Iliac artery revascularization: overview of current interventional therapies

The treatment of patients with peripheral arterial disease has evolved tremendously since the early 1960s, when Charles Dotter first successfully revascularized a superficial femoral artery occlusion in a patient with critical limb ischemia. Endovascular interventions have become the preferred therapy, as studies show equivalent, if not superior, procedural success and clinical outcomes compared with open-surgical options. Numerous devices have been developed over the last several decades, from percutaneous transluminal angioplasty to stenting with bare-metal and covered stents. Many of the stents used in vascular therapies were developed for use in the biliary system. Off-label use in the iliac and infrainguinal arteries is a regular practice, but well-designed clinical trials are needed to verify safety and effectiveness of these devices in various vascular beds. Several trials have been carried out, and are reviewed in this article, evaluating balloon-expandable, self-expandable and covered stents in the treatment of iliac occlusive disease.

KEYWORDS: balloon-expandable stent ▪ covered stent ▪ iliac occlusive disease ▪ percutaneous transluminal angioplasty ▪ self-expanding stent

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The prevalence of peripheral arterial disease (PAD) increases progressively with age. The relationship between PAD prevalence and age was illustrated in an analysis of 2174 participants at least 40 years of age, in the 1999–2000 National Health and Nutrition Examination Survey (NHANES) [1]. The prevalence of PAD, defined as an ankle-brachial index (ABI) less than 0.90 in either leg, was 0.9% between the ages of 40 and 49 years, 2.5% between the ages of 50 and 59 years, 4.7% between the ages of 60 and 69 years, and 14.5% for those aged at least 70 years. As a result, PAD is growing as a clinical problem, owing to the increasingly elderly population in the USA and globally.

The PAD Awareness, Risk and Treatment: New Resources for Survival (PARTNERS) program reported a higher prevalence of PAD among primary-care practices across the USA, in which almost 7000 patients aged at least 70 years, or 50–69 years, with a history of cigarette smoking (more than 10 years) or diabetes, were evaluated by history and by ABI (with a value ≤0.90 considered diagnostic of PAD) [2]. PAD was present in 29% of patients overall; 13% had PAD alone (55% newly diagnosed) and 16% had PAD and cardiovascular disease (35% newly diagnosed). A classic history of claudication was present in only 11% of patients with PAD. This study revealed the underdiagnosis of PAD in the general population.

The iliac arteries are vessels that are commonly diseased in patients with PAD. Although historically, surgical repair was performed for iliac artery disease, now most physicians prefer endovascular management, as rates of procedural success and long-term outcomes are similar to those achieved with surgical revascularization but with reduced morbidity and mortality [3–5]. There are several endovascular options, including percutaneous transluminal angioplasty (PTA), balloon-expandable stents, self-expanding stents and covered stents. The acute procedural success rate after stent implantation in the iliac arteries is greater than 95% [5], and excellent long-term patency has been reported [6–11].

PTA versus stenting

Several randomized studies, comparing endovascular stenting with stand-alone PTA, demonstrated stenting to be superior in both hemodynamic parameters and Rutherford classification. A meta-analysis of iliac artery intervention demonstrated that stent placement reduced the risk of long-term failure by 39% when compared with PTA alone. In a longer than 4-year follow-up, only 67% of the PTA group showed clinical improvement (one or more Fontaine class), whereas approximately 90% of the stent group improved [12]. Multiple other studies have demonstrated an increasing superiority of stents compared with balloon angioplasty [13–22].

The Dutch Iliac Stent Trial Study Group performed a randomized comparison of primary stent placement with primary angioplasty, followed by selective stent placement in 279 patients (356 limbs) with iliac artery

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occlusive disease. Less than 10% of the limbs treated were total occlusions. The investigators demonstrated that selective stent placement, in which a stent is placed after iliac artery angioplasty, when there is a pressure gradient of more than 10 mmHg across the treated site, was equally as effective in maintaining iliac patency compared with primary stent placement. They also showed that the selective stent placement is more cost effective than primary stenting of iliac artery stenosis [23,24]. However, there was a high crossover rate with nearly half (43%) of the patients randomized to balloon angioplasty, necessitating stent placement for a suboptimal result during the primary procedure. In addition, complication rates were nearly doubled (4 vs 7%) in the angioplasty group. Interpretation of these study results is difficult, owing to a mean follow-up of less than 1 year and low acute technical success rates (~80% for both groups). A later report with 5-year follow-up of this study did not find a significant difference between the groups, although repeat intervention was more common in the angioplasty group [25].

A meta-analysis of more than 1300 patients, comparing iliac angioplasty and stenting, found significantly higher acute technical success, as well as improved primary patency in both claudicants and those with limb-threatening ischemia [12]. The 4-year primary patency rates were 65% for stenosis versus 54% for total occlusions after PTA to treat claudication, and were 53% for stenosis versus 44% for occlusions after PTA to treat critical ischemia. These rates were 77% for stenosis versus 61% for occlusions after stent placement to treat claudication, and 67% for stenosis versus 53% for occlusions after stent placement for critical ischemia. In this study, stent placement was found to reduce the risk of long-term failure by 39% compared with PTA alone. In another study on 106 patients, kissing iliac stents showed good results in aortic bifurcation disease, which can be very problematic for balloon angioplasty, with primary and secondary patency rates of 78 and 98%, respectively, at 3 years [26]. Even in chronic total occlusions of the iliac artery, one can expect early technical success in up to 97% of procedures using balloon-expandable stents, with 3-year primary and secondary patency rates of 70 and 80%, respectively [23].

■ Balloon-expandable stents

Several balloon-expandable stents have been used in the iliac artery, however, they have not had a primary indication for iliac stenting. The Express® LD iliac premounted stent system (Boston Scientific, MA, USA) is currently the only available premounted balloon-expandable stent that is approved by the US FDA for the treatment of iliac artery atherosclerotic disease.

■ Express LD iliac stent

The Express LD stent was approved in March 2010 for the treatment of atherosclerotic lesions found in iliac arteries up to 100 mm in length, with a reference diameter of 6–10 mm (Figure 1). The device has been commercially available as a biliary stent in the USA since October 2002, and as a peripheral vascular stent since July 2002 in 76 countries [101,102]. The device is fabricated from 316L stainless steel tubing, laser cut into a geometric pattern consisting of large and small sinusoidal bands (Macro™ and Micro™ elements) interconnected by longitudinally oriented struts (Tandem Architecture™). The Express LD stent technology is designed to work in tandem to provide flexibility, conformability and consistent radial strength along with balanced stent deployment accuracy. The device comes in lengths of 17, 27, 37 and 57 mm, and maximum expanded diameters of 9 and 11 mm.

The device delivery system consists of a noncompliant balloon catheter available in lengths of 75 and 135 cm, and has two radiopaque balloon markers embedded in the shaft to aid in the placement of the stent. The 6 and 7 Fr stent delivery system is compatible with 0.035-inch guidewires. The balloon has a maximum inflation pressure of 12 atm (1216 kPa), which can be used for initial stent placement and post-stent dilatation.

Figure 1 illustrates a patient with an iliac artery occlusion, treated successfully with an Express LD stent.

■ MELODIE trial

The Boston Scientific Corporation Multicenter, Single-Arm Study to Obtain Additional Data on the Safety and Efficacy of the Express Vascular LD Stent Implantation in the Treatment of Stenosed or Occlusive Atherosclerotic Disease in Iliac Arteries (MELODIE) trial, is the report of the FDA study sponsored by Boston Scientific Corporation, leading to approval of the Express stent for marketing as an iliac stent [27]. The study was a prospective, single-armed clinical trial, which enrolled 152 subjects at ten centers in Europe and Canada, and was designed to assess the safety and effectiveness of the Express LD stent at 6 months, compared with historical results representative of the Palmaz balloon-expandable stent, as reported in the literature [28,29]. Subjects were treated between 7 January

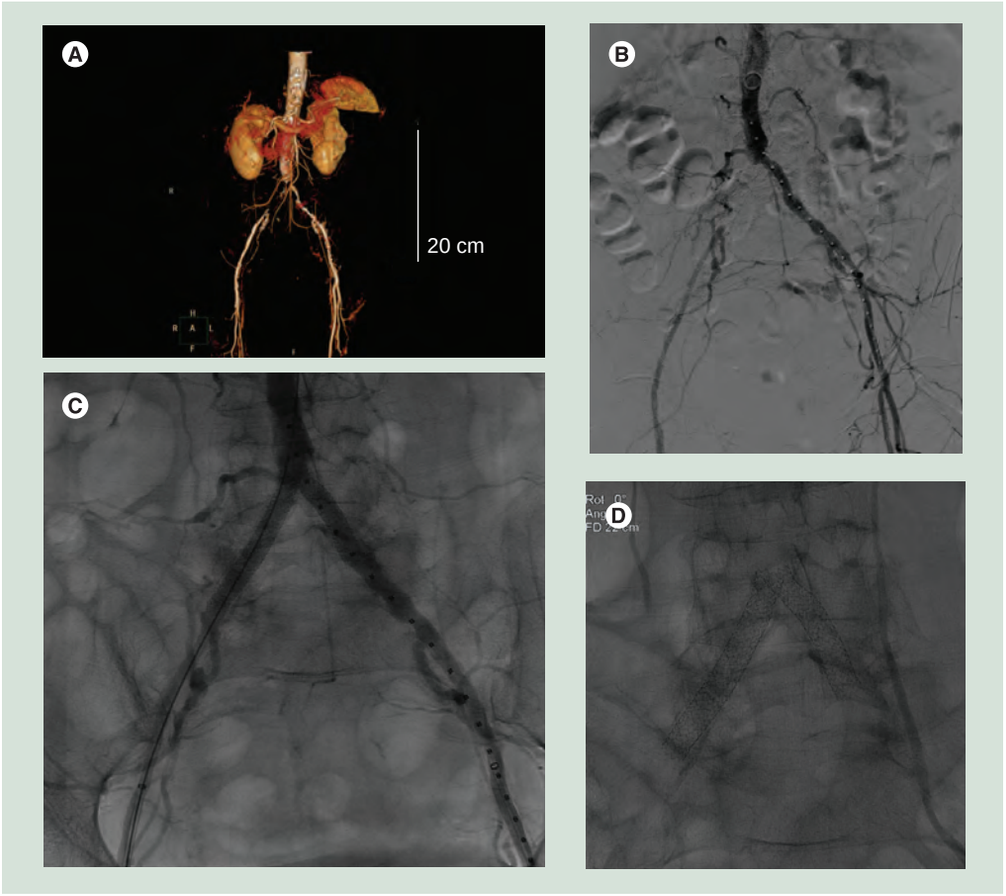

Figure 1. A 66-year-old woman presented with 6 months of right buttock and lower extremity claudication. (A) 3D reconstruction of a computed tomography angiogram demonstrates occlusion of the right common iliac artery. **(B)** Angiogram, again demonstrating the right iliac occlusion with reconstitution of the distal right common iliac artery before its bifurcation. In addition, note a prominent lumbar collateral. **(C)** Angiogram after successful recanalization of occluded right common iliac artery and placement of 'kissing' iliac Express® LD stents. **(D)** Fluoroscopic image demonstrating the details of the bilateral iliac Express LD stents.

2004 and 4 February, 2005, and included patients with chronic symptomatic *de novo* or restenotic atherosclerotic disease in the common and/or external iliac arteries (Fontaine class IIa, IIb and III), had a baseline percentage diameter stenosis of at least 50% at the target lesion, reference vessel diameter of 5–10 mm, and length of diseased segment(s) no greater than 10 cm. Prior to the stenting procedure, subjects were given anticoagulant and/or antiplatelet treatment, according to the routine practice of the participating study center. The use of heparin was permitted during the procedure according to routine practice at the participating study center. After the procedure, subjects were administered aspirin 100 mg once daily during the entire 24-month follow-up phase of the study, or clopidogrel 75 mg once daily if the use of aspirin was contraindicated. Subjects were also permitted to take additional anticoagulant/antiplatelet medications, if indicated. Follow-up included office visits at 30 days, and 6, 12 and 24 months. Angiographic follow-up was performed at 6 months, and computed tomography angiography (CTA) at 12 and 24 months.

The primary end point of the study was to assess mean percentage loss of luminal diameter at 6 months postintervention, based on core laboratory angiographic assessment. Secondary and tertiary end points included technical success of immediate postprocedure of less than 30% residual stenosis, hemodynamic success of improved ABI by more than 0.1 above preprocedure value and not deteriorated by more than 0.15 from maximum postprocedure value, clinical success by improvement of Fontaine class by at least one class compared with preprocedural classification, angiographic binary restenosis (stenosis of the target lesion of >50% of the reference vessel diameter assessed at 6 months), major adverse events, including death, target vessel revascularization, distal embolization related to the device; and CTA target lesion patency.

Technical success was 98%. The mean percentage late-loss luminal diameter at 6 months was 16.2% for the Express LD stent. This result was statistically significant and lower than the historical data on the Palmaz stent, with a p-value of 0.0061, demonstrating noninferiority of the Express stent for the treatment of atherosclerotic disease of the iliac arteries. Angiographic binary restenosis at 6 months was 5.6%. CTA target-lesion patency was 97.2 and 94.1% at 12 and 24 months, respectively. The incidence of target-lesion revascularization was 6.5, 9.0, and 10.2% at 6, 12 and 24 months, respectively. The MELODIE trial also demonstrated the safety of iliac artery revascularization with the Express LD stent, with no procedure-related death or distal embolization. Clinical improvement was observed, with the ABI increasing by more than 0.2 above the preprocedure value at 2-year follow-up.

Self-expanding stents

With the introduction of self-expanding stents, an increased number of complex diseases were treated, with success rates comparable to those of open surgery [14,15]. In a contemporary study, the use of the stainless steel Wallstent® (Boston Scientific Corporation) had a 6-year primary patency rate of nearly 80% in claudicants [14]. The Wallstent device is a self-expanding stent made from elgiloy, a 'superalloy' combining cobalt, chromium, nickel and a relatively small amount of iron and, therefore, is nonferromagnetic and MRI compatible. A platinum core renders the stent struts radiopaque. The woven-mesh design of the struts imparts flexibility, as well as an outward self-expanding force to the stent. The delivery system employs an inner shaft and outer constraining sheath, with radiopaque markers to facilitate accurate placement. The Wallstent is reconstrainable, even when it is up to 87% deployed and, therefore, can be repositioned during deployment, if necessary.

The Cordis® shape-memory alloy recoverable technology (SMART) nitinol self-expanding stent (Cordis, Inc., FL, USA) is a self-expanding crush-resistant stent, with a unique segmental design and high flexibility. The device was approved by the FDA in 2003. The SMART stent is a flexible, fine-mesh tubular prosthesis, which expands on deployment. The delivery system consists of an inner shaft and an outer sheath, locked together with a valve, with the self-expanding stent constrained in the space between the two. Radiopaque markers at the distal and proximal ends of the shaft allow fluoroscopic visualization. For deployment, the outer sheath is unlocked from the shaft, and retracted proximally relative to the inner shaft. The stent is considered fully deployed when the radiopaque marker on the distal end of the sheath is proximal to the inner-shaft marker. The stent cannot be significantly repositioned after deployment has started, and the device cannot be reconstrained.

The Cordis Randomized Iliac Stent Project (CRISP)-US trial was a prospective, randomized trial, comprising of 203 patients with chronic limb ischemia, randomized to either the SMART stent (n = 102) or the Wallstent (n = 101) after suboptimal PTA [30]. Patients were prescribed aspirin (81–325 mg) for at least 3 months postprocedure. The primary equivalent end point was a composite of 9-month restenosis, 30-day death and 9-month target vessel revascularization. Functional, clinical and hemodynamic assessments were made at hospital discharge, and at 1, 6, 9 and 12 months. The 9-month composite end-point rate was equivalent for the SMART stent and Wallstent (6.9 vs 5.9%), with low rates of restenosis (3.5 vs 2.7%), death (2.0 vs 0.0%) and revascularization (2.0 vs 4.0%) in both groups. Primary patency at 12 months was 94.7 and 91.1% with the SMART stent and Wallstent, respectively. Functional and hemodynamic improvement was also comparable between the groups. The acute procedural success rate was higher in the SMART stent group (98.2 vs 87.5%; p = 0.002). The frequency of major adverse events was similar at 1 year (4.9 vs 5.9%).

The Zilver® vascular stent (Cook, IN, USA) is a self-expanding stent made of flexible laser-cut nitinol tubing. The Zilver stent is designed to be highly flexible and to have a high radial force. Its unique geometry prevents the stent from shortening upon deployment, a property that, together with gold markers at each end, improves the accuracy of stent placement and helps ensure that the lesion is covered completely.

A prospective, multicenter, single-armed clinical trial compared the Zilver stent to an objective performance criterion of less than 16% for major adverse events rates [31,32]. A total of 151 consecutive patients were implanted with Zilver vascular stents, regardless of the results of an initial PTA, in up to two stenotic (<10 cm) or occluded (<5 cm) atherosclerotic lesions of the external or common iliac arteries. Approximately 50% of patients received aspirin, 36% of patients received clopidogrel periprocedurally,

and 76% received aspirin and/or clopidogrel at discharge. The primary end point was the rate of major adverse events up to 9 months after the procedure. Major adverse events were defined as death, myocardial infarction, target lesion revascularization and limb loss. Secondary end points included acute procedural success, 30-day clinical success, 9- and 12-month patency rate and functional status (on the basis of the validated walking-impairment questionnaire) and ABI. Results of 1-, 6-, 9- and 12-month follow-up are reported.

The 9-month device and/or procedural-related major adverse event rate was 2.7% with no increase at 12 months. The all-cause major adverse event rate was 7.5%. Both rates were substantially below the prespecified objective performance criterion of 16%. The acute procedure success rate and 30-day clinical success rate were 98.0 and 94.0%, respectively. The 9-month patency rate, measured with duplex ultrasonography, was 92.9%. At 12 months, the patency rate was 90%. There was a statistically significant improvement in the ABI, with an approximate increase of 0.2, which was maintained at 9-month follow-up. Differences in ABI between 9 and 12 months were not statistically significant. In addition, there was an improvement in walking distance and walking speed scores, relative to preprocedural values at 9 months, with a slight drop at 12 months compared with the 9-month scores.

Covered-stent grafts

Self-expanding polyethylene terephthalate and polytetrafluoroethylene (PTFE)-covered stents have been shown to decrease the need for repeat procedures in the iliac artery [33]. Similar to surgical bypass, minimal luminal diameter may affect the patency of these stents.

The Gore Viabahn® endoprosthesis (originally marketed under the name Hemobahn®) and the Gore Viabahn endoprosthesis with heparin bioactive surface (WL Gore & Associates, AZ, USA) are FDA approved for use in patients with symptomatic iliac artery lesions, with reference vessel diameters ranging from 4.0 to 12 mm, and are also FDA approved for use in patients with symptomatic superficial femoral artery lesions with reference vessel diameters ranging from 4.0 to 7.5 mm. The Viabahn is a flexible, self-expanding endoluminal endoprosthesis, consisting of an expanded PTFE lining, with an external nitinol support extending along its entire length. The device is also available with a heparin bioactive surface, where the surface of the endoprosthesis is modified with covalently bound, bioactive heparin. The endoprosthesis is compressed and attached to a dual-lumen delivery catheter. The larger central catheter lumen is used for flushing and guidewire introduction. The smaller lumen contains elements of the deployment mechanism. The delivery catheter hub assembly has one port for the deployment system, and one port for flushing and guidewire insertion. To facilitate accurate endoprosthesis placement, two radiopaque metallic bands are attached to the catheter shaft, marking the ends of the compressed endoprosthesis. The device is available in 5–13 mm diameters, and the delivery sheath ranges from 7 to 12 Fr.

The most extensive prospective multicenter data on the Hemobahn endograft comes from a trial conducted in Europe and the USA, treating 61 iliac and 80 femoral arteries for superficial femoral artery occlusive disease between 1996 and 1998 [34]. The purpose of this study was to investigate the safety and efficacy of the Hemobahn endograft. Clinical category status, ABI and color-flow duplex imaging results were recorded before treatment, at discharge, and 1, 3, 6 and 12 months after treatment. Clinical effectiveness was determined by using the chronic limb ischemia categories, proposed by the Society of Vascular Surgery and the International Society of Cardiovascular Surgery. Limb ischemia categories were scored from grade 0 for asymptomatic, to grade 6 for major tissue loss with a functional foot that can no longer be salvaged. Clinical effectiveness was defined as improvement by at least one clinical category level over the pretreatment level. Aspirin was administered throughout the study, and heparin was administered during, and 2 days after, the procedure. The Clinical Status Scale is a functional grading scale, from -3 (markedly worse), to 0 (baseline), to +3 (markedly better).

In 53 patients (61 limbs), an iliac arterial obstruction (stenosis or occlusion) was treated. The common iliac artery was treated in 32 limbs, and the external iliac artery was treated in 29 limbs. Complications occurred in ten iliac procedures, and included one major complication (infection). Early thrombosis (within 30 days) occurred in one iliac artery. Late restenosis or reocclusion was observed in five iliac arteries within the first year.

The 1-year primary and secondary patency rates in this patient population, based on color-flow duplex ultrasound findings, were 91 and

95% in the iliac arteries. In the iliac group, the mean ABIs were 0.59 before treatment and 0.92, 0.91, 0.93 and 0.85 at 1, 3, 6 and 12 months after treatment, respectively. During follow-up, early occlusion of the prosthesis (within 30 days) occurred in one limb in the iliac-treatment group, and late occlusions (30 days–12 months) occurred in an additional five limbs in the iliac group. Pretreatment chronic limb ischemia categories for the 53 patients in the iliac arterial-treatment group were as follows: no patients with grade 0, five with grade 1, 22 with grade 2, 21 with grade 3, two with grade 4 and three with grade 5. At 1 year after treatment, chronic limb ischemia grades were reported for 46 patients in the iliac-treatment group as follows: 29 with grade 0 ischemia, seven with grade 1, seven with grade 2, three with grade 3, and none with grades 4–6. In addition, Clinical Status Scale scores at 1 year after treatment were reported for 44 patients in the iliac-treatment group: one patient showed a mild decline (score: 21), four showed no change or minimal improvement (score: 0 or 11), ten showed moderate improvement (score: 12) and 29 showed marked improvement (score: 13). The authors concluded that the Hemobahn endoprosthesis can be implanted without additional risks to the patient and provided encouraging patency rates up to 1 year.

The Covered Balloon-Expandable Stent (COBEST) trial is a randomized, multicenter, prospective trial, being conducted in Australia, comparing Atrium's (Atrium Medical Corporation, NH, USA) proprietary balloon-expandable covered-stent technology (Advanta V12® covered stent; iCAST® in the USA) to bare-metal stents, commonly prescribed for iliac occlusive vessel disease [35]. The Advanta V12 covered stent is a low-profile premounted covered stent, made of a radial-expandable stainless steel stent, which is completely encapsulated with a patented microporous layer of expanded PTFE film.

The study randomized 167 limbs (123 patients) from 12 hospital centers across Australia. Patients were included if they had TransAtlantic Inter-Society Consensus (TASC) B, C or D iliac occlusive disease. A total of 83 limbs were randomized to the Atrium Advanta V12 covered-stent group, and 84 limbs were randomized to the bare-metal stent group. All patients were administered clopidogrel and aspirin postprocedurally. Patient characteristics were similar in all groups, except for a greater percentage of patients with hypertension in the bare-metal stent group, and a greater number of challenging TASC D lesions in the Atrium covered-stent group.

The primary objective of COBEST is to compare the outcome benefits of balloon-expandable covered-stent technology to the current standard of care with bare-metal stents. This clinical study comparison included binary restenosis (renarrowing of the vessel within the treated stent region), and freedom from stent occlusion (a complete blockage), primarily assessed through duplex ultrasonography up to 18 months. Secondary objectives included comparing amputation rates, noninvasive tests, including ABIs, and symptomatic patient outcomes, based on type-of-lesion classification (TASC B, C and D), target vessel revascularization, as well as patient relief at each time interval up to 18 months. The interim data represented 160 limbs with a full 12-month follow-up, with 132 limbs having reached the 18-month time frame. Of note, there were fewer patients with TASC D lesions in the bare-metal stent group (7%) compared with the covered-stent group (16.1%).

The Atrium covered-stent group had significantly less binary restenosis than the bare-metal stent group ($p < 0.0175$), and greater freedom from stent occlusion compared with bare-metal stents ($p < 0.0173$). At 18 months, 95.4% of the covered-stent group were free of binary restenosis, compared with 82.2% for the bare-metal stent group. Of the covered-stent patients, 94.2% showed a clinical improvement at 18 months compared with 76.7% in the bare-metal stent group ($p < 0.008$). The covered-stent group also experienced a lower amputation rate (1.2 vs 3.6%) and a lower complication rate (4.8 vs 10.7%). No deaths were reported in the study.

Analysis of the lesion classification showed superiority of the Advanta V12 covered stent in type C and D lesions over bare-metal stents. While no significant difference was observed in the overall patency rate of the randomized clinical trial in patients with type B lesions, the interim results of the COBEST trial demonstrated that there is a significant benefit when using the covered stent in type C and D lesions with regard to binary restenosis, freedom from occlusion and clinical improvement. Bare-metal stents in this clinical study experienced a fivefold increase in target lesion revascularization.

Conclusion

The prevalence of PAD steadily increases with age, and continues to grow as a clinical problem owing to the increasing elderly population in the

USA and globally. With the advent of endovascular techniques, the majority of patients with iliac artery occlusive disease are being treated with minimally invasive techniques with excellent outcomes. The vascular interventionalist's armamentarium has grown, as the need for improved radial force, flexibility, trackability, lower-profile devices, accurate deployment and superior long-term patency, grows to treat a wider selection of patients.

Placement of endovascular stents are the accepted therapy for iliac artery occlusive disease. The utility of selective provisional stenting to salvage iliac lesions after failed or unsatisfactory PTA, owing to elastic recoil, flow-limiting dissection or residual gradient, is well established. A primary stent philosophy offers many benefits, including improved technical success, the ability to treat complex disease and lower radiation exposure and contrast use compared with selective stenting after suboptimal PTA. In addition, complications from dissection, acute vessel closure and distal embolization are significantly decreased, and long-term restenosis rates appear to be significantly improved.

While there are no randomized clinical trials to show that primary stenting offers clinical benefit in total occlusions of the iliac vessels, numerous cohort studies and retrospective reviews have suggested improved patency and clinical outcomes compared with angioplasty alone. The Dutch Iliac Stenting trial is the only

Executive summary

Background

- The prevalence of peripheral arterial disease continues to grow as a clinical problem as the elderly population increases.
- Revascularization using endovascular techniques is the accepted treatment for many patients with critical limb ischemia.
- Endovascular technologies continue to evolve and the vascular interventionalist's armamentarium grows along with it, allowing a wider patient population to be treated.
- Numerous studies have shown that stent placement is superior to percutaneous transluminal angioplasty (PTA) alone in maintaining patency of treated vessels and improving clinical outcomes. Failure after PTA usually arises owing to dissection, elastic recoil or myointimal proliferation.
- The Dutch Iliac Stenting Trial is the only prospective randomized trial comparing primary stenting versus primary PTA, followed by selective stenting after failed PTA. The authors concluded that primary PTA and selective stenting of the iliac arteries had better long-term outcomes for symptomatic success compared with primary stenting. There were no differences in iliac patency, ankle-brachial index (ABI) or quality of life between the two groups. Repeat intervention and complication rates were higher in the primary PTA group.

Balloon-expandable stents

- The Boston Scientific Express LD premounted balloon-expandable stent is currently the first and only premounted balloon-expandable stent that has US FDA approval for use in iliac disease.
- The Multicenter, Single-Arm Study to Obtain Additional Data on the Safety and Efficacy of the Express Vascular LD Stent Implantation in the Treatment of Stenosed or Occlusive Atherosclerotic Disease in Iliac Arteries (MELODIE) trial was a multicenter, single-arm study, including 152 subjects in Europe and Canada, and showed noninferiority in terms of mean percentage luminal late loss at 6 months compared with the literature derived to objective performance criteria of the Palmaz stent.
- The original prospective multicenter trial of the Palmaz stent included 486 patients. The mean luminal late loss was 15%, plus or minus 16%. Primary patency was 92%.

Self-expanding stents

- The Cordis® Randomized Iliac Stent Project – US (CRISP-US) trial was a prospective randomized trial, including 203 patients with chronic limb ischemia, randomized to either the Cordis nitinol shape-memory alloy recoverable technology (SMART) stent or the Boston Scientific elgiloy (superalloy) Wallstent® after suboptimal PTA.
- There was no statistically significant difference in the 9-month composite end point of restenosis rate, perioperative death or target lesion revascularization between the two groups. The 12-month primary patency rates between the two groups (94.7 vs 91.1% for the SMART stent vs Wallstent, respectively) were not statistically significant.
- The authors concluded that the SMART stent was equivalent to the Wallstent in treating iliac occlusions.
- In a safety and effectiveness trial of the Cook Zilver® nitinol stent, including 151 patients, the 9-month major adverse event rate of 2.7% compared with the literature-derived objective performance criteria of 16%. The 9-month patency rate was 92.9%.

Covered stents versus bare-metal stents

- The Covered Balloon Expandable Stent (COBEST) trial is an ongoing prospective randomized trial of 123 patients, randomized to the Atrium V12® covered stent, compared with balloon-expandable bare-metal stents in the treatment of aortoiliac disease. The Cordis Palmaz stent and the Boston Scientific Express® LD stent were the primary bare-metal stents used in this trial.
- Interim results, thus far, show that, at 18 months, there were statistically significantly less binary restenosis among the covered-stent group compared with the bare-metal stent group.
- The 12-month target-lesion revascularization was 1.1% in the covered-stent group, compared with 4.7% in the bare-metal stent group.
- Of the patients in the covered-stent group, 95.4% were free from restenosis, compared with 82.2% in the bare-metal stent group.
- The amputation rate was 1.2% in the covered-stent group, compared with 3.6% in bare-metal stent group.

randomized trial comparing selective stenting after failed PTA to primary stenting and, in this trial, only a small number (<10%) of patients in either treatment arm had total occlusions. In the authors' experience, primary stenting is the preferred treatment for patients presenting with iliac stenosis and total occlusions.

Future perspective

Overall, stenting of the iliac arteries has excellent immediate and long-term results, with 12-month primary patency rates above 90% in most trials. Despite the advances made in the technology, in-stent restenosis remains a problem. In the continued drive to improve the long-term primary patency of stents, several technologies have been studied, including drug-eluting balloons, drug-eluting stents and bioabsorbable stents.

Randomized controlled studies in interventional cardiology have shown decreased restenosis and reintervention rates after coronary stenting with drug-eluting stents. Despite early favorable results, lessons learned from the interventional cardiology trials suggest that drug-eluting devices require longer-term follow-up (an order of years, not months) to evaluate safety and complications, such as late stent thrombosis. Moreover, in analyzing and comparing devices, it is important to note that each device is unique, with different pharmacologic agents, stent platform and drug-delivery polymer vehicles.

Drug-eluting balloons, drug-eluting stents and bioabsorbable stents may have a potential role in the treatment of iliac artery occlusive disease. Further studies of these technologies in this particular vascular bed are necessary.

Financial & competing interests disclosure

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Bibliography

Papers of special note have been highlighted as:
▪ of interest

1 Selvin E, Erlinger TP: Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999–2000. *Circulation* 110(6), 738–743 (2004).

2 Hirsch AT, Criqui MH, Treat-Jacobson D *et al.*: Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 286(11), 1317–1324 (2001).

3 Norgren L, Hiatt WR, Dormandy JA *et al.*: Inter-society consensus for the management of peripheral arterial disease (TASC II). *J. Vasc. Surg.* 45(Suppl. S), S5 (2007).

4 Faries P, Morrissey NJ, Teodorescu V *et al.*: Recent advances in peripheral angioplasty and stenting. *Angiology* 59, 617–626 (2002).

5 Rosanio S, Tocchi M, Uretsky BF, Stouffer GA: Use of intraluminal stents in the treatment of carotid, renal, and peripheral arterial disease. *Am. J. Med. Sci.* 319, 111–117 (2000).

6 Hood DB, Hodgson KJ: Percutaneous transluminal angioplasty and stenting for iliac artery occlusive disease. *Surg. Clin. North Am.* 79, 575–596 (1999).

7 Martin EC, Katzen BT, Benenati JF *et al.*: Multicenter trial of the Wallstent in the iliac and femoral arteries. *J. Vasc. Interv. Radiol.* 6, 843–849 (1995).

8 Henry M, Amor M, Beyar R *et al.*: Clinical experience with a new nitinol self-expanding stent in peripheral arteries. *J. Endovasc. Surg.* 3, 369–379 (1996).

9 Vorwerk D, Günther RW, Schürmann K, Wendt G: Aortic and iliac stenoses: follow-up results of stent placement after insufficient balloon angioplasty in 118 cases. *Radiology* 198, 45–48 (1996).

10 Henry M, Amor M, Ethevenot G, Henry I, Mentre B, Tzvetanov K: Percutaneous endoluminal treatment of iliac occlusions: long-term follow-up in 105 patients. *J. Endovasc. Surg.* 5, 228–235 (1998).

11 Hassen-Khodja R, Sala F, Declemy S *et al.*: Value of stent placement during percutaneous transluminal angioplasty of the iliac arteries. *J. Cardiovasc. Surg.* 42, 369–374 (2001).

12 Bosch JL, Hunink MGM: Meta-analysis of the results of percutaneous transluminal angioplasty and stent placement for aortoiliac occlusive disease. *Radiology* 204, 87–96 (1997).

13 Sullivan TM, Childs MB, Bacharach JM *et al.*: Percutaneous transluminal angioplasty and primary stenting of the iliac arteries in 288 patients. *J. Vasc. Surg.* 25, 829–838 (1997).

14 Ansel GM, Kazienko BT, Lipman JC *et al.*: Long-term and secondary patency of iliac arterial Wallstenting followed with ongoing limb surveillance. *Am. J. Cardiol.* 88(Suppl. 5A), G29 (2001).

15 Murphy TP, Webb MS, Lambiase RE *et al.*: Percutaneous revascularization of complex iliac artery stenoses and occlusions with use of Wallstents: 3-year experience. *J. Vasc. Interv. Radiol.* 7, 21–27 (1996).

16 Ballard JL, Bergan JJ, Singh P *et al.*: Aortoiliac stent deployment versus surgical reconstruction: analysis of outcome and cost. *J. Vasc. Surg.* 28, 94–101 (1998).

17 Treiman GS, Schneider PA, Lawrence PF *et al.*: Does stent placement improve the results of ineffective or complicated iliac artery angioplasty? *J. Vasc. Surg.* 28, 104–112, discussion 113–114 (1998).

18 Richter GM, Roeren T, Noeldge G *et al.*: Initial long-term results of a randomized 5 year study: iliac stent implantation versus PTA. *VASA* (*Suppl.*) 35, 192–193 (1992).

19 Rzucidlo EM, Powell RJ, Zwolak RM: Early results of stent-grafting to treat diffuse aortoiliac occlusive disease. *J. Vasc. Surg.* 37, 1175–1180 (2003).

20 Powell RJ, Fillinger M, Walsh DB *et al.*: Predicting outcome of angioplasty and selective stenting of multisegment iliac artery occlusive disease. *J. Vasc. Surg.* 32, 564–569 (2000).

21 Vorwerk D, Guenther RW, Shurmann K *et al.*: Primary stent placement for chronic iliac artery occlusions: follow-up results in 103 patients. *Radiology* 194, 745–749 (1995).

22 Henry M, Amor M, Ethevenot G *et al.*: Percutaneous endoluminal treatment of iliac occlusions: long-term follow-up in 105 patients. *J. Endovasc. Surg.* 5, 228–235 (1998).

23 Uher P, Nyman U, Lindh M *et al.*: Long-term results of stenting for chronic iliac artery occlusion. *J. Endovasc. Ther.* 9, 67–75 (2002).

24 Tetteroo E, van der Graaf Y, Bosch JL *et al.*: Randomised comparison of primary stent placement versus primary angioplasty followed by selective stent placement in patients with iliac-artery occlusive disease. Dutch Iliac Stent Trial Study Group. *Lancet* 35, 1153–1159 (1998).

▪ **Details of the Dutch Iliac Stent trial, comparing primary stenting with primary angioplasty with selective stenting.**

25 Klein WM, van der Graaf Y, Seeger J *et al.*: Long-term cardiovascular morbidity, mortality, and reintervention after endovascular treatment in patients with iliac artery disease: the Dutch Iliac Stent Trial study *Radiology* 232, 491–498 (2004).

▪ **Details the long-term results of the Dutch Iliac Stenting trial.**

26 Haulon S, Mounier-Vehier C, Gaxotte V *et al.*: Percutaneous reconstruction of the aortoiliac bifurcation with the 'kissing stents' technique: long-term follow-up in 106 patients. *J. Endovasc. Ther.* 9, 363–368 (2002).

27 Stockx L, Poncyljusz W, Falkowski A *et al.*: Express™ vascular LD stent in the treatment of iliac artery lesions: 24-month results from the MELODIE trial; *Cardiovasc. Inter. Rad.* 30(1), 282 (2007).

▪ **Summarizes the final results of the Multicenter, Single-Arm Study to Obtain Additional Data on the Safety and Efficacy of the Express Vascular LD Stent Implantation in the Treatment of Stenosed or Occlusive Atherosclerotic Disease in Iliac Arteries (MELODIE) trial, which led to approval by the US FDA for use in iliac disease.**

28 Palmaz J, Laborde J, Rivera F *et al.*: Stenting of the iliac arteries with the Palmaz stent: experience from a multicenter trial. *Cardiovasc. Interv. Radiol*. 15, 291–297 (1992).

29 Murphy KD, Encarnacion CE, Le VA *et al.*: Iliac artery stent placement with the Palmaz stent: follow-up study *J. Vasc. Interv. Radiol.* 6, 321–329 (1995).

30 Ponec D, Jaff MR, Swischuk J: The nitinol SMART stent versus Wallstent for suboptimal iliac artery angioplasty: CRISP-US trial results *J. Vasc. Interv. Radiol*. 15, 911–918 (2004).

▪ **Details of the head-to-head trial comparing shape-memory alloy recoverable technology stent with the Wallstent® in iliac disease.**

31 Krol KL, Saxon RR, Farhat N *et al.*: Clinical evaluation of the Zilver vascular stent for symptomatic iliac artery disease. *J. Vasc. Interv. Radiol*. 19, 15–22 (2008).

▪ **Details the safety and effectiveness trial of this self-expanding stent.**

32 Jaff MR, Katzen BT: 2 year clinical evaluation of the Zilver vascular stent for symptomatic iliac artery disease. *J. Vasc. Interv. Radiol.* 21, 1489–1494 (2010).

33 Ansel GM: Endoprosthesis in complex iliac stenosis and occlusion: results of the prospective, multicenter randomized trial. *Curr. Interv. Cardiol. Rep*. 1, 303–309 (1999).

34 Lammer J, Dake MD, Bleyn J *et al.*: Peripheral arterial obstruction: prospective study of treatment with a transluminally placed self-expanding stent graft. *Radiology* 217, 95–104 (2000).

▪ **Details the safety and effectiveness trial of the Hemobahn® (Viabahn®) endoprosthesis.**

35 Mwipatayi P: Covered balloon-expandable versus bare metal stents for complex iliac disease – final results of the COBEST-Study. Presented at: *The Leipzig Interventional Course 2010.* Leipzig, Germany, 27–30 January 2010.

▪ **Summarizes the results of this trial comparing covered stent with bare-metal stent in iliac disease.**

■ Websites

101 Express LD iliac stent over-the-wire premounted stent system – directions for use www.bostonscientific.com/Device.bsci?page=ResourceDetail&navRelId=1000.1003&method=DevDetailHCP&id=10121341&resource_type_category_id=1&resource_type_id=82&pageDisclaimer=Disclaimer.ProductPage
(Accessed 5 May 2010)

102 US FDA summary of safety and effectiveness data (SSED) for the express LD iliac premounted stent system www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/pma/pma.cfm?num=P090003
(Accessed 5 May 2010)