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. 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. Until recently vascular surgery by means of distal bypasses was considered the only feasible revascularisation option, 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. 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. 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), but the introduction of 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 (12–14 atm for two to three minutes) the diseased segments. 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 70–100 IU kg of unfractionated heparin. Post-procedurally, haemostasis was achieved either manually or with closure devices, 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. We also appraised the risk of major (above the ankle) and
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 paired 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 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 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.

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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        | BE BMS           |
| Sramek 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.

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 | 1 | 2 | 3 | 4 | 5 | 6 |
|--------------------|---|---|---|---|---|---|
| ABPI               | 0 | - | - | 6.6±0.11 | 0.48±0.12 | 0.3±0.06 | 0.26±0.20 |

ABPI = Ankle Brachial Pressure Index.
Follow-up Duplex ultrasound scan (n=20)  
Re-hospitalisations 6 (30%) *  
Limb salvage rate (19 CLI patients) 19 (100%)  
Minor amputations (below the ankle) in CLI patients 0  
Major amputations (above the ankle) in CLI patients 0  
Clinical follow-up 246±101 (days)  
Follow-up completion 20 (100%)  
Number of patients 20  

the Chromis Deep Stent  
Table 4: Clinical Results at Follow-up in Patients Treated with  
Procedural success 20 (100%)  
Maximum dilation pressure (atm) 9±3  
Stent length (mm)  
Stent diameter (mm)  
2.5 5 (22%)  
3.0 12 (52%)  
3.5 6 (26%)  
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  
Mean lesion length (mm) 112±35  
Mean stented length (mm) 72.2±11.7  
CLI = critical limb ischaemia.  
Re-occluded, whereas another subject showed thrombotic subocclusion at the proximal edge of  
‡ In a patient treated in the superficial femoral artery and tibio-peroneal trunk, both lesions were  
† All repeat percutaneous transluminal angioplasties were successful.  
* One patient had two re-hospitalisations.  
All repeat percutaneous transluminal angioplasties were successful.  
In-segment restenosis, but in the absence of significant in-stent restenosis.  
One hundred per cent limb salvage was achieved in all CLI patients, with no major or minor amputations.  
restenosis or re-occlusion had occurred in six (30%). All of these patients underwent angiographically and procedurally successful repeat percutaneous revascularisation with PTA angioplasty.  
(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.  
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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.

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. * 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.  
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.  
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, 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 with CLI as critical limb ischaemia.  

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Peripheral

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 (Cardis) 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 (≤33 mm), 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,6 thus the superior antiatherosclerotic 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 76 mm), 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 72.2 mm. 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.

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

| Baseline | Follow-up |
|----------|-----------|
| 0.75±0.14| 0.75±0.14 |

p<0.001

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MARIS DEEP
Infrapopliteal Self-Expanding Stent System