The Adjuvant Benefit of Angioplasty in Patients with Mild to Moderate Intermittent Claudication (MIMIC) Managed by Supervised Exercise, Smoking Cessation Advice and Best Medical Therapy: Results from Two Randomised Trials for Stenotic Femoropopliteal and Aortoiliac Arterial Disease

The MIMIC Trial Participants (See Appendix 1)

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KEYWORDS
Percutaneous transluminal angioplasty; Intermittent claudication; Femoropopliteal; Aortoiliac; Occlusive or stenotic arterial disease; Walking distance; Treadmill test; ABPI

Abstract  Background: Uncertainty exists on whether there is adjuvant benefit of percutaneous transluminal angioplasty (PTA) over supervised exercise and best medical therapy in the treatment of intermittent claudication.
Methods: Patients with symptoms of stable mild to moderate intermittent claudication (MIMIC) were randomised in two multi-centre trials, for femoropopliteal and aortoiliac arterial disease, to receive either PTA or no PTA against a background of supervised exercise and best medical therapy and followed up for 24 months. Initial claudication distance (ICD) and absolute walking distance (AWD) on treadmill were compared between randomised groups adjusting for the corresponding measure at baseline. Secondary outcomes included ankle-brachial pressure index (ABPI) and quality of life.
Findings: A total of 93 patients were randomised into the femoropopliteal trial (48 into PTA) and 34 into the aortoiliac trial (19 to PTA). The mean (standard deviation, SD) age was 66(9) years for the femoropopliteal trial (63% male) and 63(9) for the aortoiliac trial (65% male). At 24 months, there were significant improvements in both AWD and ICD in the PTA groups for both trials. The adjusted AWD was 38% greater in the PTA group for the femoropopliteal trial (95%; CI 1—90) (p = 0.04) and 78% greater in the PTA group for the aortoiliac trial (95%; CI 0—216) (p = 0.05). Further benefits were demonstrated for ABPI but not for quality of life.
There is a category of patients with lower limb occlusive peripheral arterial disease whose symptom of intermittent claudication (pain in the legs on physical exertion) may be alleviated by balloon angioplasty. Percutaneous transluminal angioplasty (PTA) has been compared with medical therapy and supervised exercise in two separate, randomised, controlled trials; a Cochrane review of these trials has concluded that there may be a short-term benefit with PTA, but there is inconclusive evidence on whether the improvement is sustained in the long term.1–3 Since these trials were performed, evidence on the beneficial effects of exercise has been demonstrated in a number of studies, with two Cochrane reviews highlighting the value of exercise in patients with intermittent claudication.6–8 Further reviews have confirmed the benefit of supervised over non-supervised exercise.9,10

Stents are routinely used to treat iliac occlusions. However, there are no data to support the routine use of stents for iliac stenoses. Stents are therefore reserved for lesions where angioplasty has left a significant residual stenosis.11 Evidence for the use of stents in the femoropopliteal segment is more controversial as the length of the lesion may determine whether it is beneficial.12–14 However, uncertainty remains on the efficacy of PTA (with or without stent) over and above treatment with supervised exercise and best medical therapy which have both been shown to benefit patients with intermittent claudication.

Thus, the multi-centre, randomised mild to moderate intermittent claudication (MIMIC) trials were instigated to test the effect of adjuvant PTA over supervised exercise, smoking cessation advice and best medical therapy in patients with stable, mild to moderate symptoms of intermittent claudication caused by aortoiliac or femoropopliteal lesions suitable for PTA. The outcomes were specified in terms of treadmill walking distances, ankle-brachial pressure indices (ABPI) and quality of life after 24 months of follow-up.

**Methods**

**Participants**

Patients presenting with symptoms of stable intermittent claudication, both new referrals or existing outpatients, were registered and screened for trial suitability, including completion of the Edinburgh Claudication Questionnaire.15 For trial purposes, the definition of MIMIC was calf or buttock pain on walking: mild enough for intervention not to be considered mandatory, yet severe enough for both patient and doctor to consider balloon angioplasty. Stability was determined at a local level by the clinical team using the suggested guideline of a 3-month history of pain on walking despite optimisation of best medical therapy and smoking cessation. The choice of target lesion was determined by the local clinician primarily on the basis of duplex mapping, and patients could only be entered into one of the two trials: an aortoiliac disease trial or femoropopliteal trial. Fig. 1 shows the trial design.

**Inclusion and exclusion criteria**

Entry criteria were the same for both the aortoiliac and femoropopliteal trials. There were no age or gender restrictions on trial participation. Suitable patients required a positive outcome on the Edinburgh Claudication Questionnaire, ABPI <0.9 or >0.9 with a positive stress test (a fall of >30 mmHg in Doppler blood pressure following a treadmill test at 4 km h⁻¹, 10° slope for 1 min) and either an aortoiliac or a femoropopliteal target lesion amenable to PTA as demonstrated by duplex mapping or diagnostic arteriography. Patients were excluded if symptoms were too mild to consider angioplasty or so severe that intervention was mandatory. Patients with critical limb ischaemia (absolute Doppler blood pressure <50 mmHg or presence of ulcers or gangrene with a Doppler pressure >50 mmHg) or concomitant disease such as musculoskeletal or cardiac which was prohibitive to exercise were also excluded.

**Randomisation**

Randomisation was performed for each trial separately and used a 1:1 ratio in randomly permuted blocks of unequal size generated by Stata version 8.0 (Stata Corporation, Texas, USA). Randomisation was stratified by centre and was performed by the trial manager via a laptop computer whilst on site at each centre after obtaining informed consent and completion of the baseline assessment. Treatment allocation was to either ‘angioplasty, supervised exercise and best medical treatment’ or ‘supervised exercise and best medical therapy alone’ within the aortoiliac trial or femoropopliteal trial depending on the location of the target lesion.

**Procedures and interventions**

Allocated treatments started immediately after randomisation, with angioplasty performed as soon as possible to coincide with the start of supervised exercise and within 3 months. Follow-up was at 6 months, 12 months and 24 months after randomisation. The trial manager, liaising with individual centre coordinators, was responsible for all aspects of patient recruitment and collection of follow-up data, attending each centre fortnightly in rotation. All data were held centrally at Charing Cross Hospital, London, UK.
**Supervised exercise**

All centres were provided with a standardised protocol of supervised exercise which was effective in the pilot study. This consisted of a 30-min continuous exercise session to a maximum pain threshold, using a walking circuit interspersed with seven lower limb training stations (e.g., stair climbing, heel raises and treadmill walking) and was supervised by physiotherapists or nursing staff. The classes were offered at least once per week, and all patients were asked to attend one or more sessions per week for 6 months and also encouraged to increase their daily exercise levels.

**Smoking cessation advice**

The importance of smoking cessation was stressed to all patients, and nicotine replacement therapy was prescribed where necessary. Smoking status was assessed using patient-reported habit and serum cotinine levels, which, as a stable metabolite of nicotine with a relatively long half-life, has been shown to be a reliable indicator of exposure to nicotine. Self-reported smoking status was measured for all follow-up appointments, whilst cotinine was measured at baseline and 24 months to assess long-term smoking cessation rates and validate self-reported smoking status.

**Best medical therapy**

Optimisation of best medical therapy was required for all participants. Blood pressure using standard cuff sphygmomanometry, total and high-density lipoprotein (HDL) serum cholesterol, serum glucose and anti-platelet treatment were assessed at baseline, and drug therapy was commenced where necessary. The general practitioner (GP) was notified for continuity of prescriptions. The threshold levels for instigating therapy were: blood pressure of >140/85 mmHg (>135/80 mmHg for patients with diabetes), total cholesterol >5 mmol/L and serum glucose >7.3 mmol/L (fasting) or >11.1 mmol/L (random). All patients, with no contraindications for anti-platelet use, were recommended to take aspirin (75 mg) or clopidogrel if intolerant to aspirin. Current medications were recorded at each follow-up to track compliance with therapy, and cholesterol was checked again at 24 months.

**Percutaneous transluminal angioplasty (PTA)**

PTA involves the inflation of a balloon catheter at the site of arterial narrowing to increase the lumen size. After arterial vascular access is achieved, heparin is administered and the diseased segment is traversed with a guide wire before inflation. For unsatisfactory results, a stent is sometimes used.
Duplex ultrasound scanning of the iliac arteries can be inaccurate if there is extreme arterial calcification or significant bowel gas impairing the scan image. Thus, accuracy of the baseline duplex examination of the iliac arteries was checked by using a diagnostic angiogram of the pelvis and lower limbs before any intervention. The severity of disease in the iliac arteries of the index limb was measured angiographically as a percentage stenosis. A resting pressure gradient along the iliac segment was assessed by either pull-back technique or using simultaneous catheters in the common femoral artery and aorta. If a resting pressure gradient of less than 10 mmHg was identified, interventionists were asked to repeat the measurement after vasodilatation using 30 mg of papaverine injected down the index limb. These angiographic findings were used to identify any patients with significant disease undetected by duplex ultrasound scanning. Patients who were randomised to femoropopliteal intervention but found to have significant aortoiliac disease had to be treated with aortoiliac angioplasty (with or without stent) in preference, followed by the femoropopliteal procedure.

Outcome measures

The primary outcome measure was AWD in metres at 24 months. AWD is defined as the maximum distance that patients can walk before they have to stop due to claudication pain or for any other reason such as breathlessness or fatigue. It was measured on a treadmill machine set at a 10° incline running at 4 km h⁻¹, up to a maximum of 15 min (i.e., 1000 m). Secondary outcomes were: AWD at 6 months and 12 months; ICD, defined as the distance the patient walks on the treadmill before onset of claudication pain; ABPI in the target limb and quality of life assessed using the Short-Form 36 questionnaire with the eight domains summarised using the mental and physical summary scales.

Ethical approval

Ethical approval was obtained from the North West Multicentre Research Ethics Committee and site-specific approval was granted locally at each centre. An international standard, randomised, controlled trial number (ISRCTN) was allocated – 37194085. All adverse events were reported to the Data Monitoring and Ethical Committee.

Statistical methods

The intended recruitment was for 170 patients in each trial. This was based on achieving 90% power to detect, at a 5% significance level, an improvement of 60 m in AWD for the PTA group compared to the control group at 24 months. The SD of AWD was assumed to be 120 m, with a correlation between baseline and follow-up of 0.5, and the target recruitment allowed for 15% loss to follow-up and a 5% cross-over rate between the randomised groups.

The analysis was carried out according to a pre-specified plan, based on intention-to-treat principles, for each trial separately. The primary outcome was the AWD at 24 months. The AWD was log transformed to achieve approximate normality; averages are reported as geometric means, and comparisons of groups as ratios. The few values of AWD >1000 m were taken as equal to 1000 m. The principal analysis of each outcome involved regression adjustment for the corresponding measure at baseline, together with age, sex, baseline smoking status and ABPI. The ICD was considered as censored by the AWD if claudication pain had not been reported by then, and so assessed using survival analysis methods (Kaplan–Meier curves and Cox regression).

Role of the funding source

These trials were funded by the Camelia Botnar Arterial Research Foundation with independent educational grants from Bard Ltd., Boston Scientific Ltd. and Cook®. Neither the study sponsor nor funding bodies had any role in the study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all of the data from the study and had final responsibility for submission of the publication.

Results

Recruitment

Over a 31-month period from August 2003 to February 2006, 1401 patients from nine UK centres were considered for inclusion in the trials. Recruitment was slower than anticipated and stopped early in order to complete the 24-month follow-up of the patients already enrolled with the available funding. Of those enrolled, 144 (10%) patients were eligible for the trials; major reasons for ineligibility were patients refusal (20%), failure to meet the Edinburgh Claudication Questionnaire criteria (19%), failure to meet the ABPI criteria (10%), unsuitable lesion (8%), being unable to walk on a treadmill (8%) or PTA being considered mandatory (7%). Of the 144 patients, 127 consented to the trial and were randomised in either the femoropopliteal or aortoiliac trial. Fig. 2 shows the flow of patients through the trials. The overall attendance at 24 months was 83% (losses shown in Fig. 2); of those attending, 89% were treadmill tested. The reasons that treadmill tests could not be performed were cardiovascular (such as unstable heart disease or angiopathy) or non-vascular (such as chest infection, twisted ankle or balance problems) in roughly equal proportions.

Table 1 shows the baseline comparability of the patients in each trial. In the femoropopliteal trial, there were slight imbalances due to chance in mean age, history of ischaemic heart disease (IHD) and use of statins. There were no apparent imbalances in the aortoiliac trial.

Femoropopliteal trial

Among the 48 patients randomised to PTA, PTA was not attempted in four patients (e.g., because symptoms improved). In the remaining 44, PTA was carried out in
After randomisation, the PTA was recorded as ‘failed’ by the local radiologist. Of the 33 successful PTAs, 21 were of the target lesion alone, seven were of a target and of a non-target lesion (mostly other femoropopliteal lesions), and five were of a non-target lesion alone (all aortoiliac lesions). No stents were used for any femoropopliteal angioplasties but for two patients who also underwent an additional aortoiliac angioplasty, a stent was placed in this segment. Four patients of the 44 randomised to the control group went on to receive PTA (all of the target lesion) during the follow-up period. There were very few complications following the angioplasty procedures: five minor haematomas and one dissected artery. Similarly, there were few adverse events in either group with no myocardial infarctions: two strokes and two distal bypass graft operations during the course of 24 months follow-up. Both randomised groups attended

![ CONSORT diagram showing flow of patients through trials.](image)

Table 1  Baseline characteristics of patients entered into the MIMIC trials, mean (SD) or number (%).

<table>
<thead>
<tr>
<th></th>
<th>Femoropopliteal trial</th>
<th>Aortoiliac trial</th>
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<tbody>
<tr>
<td></td>
<td>Control (n = 45)</td>
<td>PTA (n = 48)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.5 (9.4)</td>
<td>63.9 (9.0)</td>
</tr>
<tr>
<td>Body mass index (kg m$^{-2}$)</td>
<td>26.9 (4.5)</td>
<td>27.0 (5.1)</td>
</tr>
<tr>
<td>AWD (m)$^a$</td>
<td>126 (62)</td>
<td>133 (77)</td>
</tr>
<tr>
<td>ICD (m)$^a$</td>
<td>63 (30)</td>
<td>71 (41)</td>
</tr>
<tr>
<td>ABPI</td>
<td>0.69 (0.12)</td>
<td>0.66 (0.14)</td>
</tr>
<tr>
<td>SF36 physical health score</td>
<td>39.7 (7.4)</td>
<td>38.9 (8.5)</td>
</tr>
<tr>
<td>SF36 mental health score</td>
<td>47.6 (12.5)</td>
<td>50.4 (11.2)</td>
</tr>
<tr>
<td>Male</td>
<td>26 (58)</td>
<td>33 (69)</td>
</tr>
<tr>
<td>Ever smoker</td>
<td>38 (84)</td>
<td>38 (79)</td>
</tr>
<tr>
<td>Past history of hypertension</td>
<td>34 (76)</td>
<td>35 (73)</td>
</tr>
<tr>
<td>Past history of IHD</td>
<td>10 (22)</td>
<td>21 (44)</td>
</tr>
<tr>
<td>Using statins</td>
<td>30 (67)</td>
<td>40 (83)</td>
</tr>
<tr>
<td>Using antiplatelets</td>
<td>40 (89)</td>
<td>44 (92)</td>
</tr>
</tbody>
</table>

AWD absolute walking distance, ICD initial claudication distance, ABPI ankle-brachial pressure index, IHD ischaemic heart disease, SF36 short-form 36 summary scores.

$^a$ Geometric mean (approximate SD).
a similar proportion of the available weekly supervised exercise classes (means: 62% PTA and 61% control). Self-reported smoking status (confirmed by serum cotinine) and drug treatment remained stable throughout the trial, except that statin use increased in both groups from an average at baseline of 75% to an average of 88% during follow-up.

The geometric mean AWD in each randomised group over time is shown in Fig. 3. The mean AWD increased in both groups after baseline, but to a greater extent in the PTA group. Comparing the PTA with the control group, the ratio of geometric mean AWD at 24 months (the primary outcome) was 1.58 (i.e., a 58% increase, Table 2). This ratio was reduced to 1.38 (i.e., a 38% increase, \( p = 0.04 \)) on adjustment for baseline variables, principally because of the age imbalance.

The secondary outcome variables are also shown in Table 2. The ratios of geometric mean AWD, comparing PTA

### Table 2

<table>
<thead>
<tr>
<th>Outcomes in the MIMIC femoropopliteal trial.</th>
<th>Control</th>
<th>PTA</th>
<th>Adjusted result (95% CI)</th>
<th>p-value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWD (geometric mean, metres)</td>
<td></td>
<td></td>
<td>Ratio PTA:control</td>
<td></td>
</tr>
<tr>
<td>6 Months (n = 81)</td>
<td>167</td>
<td>202</td>
<td>1.21</td>
<td>1.06 (0.80–1.41) ( p = 0.69 )</td>
</tr>
<tr>
<td>12 Months (n = 75)</td>
<td>150</td>
<td>224</td>
<td>1.49</td>
<td>1.22 (0.88–1.67) ( p = 0.23 )</td>
</tr>
<tr>
<td>24 Months (n = 71)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>155</td>
<td>245</td>
<td>1.58</td>
<td>1.38 (1.01–1.90) ( p = 0.04 )</td>
</tr>
<tr>
<td>ICD (% attaining 200 m without claudication pain)</td>
<td></td>
<td></td>
<td>Hazard ratio</td>
<td></td>
</tr>
<tr>
<td>6 Months (n = 81)</td>
<td>23%</td>
<td>32%</td>
<td>1.56</td>
<td>1.78 (0.99–3.21) ( p = 0.05 )</td>
</tr>
<tr>
<td>12 Months (n = 75)</td>
<td>25%</td>
<td>42%</td>
<td>2.18</td>
<td>2.18 (1.15–4.12) ( p = 0.02 )</td>
</tr>
<tr>
<td>24 Months (n = 71)</td>
<td>22%</td>
<td>63%</td>
<td>2.83</td>
<td>3.11 (1.42–6.81) ( p = 0.004 )</td>
</tr>
<tr>
<td>Other outcomes at 24 months</td>
<td></td>
<td></td>
<td>Difference:</td>
<td></td>
</tr>
<tr>
<td>Mean ABPI (n = 73)</td>
<td>0.72</td>
<td>0.83</td>
<td>0.11</td>
<td>0.11 (0.03–0.20) ( p = 0.01 )</td>
</tr>
<tr>
<td>Mean SF36 physical score (n = 79)</td>
<td>39.2</td>
<td>40.9</td>
<td>1.7</td>
<td>−0.4 (−4.2 to 3.4) ( p = 0.82 )</td>
</tr>
<tr>
<td>Mean SF36 mental score (n = 79)</td>
<td>47.6</td>
<td>51.5</td>
<td>3.9</td>
<td>2.4 (−1.7 to 6.5) ( p = 0.25 )</td>
</tr>
</tbody>
</table>

AWD absolute walking distance, ICD initial claudication distance, ABPI ankle-brachial pressure index, SF36 short-form 36 summary scores.

<sup>a</sup> Pre-specified primary outcome.

<sup>b</sup> Adjusted for corresponding measure at baseline, age, sex, baseline smoking status and ABPI.

<sup>c</sup> Hazard ratio for comparing probabilities of attaining a particular ICD (see Fig. 4).
to control, at both 6 months and 12 months were also
greater than 1, but to a lesser degree than at 24 months,
and these differences were not statistically significant. The
probability of attaining a specified ICD at 24 months is
shown in Fig. 4; for example, the probabilities of attaining
200 m without claudication pain are 63% and 22% in the PTA
and control groups, respectively. Expressed as hazard ratios
(Table 2), the differences in ICD were statistically signifi-
cant at all three follow-up times. The mean ABPI was
significantly higher in the PTA group at 24 months, while the
physical and mental scores from the SF36 quality-of-life
scale showed no significant differences.

Sensitivity analyses were carried out that: (1) additionally
adjusted for baseline history of IHD and statin use
(these being apparently imbalanced); (2) adjusted for
baseline serum cotinine level rather than for reported
smoking status; (3) adjusted for attendance at supervised
exercise classes; (4) removed potential outliers from some
of the analyses; (5) compared ICD using geometric means
(replacing it by the AWD when claudication pain had not

**Figure 4** Initial claudication distance (ICD) at 24 months by randomised group in the femoropopliteal trial (Kaplan–Meier
probability of attaining a given distance without claudication pain).

### Table 3 Outcomes in the MIMIC aortoiliac trial.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PTA</th>
<th>Ratio PTA:control</th>
<th>Adjusted result (95% CI) p-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AWD (geometric mean, metres)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Months (n = 27)</td>
<td>178</td>
<td>316</td>
<td>1.78</td>
<td>1.75 (1.02–3.02) p = 0.04</td>
</tr>
<tr>
<td>12 Months (n = 24)</td>
<td>167</td>
<td>319</td>
<td>1.91</td>
<td>1.77 (0.93–3.37) p = 0.08</td>
</tr>
<tr>
<td>24 Months (n = 23)$^a$</td>
<td>168</td>
<td>354</td>
<td>2.11</td>
<td>1.78 (1.00–3.16) p = 0.05</td>
</tr>
<tr>
<td><strong>ICD (% attaining 200 m without claudication pain)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Months (n = 27)</td>
<td>0%</td>
<td>60%</td>
<td>3.2</td>
<td>3.9 (1.3–11.6) p = 0.01</td>
</tr>
<tr>
<td>12 Months (n = 24)</td>
<td>18%</td>
<td>58%</td>
<td>3.2</td>
<td>3.9 (1.1–13.6) p = 0.04</td>
</tr>
<tr>
<td>24 Months (n = 23)</td>
<td>25%</td>
<td>61%</td>
<td>3.1</td>
<td>3.6 (1.0–12.8) p = 0.05</td>
</tr>
<tr>
<td><strong>Other outcomes at 24 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ABPI (n = 25)</td>
<td>0.74</td>
<td>0.90</td>
<td>0.16</td>
<td>0.14 (0.03–0.26) p = 0.02</td>
</tr>
<tr>
<td>Mean SF36 physical score (n = 25)</td>
<td>38.6</td>
<td>46.4</td>
<td>7.8</td>
<td>7.8 (1.5–14.1) p = 0.02</td>
</tr>
<tr>
<td>Mean SF36 mental score (n = 25)</td>
<td>46.0</td>
<td>50.3</td>
<td>4.3</td>
<td>4.9 (–1.3 to 11.1) p = 0.12</td>
</tr>
</tbody>
</table>

AWD, absolute walking distance; ICD, initial claudication distance; ABPI, ankle-brachial pressure index; SF36, short-form 36 summary
scores.

$^a$ Pre-specified primary outcome.

$^b$ Adjusted for corresponding measure at baseline, age, sex and ABPI (but not smoking status because of zero cells in some groups).

$^c$ Hazard ratio for comparing probabilities of attaining a particular ICD.
been reported) and (6) compared only patients with successful PTA in the PTA group to patients without PTA in the control group. These analyses did not change the interpretation of the results presented.

**Aortoiliac trial**

For the 19 patients in the aortoiliac trial randomised to receive PTA, 17 had successful PTA of the target lesion. Amongst the 15 patients in the control group, four went on to receive PTA later during the follow-up period. A total of five stents were used across all the aortoiliac angioplasties (four in the target lesion and one in a non-target aortoiliac lesion). There were very few complications following the angioplasty procedures: three minor haematomas and one sensory deficit. Similarly, there were few adverse events in either group with no myocardial infarctions, two strokes and no distal bypass graft operations during the course of the 24 months follow-up. Both groups attended a similar proportion of the available weekly exercise classes (means: 53% PTA, 48% control). The results of the aortoiliac trial are summarised in Table 3. Despite the small size of the trial, resulting in wide confidence intervals, there were statistically significant improvements in the PTA group for AWD, ICD, ABPI and the SF36 physical score.

**Discussion**

The results achieved for these trials are surprisingly convincing despite the low recruitment rate and low rate of eligibility, and therefore one might question whether the trials are truly representative of the intended patient population. There were a number of reasons for the poor recruitment, mainly relating to the UK funding system of health care placing the budget with the primary care groups so that referral to secondary care has become less certain. For aortoiliac disease, many clinicians were unprepared to test the efficacy of angioplasty as they believed strongly that it worked. These data appear to confirm their prejudice. Moreover, it is interesting that results are apparently more impressive at 24 months than at 6 or 12 months as the earlier Cochrane review had cast some doubt on the long-term efficacy of angioplasty. From a safety perspective, it is encouraging that the rates of complication and adverse events were low for both trials. In terms of cost-effectiveness, Spronk et al. previously have reported that PTA is unlikely to be cost-effective when compared with supervised exercise; however, further analyses are required on whether the benefit presented here is cost-effective.

In our trials, best medical treatment and smoking cessation advice as well as mandatory supervised exercise were prerequisites before balloon angioplasty. We considered this imperative particularly as there are two large well-conducted studies suggesting that statins themselves can improve walking times. Thus, lipid modification to recognised standards was ensured in all study participants. There is no evidence that angioplasty alone would produce similar results, although we await the results of the CLEVER Trial which has commenced recently in the United States. In the latter trial, which intends to recruit 250 patients with claudication from aortoiliac disease, a comparison is proposed between four randomised treatment groups of medical therapy, stent placement, supervised exercise and all treatments combined.

The previous Oxford trial compared angioplasty to supervised exercise, and the Edinburgh trial compared angioplasty with medical therapy to medical therapy alone; both were smaller than the current trials. The Oxford and Edinburgh trials reported results differently, but baseline walking distances appeared to be very comparable with the trials presented here. However, their impact was to place a question mark regarding angioplasty as a form of long-term treatment, particularly as the 6-year results for the Oxford trial did not suggest any improvement with PTA. Our results provide promising evidence that the benefit of adjuvant PTA over supervised exercise may now be sustained for a considerable period of time.

It is noteworthy that the femoropopliteal results were achieved without the use of stents. Since the start of the MIMIC trials, evidence has emerged on the potential benefit of stent over plain angioplasty in the femoropopliteal segment; however, other research shows that the length of lesions may play an important role in the level of benefit. Our MIMIC trial provides no evidence on stents in the femoropopliteal segment as none were used. Operators, however, were not prepared to be denied the use of stent if considered necessary in the aortoiliac segment.

**Conclusion**

Despite some reservations relating to generalisability, these findings lend weight to the value of angioplasty as a treatment for intermittent claudication for up to 24 months, on a background of best medical treatment and supervised exercise, in MIMIC whether caused by aortoiliac or femoropopliteal disease.

**Conflict of Interest**

The author is a trustee of the Camelia Botnar Arterial Research Foundation. There are no other conflicts of interest.

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**Appendix 1**

- **MIMIC Trial Participants**

**Writing committee:** Professor RM Greenhalgh (Chair), Professor JLF Belch, Dr LC Brown, Professor PA Gaines, Mrs L Gao, Dr JA Reise and Professor SG Thompson.

**Applicants:** Professor RM Greenhalgh (Lead applicant), Professor MJ Buxton, Professor PA Gaines and Professor SG Thompson.
**Data and trial management:** Dr JA Reise (Trial manager)

**Statistical analysis:** Mrs L Gao, Dr LC Brown and Professor SG Thompson

**Trial Management Committee:** Professor RM Greenhalgh (Chair), Professor JF Belch, Professor MJ Buxton, Professor AH Davies, Professor PA Gaines, Professor A Garratt and Professor SG Thompson.

**Data Monitoring Committee:** Professor JT Powell (Chair), Sir PRF Bell, Mr J Bromley, Dr J Marsh and Dr A Nicholson.

Regional trial participants committee represented by surgeons and radiologists from each centre (number in brackets indicates number of subjects entered into the trials):

M Horrocks, J Budd, J Hardman, Bath Royal United Hospital (14); RM Greenhalgh, AH Davies, IU Franklin, AW Mitchell, P McTravers, Charing Cross Hospital, London (27); P Taylor, J Reidy, T Sabharwal, Guy’s and St. Thomas’s Hospital, London (18); J Collin, P Boardman, John Radcliffe Hospital, Oxford (1); DA Ratliff, RCJ Hicks, G Libertiny, R Kenderick, Northampton General Hospital (33); J Michaels, J Beard, P Gaines, S Thomas, T Cleveland, Northern General Hospital, Sheffield (15); G Hamilton, D Baker, F Jynt, A Platt, J Tibballs, Royal Free Hospital, London (10); M Thompson, A Belli, R Morgan, St. George’s Hospital, London (3); Mr J Wolfe, Professor N Cheshire, Mr M Jenkins, Mr R Gibbs, Dr M Clark, Dr M Hamady, St. Mary’s Hospital, London (6).

Trial co-ordinators: Louise Allen, Marion Aukett, Michelle Carmichael, Elizabeth Earby, Paul Emmanuel, Marilyn Ireland, Xun Liu, Phyl Morris-Vincent, Shelagh Murray, Claire Smith, Sinead Sweeney, Sally Wagstaff, Rachel Walker, Bridget Smith, Angela Williams.

**References**


