J CARDIOVASC SURG 2009;50:365-71

Applicability and clinical results of percutaneous transluminal angioplasty with a novel, long, conically shaped balloon dedicated for below-the knee interventions

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Aim. **The aim of this study was to assess the feasibility, safety and efficacy of percutaneous transluminal angioplasty (PTA) in patients with critical limb ischemia (CLI) using a novel balloon designed for below-the-knee (BTK) indications.**

Methods. **The authors have prospectively collected baseline, periprocedural and mid-term data of all consecutive patients with CLI due to BTK disease in which PTA was attempted using a long (210 mm), conically-shaped balloon (0.5 mm tapering from proximal to distal balloon edges). The primary objective was the assessment of acute success (composite of technical, angiographic and procedural success). The secondary assessments included limb salvage rate, major (above the ankle) and minor (below the ankle) amputation, change in Rutherford class and cutaneous oxygen tension, reocclusion/restenosis, rehospitalization, and repeat revascularization after one year.**

Results. **A total of 31 patients were treated with 36 long tapered balloons. Ten patients presented with ischemic tissue loss. Target lesions were mostly occlusive and diffuse, commonly involving the tibial arteries as well as the in-flow and out-flow vessels. Acute success was achieved in 100% of the cases without periprocedural complications. Clinical improvement in functional status was obtained and maintained after an average of 12 months, with a significant (P<0.001) decrease in Rutherford class, 100% limb salvage, no major amputation and five (16.1%) minor amputations. Duplex ultrasound control showed restenosis/reocclusion in two (6.5%) cases, whereas a total of seven (22.6%) patients underwent repeat revascularization (2 [6.5%] target lesion re-PTA).**

Conclusion. **Infra-popliteal PTA with this new, BTK dedicated, long tapered balloon in patients with CLI was feasible and safe, and was associated favorable clinical results at both acute and mid-term follow-up.**

KEY WORDS: Ischemia - Limb salvage - Peripheral arterial disease.

Increasing prevalence of diabetes and greater life expectancy are determining a progressive raise in the incidence and prevalence of critical limb ischemia (CLI).[1] Arterial revascularization is a mainstay in the management of patients with CLI due to below-the-knee (BTK) disease.[2] Whereas until recently vascular surgery by means of distal bypasses was considered the only feasible revascularization option,[1, 2] the development of specific techniques and improvement of dedicated devices has shown that percutaneous arterial revascularization by means of percutaneous transluminal angioplasty (PTA) is feasible, safe and effective.[3-6] Yet, there is still room for improvement, as PTA is still challenged by suboptimal angiographic results, and complications such as flow limiting dissections leading to abrupt vessel closure, or late restenosis/reocclusion.

Whereas stenting remains mainly reserved after failed PTA, most operators rely on plain old balloon

Conflict of interest.—The authors declare that they have no association with individuals, companies, or organizations with a vested interest in the subject matter/products mentioned in the manuscript.

Acknowledgements.—The authors wish to thank Giuseppe Biondi-Zoccai for his editorial assistance.

Received on February 4, 2009.
Accepted for publication on May 13, 2009.

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tal reference vessel diameter, as well as location of the target lesion. Indeed, when PTA was performed in tibial vessels only, balloons with a distal diameter ≥2.5 mm were used, together with higher (12-14 atm) inflation pressures. Conversely, when the distal edge of the balloon reached the pedal or the plantar artery, smaller balloons were chosen (*i.e.* with distal diameter ≤2.5 mm), and inflation pressures were limited to 7-9 atm. Inflow lesions in the iliac or femoral vessels were treated as per standard care at the above mentioned center, with standard balloon PTA and bail-out stenting, with the exception of distal superficial femoral and popliteal lesions, which were treated with the Amphirion™ Deep tapered balloons.

After such balloon inflations, the balloon was retrieved, while leaving the guidewire, to perform digital subtraction angiography and appraise post-PTA results. If angiographic success was apparent, the guidewire was retrieved and final control angiography performed. Otherwise, subsequent inflations at higher pressure, or with larger balloons were performed. The goal of PTA was to achieve a diameter stenosis <50% in all treated segments, in the absence of flow-limiting dissections. All patients were pre-treated with aspirin 75-160 mg/day and ticlopidine 500 mg/day or clopidogrel 75 mg/day for at least four days, and managed periprocedurally with 3 000-5 000 IU of i.v. unfractioned heparin.

Post-procedural and follow-up management

Postprocedurally, hemostasis was achieved with manual compression, and both aspirin and ticlopidine or clopidogrel were continued for four weeks. After discharge, clinical follow-up was routinely performed at one and then three-month intervals, including assessment of vital status and Duplex ultrasound imaging of the affected limb. In case of lack of clinical improvement, clinical recurrence (*e.g.* foot ulcer), or evidence of restenosis/reocclusion (at Duplex ultrasound), patients underwent repeat lower limb angiography, followed by revascularization where appropriate.

Definitions and end-points

Acute success was defined as the composite of: 1) technical success: ability to deliver the balloon, cross the target lesion and inflate the balloon at the desired pressure without balloon burst; 2) angiographic success: achievement of a postdilatation residual diameter stenosis of <50%; 3) procedural success: achievement of angiographic success free of periprocedural complications.

The primary objective of the study was the assessment of acute success (composite of technical, angiographic and procedural success). Up to 12 months following were also appraised: limb salvage rate; rate of major (above the ankle) and minor (below the ankle) amputations; re-hospitalizations, repeat revascularizations (distinguishing between target limb [outside the treated vessel], target vessel [outside the target lesion], and target lesion), and the occurrence of reocclusion or restenosis, change in Rutherford class (from baseline to 12 months) and change in cutaneous oxygen tension ($TcPO_2$, from baseline to 12 months, with very frequent interim measurements [*i.e.* at 1, 2, 3, 4, 5, and 6 weeks and then at three and six months]).

Statistical analysis

Continuous variables are reported as mean±standard deviation. Categorical variables are reported as N. (%), and were compared with the chi-squared test.

Results

A total of 31 consecutive patients were treated with 36 Amphirion™ Deep 210 mm tapered balloons. Baseline and procedural characteristics are reported in Tables I, II, respectively. Specifically, there were 16 (51.6%) men, age was 71±10 years, and all of them were non-insulin-dependent diabetics (100%). All subjects had CLI, with as many as 10 (32.3%) showing major tissue loss (Rutherford class 6). Most patients had severely diffused BTK disease, as well as common involvement of the superficial femoral artery (SFA) and/or popliteal artery, thus as many as 10 (32.3%) of them were treated in both the SFA and BTK district, and 10 (32.3%) in distal popliteal and BTK district. In addition, in six (19.4%) of patients disease involved the below-the-ankle vessels, which were thus treated concomitantly with the parent tibial artery. Finally, most of the lesions were occlusive (28 [90.3%]).

An average of 1.16 Amphirion™ Deep 210-mm tapered balloons were used per patient with most cases (20 [55.6%]) performed with the 2.5-2.0 mm diameter device. Balloon dilation pressure was 10±4 atm.

TABLE I.—*Characteristics of patients treated with the Amphirion™ Deep Long Cone balloon.*

	Patients N.=31
Male gender	16 (51.6%)
Age, years	71±10
Hypertension	25 (80.6%)
Dyslipidemia	18 (58.1%)
Smoking status	
— Previous smoker	19 (61.3%)
— Current smoker	12 (38.7%)
Diabetes	
— Type I	0
— Type II	31 (100%)
Rutherford class at admission – corresponding $TcPO_2$ at admission	
— 1-3	0-NA
— 4	4 (12.9%) -20±8
— 5	17 (54.8%) - 14±8
— 6	10 (32.3%) - 9±8

NA: not applicable; $TcPO_2$: cutaneous oxygen tension.

TABLE II.—*Angiographic and procedural characteristics of patients treated with the Amphirion™ Deep Long Cone balloon.*

	Patients N.=31
Location of treated lesion	
— Distal SFA+popliteal+anterior tibial arteries	5 (16.1%)
— Distal SFA+popliteal+tibio-peroneal trunk+ posterior tibial arteries	2 (6.5%)
— Distal SFA+popliteal+tibio-peroneal trunk+ peronial arteries	3 (9.7%)
— Tibio-peroneal trunk+posterior tibial arteries	5 (16.1%)
— Tibio-peroneal trunk+peronial arteries	6 (19.4%)
— Anterior tibial+pedal arteries	5 (16.1%)
— Peronial artery	4 (12.9%)
— Tibio-peroneal trunk+posterior tibial+ plantar arteries	1 (3.2%)
Total occlusion	28 (90.3%)
Lesion length, cm	35±10
Concomitant treatment of superficial femoral and popliteal artery	10 (32.3%)
Total number of Amphirion™ Deep 210 mm tapered balloons used	36
Balloon/patient ratio	1.16
Balloon diameter (proximal edge-distal edge), mm	
— 2.5-2.0	20 (55.6%)
— 3.0-2.5	12 (33.3%)
— 3.5-3.0	1 (2.8%)
— 4.0-3.5	3 (8.3%)
Maximum dilation pressure, atm	10±4
Acute success	31 (100%)

SFA: superficial femoral artery.

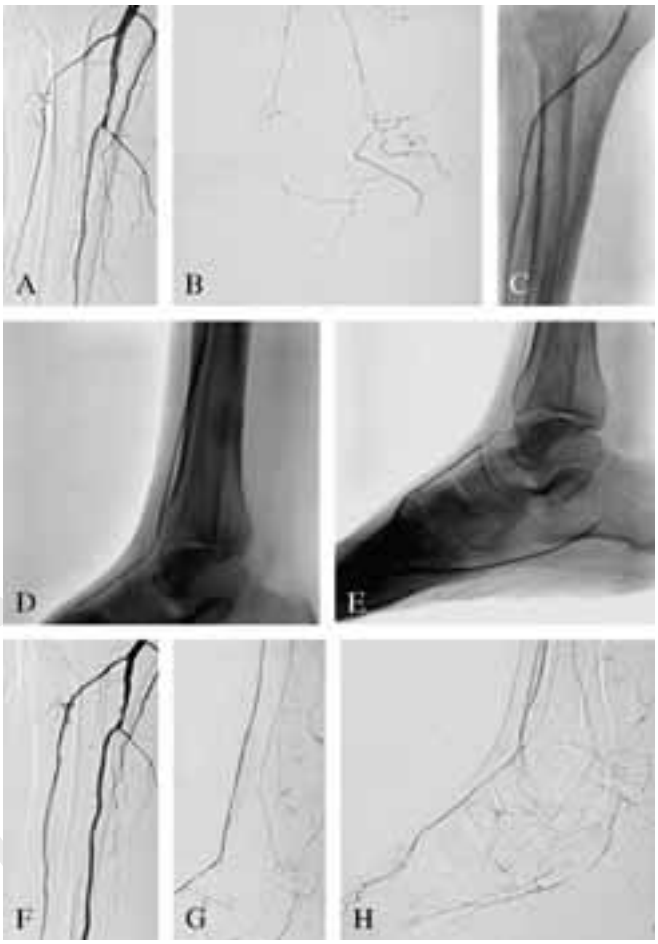

Figure 1.—PTA with the Amphirion™ Deep 210-mm tapered balloon in a patient with critical limb ischemia (Rutherford class 5) and diffuse occlusive disease of the anterior and posterior tibial arteries (A, B). He was successfully treated by means of balloon-angioplasty with the Amphirion™ Deep 210-mm tapered balloon repeatedly inflated for up to three minutes at pressures ranging between 7 and 14 atm (C-E) in both the anterior and posterior tibial arteries, as well as pedal and plantar arteries, achieving a satisfactory final angiographic and clinical result (F-H), as testified also by improvement in cutaneous oxygen tension and foot wound.

Dilation times were not systematically captured, but average one minute, as per standard practice at our center. Additional devices (*e.g.* cutting balloon, atherectomy or stents) were available routinely to the operators but were not used in any of the cases given the satisfactory results of balloon-only PTA. Technical, angiographic and procedural success were achieved in all cases, leading to an acute success rate of 100%. Figure 1 shows a typical patient with CLI undergoing PTA with the Amphirion™ Deep tapered balloon.

TABLE III.—*Clinical results at follow-up in patients treated with the 210 mm tapered Amphirion™ Deep balloon.*

	Patients N.=31
MFollow-up completion	31 (100%)
Clinical follow-up duration, months	12.0±0.5
Limb salvage rate	31 (100%)
Major amputations (above the ankle)	0
Minor amputations (below the ankle):	5 (16.1%)
— toe amputation	4 (12.9%)
— forefoot amputation	1 (3.3%)
Rutherford class– corresponding $TcPO_2$	
— 1	11 (35.4%) - 64±9
— 2	14 (45.2%) - 52±12
— 3	5 (16.1%) - 43±9
— 4	1 (3.3%) - 45±16
— 5-6	0 – NA
Re-hospitalizations	7 (22.6%)
Repeated percutaneous transluminal angioplasty (PTA)	7 (22.6%)
— Target limb (non-target vessel) PTA	4 (12.9%)
— Target vessel (non-target lesion) PTA	1 (3.3%)
— Target lesion PTA	2 (6.5%)
Duplex ultrasound scan (N.=31)	
— No restenosis	29 (93.6%)
— Restenosis	1 (3.3%)
— Reocclusion	1 (3.3%)

NA: not applicable; $TcPO_2$: cutaneous oxygen tension.

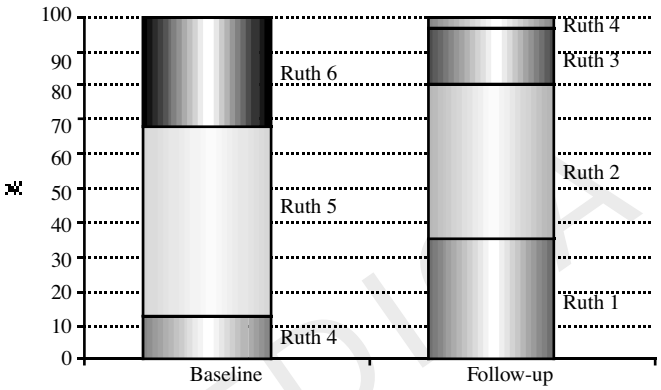

Figure 2.—Change in Rutherford class from baseline to 12 months ($P<0.001$ at χ^2 test) demonstrating the significant clinical improvements after PTA with the Amphirion™ Deep 210-mm tapered balloon.

All patients showed an improvement in their functional status, as testified at 12 months by major reductions in Rutherford class ($P<0.001$), and $TcPO_2$ (Table III and Figure 2). Indeed, no case of major amputation occurred, with only 5 (16.1%) cases of minor amputations (one forefoot amputation and four toe amputations, all with preservation of the ankle for future deambulation, and all in patients with pre-existent foot necrosis). These favorable results were supported by 12-month Duplex ultrasound control, available in all of them, showing restenosis/reocclusion in two (6.5%) cases only. Nonetheless, other five patients had atherosclerotic disease progression, leading to a total of seven (22.6%) repeat revascularizations during follow-up. Thus, four (12.9%) patients underwent target limb PTA, one (3.2%) target vessel PTA, and two (6.5%) target lesion PTA.

Discussion

This study, the first to date to report on the use of the Amphirion™ Deep 210-mm tapered balloon in patients with CLI due to diffuse infra-genicular arterial disease, suggests this device may provide favorable clinical results at mid-term follow-up.

In recent years several improvements have occurred both in the non-invasive and invasive management of symptomatic peripheral artery disease, yet the incidence and prevalence of CLI are still increasing.[1] Surgical revascularization by means of distal (*e.g.* femoro-tibial or femoro-pedal) bypasses is a well established and effective treatment for CLI, when saphenous vein grafts are available.[2] Unfortunately, many patients are poor surgical candidates. In addition, these procedures require sophisticated surgical skills that are not ubiquitous. These problems have provided the momentum for the application and development of endovascular techniques and devices for the management of CLI due to BTK atherosclerotic disease, leading to an ever increasing application of infra-genicular PTA.[3, 4] Until recently, there was uncertainty on the exact role of PTA in comparison to bypass surgery, yet current evidence supports the choice of an initial endovascular management, with bypass surgery reserved to the most severe, failing or recurrent cases.[4, 6] In this context, PTA is almost always based on balloon-only dilation, as data on other devices (eg cutting balloon, atherectomy, or stents) remain inconclusive.[7-9]

Despite its expanding clinical role and satisfactory results in comparison to surgery, balloon PTA for BTK lesions remains fraught with risks of peri-procedural complications and late recurrences. Indeed, long and diffusely diseased lesions are a rule in the BTK district, yet most of the currently available balloons have

lengths that do not match the target artery (*e.g.*, a tibial artery can be as long as 25 cm) and, more poignantly, they come in standard, cylindrical shape. Thus, at routine inflation pressures the balloon may underdilate the proximal tract of the target segment while overdilating (*i.e.* overstretching) the distal tract. This overstretch may pose an acute risk of vessel wall trauma (*e.g.* dissection or perforation),[10] as well as a later risk of constrictive remodelling and neointimal hyperplasia, both typical of overly traumatized arterial segments, possibly leading to restenosis or reocclusion.

Within this context, the availability of the Amphirion™ Deep 210-mm tapered balloon seems a useful adjunct to the armamentarium of the endovascular specialist, as this device has a length (210 mm) and a shape (conical) that best match the actual anatomic features of the typical infra-genicular target lesions. Present results support such premises and suggest that its use could lead to clinically relevant reductions in procedural and X-ray times, costs, and risk of distal dissection/perforation. Comparison of our results to other key works from the literature, as summarized by three key systematic reviews on patients with severe lower limb disease,[11-13] confirms the satisfactory findings in patients treated with the Amphirion™ Deep 210 mm tapered balloon. Specifically, Romiti *et al*. reported on works focusing on infra-genicular PTA for BTK disease, showing in patients without extensive tissue loss a limb salvage rate greater than 92%, with some studies reaching 100% limb salvage rates.[11] Met *et al*. reported on studies exploiting subintimal angioplasty for lower limb disease, with selected registries reaching limb salvage rates of 94% and overall survival rates of 100%.[12] Finally, Biondi-Zoccai *et al*. summarized results of 640 patients undergoing BTK stenting, showing limb salvage rates ranging between 94.7% and 98.1%, and repeat revascularization rates ranging between 6.2% and 13.9%.[13]

To improve outcomes when using the Amphirion™ Deep 210-mm tapered balloon, we specifically suggest to begin inflations in the most distal target segment, and then proceed proximally progressively increasing balloon pressure and/or upsizing the device diameter, and continuing each balloon inflation for at least one minute and reaching, whenever possible, pressures of 7-9 atm distally, and 12-14 more proximally. This approach appears in our experience the most effective and safe. This device cannot however be expected to address recoil in extremely fibrotic or calcific lesions. In such a setting, provisional stenting could prove useful.[9]

This study has a number of limitations, which include the lack of a control group, the reliance on duplex ultrasound to appraise patency rates and the small sample size. In addition, given the study design (retrospective single-center case series) primary patency and survival rates were beyond the scope of our work and were thus not computed. Thus, larger and controlled trials exploiting follow-up angiography are warranted to definitely appraise the risk-benefit balance of for this novel balloon device for the treatment of infra-genicular atherosclerotic disease.

Conclusions

Infra-popliteal percutaneous revascularization with the Amphirion™ Deep 210-mm tapered balloon in patients with severe lower limb ischemia and long lesions was feasible and safe, and was associated with favorable clinical results at both early and mid-term follow-up. The limited sample size does not enable however a definitive appraisal of the clinical role of this device, which awaits additional controlled studies.

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