

Cryoplasty for Treating Femoropopliteal Occlusive Disease

A single-center experience suggests that cryoplasty is effective first-line therapy and reduces target lesion revascularization.

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Conventional percutaneous transluminal angioplasty (PTA) is a well-proven minimally invasive alternative to bypass surgery for the treatment of certain atherosclerotic lesions. The acute success and long-term durability of PTA depends on several factors, including the particular artery affected, lesion length, the presence of significant calcification, and the presence of stenosis versus occlusion. The TransAtlantic Inter-Society Consensus (TASC) has suggested guidelines for treating obstructive lesions in the peripheral circulation, identifying lesions that may be more favorably treated by endovascular versus surgical means.¹

In the lower extremity, the superficial femoral artery (SFA) and popliteal artery (PA) pose significant challenges for a number of reasons, primarily due to the extent and type of disease, as well as the mechanical stresses on these vessels. Restenosis rates in the femoropopliteal and infrapopliteal arteries range from 30% to 80%,²⁻⁶ leading to a high incidence of repeat revascularization attempts. The causes of restenosis are multifactorial and include recurrent or residual plaque, dissection, and vascular recoil. Stent placement may prevent dissection and recoil, but can prompt an aggressive neointimal response, potentially leading to recurrent inflammation and late restenosis. Early experience with self-expanding and drug-eluting stent technology has shown promise,⁷ however, there have been issues with stent fractures in long lesions, not an uncommon scenario in the SFA. As such, alternative

forms of intervention are being vigorously pursued in an attempt to reduce placing stents in the SFA and PA.

The femoropopliteal segment is subject to a multitude of mechanical stresses, including compression, torsion, stretching, and shortening. The extent and type of lesions in this segment are often difficult to treat. In



Figure 1. A baseline right lower-extremity angiogram demonstrates diffuse atherosclerotic disease of the distal SFA and 90% popliteal stenosis (A). After cryoplasty therapy of the entire length of the distal SFA and the popliteal lesion, an angiogram shows markedly improved appearance (B). The patient was asymptomatic at 30-day, 6-month, and 12-month follow-up.



Figure 2. Diffuse mid- and distal-SFA disease can be seen on a bilateral lower-extremity arteriogram. Note patent right femoropopliteal graft (A). Selective left lower-extremity arteriogram further defines the SFA occlusion (B). After guidewire recanalization and cryoplasty, a completion arteriogram shows in-line flow through the SFA (C).

addition to the overall length of the femoropopliteal segment, atherosclerotic occlusive disease in the SFA is typically more diffuse than elsewhere in the vascular system. There is also a relatively higher frequency of occlusion versus stenosis in the SFA. Complex lesions, particularly with extensive or eccentric calcification, are also frequent in the SFA.

The cryoplasty procedure was designed to improve upon the outcomes of PTA and stenting by combining balloon angioplasty techniques with the delivery of cryothermal energy to the target lesion. The theoretical mechanical and biological effects of this cold therapy include altered plaque response, reduced elastic recoil, and smooth muscle cell apoptosis with the intended beneficial effects of reduced arterial dissection and the promotion of positive remodeling.⁸⁻¹²

Previous studies have reported favorable results with cryoplasty therapy in terms of initial success and reduced incidence of target lesion revascularization.^{8,9} The authors report their experience using cryoplasty therapy for treating patients with atherosclerotic femoropopliteal lesions.

MATERIALS AND METHODS

A retrospective review of 41 consecutive patients who underwent primary cryoplasty therapy of occlusive lesions in the SFA or PA from January 2004 to September 2004 was conducted. Procedures were performed at a single center by four interventionalists. All patients identified with femoropopliteal occlusive disease by any method (MRA, CTA, or angiography) were considered candidates for cryoplasty, although the treatment method was at the discretion of the treating interventionalist.

Cryoplasty was performed in 41 patients: 29 (71%)

were men and 12 (29%) were women. The mean age of patients was 69 years (range, 48 to 81 years). Of the 41 patients, 17 (42%) were diabetic, 30 (73%) were smokers, and 32 (78%) were hypertensive. Twenty-seven patients (66%) had a history of coronary artery disease (CAD). All patients were classified as grade I chronic limb ischemia, categories 1 to 3 by the Rutherford-Becker classification system.¹³ Some lesions (10 of 41, 24%) were identified by MRA before presentation to the interventional suite. All patients underwent conventional digital subtraction angiography (DSA) at the time of intervention. Isosmolar iodixanol (Visipaque 320, Amersham Health/GE HealthCare Biosciences, Little Chalfont, UK) was used during angiography.

Of the 41 lesions, 33 (80%) were SFA, eight (20%) were PA, and six (15%, four SFA, two PA) were occluded. All but one lesion were *de novo* atherosclerotic lesions. One patient with a restenotic lesion had undergone previous conventional angioplasty. Mean lesion length was 6.7 cm (range, 2 to 18.5 cm), Mean stenosis was 83% (range, 55 to 100%). All patients had at least one vessel below the knee, providing in-line flow to the foot.

Cryoplasty was performed with the PolarCath balloon angioplasty catheter (CryoVascular Systems, Los Gatos, CA [which received FDA approval in September 2002]) and standard angioplasty techniques. The cryoplasty system includes a triple-lumen balloon catheter, a nitrous oxide cylinder, an inflation unit, and a power source. During the procedure, liquid nitrous oxide travels through the lumen of the catheter to the balloon and changes to a gaseous state, expanding the balloon and reducing the temperature. Refrigerant flows continuously throughout the treatment cycle, and the temperature is regulated. The integrated process of inflation and reduction in balloon surface temperature exposes

the vessel wall to a predetermined algorithm of temperature (-10°C), pressure (8 atm), and dwell time (20 sec). At the completion of the cycle, the gas is evacuated, deflating the balloon, which is then removed.

A contralateral approach was used in the majority of cases. A 6-F or 7-F Pinnacle sheath (Terumo Medical Corporation, Somerset, NJ) was delivered for arterial access. Equipment for crossing stenoses and recanalizing occlusions was used at the discretion of the interventionist but typically involved the use of hydrophilic guidewires (GlideWire, Terumo Medical Corporation) or low-profile, .014-inch guidewires (Thruway, Boston Scientific Corporation, Natick, MA). Empiric intravenous heparin was used for anticoagulation. Balloons were sized by visual estimation or by a reference marker on the patient's leg in the area of the lesion. Cryoplasty of the lesion was performed using the step-wise instructions for use. Control angiography was used to assess immediate procedural success, and repeat dilatation was performed if the results were suboptimal. After intervention, all patients were placed on an antiplatelet regimen using aspirin and/or clopidogrel (depending on patient tolerance) for a minimum of 2 months unless other circumstances required longer-term therapy. Follow-up protocol involved clinical examination, ankle-brachial index, and duplex examination at 30 days, 6 months, and 12 months. Interval clinical evaluation was available at 9 months for 21 patients.

RESULTS

In all 41 patients (100%) who underwent cryoplasty therapy, the procedure was technically successful, defined as residual stenosis of less than 30%. Manageable dissections requiring no further therapy occurred in nine patients (22%). Flow-limiting dissection (grade C) occurred in one patient (2%) with a heavily calcified stenosis and required placement of a stent (Smart Control, Cordis Endovascular, a Johnson & Johnson company, Miami, FL).

Thirty-day follow-up was available for 38 of the 41 patients (93%). The results were targeted lesion revascularization (TLR) (0%), clinical patency (defined as <50% stenosis by duplex and/or freedom from reintervention) in all (100%), 35 (92%) experienced improvement in claudication symptoms as measured by standard Walking Impairment Questionnaire, and 36 (95%) improved Rutherford classification by +1 or +2.

Six-month follow-up was available for 23 patients (73%). The results were two patients (9%) required target lesion revascularization, clinical patency was maintained in 20 patients (87%), 20 patients (87%) experienced improvement in claudication symptoms, and 19

patients (83%) were Rutherford classified as +1 or +2 from baseline. Regarding target lesion revascularization, one patient with a history of external beam radiation therapy for pelvic malignancy experienced recurrent intermittent claudication and stenosis and underwent repeat PTA at 5 months, one patient required a femoropopliteal bypass graft, and one patient developed recurrent claudication at 4 months, but declined further intervention.

Twenty-one patients available for 9-month clinical follow-up showed consistent symptomatic improvement from preintervention baseline. Specifically, all 20 patients who noted subjective improvement at 6 months maintained this benefit and no additional patients required TLR. In addition to these patients, eight have returned thus far for 12-month evaluation. Despite this small cohort of patients for short-term follow-up, results were encouraging. Seven patients remained free of claudication symptoms or markedly improved from baseline, with no evidence of restenosis (>50%) by duplex examination. One patient developed recurrent claudication and underwent repeat cryoplasty at 13 months.

CASE PRESENTATIONS

Case 1

A 74-year-old woman with a medical history of hypertension, coronary artery disease, and recent right total knee arthroplasty had been experiencing intermittent claudication, with a maximum walking distance of 50 feet. Her ankle-brachial index was 0.71. A right lower-extremity arteriogram demonstrated diffuse atherosclerotic disease of the distal SFA and 90% popliteal stenosis (Figure 1A). She underwent 50-mm X 40-mm cryoplasty from a contralateral approach, treating the entire length of the distal SFA and the popliteal lesion. Completion angiogram showed markedly improved angiographic appearance (Figure 1B). Her 30-day ankle-brachial index was 0.90. She was asymptomatic at 30-day, 6-month, and 12-month follow-up.

Case 2

A 69-year-old woman with known peripheral arterial disease and history of right femoropopliteal graft presented with left lower-extremity claudication at 40 feet. Bilateral lower-extremity arteriography demonstrated diffuse left mid-SFA disease and 7-cm distal SFA occlusion. Selective left lower-extremity arteriography further defined the SFA occlusion with abundant mature collaterals (Figure 2B). The occlusion was recanalized using guidewire techniques and intraluminal position was confirmed in the popliteal artery. Completion angiography after SFA recanalization and 6-mm cryoplasty

shows excellent antegrade flow through the SFA and no evidence of flow-limiting dissection (Figure 2C).

DISCUSSION

The optimal treatment for patients with femoropopliteal occlusive disease has been extensively debated. The depth of these debates is beyond the scope of this article, but several observations are worth mentioning. The advancing age of the population (and likely increased prevalence of peripheral arterial disease) combined with the expanding application of devices in the "endovascular era" continually challenge yet provide opportunity for vascular specialists to improve patient outcomes. The evolution of devices (eg, low-profile balloons, atherectomy, stents) to treat this problematic arterial segment shows the importance of finding the best alternative to what has been the gold standard for patients with SFA and popliteal disease: surgical femoropopliteal bypass.

A meta-analysis of historical SFA angioplasty data has shown progressively decreasing patency rates over time, with <50% patency beyond 3 years.² Surgical outcomes for infrainguinal bypass have fared somewhat better, yet have a broad range of patency rates (83% at 1 year, 38% to 60% at 5 years) depending on numerous clinical, surgical, and anatomic variables.¹⁴⁻¹⁶ Success in early SFA stent trials was relatively modest and, similar to surgical data, was dependent on several factors to predict outcomes. The byproduct of these efforts, however, was the prompting of further advances in stent technology. Several trials have been recently completed or are underway investigating nitinol stent technology, with or without drug elution, as the next effort to improve upon existing data. Eliminating the foreign-body or hyperplastic response to stent placement remains the goal, despite initial enthusiasm of some investigators.¹⁷

Emerging technologies such as cryoplasty therapy and percutaneous atherectomy are allowing interventionists more options and enabling more aggressive endovascular treatment of femoral, popliteal, and infrapopliteal lesions. These technologies have reinvigorated interest in stent-free outcomes. The mechanism of action of the cryoplasty procedure may provide the biological as well as the mechanical means to maintain long-term patency in the SFA and PA.

CONCLUSION

Our single-center experience with cryoplasty therapy corroborates 9-month clinical trial data.¹⁰ Indeed, mean lesion length in our series was slightly greater, yet similar results were achieved. At our center, we have gone through an evolution of endovascular treatment

approaches for femoropopliteal disease and our data suggest the durability of cryoplasty to be superior to historical PTA outcomes, and to be an encouraging option for treating occlusive lesions in this challenging vascular bed. In this patient population, we now frequently use cryoplasty as a first-line approach. ■

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