ORIGINAL ARTICLE

INTRAVASCULAR LITHOTRIPSY FOR SEVERE PERIPHERAL ARTERY CALCIFICATION – A 3-YEAR SINGLE CENTRE EXPERIENCE

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Abstract

Introduction: *Severe arterial calcification is a challenging limitation in endovascular procedures leading to worse success rates and outcomes. Conventional balloon angioplasty may provide limited luminal gain, calling for adjunctive strategies of plaque modification, such as intravascular lithotripsy (IVL). The aim of this study is to describe our institutional experience with IVL in the treatment of peripheral artery disease (PAD).*

Materials and methods: *A prospectively maintained database from a tertiary academic medical centre was retrospectively enquired from October 2021 to September 2024. The study included all patients who underwent IVL (Shockwave Medical, Inc., California, USA) for vessel preparation during endovascular treatment of PAD.*

Results: *19 patients were included (79% male, median age 76 years) with a median follow-up period of 6 and total of 35 months. Most common risk factors were hypertension (90%), diabetes (68%), dislipidemia (63%) and ischaemic heart disease (63%). Clinical presentation was mostly chronic limb-threatening ischemia (Fontaine grade IV in 74% and Fontaine grade III in 10%). The target lesion undergoing IVL was most often femoropopliteal (68%). Intraprocedural lesion crossing was almost equally subintimal and intraluminal (53% vs. 47%) and definitive treatment was mostly performed with stenting (79%). Additionally, 3 patients (16%) underwent a hybrid procedure with femoral endarterectomy (11%) or femoro-femoral bypass (5%). There were no identified procedural complications. Major adverse limb events (MALE) included no reinterventions and 1 major amputation (5%), and the all-cause mortality rate was 16%. Regarding the 14 patients in Fontaine grade IV, the wound healing rate was 57%.*

Discussion/Conclusion: *IVL is a safe and effective adjunctive in vessel preparation during endovascular revascularisation procedures, particularly in the femoropopliteal sector. Procedure and/or device-related complications, MALE and mortality are infrequent. Further research is needed concerning aortoiliac and infrapopliteal sectors and comparison with other supplementary treatment alternatives.*

Keywords: *intravascular lithotripsy, severe peripheral artery calcification, peripheral artery disease, chronic limb-threatening ischaemia*

INTRODUCTION

Artery calcification is one of the main challenges in endovascular procedures for peripheral artery disease (PAD). It has been estimated that 30 to 50% of patients with PAD, especially in older age and those with diabetes mellitus and/or chronic kidney disease, have significant vascular calcification, which alone is associated with worse clinical outcomes, including higher major amputation and overall mortality rates.[1-2] Severe artery calcification carries higher difficulty in endovascular procedures, such as suboptimal vessel preparation and expansion and an increased risk of vascular complications and lower procedural success, as poor balloon expansion, early recoil, restenosis, dissection, perforation and distal embolization.[1-4]

Various techniques and devices have been proposed as adjunctive measures in these cases, including high-pressure balloon angioplasty and atherectomy devices (rotational, orbital, or directional). Recently, intravascular lithotripsy (IVL) emerged as a novel treatment option for patients with severe artery calcification. It derives from shockwave lithotripsy used for nephrolithiasis, generating

pulsatile sonic pressure waves to disrupt plaque calcification without affecting soft tissues or liberating emboli, through a single-use angioplasty balloon catheter embedded with emitters.[1-2,4]

The aim of this study is to describe our institutional experience and results with IVL in the treatment of severely calcified peripheral artery disease.

MATERIAL AND METHODS

A prospectively maintained single centre database from a tertiary academic medical institution was retrospectively enquired regarding a study period of 3 years from October 2021 to September 2024.

Study population

All patients, in a total number of nineteen, who underwent IVL (Shockwave Medical, Inc., California, USA) for vessel preparation during a revascularisation procedure for PAD from October 2021 to September 2024 in our institution were included. Both purely endovascular and hybrid procedures were included. Three patients who underwent IVL for access preparation for other procedures, such as EVAR or TAVI, were excluded.

Patients were considered for IVL after imagological confirmation, by CT angiography and/or angiography, of severe arterial calcification, defined as circumferential plaque and/or plaque occupying over 50% of the vessel lumen associated with subtotal balloon expansion. Short lesions mainly were treated with drug-coated ballooning (DCB) after intraluminal crossing and luminal gain with IVL. Long lesions were mostly treated with stenting after subintimal crossing, if a flow-limiting dissection was encountered.

Data collection

An institutional medical record review was performed and baseline characteristics, clinical presentation, and procedural and follow-up data were obtained. Reintervention was defined as a subsequent vascular revascularization procedure performed on the same limb due to clinical-driven restenosis/occlusion associated with recurrence/maintenance of symptoms of PAD. Major amputation was defined as transfemoral or transtibial amputation. In our institution, follow-up after an endovascular procedure is clinical except when a doppler ultrasound is performed in cases of failure to improve or recurrence of symptoms.

Endpoints

The primary endpoint was major adverse limb events, a composite endpoint consisting of reintervention and major amputation rates. The secondary endpoints were mortality and wound healing rates, the latter in a subgroup analysis of patients in chronic limb-threatening ischemia (CLTI) Fontaine grade IV.

Statistical analysis

Descriptive statistics were used to report data. Continuous data were presented as mean ± standard deviation or median (interquartile range). All analyses were performed using IBM SPSS Statistics version 29.0 software.

RESULTS

Between October 2021 and September 2024, nineteen patients (79% male, 21% female) with a median age of 76 (73-82) years underwent IVL for vessel preparation during a revascularisation procedure for PAD. Baseline characteristics are described in table 1. The most common comorbidities were hypertension (n=17, 90%), diabetes mellitus (n=13, 68%), hypercholesterolemia (n=12, 63%) and history of ischaemic heart disease (n=12, 63%). Most patients presented in CLTI, including 14 patients (74%) with either ulceration or gangrene – Fontaine grade IV – and two patients (10%) with rest pain – Fontaine grade III. Regarding the target lesion undergoing IVL, the most frequently treated sector was the femoropopliteal segment (n=13, 68%). Additionally, five lesions (26%) of the aortoiliac and 1 (5%) of the infrapopliteal sectors were treated.

Regarding intraprocedural details, lesion crossing was almost equally intraluminal (n=9, 47%) or subintimal (n=10, 53%). Stenting was the most frequently selected option for definitive endovascular treatment, being preferred in 15 patients (79%), followed by drug-coated ballooning and plain balloon angioplasty alone in 2 patients (11%) each. Lastly, three patients (16%) underwent a hybrid procedure: 2 patients (11%) underwent a femoral endarterectomy and one patient (5%) underwent a femoral-femoral bypass.

The median follow-up period was 6 (3-15) months. The composite endpoint of MALE occurred in 1 patient (5%). Individually, no reinterventions were reported and one major amputation was performed at 3 months of follow-up.

This population's overall all-cause mortality rate was 16% (3 patients), with all events occurring in the first 6 months after surgery. Despite this, no death was procedure or device-related.

Lastly, a subgroup analysis of patients presenting in CLTI Fontaine grade IV was performed. The wound healing rate in this population was 57% (8 patients), in a median time of 2 months. In contrast, six patients (43%) are still under wound care, with a median follow-up time of 5 months.

DISCUSSION

As life expectancy and the prevalence of other cardiovascular risk factors are on the rise, it is expected that severe peripheral artery calcification will also become more frequent in the future.[3] In our study, the most common risk factors in this population were hypertension, diabetes, dyslipidemia and history of ischaemic heart

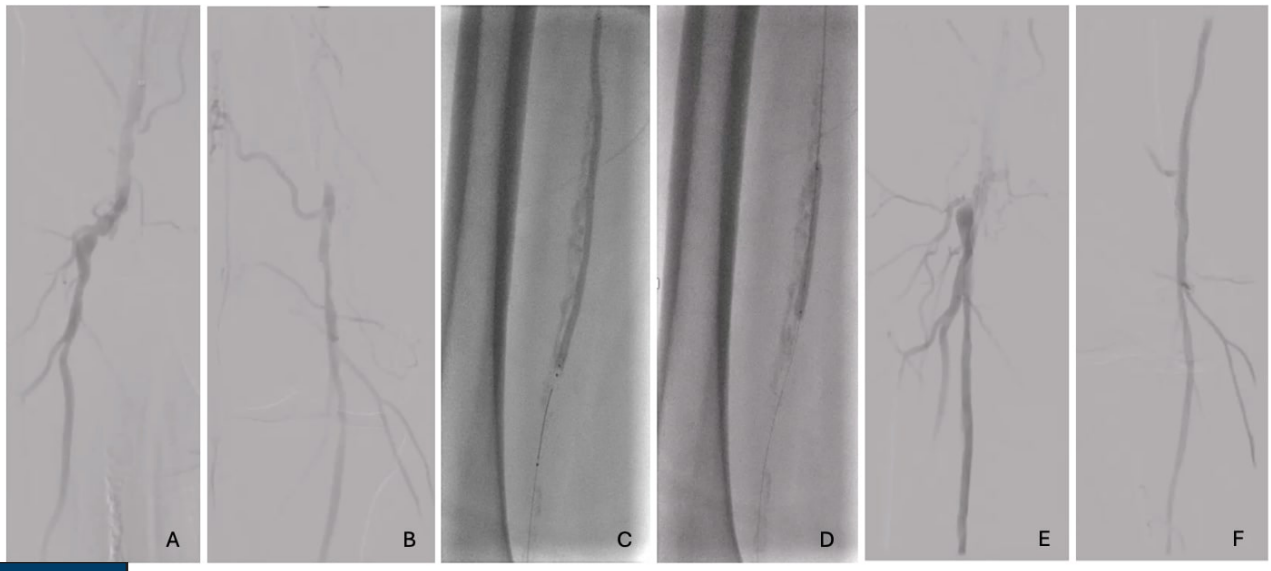

Figure 1 *Intra-operative angiographies of a femoropopliteal chronic total occlusion treated with IVL. Initial angiography shows a long and severely calcified superficial femoral artery lesion (A and B). After plain balloon angioplasty (C) with limited luminal gain and poor balloon expansion, the patient underwent IVL (D) for vessel preparation, followed by bare metal stenting. Final angiography shows patency of the femoropopliteal segment without significant residual lesions (E and F).*

disease. Additionally, the median age was found to be 76 years. According to previous studies, the most commonly found comorbidities in patients with significant artery calcification.[1] A systematic review and meta-analysis on IVL for PAD reporting demographics on this population showed similar rates of hypertension (95% of weighted mean) and coronary artery disease (61%) but lower rates of diabetes mellitus (47%) and a higher percentage of patients with a history of coronary artery disease (61%).[1] Despite chronic kidney disease being significantly associated with a higher degree of artery calcification, our study included only one patient with this comorbidity, which may be explained due to our limited sample and the fact that we only specified patients under hemodialysis. The degree of artery calcification has also been associated with the severity of limb ischemia, namely worsening limb ischemia categories in patients with PAD.[3] Accordingly, the majority of patients in our sample (84%) underwent IVL due to chronic limb-threatening ischemia (Fontaine grades III and IV).

Regarding the target lesion undergoing IVL, we mainly used it to treat the femoropopliteal sector (68%), followed by aortoiliac (26%) and infrapopliteal (6%) lesions. The mentioned meta-analysis also reports similar global rates (69%, 28% and 3%, respectively). Indeed, the femoropopliteal sector is the one with most clinical evidence for IVL usage due to its Disrupt PAD III randomized controlled trial which reports higher 1 and 2-year primary patency after IVL + DCB when compared to IVL + plain balloon angioplasty, associated with lower use of provisional stent placement in the IVL arm in heavily calcified lesions of the femoropopliteal sector.4-5 On the other hand, data regarding aortoiliac lesions mainly derives from a cohort analysis of the Disrupt PAD III study from which its early results report low residual stenosis with minimal complications, although with a higher rate of stent implantation when compared to other vascular beds, which is to be expected.[6] Lastly, infrapopliteal arteries are mainly affected by medial calcification which results in less compliance and higher recoil after balloon angioplasty and, consequently, restricting the usage and effectiveness of adjunctive treatment modalities, such as DCB, due to its limited drug uptake.[7-8] For this reason, IVL is rarely used in the below-the-knee sector. Our study performed it on one patient with a femoro-anterior tibial artery bypass with venous conduit with limb ischemia progression due to dorsalis pedis artery calcification leading to inadequate bypass run-off. After early occlusion of plain balloon angioplasty, the patient underwent IVL of the dorsalis pedis artery followed by DCB. However, due to reocclusion of the previously treated territory and wound progression at 3 months of follow-up, the patient underwent a transfemoral amputation, which is the only major amputation case we report in our series. Nonetheless, recent 30-day results from the Disrupt BTK II study report high procedural success and significant residual stenosis reduction.

As for intraprocedural specificities, lesion crossing was almost equally either intraluminal or subintimal (47% and 53%, respectively) with a complete technical success rate in both alternatives. This may benefit IVL when compared to other adjunctive vessel preparation treatment alternatives with contraindications regarding subintimal lesion crossing, such as atherectomy devices. According to our experience, IVL is mostly beneficial in long femoropopliteal calcified lesions in which subintimal lesion crossing is performed due to lack of another alternative (figure 1). In these cases, without IVL, luminal

Table 1 **Baseline characteristics of patients who underwent IVL for vessel preparation during a revascularisation procedure for PAD**

Baseline characteristics	Total
Sex	
Male	15 (79)
Female	4 (21)
Age – years	76 (73-82)
Hypertension	17 (90)
Diabetes mellitus	13 (68)
Hypercholesterolaemia	12 (63)
Active smoking	3 (16)
Chronic kidney disease under dialysis	1 (5)
Ischaemic heart disease	12 (63)
Prior cerebrovascular event	4 (21)
Fontaine classification	
Grade IIb	3 (16)
Grade III	2 (10)
Grade IV	14 (74)
Target lesion undergoing IVL	
Aortoiliac	5 (26)
Femoropopliteal	13 (69)
Infrapopliteal	1 (5)

Table 2 **Intraprocedural details of patients who underwent IVL for vessel preparation during a revascularisation procedure for PAD**

Intraprocedural details	Total
Lesion crossing	
Intraluminal	9 (47)
Subintimal	10 (53)
Definitive endovascular treatment:	
Plain balloon angioplasty alone	2 (11)
Drug-coated ballooning	2 (11)
Stenting	15 (78)
Hybrid procedure:	
Not performed	16 (84)
Femoral endarterectomy	2 (11)
Femoro-femoral bypass	1 (5)

gain is limited and immediate early recoil (after plain balloon angioplasty or DCB) or early stent thrombosis are more likely, leading to higher early revascularisation failure rates, hence IVL's benefit.

IVL may be associated with a low risk of complications such as embolization, perforation, thrombosis or a no-reflow pattern, all in less frequency than with atherectomy.[1-2,4] No procedural or device-related complications were reported in our series, including major amputation or death, which attests to its likely safety in usage.

Concerning major adverse limb events, namely reintervention or major amputation, and mortality, for our total follow-up period of 35 months, we report no reinterventions, 1 major amputation as previously described and 3 non-device or procedural related deaths, all occurring in the first 6 months of follow-up. Literature has shown that severe peripheral artery calcification is associated with an increase in the risk of amputation and all-cause mortality likely also due to calcification other vascular beds, for example coronary or intra/extracranial.[3] However, results from IVL seem promising. A study by Nugteren et al. including 29 patients reports 3 major amputations within the first 3 months and 5 deaths, comprising 1 patient in palliative care due to progressive foot ulceration.[7]

In our study, results regarding wound healing were modest, with only 57% of complete resolution of lesions within a median follow-up time of 2 months, which may be explained due to our short follow-up period. The severity of artery calcification directly impacts pedal perfusion despite revascularization procedures leading to a delay in wound healing, which may also explain these results.[3] There is little literature about the benefit of IVL in this issue, and the previously mentioned randomized controlled trial reports improvement in Rutherford classification for both IVL and plain balloon angioplasty at 1 year.[5]

This study has certain limitations. Firstly, it is a single-centre retrospective study which carries inevitable associated biases. Moreover, the small sample size may be explained by the specific patient and lesion characteristics being studied and the recent availability of the IVL device in our centre. Lastly, due to data collection restraints, there is no proper definition or classification of severity of calcification.

CONCLUSION

IVL is a safe and low-risk adjunctive measure in vessel preparation during endovascular or hybrid procedures for calcified peripheral arteries, particularly in the femoropopliteal sector, followed mostly by DCB or stenting. Despite unassuming results regarding wound healing, procedure and/or device-related complications, major adverse limb events and mortality are infrequent. Further research is needed to evaluate its results the aortoiliac and infrapopliteal sectors and for comparison with other supplementary treatment alternatives, namely atherectomy.

Conflict of interest: none.

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