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Safety and Feasibility of Intravascular Lithotripsy for Treatment of Common Femoral Artery Stenoses

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Abstract

Purpose: To evaluate the safety and feasibility of treating calcified, stenotic common femoral arteries (CFAs) using the Peripheral Intravascular Lithotripsy (IVL) System. **Methods:** An analysis was performed of 21 patients (mean age 71.9±10.1 years; 16 men) across 3 sites with calcified CFA stenoses treated with the Peripheral IVL System. The outcomes of interest were the ability to deliver IVL to the target lesion, the increase in acute gain, the reduction in diameter stenosis, the rate of provisional stenting, and angiographically defined complications. **Results:** Access to the target lesion and delivery of treatment by the IVL catheter were successful in all 21 patients. Post treatment mean diameter stenosis was 21.3%, representing an acute mean lumen gain of 3.1±1.3 mm (range 0.7–5.2). Vascular complications were minimal, with only 5 type B (non-flowing-limiting) dissections reported. The profunda femoris artery was patent in all patients following IVL, and none of the subjects experienced a perforation, distal embolization, thrombus, no reflow, or abrupt closure. **Conclusion:** These early results demonstrate that calcified, stenotic CFA lesions can be safely and successfully treated using the Peripheral IVL System.

Keywords

atherosclerosis, calcification, common femoral artery, complications, intravascular lithoplasty, lithotripsy, stenosis

Introduction

The key underlying issue of atherosclerotic common femoral artery (CFA) disease is the typically high calcium concentration. Traditionally, the standard of care for CFA disease has been common femoral endarterectomy (CFE), which has achieved high rates of long-term patency.[1–3] CFE, however, is associated with mortality between 3% and 4%[4] and a risk of morbidity >10%.[4] Surgical treatment of CFA stenosis is also associated with an extended length of stay (mean 4±7.5 days), adding to the burden on the health care system.[4] Furthermore, many patients are not ideal surgical candidates owing to diabetes, renal insufficiency, and/or the increasing incidence of obesity.[4,5]

In light of these shortcomings, endovascular interventions, including angioplasty, stenting, and atherectomy, have been evaluated for the management of CFA stenosis, although calcium is the underlying problem. While endovascular procedures were safe and technically successful, they had poorer long-term patency and more repeat interventions than surgery,[6–10] though more recent data indicate good outcomes for CFA stenting.[11,12] Given these varied results, endovascular treatment strategies for CFA disease have not been fully adopted.

Intravascular lithotripsy (IVL) is a recently introduced endovascular option that may provide an alternative to surgery for the treatment of CFA disease, especially with regard to the usually high calcium burden. The use of IVL in femoropopliteal and below-the-knee (BTK) arteries for modification of calcified plaque has been recently described, with promising results.[13–15] IVL uses pulsatile sonic pressure waves that pass through soft tissue and selectively interact strongly with calcium, producing significant shear stresses that have the ability to fracture the calcium. IVL is designed to safely and effectively modify both intimal and medial calcium across a wide range of vascular applications to increase vessel compliance,

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restore vessel mobility, and provide new versatile treatment options for patients. Furthermore, the use of IVL does not prohibit future surgical interventions. The goal of this study was to evaluate the safety and effectiveness of the Peripheral IVL System (Shockwave Medical, Fremont, CA, USA) to deliver localized lithotripsy to calcified, stenotic CFAs.

Materials and Methods

Study Device

The Peripheral IVL System consists of a generator, a connector cable, and catheter that houses an array of lithotripsy emitters enclosed in an integrated balloon.[14] The 60-mm-long IVL balloon is available in 8 diameters ranging from 3.5 to 7.0 mm in 0.5-mm increments. Once a calcified arterial lesion is crossed with a 0.014-inch guidewire, the IVL catheter is advanced to the lesion and is positioned using radiopaque markers. The generator produces 3 kV of energy that travels through the connector cable and catheter to the lithotripsy emitters at one pulse per second. With the integrated balloon expanded to 4 atm using a mixed saline and contrast solution (to achieve balloon–vessel wall apposition without significant angioplasty), a small electrical discharge at the emitters vaporizes the fluid and creates a rapidly expanding bubble within the balloon. This bubble generates a series of sonic pressure waves that travel through the fluid-filled balloon and pass through soft vascular tissue, selectively cracking the hardened calcified plaque. The emitters positioned along the length of the device create a localized field effect within the vessel. Following calcium disruption, the balloon is then inflated to nominal pressure (6 atm) to maximize lumen gain. This cycle is then repeated as needed until the desired diameter is obtained. The IVL catheter can be moved to other lesion locations to deliver lithotripsy.

Study Design and Patient Enrollment

The study was conducted prospectively in Austria between August 2015 and December 2015 and augmented with cases from 2 additional sites in Germany and the United States. In the latter 2 centers, the databases were interrogated to identify patients who had calcified CFA lesions treated with IVL between April 2017 and March 2018. The de-identified data were transferred to established data collection forms, pooled, and queried to resolve discrepancies and to ensure completion prior to database review by the investigators. All subjects were consented for the surgical procedures per institution standards. No additional consent was required for the database search or use of anonymized data.

Table 1. Characteristics of the 21 Study Patients.[a]

Age, y	71.9±10.1
Men	16
Rutherford category	
1	1
2	2
3	11
4	5
5	2
Reference vessel diameter, mm	6.1±0.8 (4.5–7.5)
Lumen diameter, mm	1.7±0.7 (0.0–2.8)
Diameter stenosis, %	72.3±12.8 (50.2–100.0)
Lesion length, mm	37.8±16.7 (12.0–72.7)
Calcification[b]	
Moderate	6
Severe	15
Calcified length, mm	61.6±30.7 (25.4–143.0)

[a]Continuous data are presented as the mean ± standard deviation (range); categorical data are given as the number.
[b]Calcification as defined by the core laboratory as readily apparent densities noted within the apparent vascular wall at the site of a stenosis. Classifications are none/mild, moderate (densities noted only prior to contrast injection), and severe (radiopacities noted prior to contrast injection generally involving both sides of the arterial wall).

Computed tomography angiography (CTA) or plain radiographs were used to confirm evidence of target vessel calcification precluding transfemoral access and suitability for IVL treatment. An independent core laboratory (Yale Angiographic Core Laboratory, New Haven, CT, USA) conducted all angiographic analyses. Moderate calcification was defined by the core laboratories as densities noted prior to contrast injection; severe calcification was defined by densities noted prior to contrast injection generally involving both sides of the arterial wall.

Patient Population

The 3 centers contributed 21 patients (mean age 71.9±10.1 years; 16 men) to the analysis. Baseline demographics and lesion characteristics are shown in Table 1. Eighteen patients enrolled in the study had Rutherford category 3 to 5 ischemia. The mean reference vessel diameter was 6.1 mm, and the mean minimum lumen diameter was 1.7 mm, with a corresponding diameter stenosis of 72.3%. The mean lesion length was 37.8±16.7 mm. The calcium burden was significant (15 patients had severe calcification), with the average length of calcium (61.6 mm) being greater than the lesion length.

Study Procedures

Vascular access, anticoagulation, introduction of guidewires, and catheter use were conducted using each institution's

Table 2. Characteristics of the 21 Procedures and Outcomes.[a]

Predilation, %	0
Successful IVL delivery	21
IVL pulses	140±58 (60–300)
Pressure, atm	6.3±1.4 (4.0–9.3)
Adjunctive technology	
Drug-coated balloon	18
Atherectomy	1
Standalone IVL	2
Stents	0
Outcomes	
Lumen diameter, mm	4.8±1.1 (2.8–6.5)
Diameter stenosis, %	21.3±10.7 (5.1–40.0)
Acute gain, mm	3.1±1.3 (0.7–5.5)
Dissection (grade B)	5
Perforation	0
Distal embolization	0
Thrombus	0
No reflow	0
Abrupt closure	0

Abbreviation: IVL, intravascular lithotripsy.
[a]Continuous data are presented as the mean ± standard deviation (range); categorical data are given as the number.

standard of care for endovascular procedures. Predilation of the target lesion was at the physician's discretion to facilitate navigation of the IVL catheter through the lesion. After the target lesion was successfully crossed, the IVL catheter was engaged to deliver multiple pulses per the instructions for use until a satisfactory result was obtained per the interventionist's assessment. Provisional stenting and planned posttreatment (eg, antiproliferative therapy) was at the discretion of the treating physician.

Study Outcomes

The primary study outcomes included the ability to deliver IVL to the target lesion, the increase in acute gain, the final percent diameter stenosis, the need for provisional stenting, and angiographically defined complications.

Results

Access to the target lesion and delivery of treatment by the IVL catheter was successful in all 21 patients without the use of predilation. IVL catheters ranged in size between 4.0×60 mm and 7.0×60 mm (mean 6.0×60 mm) and delivered an average of 140 lithotripsy pulses with a mean IVL balloon inflation pressure of 6.3 atm (range 4.0–9.3). Table 2 details the adjunctive technology used during the procedures; notably, no stents were placed for residual stenosis or for flow-limiting dissections. Pre- and postangiographic images from a representative patient are shown in Figure 1.

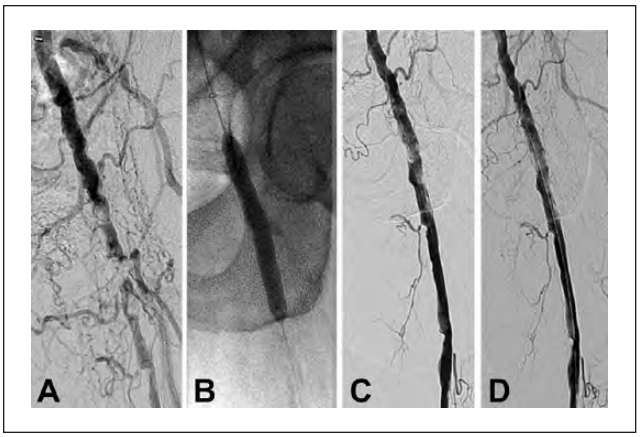

Figure 1. (A) Baseline angiography of a severely calcified, occluded common femoral artery. (B) A 7.0×60-mm intravascular lithotripsy (IVL) catheter delivering 180 pulses. (C) After IVL, there was 35% residual diameter stenosis, 3.9-mm acute gain. (D) After drug-coated balloon dilation the residual stenosis was reduced to 29%, the acute gain was 4 mm. There was no dissection, embolization, or stent placed.

Posttreatment mean diameter stenosis was 21.3%, representing an acute mean lumen gain of 3.1±1.3 mm (range 0.7–5.5). Vascular complications were minimal, with only 5 type B (non-flowing-limiting) dissections reported. The profunda femoris artery was patent in all patients following IVL, and none of the subjects experienced a perforation, distal embolization, thrombus, no reflow, or abrupt closure. The average length of stay was 2 days.

Discussion

Recent studies have reported the use of angioplasty, stenting, and/or atherectomy for treatment of symptomatic CFA disease, which presents mainly as highly calcified atherosclerotic disease. Due to this high calcium burden, plain balloon angioplasty has been associated with poor durability, risk of dissection, and need for provisional stenting.[6–8] Limited information is available for use of newer drug-coated balloons with or without atherectomy.[16–18]

Traditionally, an effort was made to avoid stenting in the CFA territory due to concerns for stent fracture caused by hip mobility. More recent studies with CFA stenting have shown improved patency and low complication rates, with longer term results similar to surgery.[11,12] Very limited information is available for the use of atherectomy in the CFA,[19] which carries a risk of embolization into the superficial femoral and profunda femoris arteries, prompting the need for multiple embolic filters.

Current treatment strategies for calcified arteries have resulted in an increased risk for adverse events. Traditional angioplasty works by exerting constant pressure (often high

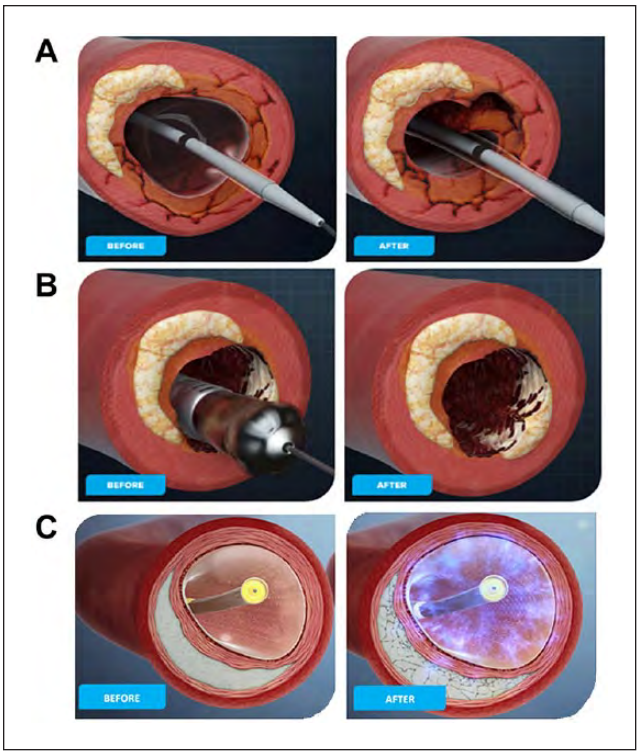

Figure 2. (A) Balloon angioplasty, before and after, uses high constant pressure in an attempt to overcome the resistance of calcified plaque and preferentially targets soft tissue. (B) Atherectomy devices remove superficial atherosclerotic plaque without differentiating between plaque and soft tissue. (C) Intravascular lithotripsy uses a low-pressure balloon catheter to deliver sonic pressure waves that pass through soft tissue and crack calcium in the intimal and medial layers.

in calcified lesions) on superficial soft tissue. This can lead to excessive force that precipitates elastic recoil, frequent dissections, and bailout stenting. Similarly, atherectomy devices are limited to the intimal tissue layer and do not differentiate between the calcified lesion and soft tissue. IVL is the only technology that addresses both intimal and medial calcium by leveraging the physics of lithotripsy, which differentiates calcium from soft tissue, in order to effectively modify calcium (Figure 2). Moreover, IVL is performed using a balloon-based catheter at subnominal pressures (4 atm) and low-pressure postdilation (6 atm).

As opposed to atherectomy, which has a risk of embolization and requires filter use, there was no embolization with IVL. The profunda artery remained patent without evidence of plaque shift and use of the IVL system did not require a filter. Additional benefits of IVL include reduced hospital length of stay, favorable periprocedural safety, and unlike stenting, no interference with future procedures. It may also offer an alternative option to patients who are poor surgical candidates.

These early results in a heavily calcified CFA cohort are consistent with outcomes obtained from the pooled DISRUPT PAD I[13] and II[15] studies and the DISRUPT BTK[14] study, which evaluated the use of the Shockwave IVL for calcified femoropopliteal and infragenicular disease. In the DISRUPT PAD I and II studies,[20] a total of 95 patients were treated with IVL, achieving a low average residual stenosis of 23.8% and acute gain of 3.0 mm; only 1 stent was implanted. In the DISRUPT BTK study,[14] 20 patients were treated with 46.5% acute reduction in diameter stenosis. The composite of major adverse events at 30 days was 0%. Vascular complications were minimal, with only 1 type B dissection and 2 stents placed. In these studies, the IVL device was reported to be simple to use, combining the calcium-disrupting capability of lithotripsy with the familiarity of traditional catheter-based interventional devices.

In addition to use of IVL in the DISRUPT PAD and BTK studies, IVL has been utilized in various other vascular areas to treat symptomatic disease, including chronic total occlusions[20] and critical limb ischemia,[21,22] to enable access for large bore procedures,[23,24] as vessel preparation prior to coronary stenting,[25,26] and to treat coronary stent underexpansion owing to calcification.[27–30] Similar to the results observed in the DISRUPT PAD and BTK studies, the experience in other vessels or conditions demonstrates that IVL can safely and successfully disrupt calcium and improve vessel compliance, reduce stenosis, and increase acute gain.

Limitations

The current study is a retrospective analysis of a small number of patients with short-term follow-up. Future studies with a larger number of patients and long-term follow-up will be needed to further evaluate this novel technology.

Conclusion

Acute results with the Peripheral Intravascular Lithotripsy System in calcified CFA lesions documented a significant reduction in stenosis with few complications, including no distal embolization or bailout stenting. The outcomes suggest that IVL is a safe and effective option for calcified, stenotic CFAs as either standalone therapy or for vessel preparation.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Professor Brodmann and Dr Schwindt have participated in physician advisory meetings for Shockwave Medical with less than $10,000 of personal compensation.

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