

## Subintimal Angioplasty in the Treatment of Patients with Intermittent Claudication: Long Term Results

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**Objectives.** Reporting the long-term results of subintimal angioplasty (SA) in patients with intermittent claudication (IC).

**Design.** A prospective study.

**Patients.** One hundred and sixteen SA procedures were performed in 104 patients, from February 1997 to January 2000.

**Methods.** This is a prospective study of patients treated for IC with infrainguinal SA. Primary assisted patency rates were calculated, also on intention to treat basis. Univariate and multivariate Cox regression tests were used to assess whether patency was correlated with co-morbidities, run-off or occlusion length.

**Results.** There was no early mortality. Technical success was achieved in 101 cases (87%). Primary assisted patency rates on intention to treat basis (116 cases) at 6, 12, 36 and 60 months were 69, 62, 57 and 54%, respectively. For successfully recanalized patients (101 cases) these respective numbers are 79, 70, 66 and 64%. Length of occlusion, age and male gender were independent risk factors for reocclusion.

**Conclusions.** The satisfactory results obtained in the present study are probably due to two main factors. First, the three participating radiologist are highly skilled and experienced. Secondly, a conscientious surveillance was adhered to, so that restenoses could be diagnosed and treated early. SA is a relevant alternative to bypass surgery in patients with disabling IC due to long femoro-popliteal occlusions. It is far less traumatic than conventional vascular reconstructions, complications are few and not serious. Very importantly, SA never interfered with later successful vascular surgery. Therefore, we have adopted SA as the primary treatment for patients with IC when medical treatment alone has not been satisfactory.

**Keywords:** Intermittent claudication; Subintimal angioplasty; Femoro-popliteal occlusions.

### Introduction

Intentional subintimal angioplasty (SA) for the treatment of occluded femoro-popliteal arteries was first described by Bolia in 1989.<sup>1</sup> Subsequent publications reaffirmed the effectiveness of SA for treating long infra-inguinal arterial occlusions as an alternative to bypass surgery.<sup>2</sup> Unfortunately, only few other centres have been able to reproduce these good results.<sup>3</sup> At the Oslo Centre for Vascular Surgery our initial results supported Bolia in his view that SA is a valuable option in the treatment of patients with symptomatic peripheral arterial disease (PAD). To substantiate our impression we followed-up 104 consecutive patients

with disabling intermittent claudication (IC) treated with SA and reviewed the long-term results.

### Patients and Methods

From February 1997 until January 2000, we performed 116 recanalizations in 104 patients with disabling IC. A patient with disabling IC was defined as having a maximum walking distance of <100 m, which made it impossible to do his/her work or live independently.

Mean age was 67 years (31–91) and 69 (64%) patients were men. The women were on average 8 years older than the male patients. Demographic data, including risk factors, are summarized in Table 1 and are not much different from other reports on patients with PAD, except for a relatively low proportion of diabetics (9%).

Eighteen patients (17%) had been operated previously in various ways. Three received an aorto-iliac

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**Table 1. Risk factors for 104 patients undergoing 116 SA**

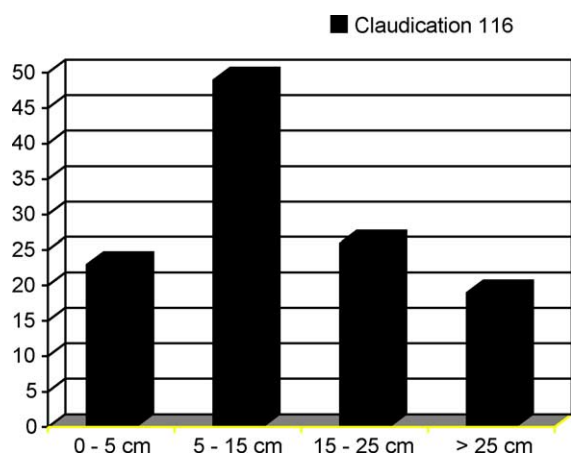
Smoking	55%
Cardiac disease	42%
Hypertension	30%
Cerebro-vascular disease	13%
Diabetes	9%
Previous PTA	34%
Previous vascular surgery	17%
Previous fem-pop bypass	3%

bypass, six a contralateral and three an ipsilateral femoro-popliteal bypass and in six cases a thrombendarterectomy in the groin was performed.

Three of them had an occluded femoro-popliteal bypass parallel to the segment currently treated. The mean arterial run-off consisted of 1.3 patent crural arteries. The mean length of treated occlusions was 16 cm (range 3–40) (Fig. 1).

Before being treated with SA all patients had been submitted to a 3–6 months period of medical treatment, which consisted of practical advice concerning smoking cessation, dietary improvements and regular walking exercise. All patients received anti-platelet drugs if not contra-indicated. The use of statins was individualized, since it was not a routine practice at the time. The indications for SA were the same as for surgical interventions in these patients with disabling IC. If it seemed feasible, patients were primarily treated with SA, since the procedure is less invasive and our initial results had been promising. The SA procedures were performed by three interventional radiologist, who had many years of experience with conventional percutaneous transluminal angioplasty (PTA). They had previously been instructed by Bolia, the pioneer of SA.<sup>1</sup>

The ipsilateral common femoral artery was punctured antegradely. A 5 French straight angiography catheter was used to enter the arterial wall



**Fig. 1.** Number of different occlusion lengths recanalized with SA.

subintimally. This entrance was used to introduce a 0.035 in. hydrophilic guidewire traversing the occluded segment subintimally. A basic technique at this point included the looping of the guidewire tip that was followed by a less-flexible 5 French catheter. Re-entry into the arterial lumen usually occurs spontaneously. Subsequent to re-entry at the distal end of the arterial occlusion the subintimal channel was dilated with either a 5 or 6 mm balloon. The procedure was considered a failure when it was not possible to obtain either of the following: an entry, a re-entry or sufficient flow, by visually assessing the passage of contrast flow. During the procedure patients received 5000 IU of heparin intravenously. All patients stayed over one night in the hospital for observation. They were prescribed 160 mg of aspirin daily, lifelong if not contra-indicated.

Patients who had undergone SA were included in the same surveillance program as patients with a femoro-popliteal bypass. They were examined with ankle/brachial blood pressure measurements and duplex ultrasound scanning at the Vascular Laboratory after 1, 3, 6 and 12 months and thereafter individually. If a significant stenosis (>50%) was suspected on duplex scanning angiography was performed. Subsequent PTA was done whenever needed (Fig. 4). Thereafter, the patients continued to be followed-up according to our routine schedule. If PTA was performed on a stenosis, the case was categorized as 'primary assisted'. All patients were thus followed-up in a prospective fashion during a period of 12 months.

#### Statistical methods

All data were entered into a computed data registry and analyzed by means of the SPSS program at the department for medical statistics. Patency rates were calculated and presented in a Kaplan–Meier curve for the 116 intention to treat as well as for the 101 primary successful recanalizations. Comparison of patency rates was done with the log rank test. Multivariate analyses were performed with the Cox proportional regression method. Means of continuous data were compared with Student's *t*-test. Statistical significance was accepted at  $p < 0.05$ . When patients did not reach a defined end-point, data were censored to the last known date of follow-up.

#### Results

In 101 of 116 cases the subintimal procedure was

successful—the primary technical success rate was 87%. The failures were mostly due to no re-entry distally. Fifty-four out of 116 procedures were multi-segmental, including two out of the three main arterial segments: femoral, popliteal and crural. The superficial femoral artery was nearly always recanalized (Fig. 2), but in eight cases (7%) the procedure was performed only at the popliteal or crural level (Fig. 3). In 50% of cases conventional intraluminal PTA was performed simultaneously proximal or distal to the subintimal recanalization.

All patients with an patent reconstruction markedly improved clinically.<sup>4</sup> Ankle/brachial pressure index increased from 0.55 (0.27–0.80) to 0.90 (0.58–1.0). In 15 cases the initial procedure failed. A second attempt was made in five patients, of which three were successful. Six patients were operated upon with a femoro-popliteal bypass because of the severe symptoms they already had before SA was attempted. Four patients abstained from further invasive treatment.

There was no mortality during the first 30 days. During the total period of follow-up 14 patients died with open subintimal reconstructions based on data from the last the outpatient clinic and/or information from a relative. Complications were minor (Table 2). Of seven haematomas only one required surgical revision because it was large and extended retro-peritoneally. In none of the six perforations there was need for any intervention and they did not influence the clinical outcome. Five of the seven cases with peripheral emboli were successfully aspirated during the same procedure. An 82-year-old male patient needed a popliteal embolectomy after which the artery has stayed open.

Median follow-up duration was 41 months (0–79). In 17 of the 101 cases (17%) angiography confirmed a significant stenosis, which was successfully redilated

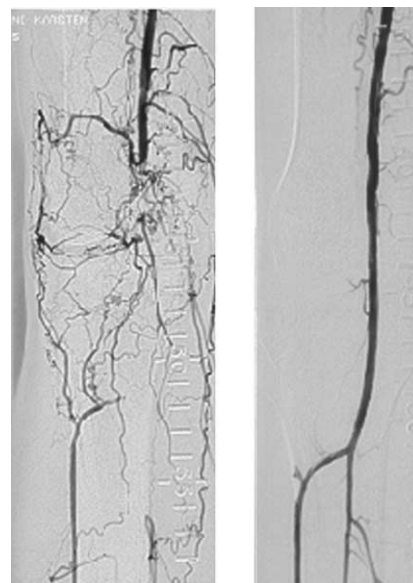


Fig. 3. SA of right popliteal artery and crural arteries.

Table 2. Complications in 116 SA procedures

Bleeding	7
Surgical treatment	1
Perforation	6
Surgical treatment	0
Peripheral emboli	7
Successfully aspirated	5
Embolectomy	1
Heparin	1

(Fig. 4). In one case an additional patch plasty of the common femoral artery was performed because of a narrow stenosis at the puncture site. Of these 17 recanalizations, which were redilated only two re-occluded (after 14 and 42 months). Two patients died with an open redilated subintimal channel and 13 are still alive with a patent reconstruction after 45–75 months.

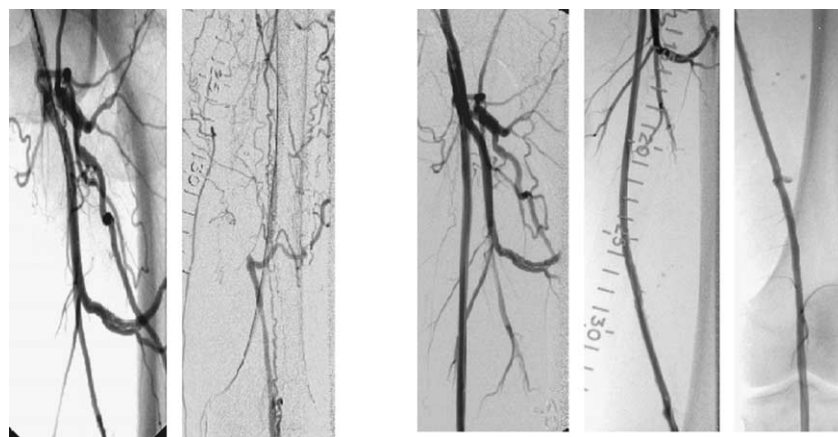
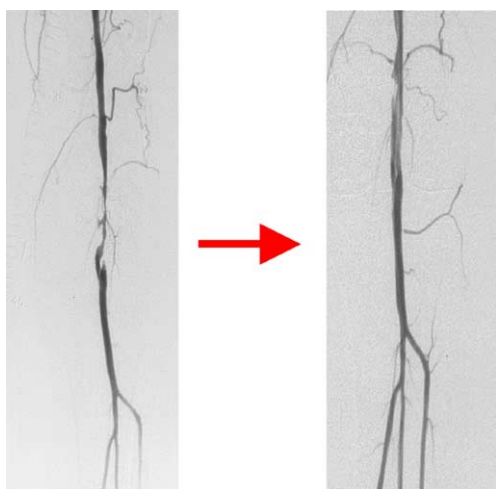


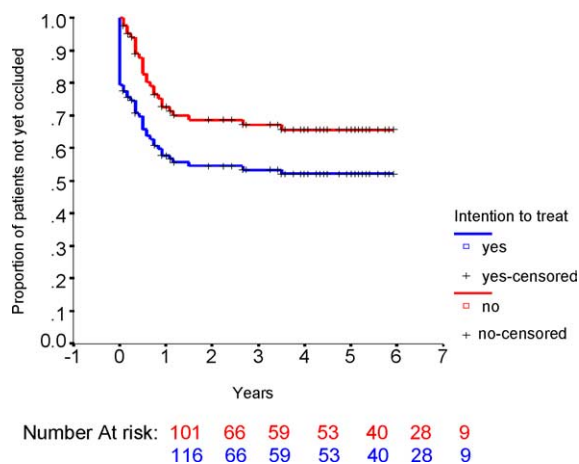
Fig. 2. SA of occluded left superficial femoral artery.



**Fig. 4.** Angioplasty of stenosis in the subintimal channel at the re-entry site.

In 33 cases (33%) the subintimal channel occluded. Thirty of those occurred within the first 15 months, all of which were acute. Three occluded arteries were reopened, one with thrombolysis and two by means of a second subintimal angioplasty.

The 5-year assisted primary patency rate for the 101 primary successful procedures was 64%. For the intention to treat recanalizations (116) the 5-year assisted primary patency rate was 56% (Fig. 5). Twenty-eight recanalized arteries are still open and under observation after more than 5 years. The Kaplan–Meier curve clearly showed that the recanalization tends to stay open once it is still patent after 15 months (Fig. 5). Fourteen patients with an initially successful recanalization died of unrelated causes with 15 open channels during follow-up one of which had been bilaterally recanalized. Multivariate



**Fig. 5.** Assisted primary patency rates for SA for intermittent claudication. Blue curve: intention to treat. Red curve: successful recanalizations.

analysis showed that longer occlusions (> 25 cm) were significantly more prone to occlude than the shorter ones ( $p < 0.002$ ) (Table 3). In female patients results were better. The risk of reocclusion increased for patients > 70 years old. The results were not related to the run-off status of the crural arteries (Table 4).

## Discussion

It is generally agreed that the treatment of patients with IC aims at increasing quality of life by means that are least invasive. Atherosclerosis is a generalized disease without a known etiology and patients do not die from IC but from heart and cerebrovascular disease. Therefore all patients with symptoms of PAD receive appropriate medical treatment and that surgical intervention principally should be reserved for patients with critical limbs ischaemia (CLI). However, there is a relatively large group of patients who have disabling symptoms of claudication despite serious attempts to stop smoking, optimal medical treatment and a training regimen.

Patients with disabling IC often have relatively long (> 5 cm) arterial occlusions unfit for conventional PTA. The present study shows that the results after SA for long arterial occlusions compare favourably with bypass surgery.<sup>5</sup> In our view it is therefore appropriate to primarily attempt SA instead of surgery in this group of patients. SA is a far less invasive, implicating a lower procedural morbidity<sup>6</sup> and it is less expensive. In the present study complications were few and not serious. In addition, during a SA procedure it is easy to simultaneously address a stenosis proximal or distal to the occlusion. Thus, the patient can be treated more completely. Finally, SA does not interfere with later successful vascular surgery.

Previous reports on SA have mainly dealt with the short-term results after SA.<sup>7–9</sup> Our results compare well with these previous studies, however, the present study includes larger number of patients with longer follow-up.

Several vascular centres have discussed why they are not able to duplicate the good results published by Bolia and associates.<sup>10</sup> We conclude that good results can be obtained if the interventional radiologist is very experienced and dedicated.<sup>11,12</sup> It goes without saying that optimal cooperation between surgeon and radiologist is necessary to obtain the best possible results. Furthermore, it is crucial that the patients get enrolled in a good surveillance program so that stenoses can be diagnosed and treated at an early stage.

We have not differentiated the results by calculating

**Table 3. Statistics showing significant risk factors for occlusion**

	Odds ratio	P-value
Intention to treat: yes		
Length of occlusion		
5–15 cm	2.0	0.27
15–25 cm	3.4	0.054
>25 cm	7.0	0.002
Gender		
Female	0.5	0.05
Intention to treat: no		
Length of occlusion		
5–15 cm	2.0	
15–25 cm	4.0	0.068
>25 cm	5.5	0.029
Age		
70–75 years	3.3	0.04

primary patency rates. There is no way of knowing whether the prophylactic redilatation of a stenotic subintimal channel was really necessary to secure patency. That is why we only have used assisted primary patency rates in the evaluation of our results. Only two of 17 redilated segments reoccluded (after 14 and 42 months, respectively). This supports the value of a careful follow-up routine and an active attitude towards reintervention.

Complications were few and minor. Of seven haematomas only one needed surgical evacuation. The six perforations did not need any intervention and they did not influence clinical outcome. Emboli into the crural vessels during the procedure could usually be aspirated. Very importantly, SA never interfered with later successful vascular surgery.

There are indications that angioplasty increases patients' quality of life, even though good disease specific questionnaires are still lacking.<sup>13</sup> It was not our aim to calculate and compare the costs of these two treatment modalities, but it seems very plausible that SA comes out well despite the relatively frequent need for a second procedure since hospital stay is much shorter than for surgery.

When results after endovascular procedures are based on intention to treat, a comparison with bypass surgery gets distorted. The results after autologous

vein bypass operations are rarely presented as intention to treat, because then all cases where a poor quality vein has to be discarded have to be counted as failures. This would give a wrong impression of the effectiveness of performing the bypass itself.

Multivariate analysis of small numbers and different subsets can be unreliable. Therefore we are careful in drawing conclusions and are uncertain in how far this information will influence our indications for SA. The finding that the length of arterial occlusion was an independent risk factor was not surprising. The longer the potentially thrombogenic subintimal channel, the greater chance for reocclusion. Our patients received 160 mg aspirin daily as life-long antiplatelet therapy. The optimal adjuvant therapy after SA is still a topic of debate. The results after SA may be improved by giving patients low molecular heparin or clopidogrel during the first 6–8 weeks after the intervention.

In contrast to what has been reported concerning femoro-popliteal bypass surgery, the status of run-off vessels did not seem to influence the results of SA. This is probably due to the fact that there are more open collateral vessels to facilitate run-off after SA than after bypass surgery. Since the diameter of arteries in women usually is smaller than in men, it was surprising that the female patients were less prone to reocclusion ( $p < 0.05$ ). Explanations are purely speculative.

In contrast to other reports,<sup>14</sup> in the few cases where we performed SA on the occluded superficial femoral artery in the presence of an occluded bypass graft, the results were encouraging. If conservative treatment seems to be of no avail in patients with critical ischaemia after occlusion of their previously inserted bypass graft, management options include thrombolysis and angioplasty, graft thrombectomy and angioplasty, remote endarterectomy,<sup>15</sup> or redo bypass surgery. Thrombolysis is our first choice giving us the opportunity to localize and address a possible cause of the occlusion. In patients who need a new revascularization procedure our second option would

**Table 4. Statistics showing controlled risk factors for occlusion**

Risk factors	Significance intention to treat (116)	Significance successful recanalization (101)
Smoking	NS	NS
Cardiac disease	NS	NS
Hypertension	NS	NS
Cerebro-vascul. dis.	NS	NS
Diabetic	NS	NS
Occl. length	0.002	0.029
Previous vasc. surg	NS	NS
Run-off	NS	NS
Age > 70 years	NS	0.04
Male gender	0.05	NS

definitely be SA, since a redo operation is technically more difficult.

The assisted patency curves flattened out after 15 months. In the majority of patients where a successful redilatation was performed during the initial 15 months, the subintimal channel stayed open during the following years. This observation accentuates the importance of careful surveillance so that it is possible to re-intervene and redilate a stenosis in progress.

In conclusion, due to the good results obtained with SA, femoro-popliteal bypass surgery is increasingly being reserved for patients in whom PTA or SA has failed or is contraindicated.

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