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Angioplasty or Bypass for Superficial Femoral Artery Disease? A Randomised Controlled Trial

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Aim. *To evaluate whether angioplasty or above-knee bypass is the best treatment for symptomatic superficial femoral artery occlusive lesions, we performed a multicentre randomised trial.*
Patients and methods. *Between October 1995 and August 1998, 56 patients were enrolled, all with symptoms related to a 5–15 cm long occlusive lesion of the superficial femoral artery. Thirty-one patients were randomly assigned to percutaneous transluminal angioplasty (PTA); 25 patients to bypass surgery. All patients were followed at 1, 6 and 12 months after the procedure. The primary outcome of our study was re-occlusion of the femoral artery.*
Results. *Thirty patients underwent the allocated PTA and 24 patients underwent bypass surgery. Cumulative 1-year primary patency after PTA was 43 and 82% after bypass surgery. After PTA more than half of the patients had a re-occlusion with an absolute risk reduction of 31% (CI: 6–56%) in favour of bypass surgery. The hazard ratio for occlusion comparing PTA with bypass surgery is 2.24 (95% CI: 0.9–5.58).*
Conclusion. *Despite 18 participating centres only 56 patients were randomised to PTA our bypass surgery. Based on our results, for every three patients treated with bypass surgery instead of PTA, one additional re-occlusion is prevented. Therefore, we conclude that with respect to patency, for long superficial femoral artery (SFA) stenoses or occlusions, surgery is better than PTA.*

Key Words: Randomised trial; Percutaneous transluminal angioplasty; Bypass surgery; Femoro-popliteal occlusive disease; Primary patency; SVS/ISCVS classification; ARR; NNT.

Introduction

Intermittent claudication is usually treated conservatively. However, if conservative treatment fails and the patient is strongly disabled, invasive treatment can be considered. percutaneous transluminal angioplasty (PTA) or bypass surgery are the possible treatment options for patients with an isolated lesion of the superficial femoral artery (SFA). The optimal method of treatment remains controversial because both treatment modalities have never been compared in a well-defined randomised trial.[1] Meta-analysis of observational cohort studies showed a pooled one-year primary patency of PTA of 85% (83–86%) against 95% (94–97%) for vein bypass surgery. After 3 years follow-up the difference in primary patency increased to 13% (75% (72–78%) versus 89% (86–91%), respectively).[2] It should be emphasised that this is not a randomised comparison.

A decision-analysis, based on the results of these cohort studies, advised PTA for stenosis or short occlusions of the SFA, whereas vein bypass surgery was recommended for long occlusions.[3] However, this recommendation was based on heterogeneous patient groups. Because of the lack of well-defined study groups, we decided to perform a multi-centre randomised clinical trial with a homogeneous patient group, according to suggested standards.[4,5]

The aim of this BASIC trial (Bypass or Angioplasty in Severe Intermittent Claudication) was to evaluate whether PTA or vein bypass is the most successful treatment for patients with an isolated SFA lesion with a length between 5 and 15 cm combined with symptoms classified according to the SVS/ISCVS classification.

Patients and Methods

Patients

Patients had to fulfil two inclusion criteria: intermittent claudication not responding to conservative

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therapy for at least 3 months and a stenosis or occlusion of the SFA with a length between 5 and 15 cm. Results of a baseline treadmill test and symptoms were recorded according to the SVS/ISCVS classification. A digital subtraction angiography was used for baseline assessment of the SFA and the outflow arteries. Exclusion criteria were: a hemodynamically significant stenosis of the aorto-iliac tract as detected by duplex scanning, absence of patent crural arteries, previous treatment of the femoropopliteal segment, life expectancy less than one year due to concomitant diseases and contra-indication for PTA or surgery, such as severe cardiopulmonary diseases.

Methods

Principal investigators of 18 participating centres in the Netherlands (16) and United Kingdom (2) consented to participate in this randomised trial. The ethical committee of all participating centres approved the study protocol. All patients signed written informed consent before randomisation. Patients were assigned to PTA or vein bypass by computer randomisation, stratified for each centre.

The PTA was carried out by conventional balloon dilatation of the lesion. A stent could be placed, according to the decision of the interventional radiologist. If the PTA procedure technically failed the patient received a bypass graft. The bypass procedure was performed according to standard vascular techniques, using an *in situ* or reversed autogenous vein graft. Both treatment groups received Aspirin 100 mg daily after treatment for at least 3 months. For both procedures hemodynamic significant re-stenosis or occlusion were treated either by PTA or bypass, according to the decision of the responsible surgeon. Follow-up continued after a redo-procedure. The patients were followed in a thorough non-invasive surveillance program consisting of a quality of life questionnaire, physical examination, blood systolic pressure measurements, treadmill test and duplex scan of the target limb. These visits were performed at 1, 6 and 12 months after the procedure and every following year or if symptoms reoccurred. The blood systolic ankle pressure and ankle brachial index (ABI) were assessed at rest and immediately after treadmill-exercise. The treadmill test was standardised: 5 min at 3 km/h, with an eight percent incline.[4,5] Patency of the treated vessel or bypass was established via duplex scanning by calculating the peak systolic velocity (PSV) and the end diastolic velocity (EDV). Both parameters were used to trace the diameter reduction of the revascularized artery. An increase of the PSV greater then 2.5 at a stenosis site was defined as hemodynamically significant.[6]

Analysis

The primary outcome of our study was re-occlusion of the femoral segment. We assumed that venous bypass surgery is more effective than PTA in achieving primary patency, with an expected difference in primary patency of 15%, after one year. Power analysis was based on this primary objective. The number of patients needed in each treatment group was 100, in order to detect a difference in primary patency of 15% (75% versus 90% for PTA and bypass surgery, respectively) with a power of 0.80 and a two-tailed alpha of 0.05. An intention to treat analysis was used.

The primary patency was defined as the natural course of the treated femoral artery until occlusion or re-intervention occurred. Secondary endpoints were clinical improvement, primary assisted patency, mortality, and adverse events, such as haemorrhage, infection or stroke. Clinical improvement was defined as a degree of improvement of at least +1, compared to pre-procedure values, according to the SVS/ISCVS classification. Primary assisted patency was defined as the history of the treated artery allowing re-intervention for hemodynamic significant re-stenosis to prevent occlusion.

Where appropriate Chi-square test, students T-test and Mann Whitney U test were used to test baseline comparability between treatment groups. Kaplan–Meier survival analysis was used to compare maintenance in primary patency.

Results

Between October 1995 and August 1998, 56 patients were enrolled by 13 participating centres. Because of this disappointing patient number the National Health Council decided to terminate the inclusion before the required number of 200 patients was realised. The analysis was based on these 56 patients consisting of 19 females and 37 males ranging in age between 42 and 84 years (Table 1). Baseline characteristics were similar for both treatment groups. Indication for intervention according to the SVS/ISCVS classification was severe intermittent claudication category 2 and 3, predominantly. Overall median lesion length was 9 cm (range: 5–15 cm). Fifty-one patients had an occlusion of the femoral artery, whereas five patients were treated for a stenotic lesion. Median follow-up for all patients was 703 days (range; 39–1430 days) (Table 2).

Table 1. Pre-procedure characteristics of PTA and Bypass study group; BASIC trial

	PTA	Bypass
Number	31	25
Male/Female	21/10	16/9
Age median (range)	68 (45–84)	66 (42–83)
Medical history		
Previous surgery	12	9
Hypertension	17	8
Hyperlipidaemia	8	6
Diabetes	5	3
Myocardinfarct	7	4
Stroke	3	4
Smoking	12	15
Rutherford classification		
Category 1	4	7
Category 2	14	10
Category 3	10	8
Category 4	3	0
Blood systolic pressure		
Ankle mmHg (range)	93 (27–170)	93 (42–137)
Ankle Brachial index % (range)	55 (15–84)	58 (22–92)
Lesion		
Stenosis	3	2
Occlusion	28	23
Length cm (range)	9 (5–15)	9 (5–15)
Number of patent crural arteries		
1	11	8
2	11	9
3	9	7

Thirty-one patients were randomly assigned to PTA; one patient was still on the waiting list at the end of the study (Fig. 1). Subsequently, 30 patients underwent the allocated PTA and were analysed. In seven patients a stent was placed. Two patients were lost to follow-up after 2 and 3 years, respectively. The last objective evaluation was used to determine study endpoints.

Table 2. Outcome measurements at study end; BASIC trial

	PTA	Bypass
Number	30	24
Follow-up		
Median days (range)	704 (39–1430)	754 (164–1082)
Degree clinical improvement		
Rutherford classification		
− 1	2	1
0	11	2
1	3	4
2	7	5
3	4	7
Reintervention	3	5
Primary patency		
Technical failure	3	0
Occlusion	9	2
Reintervention	5	5
Amputation	1	0
Primary assisted patency		
Technical failure	3	0
Occlusion	9	4
Reintervention	1	1

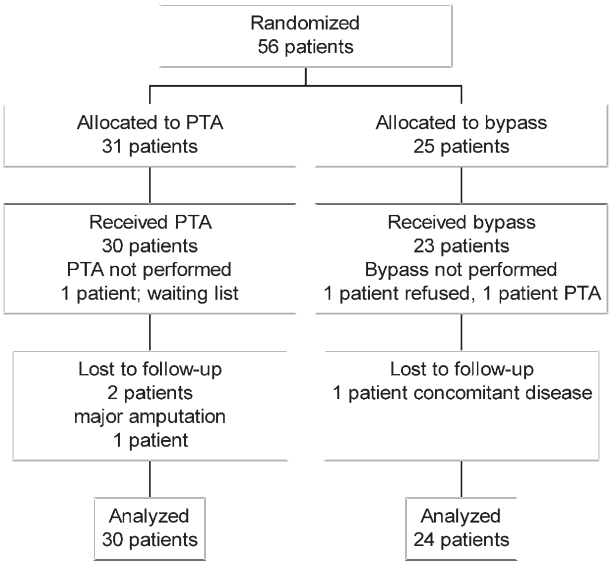

Fig. 1. Above-knee bypass procedure or percutaneous transluminal angioplasty in patients with intermittent claudication; the BASIC-trial. Flow diagram of patient progress.

Twenty-five patients were randomly assigned to bypass surgery. Despite informed consent two patients refused bypass surgery, of whom one patient underwent PTA after all. The other patient refused further study participation. In the bypass group 24 patients were analysed. Twenty-three patients received the allocated bypass procedure. A reversed vein bypass was performed 12 times, *in situ* vein bypass surgery six times. Four patients received a prosthetic bypass (polytetrafluoroethylene), as against the study protocol. In the bypass group one patient was lost to follow-up after 3 years, due to a life threatening concomitant disease.

Primary and primary assisted patency

In three of 30 patients in the PTA group (10%) the procedure technically failed because the femoral artery could not be punctured or the occlusion could not be passed (Table 2). Eighteen patients (60%) had an occlusion or re-intervention of the target limb, during follow-up. There were no technical failures in the bypass group. Seventeen of the 24 bypasses remained patent during follow-up. Seven patients (29%) had an occlusion or re-intervention of the bypass at the end of the study. Thus after bypass surgery there is an absolute risk reduction for occlusion of 31% (95% confidence interval (CI): 6–56%) compared to PTA

(Table 3). The hazard ratio for occlusion comparing PTA with bypass surgery is 2.24 (95% CI: 0.9–5.58). Life table analysis showed a cumulative 1-year primary patency after PTA of 43 and 82% after bypass surgery (Fig. 2).

Taking into account re-interventions 13 out of 30 patients (43%) in the PTA group developed an uncorrected occlusion. In the bypass group, this occurred in five patients (21%). Considering secondary patency, performing a bypass instead of a PTA resulted in an absolute risk reduction for occlusion of 22% (95% CI: −2–47%) (Table 3). The hazard ratio for re-occlusion was 2.41 (95% CI: 0.83–6.94) for patients treated with PTA compared to bypass surgery.

Clinical improvement; SVS/ISCVS classification

Sixteen patients (53%) in the PTA group failed to show a clinical improvement; in the bypass group eight patients (33%) did not improve (Table 2). This results in an absolute difference of clinical success of 20% (95% CI: −6–46%) in favour of bypass surgery.

Mortality and adverse events

In both treatment groups 30 days mortality was 0%. Forty days after PTA, one patient underwent major amputation of the target limb because occlusion of the crural arteries accidentally occurred during the percutaneous procedure. In the bypass group four adverse events occurred: one patient had a stroke. One patient developed a serious wound infection in the groin and two patients had a hematoma, which was treated conservatively.

Discussion

This paper describes a randomised trial comparing PTA with bypass surgery for the treatment of an isolated lesion of the SFA. Although power analysis showed a required number of 200 patients to detect a 15% difference in treatment success, our inclusion unfortunately ended with a total number of 56 patients. This is a major drawback limiting the power of our study. However, the difference in favour of surgery is impressive. After PTA more than half of the patients had a re-occlusion with an absolute risk reduction of 31% (CI: 6–56%) in favour of bypass surgery. The clinical impact of this reduction is clearly shown by the number needed to treat. Of three patients (CI: 2–17) treated with bypass surgery one additional occlusion is prevented if compared with PTA. Because of the small patient number the confidence interval of our primary objective is wide, but does not reach zero. Therefore, we conclude that surgery is better than PTA in terms of primary patency.

The disappointing outcome after PTA with a one-year primary patency of 43% did not correspond with the patency rates described in literature: 58–76%.[7–10]

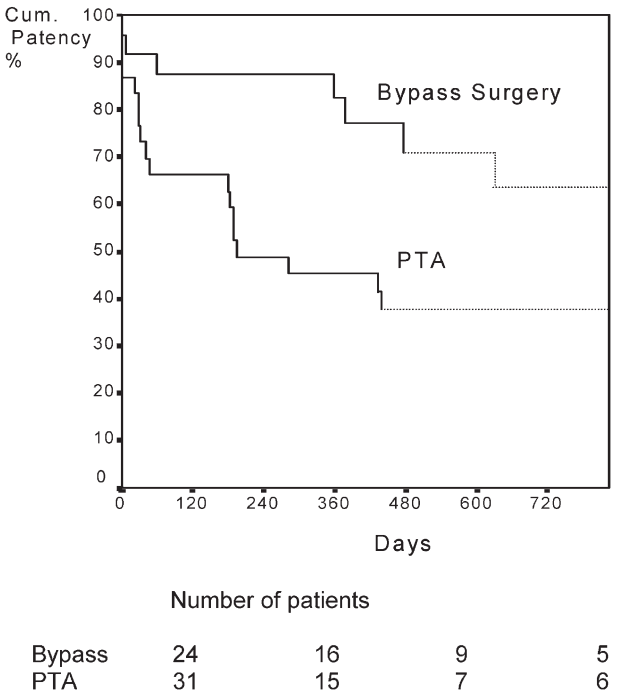

Fig. 2. Kaplan–Meier survival analysis. Primary patency after PTA and bypass surgery; BASIC trial.

Table 3. Study endpoints: PTA versus bypass surgery; BASIC trial

	PTA	Bypass	Absolute risk reduction	Number needed to treat
Number	30	24		
Occlusion + reintervention	18	7		
Primary patency	60%	29%	31% (6–56%)	3 (2–17)
Occlusion	13	5		
Primary assisted patency	43%	21%	23% (−2–47%)	5 (2–∞)
Clinical decline*	16	8		
	53%	33%	20% (−6–46%)	5 (2–∞)

*According to the SVS/ISCVS classification.

However, these authors reported a median lesion length of approximately 5 cm against 9 cm in our series. The length of the lesion negatively influences treatment outcome and, therefore, can explain our results after PTA.[11] Secondly, some authors defined patency by ABI which underestimate re-stenosis or occlusions compared to our surveillance by duplex scanning.[9,10]

More patients in the PTA than in the bypass group showed a clinical decline. Although there were no differences in demographic parameters between the two groups, the patients in the PTA group showed a slightly higher Rutherford classification. The fact that no statistical differences could be demonstrated might be due to small numbers (type II error). Theoretically this could have biased the results in favour of bypass surgery. The absolute difference between both study groups for clinical improvement was 20% (CI: −6–46%) in favour of surgery. The difference in clinical effect was less pronounced than our primary objective, probably because some patients in the PTA group showed an asymptomatic re-stenosis on duplex scanning. From a clinical point of view one might argue that our primary endpoint should have been clinical improvement, another reason to interpret our results with some caution.

Two earlier randomised trials compared PTA with bypass surgery.[12,13] Both studies described heterogeneous patients groups with both iliac- and femoropopliteal lesions. Despite the unselected study group their inclusion rate was approximately 10 patients each year in two participating centres. We performed our trial on a homogenous patient group; an isolated lesion of the femoral artery combined with symptoms classified according to the SVS/ISCVS classification. In daily practice patients eligible for our study seem to be rare; the patient either has an asymptomatic isolated lesion of the SFA or severe intermittent claudication based on multilevel peripheral arterial occlusive disease. We did not register all patients who were referred to the vascular laboratory for duplex scanning of the femoral artery, so we do not know the incidence of patients with an isolated lesion of the femoral artery.

All investigators were closely involved in the preparation of the study protocol. The centres were selected for their experience in vascular surgery, interventional radiology and the availability of a vascular laboratory. The protocol was adjusted and approved by all investigators after several central meetings. During regular site visits at the vascular laboratory, treadmill test and duplex scanning of the target limb were standardized and monitored. On a weekly basis the vascular surgeons, radiologist and trial co-ordinator reviewed all outpatient angiographies to screen for eligible study patients. Because of the large number of participating centres within a small area we had a unique opportunity to start this trial supported by the Dutch Health Council. Our strict inclusion criteria prevented the enrolment of enough study patients and, therefore, the Dutch Health Council stopped the study at an earlier date. Despite 18 participating centres our inclusion rate reached only 20 patients per year. In reflecting this decision, we obviously wondered greatly if we should have chosen more flexible criteria. We decided not to adjust these criteria and continued the follow-up of all included patients and analysed these data at the study end. Based on the practical difficulties we encountered, we doubt whether our primary study question, "which treatment is the best choice for patients with femoropopliteal occlusive disease?" will ever be answered on a basis of sufficient number of patients. However, our limited patient volume suggests the superiority of bypass surgery for long lesions of the SFA.

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