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STATE-OF-THE-ART REVIEW

Can Most Calcified Coronary Stenosis Be Optimized With Coronary Intravascular Lithotripsy?

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ABSTRACT

Intravascular lithotripsy can be used as an effective therapy for lesion preparation in severely calcified lesions. The mechanism, as shown by optical coherence tomography, is calcium fractures. The aforementioned modification is performed with minimal risk of perforation, no-reflow and a low incidence of flow-limiting dissection and myocardial infarctions. Other techniques, such as cutting or scoring balloons and rotational atherectomy have also been shown to increase luminal diameter, but other complications, such as distal embolization, induced by these treatment modalities, are a source of concern. This review describes a single-center study of all-comer patients, including those with complex characteristics. This therapy is very effective, with a very low risk of complications. In this article, we characterize the mechanism of action of the intravascular lithotripsy catheter, its optical coherence tomography validation, clinical applications, and comparison with other calcium-modifying technologies, as well as future directions, which can be used to improve the technology. (JACC: Asia 2023;3:185-197) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

In percutaneous coronary intervention (PCI) using a drug-eluting stent, coronary artery calcification poses a significant challenge to intraluminal drug delivery.[1] Coronary artery calcification has several negative effects on the outcomes of coronary treatments, including changes in drug-eluting polymer deamination[2] and drug delivery.[1] Certain approaches, such as noncompliant, cutting, and scoring balloons, as well as atheroablative mechanisms used to reduce coronary artery calcification, are frequently associated with several drawbacks. Aside from that, the high-pressure balloon dilation technology may not be able to produce the required effects to fracture the calcium and expand the artery, which can result in barotrauma-related dissection or perforation.[3] In comparison with the use of a balloon to treat coronary artery calcification, the use of atheroablative technology increases the risk of serious complications, such as myocardial infarction, flow-limiting dissection, distal embolization, and perforation.[4-6] Intravascular lithotripsy (IVL) has evolved as a therapeutic intervention for vascular calcification.[7,8] IVL works by using acoustic pressure waves to target vascular calcium. Several clinical trials involving severe peripheral arterial disease and calcified arterial disease have demonstrated the safety and efficacy of IVL in the treatment of coronary artery calcification,[9,10]

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease
IVL = intravascular lithotripsy
OA = orbital atherectomy
OCT = optical coherence tomography
PCI = percutaneous coronary intervention
RA = rotational atherectomy

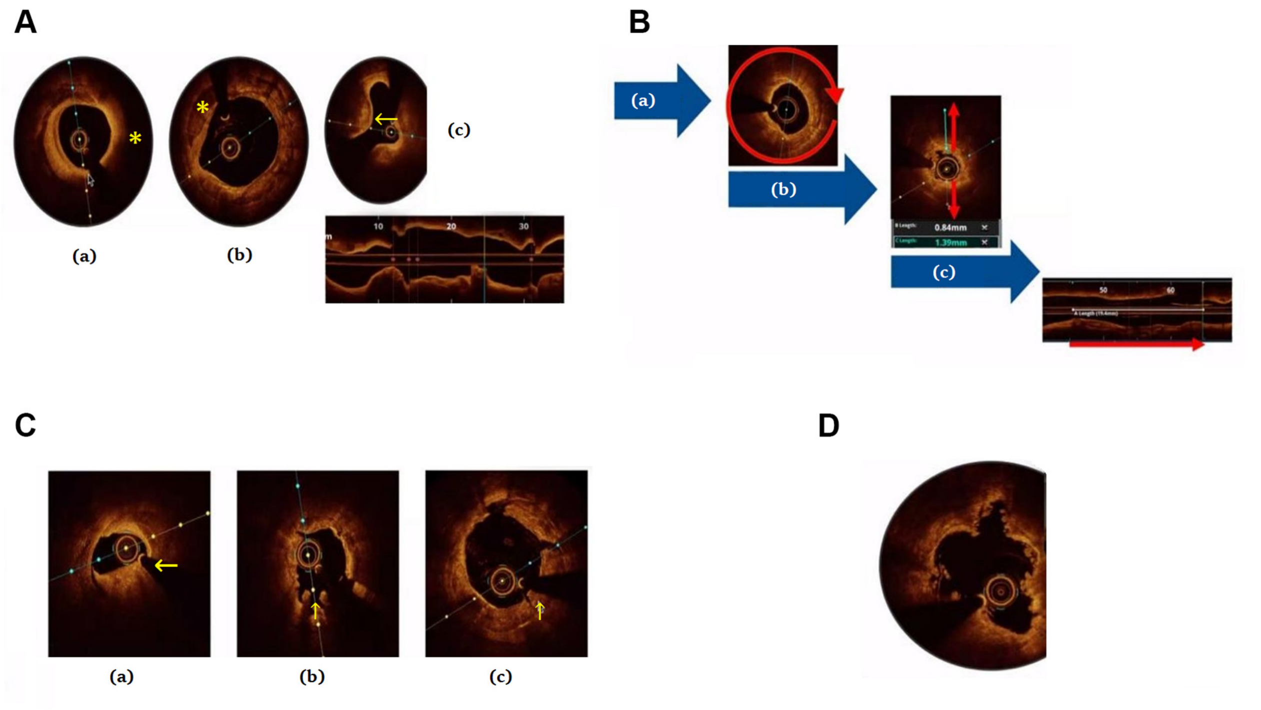
MECHANISM OF IVL

IVL emitters generate electric sparks, which cause unfocused acoustic pressure waves to spread through the vessel walls. Acoustic pressure waves fracture the calcium after inducing contraction in it by creating a small peak of negative pressure. IVL demands less energy-flux density than extracorporeal shockwave lithotripsy to fracture the calcium present in the vessel wall; as a result, the risk of injury of soft tissue with IVL is very low.[11] Figure 1 shows types of calcium and their modification by IVL. Figures 2 to 4 depict the modification of calcium by different techniques.[12]

A post hoc analysis of the Disrupt PAD II (Shockwave Lithoplasty Disrupt Trial for PAD) study demonstrated the significance of IVL balloon sizing and emitter alignment. This study looked at the effect of the IVL technique on the 12-month primary patency in superficial femoral and popliteal arterial segments when only IVL was used as a treatment.[13] In this study, the ratio of the IVL balloon to the reference vessel diameter was used as an evaluation parameter, with a ratio of ≥1 being considered optimal. In this study, there was no significant increase in adverse outcomes when the IVL balloon size crossed the reference vessel diameter.

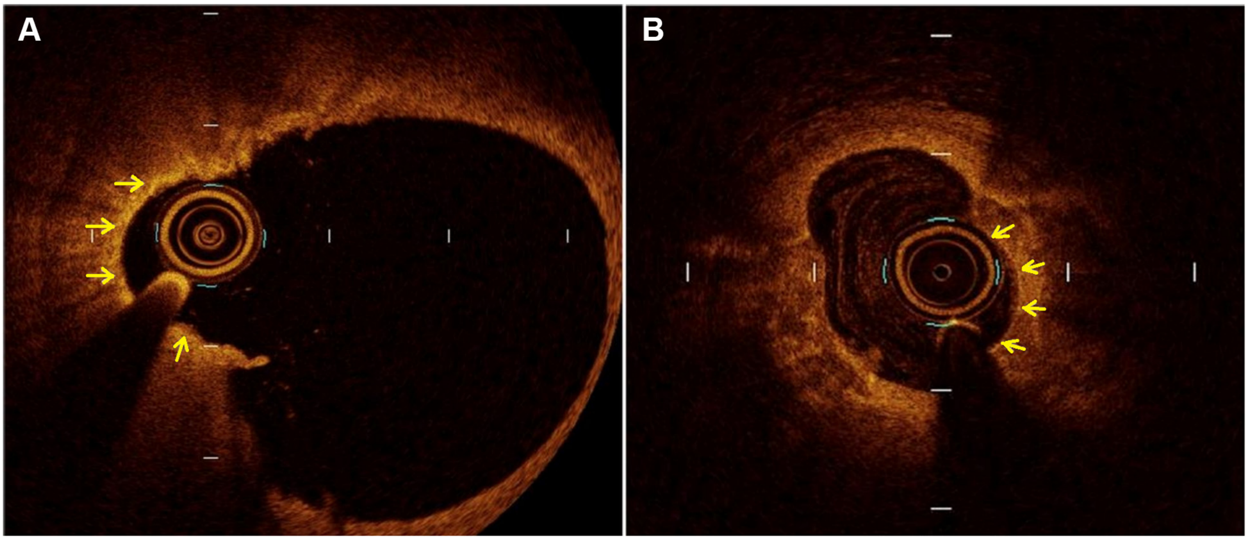
A patient-level pooled analysis of the Disrupt CAD I and Disrupt CAD II studies demonstrated the effectiveness of IVL in the treatment of eccentric calcified lesions. Patient-level data from these two studies ($n = 180$) was pooled out, and 133 concentric lesions and 47 eccentric lesions were recognized. In this study, the evaluation parameter was the final post-residual stenosis in both eccentric and concentric lesions. The study found that postresidual stenosis of <50% in both groups of patients with eccentric and

FIGURE 1 **Types and Extent of Calcium and Their Modification by IVL**



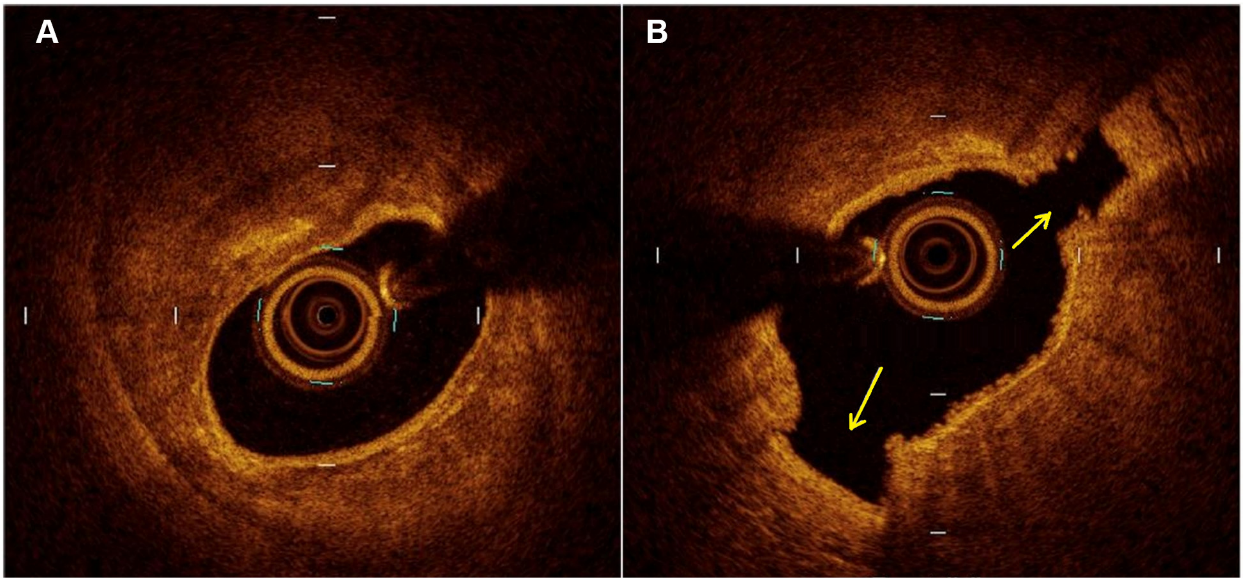
(A) Types of calcium on OCT. **(a)** Deep calcific plaque characterized by signal-poor region with sharply delineated borders located deeply **(asterisk)**. **(b)** Superficial calcific plaque characterized by signal-poor region with sharply delineated borders located superficial **(asterisk)**. **(c)** Nodular calcific plaque characterized by signal-poor region with sharply delineated borders in nodular morphology **(arrow)**. **(B)** Superficial calcified plaque determining the extent of calcified lesion. **(a)** Angle of superficial calcified plaque (**round arrow** showing the angle, which is 360°). **(b)** Calcified plaque showing thickness **(arrow)**. **(c)** Longitudinal view of calcified plaque showing length **(arrow)**. **(C)** Calcified plaque after modification. **(a)** Dissections in calcified plaque after modification **(arrow)**. **(b)** Fissures in calcified plaque after modification **(arrow)**. **(c)** Fractures in calcified plaque after modification **(arrow)**. **(D)** OCT showing post modification by IVL device with calcified plaque showing fractures. IVL = intravascular lithotripsy; OCT = optical coherence tomography.

FIGURE 2 **Effects on Calcified Plaque Induced by RA and OA**



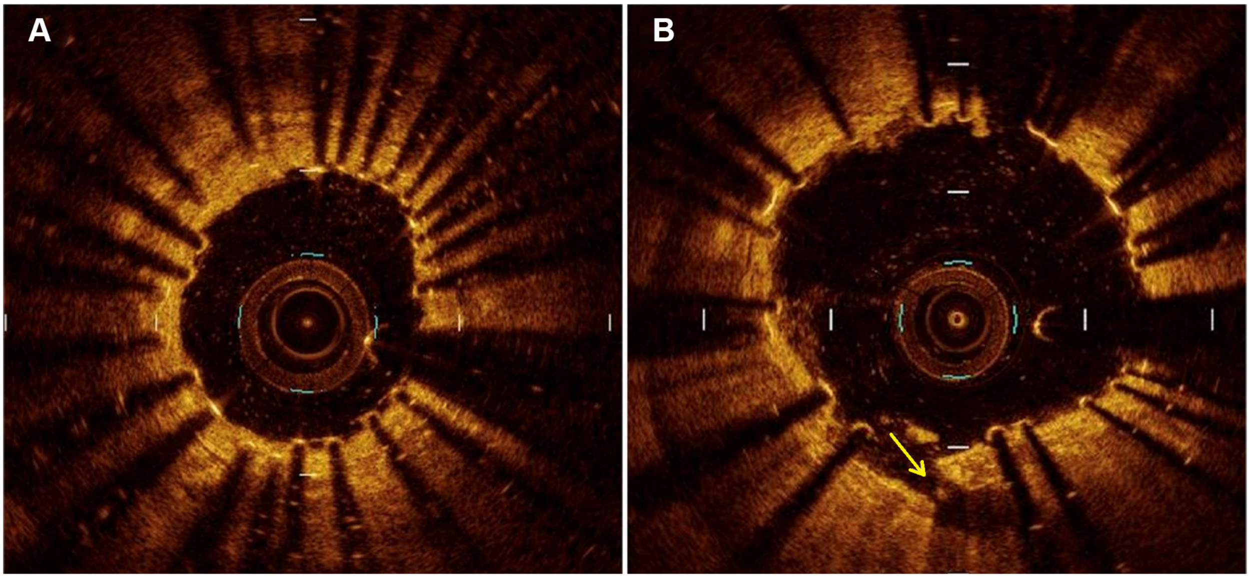
(A) In the shape of a polished groove, calcium ablation **(yellow arrows)** is demonstrated by OCT after RA. **(B)** Similar in shape to RA, calcium ablation **(yellow arrows)** is demonstrated by OCT method after OA. Ablation is highlighted by both cross sections by either device at the wire bias site, with the modification of plaque occurred in the segment adjacent to the OCT catheter and the guidewire. OA = orbital atherectomy; RA = rotational atherectomy; other abbreviations as in Figure 1.

FIGURE 3 **De Novo Calcium Modified by IVL**



(A) severe circumferential calcification in coronary artery is demonstrated by OCT cross-section method. **(B)** At the artery circumference **(yellow arrows)**, deep fractures are modified by IVL. Abbreviations as in Figure 1.

FIGURE 4 **Underexpanded Stent in a Severely Calcified Lesion Modified by ELCA**

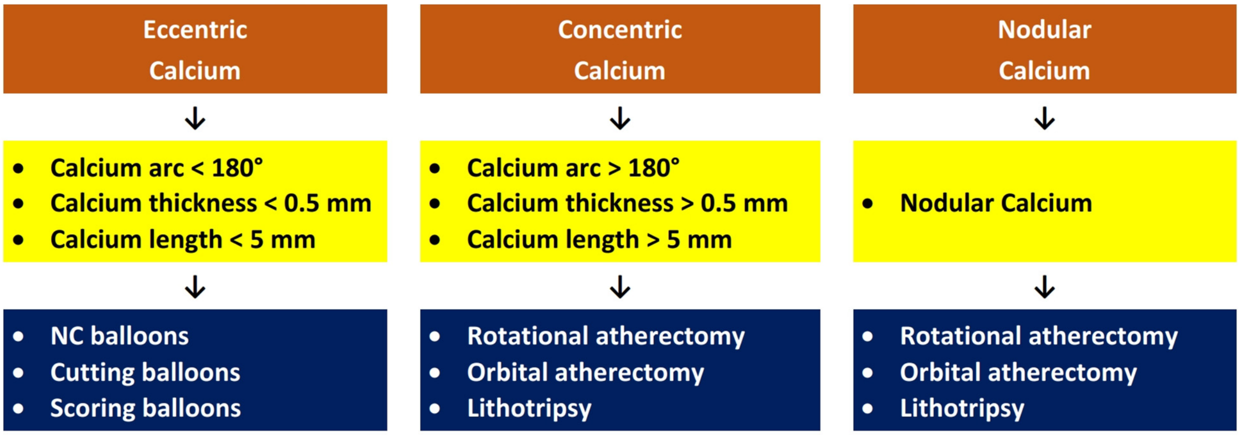


(A) In a severely calcified lesion, there is an underexpanded stent. **(B)** Luminal gain and calcium fracture **(yellow arrow)** is demonstrated by OCT after ELCA. ELCA = excimer laser coronary atherectomy. Abbreviation as in Figure 1.

concentric calcified lesions in 98.6% of patients angiographically after treatment with IVL. Furthermore, there was no evidence of various complications, such as perforations, abrupt closure, or no-flow phenomenon in either group of patients.[14]

Rola et al[15] showed the efficacy of shockwave IVL in patients with severely calcified left main disease. In this study, 16 patients with coronary artery disease (CAD) were treated with IVL followed by PCI, after several unsuccessful attempts at plaque modification

FIGURE 5 **Modification of Various Subtypes of Calcium Defined by Imaging**



The different calcium plaque morphologies by imaging and also the extent and degree of calcification and Arrow heads show the flow of the calcium modification procedure. NC = noncompliant; other abbreviations as in Figure 1.

TABLE 1 Baseline Characteristics (N = 30)

Age, y	74.0 ± 7.0
Male	29 (63)
Height, cm	170 ± 8
Weight, kg	72 ± 12
Diabetes mellitus	12 (40)
Hypertension	24 (80)
Dyslipidemia	21 (71)
Current smokers	6 (18)
Chronic renal failure[a]	6 (20)
Previous MI	6 (20)
Previous PCI	5 (16)
Unstable angina	3 (10)
Atrial fibrillation	3 (11)
Left main disease	3 (10)
Multivessel disease	20 (65)
LV ejection fraction, %	38.0 ± 10.2
Multilesion PCI	12 (38)
Unfractionated heparin	30 (100)
Bivalirudin	0 (0)
GP IIb/IIIa antagonists	2 (4.5)

Values are mean ± SD or n (%). [a]Defined as a glomerular filtration rate of <60 mL/min.

IVL = intravascular lithotripsy; LV = left ventricle; MI = myocardial infarction; PCI = percutaneous coronary intervention.

with other treatment modalities such as rotational devices and noncomplaint balloon catheters. The evaluation parameter in this study was the effective deployment and delivery of the stent. Positive clinical results were obtained in all of the patients, and the study's findings indicate that shockwave IVL is an effective and safe treatment method for patients with left main lesions.[15]

In an analysis that sought to substantiate the mechanistic effects of IVL from 4 international prospective studies (Disrupt I, II, III, IV) in 262 patients, despite having a higher calcium burden, the greater number of IVL-induced fractures in calcified nodules resulted in consistent improvements in luminal gain, minimal stent area, and stent expansion after IVL treatment of both calcified nodule and noncalcified nodule lesions.[16] Recently presented optical coherence tomography (OCT) data suggest that IVL can be effective in concentric, eccentric, and nodular calcification.[17] Different calcium morphologies on OCT or intravascular ultrasound and their mode of modification are shown in **Figure 5**.

The Disrupt PAD II OCT subanalysis,[18] as well as the OCT substudies of the Disrupt CAD I[10] (Shockwave Coronary Rx Lithoplasty Study), and Disrupt CAD II (Shockwave Coronary Lithoplasty Study) Disrupt CAD III (Disrupt CAD III With the Shockwave Coronary IVL System), demonstrated that calcium fracture after IVL treatment was comparable to micro fractures in computed tomographic and histopathologic results from cadaveric studies.[18] The most commonly used therapeutic imaging intervention in the treatment of peripheral artery disease is intravascular ultrasonography. Hence, there is a scarcity of OCT imaging studies of IVL therapy in peripheral arteries.

After IVL therapy, the vascular luminal area increased significantly in both the coronary and the peripheral vessels.[19] Furthermore, the Disrupt CAD and Disrupt PAD studies show that IVL therapy does not cause vessel perforations because IVL acoustic shockwaves penetrate deeply inside the soft tissue with minimal damage and adventitial fibrosis.[20] Furthermore, calcium fracture was observed in 67.7% of the lesions after IVL treatment, indicating that this therapy causes significant changes in vascular calcium.[19]

In Europe, the United States, and other countries around the world, the Shockwave M5 and S4 IVL are approved as therapeutic interventions for the treatment of various peripheral vascular diseases. A coherent reduction in residual luminal diameter stenosis was observed in a patients-level pooled analysis of 336 patients with moderately calcified peripheral lesions.[21]

IVL technology has several advantages over balloon-based and atheroablative technologies for the treatment of chronic calcified lesions. Because IVL relies on low-pressure acoustic waves supplied through a semicompliant balloon, the risk of barotrauma is very low in this technology when compared with other balloon-based systems. Also, the safety of atheroablative technologies is very low, because they can aggravate the thermal damage and vascular problems in the target arteries.

There are several areas where the IVL catheter system can be improved to increase its clinical applicability. The incorporation of electrohydraulic lithotripsy emitters into the shaft of the IVL catheter can improve its deliverability in the treatment of severely stenotic lesions. Second, increasing the size of the IVL balloon matrix can modulate energy transfer via the acoustic waves generated by the IVL. Finally, by potentiating the total number of pulses delivered, the maximum number of lesions can be treated with a single IVL catheter. To date, acute results with IVL therapy in severely calcified lesions have been very promising; however, long-term follow-up is required to understand fully how IVL affects long-term clinical outcomes. Randomized clinical trials are required to provide evidence of the effectiveness and safety of IVL therapy in comparison with other therapies.[22]

TABLE 2 Angiographic and Procedural Characteristics (45 Lesions)

Location	
LMCA	3 (6)
LAD	19 (43)
LCx	6 (12.5)
RCA	17 (37.9)
Reference vessel diameter, mm	3.3 ± 5.3
Lesion length, mm	29.97 ± 17.0
Diameter stenosis, %	84 ± 9
Ostial location	12 (27)
Bifurcation	20 (44.5)
Moderate/severe tortuosity	15 (34)
Chronic total occlusion	2 (4.5)
B2/C lesion	43 (96)
7F guiding catheter	40 (90)
MB diameter, mm	3.00 ± 0.57
MB pressure, atm	16.0 ± 2.8
Use of >1 MB	4 (9)
MB-to-artery ratio	0.95 ± 0.10
IVL in underdeployed stents	6 (13.33)
IVL in ISR calcified	3 (6.66)
IVL in uncrossable lesion	4 (8.8)
IVL in long lesions	5 (11.11)
Balloon predilatation	41 (91)
No. of predilatation balloons	1.77 ± 0.88
Maximum predilatation balloon diameter, mm	2.90 ± 0.45
Maximum predilatation balloon pressure, atm	19.95 ± 4.88
No. of stents per lesion	1.70 ± 0.88
Total stent length per lesion, mm	36.12 ± 18.55
Minimum stent diameter, mm	3.22 ± 0.45
Maximum stent diameter, mm	3.42 ± 0.44
Maximum stent implantation pressure, atm	17.55 ± 3.42
Balloon postdilatation	38 (84)
Maximum postdilatation balloon diameter, mm	3.80 ± 0.50
Maximum postdilatation balloon pressure, atm	22.00 ± 4.54

Values are n (%) or mean ± SD .

ISR = in-stent restenosis; LAD = left anterior descending; LCx = left circumflex coronary artery; LMCA = left main coronary artery; MB = modified balloon; RCA = right coronary artery; other abbreviation as in Table 1.

With this goal in mind, 30 patients with calcified lesions (n = 45) were treated with a shockwave IVL catheter (Translumina) followed by drug-eluting stent implantation. They were further classified into 9 categories:

1. Primary IVL group with calcified lesions, 10 lesions
2. IVL in calcified nodules, 4 lesions
3. IVL in calcified left main bifurcations, 3 bifurcation lesions
4. IVL in underdeployed stents, 6 lesions
5. IVL in in-stent restenosis-calcified, 3 lesions
6. IVL in large vessels and eccentric calcium, 5 lesions
7. IVL in chronic total occlusion PCI, 2 lesions
8. IVL in uncrossable lesions, 4 lesions
9. IVL in long lesions, 5 lesions

TABLE 3 Procedural and In-Hospital Outcome (N = 30; 45 Lesions)

Procedural duration, min	78.90 ± 41.05
Fluoroscopy time, min	19.9 ± 13.5
Contrast amount, mL	225.0 ± 94.0
Large dissection, >5 mm	2 (4.5)
Perforation	0 (0)
Pericardial effusion	0 (0)
No/slow flow	0 (0)
Final TIMI flow grade <3	0 (0)
Residual stenosis >20%	1 (2.2)
Stent failure	2 (4.5)
Crossover	7 (16)
Strategy success	44 (98)
Death	0 (0)
MI	1 (3.3)
Target vessel re-PCI	1 (3.3)
CABG	0 (0)
Stent thrombosis	0 (0)
Access site complications	2 (6.6)

Values are mean ± SD or n (%).

CABG = coronary artery bypass graft; TIMI = Thrombolysis in Myocardial Infarction; other abbreviations as in Table 1.

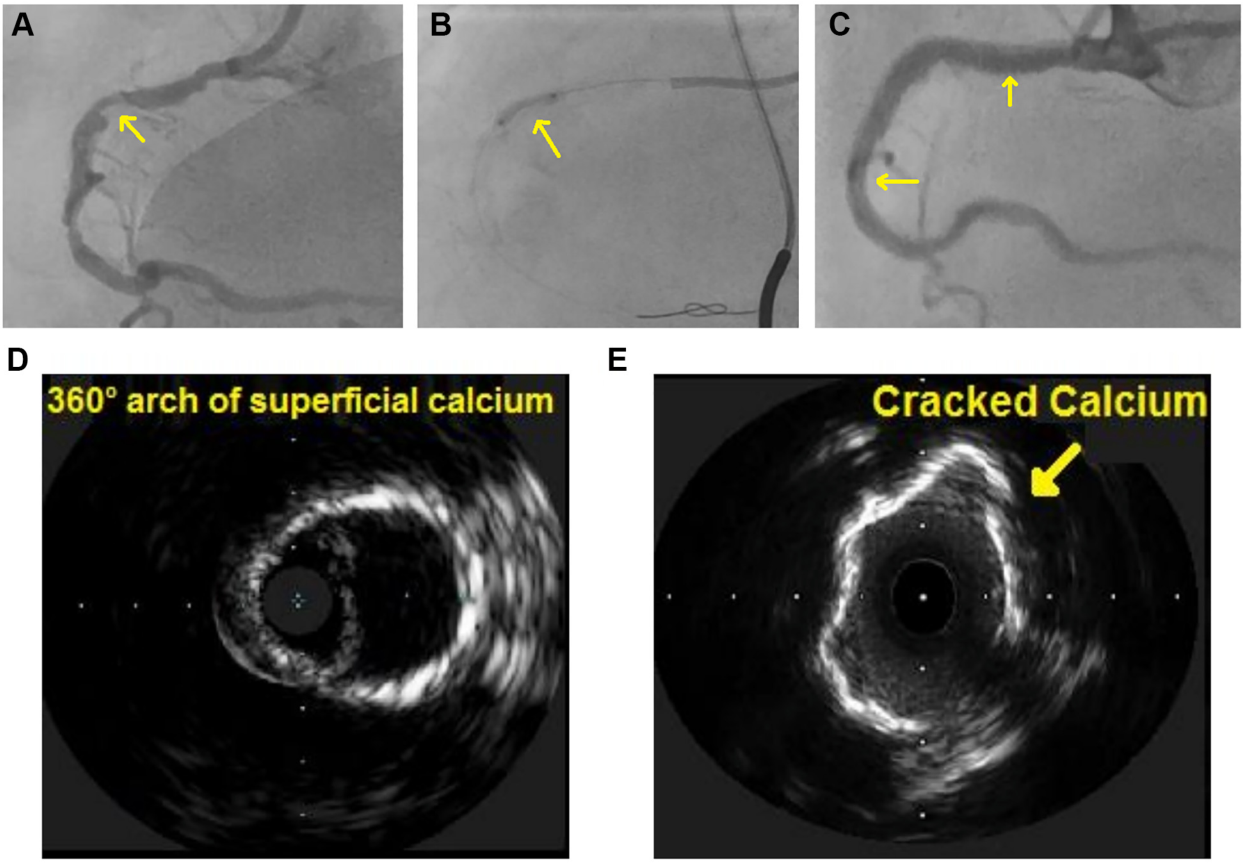
After PCI, these patients were studied angiographically and with intravascular ultrasound imaging, and clinical results were recorded, as well as several clinical events such as cardiac death, target vessel revascularization, and myocardial infraction for a 1-month follow-up. Tables 1 to 3 shows the baseline characteristics, angiographic and procedural characteristics, and in-hospital outcomes of the study. Figures 6 to 9 depict the cases of various calcium morphologies done with IVL modification.

All patients in this single-center retrospective study received IVL using a shockwave balloon-based coronary catheter system. The size of the IVL balloon was determined based on the size of the targeted vessel. A balloon catheter was used to deliver 1 pulse/second to the targeted lesion site. IVL treatment was successful in treating 45 targeted lesions. Although no serious complications were observed, 7 lesions had minor dissections (types A-C). Angiography was performed successfully in all 45 treated lesions, and better clinic results were obtained in 96% of the total cases.

FUTURE DIRECTIONS

The IVL catheter system could be iterated and improved in several areas, increasing the technology's clinical significance. First, a smaller device-crossing profile and increased flexibility in the IVL catheter may improve deliverability in severely

FIGURE 6 **A Large RCA With Concentric Calcium Treated With IVL**

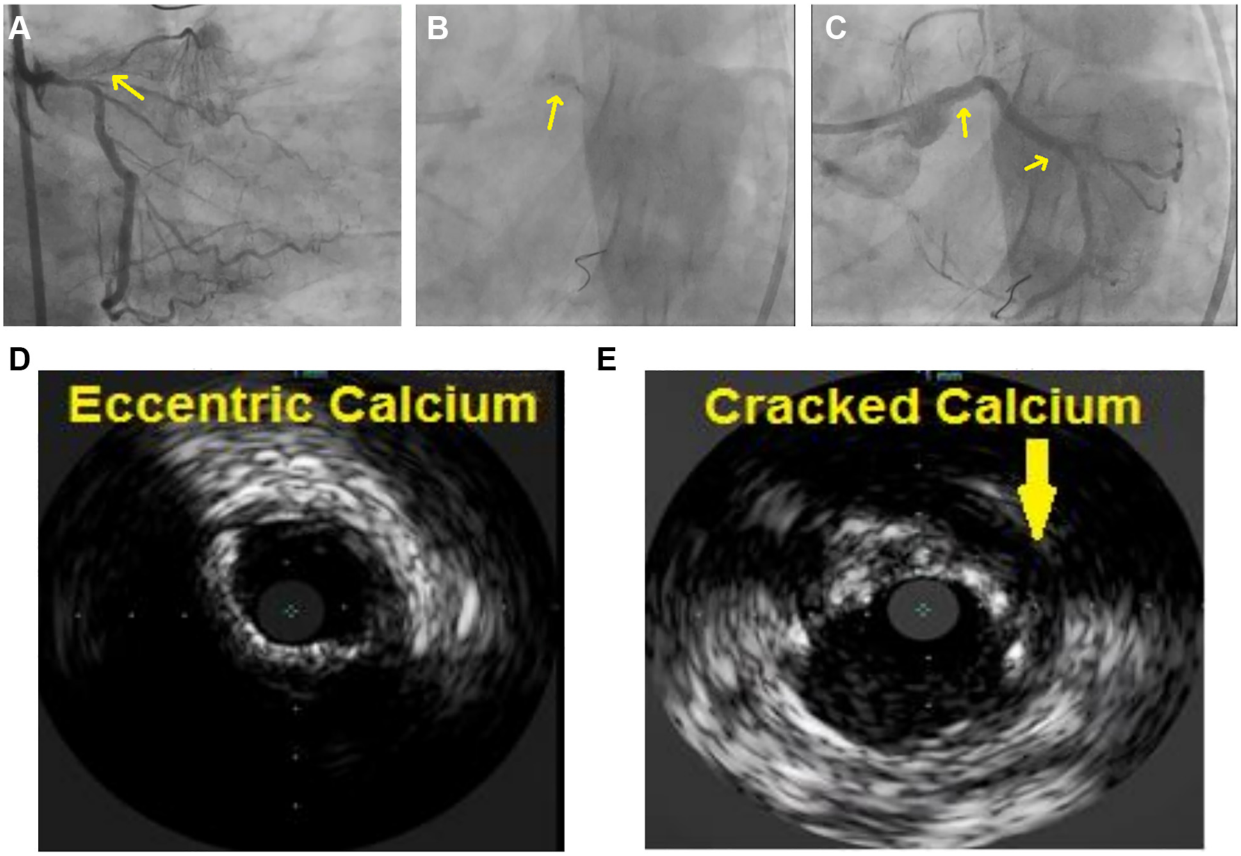


(A) Pre-PCI CAG shows significant calcified plaques in proximal and distal RCA **(arrow)**. **(B)** Inflated NC balloon shows dog boning indicating unyielding calcified lesion **(arrow)**. **(C)** Post-PCI CAG shows fully expanded stent deployed after IVL modification of the lesion **(arrows)**. **(D)** Pre-IVL IVUS imaging shows a superficial 360° arch of superficial calcium. **(E)** IVUS post-IVL shows calcified plaque after IVL, which shows fractures **(arrow)**. CAG = coronary angiogram; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention; RCA = right coronary artery; other abbreviations as in Figures 1 and 5.

stenotic or tortuous lesions. The current crossing profile is larger than that of traditional angioplasty balloon catheters because electrohydraulic lithotripsy emitters are integrated into the IVL catheter's shaft. Cross-profile and flexibility have an impact on delivery. Second, an extended IVL catheter shaft length may allow for the treatment of more distal lesions, whereas broader IVL balloon sizes may allow for appropriate sizing of larger coronary (left main) and peripheral (common iliac) vessels. As a result, improving the optimum balloon matrix for the Shockwave C2 IVL catheter for coronary arteries (4.0 mm), and the S4 (4.0 mm) and M5 (7.0 mm) IVL catheters for peripheral arteries would allow for more optimal IVL balloon-to-artery sizing and improved acoustic energy transfer. Eventually, increasing the total number of pulses delivered per catheter may allow more lesions to be treated with a single IVL catheter, diminishing the duration and cost of the procedure.

Although acute outcomes after IVL in severely calcified coronary lesions have been very reassuring thus far, long-term follow-up is required to understand how these acute results, especially optimal stent expansion and minimum stent area, may affect long-term health outcomes. Disrupt CAD III will have a 2-year follow-up period and will provide long-term clinical outcome data to assess the efficacy of improved stent insertion after intracoronary IVL use. This study included patients with unstable coronary syndromes, ostial or bifurcation coronary lesions, treatment of in-stent restenosis or underexpanded

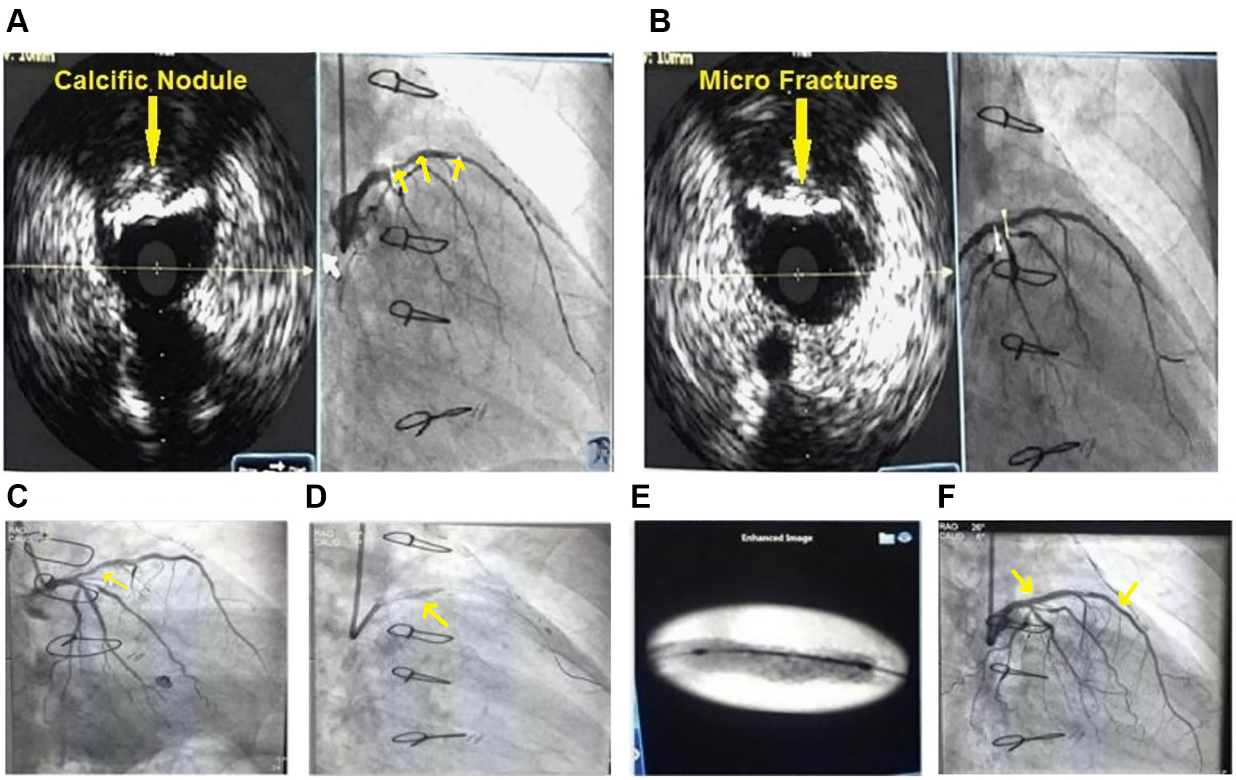
FIGURE 7 **A Case of LM to LCX With Eccentric Calcium Treated With IVL**



(A) Pre-PCI CAG shows significant calcified plaques in LM to LCx **(arrow)**. **(B)** Inflated NC balloon shows dog boning, indicating an unyielding calcified lesion **(arrow)**. **(C)** Post-PCI CAG shows the fully expanded stent deployed after IVL modification of the lesion **(arrows)**. **(D)** Pre-IVL IVUS imaging shows the eccentric calcified plaque. **(E)** IVUS imaging after IVL shows calcified plaque after IVL, which shows fractures **(arrow)**. LCx = left circumflex; LM = left main; other abbreviations as in **Figures 1, 5, and 6**.

coronary stents,[22-25] extreme calcification in upper extremity vessels (ie, carotid, subclavian/axillary, innominate) and vein grafts, as well as the infrarenal aorta, radial, and brachial arteries. After obtaining U.S. Food and Drug Administration approval of the Shockwave Coronary IVL System, an investigator-sponsored all-comers registry is currently enrolling in Spain (REPLICA [Registry of Coronary Lithotripsy in Spain; NCT04298307]; n = 400), and postmarket consent research is being evolved to use the American College of Cardiology National Cardiovascular Data Registry CathPCI Registry to provide perspectives into device safety and effectiveness in an expanded real-world setting. Additional randomized controlled pilot studies comparing IVL with cutting or scoring balloons (BALI [Balloon Lithoplasty for Preparation of Severely Calcified Coronary Lesions; NCT04253171], n = 200; CCS [Coronary Calcification Study; NCT04428177], n = 40) or rotational atherectomy (RA) and laser atherectomy (ROLLERCOASTER [Rotational Atherectomy, Lithotripsy, or Laser for the Treatment of Calcified Stenosis; NCT04181268], n = 150) are scheduled to compare the safety and effectiveness of IVL with other calcium-modifying technologies before stent implantation in severely calcified coronary lesions. There is also a lack of evidence of the effectiveness of IVL therapy in the treatment of eccentric and/or nodular calcification, and a pooled analysis of the Disrupt CAD I, Disrupt CAD II, Disrupt CAD III, and Disrupt CAD IV OCT substudies is now being performed to address these issues. To provide definitive proof of the relative safety and effectiveness of these therapies, as well as to steer algorithms for the treatment of heavily calcified lesions in the

FIGURE 8 **A Case of a Calcified Nodule Treated With IVL**



(A) IVUS examination before IVL shows the calcified nodule **(arrow)**. **(B)** IVUS examination after IVL shows the microfractures in calcified nodule **(arrow)**. **(C)** Pre-PCI CAG shows the significant calcified plaques in proximal LAD **(arrow)**. **(D)** Inflated NC balloon shows dog boning indicating unyielding calcified lesion **(arrow)**. **(E)** Syncvision image shows fully expanded balloon after IVL, indicating good modification. **(F)** Post-IVL CAG shows fully expanded stent deployed after IVL modification. LAD = left anterior descending artery; other abbreviations as in Figures 1 and 6.

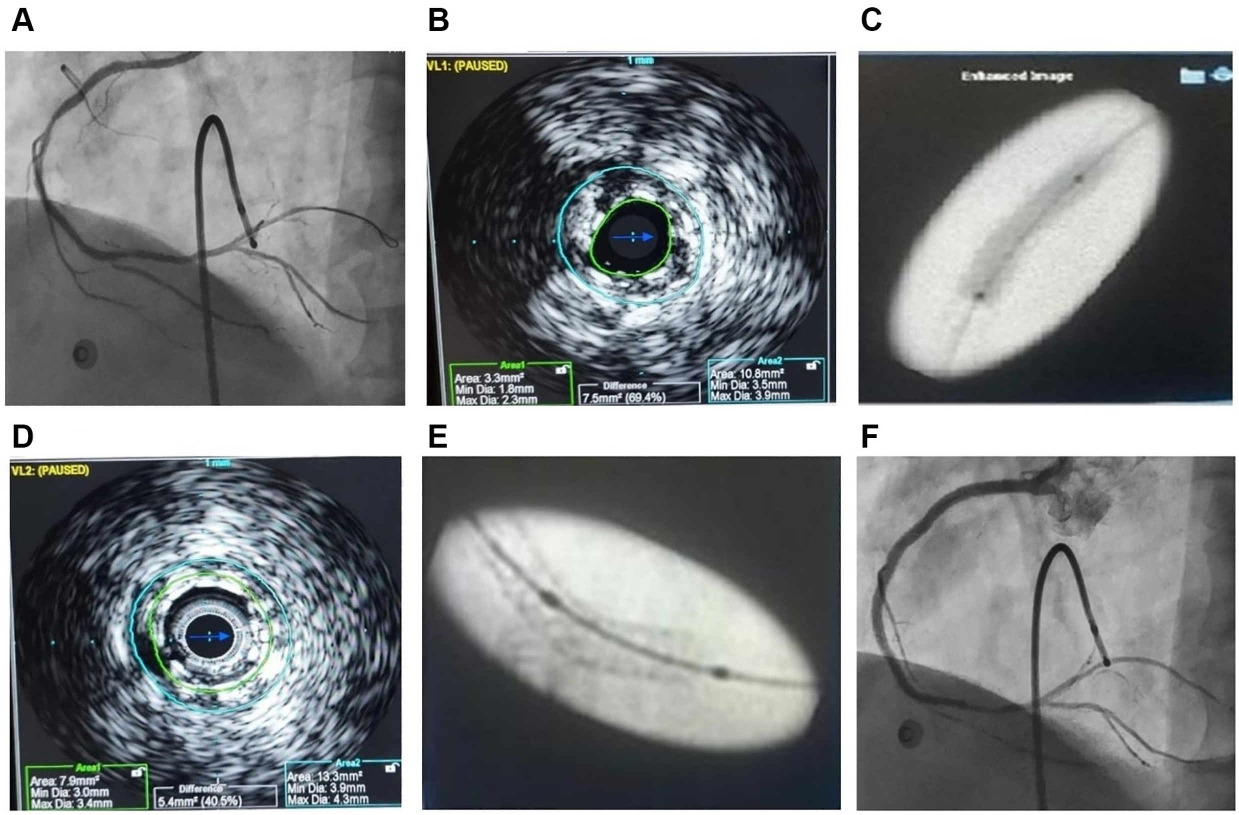
coronary and peripheral vasculature, randomized clinical trials comparing IVL with other calcium-modifying therapies (eg, high-pressure balloon, atheroablative technologies, laser atherectomy) are required. Likewise, the use of IVL to treat grievously calcified aortic valves, rheumatic mitral stenosis, and mitral annular calcification are all promising research areas.

COMPARISON WITH OTHER CALCIUM-MODIFYING TECHNOLOGIES

In the treatment of severely calcified lesions, IVL has several benefits over balloon-based technologies (such as high-pressure noncompliant and cutting/scoring balloons) and atheroablative technologies (RA or orbital atherectomy [OA]). High static pressure is used in balloon-based systems to alter plaques, whereas IVL uses acoustic shockwaves supplied and delivered via a semicompliant balloon expanded to approximately 4 atm, avoiding high-pressure inflation and the risk of barotrauma linked to noncompliant balloons. Second, atheroablative technologies depend on localized calcium debulking, which generates thermal damage and vascular problems in the target arteries. Eccentric ruts or troughs form as a result of the wire bias in their action, posing the possibility of incomplete calcium modification. Additionally, atheroablative technologies are unable to change deep calcium in the lack of indicated wire bias and/or bigger device sizes, both of which may compromise procedure safety. In contrast, IVL fractures both superficial and deep calcium in situ, decreasing the risk of vascular complications and thermal harm. The rates of vascular difficulties related to peripheral and coronary calcium-modifying technologies utilized in significantly calcified target lesions are shown in Table 4.

According to the findings of these retrospective studies suggest, IVL technology causes calcium

FIGURE 9 **A Case of an Underdeployed Stent Owing to Calcification Treated With IVL**



(A) Pre-PCI CAG showing diffuse ISR in RCA from proximal to distal. **(B)** Pre-IVL IVUS examination showing the underdeployed stent and calcified ISR. **(C)** Inflated NC shows underexpansion, indicating an unyielding calcified lesion. **(D)** Post-IVL IVUS examination shows some expansion of the stent in the lesion. **(E)** The fully expanded stent after IVL after stenting. **(F)** Post-PCI CAG showing the fully expanded stents from proximal to distal RCA. ISR = in-stent restenosis; other abbreviations as in Figures 1 and 6.

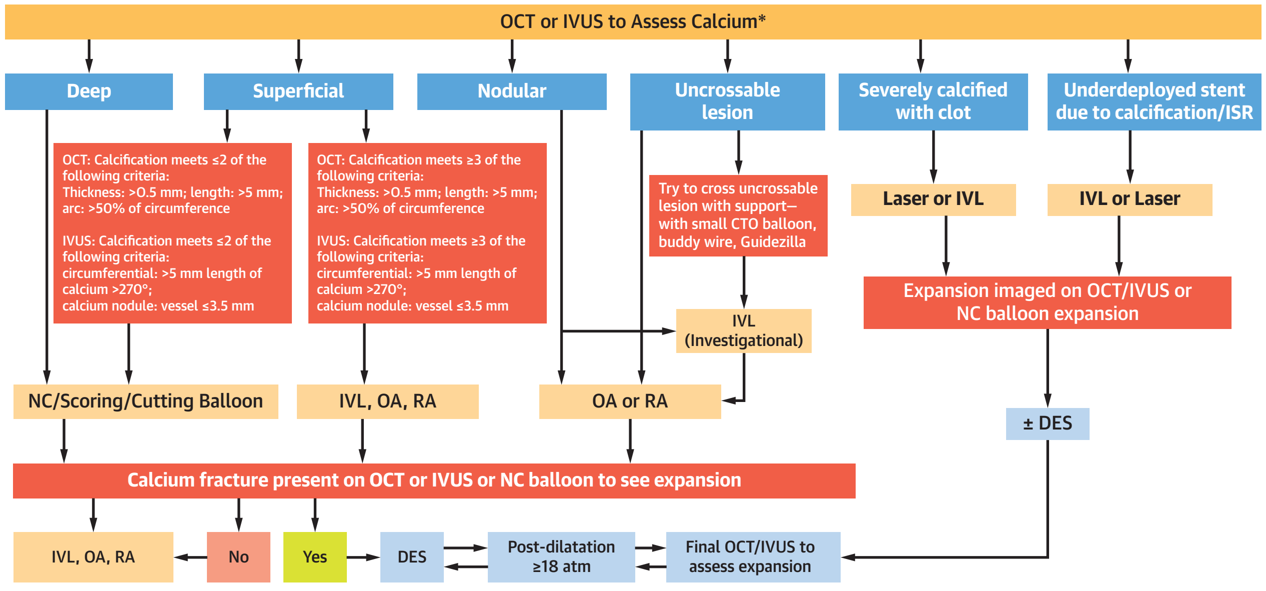
TABLE 4 **Angiographic Complications With Coronary Calcium Modification Technologies**

	IVL	RA	OA	Laser Atherectomy
	Disrupt CAD I (N = 60), Disrupt CAD II (N = 120), Disrupt CAD III (N = 384), Disrupt CAD IV (N = 64)[15,18,23,26]	**PREPARE-CALC (N = 100)**[27]	**ORBIT II (N = 443)**[28]	**Bilodeau et al.**[29] **(N = 95)**
Moderate to severe calcification, %	94.2-100.0	100	100[a]	80%[b]
Angiography core laboratory	Yes	Yes	Yes	Yes
In-hospital MI, %	5.0-6.8[c]	2.0[d]	9.3[c]	2.1
Dissection (types D-F), %	0.0-0.3	3.0[e]	0.9[f]	5.3[f]
Perforation, %	0.0-0.3	4.0	0.9	0.0
Abrupt closure, %	0.3	NR	0.2	0.0
Slow flow, %	0.0	2.0[g]	0.5	0.0
No reflow, %	0.0	–	0.0	–

Values are % unless otherwise indicated. [a]Site reported. [b]Presence of calcium noted, but severity not specified. [c]CK-MB >3 times the upper limit of normal. [d]CK-MB >3 times the URL or troponin >3 times the URL. [e]Large dissection (>5 mm). [f]Includes dissection types C-F. [g]Includes no reflow and slow flow.

CK-MB = creatine kinase myocardial band; Disrupt CAD I = Shockwave Coronary Rx Lithoplasty Study; Disrupt CAD II = Shockwave Coronary Lithoplasty Study; Disrupt CAD III = Disrupt CAD III With the Shockwave Coronary IVL System; Disrupt CAD IV = Disrupt CAD IV With the Shockwave Coronary IVL System; NR = not reported; OA = orbital atherectomy; ORBIT II = Evaluate the Safety and Efficacy of OAS in Treating Severely Calcified Coronary Lesions; PREPARECALC = Comparison of Strategies to Prepare Severely Calcified Coronary Lesions Trial; RA = rotational atherectomy; URL = upper reference limit; other abbreviations as in Tables 1 and 4.

CENTRAL ILLUSTRATION **Algorithm Flow Chart to Approach Modification of Calcified Coronaries**



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Imaging with OCT or IVUS assesses the calcified plaque and divides it into various imagining subclasses. The role of various modalities to modify calcium subtypes identified by imaging like NC, scoring, cutting (balloons), IVL, OA, RA, or laser is described in the flow chart. **Arrowheads** show the flow of the calcium modification procedure. CTO = chronic total occlusion; DES = drug-eluting stent(s); ISR = in-stent restenosis; IVL = intravascular lithotripsy; IVUS = intravascular ultrasound; OCT = optical coherence tomography; OA = orbital atherectomy; RA = rotational atherectomy.

fracture in 60% of severe cases of calcified lesions. This retrospective study also strongly suggests that IVL therapy can be used to treat all calcium subsets. With the use of an IVL balloon, several types of severe lesions that were previously difficult to cross earlier can be predilated. To summarize, the IVL technique can treat a wide variety of morphologies, calcium subtypes, and even stent failure. A flow chart to approach modification of calcified coronaries is shown in the **Central Illustration**.

KEY POINTS.

- In calcified coronaries, imaging with OCT and intravascular ultrasound helps to assess type of calcium which can be deep, superficial or nodular. Or there can be calcification associated with clot or an underdeployed stent or in-stent restenosis.
- With OCT and intravascular ultrasound imaging, we can determine whether calcification is mild, moderate, or severe in extent.
- If the calcification is moderate or severe, it will require modification with IVL, OA, or RA in most cases.
- If the calcification is mild, it may require modification with a noncompliant, scoring, or cutting balloon.
- It is prudent to palpate the artery with demonstration of expansion of a noncompliant balloon after each modification.

TABLE 5 **Calcium Modification According to Subtype of Calcium by Different Modalities: A Comparison**

	NC/Cutting/Scoring Balloon	OA	RA	IVL	Laser
Mild calcification	+++	NU	NU	++	++
Severe calcification					
Deep calcium	++	+	+	+++	NU
Superficial					
Eccentric calcium	+	++	++	+++	NU
Concentric calcium	+	+++	+++	+++	NU
Nodular calcium	+	+++	++	++	NU
Underdeployed stent	NU	NU	NU	++	+++
ISR	+	NU	NU	+++	++
Calcium with clot	+	NU	NU	++	+++

NC = noncompliant; NU = not useful; other abbreviations as in Tables 1, 2, and 4.

- In severely calcified lesions with clot, laser or IVL can be a good modification option.
- In underdeployed stent calcification or in-stent restenosis, IVL or laser can be a good modification strategy.
- Nodular calcium is always an Achilles heel in the management, but OA and RA can be used as first choices. Recently, IVL has been found effective in modifying this subset of calcium morphology.
- In lesions that are uncrossable, we can start with OA or RA. However, with adequate support and the use of smaller chronic total occlusion balloons, some of these lesions, if crossed, can be treated with IVL.
- Lesions that are modified with RA or OA, if inadequate, can be modified further with IVL, so-called rotatripsy. A comparison of different calcium-modifying modalities according to subtype of calcium is shown in Table 5.

HIGHLIGHTS

- Earlier treatment modalities for calcified lesions are associated with an increased risk of complications.
- IVL can be used wide across the spectrum of calcified lesions defined by the imaging.
- The use of IVL in early experience seems to decrease the complications versus other modalities.
- The IVL catheter system can be modified in various ways to improve its clinical applicability.

SUMMARY

To avoid stent failure, optimal plaque preparation of calcified coronary lesions is required. Current PCI techniques that have been linked to an increased complication risk include high and ultra-high-pressure dilatation, scoring or cutting balloons, and atherectomy. IVL is a novel method of preparing lesions in highly calcified coronary arteries. IVL was tested in an all-comers cohort in de novo calcified coronary lesions (primary IVL), lesions with failure of high-pressure balloon dilatation (secondary IVL), and patients with under expanded coronary stents owing to heavy calcification. IVL was a suitable method for lesion preparation with heavily calcified coronary lesions, with a high success rate, low procedural complications, and low major adverse cardiovascular event rates.

The IVL catheter system can be iterated and improved in several areas, including deliverability, size, and the number of pulses. Long-term outcome research is required. All-comers, such as vein grafts, ostial lesions, acute coronary syndrome, and in-stent restenosis, require further investigation. Randomized controlled trials comparing IVL with other calcium-modifying therapies are required.

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REFERENCES

1. Yamamoto MH, Maehara A, Karimi Galougahi K, et al. Mechanisms of orbital versus rotational atherectomy plaque modification in severely calcified lesions assessed by optical coherence tomography. *J Am Coll Cardiol Intv*. 2017;10:2584–2586.

2. 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.

3. Tzafriri AR, Garcia-Polite F, Zani B, et al. Calcified plaque modification alters local drug delivery in the treatment of peripheral atherosclerosis. *J Control Release*. 2017;264:203–210.

4. Madhavan MV, Tarigopula M, Mintz GS, Maehara A, Stone GW, Genereux P. Coronary artery calcification: pathogenesis and prognostic implications. *J Am Coll Cardiol*. 2014;63:1703–1714.

5. Abdel-Wahab M, Richardt G, Joachim Buttner H, et al. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. *J Am Coll Cardiol. Intv*. 2013;6:10.

6. Matsuo H, Watanabe S, Watanabe T, et al. Prevention of no-reflow/slowflow phenomenon during rotational atherectomy—a prospective randomized study comparing intracoronary continuous infusion of verapamil and nicorandil. *Am Heart J*. 2007;154:994.e1.

7. Powers CJ, Tinterow MM, Burpee JF. Extracorporeal shock wave lithotripsy: a study of renal stone differences. *Kans Med*. 1989;90:19–22.

8. Cleveland RO, McAteer JA. Physics of shock-wave lithotripsy. In: *Smith's Textbook of Endourology*. Hoboken, NJ: Wiley-Blackwell; 2012:527–558.

9. Ali ZA, McEntegart M, Hill JM, Spratt JC. Intravascular lithotripsy for treatment of stent underexpansion secondary to severe coronary calcification. *Eur Heart J*. 2020;41:485–486.

10. 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.

11. Li D, Pellegrino A, Hallack A, Petrinic N, Jerusalem A. Cleveland Response of single cells to shock waves and numerically optimized waveforms for cancer therapy. *Biophys J*. 2018;114:1433–1439.

12. Galougahi KK, Shlofmitz E, Jeremias A, et al. Therapeutic approach to calcified coronary lesions: disruptive technologies. *Curr Cardiol Rep*. 2021;23:33. https://doi.org/10.1007/s11886-021-01458-7

13. Brodmann M, Werner M, Holden A, et al. Primary outcomes and mechanism of action of intravascular lithotripsy in calcified, femoropopliteal lesions: results of Disrupt PAD II. *Catheter Cardiovasc Interv. 2019*. 2019;93:335–342.

14. Blachutzik F, Honton B, Escaned J, et al. Safety and effectiveness of coronary intravascular lithotripsy in eccentric calcified coronary lesions: a patient-level pooled analysis from the Disrupt CAD I and CAD II Studies. *Clin Res Cardiol*. 2021;110:228–236.

15. Rola P, Włodarczak A, Kulczycki J, et al. Efficacy and safety of shockwave intravascular lithotripsy (S-IVL) in calcified unprotected left main percutaneous coronary intervention – short-term outcomes. *Adv Interv Cardiol*. 2021;17:344–348. https://doi.org/10.5114/aic.2021.112524

16. Ali Z, Hill J, Saito S, et al. TCT-120 Optical coherence tomography characterization of shockwave intravascular lithotripsy for treatment of calcified coronary lesions: patient-level pooled analysis of the disrupt CAD OCT substudies. *J Am Coll Cardiol*. 2021;78(19 Suppl S):B50–B51.

17. Maehara A. Intravascular lithotripsy is effective in the treatment of calcified nodules: patient-level pooled analysis from the Disrupt CAD OCT substudies. Paper presented at: Transcatheter Cardiovascular Therapeutics (TCT) 2021; November 5, 2021, Orlando, FL.

18. Holden A. *Safety and Performance of the Shockwave Lithoplasty System in Treating Calcified Peripheral Vascular Lesions: Intravascular OCT Analysis*. Leipzig, Germany: LINC; 2018.

19. Hill JM, Kereiakes DJ, Shlofmitz RA, et al. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. *J Am Coll Cardiol*. 2020;76:2635–2646.

20. Brodmann M, Werner M, Brinton TJ, et al. Safety and performance of lithoplasty for treatment of calcified peripheral artery lesions. *J Am Coll Cardiol*. 2017;70:908–910.

21. Madhavan MV, Shahim B, Mena-Hurtado C, Garcia L, Crowley A, Parikh SA. Efficacy and safety of intravascular lithotripsy for the treatment of peripheral arterial disease: an individual patient level pooled data analysis. *Catheter Cardiovasc Interv*. 2020;95:959–968.

22. Di Mario C, Goodwin M, Ristalli F, et al. A prospective registry of intravascular lithotripsyenabled vascular access for transfemoral transcatheter aortic valve replacement. *J Am Coll Cardiol Intv*. 2019;12:502–504.

23. Rosseel L, De Backer O, Sondergaard L, Bieliauskas G. Intravascular iliac artery lithotripsy to enable transfemoral thoracic endovascular aortic repair. *Catheter Cardiovasc Interv*. 2020;95:E96–E99.

24. Riley RF, Corl JD, Kereiakes DJ. Intravascular lithotripsy-assisted Impella insertion: a case report. *Catheter Cardiovasc Interv*. 2019;93:1317–1319.

25. Saito S, Yamazaki S, Takahashi A, et al. Intravascular lithotripsy for vessel preparation in severely calcified coronary arteries prior to stent placement: primary outcomes from the Japanese Disrupt CAD IV study. *Circ J*. 2021;85(6):826–833.

26. Brinton TJ, Ali ZA, Hill JM, et al. Feasibility of shockwave coronary intravascular lithotripsy for the treatment of calcified coronary stenoses: first description. *Circulation*. 2019;139:834–836.

27. Abdel-Wahab M, Toelg R, Byrne RA, et al. High-speed rotational atherectomy versus modified balloons prior to drug-eluting stent implantation in severely calcified coronary lesions. *Circ Cardiovasc Interv*. 2018;11:e007415.

28. 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). *J Am Coll Cardiol Intv*. 2014;7:510–518.

29. Bilodeau L, Fretz EB, Taeymans Y, Koolen J, Taylor K, Hilton DJ. Novel use of a high-energy excimer laser catheter for calcified and complex coronary artery lesions. *Catheter Cardiovasc Interv*. 2004;62:155–1561.

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