Initial Clinical Experience with a Novel Dedicated Cobalt–Chromium Stent for the Treatment of Below-the-knee Arterial Disease

a report by

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The incidence and prevalence of critical limb ischaemia (CLI) is progressively increasing, mainly because of the widespread incidence of diabetes mellitus and longer life expectancy in developed countries.[1] Beyond lifestyle changes and medical therapy, arterial revascularisation is a mainstay in the management of patients with CLI due to below-the-knee (BTK) disease in order to improve functional class and prevent complications possibly leading to amputation and limb loss.[2] Until recently vascular surgery by means of distal bypasses was considered the only feasible revascularisation option,[1,2] but the introduction of dedicated techniques and devices has shown that percutaneous arterial revascularisation by means of percutaneous transluminal angioplasty (PTA) is feasible and safe in these patients, with satisfactory clinical results.[3,4] Furthermore, the landmark Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial indicates that a percutaneous revascularisation strategy is probably equivalent to bypass surgery in patients with CLI.[5] However, there remains room for improvement, as PTA may carry risks of suboptimal result, abrupt vessel closure or late restenosis or re-occlusion.

Stent implantation has proved highly beneficial in the coronary realm and, thanks also to the development of drug-eluting stents (DES), has become a standard for most percutaneous coronary interventions. Conversely, the role of stenting in peripheral artery disease is still debated, especially when the BTK district is considered. Indeed, only a few reports to date are available on BTK stenting (see *Table 1*),[6–17] with only one pertinent randomised trial supporting stenting versus standard PTA.[14] Among the concerns raised on the infragenicular use of stents are the risks of fracture, restenosis and thrombosis. Another major issue is the lack of dedicated and long stents able to treat the typical BTK lesion: a long and calcified segment often with diffuse occlusive disease.

Most recently, a dedicated device for BTK use has been developed: the Chromis Deep™ stent (Invatec, Roncadelle, Italy) (see *Figures 1* and *2*). Engineered as a 'BTK-lesion-specific' stent to allow treatment of long diffusely diseased infrapopliteal vessel segments (as normally encountered in CLI patients), the Chromis Deep is a BTK-dedicated stent and delivery system. The stent consists of a cobalt–chromium balloon-expandable metallic platform with closed-cell design, thin struts, diameters ranging between 2.0 and 4.0mm and lengths spanning from 10 to 76 mm. The delivery system is a 0.014-inch guidewire-compatible balloon catheter based on the BTK-dedicated PTA balloon Amphirion DEEP™ (Invatec, Roncadelle, Italy). Chromis Deep is available in over-the-wire designs, with shaft lengths of 120cm (for ipsilateral access) or 150cm (for contralateral access).

The aim of this retrospective study was to assess the safety and efficacy of the Chromis Deep stent in the treatment of patients with BTK disease following failed PTA.

Methods

We abstracted baseline procedural and follow-up data on all consecutive patients who underwent implantation of a Chromis Deep stent in our institution between June 2006 and September 2007. All patients gave written informed consent, and the retrospective study was conducted in accordance with the local ethics committee.

Patients with symptomatic peripheral artery disease (Rutherford category 3–6) underwent arterial angiography by means of ipsilateral or contralateral access.[18] After angiographic documentation of infrapopliteal stenotic (>70% diameter reduction) or occlusive disease, PTA was attempted using dedicated guidewires and semi-compliant balloons, as per routine at our centre. Specifically, BTK-dedicated 0.014-inch guidewires and over-the-wire balloons were used to cross and dilate (12–14atm for two to three minutes) the diseased segments.[4] After retrieval of the balloon, digital subtraction angiography was performed to appraise post-PTA results. Stenting with the Chromis Deep was then considered only in cases of failed PTA, classified as persistent suboptimal angiographic result (residual diameter stenosis >50%) or flow-limiting dissection in a non-bending zone.

All patients were pre-treated with aspirin and/or clopidogrel and peri-procedurally managed with 70–100IU.kg of unfractioned heparin. Post-procedurally, haemostasis was achieved either manually or with closure devices,[19] and both aspirin and clopidogrel were continued for at least four weeks.

A clinical follow-up visit was performed in all patients and included assessment of vital status and Duplex ultrasound imaging of the affected limb. In cases of lack of clinical improvement, clinical recurrence (e.g. foot ulcer) or ultrasound evidence of restenosis or re-occlusion, patients underwent repeat lower limb angiography, followed by revascularisation where appropriate.

The primary end-point of the study was limb salvage rate for patients with CLI and improvement of Rutherford classification for claudicant patients.[20] We also appraised the risk of major (above the ankle) and

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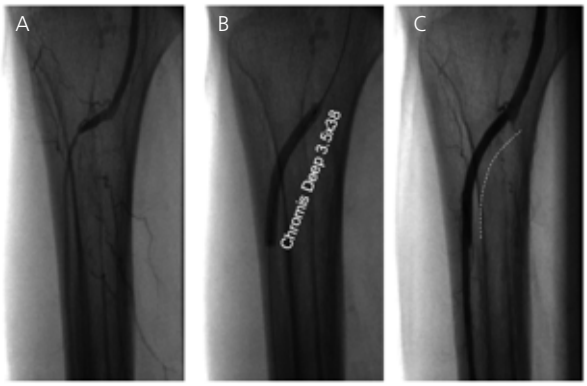
Figure 1: The Chromis Deep Stent Before Deployment (A) and Expanded (B)

Table 1: Previous Reports on Infrapopliteal Stenting for Critical Limb Ischaemia

Study	Number of Patients	Design	Stent Type
Bosiers et al., 2005	20	Registry	BE bioabsorbable stent
Bosiers et al., 2006	18	Registry	Sirolimus DES
Bosiers et al., 2007	47	Registry	SE nitinol stent
Commeau et al., 2006	30	Registry	Sirolimus DES
Feiring et al., 2004	82	Registry	BE BMS
Feiring et al., 2007	5	Case series	Sirolimus DES
Kickuth et al., 2007	35	Registry	SE nitinol stent
Morgan et al., 2005	6	Case series	BE BMS
Rand et al., 2006	24	Randomised clinical trial	BE BMS (versus PTA)
Scheinert et al., 2006	60	Non-randomised controlled study	Sirolimus DES (versus BE BMS)
Siablis et al., 2005	29	Non-randomised controlled study	Sirolimus DES (vs BE BMS)
Siablis et al., 2007	29	Registry	Paclitaxel DES
Tepe et al., 2007	18	Registry	SE nitinol stent

BE = balloon-expandable stent; BMS = bare-metal stent; DES = drug-eluting stent; SE = self-expandable stent.

Figure 2: Percutaneous Transluminal Implantation of a Chromis Deep Stent in a Patient with a Tight Stenosis of the Proximal Anterior Tibial Artery



A: baseline; B: during implantation of the stent; C: after stenting and distal balloon dilation.

Table 2: Characteristics of Patients Treated with the Chromis Deep Stent

Number of patients	20	
Male gender	15 (75%)	
Age (years)	67±16	
Hypertension	15 (75%)	
Dyslipidaemia	10 (50%)	
Smoking status		
Previous smoker	12 (60%)	
Current smoker	8 (40%)	
Diabetes mellitus		
Non-insulin-dependent	6 (30%)	
Insulin-dependent	6 (30%)	
Renal failure		
Serum creatinine >2.0mg/l	9 (45%)	
Dialysis	3 (15%)	
Rutherford class at admission	**Nr (%) of patients**	**ABPI**
1	0	–
2	0	–
3	1 (5%)	0.65±0.11
4	6 (30%)	0.48±0.12
5	10 (50%)	0.3±0.06
6	3 (15%)	0.26±0.20

ABPI = Ankle Brachial Pressure Index.

minor (below the ankle) amputation, occurrence of restenosis or re-occlusion, change in Rutherford class and repeat revascularisations.

For statistical analysis, continuous variables are reported as mean ± standard deviation and categorical variables as n (%). Ankle Brachial Pressure Index (ABPI) changes are evaluated by a pair student t-test. Rutherford class changes are evaluated by two-way analysis of variance (ANOVA). For both tests, $p<0.05$ is taken as statistically significant.

Results

Between June 2006 and September 2007, a total of of 40 patients underwent BTK revascularisation in our institution: 29 (72.5%) with CLI and 11 (27.5%) with life-limiting claudication (LLC). A total of 20 patients were treated with 23 Chromis Deep stents in the same period due to failed PTA. Baseline and procedural characteristics are reported in *Tables 2* and *3*, respectively. Specifically, there were 15 men (75%), average age was 67±16 years and 12 of the patients (60%) had diabetes, of whom six (30%) were insulin-dependent. Most patients (19 [95%]) presented with CLI: six (30%) under Rutherford class 4, 10 (50%) under Rutherford class 5 and three (15%) under Rutherford class 6, and only one patient (5%) presented with LLC under Rutherford class 3.

The target lesion was the proximal portion of the tibial artery (in overlap with the popliteal artery) in three of the patients (15%), the anterior tibial artery in eight (40%), the tibio-peroneal trunk in four (20%) and the posterior tibial artery in five (25%). Total occlusions were common (14 [70%]), as were long and diffusely diseased lesions (13 [66.7%]). Most stents had a diameter of 3.0mm (10 [50%]) and a length of 76mm (15 [75%]). Deployment pressure was 9±3atm (see *Table 4*). Short, non-compliant balloons were also employed in cases of calcific or fibrotic lesions to optimally expand the stent.

All procedures were angiographically and clinically successful. After eight months (246±101 days) of follow-up, all patients showed clinical improvement in their functional status (see *Tables 5* and *6*): the median Rutherford class change was from 5 to 3 ($p<0.01$), with most patients

Table 3: Angiographic and Procedural Characteristics of Patients Treated with the Chromis Deep Stent

Number of patients	20
Location of stented lesion	
Proximal tibial-distal popliteal*	3 (15%)*
Anterior tibial	8 (40%)
Tibio-peroneal trunk	4 (20%)
Posterior tibial artery	5 (25%)
Total occlusion	14 (70%)
Mean lesion length (mm)	112±35
Mean stented length (mm)	72.2±11.7
Concomitant treatment of superficial femoral artery	8 (40%)
Patients with two Chromis Deep stents implanted	3 (15%)
Total number of Chromis Deep stents implanted	23
Number of Chromis Deep stents per patient	1.15
Stent diameter (mm)	
2.5	5 (22%)
3.0	12 (52%)
3.5	6 (26%)
Stent length (mm)	
38	8 (35%)
76	15 (65%)
Maximum dilation pressure (atm)	9±3
Procedural success	20 (100%)

** Either the anterior tibial artery or the tibio-peroneal trunk.*

Table 4: Clinical Results at Follow-up in Patients Treated with the Chromis Deep Stent

Number of patients	20
Follow-up completion	20 (100%)
Clinical follow-up	246±101 (days)
Major amputations (above the ankle) in CLI patients	0
Minor amputations (below the ankle) in CLI patients	0
Limb salvage rate (19 CLI patients)	19 (100%)
Re-hospitalisations	6 (30%)*
Repeat percutaneous transluminal angioplasty	6 (30%)†
Follow-up Duplex ultrasound scan (n=20)	
No restenosis	14 (70%)
Restenosis or re-occlusion	6 (30%)‡

** One patient had two re-hospitalisations.*
† All repeat percutaneous transluminal angioplasties were successful.
‡ In a patient treated in the superficial femoral artery and tibio-peroneal trunk, both lesions were re-occluded, whereas another subject showed thrombotic subocclusion at the proximal edge of the stent (i.e. in-segment restenosis), but in the absence of significant in-stent restenosis.
CLI = critical limb ischaemia.

(12 [60%]) in Rutherford class 3 and none in Rutherford class >4. ABPI also showed significant improvement: the mean change was from 0.32±0.10 to 0.75±0.14 (p<0.001). One hundred per cent limb salvage was achieved in all CLI patients, with no major or minor amputations. Duplex ultrasound follow-up, completed in 20 patients (100%), showed that restenosis or re-occlusion had occurred in six (30%). All of these patients underwent angiographically and procedurally successful repeat percutaneous revascularisation with PTA angioplasty.

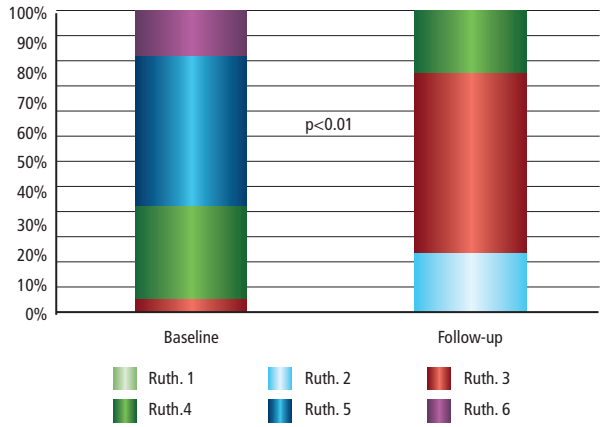
Discussion

This study, the first to date to report on this novel dedicated device for BTK disease, suggests that implantation of the Chromis Deep stent in patients with CLI after failed PTA is feasible and safe, and provides favourable clinical results. Further studies are nonetheless needed to thoroughly and further appraise the role of BTK stenting in comparison with standard PTA.

Table 5: Rutherford Class Change at Follow-up

Rutherford Class	Baseline	Follow-up
1	0	0
2	0	4 (20%)
3	1 (5%)	12 (60%)
4	6 (30%)	4(20%)
5	10 (50%)	0 (0%)
6	3 (15%)	0 (0%)

Figure 3: Rutherford Class Change at Follow-up



Despite major improvements in the non-invasive and invasive management of symptomatic peripheral artery disease, the incidence and prevalence of its most severe form, CLI, is still increasing.[1] Arterial revascularisation by means of distal bypasses is a well established and effective treatment for CLI, especially when saphenous vein grafts are available. Unfortunately, many patients are poor surgical candidates or lack suitable veins. These issues provided the impetus for the introduction of dedicated endovascular techniques and devices, leading to an ever-increasing application of infragenicular percutaneous arterial revascularisation by means of PTA.[3,4] Despite many years of uncertainty, current evidence supports the choice of an initial endovascular management, with bypass surgery reserved for the most severe or recurrent cases.[4,5] Indeed, failures of PTA are not uncommon, despite the availability of dedicated guidewires and balloons. Specifically, PTA has been shown to lead to early risk of suboptimal result due to fibrotic or calcific lesions, abrupt vessel closure due to flow-limiting dissection or thrombus and late restenosis/re-occlusion due to recoil, constrictive remodelling and/or hyperplasia.

The role of stenting in peripheral artery disease is still controversial, especially when the BTK district is considered. The main limitations of BTK stenting are the risks of stent fracture in bends,[21] restenosis due to aggressive neointimal hyperplasia (common in poorly controlled diabetics such as those with CLI) and stent thrombosis possibly due to slow flow. In addition, most patients with CLI have extensive and diffuse disease, and most available stents with infragenicular sizes (diameter between 2.0 and 4.0mm) are coronary stents and thus too short (usually 33mm or less) to adequately cover BTK lesions.

Despite these caveats, a number of studies are already available on BTK stenting (see *Table 1*). Data on the use of coronary-approved balloon-expandable bare-metal stents (BMS) in patients with CLI have been reported already by Feiring et al.,[10] Morgan et al.[13] and Rand et al. for a total of 112 treated subjects.[14] Intriguingly, the latter authors have shown, in the only randomised clinical trial published to date on BTK stenting, that elective infragenicular implantation of balloon-expandable

Table 6: Anke Brachial Pressure Index Change at Follow-up

Baseline	Follow-up	
0.32±0.10	0.75±0.14	p<0.001

Figure 4a: Ankle Brachial Pressure Index Change at Follow-up

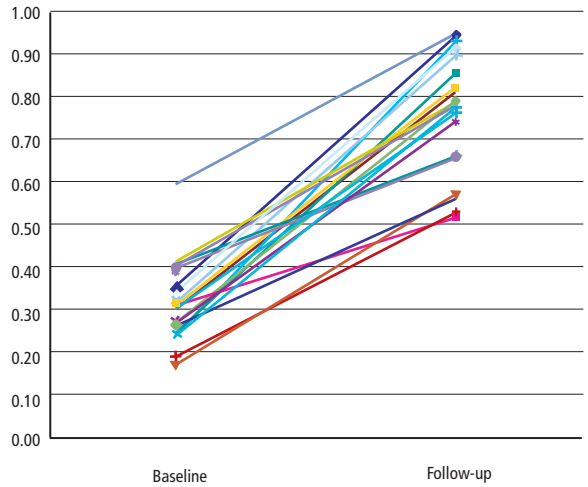
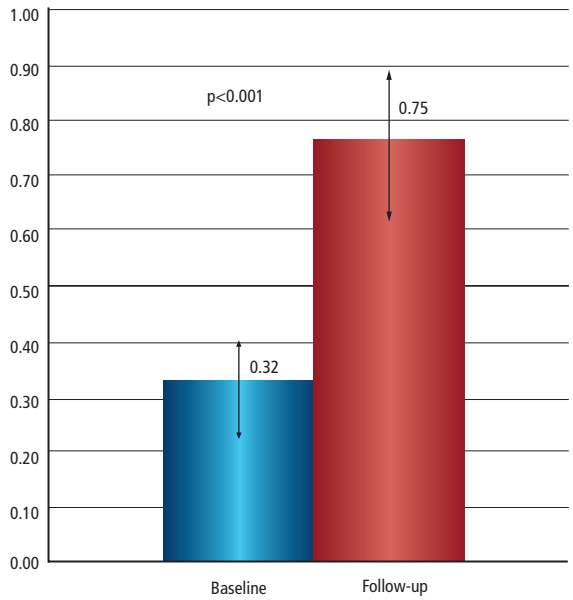


Figure 4b: Ankle Brachial Pressure Index Change at Follow-up



BMS (actually carbofilm-coated devices, yet still belonging to the BMS family) was superior to balloon-only PTA in patients with CLI in preventing restenosis and re-occlusion of the treated lesion.[14]

As many as six studies have reported on a total of 141 patients undergoing BTK implantation of a coronary-approved DES (either a sirolimus- or a paclitaxel-eluting device); of the DES, only the Cypher 3.0–33mm stent (Cordis) was approved for use in the BTK district, with an obvious off-label indication for all others.[7,9,11,15,16] While the results of this approach are quite promising, especially in light of the apparent superiority of DES in comparison with BMS, usage of DES in the BTK district seems to raise some questions and concerns. First, no study on BTK DES implantation was randomised, thus limiting internal and external validity. Second, stents developed for coronary vessels are available only in short sizes (≤33mm), thus limiting their usefulness and cost–benefit balance in the diffusely diseased tibial vessels. Finally, patients with CLI must achieve ulcer healing; in these patients avoidance of angiographic restenosis is not usually a major issue,[4] thus the superior antirestenotic effect of DES may prove futile,[22] especially in light of the increased risk of stent thrombosis.

Another focus of intense research has been the infragenicular implantation of the dedicated self-expandable nitinol Xpert stent (Abbott Vascular), a device specifically developed for BTK disease. Despite interesting and promising data from as many as 82 patients in two registries,[8,17] we await randomised controlled trials comparing this device with balloon-only PTA and/or balloon-expandable stenting.

Finally, favourable but still very preliminary data have been reported by Bosiers et al. on 20 patients with CLI treated with bioabsorbable metallic stents, which hold the promise of enabling non-invasive and repeated treatment of severe atherosclerotic disease without the need to implant a permanent endoprosthesis.[6]

Given this evidence base on BTK stenting, we believe that the present study lends further support to this endovascular approach in the treatment of patients with CLI. Furthermore, in spite of the significantly longer stented segments seen in the current study, our results with the new Chromis Deep stent appear similar to those reported in other studies in terms of restenosis, primary patency and limb salvage. On the other hand, the Chromis Deep stent has several distinct advantages over the other stents already employed in the infragenicular district, namely the large spectrum of diameters and lengths (with devices as long as 76mm), the flexible cobalt–chromium platform and low-profile delivery systems with shaft lengths compatible with both ipsilateral and contralateral access. The 30% restenosis rate seems acceptable, especially when considering the mean stented length of 72.2mm. The clinical relevance of stent restenosis in the BTK district remains debatable; however, this study has a number of limitations, including the retrospective and single-centre design, the lack of a control group and the small sample size. Thus, larger and controlled trials are warranted to definitively appraise the risk–benefit balance of this new dedicated stent for the treatment of infragenicular disease.

Conclusions

Infragenicular implantation of the new cobalt–chromium balloon-expandable stent, Chromis Deep, in patients with CLI is feasible and safe, and appears to provide favourable clinical results. Additional controlled studies are nonetheless warranted to definitively appraise the clinical role of this device. ■

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