Indian Heart Journal 74 (2022) 91–95

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Safety and procedural outcomes of intravascular lithotripsy in calcified coronaries in Indian patients

Ravindra Singh Rao [a], Govind Narayan Sharma [a, *], Shekhar Kunal [b], Kailash Garhwal [c], Suresh Bajiya [a], Pawan Mehta [a]

[a] Department of Cardiology, RHL Heart Centre, Rajasthan Hospital, Jaipur, India
[b] Department of Cardiology, GB Pant Institute of Post Graduate Medical Education and Research, Delhi, India
[c] Department of Cardiology, Maria Cecila Hospital, Cotignola, Italy

ARTICLE INFO

Article history:
Received 23 April 2021
Received in revised form
2 January 2022
Accepted 4 January 2022
Available online 5 January 2022

Keywords:
Angiogram
Calcification
Imaging
Lithotripsy
Stent

ABSTRACT

Objective: Calcified coronaries still remain a major challenge for interventional cardiologist. This study aims to evaluate safety and efficacy of intravascular lithotripsy (IVL) in management of coronary artery calcification.
Methods: This was a retrospective single centre study regarding the utility of IVL in management of calcified coronaries. Patients with hemodynamically stable acute coronary syndrome or symptomatic chronic coronary syndrome (CCS) and calcified coronaries on angiography and who underwent IVL were enrolled. Intravascular imaging was performed wherever feasible. The primary endpoint was procedural success. In addition, data regarding procedural complications were collected.
Results: A total of 29 patients underwent IVL with a majority being males and having comorbidities such as hypertension and diabetes. A procedural success rate of 93.1% was achieved with no patient having >50% residual stenosis. IVL catheter was successfully delivered in all patients. The mean catheter diameter was 3.3 ± 0.4 mm and mean number of delivered pulses was 70.3 ± 16.4. The arteries most commonly intervened were the left main coronary and the left anterior descending artery. Intracoronary imaging revealed a significant increase in minimum luminal cross-sectional area (MLA) post IVL (pre-MLA: 5.1 ± 2.5 mm^2; post-MLA: 10.7 ± 2.9 mm^2; $P<0.001$). Two patients had in-hospital MACE in form of peri-procedural non Q-wave MI. No patient had arrhythmias, stent thrombosis, coronary perforation, or slow flow/no-reflow. Two patients had a rupture of IVL balloon while four had coronary artery dissection.
Conclusions: IVL is a safe and highly effective modality with high procedural success rate in management of calcified coronaries.

1. Introduction

Calcified coronaries have been a major challenge for interventional cardiologists worldwide. Coronary calcification is highly prevalent among the elderly and those with comorbidities such as diabetes, hypertension, and chronic kidney disease.[1,2] Moderate to severe calcification, a marker of advanced atherosclerosis, is documented in more than one-third of patients with acute coronary syndrome (ACS) and is often associated with poor long-term outcomes.[3] Factors such as calcium location, distribution, and thickness are major determinants of procedural success.[4] Percutaneous coronary intervention (PCI) in heavily calcified lesions is associated with both early as well as late complications. Early complications include coronary dissection, perforation, or myocardial infarction while late events include restenosis, stent fracture, thrombosis, and repeat revascularization.[5] Heavy calcification leads to difficulty in lesion dilatation, stent delivery, and expansion resulting in an under-expanded stent with greater rates of stent thrombosis and restenosis.[6–8]

Multiple adjunctive interventions such as atherectomy, high-pressure noncompliant balloons, scoring or cutting balloons, and excimer lasers have been used to facilitate PCI in these complex lesions.[9] However, high rates of procedural complications and a low success rate in lesions with deep/eccentric calcification markedly limit their use.

---

* Corresponding author.
E-mail address: maddygov@gmail.com (G.N. Sharma).

https://doi.org/10.1016/j.ihj.2022.01.001

Intravascular lithotripsy (IVL) is a promising new technology for the treatment of severely calcified coronary lesions.[9] It consists of a semi-compliant balloon-catheter system integrated with multiple miniaturized lithotripsy emitters, which transduces electric pulse into sonic pressure waves.[10] The presence of saline and contrast within the IVL balloon facilitates transfer of these pressure waves through the soft tissue into intimal and medial calcium deposits. The mechanisms of calcific plaque modification by IVL include (a) axial splitting of calcific plaque by the impact of compressive circumferential forces which are generated by the violent collapse of cavitation bubbles induced by shock waves inside the saline-contrast filled balloon and (b) development of microfractures resulting from the shear stress of sonic pressure waves which progressively evolve into macrofractures following cumulative impact of repetitive shock wave pulses with minimal injury to the soft tissue.[9] IVL helps in a better stent apposition as well as adequate stent expansion. It induces fractures in deep-seated calcium where rotational atherectomy often fails.[9,10] Since calcium fragments remain in situ in IVL, there is no risk for distal embolization and slow flow in the coronaries.[9] In this retrospective review, we report the feasibility and safety of IVL in the management of calcified coronaries in the Indian population.

2. Methods

This is a retrospective analysis of IVL in the management of calcified coronaries at a tertiary care centre in India. Consecutive patients with stable acute coronary syndrome or symptomatic chronic coronary syndrome with severely calcified lesion on angiographic imaging (intra-lesional calcification on both sides of the vessel) and who underwent IVL were included. Patients had either circumferential deep calcified lesion (tram-track appearance) [Supplementary Figure A1] or nodular calcified lesion (Supplementary Figure A2) extending into media. Patients who underwent atherectomy or cutting/scoring balloon angioplasty were excluded. Intravascular imaging with Intravascular Ultrasound (IVUS) or Optical Coherence Tomography (OCT) were performed wherever feasible. All patients provided written informed consent before the procedure.

2.1. Study device

Shockwave Medical (Santa Clara, CA, USA) IVL system was used along with the coronary IVL catheter which is a single use, fluid-filled balloon angioplasty catheter with multiple arrays of lithotripsy emitters. This rapid exchange catheter is compatible with 0.014” coronary guidewires and is available in 2.5, 3.0, 3.5, and 4.0 mm diameters with a balloon length of 12 mm.[9,10] In order to deliver the sonic pressure shockwaves, the IVL catheter system was connected to a generator which delivers cycles of 10 pulses for a maximum of 80 pulses (8 cycles) per catheter.

2.2. Study procedure

Following written informed consent, coronary angiogram was performed via 6 F or 7 F radial/femoral access. The guiding catheter for the left coronary system was 6F/7F XB catheter (Cordis Corporation, Bridgewater, NJ, USA) while for the right coronary artery intervention was 6F/7F Judkin's Right catheter. Following this, an IVL catheter was passed over a standard 0.014″ guidewire, across the lesion and positioned using marker bands. In patients with very tight stenosis, pre-dilatation with smaller balloons was done to introduce the IVL balloon catheter. The sizing of the IVL catheter balloon was done with a 1:1 ratio with reference vessel diameter, as estimated by intravascular imaging/angiography. IVL balloon was then inflated to 4 atm to enable contact with the vessel wall and minimizing static barotrauma, followed by delivery of 10 pulses (one cycle) and then balloon inflation to 6 atm. Subsequently, the balloon was deflated to allow for distal vessel perfusion. Since most of the lesions were longer than 12 mm, the balloon was repositioned and a maximum of 80 pulses per catheter were delivered. In patients with multiple lesions, each lesion site was treated with a minimum of 20 pulses per site.[9] In case the lesion preparation was incomplete, additional IVL catheters were used. Finally, stent implantation and PCI optimization was done.

2.2.1. Intravascular imaging

Imaging was performed in a subset of patients, using either OCT or IVUS. Calcified lesion was identified on OCT by a sharply defined border with a low-attenuation signal, and on IVUS as an echo dense (hyperechoic) lesion with shadowing brighter than reference adventitia.[11,12] On an OCT image, the length of the calcified segment was determined by distance between the proximal and distal calcium edges, and the distances were summed if there were multiple separate deposits. Calcium thickness was calculated as the distance between the luminal edge and the outer border of the deposit measured throughout the lesion with the maximum value recorded per lesion. For determining the calcium arc, a protractor centred in the lumen was used to measure the calcification angle. Calcium volume index (CVI) was determined as the product of the mean calcium angle (°) and the calcium length (mm).[11] An OCT-based CVI scoring system (score: 0–4) comprising maximum calcium angle, maximum calcium thickness, and calcium length was used in the study.[13] Calcium location was deemed as superficial if the leading luminal edge of calcification was located within 0.5 mm from the surface of the calcified plaque.[11] Calcified nodule on OCT was defined as an accumulation of nodular calcification protruding into the lumen with disruption of the fibrous cap[14] while on IVUS it was determined by the presence of i) convex shape of the luminal surface, ii) convex shape of the luminal side of calcium, iii) an irregular luminal surface, and iv) irregular leading edge of calcium.[15] A post-IVL/stenting calcium fracture was identified on the OCT as the presence of a new disruption/discontinuity in the calcium sheet. In order to determine the number of fractures per lesion, the fracture lines were traced for continuity on a per frame basis and confirmed on longitudinal OCT imaging.[11]

2.2.2. Statistics

Descriptive statistics were obtained for all study subjects with continuous data being expressed as mean ± SD and categorical data as proportions. Pre and post-IVL minimum luminal cross-sectional area (MLA) on OCT were compared using paired Student's *t*-test. The primary endpoint in this study was procedural success, defined as delivering lithotripsy to the target vessel and successful stent delivery with <50% residual stenosis and without in-hospital major adverse cardiovascular events (MACE).[16–18] MACE was defined as the occurrence of cardiac death or myocardial infarction (MI), or a need for target vessel revascularization (TVR). In our study, MI was defined as CK-MB levels >3 times the upper limit of lab normal (ULN) value with or without new pathologic Q-waves occurring 12–24 h post-procedure or at discharge (peri-procedural MI) based on the Fourth Universal Definition of Myocardial Infarction.[19] In addition, data regarding procedural complications and in-hospital MACE were computed. All statistical analyses were performed on SPSS, version 24.0 (IBM Corp.). A P-value of ≤ 0.05 was considered as statistically significant.

Table 1
Baseline demographic characteristics of study population.

	N = 29
Age (years)	69.5 ± 7.9
Sex (M/F)	28 (96.5%)/1 (3.5%)
Comorbidities	
Hypertension	22 (75.8%)
Diabetes	20 (68.9%)
Dyslipidaemia	6 (20.7%)
Prior coronary artery disease	14 (48.2%)
Prior coronary artery bypass grafting	6 (20.7%)
Prior stroke	1 (3.4%)
Smoking	11 (37.9%)
Chronic coronary syndrome	20 (68.9%)
NSTEACS	9 (31.1%)
Renal insufficiency (eGFR <60 ml/min/1.73m^2)	11 (37.9%)
Mean eGFR (ml/min/1.73m^2)	87.1 ± 9.8
Mean left ventricular ejection fraction (%)	49.4 ± 3.8
Left ventricular dysfunction	16 (55.1%)
Mild (LVEF: 41–50%)	5 (17.2%)
Moderate (LVEF: 30–40%)	6 (20.7%)
Severe (LVEF: <30%)	5 (17.2%)

Abbreviations: CAD: coronary artery disease; eGFR = estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; M/F: male/female; NSTEACS: non-ST elevation acute coronary syndrome; N = number.

3. Results

A total of 29 patients underwent IVL over a period of one year. The mean age of the study population was 69.5 ± 7.9 years. Indications for coronary intervention included stable angina despite optimized medical therapy in 20/29 (68.9%) and non-ST elevation ACS in 9/29 (31.1%). No patient had ST-Elevation Myocardial Infarction. The baseline demographic data has been tabulated in Table 1. The left main (LM) coronary artery (Supplementary figure A3) and left anterior descending coronary artery were the most commonly intervened vessels. The mean baseline reference vessel diameter was 3.3 ± 0.5 mm. On coronary angiography, lesions were concentric (defined as symmetric and smooth narrowing of the coronary artery) in 23/29 (79.3%) and eccentric (defined as asymmetric narrowing of the coronary artery) in 6/29 (20.7%) cases based.[20] The angiographic profile and procedural details have been documented in Table 2. Successful delivery of IVL catheter occurred in all procedures with a mean of 70.3 ± 16.4 IVL pulses delivered. The mean diameter of the IVL catheter used was 3.3 ± 0.4 mm. In two patients, IVL as well as Transcatheter Aortic Valve replacement were done simultaneously.

Table 2
Angiographic profile and procedural details of the enrolled patients.

	N = 29
Target Vessel	
LM	15 (51.7%)
LAD	15 (51.7%)
LCX	5 (17.2%)
RCA	5 (17.2%)
Reference vessel diameter (mm)	3.3 ± 0.5
Diameter stenosis (%)	90.3 ± 5.8
Fluoroscopy time (min)	30.9 ± 16.9
Access details	
RFA	8 (27.6%)
LFA	1 (3.4%)
RRA	20 (68.9%)
IVL catheter size (mm)	3.3 ± 0.4
Number of IVL pulses	70.3 ± 16.4
Pre-dilatation	29 (100%)
Post-dilation	22 (75.8%)
Number of stents implanted	1.69 ± 0.76
1	13 (44.8%)
2	13 (44.8%)
3	2 (6.8%)
4	1 (3.4%)
Total stent length (mm)	37.3 ± 9.9
Use of IABP	2 (6.9%)
Concomitant TAVR	2 (6.9%)

Abbreviations: IABP: intra-aortic balloon pump; IVL: intravascular lithotripsy; LAD: left anterior descending artery; LCX: left circumflex; LFA: left femoral artery; LM: left main coronary artery; min: minute; mm = millimetre; N = number; RCA: right coronary artery; RFA: right femoral artery; RRA: right radial artery; TAVR: Transcatheter aortic valve replacement.

Table 3
Procedural outcomes of the study population undergoing IVL.

		N = 29
1.	Procedural success	27 (93.1%)
2.	Successful stent delivery	29 (100%)
3.	**MACE in hospital**	
	Cardiac death	0 (0%)
	Non–Q-wave MI	2 (6.9%)
	Q-wave MI	0 (0%)
	Target vessel revascularization	0 (0%)
4.	Hemodynamic instability (post-procedure)	0 (0%)
5.	Bleeding complications	0 (0%)
6.	Arrhythmias	0 (0%)
7.	Acute kidney injury	0 (0%)
Angiographic complications		
8.	**Coronary Dissection**	
	Type A	0 (0%)
	Type B	2 (6.9%)
	Type C	2 (6.9%)
	Type D-F	0 (0%)
9.	Perforations	0 (0%)
10.	Abrupt vessel closure	0 (0%)
11.	Slow flow/no reflow	0 (0%)
11.	IVL balloon rupture	2 (6.9%)
12.	Stent thrombosis	0 (0%)

Abbreviations: IVL: Intravascular lithotripsy; MACE: Major adverse cardiovascular event; MI: myocardial infarction; N = number.

3.1. *Angiographic outcomes and procedural safety*

In the study group, no patient had a post-procedural >50% in-stent residual stenosis while three patients (10.3%) had >30% in-stent residual stenosis following IVL and drug eluting stent (DES) implantation. A procedural success rate (primary endpoint) of 93.1% was achieved as MACE was documented in 2/29 (6.9%) subjects in form of peri- or post-procedural non-Q-wave MI. Intracoronary imaging (Table S1) was used in 17 patients using IVUS (8/17) or OCT (9/17). In patients, where an intracoronary imaging modality was used, the pre-procedure MLA was 5.1 ± 2.5 mm^2 while post-procedure MLA was 10.7 ± 2.9 mm^2 with a significant increase following intervention ($P<0.001$). Multiple (≥2) calcium fractures (Supplementary Figure A1C and Supplementary Figure A4) were identified after IVL in 52.9% of the lesions and was more marked in those with circumferential calcification. Procedural outcomes have been documented in Table 3. Thrombolysis in Myocardial Infarction (TIMI) III flow was observed in all patients post-procedure. In two patients, the first IVL balloon had burst during inflation necessitating a second balloon. None of the patients had any evidence of hemodynamic instability post-procedure, however, there was a prophylactic IABP was used in two due to left ventricular dysfunction and left main coronary stenting was done due to high expected risk from PCI. Major angiographic complications included Type B and Type C dissections in two patients each.

3.1.1. Discussion

The findings from our study showed IVL to be a promising and safe modality for calcified plaque modification in coronaries. In addition, IVL was an effective technique in facilitating stent delivery and achieving adequate expansion. Findings from our study were confirmatory to those in larger trials (Disrupt CAD II[16] and Disrupt CAD III[17]) done on the safety and efficacy of IVL in coronaries. In our study, the mean age was 69.5 ± 7.9 years with a majority being males and with co-morbidities such as hypertension and diabetes. Similarly, in Disrupt CAD II and Disrupt CAD III trials, a majority of patients were elderly with co-morbidities such as diabetes and hypertension, reflecting a higher prevalence of vascular calcification in this sub-group.[16,17]

Severely calcified lesions often increase the complexity of PCI leading to poor long-term outcomes.[9] Current treatment options in these calcified lesions include the use of orbital atherectomy devices, high/ultra-high pressure balloons, or cutting/scoring balloons. Most of these devices have varied success rates however, increased complications such as dissection or perforation, slow flow/no-reflow, and higher MACE rates often preclude their use.[21] IVL is a promising new modality for calcified coronaries and has been shown to be both safe as well as effective in clinical trials such as DISRUPT II and III.[16,17] IVL does offer certain advantages over atherectomy devices in terms of (i) lack of guidewire bias (ii) minimal risk of atheromatous embolization, (iii) circumferential plaque modification and (iv) simple technique with a short learning curve.[10]

Heavily calcified LM stenosis leads to an increase in procedural complexity and makes PCI a less favourable option. Though previous studies have reported good procedural success with rotational or orbital atherectomy in calcified unprotected LM disease, its use in these cases is highly limited owing to the risk of slow flow in a large vascular bed and a mismatch between atherectomy burr size and left main dimensions. IVL with its good procedural safety has shown promising results in the management of calcified LM disease.[22,23] In our series, IVL in unprotected LM stenosis was performed in 15/29 (51.7%) patients with excellent post-procedural outcomes. In 12/15 (80%) patients, provisional single-stent strategy was used while LM bifurcation stenting using double kissing crush was done in three patients (20%). In a series of 31 unprotected LM interventions with IVL, a procedural success of 97% was obtained. LM bifurcation stenting using Culotte was done in 11/31 (35%) of these patients.[24] Long-term data regarding the use of IVL in LM lesions is limited. A recent study among eight patients reported IVL to be safe in LM stenosis with MACE occurring in just one patient over a year of follow-up.[25]

3.2. Procedural safety

MACE, mostly peri-procedural MIs, has been reported in 5.8% and 6.8% of patients undergoing IVL in the Disrupt CAD II and Disrupt CAD III trial respectively.[16,17] In our study too, 6.9% patients had an in-hospital MACE, mostly peri-procedural MI. The Disrupt CAD II trial reported no incidents of abrupt vessel closure, slow flow/no-reflow, or coronary perforation.[16] In the Disrupt CAD III trial, two patients had slow flow while there were no reports of no-reflow or vessel perforation.[17] Complications such as slow/no-reflow and coronary perforation are common with atherectomy devices.[10] However, chances of slow/no-reflow are minimal in IVL as calcium fragments resulting from IVL remain in-situ, hence the low probability of distal embolization. In our study, peri- or post-procedural MI was observed in 6.9% while none had slow flow/no-reflow or coronary perforation. IVL balloon rupture is uncommon, albeit if it occurs it may lead to coronary artery dissection and acute vessel closure.[21,26,27] In our series, there were two instances of IVL balloon rupture on inflation to nominal pressures. In both these patients, circumferential calcification was evident on coronary angiogram and the IVL balloon rupture might have occurred secondary to the presence of an intra-luminal calcium spur. A review of the literature revealed four reports documenting a total of ten cases of IVL balloon rupture of which three were complicated with coronary artery dissection. In our series, there was no evidence of coronary artery dissection/perforation or acute vessel closure following IVL balloon rupture.[21,26–28] Among our patients, none had rhythm disturbances or “shocktopics” during the procedure. “Shocktopics” refers to the ventricular ectopics which are electrical signals mimicking pacing spikes seen on an ECG during the delivery of IVL pulses.[29]

One of the key limitations precluding IVL use is the bulkiness of balloon catheter with a crossing profile of 0.043″ to 0.046″ leading to poor deliverability in calcified lesions as compared to low-profile coronary balloons. This requires adequate pre-dilatation with smaller balloons before IVL or the use of adjunct techniques like atherectomy to facilitate delivery of IVL balloon catheter and adequate lesion preparation. In the Disrupt CAD II study,[16] pre-dilatation was performed in 50% patients while in the Disrupt CAD III study,[17] 55.5% underwent pre-dilation. In our study, pre-dilation with a semi-compliant balloon was performed in all patients prior to IVL in order to facilitate easy delivery of the IVL balloon catheter.

3.3. Imaging in IVL

Intracoronary imaging techniques such as IVUS or OCT helps in the assessment of extent, distribution, and thickness of calcium deposits in the coronaries.[17] Use of these imaging modalities in adjunct with IVL not only helps in localization of sites to deliver the pulses but also identifies a response to IVL therapy and the need for other modalities for plaque modification. In our study, intracoronary imaging by IVUS or OCT was used in 17/29 (58.6%) patients (Table S1). Findings on intravascular imaging revealed calcium fracture to be the predominant mechanism of action of IVL which is similar to those reported in the DISRUPT studies.[16,17] In addition, 52.9% of the plaques had multiple (≥2) calcium fractures as assessed on OCT (Supplementary Figure A4). In the DISRUPT CAD II trial,[16] multiple fractures were identified in 55.3% while in the DISRUPT CAD III trial,[17] 67.7% of lesions had multiple calcium fractures. Intracoronary imaging revealed a significant increase in MLA post IVL and DES implantation similar to that reported in the DISRUPT trials. Previous studies have shown that plaques with calcium fractures allow better stent expansion with low rates of restenosis and target lesion revascularization.[16,17] These findings were concordant with those in the OCT sub-study in DISRUPT CAD II and III trials.[16,17]

3.3.1. Limitations

The limitations of the study were the retrospective design, a small sample size and the non-randomized nature with lack of a comparative control group. Additionally, a lack of follow-up data and an absence of core laboratory analysis and intravascular imaging for the entire dataset were other limitations. Lastly, cost remains an area of concern especially in developing countries such as India, hampering widespread availability of these modalities.

3.3.2. Conclusion

Our study is a first from a developing country such as India, demonstrating the feasibility and safety of IVL in the management of complex calcified coronary stenosis. With increasing awareness and continued clinical evidence supporting the procedure, IVL is expected to see greater adoption rates by the interventional cardiologists.

Ethics approval

This retrospective observational study was conducted in accordance with all relevant guidelines and procedures.

Funding information

There was no research funding available for this study.

Declaration of competing interest

Authors have no conflict of interest to disclose.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2022.01.001.

References

1. Gruntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. *N Engl J Med*. 1979;301:61–68.
2. Lee MS, Shah N. The impact and pathophysiologic consequences of coronary artery calcium deposition in percutaneous coronary interventions. *J Invasive Cardiol*. 2015;28:160–167.
3. Généreux P, Madhavan MV, Mintz GS, et al. Ischemic outcomes after coronary intervention of calcified vessels in acute coronary syndromes. Pooled analysis from the HORIZONS-AMI and ACUITY TRIALS. *J Am Coll Cardiol*. 2014;63:1845–1854.
4. Kobayashi Y, Okura H, Kume T, et al. Impact of target lesion coronary calcification on stent expansion. *Circ J*. 2014;78:2209–2214.
5. Bourantas CV, Zhang YJ, Garg S, et al. Prognostic implications of coronary calcification in patients with obstructive coronary artery disease treated by percutaneous coronary intervention: a patient-level pooled analysis of 7 contemporary stent trials. *Heart*. 2014;100:1158–1164.
6. Mori S, Yasuda S, Kataoka Y, et al. Significant association of coronary artery calcification in stent delivery route with restenosis after sirolimus-eluting stent implantation. *Circ J*. 2009;73:1856–1863.
7. Wiemer M, Butz T, Schmidt W, et al. Scanning electron microscopic analysis of different drug eluting stents after failed implantation: from nearly undamaged to major damaged polymers. *Cathet Cardiovasc Interv*. 2010;75:905–911.
8. Tzafriri AR, Garcia-Polite F, Zani B, et al. Calcified plaque modification alters local drug delivery in the treatment of peripheral atherosclerosis. *J Contr Release*. 2017;264:203–210.
9. Forero MNT, Daemen J. The coronary intravascular lithotripsy system. *Intervent Cardiol*. 2019;14:174–181.
10. Kassimis G, Didagelos M, De Maria GL, et al. Shockwave intravascular lithotripsy for the treatment of severe vascular calcification. *Angiology*. 2020;71:677–688.
11. Ali ZA, Brinton TJ, Hill JM, et al. Optical coherence tomography characterization of coronary lithoplasty for treatment of calcified lesions: first description. *JACC Cardiovasc Imaging*. 2017;10:897–906.
12. Ueki Y, Otsuka T, Hibi K, et al. The value of intracoronary imaging and coronary physiology when treating calcified lesions. *Intervent Cardiol*. 2019;14:164–168.
13. Fujino A, Mintz GS, Matsumura M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. *EuroIntervention*. 2018;13:e2182–e2189.
14. Lee T, Mintz GS, Matsumura M, et al. Prevalence, predictors, and clinical presentation of a calcified nodule as assessed by optical coherence tomography. *JACC Cardiovasc Imaging*. 2017;10:883–891.
15. Watanabe Y, Sakakura K, Taniguchi Y, et al. Comparison of clinical outcomes of intravascular ultrasound-calcified nodule between percutaneous coronary intervention with versus without rotational atherectomy in a propensity-score matched analysis. *PLoS One*. 2020;15, e0241836.
16. Ali ZA, Nef H, Escaned J, et al. Safety and effectiveness of coronary intravascular lithotripsy for treatment of severely calcified coronary stenoses: the Disrupt CAD II study. *Circ Cardiovasc Interv*. 2019;12, e008434.
17. Hill JM, Kereiakes DJ, Shlofmitz RA, et al. Disrupt CAD III investigators. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. *J Am Coll Cardiol*. 2020;76:2635–2646.
18. Chambers JW, Feldman RL, Himmelstein SI, et al. 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.
19. Thygesen K, Alpert JS, Jaffe AS, et al. Executive group on behalf of the joint European society of cardiology (ESC)/American college of cardiology (ACC)/American heart association (AHA)/World heart federation (WHF) task force for the universal definition of myocardial infarction. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72:2231–2264.
20. Ambrose JA, Winters SL, Arora RR, et al. Coronary angiographic morphology in myocardial infarction: a link between the pathogenesis of unstable angina and myocardial infarction. *J Am Coll Cardiol*. 1985;6:1233–1238.
21. Aksoy A, Salazar C, Becher MU, et al. Intravascular lithotripsy in calcified coronary lesions: a prospective, observational, multicenter registry. *Circ Cardiovasc Interv*. 2019;12, e008154.
22. Salazar CH, Travieso A, Gonzalo N, et al. Intracoronary lithotripsy in percutaneous treatment of calcified left main coronary stenoses. *JACC (J Am Coll Cardiol): Case Rep*. 2019;1:46–49.
23. Wong B, El-Jack S, Khan A, et al. Treatment of heavily calcified unprotected left main disease with lithotripsy: the first case series. *J Invasive Cardiol*. 2019;31:E143–E147.
24. Cosgrove CS, Wilson SJ, Bogle R, et al. Intravascular lithotripsy for lesion preparation in patients with calcific distal left main disease. *EuroIntervention*. 2020;16:76–79.
25. Ocaranza-Sánchez R, Abellás-Sequeiros RA, Santás-Álvarez M, et al. First-in-man reported 12-months follow-up after intravascular lithotripsy in left main percutaneous revascularization. *Coron Artery Dis*. 2021 Feb 12.
26. López-Lluva MT, Jurado-Román A, Sánchez-Pérez I, et al. Shockwave: useful but potentially dangerous. *JACC Cardiovasc Interv*. 2019;12:500–501.
27. Soriano F, Veas N, Piccinelli E, et al. Coronary dissection due to intravascular lithoplasty balloon rupture. *EuroIntervention*. 2019;15:e558–e559.
28. Kaur N, Mehrotra S, Pruthvi CR. Intravascular lithoplasty device failure in highly calcified coronary vessel - a case report. *AJCR*. 2021;4:8–13.
29. Wilson SJ, Spratt JC, Hill J, et al. Incidence of “shocktopics” and asynchronous cardiac pacing in patients undergoing coronary intravascular lithotripsy. *EuroIntervention*. 2020;15:1429–1435.