

Infrapopliteal Stenting with Silicon Carbide-Coated Stents in Critical Limb Ischemia: A 12 Month Follow-Up Study

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ABSTRACT: **Background:** Critical limb ischemia is an increasingly common condition that has high surgical morbidity and limited non-surgical options.

Objectives: To evaluate the use of silicon carbide-coated Motion stents, as compared to reported data for bare metal stents, in elderly patients with infrapopliteal artery stenoses causing critical limb ischemia after failed or complicated percutaneous transluminal angioplasty.

Methods: Between January 2003 and March 2004, 41 stents were inserted into 17 consecutive patients (11 males, 6 females, mean age 82 years, range 75–93) following unsuccessful or complicated PTA. Seven patients had one-vessel run-off, six had two-vessel and four had three vessel run-off. All patients suffered from CLI, had up to three lesions and more than one co-morbid condition, and were considered at high surgical risk. Silicon carbide-coated Motion coronary stents, 2.5–4 mm diameter and 25 and 30 mm length, were used. Pre-intervention assessment included clinical condition, ankle brachial index, Doppler ultrasound and digital subtracted angiography. Post-intervention evaluation included clinical condition, ABI and Doppler ultrasound at 3, 6 and 12 months.

Results: The technical success rate per lesion was 100% (41/41). Two patients died of unrelated causes after 2 and 8 months respectively. Primary patency rates with duplex ultrasound were 68.7% (11/16) at 3 months, 43.7% (7/16) at 6 months and 40% (6/15) after 12 months. Nine patients developed complete occlusion in 13 stents; three of these patients underwent a below-knee amputation and two patients a partial foot amputation. Re-intervention (PTA only) was performed in 7 patients (43.7%). Secondary patency rate was 81.2% (13/16) at 6 months and 60% (9/15) at one year. Mean ABI index had improved at 6 months from 0.32 to 0.67, and to 0.53 at one year. Clinical improvement was evident in 87.5% (14/16) at 6 months and in 66.6% (10/15) at one year.

Conclusions: Silicon carbide-coated stents are comparable to bare metal stents after 6 and 12 months in infrapopliteal interventions in CLI when stenting is indicated.

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KEY WORDS: infrapopliteal artery stenosis, stent, critical limb ischemia, silicon carbide-coated stent

Critical limb ischemia will eventually occur in 10–20% of elderly patients with intermittent claudication [1]. Since elderly patients with CLI usually have several co-morbidities, minimally invasive procedures may be more suitable for this group of patients. Reported limb salvage rates after percutaneous transluminal angioplasty are comparable to those after surgery [2]. Nevertheless, the reocclusion rate of the dilated vessels is relatively high, especially in long and or distal lesions. Clinical success is superior to angiographic patency because of wound improvement and even healing during the short duration that the treated vessel remained patent, enabling better collateral flow to the foot [3]. However, the results of infrapopliteal stenting are not better than those of PTA only [4], and stents are therefore indicated for complicated or unsuccessful PTA only [5,6]. The aim of this study was to evaluate the use of coated stents in small caliber arteries, for example in the infrapopliteal region, as compared to the reported data for bare metal stents.

PATIENTS AND METHODS

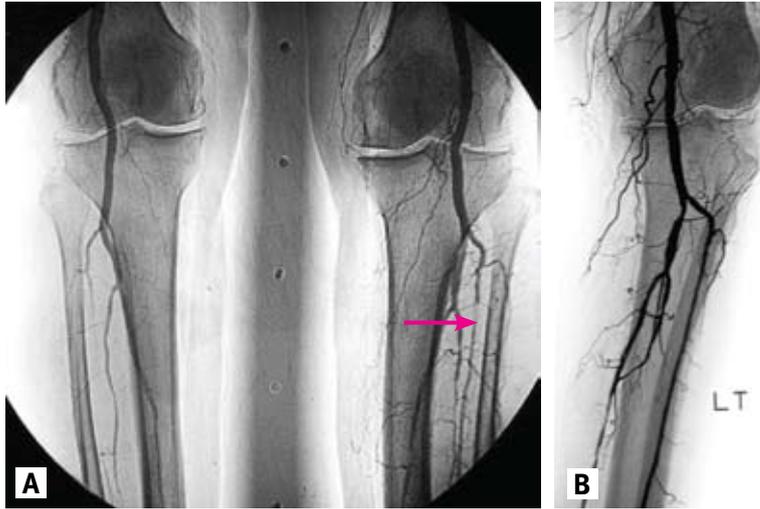
Between January 2003 and March 2004, we performed 41 stent insertions in 17 consecutive patients. The patients (11 males, 6 females), whose mean age was 82 years (range 75–93 years), presented clinically with critical chronic limb ischemia (Fontaine stages 3 and 4) defined as gangrene, ischemic ulcer and rest pain [Table 1]. All stents were secondarily placed following suboptimal or complicated PTA in the same pro-

Table 1. Patients' demographics and infrapopliteal vessels

No. of patients	16 (11 males, 6 females)
Mean age (yrs)	82 (75–93)
More than one co-morbidity	16/16
No. of visible infrapopliteal vessels	1–7 patients 2–6 patients 3–4 patients

PTA = percutaneous transluminal angioplasty
CLI = critical limb ischemia
ABI = ankle brachial index

Figure 1. [A] Peripheral run-off from right common femoral artery revealed short tight stenosis of the proximal left anterior tibial artery (arrow). **[B]** After incomplete PTA because of rapid recoiling, one 3 x 30 mm Motion stent was placed in the proximal anterior tibial artery with good result.



cedure. This accounts for about half of the patients treated only by PTA in the infrapopliteal region for CLI during this period. All patients had one or more co-morbidities and were at high surgical risk.

Seven patients had one-vessel run-off, six had two crural vessels, and four patients had three vessel run-off. A contralateral femoral approach was used in 10 patients, where angioplasty followed diagnostic angiography, replacing the diagnostic catheter with a curved 6 Fr. sheath (Cook, Bloomington, IN, USA). An antegrade femoral artery approach was performed in seven patients through 5 Fr. Sheath (Cook, or Terumo, Tokyo, Japan) in a separate session based on previous diagnostic angiographic images. Heparin, 5000 units, was administered intravenously to all patients prior to the angioplasty. There was no uniform antiplatelet therapy in the study group.

PTA was performed only for stenosis or occlusions up to 2 cm, with low profile balloons – either over-the-wire balloons (Savvy, Cordis, Roden, The Netherlands) or monorail (Gazelle, Boston Scientific, Natick, MA, USA). The diameter of the balloons ranged from 2.5 to 3.5 mm, equivalent to the diameter of the treated artery. PTA, up to three inflations and up to 3 minutes inflation time per lesion, was performed followed by digital subtracted angiography run-off. When dissection, recoiling, or inadequate dilatation with rapid recoiling occurred, resulting in patency of less than 30% of the lumen diameter adjacent to the treated area, as documented in the DSA image, a stent was implanted

across the suboptimal area. Spasm was usually ruled out by intraarterial administration of an antispasmodic agent or vasodilators (nitrites at a dose of 100–200 µg or papaverine 40 mg).

We inserted 41 stainless steel, silicon carbide-coated, balloon-expandable Motion monorail coronary stents (Biotronik, Berlin, Germany). Up to four stents were inserted, average 2.4 stents, per patient [Figure 1 A and B]. Stents with diameters of 2.5, 3, 3.5 and 4 mm and lengths of 25 and 30 mm were implanted, directed by a 0.014" coronary guide wire (Biotronik). After stent insertion a complete angiogram was performed to verify: a) lumen patency with < 30% stenosis compared to the adjacent normal lumen width, and b) unchanged vessels distal to the angioplasty sites.

Pre-intervention assessment included clinical condition, ankle brachial index, Doppler ultrasound, and digital subtracted angiography. Post-intervention evaluation included clinical condition, ABI, and Doppler ultrasound compared to the DSA images at 3, 6 and 12 months, or when symptoms recurred. Color duplex valuation of flow within the stented segments was considered as a patent segment. Clinical improvement was defined as complete healing or partial wound healing in terms of size or depth, or relief of pain at rest.

Institutional Review Board approval was not required because patients were treated according to departmental practice, in conventional procedures and with approved equipment.

RESULTS

The technical success rate per lesion was 100% (41/41). No patient's condition was worsened by the angioplasty and stent placement procedure. There were no procedure-related deaths. Two patients died of unrelated cardiac causes after 2 and 8 months respectively. Because of the small number of patients and the variety in number and sites of each crural vessel treated, primary patency rates were calculated per patient and not per targeted vessel. The primary patency rates for patients were 68.7% (11/16) at 3 months, 43.7% (7/16) at 6 months and 40% (6/15) after 12 months. Nine patients developed complete occlusion in 13 stents (7 patients with single vessel run-off and 2 with 2 vessel run-off.) Three of them underwent below-knee amputation. Another two patients underwent partial foot amputations (great toe amputation in one, and transmetatarsal amputation in the other). Secondary patency rate following reintervention (PTA only) in the stented reoccluded or stenosed lesions performed in 7 patients was 81.2% (13/16) at 6 months and 60% (9/15) at one year. Clinical improvement was 87.5% (14/16) at 6 months and 66.7% (10/15) at one year. Mean ABI index improved at 6 months from 0.32 to 0.67 and to 0.53 at one year.

DSA = digital subtracted angiography

DISCUSSION

Patients with ulceration, gangrene or rest pain of the lower limbs caused by arterial occlusive disease are defined as having critical chronic limb ischemia (Rutherford stages IV-VI or Fontaine stages III and IV). Surgical treatment for critical CLI, if there is a patent artery distal to the occlusion, is a distal bypass. It is technically more difficult to perform than proximal bypass, and the perioperative reported mortality rate of 2–6% [5,7,8] is higher than after angioplasty (< 1.7%) [6,8,9]. Non-fatal surgical complications include acute myocardial infarction (up to 3.4%), wound infection (up to 30%), and leg edema (50–100%) [10]. Distal bypass is not feasible in cases of inadequate run-off, absence of suitable veins to act as conduits for bypass, or in patients at high surgical risk. Furthermore, the 5 year patency rate of synthetic grafts is only 33% [11]. Thus, for those who cannot have surgical bypass, angioplasty may be the only therapeutic option that may minimize further amputations.

Angioplasty for CLI was first reported 44 years ago by Dotter and Judkins. The initial results were poor with a low success rate and high complication rate, but the shaft reduction and the technical improvements in guide wires, catheters and stents, together with new recanalization techniques (e.g., subintimal angioplasty) have improved the angioplasty success rate and lowered complication rates [6]. The reported technical success rates range from 78 to 98% and the clinical success rate, or the limb salvage rate, after balloon angioplasty is 72–88% at 12 months [3,10,12]. However, the angiographic patency after one year is low in most of the reports, estimated between 10 and 53%, although the short period of patency is usually sufficient for wound healing [2,3,10]. Today, the angioplasty results and the reported limb salvage rates of PTA are comparable with those after surgery [2,6,11], and according to the TASC II (Transatlantic Intersociety Consensus) document on management of peripheral arterial disease, angioplasty is recommended for group I and II lesions, and considered feasible for the more complicated groups III and IV [2,6,11]. The American Heart Association and TASC II agree that there is a need for aggressive management of such patients [11].

The early results with primary stent angioplasty or stent insertion after complicated or unsuccessful PTA were not better than with angioplasty alone; therefore, stents are advocated only for complicated PTA [2,5,6].

A recent study has shown better one year results in 82 patients (92 limbs), using different balloon-expandable and self-expanding coronary stents (bare stents, or coated with heparin or drugs) [13]. Still, only two-thirds of the study group had CLI and the rest complained of severe claudication.

To improve the long-term patency rate in the crural vessels, other approaches have been tested, and are available

or are currently being studied. These include subintimal angioplasty, lasers, cutting balloons, intravascular sonography, coated stents, drug-eluting stents, and absorbable metal stents [14–20]. Subintimal angioplasty, first presented by Bolia [14], has a reported technical success rate of about 80%, one year patency rates of 33–56% and limb salvage rate of 81–94% [14]. The main drawbacks of this technique are the reproducibility and the limited reported success rate. The largest clinical study using a cutting balloon was performed on 93 infrapopliteal vessels in CLI [15]. It reported a 80% success rate and 89.5% limb salvage rate after 12 months, but no mention of the one year patency rate. Intravascular sonotherapy and lasers are still under clinical investigation [16,17], and the reported 6 month limb salvage rate for tibial laser angioplasty is similar to that for angioplasty.

Except for one study [18], drug-eluting stents are also still under investigation. According to the non-randomized single-center 6 month angiographic results, the primary patency rate was better with the drug-eluting stents than the bare stents (92% vs. 68.1%), for in-stent and in-segment restenosis (4% and 32% vs. 53.3% and 66%) and reduction in target lesion reintervention (4% vs. 17%). In the superficial femoral artery however, the drug-eluting stents did not yield better results than the bare metal stents [19], thus further trials are needed to test drug-eluting stents in the infrapopliteal region.

Absorbable metal stents were inserted in the tibial vessels in 20 patients with CLI. At 6 and 12 months follow-up, the absorbable magnesium stent showed the best clinical and patency rates [20], but they are still at the stage of early clinical trials and are not available for use.

The results of infrapopliteal stents have so far been disappointing as compared to simple angioplasty. This is mainly because of the small vessel caliber, which plays a major role in the stent reocclusion due to intimal hyperplasia. The tissue reaction to the stent is activated by several mechanisms, such as ion release from the stent (electromechanical reaction), thrombosis formation (hemocompatible reaction) and inflammatory reaction (biocompatible response). Stent thrombogenicity is triggered by an electronic exchange at the implant surface, and the electron transfer process from proteins to stents is responsible for the activation of proteins, resulting in thrombus formation [21–23]. To diminish these reactions several solutions were applied to the stent surface, such as stent polishing, stent passive coating and ion implantation. Stents have been designed with various coatings such as carbon, carbon and hydrogen, silicon, phosphorylcholine and plasma-induced cold depositions. Their efficacy was tested *in vivo* and in limited coronary trials. The results were similar to or better than those obtained with bare metal stents [24].

There is only one reported study on the use of coated stents to treat the crural vessels [25]. This prospective multicenter randomized trial followed 24 patients (42 lesions)

with critical CLI treated with coated stent (Carbostent, Sorin, Italy), and 27 patients (53 lesions) with balloon angioplasty, for 6 to 12 months, and showed statistically better results in the former compared to the PTA-alone group after 6 months (patency rate of 83.7% in the stented group versus 61.1% in the PTA group).

The Motion stent used in our study is a balloon-expandable stainless steel stent with amorphous silicon carbide coating. The passive coating in laboratory trials showed better sealing of the bare metal surface by reduction of heavy metal diffusion leading to reduction in thrombus formation, reduction of platelet activation, better inhibition of smooth muscle cell proliferation and reduction of endothelialization compared to bare metal stents [22-24]. The 12 month patency rate results (40% primary patency rate and 60% secondary patency rate), using coated stents in the infrapopliteal area, are comparable and even superior to the results of angioplasty, and the clinical improvement is comparable (66.6%). The single reported study using a different coated stent (Carbostent) for the same indication showed better short-term results compared to PTA [24]. Since the results of infrapopliteal stenting, except for a few reports, were not better than those of PTA alone, the improved patency rate after using coated stents may be related to the stent coating, which was aimed at reducing the local tissue reaction against the stent and the heavy metal ion release.

Limitations of this study include the lack of a randomization protocol, the small number of patients, the lack of a control group, the heterogeneity of co-morbid factors, non-uniform lesions, ultrasound-only imaging follow-up, and starting point of complicated or unsuccessful PTA. Despite the small number of patients, the use of silicon carbide stents in complicated or unsuccessful PTA, in patients with CLI, has shown relatively good primary and secondary success rates after 6 and 12 months compared to PTA. Further randomized studies and follow-up are needed to determine the role of coated stents in the infrapopliteal vessels.

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