CHAPTER 5.

Midterm outcome of balloon-expandable polytetrafluoroethylene covered stents in the treatment of iliac artery chronic occlusive disease

AUTHORS
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ABSTRACT

**Purpose:** To evaluate the 4-year results of polytetrafluoroethylene (PTFE)-covered stents in the treatment of iliac artery occlusive disease.

**Methods:** Between January 2003 and September 2010, PTFE-covered stents were implanted in 115 iliac arteries of 87 patients (73 men; mean age 60±11 years) in a single center. The lesions were classified as TASC II A (n=40), B (n=41), C (n=7), and D (n=27). There were 69 primary endograft placements, while 46 procedures were performed after previous bare metal stent placement (reintervention group). Follow-up consisted of clinical investigation, ankle-brachial index (ABI) measurement, and duplex ultrasound scanning. In this retrospective analysis outcomes were reported on a per-limb basis.

**Results:** The median Rutherford classification decreased from category 3 at baseline to 0 after the procedure (P<.001) and the ABI increased from 0.66±0.24 to 0.89±0.21 (P<.001). The primary limb patency was significantly higher in the primary treatment group (P=.03): 88.7% at 1 year, 86.4% at 2 years, and 71.5% at 4 years compared to the reintervention group (77.9%, 72.1%, and 53.0%, respectively). Univariate analysis revealed prior stent placement as the only factor associated with loss of primary patency. The freedom from target lesion revascularization (TLR) in the primary treatment group was 95.2% at 1 year, 89.6% at 2 years, and 74.4% at 4 years, which did not differ significantly from rates in the reintervention group (88.0%, 82.3%, and 63.8%, respectively).

**Conclusion:** The use of PTFE-covered stents for occlusive disease in the iliac arteries is related to satisfactory limb patency rates and high freedom from TLR. Previous stent placement was related to a lower primary patency rate. Additional studies are indicated to establish subgroups that may specifically benefit from covered stents.
INTRODUCTION

Iliac artery chronic occlusive disease may be treated by surgical reconstruction or by endovascular means. The TransAtlantic Inter-Society Consensus II (TASC II) has recommended endovascular treatment for single or multiple lesions totaling 3 to 10 cm long, while surgery is advised for bilateral and more extensive lesions.\(^1\) A recent review of the literature has shown that the 12-month primary patency of endovascular treatment is 89.6% and 87.3% for TASC II C and D lesions, respectively\(^2\); corresponding rates for primary and selective bare metal stenting were 92.1% and 82.9%, respectively.

Results of endovascular treatment are affected by a range of factors, including elastic recoil, arterial remodeling, and neointimal growth leading to in-stent stenosis (ISS). A polytetrafluoroethylene (PTFE) covering may shield stents from tissue ingrowth through stent interstices and subsequently reduce ISS by intimal hyperplasia.\(^4\)-\(^7\) Case series on the results of PTFE covered stents for the treatment of iliac artery occlusive disease have shown 12-month primary patency rates between 70.0% and 91.1%.\(^8\)-\(^12\) A recently published multicenter randomized trial has demonstrated an increased patency at 18 months in favor of covered stents compared to bare metal stents in TASC C and D lesions.\(^13\) There were no significant differences in patients with TASC B lesions.

The goals of the present study were to assess the 4-year patency of PTFE covered balloon expandable stents and to elucidate differences between primary and secondary procedures after previous bare metal stenting.

METHODS

Study Design

A prospectively maintained database at a single center was interrogated to identify all patients who were treated with a PTFE covered balloon expandable stent (Advanta V12; Atrium Medical, Hudson, NH, USA) for iliac artery occlusive disease between January 2003 and September 2010. During the study period, patients with iliac artery disease were treated using a primary stenting strategy, using both bare metal stents and covered stents. Preprocedural imaging consisted of duplex ultrasound; patients did not routinely undergo computed tomography or magnetic resonance angiography before treatment. All procedures were performed by one interventional radiologist (H.S.). Patients were excluded from this analysis if their records were lost or if kissing stents had been deployed. Data on demographics, clinical status, medical history, procedure details, and follow-up
were retrieved from the database and retrospectively analyzed. The preoperative clinical status was assessed using the Rutherford classification for chronic ischemia. History of comorbidity was graded using the recommendations of Rutherford et al. Radiographic images were reviewed and scored according to the TASC II criteria.

**Procedure**

All interventions were performed percutaneously under local anesthesia with 5000 units of heparin administered intravenously. Retrograde recanalization was always attempted first; however, when this proved to be unsuccessful, an antegrade passage was performed using a crossover technique via the contralateral groin and then converted into a retrograde passage. A 35-cm-long, 7-F sheath was then inserted across the lesion to safely deliver the endograft, which was not overdilated. After the procedure, all patients were treated with acetylsalicylic acid unless warfarin was prescribed for another indication. Follow-up consisted of clinical investigation, ankle-brachial index (ABI) measurements, and duplex ultrasound scanning.

**TABLE 1: Patient Characteristics and Risk Factors**

<table>
<thead>
<tr>
<th></th>
<th>Total (N=115)</th>
<th>Primary Treatment (N=69)</th>
<th>Reintervention (N=46)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60±11</td>
<td>60±12</td>
<td>59±9</td>
<td>0.70</td>
</tr>
<tr>
<td>Men</td>
<td>73 (63.5%)</td>
<td>39 (56.5%)</td>
<td>34 (73.9%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Smoking</td>
<td>98 (85.2%)</td>
<td>58 (84.1%)</td>
<td>40 (87.0%)</td>
<td>0.79</td>
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<tr>
<td>Hypertension</td>
<td>55 (47.8%)</td>
<td>38 (55.1%)</td>
<td>17 (37.0%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (15.7%)</td>
<td>13 (18.8%)</td>
<td>5 (10.9%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>29 (25.2%)</td>
<td>19 (27.5%)</td>
<td>10 (21.7%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>26 (22.6%)</td>
<td>14 (20.3%)</td>
<td>12 (26.1%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Renal disease</td>
<td>23 (20.0%)</td>
<td>13 (18.8%)</td>
<td>10 (21.7%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Rutherford category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>17 (14.8%)</td>
<td>8 (11.6%)</td>
<td>9 (19.6%)</td>
<td>0.29</td>
</tr>
<tr>
<td>3</td>
<td>72 (62.6%)</td>
<td>42 (60.9%)</td>
<td>30 (65.2%)</td>
<td>0.70</td>
</tr>
<tr>
<td>4</td>
<td>9 (7.8%)</td>
<td>7 (10.1%)</td>
<td>2 (4.3%)</td>
<td>0.31</td>
</tr>
<tr>
<td>5</td>
<td>11 (9.6%)</td>
<td>7 (10.1%)</td>
<td>4 (8.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (5.2%)</td>
<td>5 (7.2%)</td>
<td>1 (2.2%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Ankle-brachial index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>0.66±0.24</td>
<td>0.66±0.23</td>
<td>0.66±0.27</td>
<td>0.85</td>
</tr>
<tr>
<td>After</td>
<td>0.89±0.21</td>
<td>0.89±0.20</td>
<td>0.88±0.23</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Continuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage)

*Between primary and reintervention groups using Fisher exact test
**Patient Sample**

During the study period, 628 procedures on the iliac artery were performed, of which 550 stent placements. Among the latter were 115 iliac arteries treated with balloon expandable covered stents in 87 patients (73 men; mean age 60±11 years) excluding 3 patients whose records were lost. Twenty-three patients had bilateral iliac artery disease and were treated without creating a kissing stent configuration. Five patients were treated twice.

In 77% of the cases, the procedure was performed for intermittent claudication (Table 1) and in 17% for critical limb ischemia (CLI). The common iliac artery (CIA) was treated in 95 (83%) cases, and the external iliac artery (EIA) in 9 (8%) cases (Table 2); an endograft extending from the CIA into the EIA was placed in 11 (10%) cases. For purposes of analysis, the cohort was dichotomized according to primary placement (n=69) or placement during reintervention (n=46) following previous bare stenting within the same segment.

**TABLE 2: Characteristics of the Treated Iliac Lesions**

<table>
<thead>
<tr>
<th>TASC II class</th>
<th>Total (N=115)</th>
<th>Primary Treatment (N=69)</th>
<th>Reintervention (N=46)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>40 (34.8%)</td>
<td>26 (37.7%)</td>
<td>14 (30.4%)</td>
<td>0.55</td>
</tr>
<tr>
<td>B</td>
<td>41 (35.7%)</td>
<td>23 (33.3%)</td>
<td>18 (39.1%)</td>
<td>0.56</td>
</tr>
<tr>
<td>C</td>
<td>7 (6.1%)</td>
<td>3 (4.3%)</td>
<td>4 (8.7%)</td>
<td>0.44</td>
</tr>
<tr>
<td>D</td>
<td>27 (23.5%)</td>
<td>17 (24.6%)</td>
<td>10 (21.7%)</td>
<td>0.82</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>Total (N=115)</th>
<th>Primary Treatment (N=69)</th>
<th>Reintervention (N=46)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>2 (1.7%)</td>
<td>2 (2.9%)</td>
<td>0 (0.0%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Data are given as the counts (percentage).

TASC: TransAtlantic Inter-Society Consensus.

* Differences between primary treatment and reintervention groups using Fisher exact test.

**Definitions**

The main outcome measure was primary patency, defined as a patent stent with no stenosis as measured with duplex ultrasound. Secondary outcomes were secondary patency, freedom from target lesion revascularization (TLR), correct stent placement with <30% residual stenosis (technical success), clinical improvement of at least one Rutherford category, and complications. ISS was indicated by a peak systolic value (PSV) ratio >2.5 measured in the endograft; the same threshold was used for stenotic lesions proximal or distal to the endograft edge. Secondary patency was achieved by any procedure aimed
at recanalizing an occluded endograft, thereby preserving the conduit. TLR was defined as the need for any intervention (endovascular or surgical) on the entire aortoiliac vessel proximal and distal to the treated site to treat recurrence of clinical symptoms.

**Statistical Analysis**

To be compatible with studies reported in the literature, the data were reported on a per-limb basis as the mean ± standard deviation or median (range), depending on the results of the Shapiro-Wilk test for normalcy. Paired \( t \) tests were used to compare the pre- and post-procedure ABI. Primary and secondary patency rates and freedom from TLR were estimated using the Kaplan-Meier survival analysis; a log-rank (Mantel-Cox) test was used to assess patency rates between subgroups, including primary treatment vs. reintervention, TASC II types A/B vs. C/D, claudication vs. critical limb ischemia and occlusions vs. stenoses. Univariate analyses were performed to identify factors that may have affected outcome. A multivariate analysis to identify predictors of failure was performed using the Cox proportional hazards model in which all factors with \( P < .15 \) from the univariate analysis were included; results are presented as the hazard ratio (HR) and 95\% confidence intervals (CI). Probability values were based on 2-sided testing at a significance level of 0.05.

**RESULTS**

Technical success was achieved in 114 (99\%) limbs; the endograft was dislocated in one patient and had to be removed surgically. In 90 (78\%) lesions, only one endograft was needed; 18 (16\%) lesions required two endografts, 5 (4\%) lesions received three endografts, and one (1\%) limb had four endografts. The endograft diameter was 6 mm (\( N = 4 \)), 7 mm (\( N = 32 \)), 8 mm (\( N = 52 \)), or 9 mm (\( N = 25 \)), in two cases the diameter was not reported.

During the procedure, an EIA rupture was treated with a covered stent. In 26 other procedures, additional stents were used, including 17 self-expanding bare stents, 5 balloon-expandable bare stents, and 4 self-expanding PTFE covered stents. Some of these were overlapping with the study endografts and others at a distance from them. There were no clinically apparent distal embolizations.

The median Rutherford classification decreased from category 3 (range 2–5) before the procedure to category 0 (range 0–5) post procedure (\( P < .001 \)). After the procedure, the mean ABI increased from 0.66±0.24 to 0.89±0.21 (\( P < .001 \)).
Figure 1  Kaplan-Meier survival estimates of primary patency for all PTFE-covered iliac stents and for the primary vs. reintervention groups (the latter after previous bare metal stenting)

Patency and Freedom From TLR

The median follow-up was 31 months (range 0–88). Sixteen (18%) of 87 patients (21 limbs) died, two before their first follow-up visit. One patient died nine days after the procedure from multiple organ failure following a laparotomy for duodenal bleeding. The other patient, a 92-year-old man, died at three months due to an unknown cause. Follow-up data were available for 75 (65%) of 115 limbs at 6 months, 70 (61%) limbs at 1 year, 57 (50%) limbs at 2 years, and 27 (23%) limbs at 4 years. Four-year follow-up was limited due to the fact that 16 patients died (21 limbs), three patients (3 limbs)
moved to another city, three patients (3 limbs) received a surgical bypass due to disease progression, two patients (2 limbs) did receive recent follow-up and were not invited again, four patients (4 limbs) were not able to attend follow-up, two patients (2 limbs) refused follow-up, and five patients (5 limbs) could not be reached. Twenty-two patients (32 limbs) were within the first four years after the procedure and 12 patients (16 limbs) lost primary patency within four years.

**Figure 2** Kaplan-Meier survival estimates of secondary patency for all PTFE-covered iliac stents and for the primary vs. reintervention groups (the latter after previous bare metal stenting)
Overall, the primary patency was 87.2% at 6 months, 83.6% at 1 year, 79.7% at 2 years, and 63.4% at 4 years (fig. 1). Secondary patency was 91.4%, 87.8%, 85.3%, and 71.7%, respectively (fig. 2). Freedom of TLR (fig. 3) at the same time points was 92.5%, 91.4%, 85.9%, and 67.4%.

In the primary treatment group, the primary limb patency was 92.8% at 6 months, 88.7% at 1 year, 86.4% at 2 years and 71.5% at 4 years (fig. 1).

The secondary limb patency rates within this group were 94.6%, 90.5%, 88.4% and 72.9%, respectively (fig. 2). The freedom from TLR in the primary treatment group was 95.2% at 1 year, 89.6% at 2 years, and 74.4% at 4 years (fig.3).

In the reintervention group, the primary limb patency (fig. 1) was 80.8% at 6 months, 77.9% at 1 year, 72.1% at 2 years, and 53.0% at 4 years, while the secondary patency rates were 88.8%, 85.8%, 82.7%, and 71.6%, respectively (fig. 2). The freedom from TLR in the reintervention group was 88.0% at 1 year, 82.3% at 2 years, and 63.8% at 4 years (fig. 3). Primary limb patency was significantly higher in the primary treatment group compared to the reintervention group (P=.03). There were no significant differences in secondary limb patency and freedom from TLR between these groups (P=.90 and P=.43, respectively). There were also no differences in patency between TASC II lesion types, claudication vs. CLI, or occlusion vs. stenosis.

Recurrent stenosis or occlusion resulted in 13 surgical aortobifemoral bypasses, six in the primary treatment group and seven in the reintervention group. There were three additional endograft placements in the same arterial segment, two of which were in the reintervention group.

Univariate analysis demonstrated that previous stent placement was significantly associated with loss of primary patency (P=.03). Other potential risk factors, including lesion characteristics, clinical state, and cardiovascular risk factors, were not associated with loss of primary or secondary patency. Cox regression multivariate analysis failed to identify any independent predictors of primary patency loss, including former stent placement (HR 1.94, 95% CI 0.94 to 4.03, P=.07).
Chapter 5

**DISCUSSION**

In this study, we have shown that the use of PTFE covered stents for iliac artery occlusive disease is feasible, safe, and effective, with one-year patency in primary procedures of 88.7%, which correlates well with previously described one-year patency rates of 70.0% to 91.1%.\(^8\)\(^{-}\)\(^{12}\) The four-year primary patency rate of 71.5% compares favorably with rates for bare metal stenting reported to range between 41% and 86%.\(^{15}\)\(^{-}\)\(^{22}\) The only association with failure that we identified in our analysis was prior stent placement in the same segment. Davies at al.\(^{23}\) recently showed that reintervention after iliac stenting is related to increased morbidity and worse long-term outcome, which is in

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**Figure 3** Kaplan-Meier survival estimates of freedom from target lesion revascularization (TLR) for all PTFE-covered iliac stents and for the primary vs. reintervention groups (the latter after previous bare metal stenting).
accord with our data. This emphasizes the importance of choosing the right treatment strategy for each patient and supports the need to identify those patients who might benefit from covered stents. In the recently published COovered vs. Balloon Expandable Stent Trial (COBEST), Mwipatayi et al. found that TASC II C/D lesions treated with primary placement of a covered stent were more likely to remain free of binary restenosis than lesions treated with bare metal stents, indicating that covered stents likely should be recommended for extensive disease.

In our study, the majority of patients had TASC II A/B lesions. Our observation that secondary use of a stent-graft has a poorer outcome compared to primary use supports the assumption that covered stents should not be reserved for reinterventions only. The reason for inferior outcomes after reinterventions using covered stents may be multifactorial. First, stent-grafts may perform less well owing to increased rigidity induced by placing two stents inside each other. However, an increased incidence of stent fractures related to a higher incidence of failure has never been shown. Second, in-stent stenosis is evidence of disease progression, so the severity of underlying disease in patients requiring retreatment might also partly explain the higher incidence of failure in the reintervention group.

The outcome of iliac stenting may depend on various factors, including the stenting strategy, anatomical aspects, and the clinical state of the patient. The Dutch Iliac Stent Trial (DIST) provided evidence that supported a selective stenting strategy in patients treated for intermittent claudication. In contrast, a recent meta-analysis emphasized that a primary stent strategy achieved higher patency rates within the first three years compared to selective stenting for TASC C/D lesions. After five years, however, there was no difference between the two strategies.

Selective stenting may specifically be less feasible for iliac occlusions compared to stenotic disease, as occlusion is expected to lead to a high proportion of stent placements. Five-year primary patency rates of 55% to 85% have been reported for the treatment of iliac occlusions with bare metal stents. During our study, all of our patients were treated using a primary stenting strategy. We did not observe a difference in patency rate between stenoses vs. occlusions using covered stents; similarly, Pulli et al. also found that endovascular treatment of iliac occlusions has similar results as those obtained in the treatment of stenotic lesions.
The TASC II group has recommended surgical treatment for more extensive and bilateral occlusive lesions. Previous studies, however, have shown acceptable long-term outcomes for endovascular treatment of these lesions as well, with primary patency rates varying between 53.5% and 83.0% at five years. In the meta-analysis of Ye et al., the four-year primary patency for a primary stenting strategy, as used in our cohort, was 79.1% (95% CI 55.8% to 91.9%). Our 71.5% four-year primary patency rate for the primary treatment group falls within this confidence interval. Large differences among studies in both patient and lesion characteristics and medical treatment, however, render a comparison unreliable.

We found no significant difference between patients who were treated for TASC II A/B or C/D lesions, which further supports the hypothesis that endovascular treatment of complex iliac lesions may provide a good alternative to surgery, especially in patients with severe comorbidity. Kashyap et al. compared endovascular treatment and surgical bypass for extensive aortoiliac disease; at three years, there was no difference in secondary patency (95% vs. 97%) or limb salvage (98% for both groups). Five-year estimated limb-based patency in surgical bypass is 91.0% (range 64.3%–95.4%), which is accompanied by a 3.3% mortality rate and complication rate of 8.3%. In our study, there was no procedure-related mortality among patients with TASC II C/D lesions.

In the present study, the majority of patients were treated for disabling claudication. We found no significant differences in patency rates between patients treated for CLI and patients treated for intermittent claudication and so we could not confirm previous observations that the clinical state of the patient affects the outcome of stenting. Additionally, there were no significant differences between these groups in terms of hemodynamic or clinical improvement.

**Limitations**

Limitations of this study are mainly related to the retrospective design, which may have caused a selection bias and incompleteness of data. Kissing stents were excluded from the analysis to prevent bias, which allowed results to be calculated on a per-limb basis. Had kissing stents been included, a bifurcation-based analysis per the TASC recommendations would have been more appropriate. This bifurcation-based analysis was developed mainly to compare a kissing stent configuration with a surgical bifurcated prosthesis and would have introduced a new bias in our analysis. The key reference and only randomized controlled trial in this area also used limb patency as primary outcome.
Another possible bias in the present study was the fact that follow-up to four years was limited to only 27 limbs; a larger sample size might have revealed predictors of failure.

**CONCLUSION**

The use of PTFE covered stents for occlusive disease in the iliac arteries achieves good midterm limb patency rates and a high level of freedom from TLR. Secondary stent-graft placement after previous bare metal stenting appears to produce a poorer outcome. Additional studies are indicated to establish subgroups that may specifically benefit from covered stents.

**Acknowledgments**

The assistance of Elisabeth A. Roovers with the statistical analysis of the data was greatly appreciated.
REFERENCES


