Circulation

RESEARCH LETTER

Feasibility of Shockwave Coronary Intravascular Lithotripsy for the Treatment of Calcified Coronary Stenoses

First Description

Todd J. Brinton, MD*
Ziad A. Ali, MD, DPhil*
Jonathan M. Hill, MD
Ian T. Meredith, MD, PhD
Akiko Maehara, MD
Uday Illindala, MS
Alexandra Lansky, MD
Matthias Götberg, MD, PhD
Nicolas M. Van Mieghem, MD
Robert Whitbourn, MBBS, BMedSc
Jean Fajadet, MD
Carlo Di Mario, MD, PhD

The presence of calcified coronary plaque impacts interventional outcomes by impairing stent crossing, disrupting drug polymer from the stent surface,[1] affecting drug delivery and elution,[2] and reducing stent expansion and apposition.[3] Current therapies used to overcome these challenges, including high-pressure balloon dilation and atherectomy, have inherent limitations. Balloon dilation is limited in eccentric calcium where guidewire bias may direct force toward the noncalcified segments of the artery, or in concentric calcium where insufficient force fails to induce calcium fracture. Rotational and orbital atherectomy may also have guidewire bias, resulting in eccentric ablation or ablation of noncalcified segments. Although this may improve stent deliverability, the effect on deeper calcium restricting stent expansion may be limited. Moreover, periprocedural complications and periprocedural myocardial infarction (MI) are perceived to be higher with atherectomy than traditional balloon-based therapies.

We sought to determine the feasibility of coronary intravascular lithotripsy (IVL) as a novel modality for modification of heavily calcified atherosclerotic plaques before stenting. The Disrupt CAD I Study (Shockwave Coronary Rx Lithoplasty Study; NCT02650128) was a prospective multicenter, single-arm study approved by each institutional review board and all patients gave informed consent. Patients with a clinical indication for coronary intervention were required to have ≥1 lesion requiring percutaneous coronary intervention with a diameter stenosis ≥50%, native coronary artery lesion length ≤32 mm, and heavy calcification, defined as calcification within the lesion on both sides of the vessel assessed during angiography by the operator.

The Shockwave Medical coronary IVL catheter is a single-use sterile disposable catheter that contains multiple lithotripsy emitters enclosed in an integrated balloon. The emitters create sonic pressure waves for a circumferential field effect. These sonic pressure waves selectively fracture calcium, altering vessel compliance, while minimizing barotrauma attributable to low inflation pressure (4 atm), thus maintaining the fibroelastic architecture of the vessel wall. The coronary IVL catheter, available in 2.5- to 4.0-mm diameters and 12 mm in length, is connected via a connector cable to the generator that is preprogrammed to deliver 10 pulses in sequence at a frequency of 1 pulse/s for a maximum of 80 pulses per catheter. Angiography was used to determine the appropriate number of pulses for optimal vessel preparation. Subsequent stent implantation and percutaneous coronary intervention optimization was performed at the discretion of the operator.

The primary performance end point was clinical success, defined as the ability of IVL to produce a residual diameter stenosis <50% after stenting with no evidence of in-hospital major adverse cardiac event (MACE; cardiac death,

*Drs Brinton and Ali contributed equally.

Key Words: coronary stenosis ■ lithotripsy ■ vascular calcification

https://www.ahajournals.org/journal/circ

MI [creatine kinase-muscle/brain >3× the upper limit of normal], or target vessel revascularization). The primary safety end point was freedom from MACE through 30 days defined as cardiac death, MI or target vessel revascularization. Both primary safety and clinical success end points, including the definition of MI, were selected to allow comparison with the primary end point of the Orbit II study (Evaluate the Safety and Efficacy of OAS in Treating Severely Calcified Coronary Lesions), a contemporary trial using orbital atherectomy for lesion preparation in severe coronary calcification.[4]

Between December 2015 and September 2016, 60 patients were enrolled at 7 hospitals in 5 countries. The core laboratory–adjudicated results are summarized in the Table. Median diameter stenosis on quantitative angiography was 72.5% (interquartile range, 58.5–77.0) with lesion length of 18.2 mm (interquartile range, 14.1–25.4) and severe calcification present in all patients. IVL was feasible, facilitating the delivery of stents in all patients, reducing stenosis to 12.2% (interquartile range, 6.7–20.5) with an acute gain of 1.7 mm (interquartile range, 1.3–2.1), achieving 95% clinical success (residual diameter stenosis <50% without in-hospital MACE). IVL had 3 periprocedural MIs, resulting in 95% freedom from MACE at 30 days. There were no unresolved dissections, slow-flow/no-flow, embolization, or perforations. At 6 months, MACE was 8.3%. There were 2 cardiac deaths adjudicated as unlikely related to the technology within the 6-month follow-up period. There were no new MIs or target vessel revascularizations.

IVL offers a number of specific advantages. First, IVL requires no specific training in comparison with traditional atherectomy. Second, being balloon based, IVL may reduce the risk of atheromatous embolization in comparison with atherectomy devices, but this hypothesis requires direct testing. Third, IVL is not subject to guidewire bias; instead, sonic pressure waves are distributed uniformly across the inflated balloon, addressing calcium irrespective of its circumferential location leading to fracture as recently shown by us using optical coherence tomography.[5] Fourth, unlike traditional balloon-based high-static barometric pressure vessel preparation, IVL creates peak dynamic sonic mechanical energy lasting <2 μs in a balloon inflated at low pressures, minimizing vascular injury.

In conclusion, in this pilot single-arm study performed in patients with heavy coronary artery calcification who require revascularization, IVL appeared feasible with favorable initial success and complication rates. Larger studies will be needed to establish the efficacy and safety of this procedure and to determine whether calcium-modifying technologies impact clinical outcomes.

Table. Study Results

Characteristics and Outcomes	N = 60
Characteristics	
Clinical	
Age, y	72 (66, 79)
Male	80 (48)
Diabetes mellitus	30 (18)
Hypertension	80 (48)
Hyperlipidemia	80 (48)
Myocardial infarction	40 (24)
Previous CABG	23 (14)
CVA/TIA	13 (8)
Current smoker	15 (9)
Renal insufficiency	10 (6)
Angina classification	
Class I	32 (19)
Class II	48 (29)
Class III	17 (10)
Class IV	3 (2)
Lesion	
Protected left main artery	2 (1)
Left anterior descending artery	47 (28)
Circumflex artery	13 (8)
Right coronary artery	38 (23)
Reference vessel diameter, mm	3 (2.6, 3.2)
Minimum lumen diameter, mm	0.9 (0.6, 1.1)
Diameter stenosis, %	73 (59, 77)
Lesion length, mm	18 (14, 25)
Calcified length, mm	21 (12, 25)
Severe calcification	100 (60)
Concentric	78 (47)
Eccentric	22 (13)
Side branch involvement	28 (17)
Procedural details	
Total procedure time, min	92 (70, 109)
Fluoroscopy time, min	27 (18, 41)
Device time, min	8 (12,17)
Number of catheters	2 (1, 2)
Number of pulses	72 (40, 120)
IVL pressure, atm	6 (6, 6)
Number of stents used	1 (1, 2)
Predilation	37 (22)
Postdilation	87 (52)
Outcomes	
Performance	
Clinical success	95 (57)
Device success	98 (59)

(*Continued*)

Table. Continued

Characteristics and Outcomes	N = 60
Stent delivery	100 (60)
Final in-stent angiographic outcomes (core laboratory)	
Minimum lumen diameter, mm	2.6 (2.3, 2.9)
Acute gain, mm	1.7 (1.3, 2.1)
Diameter stenosis, %	12 (7, 21)
Residual diameter stenosis <50%	100 (60)
Residual diameter stenosis <30%	92 (55)
Residual diameter stenosis <20%	73 (44)
Clinical	
Final angiographic complications	
Residual dissections	0 (0)
Perforations	0 (0)
Abrupt closure	0 (0)
Slow flow	0 (0)
No reflow	0 (0)
MACE through 30 d	5 (3)
Cardiac death	0 (0)
Non–Q-wave MI	5 (3)
Q-wave MI	0 (0)
TVR	0 (0)
MACE through 6 mo	8 (5)
Cardiac Death	3 (2)
Non-Q-Wave MI	5 (3)
Q-wave MI	0 (0)
TVR	0 (0)

Values are % (n) or median with interquartile range (25%, 75%). CABG indicates coronary artery bypass graft surgery; CVA, cerebrovascular accident; IVL, intravascular lithotripsy; MACE, major adverse cardiac event; MI, myocardial infarction; TIA, transient ischemic attack; and TVR, target vessel revascularization.

ARTICLE INFORMATION

Data Sharing: The data, analytics methods, and study materials will not be available to other researchers for the purposes of reproducing the results or replicating the procedure.

Correspondence

Todd J. Brinton, MD, Clinical Professor of Medicine, Stanford University, 318 Campus Dr, James Clark Center E-100, Stanford, CA 94305. Email tbrinton@stanford.edu

Affiliations

Stanford University, CA (T.J.B.). NewYork-Presbyterian Hospital/Columbia University Medical Center (Z.A.A.). Cardiovascular Research Foundation, New York (Z.A.A., A.M.). King's College Hospital, London, UK (J.M.H.). Monash University, Melbourne, Australia (I.T.M.). Shockwave Medical, Fremont, CA (U.I.). Yale University School of Medicine, New Haven, CT (A.L.). St. Bartholomew's Heart Center, London, UK (A.L.). The William Harvey Research Institute, Queen Mary University of London, UK (A.L.). Skane University Hospital, Lund, Sweden (M.G.). Erasmus University, Rotterdam, The Netherlands (N.M.V.M.). St Vincent's Hospital, Melbourne, Australia (R.W.). Clinique Pasteur, Toulouse, France (J.F.). University Hospital Careggi, Florence, Italy (C.D.M.). Royal Brompton Hospital, London, UK (C.D.M.).

Sources of Funding

This work was funded by Shockwave Medical, Inc.

Disclosures

Dr Ali reports grants from St. Jude Medical, personal fees from St. Jude Medical, personal fees from ACIST Medical, and personal fees from Cardiovascular Systems Inc outside the submitted work, and equity in Shockwave Medical. Dr Brinton is the cofounder of Shockwave Medical and reports personal fees from Shockwave Medical. Dr Maehara reports other support from St. Jude Medical during the conduct of the study and grants and personal fees from St. Jude Medical and Boston Scientific Corporation outside the submitted work. U. Illindala is a full-time employee of Shockwave Medical. Drs Hill, Meredith, Götberg, Lanksy, Van Mieghem, Whitbourn, Fajadet, and Di Mario have received institutional grants for the Disrupt CAD study.

REFERENCES

1. Wiemer M, Butz T, Schmidt W, Schmitz KP, Horstkotte D, Langer C. Scanning electron microscopic analysis of different drug eluting stents after failed implantation: from nearly undamaged to major damaged polymers. *Catheter Cardiovasc Interv*. 2010;75:905–911. doi: 10.1002/ccd.22347
2. Tzafriri AR, Garcia-Polite F, Zani B, Stanley J, Muraj B, Knutson J, Kohler R, Markham P, Nikanorov A, Edelman ER. Calcified plaque modification alters local drug delivery in the treatment of peripheral atherosclerosis. *J Control Release*. 2017;264:203–210. doi: 10.1016/j.jconrel.2017.08.037
3. Kini AS, Vengrenyuk Y, Pena J, Motoyama S, Feig JE, Meelu OA, Rajamanickam A, Bhat AM, Panwar S, Baber U, Sharma SK. Optical coherence tomography assessment of the mechanistic effects of rotational and orbital atherectomy in severely calcified coronary lesions. *Catheter Cardiovasc Interv*. 2015;86:1024–1032. doi: 10.1002/ccd.26000
4. Chambers JW, Feldman RL, Himmelstein SI, Bhatheja R, Villa AE, Strickman NE, Shlofmitz RA, Dulas DD, Arab D, Khanna PK, Lee AC, Ghali MG, Shah RR, Davis TP, Kim CY, Tai Z, Patel KC, Puma JA, Makam P, Bertolet BD, Nseir GY. Pivotal trial to evaluate the safety and efficacy of the orbital atherectomy system in treating de novo, severely calcified coronary lesions (ORBIT II). *JACC Cardiovasc Interv*. 2014;7:510–518. doi: 10.1016/j.jcin.2014.01.158
5. Ali ZA, Brinton TJ, Hill JM, Maehara A, Matsumura M, Karimi Galougahi K, Illindala U, Götberg M, Whitbourn R, Van Mieghem N, Meredith IT, Di Mario C, Fajadet J. Optical coherence tomography characterization of coronary lithoplasty for treatment of calcified lesions: first description. *JACC Cardiovasc Imaging*. 2017;10:897–906. doi: 10.1016/j.jcmg.2017.05.012