Conclusions—In the present study of patients with short superficial femoral artery lesions, the hypothesized absolute conceded that stents “may have a limited role in salvage of Wallstents in the management of femoropopliteal disease but aged the use of balloon-expandable stents and self-expanding Inter-Society Consensus Working Group generally discour-
achieved with stent implantation. In 2000, the TransAtlantic transluminal percutaneous angioplasty (PTA) or is best agreed on whether SFA treatment should be restricted to vascular specialists on the other hand. Even the latter do not advocated by vascular surgeons on the one hand and endo-
matter of continuing debate. Controversial viewpoints are 25-27, D-22527 Hamburg, Germany. E-mail krankenberg@herz-hh.de

Background—Endoluminal treatment of superficial femoral artery lesions is a matter of controversy. The present study was designed to investigate the impact of nitinol stenting of superficial femoral artery lesions with a maximum length of 10 cm on restenosis and clinical outcomes at 1 year.

Methods and Results—Two hundred forty-four patients (168 men; 66±9 years) with a single superficial femoral artery lesion and chronic limb ischemia were randomized to implantation of a single Bard Luminexx 3 stent (123 patients) or stand-alone percutaneous transluminal angioplasty (PTA) (121 patients). Mean lesion length was 45 mm. Technical success (residual stenosis <50% for PTA, <30% for stenting) was achieved in 96 patients assigned to PTA (79%) and 117 patients assigned to stenting (95%); 13 PTA group patients (11%) “crossed over” to stenting. At 1 year, the primary end point of ultrasound-assessed binary restenosis was reached in 39 of 101 PTA group patients (38.6%) and 32 of 101 stent group patients (31.7%; absolute treatment difference, −6.9%; 95% CI, −19.7% to 6.2%; P=0.377). Target lesion revascularization rates at 1 year were 18.3% and 14.9%, respectively (absolute treatment difference, −3.3%; 95% CI, −13.0% to 6.4%; P=0.595). No statistically significant difference between treatment groups was observed at 12 months in the improvement by at least 1 Rutherford category of peripheral arterial disease.

Conclusions—In the present study of patients with short superficial femoral artery lesions, the hypothesized absolute difference of 20% in binary restenosis at 1 year between the implantation of a single Luminexx nitinol stent and stand-alone PTA could not be demonstrated. A smaller difference requiring a larger trial might have been missed. (Circulation. 2007;116:285-292.)

Key Words: angioplasty ■ peripheral vascular disease ■ restenosis ■ stents

The optimal treatment of superficial femoral artery (SFA) disease in patients with intermittent claudication is a matter of continuing debate. Controversial viewpoints are advocated by vascular surgeons on the one hand and endo-
matter of continuing debate. Controversial viewpoints are advocated by vascular surgeons on the one hand and endo-
vascular specialists on the other hand. Even the latter do not agree on whether SFA treatment should be restricted to transluminal percutaneous angioplasty (PTA) or is best achieved with stent implantation. In 2000, the TransAtlantic Inter-Society Consensus Working Group generally discouraged the use of balloon-expandable stents and self-expanding Wallstents in the management of femoropopliteal disease but conceded that stents “may have a limited role in salvage of
multicenter trial to assess the 1-year safety and efficacy of nitinol stent implantation versus stand-alone PTA in patients with SFA disease and chronic limb ischemia.

Methods
Between January 2004 and March 2005, 244 patients (168 men [69%]; mean ±1 SD age, 66±10 years) were enrolled at 11 European centers in the Femoral Artery Stenting Trial (FAST). Patients were eligible for enrollment if they were at least 21 years of age and had a de novo SFA lesion located at least 1 cm from the SFA origin with a length between 1 and 10 cm. Target lesion diameter stenosis had to be at least 70% by visual estimate. The popliteal artery as well as 1 of the infrapopliteal (below-the-knee) vessels had to be continuously patent for sustained distal runoff. Clinically, the patients had to suffer from chronic limb ischemia of at least Rutherford category 2 (moderate claudication). Major exclusion criteria were a target lesion that required pretreatment with adjunctive devices such as lasers or debulking catheters; a target lesion that extended into the popliteal artery; previous stent implantation in the targeted SFA; multiple lesions exceeding a total length of 10 cm; acute or subacute (≤4 weeks) thrombotic occlusion; an untreated ipsilateral iliac artery stenosis; ongoing dialysis treatment; and treatment with oral anticoagulants other than antiplatelet agents.

All patients were informed about the nature of the present study and the interventional procedures involved and gave their written consent. The study was approved by the ethics committees at all participating centers.

Study Stent
The study stent was the Bard Luminexx 3 Vascular Stent (C.R. Bard, Inc, Murray Hill, NJ). This self-expanding open-cell stent made of nitinol (a nickel-titanium alloy) is available in nominal diameters of 4 to 14 mm (in 1- or 2-mm increments) and lengths of 20 to 120 mm (in 10- or 20-mm increments). In the context of the present study, only stents with a 5- to 7-mm diameter were implanted.

Interventions
All patients had to be premedicated with acetylsalicylic acid (aspirin, 100 mg/d) for at least 10 days. Patients not on this regimen were given an intravenous bolus of 500 mg of aspirin immediately before the intervention. Access to the culprit SFA lesion was achieved at the investigator’s discretion either by way of a retrograde approach from the contralateral femoral artery with the use of a dedicated 6F “crossover” sheath (Balkin, Cook Medical Inc, Bloomington, Ind) or via an antegrade (ipsilateral) approach with a standard 6F sheath (eg, Radifocus Introducer II, Terumo Medical Corp, Somerset, NJ). After sheath placement, an intravenous bolus of 3000 to 5000 U of heparin (depending on the patient’s weight) was administered. Digital subtraction angiography was subsequently performed to assess the patency status of the ipsilateral iliac arteries, the popliteal artery, and the infrapopliteal (below-the-knee) vessels. Protocol-mandated angioplasty of an arterial disease.

Secondary 12-month end points were target lesion revascularization, end points of 12-month binary restenosis rates of 45% in the PTA arm and 25% in the stent arm (an absolute difference of 20%). With

End Points
The primary study end point was binary restenosis, defined as a PVRproximal ≥2.4 on duplex ultrasound, at 12-month follow-up. Secondary 12-month end points were target lesion revascularization, absolute walking distance, ABI, Rutherford category, major adverse event including death, and stent integrity.

Statistical Analysis
The sample-size calculation for this trial was based on the assumptions of 12-month binary restenosis rates of 45% in the PTA arm and 25% in the stent arm (an absolute difference of 20%). With acceptance of a 15% lost to follow-up rate, 2-sided significance
level α of 0.05, and 80% statistical power, a total of 244 patients had to be enrolled. Data were analyzed according to the principle of intention to treat and, in a secondary “on-treatment” analysis, according to the actual treatment received.

Continuous variables are presented as mean ± 1 SD or, when appropriate, as median and interquartile range. Categorical variables are presented as counts and percentages. Differences between treatment groups in changes from baseline to 12 months of continuous variables were assessed by ANCOVA. Differences between categorical variables were assessed by Fisher exact text; 95% CIs were calculated for differences between pertinent categorical end-point variables. Logistic regression models were constructed to assess the impact of the treatment modality on 12-month restenosis in selected patient subgroups. A probability value < 0.05 indicated statistical significance. All statistical analyses were performed with the use of SAS version 9.1.3 (SAS Institute Inc, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results
Randomization assigned 121 patients to PTA and 123 patients to stenting. The resulting patient cohorts were well matched except for a lower prevalence of men, a higher prevalence of patients with renal insufficiency, and a lower baseline ABI in the stent group (Table 1). Approximately one third of patients were diabetics, and the vast majority of patients had chronic limb ischemia of Rutherford category 2 or 3 (Table 1). With respect to lesion morphology, a disparity of borderline statistical significance was evident between PTA and stent group patients in the prevalence of total occlusions (25% versus 37%, respectively; P = 0.053) (Table 2). In both treatment groups, the mean lesion length was 45 mm, yet reference vessel diameters were on average significantly smaller in women. In patients randomized to stenting, the lesions were well covered, with a mean stented segment length of 64 mm.

Intention-to-treat technical success as assessed by independent off-site ultrasound analysis was achieved in 117 stent group patients with a single stent (95%) and in 96 PTA group patients (79%). Implantation of a second study stent was required in 4 patients (3.3%). Thirteen PTA group patients (11%) “crossed over” to receive a stent, resulting in on-treatment cohorts of 108 patients actually treated with PTA and 136 patients actually treated with stents. Procedural complications are listed in Table 3.

Primary End Point Analysis
Duplex ultrasound recordings at 12 months were available from 101 PTA group patients (83%) and 101 stent group patients (82%). Intention-to-treat analysis yielded binary restenosis rates of 38.6% (39 patients) in the former and
31.7% (32 patients) in the latter (absolute treatment difference, −6.9%; 95% CI, −19.7% to 6.2%; P=0.377). Corresponding restenosis rates by on-treatment analysis were 37.8% (34/90 patients) and 33.0% (37/112 patients; absolute treatment difference, −4.7%; 95% CI, −17.8% to 8.3%; P=0.554), respectively.

Logistic regression analysis revealed no interaction of pertinent patient characteristics with the treatment modality (Figure 1) and also no interaction of gender with reference vessel diameter (P for interaction=0.222). The logistic regression showed that women had a nonsignificantly increased risk of restenosis with stenting (odds ratio, 1.52; P=0.465) and that stenting conferred marked, if statistically not significant, reductions in the risk of restenosis in various patient subsets, such as men, smokers, and diabetics, as well as patients with moderate to severe calcification, patients with total occlusions, and patients with 1 or more occluded distal runoff vessels (Figure 1). These findings were reflected in pronounced, yet statistically not significant, differences in binary restenosis rates favoring stenting in the subgroups mentioned (Figure 2). Women exhibited an increased restenosis rate with stenting (absolute difference 8.5%), but there was an imbalance in patient numbers (only 25 women underwent PTA, yet 40 underwent stenting), the 95% CI of the absolute treatment difference extended to −15% (Figure 2), and the exploratory probability value for the difference in restenosis rates was 0.579.

Stent integrity at 12 months was assessed in 83 of 101 patients; stent fractures were detected in 10 of 83 patients.
(12%). The binary restenosis rate in patients with stent fractures was statistically not different from that in patients without stent fractures (20.0% versus 28.8%, respectively; P = 0.719).

Clinical Outcomes

Clinical follow-up at 12 months was assessed in 115 PTA group patients (95%) and 114 stent group patients (93%). There was 1 death (of a carcinoma) at 11.6 months in the PTA group patients (95%) and 114 stent group patients (93%). The cause of death in the latter patients was a carcinoma, multiple organ failure, and severe 3-vessel coronary artery disease; it remains unknown in 1 patient. Lower-limb amputations because of preexisting gangrene had to be performed in 2 stent group patients (1.8%).

Target lesion revascularizations were performed only if 2 conditions were met: (1) the patient complained of recurrent claudication, and (2) on-site duplex ultrasonography revealed target lesion restenosis. The cumulative incidence of target lesion revascularizations at 12 months was 18.3% (21 patients) in the PTA group and 14.9% (17 patients) in the stent group (absolute treatment difference, −3.4%; 95% CI, −13.0% to 6.4%; P = 0.595). By on-treatment analysis, the corresponding incidences were 18.6% (19/102 patients) and 15.0% (19/127 patients); absolute treatment difference, −3.7%; 95% CI, −13.7% to 6.0%; P = 0.479).

The change in the patients’ clinical and hemodynamic status in terms of absolute walking distance, ABI at rest, and Rutherford category was assessed in a subset of 61 stent group patients (50%) and 75 PTA group patients (62%) who were able to undergo treadmill testing both at baseline and at 12-month follow-up. At 12 months, PTA and stent group patients were able to maximally walk a median of 185 m and 150 m, respectively, on the treadmill, which corresponded to a statistically significant difference in median walking distance improvement (52 versus 20 m, respectively; ANCOVA P = 0.028 [Figure 3A]). The resting ABI had improved at 12 months by approximately the same median amount in both treatment groups (PTA, 0.15; stent, 0.21; ANCOVA P = 0.560 [Figure 3B]). An improvement by at least 1 Rutherford category of peripheral arterial disease was observed at 12 months in a total of 122 patients (90%), with no statistically significant difference between treatment modalities either by intention-to-treat or by on-treatment analysis (Figure 4).

Discussion

In this randomized controlled trial of implantation of a single Luminexx 3 nitinol stent versus stand-alone PTA in 244 patients with a SFA lesion up to 10 cm in length (mean 4.5 cm), no statistically significant difference was found between the 2 treatment modalities in the primary end point of ultrasound-assessed binary restenosis at 12 months. Pronounced reductions in restenosis rates associated with stenting were observed in subgroups such as men, diabetics, and smokers, as well as patients with totally occluded lesions, patients with calcified lesions, and patients with impaired distal runoff. However, in none of these subgroups did the difference versus PTA reach statistical significance. Of note, no interaction of these patient characteristics with the treatment modality or of gender with reference vessel diameter was observed.
The lack of a statistically significant difference in binary restenosis was reflected in the patients’ clinical outcomes. At 12 months, no statistically significant differences between stent and PTA treatment were seen in target lesion revascularizations (15% and 18%, respectively), improvement in resting ABI (median 0.15 and 0.21, respectively), and improvement by at least 1 Rutherford category of peripheral arterial disease (89% and 92% of patients, respectively). The improvement in absolute walking distance (52 and 20 m, respectively) reached statistical significance, but significance testing for this variable was performed on an exploratory, not confirmatory, basis, implying that the difference could be due to random variation. The difference could also be due to bias because of the low proportion of patients who had this outcome assessed.

At the time of conception of our trial, no randomized data were available on nitinol stenting versus PTA in the treatment of SFA disease. We therefore based our assumptions of restenosis rates in either treatment arm on a then-recent review of PTA results, on the 9-month results of the small-size (49 patients total) SIROCCO II trial of sirolimus-eluting versus bare-metal nitinol stenting of SFA lesions, and on a retrospective single-center analysis of nitinol stenting in the SFA and hypothesized binary restenosis rates in the PTA and stent arm of 45% and 25%, respectively (an absolute difference of 20%). However, we observed rates of 39% and 32%, respectively (an absolute difference of 7%). The trial was not powered to establish this observed difference in restenosis rates with statistical significance. Our results therefore suggest that, in patients with short SFA lesions, implantation of a single Luminexx 3 nitinol stent provides no, or possibly only little, additional benefit compared with stand-alone PTA.

Our results appear to contradict those of a previous single-center randomized trial of nitinol stenting versus PTA in patients with SFA disease, in which the superiority of nitinol stenting was demonstrated in terms of angiographic restenosis at 6 months and ultrasound-determined restenosis at 12 months. Obvious differences between that study and ours are that Schillinger et al used different stents (Dynalink or Absolute, Guidant Corp, Santa Clara, Calif), allowed multiple-stent implantation, and treated lesions that were on average twice as long (101 mm in the stent group and 92 mm in the PTA group). At 12 months, they observed a binary restenosis rate in their 49 stent group patients of 36.7%, which is statistically not different from the 31.7% (5.1%; 95% CI, −21.3% to 10.4%) found in our study. However, in 52 PTA group patients, Schillinger et al found a restenosis rate of 63.5% as opposed to 38.6% in the present study, a difference (−24.9%; 95% CI, −8.1% to −39.6%) that is statistically highly significant (P=0.004). Thus, the striking difference between the 2 studies in patient outcomes at 12 months in absolute walking distance (AWD) and ABI in patients who were able to undergo treadmill testing at both baseline and 12-month follow-up. In both panels, bars denote medians, and error bars denote interquartile ranges.
months is most probably due to the fact that PTA is significantly less effective in longer lesions, whereas lesion length, the type of stent used, and the implantation of multiple versus single stents appear to have no major impact on 12-month restenosis in patients treated with stenting.

Another factor that may have contributed to the lack of a significant difference in effectiveness between the 2 treatment modalities noted in our study is the discrepant prevalence of total occlusions in the treatment arms. Total occlusions are known to be associated with markedly higher restenosis rates than stenoses, and their lower prevalence in the PTA group (25% versus 37% in stent-group patients) may have resulted in a lower PTA group restenosis rate than would have been found if total occlusions had been equally prevalent in both treatment arms. Finally, gender appeared to affect 12-month restenosis exclusively in the PTA arm, such that women assigned to PTA had a markedly lower restenosis rate (24.0%) than men (43.4%). However, this difference (with an exploratory \( P=0.101 \)) may have been due to chance because of the marked imbalance in patient numbers (only 25 women, yet 76 men, underwent PTA).

Nitinol stenting was associated with trends toward absolute reductions in restenosis on the order of 15% in diabetics and, surprisingly, smokers, as well as in patients with totally occluded or calcified lesions and patients with impaired distal runoff. The reasons for reduced restenosis rates by nitinol stenting in these generally “sicker” patients with comorbidities and/or advanced atherosclerosis are unknown and warrant further investigation in properly powered trials.

The incidence of stent fractures in our study was at 12% on the same order of magnitude as that reported in a recent study. An impact of stent fractures on the 12-month restenosis rate was not noted.

Limitations
The present study was powered to detect an absolute difference in restenosis rates between stenting and PTA of 20%. It was not powered to find an absolute difference of <20% that may be clinically relevant. To test whether the observed absolute difference in binary restenosis rates of 7% was statistically significant, a prohibitive number of patients (≈1500 total) would be required.

We restricted the ANCOVA of the improvement in the clinical and hemodynamic status of our patients to those who were able to undergo treadmill testing at both baseline and 12-month follow-up. Data were available from only 136 (56%) of the 244 patients because patients refused treadmill testing or had comorbidities or an impairment of the contralateral leg that prevented them from treadmill testing at either date.

Conclusions
In this randomized controlled trial that incorporated independent ultrasound analysis and data management, the hypothesized difference in 12-month restenosis of Luminexx 3 nitinol stenting versus stand-alone PTA of short SFA lesions could not be demonstrated. However, it cannot be excluded that a smaller than hypothesized benefit by stenting does exist, such as the overall 7% absolute reduction in binary restenosis at 12 months or the ≈15% absolute reduction observed in diabetics and patients with total occlusions. The study was underpowered to detect such differences with statistical significance. Properly powered trials to assess the value of nitinol stenting in selected patients with short SFA lesions, particularly diabetics or patients with advanced atherosclerotic disease, appear warranted.

Appendix
Committee to Assess Stent Fractures: J.O. Balzer (Johann Wolfgang Goethe University, Frankfurt, Germany), R. Schmiedel (Kaiserslautern, Germany), G. Wittenberg (University of Würzburg, Würzburg, Germany).

Source of Funding
This work was sponsored by C.R. Bard Inc, Murray Hill, NJ.

Disclosures
Drs Krankenberg and Zeller report having received reimbursement of travel expenses, and Dr Minar reports having received modest speaker honoraria, all from C.R. Bard Inc. The other authors report no conflicts.

References

![Figure 4. Change in Rutherford category in patients who were able to undergo treadmill testing at both baseline and 12-month follow-up. Positive and negative numbers on the abscissa indicate worsening and improvement, respectively. A, Intention-to-treat analysis. B, On-treatment analysis.](image-url)


CLINICAL PERSPECTIVE

The Femoral Artery Stenting Trial was a randomized controlled multicenter trial designed to demonstrate a 20% absolute reduction in ultrasound-assessed binary restenosis at 12 months (25% versus 45%) by implantation of a single Bard Luminexx 3 nitinol stent versus stand-alone percutaneous transluminal balloon angioplasty in patients with short superficial femoral artery lesions. Of a total of 244 consecutive patients enrolled, 123 and 121 were assigned stenting and percutaneous transluminal balloon angioplasty, respectively. Mean lesion length was 4.5 cm in both patient groups. By intention to treat, the primary study end point was reached in 39 of 101 percutaneous transluminal balloon angioplasty group patients (39%) and 32 of 101 stent group patients (32%), which corresponded to a statistically not significant absolute reduction in 12-month restenosis by stenting of only 7% (95% CI, 20% to −6%). The hypothesized absolute difference of 20% could not be shown. A larger trial of patients with short superficial femoral artery lesions was needed to demonstrate a possibly smaller benefit conferred by stenting. The clinical and hemodynamic status at 12 months assessed in a subset of patients was also not different between treatment groups. Thus, in the overall, unselected cohort of patients with short superficial femoral artery lesions treated in the present study, nitinol stenting as opposed to percutaneous transluminal balloon angioplasty did not improve the patients’ angiographic and clinical outcomes.
Nitinol Stent Implantation Versus Percutaneous Transluminal Angioplasty in Superficial Femoral Artery Lesions up to 10 cm in Length: The Femoral Artery Stenting Trial (FAST)


Circulation. 2007;116:285-292; originally published online June 25, 2007;
doi: 10.1161/CIRCULATIONAHA.107.689141
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/116/3/285

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/