Nitinol Stent Implantation Versus Balloon Angioplasty for Lesions in the Superficial Femoral Artery and Proximal Popliteal Artery

Twelve-Month Results From the RESILIENT Randomized Trial

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Background—Controversy still exists regarding the best endovascular treatment strategy for patients with symptomatic disease of the superficial femoral artery. There are conflicting data regarding the benefits of superficial femoral artery stenting and the role of primary stenting compared with balloon angioplasty with provisional stent implantation.

Methods and Results—A total of 206 patients from 24 centers in the United States and Europe with obstructive lesions of the superficial femoral artery and proximal popliteal artery and intermittent claudication were randomized to implantation of nitinol stents or percutaneous transluminal angioplasty. The mean total lesion length was 71 mm for the stent group and 64 mm for the angioplasty group. Acute lesion success (<30% residual stenosis) was superior for the stent group compared with the angioplasty group (95.8% versus 83.9%; P<0.01). Twenty-nine (40.3%) patients in the angioplasty group underwent bailout stenting because of a suboptimal angiographic result or flow-limiting dissection. Bailout stenting was treated as a target lesion revascularization and loss of primary patency in the final analysis. At 12 months, freedom from target lesion revascularization was 87.3% for the stent group compared with 45.1% for the angioplasty group (P<0.0001). Duplex ultrasound-derived primary patency at 12 months was better for the stent group (81.3% versus 36.7%; P<0.0001). Through 12 months, fractures occurred in 3.1% of stents implanted. No stent fractures resulted in loss of patency or target lesion revascularization.

Conclusions—In this multicenter trial, primary implantation of a self-expanding nitinol stent for moderate-length lesions in the superficial femoral artery and proximal popliteal artery was associated with better acute angiographic results and improved patency compared with balloon angioplasty alone.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00673985.


Key Words: angioplasty • stents • peripheral vascular disease

There is uncertainty regarding the best endovascular treatment strategy for symptomatic patients with atherosclerotic disease of the superficial femoral artery (SFA). Percutaneous transluminal angioplasty (PTA) has been shown to work well for focal SFA lesions in patients with patent infrapopliteal arteries.1,2 PTA patency rates for stenoses of <4 cm in length have been reported to be as high as 87% at 6 months and 78% at 3 years.2 For more complex disease and longer lesions, the results with PTA are poor.3–8 A recent analysis of the published experience of PTA for SFA lesions up to 15 cm in length (mean, 8.7 cm) revealed a 12-month primary patency rate of only 33%.4 For lesions >10 cm in length, primary patency rates have been reported to be as low as 20% at 1 year.5–8

Clinical Perspective on p 276

Stenting holds the promise of improving the results of SFA intervention by providing a better initial angiographic result,
reducing elastic recoil, and scaffolding dissection. Initial results with first-generation stents, including the balloon-expandable stainless steel Palmaz stent, were disappointing.9–12 Several randomized controlled clinical trials failed to demonstrate any restenosis benefit of balloon-expandable stents over angioplasty alone.13–16 Recent experience has suggested better outcomes with second-generation, self-expanding nitinol stents.17–20 Two randomized trials, however, have provided conflicting data regarding the benefits of primary nitinol stent implantation compared with balloon angioplasty with provisional stent implantation in the SFA.21–23 Schillinger et al17 randomized 104 patients with SFA disease to balloon angioplasty with provisional and bailout stent implantation (n=53; mean lesion length, 92±64 mm) versus primary nitinol stent implantation (n=51; mean lesion length, 101±75 mm). At 12 months, there was a significantly lower rate of restenosis (as determined by duplex ultrasonography [DUS]) in the primary stent group compared with the angioplasty group (37% versus 63%, respectively; P=0.01). Krankenberg et al23 randomized 244 patients with shorter SFA lesions (mean lesion length, 45±28 mm) to balloon angioplasty versus implantation of a single nitinol stent. At 12 months, there was no significant difference in restenosis between the treatment groups (31.7% versus 38.6%, respectively; P=0.38).

These conflicting results have added to the uncertainty regarding the role of stents in SFA intervention. In addition, concerns exist about the potential for stent fracture and late stent restenosis.24 Until recently, only 2 devices (a nitinol coil stent and a stent graft) were approved by the Food and Drug Administration for femoral artery use. We initiated this randomized, multicenter (international) trial to compare a new, flexible nitinol stent to PTA for the treatment of obstructive lesions of the SFA and proximal popliteal artery in patients with intermittent claudication. This trial was conducted under a Food and Drug Administration-approved clinical protocol in support of an investigational device exemption.

Methods

Between December 2004 and August 2006, 206 patients with obstructive lesions of the SFA, proximal popliteal artery, or both were prospectively enrolled in the RESILIENT (Randomized Study Comparing the Edwards Self-Expanding Lifestent versus Angioplasty Alone In LEsions INVolving The SFA and/or Proximal Popliteal Artery) trial at 24 centers in the United States and Europe. Patients were randomly assigned using a 2:1 randomization ratio to treatment with either a self-expanding nitinol stent after predilation (n=134) or PTA (n=72). All patients were informed of the risks and benefits of participating in the study and gave written informed consent to participate before enrollment. The protocol was approved by the institutional review board or ethics committee at each study site, and all study procedures were conducted in accordance with good clinical practices and the applicable laws of various governing bodies.

Patients eligible for inclusion in the study were aged ≥18 years; had symptoms of intermittent claudication (Rutherford categories 1 to 3); were candidates for angioplasty or stenting; had de novo stenotic, occlusive, or restenotic lesions in the SFA, proximal popliteal artery, or both; and had at least 1 patent infrapopliteal runoff vessel to the foot. The treatment area in the SFA and popliteal artery extended from 1 cm below the origin of the profunda femoris artery to ~3 cm above the intercondylar notch of the femur. Target lesions were examined angiographically to verify stenosis or restenosis ≥50% and a total lesion length of ≤150 mm. More than 1 lesion in the target vessel could be treated as long as the total length of the lesions did not exceed 150 mm. To allow for proper stent sizing, the reference vessel diameter was required to be between 4 mm and 6.5 mm. If a restenosed or reoccluded lesion was treated, previous intervention must have occurred >6 months before the study procedure and must not have included stenting. If a patient had multiple lesions in the SFA and popliteal arteries of both limbs (ie, bilateral disease), only 1 limb could be enrolled in the study. Patients with critical limb ischemia (Rutherford categories 4 to 6); sensitivity to contrast media that was not amenable to pretreatment with steroids, antiinflammatories, or both; known allergies to study medications or materials; renal failure (serum creatinine >2.0 mg/dL) or hepatic insufficiency; previous bypass surgery of the target limb; extensive peripheral vascular disease that precluded safe insertion of an introducer sheath; aneurysmal disease in the vessel segment to be treated; thrombus in the area to be treated that could not be resolved; or angiographic evidence of poor inflow that was inadequate to support vascular bypass or who were receiving dialysis or immunosuppressive therapy were ineligible for inclusion in the trial.

End Points

The primary effectiveness end point in this study was the rate of target lesion revascularization (TLR) at 12 months postprocedure. Secondary endpoints included primary and secondary patency at 6 and 12 months using DUS, acute lesion and hemodynamic success, the rates of TLR at 6 months, target vessel revascularization (TVR) and clinical success at 6 and 12 months postprocedure, and quality-of-life (QOL) assessments using the Short Form 8 Question Health Survey and the Walking Impairment Questionnaire.

TLR and TVR were defined as any repeat percutaneous intervention or bypass surgery of the target lesion or vessel because of a return of ischemic symptoms, decrease of at least 1 Rutherford category, decrease in the ankle brachial index of >0.15, or loss of patency as measured by angiography or DUS. In addition, the need for bailout or provisional stenting due to a failed angioplasty procedure in the PTA control arm (ie, flow-limiting dissection or a residual stenosis >30%) was classified as a TLR (day 0) and loss of primary patency. The patients receiving bailout stents were followed as a part of the angioplasty group (intention to treat) for all long-term follow-up analyses. The angiograms of all patients receiving a bailout stent were reviewed by the angiographic core laboratory and the clinical events committee to assess the appropriateness of the bailout stent procedure. QOL data were analyzed based on intention to treat, and if a patient underwent TLR, they were still eligible for the QOL surveys.

Acute lesion success was defined as attainment of ≤30% residual stenosis of the treatment area after intervention and was measured on a per-lesion and per-patient basis (ie, all target lesions in a patient were successfully treated). Acute hemodynamic success was defined as a >0.10 improvement in the ankle brachial index from preproce- dure to immediately postprocedure (discharge). Clinical success was defined as an improvement of baseline symptoms by at least 1 Rutherford category that was sustained through follow-up with no additional intervention (bailout stenting was considered an additional intervention and loss of clinical success). Patency was defined as continuous flow through the target lesion as evidenced by DUS (analyzed independently by VasCore, Massachusetts General Hospital, Boston, Mass). Treatment areas that demonstrated an increase in the peak systolic velocity ratio (PSVR) ≥2.5 (PSVR=peak systolic velocity within the area of stenosis divided by peak systolic velocity in a normal adjacent proximal artery segment) suggesting >50% reduction in luminal diameter, that underwent TLR, or both (including bailout stenting) were considered to have lost primary patency. Secondary patency was defined as patency achieved after reinvention for restenosis or reocclusion of the treated vessel and was assessed in the same manner with DUS after the reinvention procedure.

The primary safety end point of the trial was death within 30 days of the procedure. In addition, safety of the treatment procedures was

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The primary safety end point of the trial was death within 30 days of the procedure. In addition, safety of the treatment procedures was
assessed by freedom from major adverse clinical events (MACE) at 6 and 12 months postprocedure. MACE was a composite end point consisting of 30-day death, stroke, myocardial infarction, emergent surgical revascularization, significant embolization in the target limb, thrombosis of the target vessel, and worsening of at least 1 Rutherford category of chronic limb ischemia. All adverse events were reviewed and adjudicated by an independent clinical events committee.

**Angiographic and Radiographic Methodology**

Angiograms were acquired in at least 2 orthogonal views at baseline, after PTA, and after final intervention using a standardized protocol and were independently evaluated by a core laboratory (Cardiovascular Research Foundation Angiographic Core Laboratory, New York, NY). A radiopaque ruler was used for calibration for angiographic measurements. Target lesion length, target lesion minimum lumen diameter (MLD), and mean reference vessel diameter were measured at baseline. The percent diameter stenosis (%DS) was calculated \[ \text{\%DS} = \left(1 - \frac{\text{MLD}}{\text{reference vessel diameter}}\right) \times 100 \] at baseline and immediately after treatment, along with the change in percent diameter stenosis [baseline \%DS – final \%DS]. Acute gain was the change in MLD from baseline to final intervention. Acute lesion success was defined as a ≤30% residual stenosis after final intervention. In addition to quantitative evaluation of the treatment site, lesion calcification was evaluated (classified as none/mild, moderate, or severe), and distal runoff was assessed on the completion of angiograms to evaluate for evidence of distal embolization.

Radiographs of the stented limbs were taken at 6- and 12-months postprocedure and assessed for stent fractures by the angiographic core laboratory. Anterior-posterior and lateral views were taken at the highest magnification possible in straight leg and bent knee positions (90° of flexion) while maintaining the entire stent in the field of view. Stent fractures were classified by anatomic location (proximal, mid, or distal SFA or proximal popliteal) and type (type 1 to 4).²⁵

**Interventions**

Patients received a minimum of 81 mg of acetylsalicylic acid (aspirin) and 75 mg of clopidogrel per day, starting the day of the procedure. Patients were instructed to continue aspirin for at least 6 months and clopidogrel for a minimum of 12 weeks after the procedure. Unfractionated heparin was recommended during the procedure. Unfractionated heparin was recommended during the postprocedure baseline study. Patients randomized to the stent group received a self-expanding, nitinol stent after predilatation (LifeStent Self-Expanding Stent; Bard Peripheral Vascular; Tempe, AZ). Stent sizes available for the study were the 6-mm and 7-mm diameters in 40-mm, 60-mm, and 80-mm lengths. Stent selection was based on the manufacturer’s recommendation that 4- to 5.5-mm vessels should be treated with a 6-mm stent and that 5.6- to 7-mm vessels should be treated with a 7-mm stent (visual estimate). Sequential stents were deployed in cases involving longer lesions (eg, 2 80-mm long stents could be deployed to treat lesion lengths up to 150 mm). After stent deployment, postdilation was left to the discretion of the investigator. Completion angiography was performed using the same angles and technique used during the preprocedure baseline study.

**Statistical Analysis**

A minimum sample size of 206 patients was needed to detect a 14% difference in the TVR and TLR rate at 6 months postprocedure with a statistical power of 80% (1-sided simple log-rank test with a significance level of \( \alpha = 0.05 \)). The 14% difference was based on calculated TVR rates of 26% for the control group and 12% for the test group at 6 months postprocedure.²⁶–²⁹ A crossover rate of up to 16% was assumed for the RESILIENT trial.²⁹ A dropout rate of 7% (2% death; 5% lost to follow-up) was assumed for the log-rank-test-based sample size calculation.

All end points were analyzed on an intention-to-treat (as randomized) basis. All analyses were on a per patient basis except for lesion success. A secondary, post hoc analysis comparing the treatment actually received (as treated) compared the results of stent implantation (primary or provisional) with those of PTA alone. An additional post hoc analysis comparing the results of PTA plus PTA with provisional stent implantation to that of primary stent implantation was performed. In this post hoc analysis, bailout/provisional stenting was not considered a TLR or immediate (day 0) loss of primary patency. The value \( \alpha = 0.05 \) was used to determine significance, and CIs were set at 95%. Descriptive data were presented as mean±SD. Continuous variables were analyzed using \( t \) tests, dichotomized variables were analyzed with Fisher exact test, and \( \chi^2 \) tests were used for categorical variables (all with 2-sided \( P \) values).

**Results**

**Pretreatment Patient and Lesion Characteristics**

Baseline demographic and clinical characteristics for the 2 treatment groups are summarized in Table 1. Baseline patient demographics (age, sex, and race) and preprocedure classification of symptoms (Rutherford category and ankle brachial index) were not significantly different between treatment groups (\( P > 0.05 \)). In addition, preexisting risk factors (hypercholesterolemia, diabetes, smoking status, coronary artery disease, and myocardial infarction) were not significantly different between patient groups (\( P > 0.09 \)), except the angioplasty group had a significantly higher reported prevalence of hypertension than the stent group (\( P = 0.03 \)).

A total of 234 lesions were treated in the 206 randomized patients, with 28 (14%) patients having 2 lesions treated in the same SFA, popliteal artery, or both. Lesion characteristics were similar between the 2 treatment groups (Table 2). The mean lesion length per patient (taking into account multiple lesions in some patients) was 70.5±44.3 mm (minimum to maximum, 5.0 to 170.0 mm) in the stent group and 64.4±40.7 mm (minimum to maximum, 7.3 to 150.0 mm) for the angioplasty group (\( P = 0.33 \)). The mean stented length in the
stent group was 99.2 ± 49.9 mm. A mean of 1.6 stents were implanted per patient; 50% (67 of 134) of patients received 1 stent, 44% (59 of 134) received 2 stents, and 6% (8 of 134) received 3 stents.

Of the 72 patients in the angioplasty group, 29 (40.3%) underwent a secondary bailout stenting procedure because of an inadequate PTA result, either a flow-limiting dissection or a residual stenosis (n = 270 Circ Cardiovasc Interv June 2010

Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Stent (n=134)</th>
<th>PTA (n=72)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68 ± 10</td>
<td>66 ± 9</td>
<td>0.11</td>
</tr>
<tr>
<td>Men</td>
<td>95 (70.9)</td>
<td>48 (66.7)</td>
<td>0.53</td>
</tr>
<tr>
<td>Race</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>12 (9.0)</td>
<td>7 (9.7)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>120 (89.6)</td>
<td>61 (84.7)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.5)</td>
<td>4 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>112 (83.6)</td>
<td>68 (94.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>107 (79.9)</td>
<td>55 (76.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diabetes</td>
<td>51 (38.1)</td>
<td>39 (54.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Smoking status (current or past)</td>
<td>96 (71.6)</td>
<td>60 (83.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>75 (56.0)</td>
<td>54 (72.4)</td>
<td>0.88</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>27 (20.1)</td>
<td>19 (26.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>Rutherford category</td>
<td>0.17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1: Mild calcification | 4 (3.0) | 5 (6.9) |
2: Moderate calcification | 48 (35.8) | 30 (41.7) |
3: Severe calcification | 82 (61.2) | 30 (40.5) |
Target limb ABI | 0.71 ± 0.19 | 0.72 ± 0.19 | 0.85|
Contralateral limb ABI | 0.86 ± 0.21 | 0.84 ± 0.21 | 0.19|

Data are presented as n (%) or mean ± SD. ABI indicates ankle brachial index.
* Fisher exact test was used for dichotomized variables; and χ² tests were used for other categorical variables. All P values are 2-sided.

Lesion location (per lesion), n | 0.44
None or mild | 90 (64.7) | 46 (65.7) |
Moderate | 15 (10.8) | 11 (15.7) |
Severe | 34 (24.5) | 13 (18.6) |
Reference vessel diameter, mm | 0.96
5.1 ± 0.8 | 5.1 ± 0.8 |
Minimum lumen diameter, mm | 0.33
1.4 ± 0.9 | 1.3 ± 0.9 |
Degree of stenosis, % | 0.40
72.7 ± 17.6 | 74.9 ± 18.3 |
Length per patient, mm | 0.33
70.5 ± 44.3 | 64.4 ± 40.7 |

Data are presented as n (%) or mean ± SD. * Fisher exact test was used for dichotomized variables and χ² tests were used for other categorical variables. All P values are 2-sided.

Moderate calcification was defined as radiopaque density seen on 1 side of the vessel, and severe calcification was defined as radiopaque density on both sides of the vessel.

angioplasty group (P < 0.001). Acute lesion success presented per patient (ie, all target lesions per patient were treated successfully) was superior for the stent group compared with the angioplasty group (95.8% versus 83.9%; P < 0.01), and acute hemodynamic success was significantly better for the angioplasty group (P < 0.001). Acute lesion success presented per patient (ie, all target lesions per patient were treated successfully) was superior for the stent group compared with the angioplasty group (95.8% versus 83.9%; P < 0.01), and acute hemodynamic success was significantly better for the

Table 2. Baseline Lesion Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Stent (n=134)</th>
<th>PTA (n=72)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lesions, n</td>
<td>153</td>
<td>81</td>
<td>0.83</td>
</tr>
<tr>
<td>Lesions per patient</td>
<td>0.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>115 (85.8)</td>
<td>63 (87.5)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>19 (14.2)</td>
<td>9 (12.5)</td>
<td></td>
</tr>
</tbody>
</table>
| Lesion location (per lesion), n | 0.44
Proximal SFA | 20 (13.1) | 12 (14.8) |
Middle SFA | 49 (32.0) | 31 (38.3) |
Distal SFA | 77 (50.3) | 37 (45.7) |
Proximal popliteal | 7 (4.6) | 1 (1.2) |
Lesion classification (per lesion) | 0.96
Stenosis—de novo | 123 (80.4) | 64 (79.0) |
Occlusion | 26 (17.0) | 15 (18.5) |
Restenosis | 4 (2.6) | 2 (2.5) |

Data are presented as n (%) or mean ± SD. * Fisher exact test was used for dichotomized variables and χ² tests were used for other categorical variables. All P values are 2-sided.

Moderate calcification was defined as radiopaque density seen on 1 side of the vessel, and severe calcification was defined as radiopaque density on both sides of the vessel.

Table 3. Postprocedure Lesion Characteristics and Acute Effectiveness

<table>
<thead>
<tr>
<th></th>
<th>Stent (n=134)</th>
<th>PTA (n=72)</th>
<th>Percent Difference</th>
<th>P*</th>
</tr>
</thead>
</table>
| Reference vessel diameter, mm | 0.86
5.2 ± 0.8 | 5.2 ± 0.8 |
Minimum lumen diameter, mm | 0.02
4.4 ± 0.7 | 4.1 ± 0.8 |
Change in MLD (acute gain), mm | 0.45
2.9 ± 1.1 | 2.8 ± 1.1 |
Degree of stenosis, % | <0.001
16.9 ± 7.0 | 21.5 ± 9.3 |
Acute effectiveness, % | <0.01
Lesion success | 95.8 | 83.9 | 11.9 |
Hemodynamic success | 73.0 | 56.9 | 16.1 |
Procedural success | 95.8 | 83.9 | 11.9 |

Data are presented as mean ± SD, unless otherwise indicated.
* Fisher exact test was used for other categorical variables. All P values are 2-sided.
† Fisher exact test.
stent group compared with the angioplasty group (73.0% versus 56.9%; \( P < 0.05 \)).

Postprocedure Follow-Up
Follow-up data were available on 87% of patients at 12 months (87.5% for the stent group and 86.8% for the angioplasty group). Seven patients died, 9 patients withdrew consent to be evaluated, and 3 patients were lost to follow-up (Figure 1). Table 4 summarizes the effectiveness measures of the RESILIENT trial. Freedom from TLR at 6 months postprocedure was significantly better for the stent group than for the angioplasty group (98.5% versus 52.6%; \( P < 0.0001 \)) and remained significantly better for the stent group (87.3% versus 45.1%; \( P < 0.0001 \)) at 12 months. Primary patency, a combination of ultrasound-confirmed patency and absence of TLR, was significantly better for the stent group than for the angioplasty group at 6 months and 12 months postprocedure (\( P < 0.0001 \)). The 6-month primary patency rate for the stent group was 94.2% compared with 47.4% for the angioplasty group, whereas the 12-month primary patency rate was 81.3% for the stent group versus 36.7% for the angioplasty group (Figure 2A). Clinical success was significantly better for the stent group compared with the angioplasty group at both 6 months (81.4% versus 30.9%; \( P < 0.0001 \)) and 12 months (72.3% versus 32.3%; \( P < 0.0001 \)). Both treatment groups demonstrated a significant improvement in all QOL measures (ie, both Short Form 8 Question Heath Survey and Walking Impairment Questionnaire) at 6 and 12 months compared with baseline. The baseline Short Form 8 Question Heath Survey physical score was 41.0±10.5 in the angioplasty group and 41.4±9.2 in the stent group. At 12 months, the Short Form 8 Question Heath Survey scores had increased similarly in both groups (5.9±11.2 versus 5.7±11.2; \( P = 0.0001 \) versus baseline). The 12-month walking distance score was 22.3±23.2 in the angioplasty group and 22.8±24.2 in the stent group. At 12 months, walking distance scores had increased similarly in both groups (29.4±37.4 versus 25.6±34.6; \( P < 0.0001 \) versus baseline). Patients in the angioplasty group reported more claudication pain at 12 months than patients in the stent group (Walking Impairment Questionnaire evaluation, \( P = 0.009 \)), but there were no other significant differences in QOL measures between treatment groups (t test \( P > 0.05 \)).

As-Treated Analysis
The data also were analyzed according to the actual treatment received (primary and provisional stents versus PTA only). Lesions were significantly shorter in the PTA-only group compared with the combined-stent group (47.7±32.6 mm versus 63.3±41.9 mm; \( P < 0.01 \)). Despite this difference,
Table 4. Chronic Safety and Effectiveness Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Stent (n=134)</th>
<th>PTA (n=72)</th>
<th>Percent Difference</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-month freedom from MACE†</td>
<td>93.1</td>
<td>92.8</td>
<td>0.3</td>
<td>0.95</td>
</tr>
<tr>
<td>12-month freedom from MACE</td>
<td>85.8</td>
<td>86.6</td>
<td>-0.8</td>
<td>0.88</td>
</tr>
<tr>
<td>6-month effectiveness measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freedom from TLR</td>
<td>98.5</td>
<td>52.6</td>
<td>45.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Freedom from TLR/TVR</td>
<td>94.6</td>
<td>52.6</td>
<td>42.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Primary patency</td>
<td>94.2</td>
<td>47.4</td>
<td>46.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>100</td>
<td>98.3</td>
<td>1.7</td>
<td>0.31</td>
</tr>
<tr>
<td>Clinical success</td>
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<td>50.5</td>
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<td>Freedom from TLR</td>
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<tr>
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<td>72.3</td>
<td>32.3</td>
<td>40.0</td>
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</tbody>
</table>

Data are presented as %.

†MACE is defined as death within 30 days, stroke, myocardial infarction, significant distal embolization, emergent surgical revascularization of target limb; thrombosis, and worsening Rutherford category in the specified interval (6-months and 12-months).

Acute lesion success was better for the combined-stent group (97.0% versus 74.4%; P<0.0001). Primary patency was better for the combined-stent group both at 6 months (94.4% versus 79.3%; P=0.03) and 12 months (80.4% versus 61.5%; P=0.03) (Figure 2B). Freedom from TLR was also significantly better for the combined-stent group at 6 months (98.1% versus 88.1%; P=0.05), but there was no difference in the need for TLR at 12 months (86.1% versus 75.5%; P=0.15) (Figure 3).

Primary Versus Provisional Stenting

A post hoc analysis of the data was performed to compare the results of PTA plus PTA with provisional stenting to that of primary stenting. In this analysis, provisional stenting was not considered as a TLR or immediate (day 0) loss of primary patency. Freedom from TLR at 6 months was significantly better for the primary stent group compared with the PTA with provisional stent group (98.1% versus 91.1%; P=0.04). At 12 months, some of this benefit was lost, and the difference in TLR rates was not statistically significant (87.3% versus 77.3%; P=0.09) (Figure 3 and Table 5). However, primary patency at 12 months was better for the primary stent group (81.3% versus 66.9%; P=0.05) (Figure 2C).

Adverse Events

No patients in either arm of the study died within 30 days of the procedure. There was no statistically significant difference between the MACE rates for the treatment groups. Freedom from MACE at 6 months for the stent group was 93.1% and for the angioplasty group, 92.8% (P=0.95). At 12 months, freedom from MACE was 85.8% for the stent group and 86.6% for the angioplasty group (P=0.88). There were 2 unplanned amputations reported in the angioplasty group through 12 months. Both were minor, below-the-level-of-the-ankle (single-toe) amputations. No amputations were reported in the stent group.

Radiographic analysis of all stents in all phases and arms of the RESILIENT study (including bailout stents) revealed 1 (0.3%) type 4 fracture at 6 months postprocedure and a total of 9 (3.1%) fractures (4 type 1 and 5 type 4) at 12 months. Core laboratory analysis of the angiograms revealed that the stents that exhibited type 4 fractures were all elongated at deployment (118% to 143% of the nominal stent length). An additional 8 cases of stent elongation in excess of 110% that did not result in stent fracture were identified by the core laboratory. Four (80%) of the 5 type 4 fractures occurred in the mid-SFA, 4 (80%) occurred proximal or distal to a point of overlap, and 3 (60%) occurred in lesions classified as moderate or severely calcified. None of the patients with stent fractures lost primary patency or experienced a revascularization procedure.

Discussion

The RESILIENT study demonstrated that for moderate-length lesions (up to 15 cm) in the SFA and proximal popliteal artery, use of the LifeStent self-expanding nitinol stent provided superior outcomes compared with balloon angioplasty. The immediate angiographic result was better, and in the prespecified intention-to-treat analysis (bailout/provisional stent=TLR and loss of primary patency), freedom from TLR and primary patency were significantly better in the stent group up to 1 year. When the results were analyzed with regard to the actual treatment received (primary and provisional stents versus PTA only), primary patency at 12 months was better for the stent group. In addition, in a second post hoc analysis of the data comparing PTA plus PTA with provisional stent implantation to primary stent implantation, primary patency at 12 months was better for the primary stent group. Patients in the stent group reported significantly less claudication pain at 12 months than patients in the angioplasty group, whereas both groups had a statistically significant improvement in QOL compared to baseline.

Concerns exist about the potential for nitinol stents to fracture and the clinical implications of femoropopliteal stent fracture. Higher stent-fracture rates have been reported with certain nitinol stent designs, and stent fracture may for some stents be more closely linked to restenosis. In a retrospective analysis of nitinol stent procedures performed at a single institution, Scheinert et al demonstrated a 37.2% stent fracture rate when performing long-segment SFA stenting with 3 different nitinol stents. The rate of fracture was related to the length of the stented segment and the number and type of stents implanted. In the study by Krankenberg et al., a 12% fracture rate was seen after stenting of shorter lesions. In the SIROCCO (Sirolimus-Coated Cordis Self-
expandable Stent) I study, an 18.2% fracture rate at 6 months was identified with the S.M.A.R.T. stent when treating lesions with a mean length of 85 mm. In SIROCCO II, the 6-month fracture rate decreased to 8% as the lesion length was shortened to 81.5 mm and the number of stents implanted decreased. The fracture rate with the LifeStent in the current study was only 3.1% at 12 months, suggesting that this stent design may afford some degree of fracture resistance. Five type 4 fractures occurred in this study. Although a direct causative link cannot be established, all of these occurred in the setting of inappropriate elongation of the stent during deployment. Improvement in the stent delivery system and increased operator experience should reduce the likelihood of stent elongation in the future.

Lesion length is an important determinant of patency after femoropopliteal PTA and stenting. Angioplasty alone seems to provide satisfactory results for focal SFA lesions; in fact, the Krankenberg et al trial suggested that for shorter lesions (mean lesion length, 45 mm), there is minimal incremental benefit in 12-month patency when using a primary stent strategy. The present study confirmed that shorter lesions (mean lesion length, 48 mm) responded adequately to a PTA-only strategy. These lesions were also less heavily calcified, and the patients had less-severe symptoms of claudication. PTA provides less satisfactory results for longer lesions. In the Schillinger et al trial, lesion length was significantly greater (101±75 mm in the stent group and 92±64 mm in the angioplasty group), and a benefit for primary stent implantation was more easily demonstrated. The lesion length in the RESILIENT study was intermediate between the 2 previous studies (70.5±44.3 mm in the stent group versus 64.4±40.7 mm in the angioplasty group), and a benefit for stenting was again demonstrated. The high crossover rate in this trial and the fact that crossover occurred more commonly for longer, more calcified lesions again highlight the inadequacy of balloon angioplasty alone for more-complex lesions. The 12-month primary patency rate of 81.3% for the stent group in this trial compares favorably with the stent results in the Krankenberg et al and Schillinger et al studies. The lower primary patency rate seen in Schillinger et al (63%) is likely a reflection of the longer lesions that were treated, although an effect of stent design or other unidentified cofounders cannot be completely excluded.
Limitations
Despite attempts to minimize crossover to stent implantation in the angioplasty arm of this trial, there was still a relatively high crossover rate of 40.3%, leaving 43 patients who underwent PTA only. Although subsequent angiographic review demonstrated that the majority of these crossovers were justified based on the prespecified study criteria, this crossover rate is higher than was seen in the studies by Krankenberg et al23 (11%) and Schillinger et al21 (32%), and it complicates analysis of these data. Although some of the difference in crossover rates between the present study and that of Krankenberg et al can be attributed to lesion length, investigator bias also may have played a role. The decision to consider crossover to stent implantation as a TLR is certainly a controversial aspect of this trial design and a departure from previous trial designs. The decision to define bailout/provisional stenting as a TLR was based on the limitations of the more traditional intention-to-treat analysis to evaluate the benefit of stenting in the face of a high crossover rate. Inclusion of patients who undergo provisional stenting in the PTA group would tend to bias the results in favor of PTA. Importantly, data also were analyzed according to the actual treatment received. This analysis demonstrated a better primary patency rate for the combined-stent group compared with PTA alone at both 6 and 12 months.

The results of DUS have been shown to correlate well with digital subtraction angiography, although there is some debate about the optimal PSVR for the detection of a significant (≥50%) stenosis. For the present study, a PSVR of ≥2.5 was chosen based on studies suggesting that a PSVR of >2.4 to 2.5 is more accurate and specific for the detection of >50% stenosis than the traditional criteria of PSVR ≥2.0.31–33

Conclusions
In the RESILIENT trial, primary treatment with a flexible, self-expanding nitinol stent for moderate-length lesions in the SFA and proximal popliteal artery was associated with better acute angiographic results and improved clinical outcomes compared with balloon angioplasty alone. The rate of stent fracture was low, and stent fracture was not associated with any adverse clinical sequelae.

Table 5. PTA Plus Provisional Stenting Versus Primary Stent Implantation (Chronic Effectiveness Measures)

<table>
<thead>
<tr>
<th></th>
<th>Stent (n=134)</th>
<th>PTA + Stent (n=72)</th>
<th>Percent Difference</th>
<th>P*</th>
</tr>
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<tr>
<td>6-month effectiveness measures</td>
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<tr>
<td>Freedom from TLR</td>
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<td>91.2</td>
<td>7.3</td>
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<tr>
<td>Freedom from TLR/TVR</td>
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<td>91.2</td>
<td>3.4</td>
<td>0.38</td>
</tr>
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<td>Primary patency</td>
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<td>85.6</td>
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<td>0.08</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>100</td>
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</tr>
<tr>
<td>12-month effectiveness measures</td>
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<td></td>
</tr>
<tr>
<td>Freedom from TLR</td>
<td>87.3</td>
<td>77.3</td>
<td>10.0</td>
<td>0.09</td>
</tr>
<tr>
<td>Freedom from TLR/TVR</td>
<td>83.5</td>
<td>77.3</td>
<td>6.2</td>
<td>0.31</td>
</tr>
<tr>
<td>Primary patency</td>
<td>81.3</td>
<td>66.9</td>
<td>14.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>100</td>
<td>100</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as %. This intention-to-treat subset analysis does not treat the provisionally stented population as immediate (day 0) PTA failures. The P values are 2-sided and are based on the Fisher Exact test for dichotomized variables and a normal approximation from the Kaplan–Meier curves for patency, TLR, and TLR/TVR.

Figure 3. Freedom from target lesion revascularization is presented at 12 months for the per-protocol and post hoc analyses. Left to right: first, the PTA group and stent group by intention to treat (per protocol); second, as-treated analysis comparing the PTA-only group to the combined (primary plus provisional)-stent group; and third, PTA plus PTA with provisional stent group compared to the primary stent group. Bars represent 95% CIs.

Appendix
The following investigators and institutions participated in the RESILIENT trial: John R. Laird, MD, Washington Hospital Center, Washington, DC; Barry T. Katzen, MD, Baptist Heart and Vascular Center, Miami, Fla; Dierk Scheinert, MD, and Giancarlo Biamino, MD, Leipzig Heart Center, Leipzig, Germany; Johannes Lammer, MD, Martin Funovics, MD, and Maria Schoder, MD, Medical University of Vienna, Vienna, Austria; Jeffrey Carpenter, MD, University of Pennsylvania, Philadelphia, Pa; Maurice Buchbinder, MD, Scripps Clinic, San Diego, Calif; Rajesh Dave, MD, Pinnacle
Acknowledgments

We thank Kevin Drisko for his assistance with data management and Dr Annie Cao for her expert statistical analysis.

Disclosures

Dr Laird is a paid consultant to Bard Peripheral Vascular and a past advisory board member for Edwards Lifesciences (2005–2007). Dr Lansky receives research support from Bard Peripheral Vascular. Dr Lammer is a past advisory board member for Edwards Lifesciences (2005–2007). Dr Katzen is a past advisory board member for Edwards Lifesciences (2005–2007). Dr Laird is a paid consultant to Bard Peripheral Vascular and a past advisory board member for Edwards Lifesciences (2005–2007). Dr Annie Cao for her expert statistical analysis.

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References


CLINICAL PERSPECTIVE

There is uncertainty regarding the optimal endovascular treatment strategy for patients with lifestyle-limiting claudication and disease in the superficial femoral artery. Previous clinical trials have demonstrated conflicting data regarding the benefits of stenting compared with balloon angioplasty for lesions in this location. There continue to be concerns about the potential for superficial femoral artery stent fracture. The RESILIENT (Randomized Study Comparing the Edwards Self-Expansion Lifestent versus Angioplasty Alone in Lesions Involving the SFA and/or Proximal Popliteal Artery) trial compared the safety and efficacy of a self-expanding nitinol stent to balloon angioplasty for lesions in the superficial femoral artery and proximal popliteal artery. In RESILIENT, 206 patients were randomly assigned to stent implantation versus balloon angioplasty (2:1 randomization). Stenoses or occlusions up to 15 cm in length could be treated. The acute angiographic results were better after stenting, and at 12-months, primary patency rate was significantly higher in the stent group. There was a reduced need for target lesion revascularization after stenting. The rate of stent fracture was low (3.1%), and none of these stent fractures were associated with adverse clinical consequences. In this multicenter, randomized trial, stenting with a self-expanding nitinol stent was superior to balloon angioplasty for moderate-length lesions in the superficial femoral artery and proximal popliteal artery.
Nitinol Stent Implantation Versus Balloon Angioplasty for Lesions in the Superficial Femoral Artery and Proximal Popliteal Artery: Twelve-Month Results From the RESILIENT Randomized Trial

John R. Laird, Barry T. Katzen, Dierk Scheinert, Johannes Lammer, Jeffrey Carpenter, Maurice Buchbinder, Rajesh Dave, Gary Ansel, Alexandra Lansky, Ecaterina Cristea, Tyrone J. Collins, Jeffrey Goldstein, Michael R. Jaff and for the RESILIENT Investigators

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