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# Randomised comparison of primary stent placement versus primary angioplasty followed by selective stent placement in patients with iliac-artery occlusive disease

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## Summary

**Background** Percutaneous transluminal angioplasty (PTA) is a safe, simple, and successful treatment for intermittent claudication caused by iliac-artery occlusive disease. Primary stent placement has been proposed as more effective than PTA. We compared the technical results and clinical outcomes of two treatment strategies—primary placement of a stent across the stenotic segment of the iliac artery, or primary PTA followed by selective stent placement when haemodynamic results were inadequate.

**Methods** We randomly assigned 279 patients with intermittent claudication, recruited from departments of vascular surgery, either to direct stent placement (group I, n=143) or primary angioplasty (group II, n=136), with subsequent stent placement in case of a residual mean pressure gradient greater than 10 mm Hg across the treated site. The main inclusion criterion was intermittent claudication on the basis of iliac-artery stenosis of more than 50%, proven by angiography. All patients had a clinical assessment before intervention and at 3, 12, and 24 months. Clinical success was defined as improvement of at least one clinical category. Secondary endpoints were initial technical results, procedural complications, cumulative patency as assessed by duplex ultrasonography, and quality of life.

**Findings** In group II, selective stent placement was done in 59 (43%) of the 136 patients. The mean follow-up was 9.3 months (range 3–24). Initial haemodynamic success and complication rates were 119 (81%) of 149 limbs and 6 (4%) of 143 limbs (group I) versus 103 (82%) of 126 limbs and 10 (7%) of 136 limbs (group II), respectively. Clinical success rates at 2 years were 29 (78%) of 37 patients and 26 (77%) of 34 patients in groups I and II, respectively (p=0.6); however, 43% and 35% of the patients, respectively, still had symptoms. Quality of life improved significantly after intervention (p<0.05) but we found no difference between the groups during follow-up. 2-year cumulative patency rates were similar at 71% versus 70% (p=0.2), respectively, as were reintervention rates at 7% versus 4%, respectively (95% CI –2% to 9%).

**Interpretation** There were no substantial differences in technical results and clinical outcomes of the two

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treatment strategies both at short-term and long-term follow-up. Since angioplasty followed by selective stent placement is less expensive than direct placement of a stent, the former seems to be the treatment of choice for lifestyle-limiting intermittent claudication caused by iliac artery occlusive disease.

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## Introduction

Intermittent claudication caused by atherosclerotic disease of the iliac artery can be a lifestyle-limiting condition. The initial treatment of patients with this disease is physical exercise.<sup>1</sup> Supervised exercise programmes may significantly improve walking distance, but they require a great deal of time and the cost-effectiveness has not been established. Until now, such programmes were not widely available. Percutaneous transluminal angioplasty (PTA) is generally regarded as a safe, simple, and successful alternative for patients with this disease.<sup>2</sup> However, the success of PTA is reduced by residual stenosis and late restenosis. Vascular stents are being increasingly used as an adjunct to iliac-artery PTA. The indications for stent placement, as defined by the US Food and Drug Administration, include suboptimal effect of iliac angioplasty on the basis of either a residual stenosis of more than 30% measured by angiography, a mean pressure gradient of 5 mm Hg or more across the treated site, or extensive intimal dissection. Several investigators in follow-up studies on iliac-artery stenting used the criteria of the US Food and Drug Administration without indicating the specific criteria for secondary stent placement.<sup>3–9</sup> Angiography is generally regarded as an inadequate test for detection of residual, haemodynamically significant stenosis after PTA, and measurement of the intra-arterial pressure gradient provides a better assessment of the effect of treatment.<sup>10–13</sup>

Endovascular stent placement is reported to improve the immediate angiographic and haemodynamic results of iliac balloon angioplasty in cases of residual stenosis caused by elastic recoil or intimal dissection.<sup>3–9</sup> No conclusive evidence exists, however, that stent placement is better in the long term when used as an adjunct to failed angioplasty. A search of research published between 1984 and 1996 (in English) revealed no reports of randomised clinical trials of the long-term results of peripheral-artery stenting. The value of stent placement as the primary treatment of iliac atherosclerotic lesions compared with its use as an adjunct to suboptimal angioplasty has not been established either. However, a potential advantage of stent placement as primary therapy is that it provides better initial angiographic and haemodynamic results with less chance of elastic recoil, and an improved sealing of intimal flaps.<sup>3–9</sup> But the efficacy of the stents is widely recognised as limited in the long term owing to the narrowing of the luminal diameter of the devices caused by intimal

proliferations,<sup>14</sup> and there may be risks associated with the presence of a foreign body. In addition, since the stents are expensive devices and the long-term results are unknown, a selective approach to stent use seems warranted.

To assess the role of stent placement in the treatment of iliac-artery occlusive disease, we carried out a prospective, randomised, multicentre trial to compare two treatment strategies. Patients either received stent placement as the primary method of treatment for their disease (group I) or initially underwent PTA followed by placement of a stent when PTA provided suboptimal results on the basis of intra-arterial pressure measurements (group II).

## Patients and methods

### Study population

Patients were recruited from the departments of vascular surgery in six study centres from November, 1993, to March, 1997. The centres included two university hospitals and four large regional hospitals, selected on the basis of experience with peripheral-vascular intervention techniques, including endovascular stent placement. The study protocol was approved by the local institutional review boards. All patients gave informed, written consent. Inclusion criteria for patients were intermittent claudication consisting of pain localised in the buttock, upper leg, or calf; reduced pulsation of the femoral artery and reduced ankle-brachial index (ABI); reduction, evident by angiography, in arterial diameter greater than 50%; and stenosis of 10 cm or less in length in the common or external iliac artery or occlusion of 5 cm or less that allowed passage with a guide wire. Exclusion criteria were stenosis of more than 10 cm in length; arterial occlusion of more than 5 cm in length, or of 5 cm or less not allowing the passage of a guide wire; stenosis involving the distal aorta; severe comorbidity (eg, severe cardiac or cerebrovascular abnormality, malignant disease); and non-medical factors such as inability to understand Dutch, or expected poor compliance. Patients with recurrent symptoms after vascular surgery of the iliac artery or PTA more than 12 months before were not excluded. In patients with multiple unilateral or bilateral iliac stenoses, all lesions were assigned to the same treatment regimen. Multiple stenosis localised in one arterial segment (ie, common iliac artery or external iliac artery) were classified as a single lesion.

### Randomisation

Patients were randomly assigned to either primary stent placement (group I) or primary PTA with selective stent placement (group II). For each hospital, a separate computer-generated randomisation table was produced to limit imbalance between treatment assignments to four. This table was kept at the trial office and was not available to the treating physicians. The treatment assignment was revealed in the angiography suite by a trial co-worker after the diagnostic arterial angiography was done, and before intervention was started. In the event of an occlusion, randomisation was postponed until mechanical passage of the occluded segment by a guide wire proved possible. We decided that to conceal the assigned treatment from patients or physicians was not feasible.

### Treatment protocols

For diagnosis of the extent and severity of stenosis, all patients considered for intervention underwent intra-arterial digital subtraction angiography of the aorto-iliac tract in two projections. In all patients, mean intra-arterial pressures were acquired before intervention. The pressure-gradient measurements were obtained by simultaneous recording of the pressure proximal and distal to the lesion. If the lesion was of questionable haemodynamic significance (translesional gradient <10 mm Hg), additional measurement with intra-arterial vasodilation (by the use of 25 mg papaverine, 40 mg tolazoline, or 100 µg glyceryl trinitrate) was obtained for definitive quantification.

	Group I (n=143)	Group II (n=136)
<b>Mean age (SD) in years</b>	59 (11)	60 (10)
<b>Male/female</b>	102/41	99/37
<b>Medical history</b>		
Tobacco use	124 (87%)	128 (94%)
Diabetes mellitus	13 (9%)	15 (11%)
Hypertension	40 (28%)	37 (27%)
Cerebrovascular accident	20 (14%)	9 (7%)
Cholesterol >6.5 mmol/L	34 (24%)	36 (26%)
<b>Clinical grade (SVS/ISCVS classification)*</b>		
1	35 (24%)	37 (27%)
2	77 (54%)	69 (51%)
3	23 (16%)	18 (13%)
4	7 (5%)	11 (8%)
5	1 (1%)	1 (1%)
<b>Former recanalisation of same arterial segment</b>		
PTA	12 (8%)	12 (9%)
Vascular surgery	5 (3%)	2 (1%)
<b>Mean (SD) exercise data†</b>		
ABI at rest	0.78 (0.20)	0.77 (0.20)
ABI after exercise	0.55 (0.26)	0.54 (0.26)
Walking distance (m)	211 (92)	224 (88)
<b>Prescription of anticoagulants</b>		
Aspirin	128 (90%)	115 (85%)
Coumarin	13 (9%)	18 (13%)
Aspirin and coumarin	2 (1%)	3 (2%)
<b>Mean (SD) RAND-36 dimensions</b>		
Role functioning as limited by		
Physical difficulties	27 (36)	32 (40)
Emotional difficulties	59 (45)	56 (45)
Physical functioning	39 (19)	42 (20)
Bodily pain	50 (22)	50 (25)
Social functioning	64 (27)	69 (28)
Mental health	70 (22)	69 (22)
Vitality	51 (23)	53 (21)
General health perception	56 (21)	54 (23)

\*Society of Vascular Surgery and International Society for Cardiovascular Surgery.

†Number of limbs with symptoms in groups I and II, respectively: 173 and 151 for ABI at rest; 162 and 147 for ABI after exercise; 129 and 119 for walking distance.

Table 1: **Baseline clinical characteristics**

In group-I patients undergoing primary stent placement, a long 7-F introducer sheath was placed across the targeted segment. The stent (Palmaz, Johnson and Johnson Interventional Systems, Warren, NY, USA) was mounted by hand on a folded angioplasty balloon catheter. The stent-balloon assembly was positioned at the site of the intended intervention, the sheath withdrawn, and the stent deployed by inflation of the balloon. The stent diameter was determined by the width of the uninvolved portion of the vessel.

In the group-II patients, PTA was done according to standard techniques.<sup>2</sup> When elastic recoil or inappropriate results by angiography were found after angioplasty, larger balloon inflation and larger balloons were applied. In all cases, measurement of the arterial pressures was also done after intervention. The results of intra-arterial-pressure measurements were used as the only criterion for selective stent placement after PTA. When a haemodynamically significant gradient (>10 mm Hg) was found after PTA, stent placement was done at the same session, irrespective of evidence of angiography by residual stenosis. When we found evidence of residual stenosis but no haemodynamically significant gradient, we did not carry out stent placement.

All patients received anticoagulant medication (aspirin or oral anticoagulants) in accordance with local guidelines or the individual preference of the physician who initially referred the patient for treatment. Medication was independent of the type of intervention. We did colour duplex ultrasonography within 24 h of each intervention to verify local arterial patency.

### Clinical examination

Clinical assessment was carried out in all patients before intervention, and at 3, 12, and 24 months; assessment included physical examination, treadmill exercise with measurement of ABI, and colour duplex ultrasonography. Recurrent stenosis

	Group I	Group II
<b>Number of lesions</b>	187	169
<b>Arterial segment</b>		
Common iliac artery	131 (70%)	114 (67%)
External iliac artery	56 (30%)	55 (33%)
<b>Angiographic stenosis grade</b>		
<50% diameter reduction	21 (11%)	19 (11%)
≥50% diameter reduction	149 (80%)	138 (82%)
Total occlusion	17 (9%)	12 (7%)
<b>Disease severity (SVS/ISCVS grading)*</b>		
Type A	96 (51%)	80 (47%)
Type B1	48 (26%)	47 (28%)
Type B2	43 (23%)	42 (25%)
<b>Patency of runoff vessels</b>		
Occlusion of superficial femoral artery	18 (10%)	19 (11%)
Occlusion of deep femoral artery	4 (2%)	9 (5%)

\*Society of Vascular Surgery and International Society for Cardiovascular Surgery.

Table 2: **Baseline angiographic characteristics of iliac-artery lesions**

detected at follow-up examinations required no specific treatment under the trial protocol. To assess quality-of-life effects, we interviewed all patients by telephone before treatment and at 1, 3, 12, and 24 months after the procedure. The interview consisted of a generic, descriptive, health-status measure, and the RAND 36-item health survey 1.0 (RAND-36), which is equivalent to the Medical Outcomes Study Short Form-36.<sup>15</sup> The interviewers who carried out the surveys were not aware of the patient's treatment.

#### Definition of success and endpoints

We defined clinical and haemodynamic success according to the criteria proposed by the Society of Vascular Surgery and the International Society for Cardiovascular Surgery:<sup>16</sup> clinical success was defined as improvement of at least one clinical category compared with the pretreatment assessment; haemodynamic success as improvement of the ABI by 0.10 or more and no more than 0.15 deterioration from the first postprocedural measurement obtained at 3 months. The iliac artery was deemed patent if a peak-systolic-velocity ratio of less than 2.5 was found at duplex ultrasonography.<sup>17-19</sup>

We defined the primary endpoint of the study as no improvement or a worsening of the clinical category compared with the preprocedural clinical assessment. If we found a discrepancy between clinical symptoms and objective criteria of the treadmill-exercise test (ie, ABI, walking distance), we gave clinical symptoms precedence when assigning the category.<sup>4</sup> Secondary endpoints of interest were cessation of the study protocol owing to the complications of the intervention; postprocedural pressure gradient greater than 10 mm Hg across the treated site; restenosis diagnosed by colour duplex ultrasonography and defined as a peak-systolic-velocity-ratio greater than 2.5;<sup>17-19</sup> ABI improvement of less than 0.10 or deterioration by more than 0.15 compared with the maximum postprocedural value at 3 months; and repeated intervention at the treated site.

Quality-of-life effects were assessed in eight health dimensions (RAND-36): physical functioning, role functioning as limited by physical difficulties and emotional difficulties, bodily pain, social functioning, mental health, vitality, and general health perception. For each dimension we calculated a score from 0 to 100; higher scores indicated a better state of health.

#### Statistical analysis

We calculated that a sample size of 180 patients in each group of the trial would be sufficient to show a difference between groups of 10% in patency at 12 months with power 90% and  $p < 0.05$ . During the trial the accrual rate was less than expected, and funding did not allow recruitment of patients to continue beyond 3 years.

We analysed data according to the intention-to-treat principle. Discrete variables were expressed as counts and percentages; continuous data as means with SD, with calculation of 95% CIs

to measure the significance of differences. We analysed differences between preprocedural and postprocedural haemodynamic and clinical values within the treatment groups with the Wilcoxon matched-pairs signed rank-sum test. The Mann-Whitney  $U$  test was used to calculate the significance of differences between cumulative-frequency distribution curves of the two groups.

2-year arterial patency rates based on duplex ultrasound were calculated by life-table analysis. We compared cumulative patencies in both trial groups using the Wilcoxon (Gehan) test, and defined significance as a two-tailed  $p$  value of less than 0.05. Calculations were done with SPSS/PC statistical software (version 6.0).

## Results

### Patient enrolment

During the accrual period, 365 potentially eligible patients were identified and screened for participation. Patients were deemed potentially eligible when instead of diagnostic arterial angiography, colour duplex indicated significant iliac-artery stenosis. Of these 365, 27 (8%) patients refused participation, and 59 (17%) were excluded owing to specific protocol restrictions (21 had stenoses extending into the distal aorta detected by angiography; in 20 angiography could not confirm the extent of disease as assessed by the screening colour duplex ultrasonography; eight had stenosis >10 cm or occlusion >5 cm; in seven the lesion could not be crossed with a guide wire; and three had extensive, diffuse atherosclerotic changes of the vessels for which PTA or stenting under the protocol would have been insufficient). The baseline characteristics of the remaining 279 randomised patients were similar in the two treatment groups (table 1). The groups were also similar with regard to the characteristics by angiography of the lesions (table 2).

### Outcome of procedures

Group I included 143 patients randomly assigned primary stent placement, and 187 lesions were treated in this group with a total of 208 stents. One patient experienced severe vascular spasm during an attempted stent placement, which made angiographic or haemodynamic identification of the stenosis impossible, and no stent was placed. Five patients had a history of vascular surgery of the same arterial segment, of whom two had undergone endarterectomy and three had had iliac-femoral bypass. Of the latter three, one patient had developed a stenosis at the anastomosis site. The results of intra-arterial pressure measurements are given in table 3. The mean pressure gradient across the treated segments decreased from 16 mm Hg before treatment to post-treatment values of 3 mm Hg at rest (95% CI for the decrease 12-15), and to 6 mm Hg during vasodilation.

Group II included 136 patients randomly assigned to

Outcome measure	Group I		Group II	
	Number of lesions	Mean (SD) value	Number of lesions	Mean (SD) value
<b>Pressure gradient (mm Hg)</b>				
Before procedure	148	16 (11)	134	17 (11)
After procedure, at rest	163	3 (4)	150	3 (3)
After procedure, after vasodilation	151	6 (4)	138	6 (3)
<b>Peak systolic velocity ratio*</b>				
Before procedure	109	4.8 (3.4)	94	4.9 (3.1)
After procedure	152	1.2 (0.8)	132	1.2 (0.5)

\*As measured by colour duplex ultrasonography.

Table 3: **Outcome of procedures**

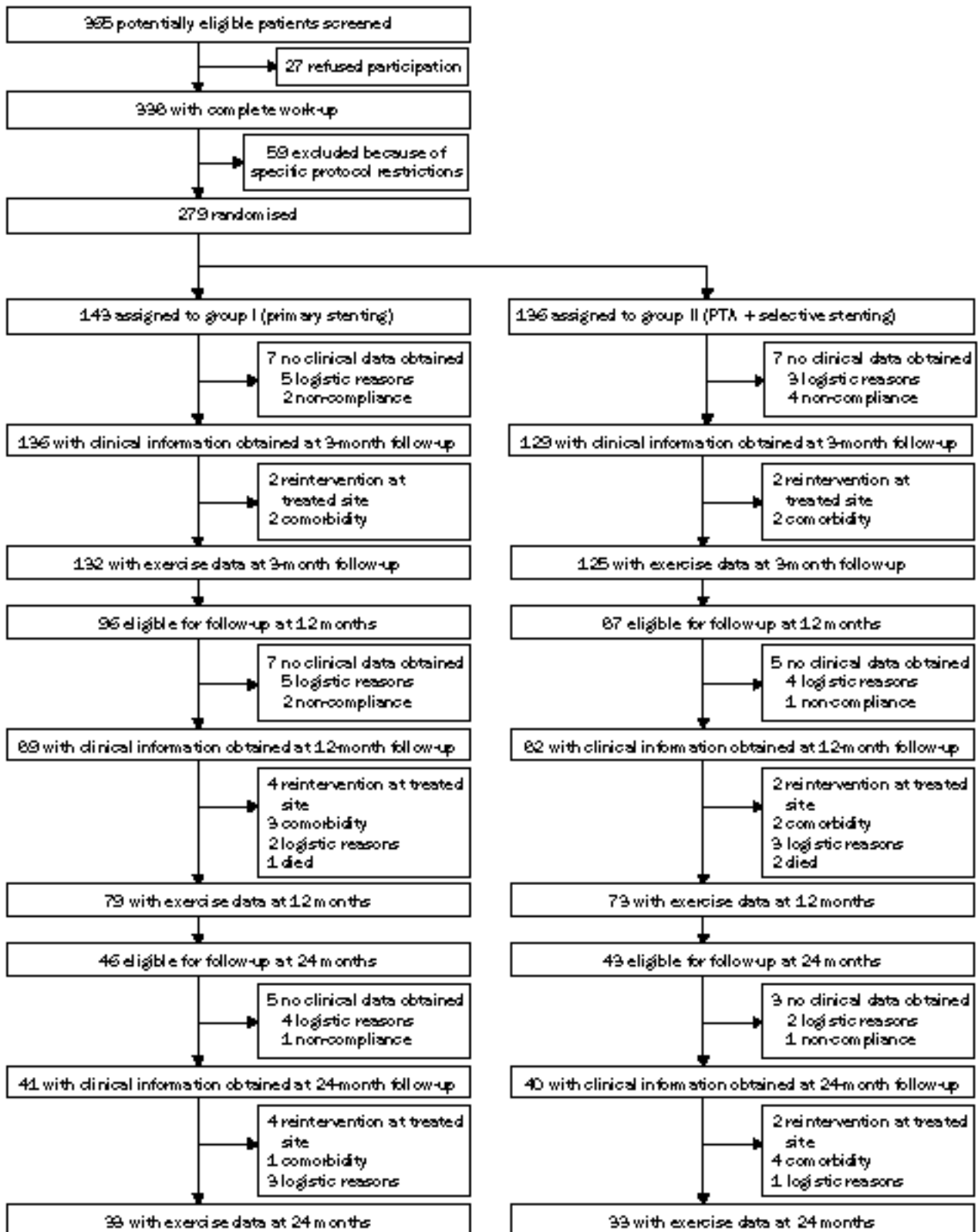


Figure 1: Trial profile

Patients from whom clinical data were not obtained at any follow-up time were asked to attend subsequent follow-up examinations.

primary PTA, and 169 lesions were treated with PTA in this group. Angioplasty was followed by selective stent placement in 59 (43%; 65 lesions; 77 stents) of these patients because a haemodynamically significant residual pressure gradient across the angioplasty site was found. In nine (7%) patients in this group, treatment was not in

accordance with the study protocol. Three of the nine patients were inappropriately treated with stent placement in the first months of the study after angioplasty-induced dissections, without substantial translesional pressure gradients; the other six were denied selective stent placement owing either to complications related to

Endpoint	Number with improvement/total (%)	
	Group I	Group II
<b>Clinical success*</b>		
3 months	103/135 (76%)	101/123 (82%)
12 months	64/80 (80%)	62/77 (81%)
24 months	29/37 (78%)	26/34 (76%)
<b>Haemodynamic success</b>		
3 months	119/149 (80%)	103/126 (82%)
12 months	71/91 (78%)	72/87 (83%)
24 months	35/41 (85%)	33/39 (85%)

\*Improvement of at least one clinical grade category.

†Improvement in ABI of >0.10; total is total number of limbs.

Table 4: Rates of clinical and haemodynamic success

angioplasty (four) or to absence of residual stenosis visible by angiography after PTA in the presence of a haemodynamically significant gradient (two). Two patients had a history of vascular surgery of the same arterial segment; one had undergone endarterectomy and was treated with stent placement, the other had had an iliac-femoral bypass with a patent anastomosis and was treated with PTA alone. In group II, the mean pressure gradient across the treated segments decreased from 17 mm Hg before treatment to post-treatment values of 3 mm Hg at rest (95% CI for the decrease 12–15) and to 6 mm Hg during vasodilation (table 3).

We found no significant differences between groups I and II in the mean pressure gradient after intervention (95% CI for the difference between means -1 to 1 mm Hg) or the percentage of post-treatment gradients exceeding 10 mm Hg at rest (five [3%] in both groups) or during vasodilation (24 [16%] in group I vs 16 [12%] in group II; 95% CI for difference in proportions -4% to 12%). Detailed information on the intra-arterial pressure measurements has been given elsewhere.<sup>20</sup>

Complications occurred in six (4%) patients in group I and in ten (7%) in group II (95% CI for difference -2% to 9%). Complications included haematoma at the puncture site, arterial-wall perforation, acute occlusion of the treated arterial segment, embolism, and vasovagal collapse. Surgical intervention was necessary in two patients in group II. Stent occlusion as indicated by arterial thrombosis did not occur.

#### Clinical and haemodynamic results

At 3 months after intervention, clinical data were obtained in 265 (95%) of the 279 randomised patients and treadmill exercise testing was done in 257 patients (figure 1). At 12 months, follow-up clinical data were obtained in 171 (93%) of 183 patients eligible for follow-up and

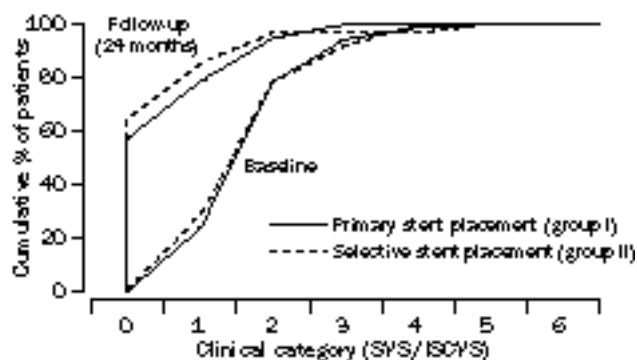


Figure 2: Cumulative distribution curves of clinical grade (categories of Society of Vascular Surgery and International Society for Cardiovascular Surgery) at baseline and at 24 months' follow-up

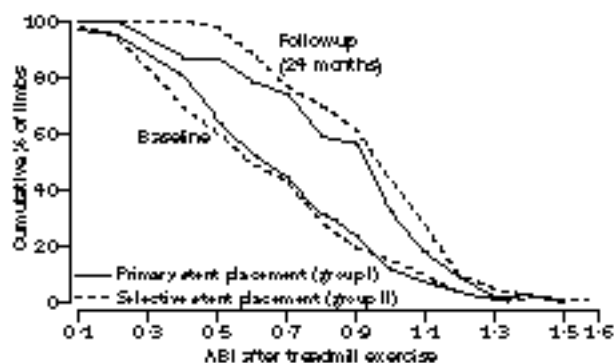


Figure 3: Cumulative distribution curves of a particular ABI exercise or better at baseline and 24 months' follow-up

treadmill testing was done in 152 patients. At 24 months, we obtained clinical data in 81 (91%) of 89 patients eligible for follow-up and treadmill exercise testing was done in 66 patients. Missing data were distributed equally across the groups. We found no difference between the two groups in the rate of repeated intervention at the treated site; repeated intervention occurred in ten (7%) patients in group I, and in six (4%) patients in group II (95% CI for difference -3% to 8%). Vascular interventions at levels distal to the iliac arteries (ie, femoropopliteal arteries) were also distributed equally in both groups during the follow-up period. The mean follow-up for all patients was 9.3 months (range 3–24).

We found no significant differences between the treatment groups in post-treatment improvement of at least one clinical category ( $p=0.6$  at 24 months; figure 2). Clinical success rates at 3, 12, and 24 months' follow-up are given in table 4. From figure 2 can be derived that 43% (16/37 patients) in group I and 35% (12/34 patients) in group II still had symptoms and signs of intermittent claudication after 2 years.

The treatment groups showed similar haemodynamic success (table 4 and figure 2;  $p$  values at 3, 12, and 24 months were 0.7, 0.4, and 0.9, respectively). For the patients in each treatment group, the results of both clinical and haemodynamic assessments were significantly improved at 3 months' follow-up ( $p<0.05$ ), and we found no deterioration during follow-up at 12 and 24 months.

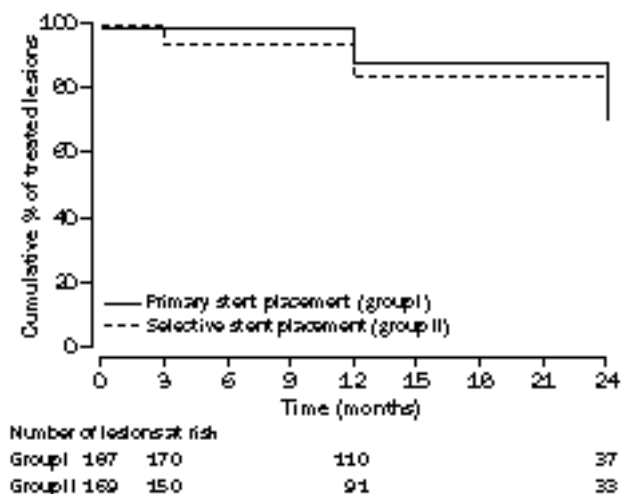


Figure 4: Cumulative patency rates as measured by colour duplex ultrasonography (peak systolic velocity ratio >2.5) of 356 iliac arteries in 279 patients

### Colour duplex sonography

The mean peak-systolic-velocity ratio decreased substantially after the intervention in both groups (table 3). Cumulative primary-patency rates on the basis of duplex examination are shown in figure 4. At 2-years' follow-up, patency rates were similar for groups I and II (71.3% *vs* 69.9%). Overall comparison of the cumulative patencies in the two treatment groups showed no difference ( $p=0.2$ ).

### Quality-of-life analysis

Quality-of-life assessment was completed in 255 (91%) of all 279 patients. All eight health dimensions of the RAND-36 survey were significantly improved in patients after intervention ( $p<0.05$ ); physical functioning, pain, and role-functioning limited by physical difficulties were improved most. After the first follow-up, quality-of-life scores did not change further over time. The improvements in quality-of-life measures were similar in both treatment groups, and we found no significant differences.

### Discussion

We found no significant differences in technical results or clinical outcomes of the two treatment strategies. Our investigation showed, moreover, that both at 3-month follow-up and during the 2-year follow-up the results remained the same irrespective of whether the intervention consisted of primary placement of a stent across the arterial stenosis or primary angioplasty followed by selective stent placement in case of a failed balloon procedure. Immediately after intervention the haemodynamically significant pressure gradients across the vascular segments resolved with both treatments, resulting in substantial improvement of the peak-systolic-velocity ratios. During the 2-year follow-up the results remained similar with substantial improvements in quality of life for both groups. Although the clinical success ratios (defined as improvement of at least one clinical category) were equally high for groups I and II (78% and 77%, respectively), a large proportion of patients still had symptoms after 2 years (43% and 35%, respectively). Although in the vast majority of these patients good results were obtained at the time of the intervention (ie, the vascular patency at the iliac stenosis was restored and remained patent at duplex sonography during follow-up), the disappointingly high number of patients with residual symptoms probably reflects the diffuse nature of atherosclerosis, which affects all vessels and not just the area of the treated stenosis. Nevertheless, since we did not find significant differences in the number of immediate complications or in the rate of reinterventions between the treatment methods, primary angioplasty followed by selective stent placement seems to be the strategy of choice for treatment of lifestyle-limiting intermittent claudication—particularly since the strategy also seems the most cost-effective, requiring only a fraction of the stents needed in a strategy of primary stent placement (65 [38%] of 169 in our study).

A review of several non-randomised studies on the clinical benefits of percutaneous treatment for iliac-artery occlusive disease showed substantial variation in reported success rates. Immediately after intervention, success rates ranged from 97% to 100% after stent placement and from 91% to 97% after PTA, at 1 year from 80% to 95% and

73% to 91%, and at 2 years from 71% to 91% and 65% to 89%, respectively.<sup>3-9,21-24</sup> A 1997 meta-analysis that compared the results of eight non-randomised stent-placement studies and six PTA studies showed that stenting reduced the risk of long-term failure by 39% compared with PTA.<sup>25</sup> Study selection ensured that a comparison was made with contemporary controls, and the investigators adjusted the data for differences in case-mix and reporting methods across studies. Nevertheless, the results should be interpreted with caution because long-term success was not uniformly defined in the analysed studies, and patients were not randomly assigned to one treatment versus the other. In general, non-randomised studies tend to overestimate the effect of new treatments, which may, at least in part, explain the differences in results after PTA and stent placement.<sup>26</sup> Whereas the meta-analysis compared stent placement, either primary or selectively, with PTA, our study was designed to assess the difference between pulmonary stent placement and primary PTA followed by stent placement in selected cases. We know of only one randomised comparison of stent placement versus PTA for peripheral-vascular occlusive disease, by Richter and colleagues from Germany. Although this study has not yet been published in full, its findings are widely quoted and provide reasons to conclude that the outcomes with stent placement are more durable than those with angioplasty alone, since cumulative clinical success at 5 years was 70% in the PTA group and 93% in the stent group.<sup>27</sup> However, no specific information is given on the definition of clinical success. In the light of our present knowledge, we might have decided on a different study design to compare direct stent placement with angioplasty alone.

All these findings taken together suggest that angioplasty followed by stent placement for failures may be preferred. Whether the gain in quality of life after selective stent placement compared with angioplasty alone justifies the additional cost, however, has yet to be established.

The criteria we used for carrying out selective stent placement were different from those recommended by the US Food and Drug Administration. In particular, we chose a mean pressure gradient of more than 10 mm Hg across the PTA site<sup>13,28-31</sup> as indication for stent placement after PTA, rather than the 5 mm Hg proposed by the Administration. Use of our more lenient criterion for definition of a haemodynamic success after PTA represents a more conservative approach to selective stent placement, which we believed would avoid unnecessary stent placements in a substantial number of patients.

Interpretation of our results is limited in several ways. First, most of our patients (94%) were treated for intermittent claudication and, in the majority of them (92%), the disorder was caused by an iliac-artery stenosis. Our results cannot therefore be extended to patients with critical ischaemia or occlusion. A selective stent-placement strategy in patients with occlusions would probably result in a high proportion of stent placements. In the 12 occlusions in our study treated with initial PTA, ten (83%) required stent placement. Total occlusions, therefore, may not be appropriate for a selective approach. Ten patients could not be treated in accordance with the study protocol; these protocol violations reflect clinical practice in the type of study we have done. To avoid a biased patient selection associated with exclusion of these cases, we adhered to the intention-to-treat principle during data analysis.

We had also expected a higher patency in the primary-stent group than in the primary-angioplasty group, but we found that the two treatments were equally effective. To prove with confidence that two treatment strategies have similar effects, a substantial number of patients are required. At 3 months the patency rate, based on peak-systolic-velocity measurements, was 95% in both trial groups. The number of the treated segments was high enough to state with 95% confidence and power 80% that the difference in 3-month patency rates was 6.5% at most. At 1 year the patency rate in both groups was 90%, and the number of treated segments was sufficiently high to state that the difference was 12% at most.

Although 67% of the patients were followed up for at least 1 year, the mean follow-up of our study was only 9.3 months. Studies that investigated PTA have shown that the failure rate is higher in the first year after treatment.<sup>23,24</sup> Thus, a difference in failure rates between the treatment groups could probably not be shown beyond 1 year. Long-term follow-up data on patients with vascular stents are still scarce. With longer follow-up (2–5 years) late complications of stent placement may be recorded.

Although our results showed no difference in patency or complication rates, functional status, or quality of life, a small difference might have gone undetected. In particular, the incidence of complications is reported as significantly higher in PTA procedures compared with endovascular stent placement.<sup>25</sup> In our study, surgical intervention was necessary in two patients in the primary angioplasty group; such intervention may be a potential drawback of this strategy.

Since we could not use a control group in our trial, the improvement in quality of life after intervention may be explained by a placebo effect rather than by the intervention itself. However, improvement of other clinical and haemodynamic values does not suggest a placebo effect.

#### Participating centres in Dutch Iliac Stent Trial Study

St Antonius Hospital, Nieuwegein (T Th C Overtoom, J C de Valois, F L Moll, H D W M van de Pavoordt); Slingeland Hospital, Doetinchem (J H Spithoven, J G J M van Iersel, J Seegers); University Hospital, Utrecht (J P J van Schaik, F J A Beek); University Hospital Rotterdam Dijkzigt (H Pieterman, H van Urk); Twenteborg Hospital, Almelo (J J Kouwenberg, F H B Tuynman, J W van den Heuvel, J G van Baal); Catharina Hospital, Eindhoven (G H M Landman, A V Tielbeek, J Buth); University of Groningen (E E E van Wijck); and University of Virginia, USA (E E de Lange).

#### Contributors

Willem P Th M Mali and Yolanda van der Graaf were the principal investigators; they designed the study, advised on data analysis, and applied for grants. Eric Tetteroo coordinated the project, and collected, checked, and analysed the data. Johanna L Bosch and Maria G M Hunink were responsible for design, data collection, and analysis of quality-of-life and cost-effectiveness studies. Andries D van Engelen participated in trial coordination, data management, and analysis. Bert C Eikelboom advised on design of the trial and data analysis. All authors contributed to the writing of the paper.

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