ELSEVIER

Early Outcomes From a Randomized, Controlled Trial of Supervised Exercise, Angioplasty, and Combined Therapy in Intermittent Claudication

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Background: To compare angioplasty (PTA), supervised exercise (SEP) and PTA + SEP in the treatment of intermittent claudication (IC) due to femoropopliteal disease.

Methods: Over a 6-year period, 178 patients (108 men; median age, 70 years) with femoropopliteal lesions suitable for angioplasty were randomized to PTA, SEP, or PTA + SEP. Patients were assessed prior to and at 1 and 3 months post treatment. ISCVS outcome criteria (ankle pressures, treadmill walking distances) and quality of life (QoL) questionnaires (SF-36 and VascuQoL) were analyzed.

Results: All groups were well matched at baseline. Twenty-one patients withdrew. Results are as follows: *Intragroup analysis:* All groups demonstrated significant clinical and QoL improvements (Friedman test, $p < 0.05$). *SEP* (60 patients, 8 withdrew)—62.7% of patients (n = 32) improved following treatment [20 mild, 9 moderate, 3 marked], 27.4% (n = 14) demonstrated no improvement, and 9.8% (n = 5) deteriorated. *PTA* (60 patients, 3 withdrew)—66.6% patients (n = 38) improved following treatment [19 mild, 10 moderate, 9 marked], 22.8% (n = 13) demonstrated no improvement, and 10.5% (n = 6) deteriorated. *PTA + SEP* (58 patients, 10 withdrew)—81.6% of patients (n = 40) improved following treatment [10 mild, 17 moderate, 3 marked], 14.2% (n = 7) demonstrated no improvement, and 4.0% (n = 2) deteriorated. *Intergroup analysis:* PTA + SEP produce a much greater improvement in clinical outcome measures than PTA or SEP alone, but there was no significant QoL advantage (Kruskal-Wallis test, $p > 0.05$).

Conclusion: SEP should be the primary treatment for the patients with claudication and PTA should be supplemented by an SEP.

INTRODUCTION

Peripheral arterial occlusive disease (PAD) is common, affecting 5% of people over the age of 55 years.[1] Intermittent claudication (IC) is the most frequent clinical presentation with symptoms varying according to the site and severity of PAD. Percutaneous transluminal angioplasty (PTA) has long been established as the treatment of choice in aortoiliac PAD but there is no current consensus for the treatment of IC due to infrainguinal PAD.[2] Evidence for treatment efficacy of supervised exercise program (SEP) over PTA is scarce, and it is unclear if combining both treatments gives additional benefit. Two prospective randomized trials comparing PTA with SEP in infrainguinal disease[3-5] were limited by small patient numbers. A Cochrane Review on this subject also highlighted difficulties related to lack of blinding and possibility of bias.

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The review further emphasized the need for larger trials.[6] Furthermore, current evidence suggests that changes in walking distances are poorly correlated with changes in quality of life, which must therefore be studied directly with quality of life (QoL) instruments.[7] Moreover, generic QoL and disease-specific QoL need to be assessed separately.[7,8]

This single-center prospective randomized controlled trial was designed to investigate whether patients with IC secondary to femoropopliteal lesions are best treated with SEP, PTA, or a combination.

PATIENTS AND METHODS

Between September 2002 and April 2007, patients were seen in consultant-led vascular outpatient clinics. All patients with symptomatic unilateral infrainguinal disease claudication were referred for assessment of suitability for inclusion in this trial.

Patients underwent duplex ultrasonography and/or angiography to assess the site and nature of their disease. All scans were discussed in a multidisciplinary vascular team (MDT) meeting consisting of a vascular surgeon, interventional radiologist, specialist vascular nurse, and vascular technologist, and only those with unilateral disease suitable for angioplasty were managed conservatively for 3 months as noted later.

All patients were prescribed antiplatelet therapy (aspirin and/or clopidogrel), received smoking cessation advice and support (including nicotine replacement therapy and NHS smoking cessation program), and risk factor modification (target oriented management of hypertension, hypercholesterolemia, and diabetes according to evidence-based care pathways within a dedicated clinic). All patients also received an advice leaflet regarding exercise. These changes were monitored by the patient's general practitioner and consultant vascular surgeon on an outpatient basis. At the end of the 3 months, patients whose symptoms were stable on this regimen were included in the trial and were randomized, using sealed envelopes, to one of the three treatments; PTA, SEP, or PTA + SEP. Inclusion criteria and exclusion criteria are summarized in Table I.

Table I. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Symptomatic unilateral IC	Critical ischemia
Angioplastiable lesion (ss discussed in MDT)	Severe limitation of physical activity due to systemic disease
Femoropopliteal lesion	Inability to tolerate treadmill testing (unrelated to limb ischemia)
>3 mo on BMT	Significant ischemic ECG during treadmill testing
	Ipsilateral surgery, previous 6 mo
	Ipsilateral angioplasty, previous 6 mo

See text for abbreviations.

Interventions by Patient Groups

Percutaneous Transluminal Angioplasty. PTA was performed by a consultant vascular radiologist as per normal operating practice at a dedicated vascular radiology suite in a tertiary referral center. Contralateral up and over access was used in all cases followed by angiogram and balloon angioplasty. Primary stenting or adjunctive procedures were not performed in any case.

Supervised Exercise Program. SEP patients attended three sessions of supervised exercise per week, for a total of 12 weeks. Each session started with some gentle warm-up exercises followed by a circuit of exercise stations. For the first 6 weeks, patients completed one full circuit; thereafter, the circuit was increased by one station per week, with the result that by the end of the exercise program, patients were completing 12 stations per session. Patients spent 2 minutes at each exercise station and performed 2-minute walking circuits between exercise stations. The sessions ended with gentle stretching and cool-down exercises. All sessions were supervised by trained physiotherapists or physicians.

There were six exercise stations, arranged in the following order:

Station 1: Walking up and down a 6-inch step

Patients started with the left foot first, and then changed the starting foot every 10 steps. This was continued for 2 minutes

Station 2: Double heel raise

Standing erect, with both feet flat on the floor and holding hand rails for support, patients stood on tiptoes. This was held for approximately 2 seconds; then the patient slowly returned their weight to the floor. This was repeated for 2 minutes.

Station 3: Single leg press

Patients stood on one leg between two parallel bars, used for stability rather than weight-bearing, and slowly lowered their weight by flexing the knee of the standing leg, then straightened the leg

Table II. ISCVS outcome criteria

Outcome		Description
+3	Marked improvement	No ischemic symptoms, any foot lesions healed, ABI normalized (>0.90)
+2	Moderate improvement	Improved by at least 1 category and ABI improved by >0.10
+1	Mild improvement	ABI improved by >0.10 but no categorical improvement or vice versa
0	No change	No categorical shift and <0.10 change in ABI
−1	Mild deterioration	ABI decrease >0.10 but no categorical deterioration or vice versa
−2	Moderate deterioration	One category worse or unexpected minor amputation
−3	Marked deterioration	More than one category worse or unexpected major amputation

See text for abbreviations.

against their own weight. After 10 repetitions, the contra lateral leg was exercised.

Station 4: Exercise bicycle

The patients pedaled for 2 minutes on an exercise bicycle. Exercise resistance was sufficient to produce perspiration and dyspnea but still allowing conversation in complete sentences.

Station 5: Knee extension

Patients sat on a high stool, knees flexed, with 2.5-kg weights attached to each ankle. One leg was slowly straightened to maximum extension, before being slowly returned to 90 degrees of flexion. Ten repetitions were performed with each leg in alternating fashion for 2 minutes.

Station 6: Elbow flexion

While holding 1.5-kg dumbbells, patients flexed and extended their elbows for 2 minutes.

This was a validated exercise regimen with established clinical and cost effectiveness.[9]

Combined Therapy (PTA + SEP)

Patients received PTA as described and then were enrolled into an SEP in the following week.

Assessments

Patients were assessed preintervention (Visit 0) and at 1 and 3 months postintervention (Visits 1 and 3, respectively).

Clinical Indicators of Lower Limb Ischemia. At each assessment visit, patient reported walking distance (PRWD) was recorded to a maximum of 1000 m. Ankle brachial pressure index (ABIRe) was measured using a standard sphygmomanometer and a handheld Doppler flow detector with an 8-MHz probe (Huntleigh Technology plc, Cardiff, UK).

Treadmill Exercise Test. Subjects then underwent a standardized, constant-load treadmill exercise test (2.5 km/hr at a 10-degree incline) for a maximum of 5 minutes. Intermittent claudication distance (ICD) and maximal treadmill walking distance (MWD) were recorded up to a maximum of 207 m (equivalent of 5 minutes walking). Following treadmill testing, postexercise ABI (ABIPE) was measured using the method described above.

Outcome following treatment was assessed using the International Society of Cardiovascular Surgery (ISCVS) outcome criteria (Table II).[10]

Quality of Life and Effect Sizes. At each visit, patients completed questionnaires to assess QoL. Generic and disease-specific QoL was analyzed using the MOS Short-Form 36 (SF-36) instrument and the Kings College VascuQoL questionnaire, respectively. Both are standard questionnaires that have been demonstrated to be valid, reliable, and responsive specifically in patients with IC.[11,12]

Effect sizes supplement standard statistical testing to give a more complete and relevant picture of health status change.[13] Effect size is calculated by dividing the difference between the median value before and after treatment, by the pretreatment interquartile range (IQR). An effect size greater than 0.5 is considered clinically relevant.[13]

Sample Size Calculations

For sample size calculations, we used an alpha of 5% and calculated for 80% power, giving a K (constant) value of 7.9. A 20% change in the outcome measure was considered significant. Calculations were performed for the following outcomes:

1. Walking distances: ICD and MWD
2. ABPI
3. Generic quality of life: SF-36
4. Disease-specific quality of life: VascuQol

We obtained results from previously published studies and, using the above values, calculated sample sizes for all primary outcome measures.

The largest sample size was calculated from the SF-36 domains. Based on previously published data,[14] the mean score of physical functioning domain (SF-36) in a group of claudicants is 43 (SD, 17.7), which improved to 52 (SD, 22.2) with

Table III. Patient profile preintervention

	SEP (n = 60)	PTA (n = 60)	PTA + SEP (n = 58)	*p* value*
Male (n)	37	37	33	0.6590
Median age (IQR) (yr)	69 (63–76)	70 (63–75)	69.5 (64–79)	1.0000
Diabetic (n)	9	8	8	0.9210
Hypertensive (n)	40	40	34	0.5610
Hypercholesterolemia (n)	47	45	43	0.7050
Smoking (n)	18	18	19	0.9720
PRWD[a] (m)	100 (50–200)	150 (81–300)	150 (69–300)	0.2693
ABIRe[a]	0.65 (0.53–0.80)	0.70 (0.57–0.87)	0.65 (0.53–0.86)	0.4735
ICD[a] (m)	33.5 (18.7–62.1)	27.4 (19.2–65.9)	40.0 (20.7–67.6)	0.4185
MWD[a] (m)	46.2 (32.0–85.4)	51.8 (33.6–81.9)	63.1 (40.2–98.0)	0.4565
ABIPE[a]	0.31 (0.25–0.56)	0.41 (0.26–0.57)	0.44 (0.22–0.59)	0.3429
SF–36 PF[a]	30 (20–55)	35 (25–55)	40 (20–50)	0.5950
SF–36 RP[a]	20 (20–50)	25 (0–65)	25 (0–75)	0.1916
SF–36 BP[a]	41 (22–64)	41 (31–71)	41 (31–62)	0.5950
SF–36 GH[a]	55 (35–72)	57 (35–72)	55 (42–67)	0.9671
SF–36 V[a]	45 (35–55)	50 (35–70)	45 (35–56)	0.3140
SF–36 SF[a]	62 (37–87)	75 (50–100)	62 (52–87)	0.3108
SF–36 ER[a]	33 (0–100)	66 (0–100)	66 (33–100)	0.1070
SF–36 MH[a]	68 (56–84)	72 (56–84)	70 (59–84)	0.6760
SF–36 Index[a]	0.57 (0.53–0.62)	0.59 (0.52–0.69)	0.63 (0.52–0.69)	0.5000
VascuQol[a]	3.7 (2.7–5.0)	4.3 (3.3–5.1)	4.2 (2.9–5.2)	0.2342

See text for abbreviations.
[a]Median (range).
*Kruskal-Wallis ANOVA.

Table IV. ISCVS outcome by treatment groups

	ISCVS outcome (n)				
Treatment arm	Marked improvement (+3)	Moderate improvement (+2)	Mild improvement (+1)	No change(0)	Mild deterioration(−1)
SEP	3	9	20	14	5
PTA	9	10	19	13	6
PTA + SEP	13	17	10	7	2

See text for abbreviations.

intervention. Thus, a change of at least 10 points (20% to 25% of base value) would be worth detecting. The required sample size for 80% power is 50 patients. Considering 20% dropout, we aimed to recruit 60 patients in each arm of the study.

Data and Statistical Analysis

Data were recorded in Excel 2002 for Windows (Microsoft Corp.) and analyzed using SPSS for Windows, version 16.0 (SPSS Corp.).

Nonparametric statistical tests were used throughout the study after appropriate testing for normality. Intergroup analysis was performed at each time point using the Kruskal-Wallis analysis of variance (ANOVA) and Mann-Whitney test. Intragroup analysis was performed using Friedman test to compare differences over the time course of the study and Wilcoxon signed rank test to compare differences between each pair of time points.

This study was approved by the local research ethics committee and the NHS Trust R&D Committee, and each patient gave informed consent prior to participating in this study.

RESULTS

There were 1157 patients assessed, of whom 185 (16%) had inflow rather than femoropopliteal disease, 324 (28%) were unsuitable for angioplasty after discussion in the MDT meeting, and 81 (7%)

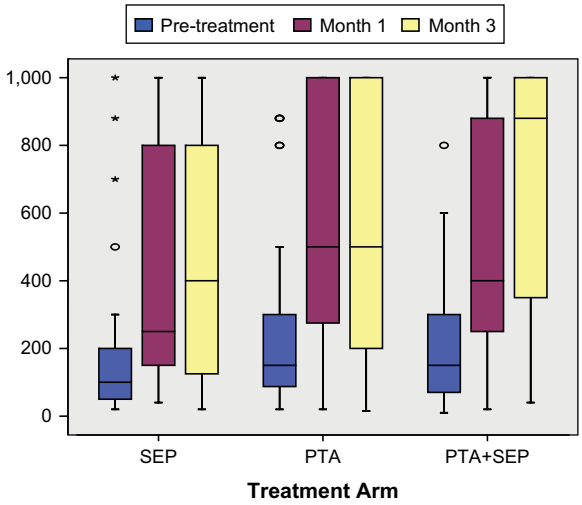

Fig. 1. Patient reported walking (PRWD).

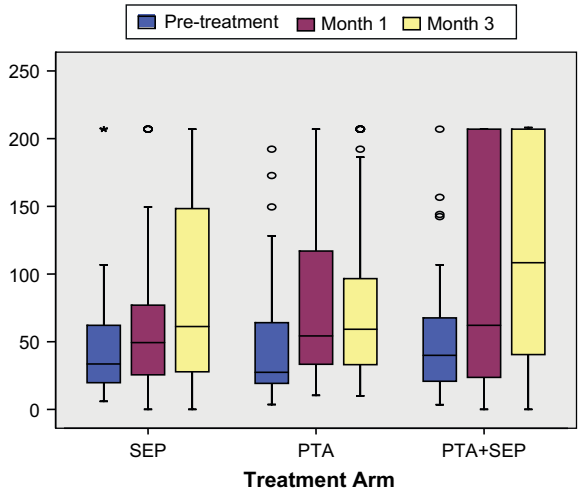

Fig. 3. Treadmill intermittent claudication distance (ICD).

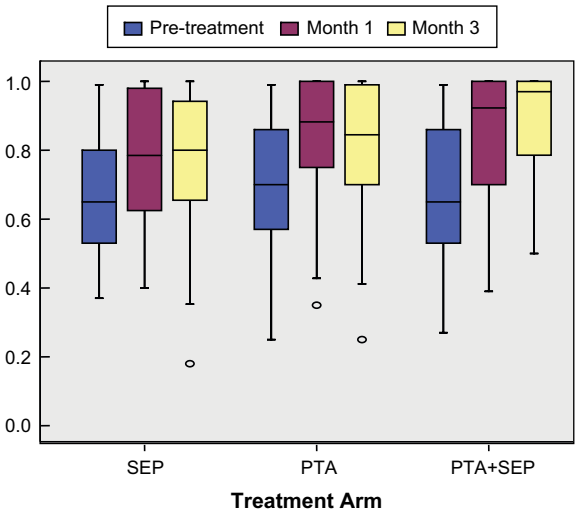

Fig. 2. Resting ankle brachial pressure index (ABIRe).

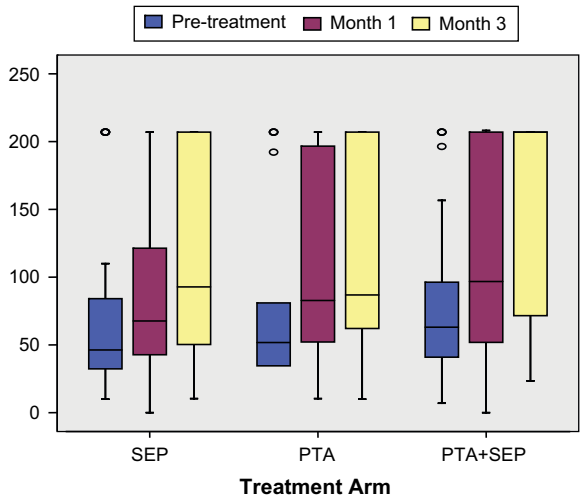

Fig. 4. Maximal treadmill walking distance (MWD).

had infragenicular disease. Of the remaining 414 patients, 236 (20%) had symptomatic improvement on best medical treatment, and 153 (13%) patients declined to participate.

One hundred seventy-eight patients (15.3%) were recruited and randomized into the three treatment arms (PTA, 60; SEP, 60; PTA + SEP, 58). No significant difference was observed at baseline between the three groups in terms in demographic factors, comorbidities, and QoL ($p > 0.05$, Kruskal-Wallis ANOVA; Table III).

Twenty-one patients (11.7%) withdrew over the course of the study, of whom 4.4% (n = 8) were from the SEP group, 1.6% (n = 3) were from the PTA group, and 5.6% (n = 10) were from the PTA + SEP group. Arterial duplex at 3 months demonstrated significant postangioplasty restenosis (doubling of peak systolic velocity used as standard measure) in 11 patients: 7 from the PTA group and 4 from the PTA + SEP group. None of these patients required revascularization at this point.

Intragroup Analyses

Clinical Outcome (ISCVS Score: Table IV)

- SEP: 62.7% of patients improved following treatment, 27.4% demonstrated no change, and 9.8% deteriorated.
- PTA: 66.6% of patients improved following treatment, 22.8% demonstrated no change, and 10.5% deteriorated.

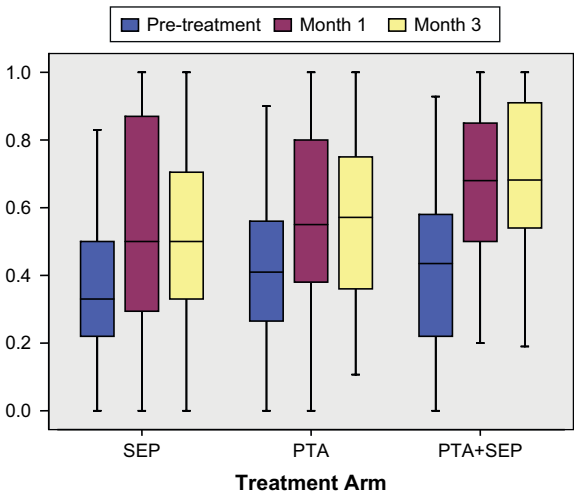

Fig. 5. Postexercise ankle brachial pressure index (ABIPE).

- PTA + SEP: 81.6% of patients improved following treatment, 14.2% demonstrated no change, and 4.0% deteriorated.

Clinical Indicators of Lower Limb Ischemia (PRWD, ABIRe, ICD, MWD, ABIPE: Figs. 1-5; Table V). Patients in all three groups demonstrated increased PRWD, ABIRe, ICD, MWD, and ABIPE over baseline at 3 months. This was statistically significant (Wilcoxon signed rank test, $p < 0.05$).

Quality of Life: SF-36 Domains, SF-36 Index, and VascuQoL (Table V). SEP patients had statistically significant improvements in SF-36 domain scores for Physical Function (PF), Role Physical (RP), Role Emotional (RE), and Vitality (V) but not in the domains of Bodily Pain (BP), General Health (GH), Social Functioning (SF), and Mental Health (MH). Statistically significant improvements were also seen in SF-36 index and VascuQol scores.

PTA patients had statistically significant improvements in SF-36 domain scores for BP, PF, RP, and MH but not in the domains of GH, V, SF, and ER. Statistically significant improvements were also observed in the SF-36 index and VascuQol scores.

PTA + SEP patients had statistically significant improvements in the SF-36 domain scores for PF, RP, BP, SF, V, and MH but not in the domains of GH and ER. Statistically significant improvements were also observed in the SF-36 index and VascuQol scores.

Intergroup Analyses

Clinical Outcome ISCVS Score (Table VI, Fig. 6). When the groups were compared at 3 months, PTA + SEP patients demonstrated significantly better ISCVS outcome criteria scores than SEP and PTA (Mann-Whitney U test, $p < 0.05$). No significant difference was found between the SEP and PTA groups.

Clinical Indicators of Lower Limb Ischaemia

- *SEP vs. PTA:* Over the duration of this study, SEP patients did not show a significant difference in any of the clinical indicators of lower limb ischemia from patients undergoing PTA.
- *SEP vs. PTA + SEP:* Patients undergoing PTA + SEP had significantly greater improvements than SEP patients in all the clinical indicators of lower limb ischemia (PRWD, ABIRe, ICD, ABIPE) except MWD.
- *PTA vs. PTA + SEP:* Patients undergoing PTA + SEP had significantly greater improvement in all the clinical indicators of lower limb ischemia (ABIRe, ICD, MWD, ABIPE) except PRWD.

Quality of Life (Effects Size, Table VI, Fig. 7)

- *SEP vs. PTA:* Both these treatments resulted in significant improvements (effect size >0.5) in the SF-36 domains of PF and BP and the VascuQol. SEP was superior to PTA in the SF-36 domains of RP, V, and RE and in the SF-36 index. PTA was superior to SEP only in the SF domain of SF.
- *SEP vs. PTA + SEP:* Both these treatments resulted in significant improvements (effect size >0.5) in the SF-36 domains of PF, RP, BP, V, and RE and the VascuQol. SEP was superior to PTA + SEP in the SF-36 index, while PTA + SEP was superior in the SF-36 domains of SF and MH.
- *PTA vs. PTA + SEP:* Both these treatments resulted in significant improvements (effect size >0.5) in the SF-36 domains of PF, BP, and SF and the VascuQol. PTA + SEP was superior to PTA in the SF-36 domains of RP, V, RE, and MH, while PTA did not demonstrate superiority to PTA + SEP in any domain. There was no improvement (effect size <0.5) in the SF-36 index with PTA or PTA + SEP. Interestingly, there was no significant improvement (effect size <0.5) in the SF-36 domain of GH following any of the three interventions.

DISCUSSION

Treatment options for patients with infrainguinal peripheral arterial disease are pharmacotherapy, SEP, PTA, or surgery. Due to the lack of consensus, current practice in the United Kingdom is highly

Table V. Results of intragroup analysis for clinical and QoL variables

	SEP		PTA		PTA + SEP	
	Visit 0	Visit 3	Visit 0	Visit 3	Visit 0	Visit 3
PRWD (m)	100 (50–200)	400 (100–800)*	150 (81–300)	500 (200–1000)*	150 (69–300)	880 (325–1000)*
ABIRe	0.65 (0.53–0.80)	0.8 (0.65–0.94)*	0.70 (0.57–0.87)	0.84 (0.69–0.99)*	0.65 (0.53–0.86)	0.97 (0.78–1.00)*
ICD (m)	33.5 (18.7–62.1)	61.2 (24.9–165.6)*	27.4 (19.2–65.9)	59.0 (33.0–96.0)*	40.0 (20.7–67.6)	108.0 (40.0–207.0)*
MWD (m)	46.2 (32.0–85.4)	92.8 (49.3–207.0)*	51.8 (33.6–81.9)	87.0 (61.0–207.0)*	63.1 (40.2–98.0)	207.0 (71.4–207.0)*
ABIPE	0.31 (0.25–0.56)	0.50 (0.33–0.71)*	0.41 (0.26–0.57)	0.57 (0.35–0.77)*	0.44 (0.22–0.59)	0.68 (0.54–0.91)*
SF-36 PF	30 (20–55)	55 (27–75)*	35 (25–55)	52 (35–75)*	40 (20–50)	60 (36–79)*
SF-36 RP	5 (0–50)	25 (0–100)*	25 (0–65)	25 (00–75)*	25 (0–75)	75 (25–100)*
SF-36 BP	41 (22–64)	55 (32–75)	41 (31–71)	61 (38–84)*	41 (31–62)	62 (42–74)*
SF-36 GH	55 (35–72)	60 (42–72)	57 (35–72)	54 (35–76)	55 (42–67)	62 (47–67)
SF-36 V	45 (35–55)	50 (35–70)*	50 (35–70)	55 (35–70)	45 (35–56)	55 (40–70)*
SF-36 SF	62 (37–87)	75 (50–100)	75 (50–100)	88(50–100)	62 (52–87)	75 (50–100)*
SF-36 ER	33 (0–100)	83 (0–100)*	66 (0–100)	100 (0–100)	66 (33–100)	83 (33–100)
SF-36 MH	68 (56–84)	72 (62–92)	72 (56–84)	82 (67–92)*	70 (59–84)	82 (65–92)*
SF-36 Index	0.57 (0.53–0.62)	0.64 (0.57–0.79)*	0.59 (0.52–0.69)	0.63 (0.57–0.76)*	0.63 (0.52–.69)	0.68 (0.60–0.75)*
VascuQol	3.7 (2.7–5.0)	5.24 (4.08–6.16)*	4.3 (3.3–5.1)	5.36 (4.51–6.52)*	4.2 (2.9–5.2)	5.80 (4.88–6.40)*

All values expressed as median (range).
See text for abbreviations.
*Wilcoxon rank sum test, $p < 0.05$.

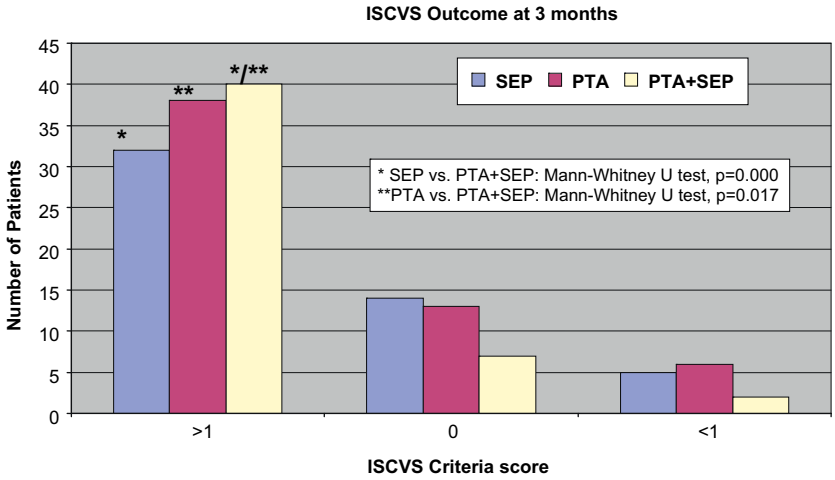

Fig. 6. ISCVS outcome criteria.

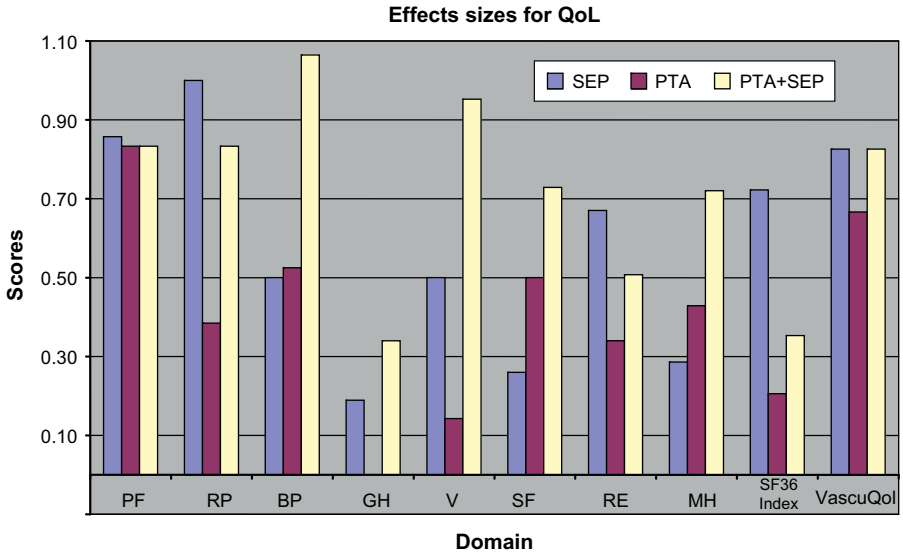

Fig. 7. Effect sizes for SF-36 domains, SF-36 Index, and VascuQoL

variable with some units initially treating IC with medical treatment and exercise advice using invasive procedures like PTA if exercise fails to alleviate symptoms and others using PTA and other invasive treatments routinely as first-line therapy.

PTA is a commonly performed procedure with its own limitations. A systematic review of PTA with or without stenting demonstrated primary patency rates at 12 months of 71.1% for PTA plus stenting and 58.3% for PTA alone.[15] This limits the utility of PTA and necessitates repeat treatments with attendant risks, complications, and costs. On the other hand, evidence shows that SEP is superior to best medical therapy and unsupervised exercise.[16] A Cochrane Review showed that SEP resulted in increased walking distances,[6] while a meta-analysis suggested that the most effective SEPs involve exercising to the point of maximal claudication pain, with sessions lasting longer than 30 minutes, three times per week for at least 3 months.[14]

Comparisons of SEP and PTA are relatively scarce and are often limited by small sample size. A systematic review comparing SEP and PTA in claudicants demonstrated that PTA resulted in a greater increase in ABI but similar improvements in QoL. However, none of the included studies directly compared SEP and PTA.[17-24]There is no published literature of a three-way comparison between SEP, PTA, and SEP + PTA; thus, this study is the first of its kind.

Analysis

Individual analysis of outcome indicators is as follows.

Table VI. Results of intergroup analysis at 3 months for clinical and QoL variables

	SEP	PTA	PTA + SEP
PRWD (m)	400 (100–800)*	500 (200–1000)	880 (325–1000)*
ABIRe	0.80 (0.65–0.94)*	0.84 (0.69–0.99)[a]	0.97 (0.78–1.00)*,[a]
ICD (m)	61.2 (24.9–165.6)*	59 (33–96)[a]	108 (40–207)*,[a]
MWD (m)	92.8 (49.3–207.0)	87 (61–207)[a]	207.0 (71.4–207.0)[a]
ABIPE	0.50 (0.33–0.71)*	0.57 (0.35–0.77)[a]	0.68 (0.54–0.91)*,[a]
SF-36 PF	55 (27–75)	52 (35–75)	60 (36–79)
SF-36 RP	25 (0–100)	25 (00–75)[a]	75 (25–100)[a]
SF-36 BP	55 (32–75)	61 (38–84)	62 (42–74)
SF-36 GH	60 (42–72)	54 (35–76)	62 (47–67)
SF-36 V	50 (35–70)	55 (35–70)	55 (40–70)
SF-36 SF	75 (50–100)	88 (50–100)	75 (50–100)
SF-36 ER	83 (0–100)	100 (0–100)	83 (33–100)
SF-36 MH	72 (62–92)	82 (67–92)	82 (65–92)
SF-36 Index	0.64 (0.57–0.79)	0.63 (0.57–0.76)	0.68 (0.60–0.75)
VascuQol	5.24 (4.08–6.16)	5.36 (4.51–6.52)	5.80 (4.88–6.40)

See text for abbreviations.
*Mann–Whitney *U* test, $p < 0.05$, SEP vs. PTA + SEP.
[a]Mann–Whitney *U* test, $p < 0.05$, PTA vs. PTA + SEP.

- **PRWD.** Despite the significant improvements in PRWD over the 3-month duration of the study with the smallest increase seen in SEP group and the greatest increase seen in PTA + SEP patients, it has been previously demonstrated that PRWD is a subjective measure and correlates poorly with QoL.[8]
- **ABIRe.** Increases in the ABI with PTA and PTA + SEP are expected and self-explanatory. However, ABI increase in SEP group is not in agreement with previous studies.[4,25] It is possible that patients with SFA disease undergo a process of remodeling of collateral circulation. Although establishment of collateral pathways to improve ABIRe is unlikely to happen within 3 months, there is a possibility that such pathways may have been established in these patients as a consequence of ongoing ischemia, and SEP leads to dilatation or expansion of these already present collaterals. This, however, needs further investigation.
- **ICD and MWD.** As both ICD and MWD were significantly improved within each of the three groups over the 3-month duration of the study, the three different intervention regimens are broadly equivalent in clinical terms. MWD is the most reliable subjective measure of treatment outcome. PTA + SEP patients performed better in all clinical indicators except in MWD. However, our data were censored at 207 m, introducing a ceiling effect. PTA + SEP patients undergoing treadmill exercise testing at 3 months postintervention were mostly symptom free at 207 m and indicated a willingness to continue on the treadmill beyond that point. Full walking to absolute claudication may demonstrate a difference; however, this can be difficult to achieve due to time limitations.
- **QoL.** As IC is by definition a condition that is neither limb nor life threatening, the primary goal of treatment for IC is improvement in quality of life. Establishing the impact of treatment on QoL has been difficult because of the small number of studies with complete information. Previous studies on SEP for treatment of IC have shown improvements in QoL following treatment.[9,14,26] Similarly, PTA has been previously studied and shown to be beneficial to QoL.[18-20,27] However, ours is the first study to directly compare QoL following PTA and SEP in the treatment of IC. Ours is also the first study to directly compare these two treatments against combined therapy (PTA + SEP).

In previous studies, the subjective benefits of PTA have not been sustained, often being lost by 1 year compared to SEP.[4,27] In our study, the three groups of patients show very similar QoL benefits post intervention. However, the two interventions including SEP seemed to have additional benefits in the psychological SF-36 domains (V, RE, MH). No intervention had any impact on the SF-36 domain of GH. Given the recorded improvements in other domains with all three treatments, the validity of this domain has to be seriously questioned.

Complications and Attrition

The 3-month PTA patency rate was 93.9% in our study. There were no complications associated

with SEP or with PTA in any of the three groups. The dropout rate and unwillingness of some patients to participate arose from distance between their homes and hospital and unavailability of transportation. The development of a community-based SEP may improve treatment compliance, and a recent study has demonstrated the efficacy[28] and the cost-effectiveness of such an approach.[9]

Study Limitations

Our study has a few limitations. First, femoropopliteal disease represents 15% to 20% of the total claudicant population. This makes it a relatively pure sample. However, this is the group where the treatment decisions are disputed. Therefore, we wanted to study the difference in treatment outcomes in this particular population. Second, as the study predates the TASC grading system for femoropopliteal lesions, we did not classify patients prospectively into these categories. This policy was maintained throughout the recruitment process for uniformity. However, a retrospective TASC grading is currently under way, and we should be able to report that with the long-term results. Third, the ICD and MWD were capped at 5 minutes, making it difficult to assess the true improvement in the absolute distances. However, the fixed load treadmill testing used in this study is a standard practice in modern vascular clinical practice, and the obvious time constraints in outpatient clinics justify this as a realistic compromise. And finally, we acknowledge that patient follow-up is relatively limited in this study but is continuing and we hope to report longer-term follow-up in due course. However, results thus far demonstrate interesting findings that may influence the management of patients with IC.

Third Party and Insurance Implications

The cost effectiveness of SEPs has been established in previous studies.[9] However, there are no community-based SEPs currently available in NHS to support this type of intervention. Provision of these services is rarer in insurance-based health care systems like the United States as they are not covered by most of the insurance providers. We found this to be a major barrier in our study population as well, as most of the patients declined to take part or dropped out because of unavailability of these services in community, fiscal and time expense of traveling to hospital, and commitment to a hospital-based intervention program. These difficulties can be overcome by provision of these services at primary care level. This can provide a cheaper alternative to PTA, thus reducing the cost of intervention and re-intervention by providing a more holistic improvement in lifestyle rather than providing a ''nondurable quick fix solution.'' Further cost effectiveness studies need to be undertaken in this field, and we aim to undertake such analysis on conclusion of this trial.

CONCLUSIONS

The early findings of this study and those preceding it support the continued provision of SEP in the treatment of IC, whether as monotherapy or combined with PTA. Maximal treatment benefit can be achieved by combining PTA and SEP in patients with intermittent claudication due to femoropopliteal disease. However, community-based SEPs can provide a cost-effective first-line treatment for these patients.

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