Table 1
Classification of variants identified in *LZTR1*

Patient	Nucleotide change in *LZTR1*	Aminoacid change	Frequency control populations (gnomAD;ExAC)	*In silico* studies (computational pathogenicity predictors)	Cosegregation analysis	Pathogenicity classification of the variant
Case 1, Allele 1	NM_006767.3: c.1084C>T	p.Arg362*	< 0.01 No homozygous carriers	Premature stop codon, causing a nonsense variant	Mother carrier. Father noncarrier.	Likely pathogenic
Case 1, Allele 2	NM_006767.3: c.1149+1G>T	Splice site (donor)	< 0.01 No homozygous carriers	Abnormal gene splicing (SSF, HSF, MaxEnt, Nnsplice, GeneSplicer, dbscSNV predict)	Father carrier. Mother noncarrier.	Likely pathogenic
Case 2, Allele 1	NM_006767.3: c.2070-2A>G	Splice site (acceptor)	< 0.01 No homozygous carriers	Abnormal gene splicing (SSF, HSF, MaxEnt, Nnsplice, GeneSplicer, dbscSNV predict)	Father carrier. Mother noncarrier.	Likely pathogenic
Case 2, Allele 2	NM_006767.3: c.1735G>A	p.Val579Met	< 0.01 No homozygous carriers	Probably damaging (in silico analysis: SIFT, Mutation Taster, Polyphen-2, DANN, and FATHMM predictors)	Mother carrier. Father noncarrier.	Likely pathogenic

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Shockwave Lithoplasty-facilitated Transfemoral Access for Transcatheter Aortic Valve Replacement. An Initial Single-center Experience in Spain

Implante percutáneo de válvula aórtica transfemoral facilitado con Shockwave Lithoplasty. Experiencia inicial en un centro español

To the Editor,

Lithoplasty has been demonstrated to be safe and effective in the treatment of moderately or severely calcified lesions of the femoropopliteal arteries, including chronic occlusions.[1] Results have shown a significant reduction in stenosis, with a low need for stent implantation or revascularization at follow-up. More recently, experiences with lithoplasty have been published, with good outcomes for the treatment of calcified coronary lesions.[2]

There is little experience with the use of lithoplasty on peripheral vessels to allow facilitated transfemoral access in transcatheter aortic valve implantation.[3] Evidence on its efficacy in this context would likely increase the percentage of patients treated via the transfemoral route—an important point given that this has been demonstrated to have a lower mortality rate and better outcomes than other access routes.[4]

We present our initial experience with 4 patients—which to the best of our knowledge is the largest series described so far—with severe, highly-calcified lesions in both iliac vessels, who underwent lithoplasty with the Shockwave Lithoplasty system (Shockwave Medical Inc).

The Shockwave Lithoplasty balloon (Figure 1A) is a system that allows treatment of calcified stenotic lesions in peripheral arteries using the emission of sonic pressure waves that generate high mechanical energy. This energy cracks the superficial and deep calcium in the vessel with minimal impact on healthy tissue. The end objective is to convert the calcified plaque from a rigid, undilatable plaque to a more distensible plaque through which materials can be passed, minimizing trauma to the vessel compared with conventional balloon angioplasty.

The device consists of a small control panel that contains the pulse generator and a small monitor where the pulses delivered are counted. The control panel is attached to a cable, which at the distal end has a button that activates and deactivates the delivery of pulses as required. This cable in turn connects to the lithoplasty balloon catheter. It is a semicompliant balloon, with an over-the-wire design, which contains 6 miniature sonic wave emitters. It is compatible with 6 or 7-Fr introducer sheaths (6.5 or 7 mm balloons) and is mounted on a 0.014 inch guidewire. It is currently available in sizes from 3.5 mm to 7 mm, all of

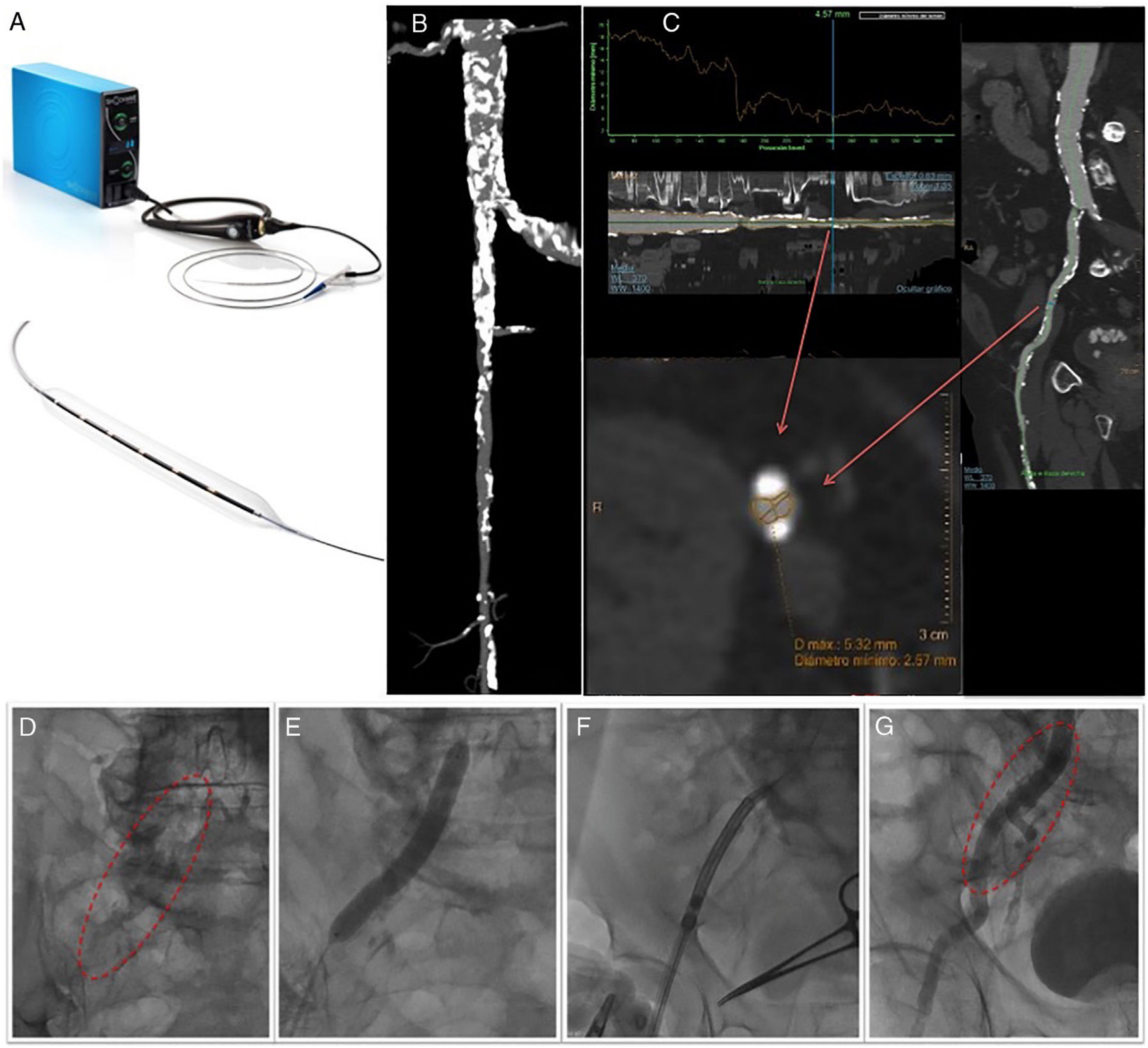

Figure 1. A: Shockwave Lithoplasty system. B and C: computed tomography images showing extensive calcification of the common iliac artery and the origin of the right external iliac artery, as well as the common femoral artery, which also had severe lesions in all segments with a minimum lumen diameter of 5.3×2.4 mm. D: extensive calcification observed on fluoroscopy. E: lithoplasty balloon inflated to 7×60 mm, over a 330 cm Asahi RG3 0.014-inch guidewire. F: advancing a CoreValve Evolute Pro 29 mm prosthesis across the calcified lesion. G: final condition of the artery after finishing the procedure; the fracture produced in the calcium can be seen without images of associated dissection.

which have a balloon length of 60 mm and total catheter length of 110 mm. Each catheter can be used to deliver up to 10 cycles of 30 pulses (total 300 pulses per balloon). Once the desired position is achieved, to deliver the sonic waves, the balloon is first inflated to 4 atm, 30 pulses are delivered, and then the pressure is increased to 6 atm (nominal value); the burst pressure is 10 atm. Since the energy propagation that leads to the calcium fragmentation is transmitted when the balloon comes into contact with the intima of the vessel, it is important to choose a balloon with a 1:1 ratio with the artery diameter to achieve good apposition between the balloon and the calcium of the lesion when the balloon is inflated to 4 atm (2 atm lower than the nominal value).

Table 1 shows the baseline characteristics of the patients and the procedure. Most patients were male with medium or high surgical risk, and previously undiagnosed peripheral arterial disease. All of the procedures were performed under conscious sedation, and in all bar one, radial access was chosen as secondary access, given the contralateral femoral disease. In most cases, the balloon length (60 mm) covered the area to be treated and it was not necessary in any of the patients to use all of the 300 available pulses to achieve the desired result. There were no device-related complications.

Figure 1 is taken from one patient. It shows computed tomography images of the iliofemoral vascular section prior to implantation and images from the procedure.

Based on the outcomes observed in our series, we can say that this is a simple, highly reproducible procedure that is effective in the treatment of severe, highly-calcified stenosis, as it allowed transfemoral implantation in all patients. Its usefulness in different types of vascular diseases remain to be determined.

CONFLICTS OF INTEREST

R. Trillo Nouche is a proctor for Medtronic.

Table 1
Baseline characteristics of the patients and the procedure

	Patient 1	Patient 2	Patient 3	Patient 4
General information				
Age, y	86	83	84	84
Sex	Male	Male	Female	Male
BMI	25	34	29	26
DM	No	No	No	No
Dyslipidemia	No	Yes	Yes	Yes
HTN	Yes	Yes	Yes	Yes
AF	Yes	Yes	No	No
Peripheral arterial disease	Yes	Yes	Yes	No
Previous stroke	No	Yes	No	No
Previous CHD	No	Yes	No	No
COPD	No	No	No	No
EuroSCORE II	5.4	3.2	3.5	8.8
STS score	4.1	2.2	2.2	3.2
Hemoglobin, g/dL	11.8	12.5	13.5	13.6
Hematocrit, %	37.2	37.5	39.6	38.4
Glomerular filtration rate	28.8	90.5	81.3	36.7
Procedure				
Anesthesia	CS	CS	CS	CS
Primary access	LFA	LFA	LFA	RFA
Calcification	Severe	Severe	Severe	Severe
Tortuosity	Mild	Mild	Mild	Mild
MLD, mm	5.3 × 2.4	4.4 × 4.8	4.3 × 6.4	4.5 × 5.1
Secondary access	LRA	RRA	RFA	LRA
Aortic valve prosthesis	Evolute R 34	Accurate M	Evolute Pro 26	Evolute R 34
Introducer sheath	iSleeve (14-Fr)	iSleeve (14-Fr)	DrySeal (16-Fr)	DrySeal (16-Fr)
Lithoplasty balloon, mm	7	6	6	6
Length treated, mm	60	60	60	90
Number of pulses	150	90	90	120
VC associated with the device	No	No	No	No
Implant successful	Yes	Yes	Yes	Yes

AF, atrial fibrillation; BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CS, conscious sedation; DM, diabetes mellitus; HTN, hypertension; LFA, left femoral artery; LRA, left radial artery; MLD, minimum lumen diameter; RFA, right femoral artery; RRA, right radial artery; STS: Society of Thoracic Surgeons; VC, vascular complication.

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