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Indian Journal of Cardiovascular Disease in Women

Cardiovascular Interventional Round

Shock Wave Intravascular Lithotripsy: Shock the Rock

Sarita Rao[1], Roshan Rao[1], Sonya Burgess[2], Achukatla Kumar[3]

[1]Department of Cardiology, Apollo Hospitals, Indore, Madhya Pradesh, India, [2]Department of Cardiology, Nepean Hospital, Kingswood, Australia, [3]Department of Health Research, ICMR, Port Blair, India.

***Corresponding author:**
Sarita Rao,
Department of Cardiology,
Apollo Hospitals, Indore,
Madhya Pradesh, India.

saritarosh@yahoo.com

Received: 29 November 2022
Accepted: 16 December 2022
EPub Ahead of Print: 10 January 2023
Published: 01 March 2023

DOI
10.25259/IJCDW_16_2022

Quick Response Code:

ABSTRACT

Complex coronary artery disease with severe coronary calcification can be challenging to treat, with a higher risk of procedural complications and major adverse cardiac events. Intravascular lithotripsy (IVL) is a pioneering technology for the treatment of critically calcified coronaries. IVL utilizing localized pulsatile sonic pressure waves at low pressure provides a novel approach for lesion preparation of severely calcified plaques. The deliverability and ease of use are also likely to increase access and use of IVL, and combination therapy with other devices shows promise.

Keywords: Shock wave, Intravascular lithotripsy, Coronary artery calcification

INTRODUCTION

Complex coronary artery disease with severe coronary calcification can be challenging to treat, with a higher risk of procedural complications and major adverse cardiac events (MACE). Severe coronary artery calcification (CAC) is a frequent cause of percutaneous coronary intervention (PCI) failure.[1,2] CAC is associated with higher rates of stent under-expansion, restenosis, thrombosis, target vessel revascularization, and drug and polymer stent coating disruption during stent delivery. Contemporary tools have been developed to improve procedural success and short- and long-term outcomes. These techniques include tools for calcium modification and intravascular imaging. These tools make PCI of heavily calcified lesions, more predictable, safer, and more likely to be successful.

CAC is common, between 17 and 35% of patients under-going PCI are reported to have CAC. Severe CAC is more common with advanced age, diabetes, and chronic kidney disease, male sex, and more frequently observed in the previous coronary artery bypass grafting (CABG) patients,[2,3] The prevalence of CAC also changes with ethnicity/race, and cardiovascular disease risk factors.[4] The strongest predictor of CAC incidence is advanced age; by the age of 70, more than 90% of men and 67% of women develop CAC.[5-8] A study by Kanaya *et al*. evaluating CAC rates using computed tomography assessment amongst differing ethnicities found a significantly higher prevalence of CAC in men who were white or south Asian compared to men who were Chinese, black or Latino post multivariate risk adjustment, but no reported ethnic differences in CAC rates among women.[4-9] Several studies have reported higher rates of CAC in men when compared to women post multivariate risk adjustment.[6]

The prevalence of CAC varies significantly between studies and patient cohorts. Higher reported rates have been reported seen in more contemporary PCI cohorts. In the 2004 (C-SIRIUS) study

rates of CAC were reported at only 12%, in the Horizons-AMI study,[7] reported rates of CAC were 37.7% in (ST-segment elevated myocardial infarction patients), and 26.7% (in non-ST-elevated acute coronary syndrome), rates of CAC in the 2011 COMPARE study were 38%.[8,9]

Substantially higher rates of CAC are detected with intravascular imaging, with one study reporting angiographically evident rates of CAC in 38% of patients, which increased to 73% when intravascular ultrasound was used.[10]

PATHOPHYSIOLOGY OF CAC

Inflammation is an important mediator of CAC. Inflammation proceeds coronary calcification and facilitates its progression. The apoptosis of inflammatory cells and smooth muscle cells cause's dysmorphic calcium precipitation, macrophage, and foam cell cytokines also play an important role.[11] The pathological changes begin when the cholesterol plaques underneath the endothelium trigger an inflammatory reaction, which comprises macrophages, foam cells, chondrocyte-like cells, and cytokines. These changes lead to the formation of microcalcifications, within the coronary artery plaques. It is a intricate process involves multiple inhibitors and activators that is similar to osteogenesis elsewhere in the body.[12]

IMPACT OF CAC ON PCI OUTCOMES

Complex coronary artery disease with severe coronary calcification predicts PCI failure and MACE.[13-16] Survival rate, target lesion revascularization, and MI incidence rates are predominantly affected by the severity of calcification[13-15] calcified lesions which are circumferential, and extensive are more likely to be resistant, and non-distensible during conventional balloon angioplasty.[15,16] The length, depth, and circumference of coronary calcification on intravascular imaging predicts the need for advanced calcium modification techniques such as lithotripsy or atherectomy and have been used to develop prognostically validated risk scores to guide PCI decision making. Where CAC extends beyond 180°, is thicker than >0.5 mm, and longer than >5 mm stent under-expansion is likely without advanced techniques for calcium modification.[17]

Calcification remodeling and debulking can be done with contemporary tools for advanced calcium modification. Advanced calcium modification tools include orbital and rotational atherectomy, and scoring balloons, cutting balloons, super high pressure balloons, laser atherectomy, and intravascular lithotripsy (IVL).[16,18,19] These are chosen based on calcium distribution within the specific lesion, and together constitute the armory of equipment accessible for CAC.

Cutting balloons, high-pressure non-compliant balloon catheters, rotational and orbital atherectomy, lithotripsy and excimer lasers can be utilized to modify calcified stenoses, allowing for more optional stent delivery and expansion in complex coronary situations. Adequate lesion preparation with optimal calcium modification is required to minimize the higher risk of complication associated with severe CAC, as heavy unmodified or poorly modified calcified lesions may result in stent damage, stent under expansion, or malposition, restenosis and stent thrombosis secondary to suboptimal PCI.[13,20,21] Advanced calcium modification techniques such as rotation and orbital atherectomy can be used to successful debulk, fracture and modify severely calcified stenoses but learning curves, cost, along with complications such as with periprocedural MI, complex dissection, slow flow, and perforation, and arrhythmia can impede of atherectomy procedures and may limit their use and accessibility.[22] In up to 1 third of cardiac catheterization laboratories in the United States coronary atherectomy is not available[23] [Table 1].

Intravascular coronary lithotripsy provides a feasible and user-friendly alternative to rotablation to modify severe CAC. Lithotripsy is an established tool successfully used for renal and gastroenterological procedures for many years. IVL has also been used with FDA clearance since 2016 for peripheral arterial disease patients with critically calcified lesions [Table 2]. Coronary IVL (using the Shockwave IVL (S-IVL) (shockwave medical, Ins., Santa Clara, CA, USA), was approved in 2021.[24] IVL utilizing localized pulsatile sonic pressure waves at low pressure provides a novel approach for lesion preparation of severely calcified plaques. Electrohydraulic waves produced by IVL can disrupt subendothelial calcification, successfully fracturing circumferential calcium[25,26] [Table 2].

IVL

Origination of IVL

Shock wave lithotripsy was primarily used medically to treat urolithiasis in the 1980s.[27] Before lithotripsy use the predominant method of stone extraction was surgery, and treatment carried a significant risk of surgery related complications. The introduction of a novel, non-invasive medical approach to treat renal stones revolutionized treatment, as extracorporeal shockwave lithotripsy allowed minimally invasive management of urinary tract stones. Evaluation the safety and effectiveness of extracorporeal shock wave liothotripsy have been favorable,[28] but not complication free. Vascular rupture, actual kidney injury (secondary to tubular involvement), scarring and inflammation, with persistent impairment of kidney function are possible. These complications are reduced when utilizing

Table 1: Comparison of characteristics between rotational atherectomy, orbital atherectomy, and intravascular lithotripsy.

Characteristics	RA	OA	IVL
Guidewire	0.09" proprietary wire	0.014" proprietary wire	0.014" guidewire of choice
Effect of wire bias on calcium modification	Wire-bias dependent	Wire-bias dependent	Independent, circumferential calcium modification
Side branch protection	Side branch wire must be removed during atherectomy	Side branch wire must be removed during atherectomy	No interaction with side branch wire
Distal embolization	Atherectomy releases debris and microparticles	Atherectomy releases debris and microparticles	Theoretically same risk as angioplasty balloons
Perforation	Up to 1.5%	Up to 1.8%	Low (<1%)
Bradyarrhythmia	Temporary pacemaker needed in atherectomy in dominant coronary artery	Temporary pacemaker may be considered in atherectomy in dominant coronary artery	No recorded bradyarrhythmia
Plaque ablation	Dependent on selected burr size	Dependent on minimal lumen area	No plaque ablation
Effect on intimal (superficial) and medial (deep) calcium	Ablates superficial calcium	Ablates superficial calcium	Modifies superficial and possibly deep calcium

Table 2: Characteristics of coronary, peripheral (iliac/femoral), and peripheral (below the knee) IVL.

IVL	Coronary	Peripheral (iliac/femoral)	Peripheral (below the knee)
Guide/sheath compatibility (Fr)	6 guide catheter	6 sheath for 3.5–6.0 mm balloons 7 sheath for 6.5–7.0 mm balloons	5 sheath
Guide extender compatibility	≥5.5 Fr	-	-
Catheter length (cm)	138	110	135
Guidewire compatibility (inch)	0.014"	0.014"	0.014"
Balloon diameter (mm)	2.5–4.0	3.5–7.0	2.5–4.0
Balloon length (mm)	12	60	40
Balloon diameter (mm)/ crossing profile (inch)	2.5-2.75 mm: 0.043" 3.0-3.5 mm: 0.044" 3.75-4.0 mm: 0.046"	3.5 mm: 0.054" 4.0 mm: 0.057" 4.5 mm: 0.058" 5.0 mm: 0.062" 5.5 mm: 0.064" 6.0 mm: 0.066"	2.5-3.0 mm: 0.045" 3.5 mm: 0.045" 4.0 mm: 0.050"
Number lithotripsy emitters/ balloons	3	5	5
Pulse frequency	1 pulse/s	1 pulse/sec	1 pulse/sec
Maximal duration of energy delivery (sec)	10	30	20
Emitted energy/balloon atm (MPa)	50 atm (5 MPa)	50 atm (5 MPa)	50 atm (5 MPa)
Maximum pulses/balloon	80 (8 cycles with 10 pulses each)	300 (10 cycles with 30 pulses each)	160 (8 cycles with 20 pulses each)
Minimal balloon pressure during energy delivery (atm)	4	4	4
Nominal pressure (atm)	6	6	6
Rated burst pressure (atm)	10	10	10
CE mark	2015	2017	2018
FDA registration	2021	2017	-

a lower rate of shock-wave and stopping between each phase of the treatment.[27] Further innovation has allowed for use of lithotripsy to treat stones in the gallbladder and bile duct, and within the coronary and peripheral vasculature.[29] Using pulsatile sonic pressure waves to shatter and crack the calcium.

IVL: Device and procedure

Coronary IVL is currently performed using the Shockwave Medical device (Shockwave Medical, Inc, Santa Clara, CA). This is a single use disposable monorail catheter with an fluid filled 12 mm angioplasty balloon surrounding the shockwave emitters [Figure 1] connected to a portable energy generator. The balloon has a diameter ranging from 2.5 to 4.0 mm, with crossing profiles of 0.043" to 0.046" [Figure 1]. Catheter is inserted through a conventional coronary wire (0.014") with a fast exchange platform. There are two lithotripsy emitters in the balloon shaft[30] emanate IVL waves. These emitters produce acoustic pressure waves within the balloon. The electrical current from the emitters allows the fluid within the balloon to vaporize, creating sonic pressure waves as the gaseous bubble within the balloon rapidly expands and collapses. The shock waves travels through the vasculature soft tissue, selectively modifying calcification within the vessel wall, causing fractures evident with subsequent intravascular imaging.[26,31] The both blood vessel layers (intima and medial layers) are affected. The calcium modification and fracture enhances vascular compliance, enabling controlled balloon dilation and better stent delivery and expansion.[30] The balloon is filled with fluid to limit thermic damage to the vaculature, and several emitters across the shaft to permit shock waves to the extent of the lesion. The positive and negative peak pressures are monitored closely and lowered to minimize the tensile stress on the vessel wall, which can be compared to extracorporeal SWL.[31]

Balloon size is choosed depend on the diameter of the reference vessel (1:1 sizing). The indeflator device and balloon are developed by conventional procedure applying a solution of contrast dye and saline (50:50). Following a guidewire flush, saline is applied to the balloon and distal shaft to activate the hydrophilic coating. The cable connector is connected to one side of IVL and catheter on the another side [Figure 1]. The IVL balloon is positioned at the treatment site using proximal and distal markers, and then it is inflated to a pressure of no more than 4.0 atm. The balloon must be fully apposed to the vessel wall. When the connector button is switched on, ten pulses of IVL therapy are administered over 10 s. The balloon is expanded to 6.0 atm to a greater extent as per the balloon compliance and thereafter compressed, to admit blood flow to be restored. The process can be performed as many times as required to administer numerous cycles of IVL to the lesion with a maximal of 80 pulses per therapy segment. To ensure and maintain optimal distal perfusion, each cycle of 10 pulses must always be followed by an pause of at least 10 s. The balloon can be maneuvered across the lesion among rounds.[32] Particular risks are linked with the coronary IVL procedure which includes vessel dissection, atrial or ventricular capture/extrasystole, device embolization, and allergic responses to any component of the device reported by the manufacturer.[32] This is in contrast to the known risks of catheter-based therapies and general coronary interventional procedures. Coronary IVL is now approved for use in the balloon dilation of stenotic, severely calcified *de novo* coronary arteries preliminary to stenting. When performing IVL for lesions within 5 mm of prior stenting, advised with caution.[32] off-label applications of the IVL method encompass in-stent restenosis (ISR), lesions post CABG, and stent under expansion [Figures 2 and 3].

PRE-CLINICAL RESEARCH

Shockwave medical performed two studies, one acute and one chronic swine animal study with the use of S-IVL system. Shockwave coronary IVL catheter is in accordance with Good

Figure 1: Intravascular lithotripsy device.

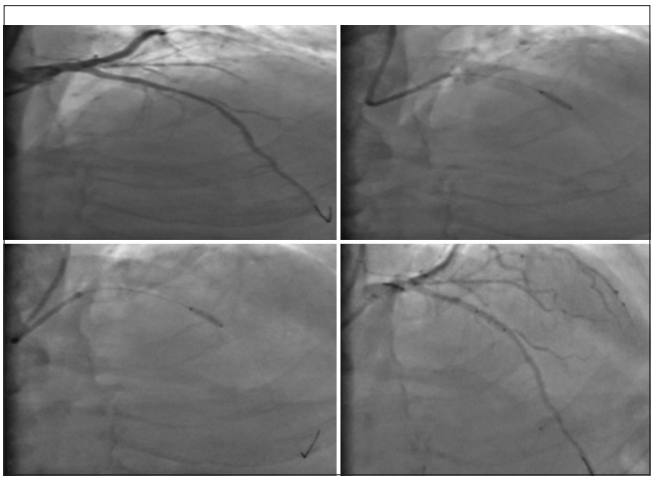

Figure 2: Coronary angiography pre- and post-intravascular lithotripsy therapy.

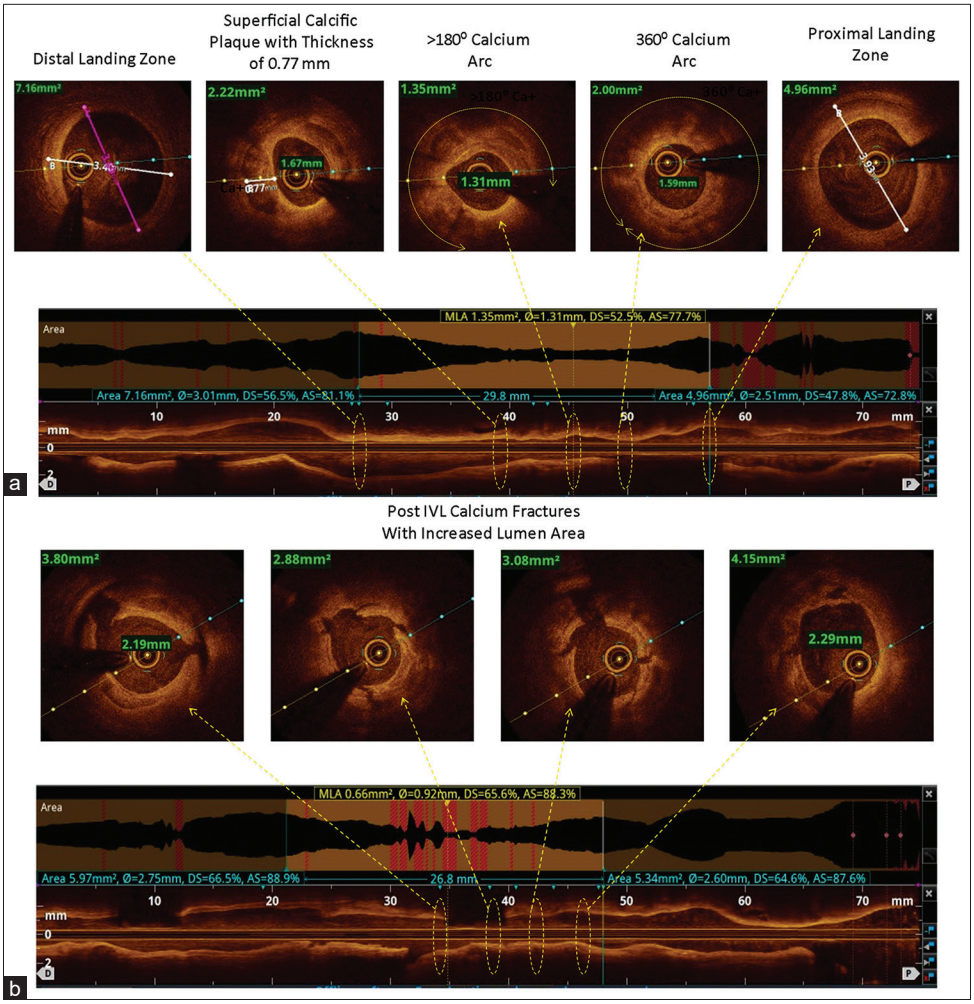

Figure 3: (a) Pre-intravascular lithotripsy (IVL) OCT of calcification (b) post-IVL OCT of calcium fractures with increased lumen area.

Laboratory Practices (GLP) regulations 21 CFR58 to assess the safety. The ultimate goal of this research was to evaluate the safety of mechanical energy used during the IVL versus balloon angioplasty alone accompanied by stenting. The IVL test group examined a clinical use case involving possible therapy overlap when two separate IVL balloons were used. Neither study reported significant morbidity or any adverse events, or any fatality during the experimentations or follow-up. Pathological observations in the acute study indicated epicardial bleeding with fat necrosis underlying almost entire test article treated arteries on gross inspection, as well as histology which was missing in the controls who had undergone balloon angioplasty. Significant epicardial fat accumulation was also observed on the superficial regions of the heart in the subacute investigation, but it's unclear whether the observations were related to both, or the test, or control-treated arteries. Vascular wall inflammation and mean diameter stenosis was moderate and comparable across the group in both studies, and the operator noted <50% in-stent lumen constriction in stented arteries at terminal angiography. The results could be attributed to a excessive mechanical outstretch, therapy of non-diseased, non-calcified arteries, and constraints of animal models. The trials conducted by GLP (i.e., procedural observations, histological data findings, and angiographic findings) indicate that IVL can be safely and efficiently delivered in tandem with the clinical setting of care (stenting). The investigations found no significant differences among the balloon angioplasty control and IVL test groups. These studies corroborate the conclusion that the S-IVL procedure poses no safety risk.[32]

CLINICAL TRIALS

DISRUPT trial for CAD I

This trial,[25] a small (n = 60) prospective multicenter study, evaluating the feasibility of IVL use in patients with severely calcified coronary lesions IVL. A clinical endpoint of

MACE was used (defined in this trial as cardiac mortality, myocardial infarction, and target vessel revascularization), DISRUPT trial patients had MACE rates of 5.0% at 30 days and 8.6% at 6 months. The instrument success rate (defined as successful device delivery and IVL therapy at target lesion) and clinical success rate (defined as a residual stenosis of less than 50% and no in-hospital MACE) were both high (98.3% and 95.0%, respectively). According to OCT results, fracture was the main mechanism for calcium alteration, and it was independent of depth.[25]

DISRUPT trial for CAD II

The DISRUPT II trial,[33] followed on from DISRUPT I and was designed to evaluate safety and effectiveness of IVL, was a slightly larger (n = 120) prospective multicenter study, evaluating IVL use in patients with severely calcified coronary lesions IVL. The in-hospital MACE was an primary endpoint (MI, target vessel revascularization, and cardiac death). An OCT sub study was also conducted to evaluate the mechanism of calcium modification, and characteristics of the plaque fracture achieved. In hospital MACE was reported in 5.8% (due to 7 myocardial infarctions), no perforation or slow flow-no reflow, abrupt closure was noted in any of the DISRUPT II patients. There is 78.7% lesions having calcium fractures were showed in the te Post PCI OCT, with average of 2.6 fractures per lesion.[33]

DISRUPT trial for CAD III

The DISRUPT III trial,[30] followed on from DISRUPT II and was considered the pivotal study to confirm safety and effectiveness of coronary IVL, still a single arm prospective multicenter study it was performed in 4 countries and studied a larger (n = 431) cohort, evaluating IVL use in patients with severely calcified coronary lesions IVL. Freedom from MACE at 30 days was the major safety endpoint, while procedural success was the efficacy endpoint. While the procedural success rate was 92.4%, the overall primary safety endpoint reached was 92.2%. The procedure was well tolerated, and there were few periprocedural complications. The associated OCT sub study found 67.4% of the lesions had calcium fracture.[30]

DISRUPT trial for CAD IV

This trial[34] followed on from DISRUPT III and was designed to for regulatory approval of coronary IVL in Japan, still a single arm prospective multicenter study it studied only 64 patients, specifically evaluating IVL use in Japanese patients with severely calcified coronary lesions IVL. Again, freedom from MACE at 30 days was the primary endpoint, and operative success (residual stenosis <50%) was the major efficacy endpoint. Results from DISRUPT IV patients were also compared using propensity matching to previously published IVL control group from outside of Japan. The main outcomes were procedural success (cases 93.8% vs. control 91.6%, P = 0.007) and noninferiority for freedom from MACE at 30 d (cases 93.8% vs. control 91.2%, P = 0.008). During the procedure, no complications such as perforations, abrupt closure, or slow flow/no reflow were occurred.[34]

Pooled evidence disrupt I-IV

Data from all 4 DISRUPT trials have been pooled and recently published[31] discussing outcomes of all 628 patients in these single arm IVL trials from Japan, Northern American, Australia, and Europe. Major reported findings were that coronary IVL had a high rate of procedural success and facilitated safe successful stent implantation in severely calcified coronary lesions. The average length of calcified stenosis treated over all 4 studies was found to be 41.5 ± 20.0 mm. Safety and efficiency endpoint were met in ≥92% of patients. Reported rates of target lesion failure were 7.2%, cardiac death 0.5%, and stent thrombosis 0.8%. Rates of post-IVL complications were 2.1% and rates of serious angiographic complications were 0.3%, no IVL-associated perforations, abrupt closure, or episodes of no reflow in the entire pooled cohort. Editorial comment was primarily positive but also noted the need for future control group comparison where PCI was used without lithotripsy, and the issue of lesion choice where calcium may not be circumferential, and therefore less favorable for IVL, concluding more data, particularly RCT data were required[23] [Table 3].

REAL WORLD EVIDENCE STUDIES (CLINICAL REGISTRIES)

Several clinical registries also provide real world data describe IVL use. A prospective 3 center registry described by Aksoy *et al.*[35] with 71 enrolled patients treated with for IVL, reported results in patients divided into three patient groups. Group A (received primary IVL therapy with calcified *de novo* lesions (n = 39), Group B received secondary IVL therapy for patients who failed to dilate a lesion with a noncompliant balloon (n = 22), and Group C received tertiary IVL therapy for patients who experienced stent under-expansion following prior stenting (n = 17). Procedural success (defined as <20% residual stenosis) and safety results were the primary endpoints. Aksoy *et al*. found Groups A, B, and C experienced procedural success rates of 84.6%, 77.3%, and 64.7%, respectively, with no reported in- hospital MACE.[35]

Further registry data (n = 45) from Umapathy *et al*., retrospectively evaluated the clinical and angiographic

Table 3: Randomized clinical trials of IVL (Disrupt CAD studies).

RCT	CAD I	CAD II	CAD III	CAD IV
Date Published	February 2019	October 2019	October 2020	May 2021
Type of study	Prospective single-arm multicenter study	Prospective single-arm multicnter study	Prospective single-arm multicenter study	Prospective single-arm multicenter study
Number of patients	60	120	384	64
Number of centres	7	15	47	8
Inclusion criteria	Patients with a clinical indication for coronary intervention were required to have one or more lesions requiring percutaneous coronary intervention with a diameter stenosis≥50%, native coronary artery lesion length≤32 mm, and heavy calcification	Patients had silent ischemia, unstable or stable angina with evidence of myocardial ischemia, or stabilized acute coronary syndrome without elevation in the cardiac biomarkers. Participants were required to have a single target lesion requiring percutaneous coronary intervention with a diameter stenosis≥50%, lesion length≤32 mm in native coronary arteries, and severe calcification	Patients presenting with stable, unstable, or silent ischemia and severely calcified *de novo* coronary artery lesions undergoing percutaneous coronary intervention were eligible for enrollment. Target lesions were≤40 mm in length with reference vessel diameters of 2.5–4.0 mm	Eligible patients were scheduled for percutaneous coronary intervention and presented with stable, unstable, or silent ischemia and severely calcified *de novo* coronary artery lesions. Target lesions were≤40 mm in length and the target vessel reference diameter ranged from 2.5 to 4.0 mm
Exclusion criteria	Not reported	Participants were excluded if there was planned use of atherectomy, specialty balloons, or investigational coronary devices	Patients with acute myocardial infarction and specific complex lesion features were excluded	Patients with New York Heart Association class III or IV heart failure, renal failure, or recent myocardial infarction, stroke, or transient ischemic attack were excluded
Age (Years)	72 (66, 79)	72.1±9.8	71.2±8.6	75±8
% Male	80.0%	78.3%	76.6%	75%
Lesion length	18 mm (14, 25)	19.5 mm±9.8	26.1 mm±11.7	27.5 mm±10.4
Severe calcification at baseline	100%	94.3%	100%	100%
Concentric calcification *n* (%)	47 (78)	86 (71.7)	NA	46 (74.4)
Eccentric calcification *n* (%)	13 (22)	34 (28.3)	NA	NA
Calcified length	22.3 mm±12.3	25.7 mm±12.4	47.9 mm±18.8	49.8 mm±15.5
Number of IVL pulses	72 (40-120)	70.7±43.3	68.8±31.9	104±56
Number of stents	1 (1, 2)	1.3±0.6	1.3±0.5	1.1±0.3
No. of lithotripsy catheters (median with IQR range or mean±SD)	2 (1, 2)	1.2±0.6	1.2±0.5	NA
IVL Pressure pre/post IVL, atm	6/6, atm	4/6, atm	6/6, atm	NA
Pre-dilation	37%	41.7%	55.2%	20.3%
Post-dilation	87%	79.2%	99%	1.6%
Total procedure time min	92 (70–109)	68.3±34.2	53.0 (38.0–74.0)	NA
Primary endpoints	30 d MACE	In-hospital MACE	Freedom from in-hospital MACE, procedural success	Freedom from in-hospital MACE, procedural success

(Contd...)

Table 3: *(Continued).*

RCT	CAD I	CAD II	CAD III	CAD IV
Outcome	5% MACE observed	MACE occurred 5.8% patients	Freedom from in-hospital MACE occurred in 92.2%; Procedural success in 92.4%	Freedom from in-hospital MACE occurred in 93.8%, Procedural success in 93.8%
Procedural success	95%	100%	92.4%	93.8%
In-hospital MACE	5%	5.8%	7%	N/A
MACE at 30 days	5%	7.6%	7.8%	6.2%
MACE at 6 months	8.3%	N/A	N/A	N/A
MACE at 1 year	N/A	N/A	13.8%	N/A
Luminal gain post IVL	N/A	0.83±0.47 mm	N/A	1.42±0.42 mm
Luminal gain post stenting	1.7 mm	N/A	1.7 mm	1.67±0.37 mm
Residual stenosis	<50% in 100 lesions; <30% in 92% lesions; <20% in 73% lesions	7.8±7.1%	11.9%	Residual diameter stenosis<50% and<30% in all
Calcium fracture on OCT	78%	78.7%	67.4%	53.5%

IVL: Intravascular lithotripsy, MACE: Major adverse cardiac events

outcomes of coronary IVL use in patients with moderate to severe calcified coronary lesions who underwent IVL. Cardiovascular death, myocardial infarction, and target vessel revascularization were the primary endpoints, with secondary endpoints of clinical success (stent expansion with <30% ISR and no in-hospital MACE) and angiographic success. Patients received either primary IVL therapy (n = 23 lesions), secondary IVL (n = 15 lesions), and tertiary IVL (n = 12 lesions). The total clinical success rate was 90%, and the angiographic success rate was 94%.[36] At baseline, the mean diameter of the stenosis was decreased from 63.2% ± 10.2% to 33.5% ± 10.9% (P = 0.001) after IVL, after stenting, it was 15.0% ± 7.1% (P = 0.001). The mean minimum lumen diameter in this study increased after IVL from 1.1 ± 0.3 mm at baseline to 1.90 ± 0.5 mm and 2.80 ± 0.50 mm after stenting.

Acute coronary syndrome (ACS)

Data describing IVL in the setting of ACS have also been described in a small number of patients.[37-41]

Wong *et al.* reported real world data in patients treated with IVL (n = 44). In this registry 57% of patients had ACS at presentation. Wong reported that angiographic success in all 44 cases of angiographic success were documented. There were no adverse outcomes or in-hospital complications were observed. At 1-year follow up 1 cardiovascular death due to hemorrhagic stroke, 3 NSTEMIs, (and 3 non-cardiac deaths were reported) three NSTEMIs occurred at 1 year. More IVL treated ACS cases are reported by Aziz *et al.* in their registry (n = 190) of ACS data collected from 6 centers in the United kingdom and Italy.[39] In this cohort 47.8% were ACS. Procedural success was achieved in every patients except one. The complications rate was 3%. Six coronary perforations were reported. There was one in-hospital death. At final follow up (median 222 days) a MACE rate of 2.6% was reported. There were three cases of TVR, two cardiac mortality, and one MI.

A lower rate of IVL use in ACS was reported by El Jattari *et al.*, evaluating German registry data (n = 134).[40] El Jattari *et al.* reported 29.9% of the patients selected for IVL treatment presented with ISR, and 70.1% had *de novo* lesions. In this registry 88.1% of cases had successful procedural outcomes. MACE at 1 month was 3%, with 2 cardiovascular deaths, and 2 of non-cardiac deaths, 1 case of stent thrombosis occurred, and 1 dissection that requiring further stenting, 13 IVL balloon ruptures occurred (9.7%) (with no adverse sequelae), and 1 coronary artery perforation causing death was reported.

Rola *et al.* evaluated polish registry data (n = 52), including patients with lesion described as previously "un-dilatable" 82.7% of whom had ACS.[41] In this case series, clinical success with IVL was attained in 98.1% of cases. One patient experienced ventricular arrhythmia due to ongoing ischemia rather than IVL therapy. One balloon ruptured, and one patient had a residual stenosis more than 50% (despite 100 IVL pulses). Two significant bleeding events were reported, and one in-hospital stroke.

Under expansion of stents

IVL has also been used successfully for stent under expansion. Data from the multicenter SMILE registry, (n = 34) found a

success rate of 87.1% with IVL.[42] Authors reported 30 days outcomes in this cohort of no, stent thrombosis, artery perforation, TLR, and cardiac mortality. At median of 13 months this registry reported, 1 non-fatal peri-procedural MI post rupture of IVL balloon.

Combined therapy "Rotatripsy"

Calcium modification with a combination of both IVL and rotablation has also been described. Aziz *et al*. reported cause of ombined therapy with both IVL and rotablation in 34/190 (18%) of patients treated with IVL, but did not report subgroup outcomes for those treated with "rotatripsy."[39] Buono *et al*.,[43] report outcomes of a retrospective analysis of thirty-four "Rotatripsy" cases. In all cases rotablation preceded IVL, either during the index procedure (79%) or staged procedure during the same hospital admission. The procedures success was reported in 100% of cases. Adverse outcomes at 1 year were reported and included t2 target vessel MIs, and the all cause at a rate of 9%. Three coronary perforations occurred; they were successful treated without further deterioration.

CONCLUSION

Severe coronary calcification is common. The presence of complex calcified coronary artery disease significantly increases the risk of complications both peri-procedurally and at longer term follow-up. If lesion preparation is inadequate incomplete stent expansion, stent thrombosis and restenosis are more likely to follow. IVL is an effective calcium modification tool. IVL can offer significant benefits over other calcium modification techniques and while no RCT comparing lithotripsy to non-lithotripsy based treatment is currently published, contemporary observational data suggests this technology offers significant benefits to patients and to interventional cardiologists. The deliverability and ease of use are also likely to increase access and use of IVL, and combination therapy with other devices show promise.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Rao S, Rao R, Burgess S, Kumar A. Shock wave intravascular lithotripsy: Shock the rock. Indian J Cardiovasc Dis Women 2023;8:75-85.