Covered stents in aortoiliac occlusive disease

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CHAPTER 6.

Endovascular treatment of occlusive lesions in the aortic bifurcation with kissing polytetrafluoroethylene covered stents

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ABSTRACT

**Purpose:** To determine the clinical outcomes of polytetrafluoroethylene covered balloon expandable stents (CBES) in occlusive lesions of the aortic bifurcation in a kissing stent configuration.

**Material and Methods:** The study included a total of 69 consecutive patients (29 men, 40 women) who underwent kissing stent procedures with CBES between January 2003 and April 2009 in a single center. Patients who were previously treated with CBES were excluded. Follow-up consisted of clinical investigation and duplex ultrasound examination.

**Results:** The primary patency was 88.1% at one year and 71.5% at four years, with secondary patency rates of 88.1% and 75.3%, respectively. For primary treated patients primary patency was 91.3% at one year and 77.1% at four years and for the group that had undergone previous stenting 83.6% and 65.2%, respectively (P=.83). There were also no differences in secondary patency and freedom from TLR. Loss of primary patency was mainly caused by stent occlusions (14 cases, [78%]). The freedom from target lesion reintervention at four years was 76.8%.

**Conclusions:** Patency rates and freedom from target lesion reintervention of CBES in the kissing stent configuration with up to four years follow-up are acceptable and mainly affected by stent occlusions. Studies focusing on optimizing stent configuration and medical care to reduce the incidence of thrombosis are indicated to further improve results.
INTRODUCTION
Symptomatic occlusive lesions of the aortic bifurcation are traditionally treated surgically, when indicated. Patency rates are good, with primary patency rates up to 86% at five years.\textsuperscript{1} Surgical interventions, however, may not always be suitable in patients with co-morbidities or with a hostile abdomen due to previous surgery. The reported 30-day mortality for aorto-bi-femoral bypass is 4.1%, and local and systemic morbidity rates are estimated at 6.3% and 16%, respectively.\textsuperscript{1,2} In addition, late complications may include incisional hernia, with an incidence of approximately 10%, sexual dysfunction with an incidence of 15-25% and small bowel obstruction caused by postoperative adhesion formation.\textsuperscript{3,4}
Endovascular procedures for aortoiliac occlusive disease (AIOD) include the kissing stent technique, in which bilateral iliac stents are simultaneously deployed.\textsuperscript{5-7} Cohort studies describe patency rates of kissing stents between 73% and 100% at one year\textsuperscript{8} and 65% at four years.\textsuperscript{9} Polytetrafluoroethylene covered balloon expandable stents (CBES) may improve patency rates by preventing in-stent restenosis caused by tissue ingrowth and intimal hyperplasia.\textsuperscript{10-14} The aim of this study was to describe the performance of kissing CBES after a follow-up of up to four years for AIOD at the level of the aortic bifurcation.

MATERIALS AND METHODS
Patients
The study included all patients treated with kissing CBES in the aortic bifurcation between September 2003 and April 2009 in a single center. A primary stenting strategy was used to perform approximately 400 procedures for iliac artery using both BMS and CBES. Patients previously treated with CBES in the same segment were excluded from the analysis.

During the study period, 73 kissing CBES procedures in 70 patients were performed. There were 42 primary procedures and 31 secondary procedures after previous endovascular interventions, including 27 BMS placements (4.6±3.1 years earlier) and four covered stent placements. The latter four were excluded from the study, leaving 69 patients for further analysis. One patient underwent BMS placement twice before treatment with kissing CBES, whereas the other 26 patients had one previous BMS placement.
Chapter 6

TABLE 1: Patient characteristics

<table>
<thead>
<tr>
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<th>N</th>
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<tbody>
<tr>
<td>Men</td>
<td>29</td>
<td>42%</td>
</tr>
<tr>
<td>Rutherford Category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2; moderate intermittent claudication</td>
<td>18</td>
<td>26%</td>
</tr>
<tr>
<td>3; severe intermittent claudication</td>
<td>40</td>
<td>58%</td>
</tr>
<tr>
<td>4; ischemic rest pain</td>
<td>4</td>
<td>6%</td>
</tr>
<tr>
<td>5; focal tissue loss</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>6%</td>
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<tr>
<td>Tobacco use</td>
<td>61</td>
<td>88%</td>
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<tr>
<td>Diabetes Mellitus</td>
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<td>Hypertension</td>
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<tr>
<td>Hyperlipidemia</td>
<td>50</td>
<td>72%</td>
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<tr>
<td>Cardiac disease</td>
<td>18</td>
<td>26%</td>
</tr>
<tr>
<td>Carotid disease</td>
<td>9</td>
<td>13%</td>
</tr>
<tr>
<td>Renal disease</td>
<td>6</td>
<td>9%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.2±8.9</td>
<td></td>
</tr>
</tbody>
</table>

There were 29 men and 40 women included in the analysis, with a mean age of 59±9 years. Data were retrospectively collected and anonymously analyzed. Retrospective research of patient’s medical records is not in the scope of the Dutch Law on Human Bound Research, and therefore, Institutional Review Board approval was not required. As a consequence, patient informed consent was not obtained.

Patients’ medical records were analyzed for medical history, demographic data, and co-morbidities, which were graded according the medical co-morbidity scoring system from the Society for Vascular Surgery and the American Association for Vascular Surgery. Intra-operative angiograms were reviewed for TransAtlantic Inter-Society Consensus (TASC)-II-classification. Cardiovascular risk management, including the prescription of statins, was performed in accordance with national guidelines.

Procedure

All procedures were performed in one center by a single interventional radiologist. Procedures were performed under local anesthesia. Femoral access was obtained percutaneous. All patients received 5000 units of heparin intravenously. The Seldinger technique was used to introduce two 7Fr. sheaths, and after recanalization two Advanta V12 stents (Atrium Medical, Maquet Getinge Group, Hudson, NH, USA) were positioned at the aortic bifurcation and deployed simultaneously. When lesions extended distal from the kissing stents, additional stents were placed with minimal stent overlap. Angiographic
images of a case example are provided in fig. 1A and B. Post-operatively, all patients received single antiplatelet therapy using acetyl-salicylic acid orally (80-100 mg). When coumadin derivates or warfarin were indicated for other indications, no acetyl-salicylic acid was added.

**Figure 1A** Preoperative angiography of a 52-year old man suffering from disabling intermittent claudication, not responding to walking exercise, showing significant stenosis of the right common iliac artery and an occlusion of the left common iliac artery.

**Figure 1B** Postoperative angiography after placement of two 8x58mm Advanta V12 covered stents in the iliac arteries. The ankle brachial index increased from 0.65 to 1.10 on the left and from 0.83 to 1.20 on the right side.

**Definitions**

Primary outcomes were primary patency and freedom from target lesion reintervention (TLR). Secondary outcomes were secondary patency, clinical improvement and mortality. The definitions used were according the reporting standards.\textsuperscript{18,19}

Loss of primary patency was defined as a CBES that occluded, a CBES with re-stenosis or a CBES that required reintervention. Re-stenosis was defined as a lesion with a peak systolic value (PSV) ratio ≥ 2.5 as measured with duplex ultrasound, comparing PSV at the site of the lesion to the PSV proximal or distal from the lesion.\textsuperscript{19,20}

Freedom from TLR was defined as the time from the procedure to any new surgical or endovascular procedure performed at the aortoiliac segment to treat recurrent symptoms.
Secondary patency was defined as patent CBES, with all procedures performed aimed at recanalizing an occluded CBES, thereby preserving it. An Ankle-Brachial Index (ABI) improvement of 0.10 was considered clinically relevant.\textsuperscript{18}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Kaplan-Meier survival curves showing patency rates}
\end{figure}

\textbf{Statistics}

Data are presented as mean and standard variation or median and range, depending on the distribution of the variables.
Survival, freedom from TLR, and patency estimates were determined by Kaplan-Meier analysis. Univariate analysis, using the Cox proportional hazard model, was performed
to identify factors that could have affected outcome. Hazard ratios are outlined in forest plots with a 95% confidence interval. Log-rank tests were used to address differences between categorical variables. Paired $t$-tests were used to compare pre- and post-procedural ABI, both for the right and the left limb. Probability values given are based on two-sided analyses of test results. A significance level of 5% was used. All statistical analysis were performed with SPSS 19.0 software (IBM Corp., Armonk, NY, USA).

Figure 3  Kaplan-Meier survival curves show the primary patency of kissing CBES as primary treatment or reintervention after previous treatment.
RESULTS

Of the 69 patients included in the study, 58 were treated for disabling claudication, four for ischemic rest pain, and three for focal tissue loss. No Rutherford category was documented in four patients. According to the TASC-II criteria, 22 TASC A (including 10 patients after previous stent treatment, 9 with bilateral lesions of the common iliac artery [CIA], 3 with lesions in the proximal CIA), 21 TASC B (including 12 patients after previous stent treatment, 7 with bilateral lesions, and 2 with CIA occlusion), 3 TASC C and 23 TASC D lesions were treated with the kissing stent technique.

The stent diameters used in the kissing stent configuration were 7 mm (31% of the stents used), 8 mm (44%), and 9 mm (25%). The stent lengths used were 38 mm (46% of the stents used) and 59 mm (54%). The procedure was completed with the use of two stents (72%) in 50 cases, with three stents (23%) in 16, and in four stents (3%) in one. Five stents were used in one patient (1%) and six stents were used (1%) in another patient to cover the complete lesion length. In seven patients (10%) an additional bare metal stent was placed in the external iliac artery.

Patient survival and follow up

During four years of follow-up, eight patients died, one within 30 days after the procedure. This patient, who was severely obese, died at home, presumably the result of sepsis due to erysipelas, as diagnosed by the general practitioner. Unfortunately, the patient could not be transported to hospital due to severe obesity. A postmortem investigation was not performed, and thus, a stent infection could not be ruled out. The 30-day mortality rate was 1.4%.

Duplex follow-up examination was available for 51 patients at one year, 41 at two years, and 25 at four years. Reasons for loss to duplex follow-up at four years were stent placement of less than four years after inclusion in twelve patients, ten had loss of secondary patency, or surgical replacement. Twelve patients were lost to follow-up due to end-stage non-vascular disease (N=3), refusal/no-show (N=3), follow-up elsewhere (N=4), and unknown whereabouts (N=1). Data on these patients lost to follow-up were included in pre-operative findings, procedural data, and available duplex follow-up. Twenty patients accepted the offer for new duplex investigation at the time of analysis. The resting ABI at the right limb increased significantly from 0.82±0.22 to 1.00±0.17 after treatment (P<.001), the resting ABI at the left limb increased from 0.72±0.22 to 0.97±0.17 (P<.001). A clinical relevant improvement of a mean resting ABI (mean measured over
Kissing covered stents for the aortic bifurcation

both limbs) was found in 43 of 59 patients (73%), no relevant improvement was seen in 12 patients (20%) and in four patients the ABI decreased after treatment (6%). In one patient the decrease was based on an occlusion of the kissing stents, in one patient, the decrease was asymptomatic and the kissing stents were patent. In the latter two patients the ABI decreased from 1.04 to 1.00 and from 1.00 to 0.97, respectively. In ten patients no pre operative or post operative ABI was recorded. In eight patients, no Rutherford category was documented and no treadmill testing was performed. Fifty-one patients of 61 patients (84%) did improve at least one Rutherford category. In ten of the patients treated, no clinical improvement was seen in the Rutherford classification, whereas the mean ABI increased with at least 0.10 in seven of the patients and increased 0.05-0.07 in the other three patients. Why the increased blood flow did not lead to an improved Rutherford category in these patients was not clear from the case files. There were no patients with worsening of symptoms after treatment.

Figure 4A  Influences on primary patency

Patency and freedom from TLR

Primary patency was 96.9% at six months, 88.1% at 12 months, 78.8% at two years and 71.5% at four years (fig. 2). For primary treated patients primary patency was 91.3% at one year and 77.1% at four years, for the reintervention group 83.6% and 65.2%, respectively (P=.83).

Loss of primary patency occurred in 18 patients; this was based on occlusion in 14 patients (78%) and by re-stenosis in four (22%). Twelve of the 14 occlusions occurred in only one stent, and both stents occluded in two patients.
Secondary patency rates were 96.9%, 88.1%, and 82.8% at six, twelve and 24 months, respectively. Estimated secondary patency was 75.3% at four years (fig. 2). For primary treated patients secondary patency was 91.3% at one year and 80.7% at four years, for the reintervention group 83.6% and 69.0%, respectively (P=.67).

Freedom from TLR was 92.4% at one year and 76.5% at four years (fig. 2). For primary treated patients freedom from TLR was 94.9% at one year and 77.9% at four years, for the reintervention group 88.9% and 76.6%, respectively (P=.81).

In three of the 18 cases with loss of primary patency, no reintervention was performed; in the other 15 patients, eight endovascular reinterventions (all but one including new stent placement) and seven surgical bypass procedures were performed.

Univariate analysis showed no significant influence of smoking (P=.20 and P=.59), diabetes mellitus (P=.28 and P=.39), hypertension (P=.09 and P=.08), hyperlipidemia (P=.76 and P=.84), cardiac disease (P=.13 and P=.19), neurologic disease (P=.31 and P=.45), renal disease (P=.33 and P=.46), TASC classification (TASC A/B vs TASC C/D) (P=.87 and P=.79) (fig. 4A and 4B).

One patient experienced abdominal pain after intraluminal stent insertion. The pain did not respond to drug treatment. The patent CBES were removed surgically 15 months later and an aortobifemoral bypass was constructed. Histopathologic examination of the involved stents showed extensive foreign body giant cell reaction. The patient declared to have no allergies before the procedure. There were no tests performed.
DISCUSSION

In this cohort study, we showed that the use of PTFE CBES in the kissing stent technique has acceptable primary patency rates up to four years.

In one randomized controlled trial the use of CBES in TASC C and D lesions resulted in a significantly lower re-stenosis rate compared to the use of BMS\textsuperscript{21}; however, whether CBES also performed better in a kissing configuration, remained unclear in that study.

Only one historical cohort study, by Sabri et al.\textsuperscript{14} favored the use of CBES in this configuration, whereas a more recent cohort study by Humphries et al.\textsuperscript{22} showed significantly better patency rates of BMS compared with CBES.\textsuperscript{14,22} The conclusions of these studies might be contradictory because of different definitions of patency. In the study by Humphries et al.\textsuperscript{22}, patency rates were only calculated by the number of stent occlusions or reinterventions. No follow-up was done for re-occurrence of stenosis. Sabri et al.\textsuperscript{14}, in contrast, included re-stenosis in the definition of loss of primary patency. Furthermore, the choice of the type of stents used (BMS vs CBES) and the choice for reintervention were made on a case-by-case basis in the study by Humphries et al.\textsuperscript{22}, which could have influenced the performance of CBES. Published results of kissing stents in the aortic bifurcation in other cohort studies are difficult to compare because of the use of different definitions, techniques and case mixture. Hopefully the DISCOVER (Dutch Iliac Stent trial: COVERed balloon-expandable versus uncovered balloon-expandable stents in the common iliac artery) trial may clarify if CBES have less binary re-stenosis in the iliac tract than BMS.\textsuperscript{23}

A comparison of endovascular results with more historical results of surgical procedures may also not be reliable due to changes in peri-operative risk management, medication and lesion morphology. Possibly, the percentage of TASC-II D lesions is higher in surgically treated patients, whereas in our cohort, only 33% were classified as TASC-II D.

In our study, primary patency at two years was 79%, which was lower than the reported 92% at two years by Sabri et al.\textsuperscript{14} Possibly our results were influenced by the large number of patients (45%) treated for recurrent disease. However, at univariate analysis, we did not find significant differences between the primary and the reintervention treatment group (fig. 3). In another patient cohort treated with single CBES in the iliac artery, we found that previous stent placement was a factor that might have influenced the outcome.\textsuperscript{24} The sample size of the cohort in this study might have been too small to demonstrate such an influence, accounting for a possible type 2 statistical error. The difference might also be explained by the difference in antiplatelet therapy. In contrast
to the Covered Versus Balloon Expandable Stent Trial (COBEST)\textsuperscript{21} and the comparative cohort study by Humpries et al.\textsuperscript{22}, our patients received single antiplatelet therapy only. Patients in the studies mentioned received dual antiplatelet therapy for at least one month and acetyl salicylic acid solely thereafter, and continued dual antiplatelet use was associated with better overall primary patency rates.\textsuperscript{22} At the time of treatment of our cohort, this information was not available yet.

A submitted systematic review that included 10 kissing stent studies found a mean primary patency rate of 88.8\% at one year and 68.5\% at five years. These results were comparable to the primary patency rates in this patient cohort of 88.1\% at one year and 71.5\% at four years.

Loss of primary patency in 78\% of the cases was caused by occlusion and only in 22\% by re-stenosis. The reason for the high number of occlusions may be threefold: First, the study had a retrospective character, and follow-up by duplex ultrasound imaging was not performed at regular follow-up intervals. Patients may only experience clinical deterioration in case of stent occlusion and less in case of re-stenosis; therefore, a duplex ultrasound examination performed for clinical deterioration may show more occlusions. However, in half of the patients, the duplex ultrasound assessment before to the occlusion showed no signs of abnormalities. Second, compliance with therapy was not routinely checked or documented, even after a demonstrated occlusion. Only in three patients possible causes for occlusion were documented. The first was an occlusion that occurred after a knee arthroscopy with the use of a tourniquet, 11 months after the procedure. The second occurred after severe dehydration that was accompanied by a low flow state. No possible cause could be pointed out or was documented in the other 12 occlusions. Third, the geometry of the kissing stent configuration, especially radial mismatch, might have contributed to thrombus formation and subsequent stent occlusion.\textsuperscript{25-27} CBES in a kissing stent configuration create a higher radial mismatch compared with the use of BMS, in theory leading to thrombus formation by dead space perfusion.\textsuperscript{28} To create a more physiologic situation, the use of endovascular aneurysm repair devices and the Covered Endovascular Reconstruction of the Aortic Bifurcation technique have been described.\textsuperscript{29,30}

Limitations of this study are related to its retrospective design, which lacks information on indication, technical failures, and also routine ABI measurements and pulse volume recording. Moreover, information on complications could not be retrieved reliably. Another limitation is the small number of patients (N=25) at risk at four years. At the
time of data collection, however, 12 patients had undergone an intervention before the year assessments. Eight patients died within four years of the procedure, and there were nine failures; thus, only 40 patients were available for four year follow-up. We could provide duplex follow-up data on 25 of 40 patients (63%), and we therefore think this patient cohort gives a good representation of current clinical practice. Moreover, a stent infection could not be ruled out in one patient that died within 30 days due to a sepsis. One patient treated with CBES for isolated stenosis of the infrarenal aorta was described earlier with a stent infection. Although there is no literature confirming this, CBES might be more prone to infection than BMS. Implantation should therefore preferably be performed in a sterile environment under antibiotic prophylaxis. Most of our procedures were performed at the radiology department with percutaneous access. In this study, patency rates and freedom from TLR of PTFE covered stents in the kissing stent configuration are within acceptable range within four years of intervention. Because patency rates were mainly affected by stent occlusions, future studies are indicated to reduce thrombus formation by optimizing medical care and stent configuration.
REFERENCE LIST


