EuroIntervention

Infragenicular angioplasty and stenting in the management of critical limb ischaemia: one year outcome following the use of the MULTI-LINK VISION stent

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The authors have no conflict of interest to declare.

KEYWORDS
Critical limb ischaemia, CoCr, stent, revascularisation, peripheral artery disease, below the knee, infragenicular, crural, limb salvage

Abstract

Background: Use of stents following angioplasty for infragenicular lesions appears to be superior to angioplasty alone. We investigated the safety and efficacy of MULTI-LINK VISION stent (Abbott Vascular, Brussels, Belgium) for the treatment of infragenicular lesions in patients with critical limb ischaemia (CLI).

Methods and results: During the period between February 2005 and October 2005, fifty patients with CLI (Rutherford 4 and 5) due to infragenicular disease were included in the study. The studied patient population included 28 males (56.0%) and 22 females (44.0%) with a mean age of 76 years (range 59-90 years). The medical history was significant for hypertension in 43 patients (86.0%), diabetes in 23 (46%) and hypercholesterolaemia in 37 (74%) patients. Fourteen patients (28%) admitted to the use of nicotine. Thirty-four (68%) belonged to Rutherford class 4 and 16 were class 5 (32%). All patients underwent clinical evaluation before and after the intervention. A pre-procedure Duplex ultrasound examination followed by angiography and intervention were performed on all patients included in the study. Sixty-two lesions were treated with angioplasty followed by insertion of 68 MULTI-LINK VISION stents. After intervention, patients were followed at one, six and 12 month intervals with clinical examination and arterial duplex study.

The survival of the studied population was 83.3%, the limb salvage was 89.3% and primary patency of treated vessel was 62.8% at 12 months.

Conclusions: Treatment of infragenicular lesions in CLI with MULTI-LINK VISION stent is safe and effective with satisfactory limb salvage. The primary patency was acceptable, but less compared to dedicated below the knee devices.

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Introduction

Patients with critical limb ischaemia (CLI) present with ischaemic rest pain or with ischaemic skin lesions, either ulcers or gangrene and with either rest pain or non-healing wounds and are classified as Category 4, 5 and 6 according to the Rutherford Categorisation[1], respectively. CLI patients have multi-segmental stenotic or occlusive lesions, often with involvement of the infragenicular vascular bed. Patients presenting with CLI are known to have high mortality due to cardiovascular events, and untreated CLI often leads to primary amputation[1]. Surgical revascularisation by bypass surgery is associated with a peri-operative mortality rate of 1.8-6% and a variable primary clinical success reported between 50%-77%[2,3]. The majority of patients with CLI have profound comorbid factors which preclude a major surgical intervention. In addition, absence of a suitable target vessel and/or infected soft tissues may preclude bypass surgery. Endovascular techniques, such as percutaneous transluminal angioplasty (PTA) or subintimal angioplasty, have shown promising results[4,5]. The BASIL trial has shown that PTA is an effective and cost-efficient alternative to traditional surgical approach in this elderly, fragile population[6]. The role of stents in the infragenicular lesions was limited because of lack of devices designed for this vascular bed. The stents were used selectively as a bailout following PTA for flow limiting dissections or residual stenosis[7]. However the results of routine stenting following an uncomplicated angioplasty were reported to be superior to PTA alone[8-10]. It is possible that stent implantation overcomes the early plaque remodelling and consequent loss of lumen after PTA alone. The primary objective of this prospective, single-arm study was to evaluate the safety and clinical efficacy of MULTI-LINK VISION (Abbott Vascular) stent in the treatment of CLI due to infragenicular vessel involvement.

Methods

This prospective, non-randomised clinical trial using the MULTI-LINK VISION (Abbott Vascular) stent system for the treatment of CLI involving the infragenicular vessels was performed with institutional ethics committee approval between February 2005 and October 2005 at AZ-St Blasius hospital, Dendermonde and Imelda hospital, Bonheiden, Belgium. The inclusion and exclusion criteria are given in Table 1. Fifty patients with CLI (Rutherford 4 and 5) and diagnosed with infragenicular occlusive arterial disease were included in the study. The studied population included 28 males (56.0%) and 22 females (44.0%) with a mean age of 76 years (range 59-90 years). The medical history was significant for hypertension in 43 patients (86.0%), diabetes in 23 (46%) and hypercholesterolaemia in 37 (74%) patients. Fourteen patients (28%) admitted to the use of nicotine. Based on the patients' clinical description, 34 (68%) belonged to Rutherford class 4, and 16 were class 5 (32%). All patients underwent clinical evaluation, Duplex ultrasound examination and angiography. Sixty-two lesions were treated with angioplasty followed by insertion of the MULTI-LINK VISION stent.

Device description

The MULTI-LINK VISION is a pre-mounted L-605 cobalt chromium alloy (CoCr) coronary stent with radial strength and fluoroscopic visibility superior to stainless steel stents. The stents are available in 2.75, 3.00, 3.50 and 4.00 mm diameter and lengths of 8, 12, 15, 18, 23 and 28 mm.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria
Stenotic (> 50%) or occlusive atherosclerotic disease of the infragenicular arteries
Length of lesion <55 mm
Reference vessel diameter should be 2.5-3.5 mm
A maximum of 2 lesions in one or more infragenicular vessels
Symptomatic critical limb ischaemia (Rutherford 4, 5)
Patients with one stenosed and one patent artery may also be included on the pre-condition that the stenosed artery supplies the wounded area
At least single vessel run-off until the ankle
The patient must be > 50 years
Life-expectancy of more than 12 months
The subject or legal guardian has been informed of the nature of the study; agrees to its provisions and has signed informed consent
The patient must be available for the appropriate follow-up times for the duration of the study
The patient is capable to follow all study requirements
Exclusion criteria
Patient refusing treatment
The reference segment diameter is not suitable for available stent design
Length of lesion requires more than two stent implantations
More than two infragenicular lesions in the same limb
Previously implanted stent(s) or PTA at the same lesion site
Lesion lies within or adjacent to an aneurysm
Inflow-limiting arterial lesions left untreated
The patient has a known allergy to heparin, aspirin or other anticoagulant/antiplatelet therapies or a bleeding diatheses or is unable, or unwilling, to tolerate such therapies
The patient takes Phenprocoumon (Marcumar)
The patient has a history of prior life-threatening contrast media reaction
The patient is currently enrolled in another investigational device or drug trial
The patient is currently breast-feeding, pregnant or intends to become pregnant
The patient is mentally ill or retarded

Follow-up visits

Following intervention, according to the standard care of CLI, patients are followed at one, six and 12 months with clinical assessment, Rutherford categorisation and arterial duplex examination. Patients with clinical deterioration were referred for arteriography.

Endpoints

The primary endpoint was 12-month primary patency of the MULTI-LINK VISION stent (Abbott Vascular) in patients with stenotic or

occlusive atherosclerotic disease involving the infragenicular vessels and CLI. Primary patency is defined as the absence of:

A. Any reintervention to restore the blood flow.
B. Major amputation.
C. Conversion to bypass surgery to restore the blood flow.
D. Untreated restenosis (>50%) or occlusion as determined by colour flow Duplex ultrasonography (CFDU), a haemodynamically significant restenosis (>50%) was defined as a Proximal Velocity Ratio (PVR) of ≥ 2.4. PVR is the ratio of the Peak Systolic Velocity (PSV) at the lesion segment over the PSV at the proximal reference vessel.

The secondary endpoints of the study were:

A. Immediate angiographic procedural success, defined as maximal 30% residual stenosis on visual assessment of the treated lesion.
B. Limb salvage (defined as avoidance of a major amputation).
C. Survival of the patient.

Anticoagulation regime

Patients were given 100 mg /day of aspirin and clopidogrel 75 mg daily for four days, or one loading dose of 300 mg the day prior to the procedure. Unfractionated heparin (150 IU/Kg body weight) was given during the procedure. The post-procedure antithrombotic regimen consisted of clopidogrel 75 mg daily for at least one month and aspirin, 100 mg daily, indefinitely. Nadroparin was administered daily for three weeks.

Statistics

The statistical analysis on the follow-up data of the entire patient group was done by Kaplan-Meier estimation. All calculations were performed using the MEDCALC statistical software version 9.2.0.1.

Results

Contralateral access was the preferred approach at our institution, and this was obtained in 48 patients (96.0%). Ipsilateral access to the tibial vessels was obtained in two patients (4%) because of the presence of aortic endograft in one patient and a history of common femoral artery pseudo-aneurysm in the contralateral groin in the second. The mean procedural time was 52 min (range of 25-90 min), mean volume of contrast used was 115 ml (range of 40-250 ml) and the mean fluoroscopy time was 16 min (range of 2-47 min).

The 62 lesions treated had a mean stenosis of 92.7% (range of 50-100%). The mean lesion length was 21.1 mm (range of 5.0-52.0) and the reference diameter of the vessel was 3.1 mm (range of 2.5-3.5). Thirty-four lesions were calcified (54 .8%), seven were ulcerative (11.3%) and vessel dissection was noted in two (3.3%). Two below-the-knee popliteal (BTK P3) arteries (3.2%), 18 tibio-fibular trunks (29.0%), 10 anterior tibial (16.2%), 16 posterior tibial (25.8%) and 16 fibular arteries (25.8%) were treated successfully with a total of 68 MULTI-LINK VISION stents. The description of the stent sizes used is given in Table 2. A predilation of the lesion was routinely performed. Twenty-three of the 62 lesions were occlusive and the remaining 39 were stenotic. The immediate procedural success was achieved in all patients (100%). As found by Kaplan Meier estimation (Figures 1-3), the survival of the studied population was 83.3%, the limb salvage was 89.3% and the primary patency of the treated vessel was 62.8% at 12 months.

Table 2. Stent size distribution (n=68).

Diameter	Length	Distribution (absolute)	Distribution (percentage)
3.0	15	22	32.4
3.0	28	16	23.5
3.5	15	10	14.7
3.5	28	20	29.4

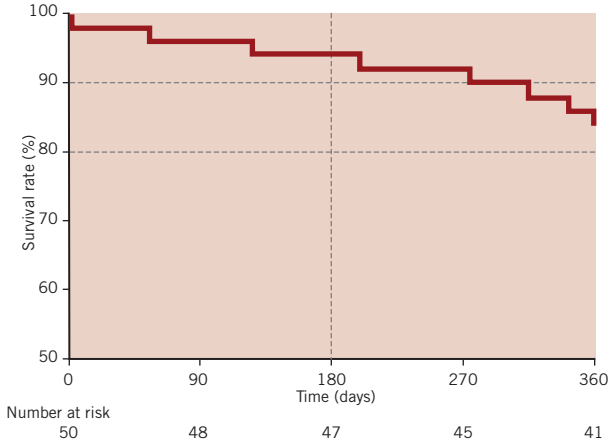

Figure 1. Kaplan-Meier estimation of survival

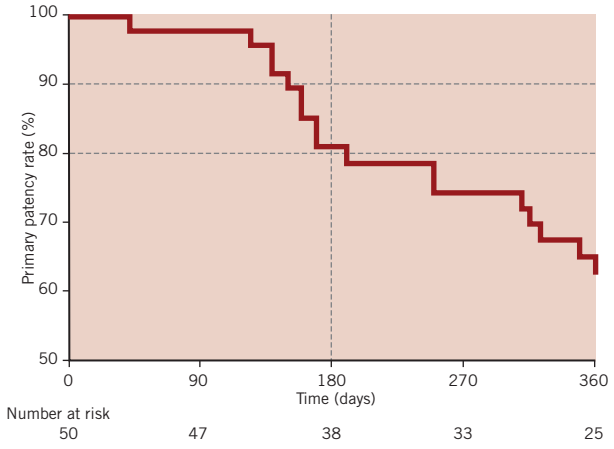

Figure 2. Kaplan-Meier estimation of primary patency

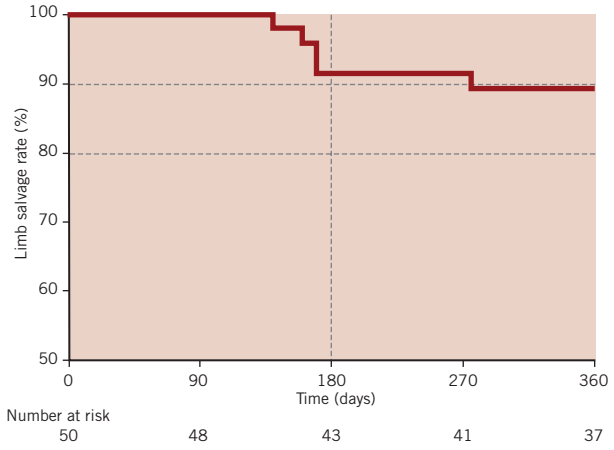

Figure 3. Kaplan-Meier estimation of limb salvage

Discussion

Critical limb ischaemia (CLI), the result of advanced, multi-segmental atherosclerotic lesions is one of the major causes of morbidity and mortality in the increasing elderly population. The increasing incidence of diabetes in the general population is also a major contributing factor for this epidemic of CLI. Despite the advances made in the treatment strategies of CLI, the management of this subset of patients is still a difficult task.

CLI manifests with rest pain, ulceration and gangrene of the lower extremity and affects 500-1000 individuals per million population every year with a significant economic impact on health care resources[1]. The mortality rate amongst these patients is 25% in one year5 and more than 50% in 3 years[1,11]. Untreated CLI often results in a primary major amputation, with markedly diminished quality-of-life and emotional stress to the patient and the family. Moreover, it translates into high costs to the society[12,13]. Many studies have shown significant improvement in the functional status and quality-of-life in patients with limb salvage by revascularisation rather than primary amputation[14]. Revascularisation is also more cost-effective than primary amputation in patients with critical ischaemia[15]. Improved survival rate is noted after revascularisation by distal bypass surgery as compared to primary amputation[16,17] and current data unequivocally supports aggressive revascularisation of critically ischaemic limbs[18].

Many investigators recommend that in patients with CLI and concomitant infragenicular lesions, the endovascular strategy should be considered first, prior to surgery[10,19,20]. The goal of any intervention is to achieve an in-line pulsatile flow of blood to the ischaemic region. The endovascular intervention has shown to be an effective tool[10,19-21] for CLI with reduced mortality[6,22], hospital stay[22] and costs[6,22] compared to bypass surgery. Moreover, a failed angioplasty does not preclude surgical revascularisation[6,10,22] at a later time.

Although the reported high clinical and technical success[23-25] of endovascular infragenicular strategies, the BASIL trial documented high immediate failure and re-intervention in a 12 month follow-up for angioplasty group compared to bypass surgery[6]. The infragenicular vessels are of smaller calibre and the atherosclerotic process involving these is often diffuse and multi-segmental[9]. Angioplasty and stenting may achieve superior outcome compared to angioplasty without stenting[9,26] in this hostile vascular bed. However the restenosis rate following angioplasty and stenting may be more than 50% after 12 months[1]. To overcome this, and to improve the primary patency rate, drug eluting stents and stents of different material were studied by several investigators. Improved patency rates were reported for sirolimus-eluting stents[27,28], absorbable metal stents[29] and nitinol stents[30].

In an earlier publication of our group[10], we reported on our global experience using all the available, different endovascular tools, including the above mentioned newer generation devices, and found at 12 months a limb salvage rate of 96.6%. This result is comparable to the 89.3% limb salvage rate with the bare metal MULTI-LINK VISION stent as found in the present study. However, the MULTLINK VISION stent's primary patency rate of 62.8% at 12 months is inferior to this in our earlier global publication (74.2%) and other published reports of dedicated last generation below the knee stents[27-30], but is still better compared to PTA alone.

Endovascular management will become the primary modality of treatment in patients with CLI due to infragenicular disease. Development in the field of endovascular techniques and devices will certainly further improve the patency rates of the infragenicular interventions and achieve higher clinical success rates in this subset of fragile patients.

Study limitations

This is a prospective, non-randomised study limited to two centres and with a small number of patients. The other limitation was that the patency of the device was determined by Duplex ultrasound examination rather than the conventional angiography. Recently after the finalisation of the follow-up, Favaretta et al brought to light that Duplex ultrasound has only limited value for the investigation of infragenicular lesions[31]. Therefore, any future investigation into the efficacy of the MULIT-LINK VISION stent – or any other endovascular device for infragenicular revascularisation – should be controlled by means of an angiographic control rather than a Duplex ultrasound examination.

Conclusion

The MULTI-LINK VISION stent is a safe device for the management of CLI due to infragenicular lesions. The 12 month limb salvage rate was comparable to the published reports on dedicated below the knee devices. Although better then what was seen with PTA alone, the primary patency seems to be lower when compared to other dedicated below the knee stent types.

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