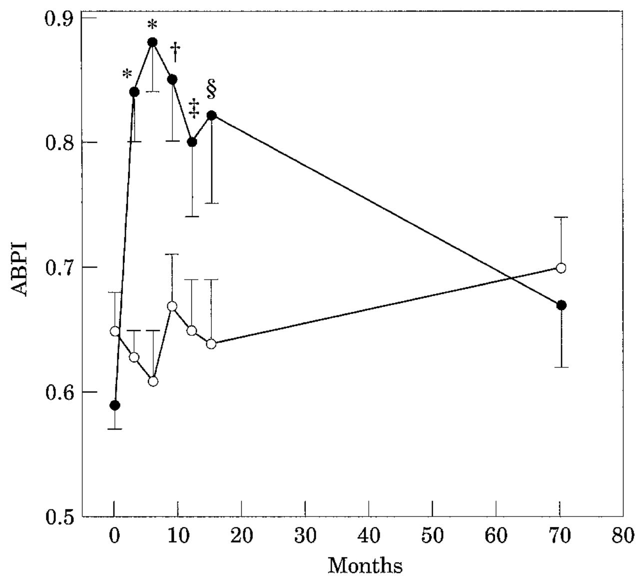

Fig. 1. Median ABPI *vs.* time (standard error bars). *$p = 0.0001$, †$p = 0.001$, ‡$p = 0.005$, §$p = 0.02$ (Wilcoxon paired test). (●) PTA; (○) exercise.

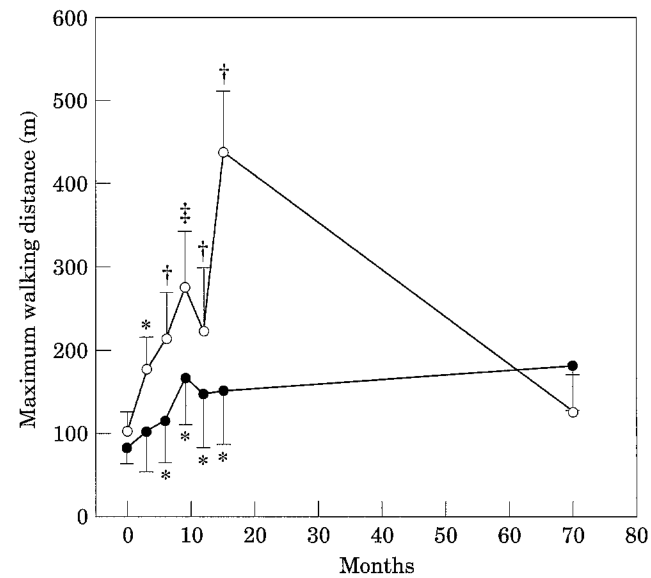

Fig. 3. Median maximum walking distance *vs.* time (standard error bars). *$p < 0.005$, †$p < 0.001$, ‡$p = 0.0001$ (Wilcoxon paired test). (●) PTA; (○) exercise.

walking ability in patients with a proximal iliac artery lesion (IA) was compared with that of patients who had disease confined to the superficial femoral artery only (SFA). The changes in claudication distance and maximum walking distance for patients with IA or SFA disease are shown in Figs. 4 and 5. Significant increases in ABPI were seen only in the group receiving PTA, regardless of the site of disease. The ABPI showed an increase at 3 ($p = 0.002$), 6 ($p = 0.01$), 9 ($p = 0.01$), and 15 ($p = 0.04$) months for the SFA group treated with angioplasty, and at 3 ($p = 0.03$), 6 ($p = 0.003$) and 9 ($p = 0.02$) months for the IA group. In contrast, none of the exercise training patients (both IA and SFA) had any significant increase in ABPI during this same time.

At long term follow-up, only two patients admitted to continuing to perform the exercises every day, and a further three patients exercised more than twice in

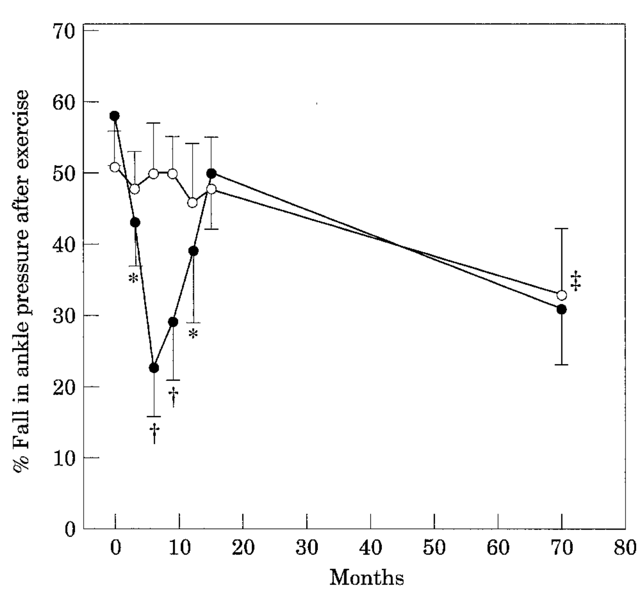

Fig. 2. Median % fall in ankle pressure *vs.* time (standard error bars). *$p = 0.01$, †$p = 0.005$, ‡$p = 0.02$ (Wilcoxon paired test). (●) PTA; (○) exercise.

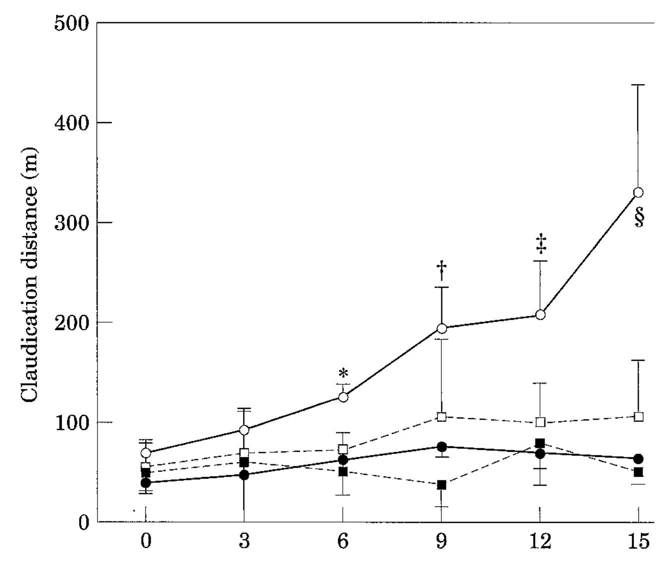

Fig. 4. Median claudication distance *vs.* time (standard error bars). Subgroup analysis according to site of disease (IA or SFA). *$p = 0.01$, †$p = 0.009$, ‡$p = 0.008$ (Wilcoxon paired test). (●) SFA PTA; (○) SFA exercise; (■) IA PTA; (□) IA exercise.

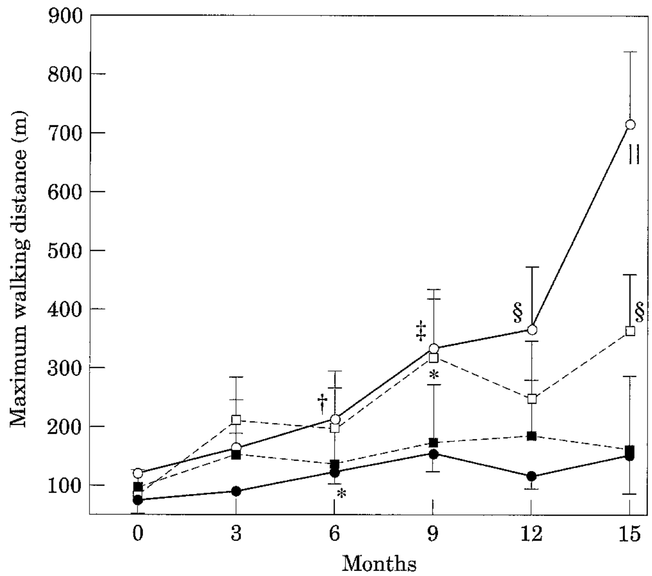

Fig. 5. Median maximum walking distance *vs.* time (standard error bars). Subgroup analysis according to site of disease (IA or SFA). *$p = 0.02$, †$p = 0.004$, ‡$p = 0.003$, §$p = 0.005$, | |; $p = 0.001$ (Wilcoxon paired test). (●) SFA PTA; (○) SFA exercise; (■) IA PTA; (□) IA exercise.

each week. The remainder exercised only sporadically. Nine of the 22 patients (41%) reviewed in the PTA group and 8 out of 15 (53%) in the exercise group continued to smoke.

Discussion

Over the past decade percutaneous transluminal angioplasty (PTA) has been increasingly used as the first-line treatment for lower limb ischaemia, either alone or in conjunction with reconstructive surgery.[6] This preference for the use of PTA over the more conservative management of exercise training appears to have arisen from an unproven perception that PTA produced a better outcome for patients. This prospective, randomised study clearly shows that the increases in claudication distance and maximum walking distance experienced by patients enrolled into an exercise programme were significantly greater than those in patients undergoing PTA. These increases in both claudication distance and maximum walking distance in those randomised to the exercise programme are in line with those in non-randomised observational studies on exercise training.[2,3]

The beneficial effects of exercise training are not simply produced by an increase in collateral blood flow. The studies of Larsen and Lassen[2] and Ekroth *et al.*[3] showed no increase in limb blood flow as measured by Xenon-133 clearance studies[2] or strain gauge plethysmography,[3] observations that are supported by the lack of increase in ABPI seen in the exercise group in our study. At a cellular level, exercise promotes changes in the enzymatic activity,[7,8] and the size and numbers of mitochondria within the muscle,[9] this allowing more efficient utilisation of oxygen. Substrate extraction from blood is enhanced.[10] Within muscle, there is a change of fibre type, with an increase in Type 1 fibres,[11] which are characterised by a more dense capillary network, thus allowing more efficient delivery of substrate to the muscle. Blood fluidity, characterised by an increase in red cell deformity and a reduction in blood viscosity,[12] is increased by exercise training.

Previous studies have suggested that the beneficial effects of exercise training are seen regardless of the site of disease.[3] The subgroup analysis of the patients in this study according to the site of the lesion, does not support this view, although the numbers in each group are small. The most significant improvement was seen in patients with disease confined to the superficial femoral artery. Disease in this arterial segment is often multifocal, and the results of angioplasty within the femoropopliteal segment are less convincing. The relatively small number of patients in each subgroup prevent absolutely definitive conclusions from being reached, but would support recommending exercise training as the initial management of choice in stable claudicants with lesions in the SFA only. This is an area for further investigation.

In the long-term the functional outcome between the two groups was identical. The results show a small, but non-significant increase in all parameters in both groups compared to pre-treatment values, with an encouragingly benign long-term progress regardless of treatment option. The amputation rate for the entire randomised group of patients and the rate of surgical intervention are similar to those reported in studies of the natural history of intermittent claudication.[13–15] The benign natural history of intermittent claudication is confirmed by our study irrespective of whether the treatment given initially was PTA or exercise therapy.

In conclusion, we suggest that many patients currently treated with PTA would be suitable for, and benefit from exercise training. Although the complication rate of PTA is low, nonetheless a small percentage (2%) of patients will require surgery to correct complications.[16] There are no complications of exercise training, nor does it compromise subsequent PTA or surgery should they be necessary. Exercise training has the additional merit of promoting a generalised feeling of well-being.[2] Some patients with coexisting cardiac or arthritic conditions may be prevented from exercising, and some younger patients who are still in full employment may find the exercise programme excessively time-consuming, but these are small subgroups and the majority of patients with stable intermittent claudication would gain a significant improvement in walking performance from enrolment into an exercise programme. The use of exercise training as an adjunctive treatment following reconstructive surgery has been shown to improve the benefit conferred by such surgery[17] and it is possible that the combination of PTA and exercise training may confer the maximal advantage to the patient. This requires further investigation. Long-term fears for the viability of limbs in patients treated with exercise training are not justified. Although the benefits of exercise therapy are not sustained in the long term, because patients tend to stop exercising as time goes by, the long term outcome is identical to patients who receive treatment with PTA.

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