Cryoplasty for the Treatment of Femoropopliteal Arterial Disease: Results of a Prospective, Multicenter Registry

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PURPOSE: Despite suboptimal results, angioplasty of femoropopliteal arterial lesions has been a mainstay of endovascular therapy for many years. The recent introduction of cryoplasty marks a potential advance in the ability to effectively treat peripheral arterial atherosclerotic stenoses. This article presents the results of a prospective, multicenter trial that evaluated the efficacy of cryoplasty for femoropopliteal disease.

MATERIALS AND METHODS: One hundred two patients with claudication and lesions of the superficial femoral and popliteal arteries of no greater than 10 cm were studied. All patients were treated with a primary strategy of stand-alone cryoplasty with use of the PolarCath cryoplasty system. The primary endpoints of the study were acute technical success and clinical patency at 9 months. Technical success was defined as the ability to achieve residual angiographic stenosis no greater than 30% and residual stenosis less than 50% by duplex ultrasound (US) imaging. Clinical patency was defined as freedom from target lesion revascularization within 9 months. Primary patency was defined by a duplex US systolic velocity ratio no greater than 2.0.

RESULTS: A total of 102 patients were enrolled at 16 centers. Of those treated, 31% had diabetes and 31% were active cigarette smokers. The majority of the lesions were confined to the superficial femoral artery (84.3%) and 14.7% presented with total occlusions. The mean vessel diameter treated was 5.5 mm ± 0.5, the mean stenosis diameter was 87% ± 10%, and the mean lesion length was 4.7 cm ± 2.6. The technical success rate was 85.3% with a mean residual stenosis after cryoplasty of 11.2% ± 11.2% ($P < .05$ vs baseline). Clinical patency in this group was 82.2%, as only 16 patients required target lesion revascularization during the 9-month surveillance period. Primary patency determined by duplex US was 70.1%.

CONCLUSIONS: Cryoplasty demonstrated a high degree of acute angiographic success and a low frequency of target lesion revascularization. The patency rate observed compares favorably to that previously documented with conventional angioplasty.

J Vasc Interv Radiol 2005; 16:1067–1073

Abbreviations: ABI = ankle-brachial index, PSV = peak systolic velocity, SMC = smooth muscle cell, SVR = systolic velocity ratio, TASC = TransAtlantic Inter-Society Consensus

SINCE the development of percutaneous transluminal angioplasty 40 years ago, this technique has become the mainstay of endovascular therapy for intermittent claudication of the lower extremities (1). However, despite widespread practice, angioplasty continues to be limited acutely by arterial dissection and recoil and by suboptimal long-term patency rates, especially in more challenging lesions. Although some degree of acute dissection is inherent in most angioplasty procedures, a recent analysis demonstrated greater than desired dissection in a significant number of treated vessels (2). In addition, a contemporary metaanalysis of femoropopliteal angioplasty has demonstrated a 1-year patency rate of 59% among multiple lesion subsets (3).

Stent implantation at the time of angioplasty has been used in an effort to improve endovascular outcomes.

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J.D.J. is a shareholder and has intellectual property in Cryovascular Systems Inc. None of the other authors have identified a conflict of interest.

DOI: 10.1097/01.RVI.0000167866.86201.4E

Stent placement has improved the acute technical results of angioplasty by eliminating vascular recoil and resolving arterial dissection (4). Because of the aggressive neointimal proliferation, stent implantation of femoropopliteal arteries has done little to extend the durability of endovascular interventions, limiting their application to a "bailout" indication (5–8).

Endovascular cryotherapy, also known as cryoplasty, represents a new method of peripheral vascular intervention. Cryoplasty combines the dilation force of angioplasty with the simultaneous delivery of cold thermal energy to the arterial wall. Both mechanisms are achieved by filling the catheter with nitrous oxide instead of the usual contrast material/saline solution mixture. Cryotherapy has been shown to biologically alter the behavior of arterial cellular components in a manner that results in a benign healing process (9). In particular, collagen fibers are unperturbed and therefore maintain the architectural integrity of the artery, whereas elastin fibers undergo a morphologic change that may limit vascular recoil. In addition, cryotherapy is capable of inducing apoptosis in smooth muscle cells (SMCs) and other cell lines that participate in the restenosis process (10).

Early clinical reports of cryoplasty for femoropopliteal disease have shown encouraging results (11). The purpose of this study was to evaluate the safety and efficacy of femoropopliteal cryoplasty in a prospective multicenter registry.

MATERIALS AND METHODS

Patient Group

The study was approved by the United States Food and Drug Administration. One hundred two patients with intermittent claudication caused by femoropopliteal arterial disease were enrolled in a prospective, nonrandomized, multicenter registry. Patients were eligible for the study if they had intermittent claudication (Rutherford category 2/3) of the lower extremities caused by de novo or restenotic lesions of the superficial femoral artery or popliteal artery that were amenable to endovascular intervention. Target lesions were classified as TransAtlantic Inter-Society Consensus (TASC) class A, B, or C stenoses or occlusions (12) with a percent diameter stenosis of at least 50%, lesion length no greater than 10 cm, and at least one vessel runoff to the foot. Tandem lesions were included in the study provided they were located within the maximum specified treatment length of 10 cm. Patients with recent myocardial infarction or stroke and those with serum creatinine levels greater than 2.5 mg/dL were excluded from the study. Additionally, patients with rest pain, ischemic foot ulceration, or in-stent restenotic lesions were not eligible for enrollment.

The study protocol received institutional review board approval at all enrolling centers and informed consent was obtained from all patients.

Technique

All patients who met the enrollment criteria of the study underwent a baseline clinical examination, resting ankle-brachial index (ABI) measurement, and lower-extremity arterial duplex ultrasound (US) examination. Before intervention, all patients were administered 325 mg of aspirin, clopidogrel (75 mg daily for 4 days before intervention or 300-mg preprocedural loading dose), and intravenous heparin or bivalirudin to maintain an activated clotting time greater than 200 seconds. Angiography was performed with use of conventional methods to identify the target lesion and confirm its suitability for the trial.

The intent of the study was to conduct cryoplasty as a stand-alone therapy, reserving stent placement as a bailout procedure for suboptimal results, and adjunct angioplasty at the discretion of the investigator. Cryoplasty was performed with use of standard interventional technique with a 0.035-inch angioplasty wire through a 7-F arterial sheath. When the lesion was identified, cryoplasty was performed with the PolarCath cryoplasty system (Cryovascular Systems, Los Gatos, CA). The components of the system include a cryoplasty catheter, a microprocessor-based inflation unit, and a nitrous oxide cylinder (**Fig 1**).

The system is based on traditional balloon angioplasty technology but has been modified to incorporate nitrous oxide as the inflation medium instead of the standard mixture of saline solution and contrast medium. On initiation of cryoplasty, pressurized liquid nitrous oxide is delivered via a hypotube to a balloon reservoir at the distal end of the catheter. As the liquid nitrous oxide enters the balloon, it undergoes a phase shift to a gaseous form, which causes expansion and a dilation force of 8 atm. This phase change causes an endothermic reaction that simultaneously creates a heat sink that reduces the temperature at the interface of the balloon and the vessel wall to −10°C. The treatment cycle of simultaneous dilation and cooling lasts 20 seconds, and after passive warming of the catheter by body temperature and surrounding blood flow, the balloon is manually deflated and can be repositioned or removed.

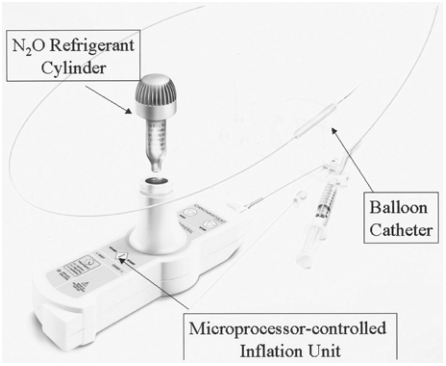

Figure 1. The three components of the cryoplasty system consist of a cryoplasty catheter, a microprocessor-controlled inflation unit, and a nitrous oxide cylinder.

After cryoplasty, patients received clopidogrel for 30 days and were encouraged to take aspirin indefinitely. Postprocedural examinations included an ABI measurement within 24 hours and a lower-extremity arterial duplex scan within 7 days of cryoplasty. At 3 and 9 months, patients returned for clinical assessment, ABI measurement, and arterial duplex US. All US images were obtained by the local site personnel in accordance with instructions by an independent duplex US core laboratory (Vascular Ultrasound Core Laboratory, Boston, MA).

Arterial Duplex Imaging Protocol

All sites considered for entry into the trial were surveyed by the core laboratory to determine the available