Dutch iliac stent trial

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Published in:
RADIOLOGY

Dutch Iliac Stent Trial: Long-term Results in Patients Randomized for Primary or Selective Stent Placement[1]

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Purpose: To determine long-term results of the prospective Dutch Iliac Stent Trial.

Materials and Methods: The study protocol was approved by local institutional review boards. All patients gave written informed consent. Two hundred seventy-nine patients (201 men, 78 women; mean age, 58 years) with iliac artery disease were randomly assigned to undergo primary stent placement (143 patients) or percutaneous transluminal angioplasty (PTA) with selective stent placement in cases in which the residual mean pressure gradient was greater than 10 mm Hg across the treated site (136 patients). Before and at 3, 12, and 24 months and 5–8 years after treatment, all patients underwent assessment, which included duplex ultrasonography (US), ankle-brachial index (ABI) measurement, Fontaine classification of symptoms, and completion of the Rand 36-Item Health survey for quality-of-life assessment. Treatment was considered successful for symptoms if symptoms increased at least one Fontaine grade, for ABI if ABI increased more than 0.10, for patency if peak systolic velocity ratio at duplex US was less than 2.5, and for quality of life if the RAND 36-Item Health Survey score increased more than 15 points. Effects of both treatments on symptoms, quality of life, patency, and ABI were compared by using survival analyses.

Results: Patients who underwent PTA and selective stent placement had better improvement of symptoms (hazard ratio [HR], 0.8; 95% confidence limits [CLs]: 0.6, 1.0) than did patients treated with primary stent placement, whereas ABI (HR, 0.9; 95% CLs: 0.7, 1.3), iliac patency (HR, 1.3; 95% CLs: 0.8, 2.1), and score for quality of life for nine survey dimensions did not support a difference between treatment groups.

Conclusion: Patients treated with PTA and selective stent placement in the iliac artery had a better outcome for symptomatic success compared with patients treated with primary stent placement, whereas data about iliac patency, ABI, and quality of life did not support a difference between groups.

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In 1964, Dotter and Judkins published an article in *Circulation* (1964; 30:654–670) that was later reprinted in *Radiology* (1) in which they proposed the use of percutaneous transluminal angioplasty (PTA) to improve signs and symptoms of peripheral arterial disease (PAD) in patients. In the past few decades, endovascular treatment of iliac artery lesions has become safe and effective. When stent placement was introduced in the 1990s, selective stent placement soon became an accepted treatment for unsatisfactory PTA results or occlusion. This change in medical practice was based on results in short-term nonrandomized studies. Nowadays, there is a tendency to place stents primarily. There is, however, limited evidence to prove which of the different endovascular treatment strategies is best for iliac artery lesions. Most studies on this subject were cohort studies, and they provided only short- or midterm results. The long-term effects of stent placement are unknown. The best way to study these effects is in a randomized trial. To the best of our knowledge, the only study in which randomization was used for endovascular treatment in the iliac arteries is the Dutch Iliac Stent Trial (DIST). In the DIST study, patients with iliac artery lesions were randomized to undergo primary stent placement or PTA with selective stent placement. Short-term (3-month) and midterm (12- and 24-month) results have been published (2,3). Thus, the purpose of our current study was to determine the long-term results of the prospective DIST.

Materials and Methods

General Information

Methods have been described extensively in previous articles (2,3). Accordingly, we present a short description of the DIST study with a detailed description of methods in regard to the long-term follow-up. The study protocol was approved by the local institutional review boards. All patients gave written informed consent. The long-term follow-up assessment was financially supported by Cordis, Roden, the Netherlands. Authors had full control over the data and analyses, without any interference of Cordis.

Study Population

Two hundred seventy-nine patients (201 men, 78 women; mean age, 58 years) with intermittent claudication or critical ischemia caused by stenosis or short occlusion (< 5 cm) in the iliac arteries were examined in the departments of vascular surgery in six study centers (see Acknowledgments) from November 1993 to November 1996 and were included in the study. Radiologists involved included three authors of this article (J.H.S., T.T.C.O., W.P.T.M.M.), and all had at least 5 years of experience with interventional procedures at the start of the trial. Inclusion criteria for patients were *(a)* clinical signs and symptoms of PAD—such as pain localized in the buttock, upper area of the leg, or the calf—and/or reduced pulsation of the femoral artery and/or reduced ankle-brachial index (ABI); *(b)* significant stenosis in the common or external iliac artery—as evident by an arterial diameter reduction of more than 50% at angiography—and/or a peak systolic velocity ratio of more than 2.5 and/or a mean pressure gradient of more than 10 mm Hg over the stenosis (with intraarterial vasodilation); and *(c)* stenosis of 10 cm or less in length or occlusion of 5 cm or less in length that allowed passage with a guidewire.

Other than the 279 patients, 86 patients were excluded for the following reasons: unwillingness to participate ($n = 27$), protocol restrictions ($n = 59$) (21 patients had stenoses extending into the distal aorta; in 20, results of angiography could not confirm the extent of disease as assessed with duplex ultrasonography [US]; eight had stenosis of more than 10 cm in length or occlusion of more than 5 cm; in seven patients, the lesion could not be passed with a guidewire; and three patients had extensive diffuse atherosclerotic changes of the vessels for which PTA or stent placement that, according to the protocol, would have been insufficient). In patients with multiple unilateral or bilateral iliac stenoses, all lesions were assigned to receive the same treatment. Multiple stenoses localized in one arterial segment (ie, common iliac artery or external iliac artery) were classified as a single lesion. For the survival analyses, we used only one lesion per person: In cases in which more than one lesion was present per person, the most severe lesion was selected on the basis of symptoms and angiographically determined percentage of stenosis or, when this was not sufficient for discrimination, on the basis of the peak systolic velocity ratio determined at duplex US.

Patients were randomly assigned to undergo either primary stent placement (group 1, 143 patients with 187 lesions in 181 legs) or primary PTA with selective stent placement, such as in cases in which the residual mean pressure gradient was greater than 10 mm Hg (group 2, 136 patients with 169 lesions in 164 legs). In group 2, 59 (43%) of 136 patients (65 [38%] of 169 lesions) needed stent placement. Comparison of the risk profile in both groups did not reveal differences (Table 1) (2).

In patients who underwent primary stent placement, a long 7-F introducer sheath was placed across the targeted

Published online before print
10.1148/radiol.2382041053

Radiology 2006; 238:734–744

Abbreviations:
ABI = ankle-brachial index
CL = confidence limit
DIST = Dutch Iliac Stent Trial
HR = hazard ratio
PAD = peripheral arterial disease
PTA = percutaneous transluminal angioplasty

Author contributions:
Guarantors of integrity of entire study, Y.v.d.G., W.P.T.M.M.; study concepts and study design, Y.v.d.G., W.P.T.M.M.; literature research, W.M.K., Y.v.d.G., W.P.T.M.M., E.B.; clinical studies, all authors; data acquisition, all authors; data analysis/interpretation, Y.v.d.G., W.P.T.M.M., W.M.K., E.B.; statistical analysis, W.M.K., W.P.T.M.M., Y.v.d.G., E.B.; manuscript preparation, definition of intellectual content, editing, revision/review, and final version approval, all authors

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See Materials and Methods for pertinent disclosures.

segment. The stent (Palmaz; Johnson and Johnson Interventional Systems, Warren, NY) 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 was withdrawn, and the stent was deployed by means of inflation of the balloon. The stent diameter was determined according to the width of the uninvolved portion of the vessel. In the patients randomized to undergo PTA and selective stent placement, PTA was performed according to standard techniques (4). When elastic recoil or inappropriate results at angiography were found after angioplasty, larger balloon inflation and larger balloons were applied. When a hemodynamically significant gradient of greater than 10 mm Hg was found after the final PTA, stent placement was performed at the same session, irrespective of evidence of residual stenosis with angiography. When evidence of residual stenosis but no hemodynamically significant gradient was found, we did not perform stent placement. All patients received anticoagulant medication (aspirin or oral anticoagulants) in accordance with local guidelines or individual preference of the referring physician, independent of the type of intervention. On the angiogram obtained during the intervention, the radiologist noted the angiographic characteristics of the iliac artery lesions (Table 1). Short- and midterm technical and clinical results and complications determined as long as 24 months after the procedure have already been published (2).

Table 1

Patient and Angiographic Characteristics at Baseline and after Treatment

Characteristic	Primary Stent Placement	PTA and Selective Stent Placement
No. of patients	143	136
Sex		
M	102	99
F	41	37
Age (y)*	58 ± 11	58 ± 10
Fontaine classification†		
I	4 (3)	5 (4)
II	132 (92)	120 (88)
III and/or IV	7 (5)	11 (8)
ABI at rest*	0.75 ± 0.18	0.77 ± 0.18
Location†		
Common iliac artery	106 (74)	93 (68)
External iliac artery	37 (26)	43 (32)
Percentage of stenosis at angiography†		
<50% stenosis	9 (6)	11 (8)
>50% stenosis	119 (83)	113 (83)
100% or total occlusion	15 (10)	12 (9)
Length of stenosis†		
<2 cm	83 (58)	74 (54)
2–10 cm	60 (42)	62 (46)
Runoff patency†		
Occlusion of superficial femoral artery	23 (16)	24 (18)
Occlusion of deep femoral artery	8 (6)	14 (10)
Stent placement†	139 (97)‡	55 (40)§
Direct results of treatment		
Residual stenosis ≥50% on angiogram after treatment†	1 (1)	4 (3)
ABI at rest*	0.94 ± 0.20	0.96 ± 0.24
Peak systolic velocity ratio*	1.2 ± 0.9	1.3 ± 0.6

* Data are the mean ± standard deviation.

† Data are numbers of patients. Numbers in parentheses are percentages.

‡ Protocol violation and denial of primary stent placement occurred in four patients.

§ Denial of selective stent placement occurred in six patients; inappropriate stent placement, in five patients.

Follow-up Protocol

Follow-up assessments.—Data in all patients were collected before and directly after intervention and at 3, 12, and 24 months thereafter, or as close to these dates as logistically possible. A final collection of data was conducted in 2002 (ie, between 6 and 8 years after trial intervention) by a few authors (W.M.K., J.S., and W.P.T.M.M.). All assessments were equal for both treatment groups and included assessment of symptoms, measurement of ABI at rest, and color duplex US of the treated iliac artery segment (left or right; common or external iliac artery). Symptoms were recorded according to the Fontaine classification (Table 2). We did not use the Rutherford classification (classification of the Society of Vascular Surgery and the International Society of Cardiovascular Surgery [5]), which combines symptoms and ABI, because in the DIST study, we experienced that use of the Rutherford classification leaves about one-third of the patients unclassifiable at short- and midterm follow-up. With the Rutherford classification, the classification of patients with PAD is performed in a theoretical way, whereas with the Fontaine classification, classification can be performed clinically for all patients.

To prevent patients from dropping out at the final follow-up, patients were offered a home visit in case they were

Table 2

Fontaine Classification of Symptoms

Fontaine Stage	Definition or Clinical Manifestation
I	No symptoms
II	Intermittent claudication
III	Pain at rest
IV	Critical ischemia, ulceration, or gangrene

unable to come to the hospital, and this visit included color duplex US performed with a portable unit.

Reinterventions.—The trial did not stipulate the criteria for or the manner in which to reintervene. Treatment of recurrent stenosis or of symptoms of PAD detected at follow-up examinations was the choice of the clinician and the patient. Five years after treatment, we recorded endovascular and surgical reinterventions for the iliac artery segment (either common iliac artery or external iliac artery) that was treated in the DIST study after we consulted the general practitioner and the referring clinician (6).

Quality-of-Life Assessments

Quality of life was measured with the RAND 36-Item Health Survey 1.0 (7), which refers to the patient's health over the previous 4 weeks. Quality of life was assessed by means of questionnaires administered over the telephone before treatment and at 1, 3, 12, and 24 months after treatment (University of Groningen). The 5-year measurement was assessed by means of the same questionnaires sent to the patients by regular mail (W.M.K., W.P.T.M.M.).

The RAND 36-Item Health Survey is equivalent to the Medical Outcomes Study Short Form 36 and includes nine health dimensions. For each dimension, responses to items are summed and scores are converted on a 0–100 scale, in which 100 indicates optimal functioning or well-being.

Table 3

Available Data in Living Patients at Inclusion and during Follow-up

Data	No. of Patients with Primary Stent Placement	No. of Patients with PTA and Selective Stent Placement
At inclusion		
Symptom assessment results	143/143 (100)	136/136 (100)
ABI measurements	135/143 (94)	124/136 (91)
Duplex US results for iliac arteries	81/143 (57)	72/136 (53)
Quality-of-life assessment results	128/143 (90)	121/136 (89)
At follow-up		
1 Month after treatment		
Quality-of-life assessment results	126/143 (88)	119/136 (88)
3 Months after treatment		
Symptom assessment results	138/143 (97)	125/136 (92)
ABI measurements	137/143 (96)	126/136 (93)
Duplex US results for iliac arteries	126/143 (88)	120/136 (88)
Quality-of-life assessment results	124/143 (87)	116/136 (85)
12 Months after treatment		
Symptom assessment results	112/142 (79)	107/134 (80)
ABI measurements	118/142 (83)	112/134 (84)
Duplex US results for iliac arteries	109/142 (77)	107/134 (80)
Quality-of-life assessment results	118/142 (83)	104/134 (78)
24 Months after treatment		
Symptom assessment results	92/141 (65)	91/131 (69)
ABI measurements	107/141 (76)	99/131 (76)
Duplex US results for iliac arteries	96/141 (68)	85/131 (65)
Quality-of-life assessment results	103/141 (73)	98/131 (75)
5 Years after treatment		
Quality-of-life assessment results	91/129 (71)	89/116 (77)
6–8 Years after treatment		
Symptom assessment results	95/118 (81)	80/110 (73)
ABI measurements	101/118 (86)	85/110 (77)
Duplex US results for iliac arteries	109/118 (92)	90/110 (82)

Note.—Numerators indicate the number of patients who attended a follow-up session. The denominators decreased from inclusion to 6–8 years after treatment because some patients died. Numbers in parentheses are percentages.

Definition of Long-term Outcome

Symptomatic success was defined as an increase of at least one Fontaine grade during the whole follow-up period compared with that at the pretreatment assessment. Hemodynamic success was defined as an increase of the ABI of 0.10 or more during the whole follow-up period compared with the value at the pretreatment assessment. Patency of the (common or external) iliac artery segment initially treated in the DIST study was defined as a peak systolic velocity ratio of less than 2.5 at duplex US (8) during the whole follow-up period. Reintervention was defined as any surgical or endovascular intervention for PAD that involved the iliac artery segment that was treated in the DIST study. We chose the whole common iliac artery or the whole external iliac artery that was treated as the site of iliac patency or reintervention, and not only the part in which a stent was placed or the part that was treated with PTA, because the site treated with PTA alone is hard to recognize. Also, in this way, the segments treated with either of the two strategies were identical. Successful outcome for quality of life was defined as an increase of 15 or more in the score on the RAND 36-Item Health Survey during the whole follow-up period compared with the score at the pretreatment assessment.

Statistical Analysis

We analyzed data according to the intention-to-treat principle, which implies that we did not exclude any of the 279 patients after randomization. Furthermore, the reported outcomes are secondary results, because we did not exclude patients after failure or reintervention. For the analyses, we used one lesion (the least favorable one) per patient. Symptomatic success, hemodynamic success, patency, and reintervention were quantified with calculation of the hazard ratios (HRs) and corresponding 95% confidence limits (CLs).

Kaplan-Meier curves are presented for graphic comparison. The time to event was set as the date of the clinical assessment for symptomatic and hemodynamic success and patency, as the date of interview for quality of life, and as the actual date of intervention for the analyses of reintervention. Quality-of-life assessment scores were calculated, and differences between the two treatment arms were tested by calculating HRs and 95% CLs. Also, data of age-matched controls were obtained from published literature on 1063 randomly chosen Dutch persons (9). We compared quality-of-life assessment scores 5 years after treatment for the two treatment groups with those of the age-matched controls by using the Student *t* test. Statistical tests were performed with statistical software (SPSS 10.0; SPSS, Chicago, Ill) by several authors (W.M.K., Y.v.d.G., E.B., F.L.M., W.P.T.M.M.) and a statistician. Evaluation and interpretation of results was performed by all authors.

All of the previously mentioned survival analyses were also performed in the patients treated with PTA alone versus the patients treated with primary or selective stent placement.

Results

Follow-up Data

All but one of the 279 patients underwent at least one follow-up examination. One patient was lost to follow-up. Twenty-six patients (eight treated with primary stent placement; 18 treated with PTA and selective stent placement) did not want to undergo the last follow-up examination: Eleven patients refused because of health reasons other than PAD (Alzheimer disease, stroke, cancer), and 15 patients refused because of personal reasons. Six patients (other than the 26 who refused to undergo the last follow-up examination) had just undergone a routine clinical examination that included duplex US of the iliac arteries, and we used the results of that examination for this study. A further 13 patients (11 treated with primary stent placement and two treated with PTA and selective stent placement) underwent their last follow-up examination at their home. In 12 patients, this was so because of health reasons; and in one patient, because of his busy schedule. Available data are given in Table 3. The mean duration until the last follow-up examination or death was 6.3 years ± 1.8 (standard deviation), with a range of 0.7–8.6 years, for the patients with primary stent placement and 5.7 years ± 2.2, with a range of 0.3–8.7 years, for the patients with PTA and selective stent placement ($P = .01$).

During this follow-up period, in the group with primary stent placement, 25 (17%) of 143 patients died, whereas in the group with PTA and selective stent placement, 26 (19%) of 136 patients died (HR = 1.3; 95% CLs: 0.7, 2.2) (6).

Table 4

Results of Follow-up Assessments per Lesion in Both Treatment Groups

Assessment	Primary Stent Placement	PTA and Selective Stent Placement
At 3 months		
Fontaine classification		
I	88/138 (64)	85/125 (68)
II	49/138 (36)	40/125 (32)
III and/or IV	1/138 (1)	0/125 (0)
ABI measurement*	0.96 ± 0.18	0.96 ± 0.21
Occlusion at duplex US	1/126 (1)	1/120 (1)
Peak systolic velocity ratio*	1.3 ± 0.9	1.5 ± 0.6
Reinterventions†	2/143 (1)	1/136 (1)
At 12 months		
Fontaine classification		
I	72/112 (64)	72/107 (67)
II	40/112 (36)	35/107 (33)
III and/or IV	0/112 (0)	0/107 (0)
ABI measurement*	0.94 ± 0.19	0.98 ± 0.18
Occlusion at duplex US	0/109 (0)	0/107 (0)
Peak systolic velocity ratio*	1.5 ± 1.0	1.6 ± 0.8
Reinterventions†	5/142 (4)	4/134 (3)
At 24 months		
Fontaine classification		
I	59/92 (64)	56/91 (62)
II	33/92 (36)	34/91 (37)
III and/or IV	0/92 (0)	1/91 (1)
ABI measurement*	0.91 ± 0.21	1.0 ± 0.19
Occlusion at duplex US	0/96 (0)	0/85 (0)
Peak systolic velocity ratio*	1.7 ± 0.9	1.8 ± 1.0
Reinterventions†	8/141 (6)	2/131 (2)
At 6–8 years		
Fontaine classification		
I	31/90 (34)	38/78 (49)
II	45/90 (50)	27/78 (35)
III and/or IV	14/90 (16)	13/78 (17)
ABI measurement*	0.90 ± 0.20	0.96 ± 0.22
Occlusion at duplex US	5/109 (5)	10/90 (11)
Peak systolic velocity ratio*	1.9 ± 1.6	1.7 ± 1.1
Reinterventions†	12/118 (10)	21/110 (19)

Note.—Unless otherwise indicated, data are numbers of lesions. The denominators correspond to the numerators in Table 3 (ie, available data). Numbers in parentheses are percentages.

* Data are the mean ± standard deviation.

† Data are numbers of patients. Numbers in parentheses are percentages.

All results of follow-up assessments per lesion are presented in Table 4.

Symptomatic Success

At the follow-up assessment at 3 months, symptomatic success was achieved in about 70% of the patients in both treatment groups (Fig 1). At the final follow-up assessment, 59 (66%) of 90 of the patients treated with primary stent placement and 40 (51%) of 78 of the patients treated with PTA and selective stent placement still had symptoms of PAD. With the Cox survival analysis, an HR of 0.8 (95% CLs: 0.6, 1.0) was calculated, and this result was in favor of the lesions treated with PTA and selective stent placement (Fig 1).

Hemodynamic Success

The mean ± standard deviation for ABI increased from 0.75 ± 0.18 before treatment to 0.94 ± 0.20 after treatment and then decreased to 0.90 ± 0.20 at the final follow-up for the patients with primary stent placement. For the patients treated with PTA and selective stent placement, the ABI increased from 0.77 ± 0.18 before treatment to 0.96 ± 0.24 after treatment and remained as 0.96 ± 0.22 at the final follow-up. Hemodynamic success was achieved in about 70% of the patients in both groups at the 3-month follow-up assessment (Fig 2). With the Cox survival analysis, an HR of 0.9 (95% CLs: 0.7, 1.3) was calculated.

Patency

Iliac patency decreased from 97% (122 of 126 patients) at 3 months after treatment to 83% (90 of 109 patients) at the final follow-up in the patients with primary stent placement and from 94% (113 of 120 patients) to 74% (67 of 90 patients) in the patients treated with PTA and selective stent placement. The HR was 1.3 (95% CLs: 0.8, 2.1) (Fig 3).

Reintervention

Twenty-five (17%) of 143 patients treated with primary stent placement needed reintervention in the iliac artery segment that was initially treated in the DIST study because of symptoms or signs (in noninvasive measurements) of restenosis. In the group that was treated with PTA and selective stent placement, 28 (21%) of 136 patients needed reintervention (HR = 1.1; 95% CLs: 0.6, 1.9). There was no difference in the number of endovascular and surgical procedures between the two treatment groups (6).

Quality of Life

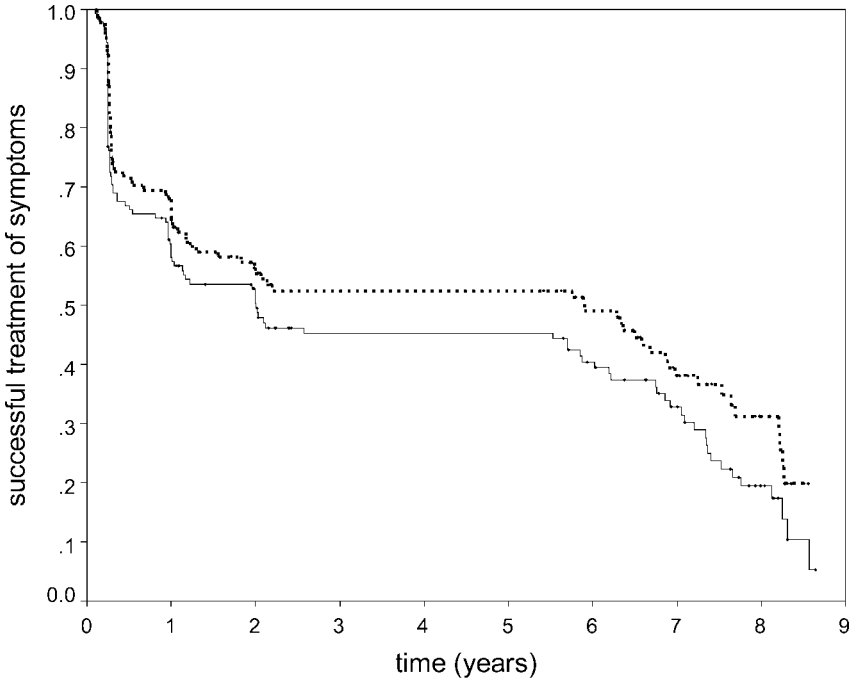
All RAND 36-Item Health Survey scores increased substantially in both groups after treatment (3) (Table 5). At 5 years after treatment, all scores, except the score for general health perception, were still markedly higher than they were before treatment in both groups. Survival analyses showed no differences in RAND 36-Item Health Survey scores between the two treatment groups over the whole follow-up period.

When we compared the quality-of-life scores of the two treatment groups 5 years after treatment with data in age-matched controls from the literature, patients treated with PTA and selective stent placement had scores that were equally as high as the age-matched controls for all dimensions. On the other hand, patients treated with primary stent placement had scores that were substantially lower for physical functioning, physical role functioning, vitality, bodily pain, and general health perception, whereas scores for emotional role functioning, social functioning, mental health, and health change were equivalent to those in age-matched controls (Fig 4).

PTA Alone versus Stent Placement

When we compared the patients treated with selective or primary stent placement versus the patients treated with PTA alone, we could not show any difference with regard to symptomatic and hemodynamic success, iliac pa-

Figure 1



Primary stent	143	82	63	48	-	-	40	27	10
Failure	56	12	7	-	-	5	7	10	4
PTA with selective stent	134	86	60	51	-	-	44	28	13
Failure	42	14	4	-	-	3	9	4	4

Figure 1: Kaplan-Meier survival curves for symptomatic success. Solid line signifies primary stent placement (101 of 143 patients); and dotted line, PTA with selective stent placement (80 of 134 patients).

tency, and quality-of-life assessment scores. Also, iliac reinterventions and ipsilateral interventions were not different for patients with and without stent placement.

Discussion

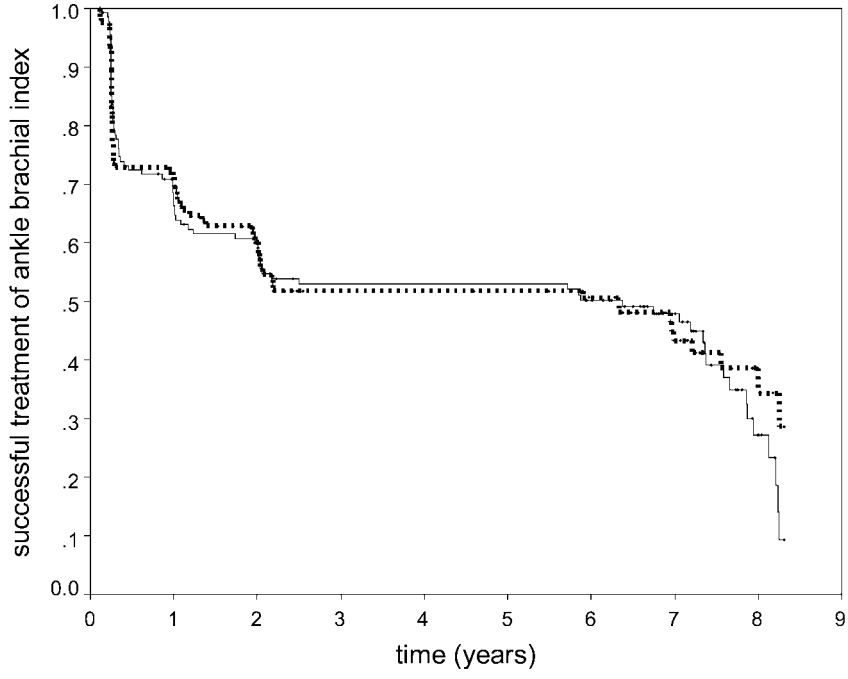
Selective stent placement for iliac artery lesions results in a better preservation of symptomatic success in the long term, without a difference in the results for hemodynamic success, iliac artery patency, and quality of life. Therefore, selective stent placement should be the treatment of preference for iliac artery lesions.

Although the data did not support a difference between treatment groups for iliac artery patency and ABI, PTA and selective stent placement should be the treatment of choice over primary stent placement. Besides better results for symptomatic success, selective stent placement has several other advantages over primary stent placement. Long-term quality of life of patients treated with selective stent placement was not different from that in age-matched controls, while patients treated with primary stent placement had lower scores. Another advantage is that use of PTA and selective stent placement results in a considerable cost savings, as only 40% of the patients actually needed stent placement and thus required only a small number of the stents needed in the strategy of primary stent placement. Further, it is usually preferred in medicine both by patients and physicians not to use foreign bodies unnecessarily. In this study, we showed that primary stent placement is not necessary.

Despite the technically successful treatment in both groups, as is apparent from the long-term patency results, the patients treated with PTA and selective stent placement tended to have a clinically better outcome than did the patients treated with primary stent placement. Because patients were randomized for treatment, we assumed that predictors of outcome were equally distributed over the two treatment groups, and the differences between the groups in the long term could only be explained by the difference in treatment. The tendency toward fewer symptoms in the group with selective stent placement cannot be explained by better patency or hemodynamic success. We do not know the reason for this more rapid deterioration of symptoms in patients treated with primary stent placement. The deterioration may be caused by the breakdown of stent material. Also, allergic reactions to metal released from stents have been proposed as the triggering mechanisms for in-stent restenosis (10). This difference, however, was not found when we compared patients treated with PTA alone versus patients treated with primary or selective stent placement, and this finding indicates that some patients benefit from selective stent placement (in this study, that meant that the stent was placed when a residual pressure gradient of >10 mm Hg was present). This late chronic effect of primary stent placement, to our knowledge, has not been demonstrated before in studies in patients with iliac artery disease, as there have been no other randomized trials with long-term follow-up of peripheral arterial lesions in which primary stent placement was compared with PTA and selective stent placement. Only in randomized trials with long-term follow-up can the actual differences in outcome of patients treated with primary stent placement versus those treated with PTA and selective stent placement be detected. Cohort studies provide biased evidence if treatments are compared.

To the best of our knowledge, this study is the first in which two endovascular treatment methods for iliac artery disease were compared in a randomized way and with long-term follow-up. We presented a complete spectrum with both subjective and objective results.

Figure 2



Primary stent	136	86	72	57	-	-	52	34	9
Failure	44	9	8	-	-	3	2	10	5
PTA with selective stent	126	88	65	50	-	49	42	26	9
Failure	35	14	9	-	0	1	5	2	2

Figure 2: Kaplan-Meier survival curves for hemodynamic success measured with ABI. Solid line signifies primary stent placement (81 of 136 events); and dotted line, PTA with selective stent placement (68 of 126 events).

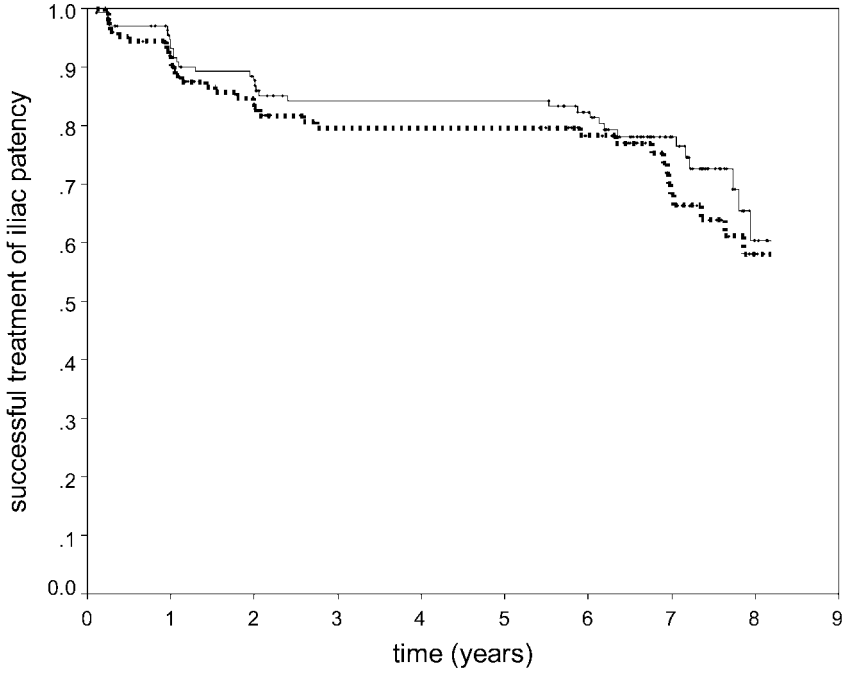
Data about cardiovascular morbidity and mortality in these patients have been published before (6). Some studies about endovascular treatment of the iliac arteries with a follow-up of 4 years or longer have been published (11–16). Researchers in most of these studies reported results for iliac patency, and these results seem to be in accordance with our outcomes: 72%–92% secondary iliac artery patency after a follow-up of 4.0–7.5 years. The definition of successful patency, however, was dissimilar in the different studies; in none of the studies were solely duplex US results used for defining patency, and in most of them, clinical success was incorporated within the definition of successful patency.

In none of these studies did researchers report the results for assessment of symptomatic success separately from those for assessment of technical success, as we did. Also in none of the studies did the researchers report the results for quality-of-life evaluation. In a meta-analysis in which PTA was compared with primary or selective stent placement for iliac artery disease, it was found that stent placement had lower long-term failure rates (17). In none of the studies that were included in this meta-analysis were the analyses randomized.

In studies about the quality of life in patients with PAD, the endovascular treatment was not randomized, and in none of these studies was the follow-up period longer than 2 years (18–20). Chetter et al (21) found that PTA of iliac artery lesions resulted in immediate improvement of quality of life and that the quality of life approached the level of that of age-matched controls. It was found that patency and ABI had no effect on quality of life but that the presence of symptoms of PAD had negative effects on the quality of life (19,22,23). Physical functioning and bodily pain contributed most to the reduction of quality of life in patients with claudication (24,25). These findings seem to be in accordance with our findings; in our study, the patients treated with PTA and selective stent placement had better preservation of symptomatic success and also had higher scores for quality-of-life assessment compared with those in age-matched controls.

We noticed a preference for primary stent placement—not only for the iliac artery and more peripheral arteries but also for the coronary, carotid, and renal arteries—in clinical practice all over the world. There is no convincing evidence, however, that primary stent placement is actually better than PTA and selective stent placement in any of these arteries. As for the coronary arteries, there have been several randomized trials in which primary stent placement was compared with PTA with selective stent placement (26–30). The longest follow-up period in these studies was 5 years (26). The general conclusion of these studies is that PTA with selective stent placement is as good as primary stent placement in regard to symptoms of angina, myocardial infarction, and survival. In the long term, however, primary stent placement results in fewer reinterventions in the target lesion. The majority of cardiologists have therefore chosen primary stent placement, and they have also done so because stent placement is an easy and fast procedure, unlike the complex procedure that is necessary to decide whether selective stent placement after PTA is needed (31,32). In the Dutch Iliac Stent Trial, the criterion for selective stent placement was based on the presence of a pressure gradient over the stenosis. Determination of this gradient is complex and time consuming. Since we have shown that selective stent placement leads to better symptomatic success in the long term, it is the treatment of choice for the iliac arteries. Difficulties in measuring the pressure gradient should be dealt with. Also, in the carotid and renal arteries,

Figure 3



Primary stent	139	121	110	93	-	-	82	47	11
Failure	7	9	4	-	-	2	4	6	1
PTA with selective stent	130	108	86	73	-	-	61	38	14
Failure	10	9	4	-	-	1	6	4	4

Figure 3: Kaplan-Meier survival curves for iliac patency measured with duplex US. Solid line signifies primary stent placement (33 of 139 patients); and dotted line, PTA with selective stent placement (38 of 130 patients).

Figure 4

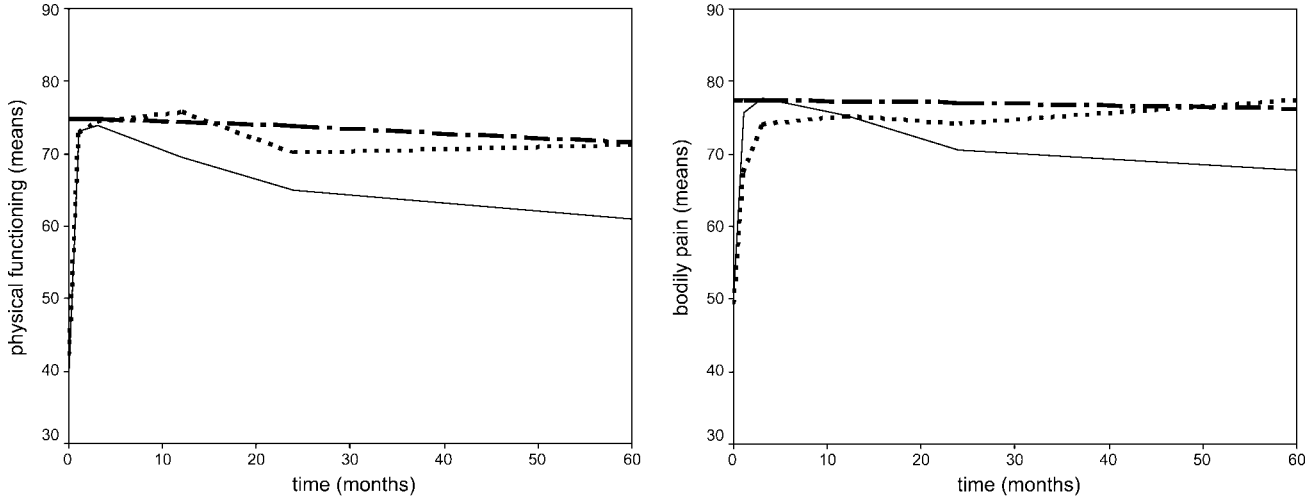


Figure 4: Graphs show RAND 36-Item Health Survey scores for **(a)** physical functioning and **(b)** bodily pain in two treatment groups of the DIST study and in age-matched controls. Solid line signifies group with primary stent placement; dotted line, group with PTA and selective stent placement; and dashed and dotted line, age-matched controls. At long term, scores of patients treated with selective stent placement were not different from data in age-matched controls, whereas patients with primary stent placement had lower scores.

Table 5

RAND 36-Item Health Survey Scores at Baseline and during Follow-up

	Primary Stent Placement			PTA with Selective Stent Placement		
Dimension	At Baseline	At 1-month Follow-up	At 5-year Follow-up	At Baseline	At 1-month Follow-up	At 5-year Follow-up
Physical functioning	39.6 ± 18.9	73.0 ± 25.2	61.0 ± 27.3	42.1 ± 20.4	72.9 ± 25.4	71.2 ± 26.1
Physical role functioning	27.1 ± 36.3	58.5 ± 44.3	61.2 ± 41.2	32.0 ± 40.5	55.9 ± 45.2	70.0 ± 39.2
Emotional role functioning	59.9 ± 44.5	72.2 ± 40.6	80.7 ± 35.3	54.8 ± 44.7	66.4 ± 41.3	86.4 ± 28.2
Social functioning	63.8 ± 27.0	77.8 ± 25.9	80.4 ± 25.1	68.5 ± 28.2	76.4 ± 26.0	80.2 ± 23.6
Bodily pain	50.3 ± 22.2	75.8 ± 24.6	67.8 ± 25.8	49.3 ± 24.6	67.5 ± 27.8	77.5 ± 24.2
General health perception	56.7 ± 21.0	63.2 ± 22.4	53.7 ± 21.1	53.5 ± 22.8	57.2 ± 21.5	59.7 ± 24.4
Mental health	70.4 ± 21.4	75.3 ± 20.2	75.2 ± 17.9	69.1 ± 21.9	74.2 ± 19.2	76.7 ± 17.3
Vitality	50.9 ± 23.3	62.2 ± 23.5	61.1 ± 20.6	52.6 ± 21.5	61.3 ± 21.9	64.3 ± 20.6
Health change	30.9 ± 22.5	71.2 ± 27.4	47.9 ± 22.1	31.2 ± 21.0	62.4 ± 30.0	47.5 ± 18.9

Note.—Values are the mean ± standard deviation.

primary stent placement is in vogue because of the ease and quickness of the procedure. Here, too, no sound evidence is available that this method is actually better, as there are no randomized trials in which PTA with selective stent placement was compared with primary stent placement.

About half of the patients in both treatment groups of the DIST study had recurrence or progression of symptoms of PAD in the long term (and this was more extensive in the patients with primary stent placement). In a limited number of patients, this recurrence or progression of symptoms could be caused by recurrence of the iliac artery stenosis; however, this cause cannot explain all cases of recurrence or progression of symptoms, as the iliac artery patency is high. Progression of atherosclerotic disease in the more peripheral arteries is a more valid explanation of the recurrence or progression of PAD symptoms. Patients ought to be informed about their high risk of lasting or recurrent symptoms after endovascular treatment. Secondary preventive measures, such as treatment of risk factors and exercise training, must be intensive, and, when possible and necessary, further invasive treatment must be considered.

This study had some limitations that need to be discussed. The finding that patients treated with primary stent placement on average had a slightly longer follow-up time than did patients treated with PTA and selective stent placement could possibly have influenced the outcome of the study. The longer follow-up might have led to biased results, even with follow-up time being taken into account with survival analyses. Patients in both treatment groups were subject to the same follow-up protocol; however, they were aware as to whether or not they had been treated with PTA alone or stent placement (2), and this awareness could have caused a difference in attendance of follow-up assessments.

Another limitation was that we used the RAND 36-Item Health Survey questionnaire, which is not disease specific. At the time the DIST study was started, this questionnaire was the most widely used and best available for quality-of-life assessment, and it was validated and translated into Dutch. Also, researchers in other studies about the quality of life in patients with PAD used nondisease-specific questionnaires (18–20,23), and they too measured an effect of treatment. A disease-specific questionnaire could enable a more detailed assessment of the effect of treatment on the quality of life in these patients.

A possible limitation was that the questionnaire was completed with a telephone interview until 24 months after treatment. At 5 years, a paper version was sent to the patients' homes. This difference may have caused patients in both groups to give different answers. Patients were informed about the treatment they had undergone. Patients' knowledge of whether or not they had a stent may have caused different scores on the RAND 36-Item Health Survey and could have resulted in some bias across treatment groups.

We conclude that, for patients with iliac artery disease, treatment with PTA and selective stent placement is at least as good as treatment with primary stent placement in the long term. Selective stent placement tended to lead to a better preservation of symptomatic success and quality of life. Therefore, selective stent placement should be the preferred method.

Acknowledgments: We thank Michael Edlinger, MSc, for assistance in the statistical analysis and Rudy Meijer, BA, for performing the home visits for follow-up assessments. Centers in the Netherlands that participated in the Dutch Iliac Stent Trial study group included the following: St Antonius Hospital, Nieuwegein: T. T. C. Overtoom, MD, and J. C. de Valois, MD, PhD (Radiology), F. L. Moll, MD, PhD, and H. D. W. M. van de Pavoordt, MD, PhD (Vascular Surgery); Slingeland Hospital, Doetinchem: J. H. Spithoven, MD (Radiology), and J. G. J. M. van Iersel, MD, and J. Seegers, MD (Vascular Surgery); University Medical Center Utrecht, Utrecht: B. C. Eikelboom, MD, PhD (Vascular Surgery), W. P. T. M. Mali, MD, PhD, J. P. van Schaik, MD, PhD, F. J. A. Beek, MD, PhD, E. Tetteroo, MD, PhD, C. Haaring, BA, and A. D. van Engelen, MD (Radiology), and Y. van der Graaf, MD, PhD (Julius Center for Health Sciences and Primary Care); University Hospital Rotterdam, Rotterdam: H. Pieterman, MD (Radiology), and H. van Urk, MD, PhD, and M. R. H. M. van Sambeek, MD, PhD (Vascular Surgery); Twenteborg Hospital, Almelo: J. J. Kouwenberg, MD, and F. H. B. Tuynman, MD (Radiology), and J. W. van den Heuvel, MD, and J. G. van Baal, MD, PhD (Vascular Surgery); Catharina Hospital, Eindhoven: G. H. M. Landman, MD, PhD, A. V. Tielbeek, MD, PhD, and D. VroegindeWeij, MD (Radiology), and J Buth, MD, PhD (Vascular Surgery); and University of Groningen (Quality of Life Studies), Groningen: M. G. M. Hunink, MD, PhD, J. L. Bosch, MD, PhD, J. J. Bos, MD, and E. E. E. van Wijck, MSc (Health Sciences, Medical Decision Making).

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