



A Single-Center Experience with Intravascular Lithotripsy in the Treatment of Claudication

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Abstract

Objectives: Presence of calcification is a significant risk factor for treatment resistance during endovascular therapy, limiting vessel expansion and increasing rates of complication. The goal of this study is to assess the safety and efficacy of intravascular lithotripsy (IVL) in the treatment of calcified peripheral arterial lesions in patients with claudication. **Materials and Methods:** Patients within our institution treated with IVL in lower extremity calcified lesions from 2018 to 2022 were identified. Our study population was limited to patients classified as Rutherford 1 to 3. The following data points were obtained: pre-/post-IVL luminal stenosis (measured by digital subtraction angiography), pre-/post-IVL ankle-brachial index (ABI), lesion location, adjunctive therapies used at the target lesion, and intraprocedural complications. Overall, 22 target lesions in 18 patients were identified. Pre- and post-treatment ABI measurements were available in 14 treated lower extremities. **Results:** Mean luminal gain in all target lesions treated with IVL was 81.3%. Analysis of vessel location subgroups demonstrated a luminal gain of 80.6% in the aortoiliac segment ($n = 8$), 76.7% in the common femoral artery ($n = 3$), and 83.1% in the femoropopliteal segment ($n = 11$). Luminal gain in lesions treated with IVL alone and IVL with adjunctive therapies was 75.4% and 85.38%, respectively. A mean improvement in ABI of 0.20 ($P < .0001$) was observed across 14 treated limbs. Intraprocedural complications occurred in 1 out of 22 target lesions, which was 1 case of distal embolization successfully managed with aspiration thrombectomy. **Conclusion:** Treatment with IVL may facilitate safe and effective luminal gain and vessel preparation in patients with claudication.

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Peripheral artery disease (PAD) affects over 230 million people worldwide and is a significant cause of cardiovascular morbidity and mortality.¹ Although early management focuses on lifestyle intervention and medical therapy, the mainstay of treatment in refractory patients remains revascularization.

Endovascular techniques are the primary revascularization approach in PAD.² Nonetheless, the presence of calcified vessel occlusions poses a significant challenge. Vascular calcification limits the efficacy of endovascular treatment and is associated with poor clinical outcomes.^{3,4} This includes an increased risk of periprocedural complications, such as dissection and perforation. Treatment modalities such as balloon angioplasty may be limited by poor balloon expansion in rigid, calcified vessels.⁵ Other definitive interventions can also be limited. Drug-coated balloon (DCB) angioplasty is dependent on diffusion

of antiproliferative therapy through the vessel wall; however, calcification may stunt this process.³ Stent placement has an increased risk of under-expansion and in-stent restenosis.^{3,4} Because of this, various devices have emerged to address vessel calcification, including atherectomy. While this approach can be effective at removing intimal calcium, it is unable to treat deeper calcium deposits and is associated with dissection, perforation, and distal emboli.^{2,6} For all these reasons, lesions with severe calcification are often excluded from clinical trials.⁵

Intravascular lithotripsy (IVL) is a novel tool designed to overcome the challenges posed by vessel calcification. Using a percutaneous balloon-based device with the ability to generate sonic pressure waves, IVL fragments both intimal and medial calcification while maintaining the integrity of surrounding soft tissue.⁷ Pre-treatment with this device (vessel preparation)

can improve the success of subsequent definitive interventions, although IVL may also be used as standalone therapy.

Currently, most existing evidence on IVL has been gained from the Disrupt studies, sponsored by the device's developers (Shockwave Medical). These ongoing studies have collectively shown promising luminal gain with minimal complications.⁷⁻¹² Most recently, interim data from the Disrupt PAD III randomized controlled trial has shown IVL to have superior procedural success compared with plain balloon angioplasty when used prior to DCB angioplasty.⁹ The Disrupt PAD III observational study, a large multicenter registry investigating IVL alongside adjunctive modalities to mirror real-world applications, has so far shown short-term safety and effectiveness in iliac and infrapopliteal lesions.¹⁰ Both these studies are yet to reach completion.

As IVL remains a fairly new technology, there are a few single-center experiences published in the literature, with each containing limited sample sizes.^{13,14} In addition, there remains little performance data available on IVL in real-world clinical settings. The goal of this study is therefore to evaluate the safety and efficacy of IVL in the treatment of calcified peripheral lesions among patients with claudication in our institution.

Methods

A retrospective study was conducted in patients with claudication treated with IVL within a single institution. Following Institutional Review Board approval, Philips IntelliSpace PACS Radiology with Prism primordial search was used to identify all patients from 2018 to 2022 who underwent IVL for treatment of calcified lesions. Prism search terms used included *intravascular*, *endovascular*, *shockwave*, and *lithotripsy*. Chart review using Cerner electronic health record software was used to identify those patients meeting the criteria for claudication, which was defined using Rutherford classification previously recorded at the time of patient evaluation. All patients with Rutherford 1 to 3 claudication were included in the study sample. Patients who underwent IVL treatment of 1 or more target lesions during the same operative case were included, with each lesion recorded as a separate data point. All target lesions undergoing additional treatment with other modalities, such as standard balloon angioplasty, DCB angioplasty, and stent placement (ie, adjunctive therapies) following IVL were included. Of note, atherectomy or any other calcium-modifying therapy was not used alongside IVL in our institution.

Procedural data for each target lesion including pre- and post-IVL luminal stenosis (expressed as percentage of luminal diameter), lesion location, types of adjunctive therapies used at the site of the lesion(s), intraprocedural complications (eg, thrombus, distal embolization, flow-limiting dissection, perforation), date of intervention, and fluoroscopic time was collected using PACS Radiology. The location of target lesions was categorized as aortoiliac (aorta, common iliac artery, external iliac artery),

common femoral, or femoropopliteal (superficial femoral artery, profunda femoral artery, popliteal artery, anterior tibial artery, posterior tibial artery, or peroneal artery). ABI readings were included in the study if a post-IVL measurement was obtained prior to another subsequent vascular intervention in the same treated limb. All patient data was de-identified and compiled into a Microsoft Excel spreadsheet.

Selection criteria for treatment of a target lesion with IVL included the presence of significant vessel calcification as judged by the case operator. In all cases, access was obtained using the Seldinger technique under ultrasound guidance at the common femoral artery. Upon advancement of the guidewire and catheter to the level of the lesion, the percentage of luminal stenosis prior to treatment was quantified using digital subtraction angiography. These measurements were obtained in a single plane and interpreted by the operator (ie, single reader) and were thus non-blinded. Size of the IVL balloon was determined using measurement of the target vessel diameter at the time of angiography and sizing to a ratio of 1.1:1. The target lesion was then crossed and the balloon was approximated to the site of calcification; in some cases, pre-dilation of the lesion with standard balloon angioplasty was used to help deliver the IVL balloon. At the target lesion, the IVL balloon was inflated to low pressure at 2 atm. The number of IVL pulses administered and the location of the emitters in respect to the lesion was left at the discretion of the operator. Treatment was complete when there was full expansion of the waist of the IVL balloon at low pressure.

The use of adjunctive techniques was determined by the operator. Within the study sample, there was no threshold to determine the need or type of adjunctive therapy. IVL was used as a vessel preparation method aimed at maximizing the effectiveness of subsequent balloon angioplasty, DCB angioplasty, or stenting in the calcified vessel. Following completion of the procedure, the luminal stenosis of the target lesion at the lesion was measured in a similar fashion. Both Shockwave S4 and M5 IVL devices (Shockwave Medical) were used at this institution, with most cases performed with the S4 device.

Statistical Analysis

Following data collection, statistical analysis was performed using Microsoft Excel and GraphPad PRISM. Luminal gain following IVL was calculated from pre- and post-IVL stenosis measurements for each target lesion. Pre- and post-IVL ABI was used to calculate improvement in ABI for each treated limb. Mean and standard deviation were calculated for continuous variables, and ratios or percentages were calculated for all categorical variables. Normal distribution of ABI values was determined using the Shapiro-Wilk test. Paired sample t-test was applied for statistical analysis of ABI measurements. A *P* value of <.05 was used as the threshold for statistical significance.

TABLE 1. BASELINE CHARACTERISTICS OF ALL 22 PATIENTS WITH CLAUDICATION TREATED WITH INTRAVASCULAR LITHOTRIPSY

Baseline Characteristics	
Age	71.5 ± 9.4
Race (%)	
White/Non-Hispanic	8/22 (36%)
White/Hispanic	13/22 (59%)
Black or African American	1/22 (5%)
Sex (%)	
Male	12/22 (55%)
Female	10/22 (45%)
Comorbidities (%)	
Hypertension	22/22 (100%)
Hyperlipidemia	18/22 (82%)
Diabetes mellitus	10/22 (45%)
Coronary artery disease	13/22 (59%)
End-stage renal disease	0/22 (0%)
Dialysis	0/22 (0%)
Smoker (current or former)	19/22 (86%)

Results

Within our institution, a total of 22 patients with claudication who were treated with IVL were identified. This sample included 22 patients classified as Rutherford 3. Characteristics of patients in the study sample are described in **Table 1**. Pre- and post-IVL luminal stenosis measurements for 22 target lesions treated in 18 patients were available and included in the study analysis. Pre- and post-IVL ABI measurements for 14 treated lower extremities in 14 patients were included.

Pre-IVL luminal stenosis, post-IVL luminal stenosis, and luminal gain outcomes for all treated lesions and vessel segments are reported in **Table 2**. IVL produced a clinically significant mean improvement in luminal gain among all 22 target lesions and in all therapies. This finding was observed in all vessel segments—aortoiliac, common femoral, and femoropopliteal—with similar degrees of luminal gain irrespective of lesion location. The observed luminal gain in lesions treated with IVL as a sole intervention (ie, without adjunctive therapies) was comparable to that in lesions intervened with both IVL and adjunctive therapies. Of the lesions treated with IVL alone (n = 9), 3 were in the aortoiliac segment and 6 in the femoropopliteal segment. In 14 treated limbs for which ABI was recorded, pre-IVL ABI was measured at 0.69 ± 0.21 . Following IVL, ABI was measured at 0.89 ± 0.20 , producing a statistically significant ABI gain at

TABLE 2. LUMINAL STENOSIS OUTCOMES IN 22 TARGET LESIONS TREATED WITH INTRAVASCULAR LITHOTRIPSY BY VESSEL LOCATION AND MODALITY

	Pre-IVL Luminal Stenosis (%)	Post-IVL Luminal Stenosis (%)	Luminal Gain (%)
All vessel locations (n = 22)	85.5 ± 13.6	4.1 ± 8.0	81.3 ± 12.9
Aortoiliac (n = 8)	81.9 ± 9.6	1.3 ± 3.5	80.6 ± 9.0
Common femoral (n = 3)	86.7 ± 14.4	10 ± 17.3	76.7 ± 16.0
Femoropopliteal (n = 11)	87.6 ± 16.3	4.6 ± 6.9	83.1 ± 15.2
IVL alone (n = 9)	79.9 ± 15.5	4.4 ± 7.3	75.4 ± 13.0
IVL + any adjunctive therapy (n = 13)	89.2 ± 11.2	3.9 ± 8.7	85.4 ± 11.6

Clinically significant luminal gain of $81.3\% \pm 12.9$ was observed across all vessel locations with IVL treatment. Luminal gain was $80.6\% \pm 9.0$, $76.7\% \pm 16.0$, and $83.1\% \pm 15.2$ for target lesions in the aortoiliac (n = 8), common femoral (n = 3), and femoropopliteal (n = 11) segments, respectively. Luminal gain of $75.4\% \pm 13.0$ was measured in cases where IVL was used as the sole intervention (n = 9), while IVL alongside adjunctive therapy (n = 13) yielded a luminal gain of $85.4\% \pm 11.6$. Abbreviation: IVL, intravascular lithotripsy.

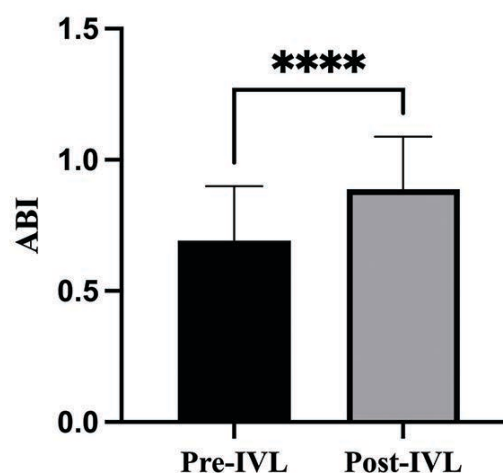


FIGURE. Ankle-brachial index outcomes in 14 limbs treated with intravascular lithotripsy. In the 14 treated limbs for which ABI data was recorded, pre-IVL ABI was measured at 0.69 ± 0.21 . Following IVL, ABI was measured at 0.89 ± 0.20 , yielding a statically significant mean improvement of 0.20 ± 0.11 ($P = .0001$). Abbreviations: ABI, ankle-brachial index; IVL, intravascular lithotripsy.

0.20 ± 0.11 ($P < .0001$) (**Figure**). This included patients receiving IVL alone or with adjunctive therapy.

The types and frequencies of utilized adjunctive therapies are detailed in **Table 3**. Adjunctive therapies were frequently used in the treatment of most lesions (59%), with operators commonly employing more than 1 per lesion. The most frequently performed

TABLE 3. ADJUNCTIVE THERAPIES PERFORMED IN 22 TARGET LESIONS TREATED WITH INTRAVASCULAR LITHOTRIPSY

Adjunctive Therapy	Target Lesions Receiving
Any	13/22 (59%)
Standard balloon angioplasty	9/22 (41%)
Pre-IVL dilation	4/22 (18%)
Post-IVL dilation	6/22 (27%)
Drug-coated balloon angioplasty	1/22 (5%)
Stenting	9/22 (41%)
Atherectomy	0/22 (0%)

Adjunctive therapies were performed in 13/22 (59%) of target lesions, including standard balloon angioplasty, drug-coated balloon angioplasty, and stenting. Atherectomy was not performed in patients receiving IVL. Abbreviation: IVL, intravascular lithotripsy.

TABLE 4. ADDITIONAL OUTCOMES IN ALL 22 CLAUDICATION PATIENTS TREATED WITH INTRAVASCULAR LITHOTRIPSY

Fluoroscopy time (minutes)	19.6 ± 12.4
Days from intervention to discharge	0.8 ± 1.2
Discharged on dual-antiplatelet therapy	10/22 (52%)

of these was stenting and standard balloon angioplasty used either prior (to aid in traversing the lesion) or after (to further expand the lesion diameter) IVL treatment. Fluoroscopy time, days from intervention to discharge, and percentage of patients discharged on dual-antiplatelet therapy are highlighted in **Table 4**.

Within the sample, intraprocedural complication was recorded in 1 out of 22 target lesions. This included a case of distal embolization to the posterior tibial artery following treatment of a multifocal superficial femoral artery lesion. This was successfully managed with aspiration thrombectomy. No other instances of thrombus, distal embolization, flow-limiting dissection, perforation, or abrupt closure were noted.

Discussion

Currently, there is a need to further support the safety and efficacy of peripheral IVL beyond the Disrupt studies due to the novelty of the therapy. Here, we report a single-center experience with IVL in a real-world clinical setting in patients with claudication, who comprise the majority of PAD. In our institution, treatment and vessel preparation of calcified occlusions with IVL produced a clinically significant luminal gain of 81.3% and a low residual stenosis of 4.1%. Similar luminal gain was seen across all vessel locations. These results compare favorably to a recent meta-analysis, where mean luminal gain of 59.3% was reported across several studies.¹⁴ Reasons for this success may include

rising operator experience with the device in recent years and the presence of a dedicated multidisciplinary vascular center. Overall, alongside minimal complications and improvement in ABI, these results suggest a beneficial role for IVL in managing challenging calcified lesions in patients with claudication.

Vessel preparation with IVL is a valuable strategy to address calcification. This approach is crucial in the overall management of PAD, where heavily calcified lesions reduce the efficacy and safety of definitive interventions. In this study, several patients were treated with IVL balloons as standalone therapy, although the potential risk of intimal hyperplasia may raise concerns with this approach. Adjunctive therapies were employed in the majority of treated lesions. Standard balloon angioplasty was used prior to IVL for pre-dilatation and after calcium modification to provide further increase in luminal caliber. DCB angioplasty was used in 1 lesion to limit restenosis, and stenting was commonly utilized to sustain luminal gain in complex lesions. No lesions in this sample were treated with atherectomy or scoring balloons, with IVL as the only modality used for calcium modification. The promising luminal gain observed in this study supports this role of IVL as an important tool for vessel preparation.

This study reports 1 complication in patients with claudication at our institution. Following treatment of 3 locations within a long-segment superficial femoral artery lesion, repeat angiography revealed an abrupt cutoff of flow in a previously patent posterior tibial artery near the level of the ankle. Aspiration thrombectomy was successfully used to reconstitute flow. During the case, no other interventions were performed in the extremity and the lesion was treated solely with IVL. Despite this, it remains possible the event may be attributed to wire or catheter manipulation. To the knowledge of the authors, no embolic protection was used in cases at this institution. An instance of distal embolization has not been previously reported in the IVL literature. Nonetheless, no other complications were noted at this institution. These safety results remain promising considering the risk of vessel rupture and flow-limiting dissection in the setting of calcification. A high degree of safety with IVL has been previously demonstrated across all other literature, with complications rarely reported.^{14,15} Generally, one of the benefits of the IVL system is the avoidance of damage to the vessel wall and surrounding soft tissues. In the management of calcification, IVL appears to hold this distinct safety advantage in comparison with modalities such as atherectomy.

Due to operator preferences and lack of standardization in technique (eg, number of pulses delivered, location of emitters, etc), the results of this study may have limited generalizability. Other limitations include the absence of a control group as well as lack of an angiography core lab to quantify stenosis measurements. These would assist in drawing definitive conclusions of safety and efficacy relative to other modalities and more accurate assessment of luminal gain measurements, respectively. As a retrospective study with data obtained through chart review,

certain results, including lesion length, were unable to be provided. Data was limited to what was previously recorded. Outcomes of interest outside the intraoperative period, including restenosis, post-procedural complications, and maintenance of ABI improvement, were also not able to be assessed in this study. Finally, geographic location and predominantly White/Hispanic demographics may not be entirely representative of the population at other institutions.

Conclusion

Treatment with IVL may facilitate safe and effective luminal gain and vessel preparation in patients with claudication.

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