

Editorial

Coronary lithoplasty: applying a pulse to calcified lesions

Litoplastia coronaria: un pulso al calcio

Cristóbal A. Urbano-Carrillo,* Luz D. Muñoz-Jiménez, and Macarena Cano-García

Unidad de Hemodinámica y Cardiología Intervencionista, Servicio de Cardiología, Hospital Regional Universitario de Málaga, Málaga, Spain



Article history:

Available online 10 August 2020

Calcified coronary lesions are a major challenge in interventional cardiology, adversely affecting the short- and long-term results of coronary procedures. According to recent studies, moderate-to-severe calcification is estimated to be present in 18% to 26% of coronary lesions.¹ The lesions are associated with advanced age, hypertension, diabetes, and chronic kidney failure. As the population gradually ages and these comorbidities become more common, the prevalence of significantly calcified coronary lesions can be expected to rise.

Percutaneous interventions in calcified coronary lesions are associated with greater stent underexpansion and malapposition, more postprocedure complications, and consequently a higher percentage of restenosis and thrombosis. The presence of coronary calcium has been shown to be an independent predictor of adverse clinical outcome and is associated with higher mortality, a higher number of cardiovascular events, and higher risk of procedural failures.² Additionally, friction between the calcium and the drug-eluting stent during angioplasty could damage the stent polymer and affect the drug-release kinetics.

Coronary angiography often underestimates the presence of calcium and is also unable to assess its position or depth within coronary plaque. Before angiographic contrast is injected, calcified coronary lesions are seen as attenuated linear areas that follow the silhouette of the coronary artery, with synchronous motion during cardiac contraction and relaxation. Severe coronary calcification is angiographically defined when these lines can be observed prior to contrast injection on both sides of the arterial wall during cardiac motion. The calcium component occasionally appears as diffuse areas with nonhomogeneous contrast uptake, and it is often difficult to differentiate from thrombi on angiography alone. Wang et al.³ assessed 440 lesions by angiography, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) and found that IVUS is a particularly sensitive method. This study detected calcium in 40.2% of lesions by angiography, 76.8% by OCT, and 82.7% by IVUS. The latter is the most reliable intravascular technique used to detect calcium; however, calcium thickness cannot be measured because it produces an acoustic shadow. Conversely, the advantage of OCT over IVUS is that, despite minimal imaging penetration, the technique is highly sensitive and highly specific for calcified areas and can evaluate thickness, thus allowing estimation of the total

calcified mass.⁴ Fujino et al.⁵ used OCT to validate a risk score for predicting potential stent underexpansion. The score combines 3 parameters: maximum calcium angle $>180^\circ$ (2 points), maximum calcium thickness >0.5 mm (1 point), and calcium length >5 mm (1 point). The study observed a high risk of stent underexpansion in coronary lesions with a score of 4 points.

Current methods used to treat calcified coronary lesions are classified into 2 groups: ablation and balloon-based plaque rupture. Ablation techniques include rotational atherectomy (RA), orbital atherectomy, and coronary laser. Angioplasty balloon techniques do not eliminate calcium, but do improve plaque elasticity and allow stent expansion once the calcium component is ruptured.⁶

Rotational atherectomy was introduced for atherosclerotic plaque debulking more than 30 years ago, as an alternative or complementary strategy to percutaneous balloon angioplasty. Although positive early experience indicated increased luminal gain, the technique also had a high rate of target lesion revascularization due to cell proliferation and restenosis. Once drug-eluting stents were introduced and the rate of restenosis dropped, RA was reserved for lesion preparation before stent implantation in cases of highly calcified stenosis. Although many hospitals only have access to RA for the treatment of severely calcified lesions when the lesion cannot be crossed with a balloon, published studies have not shown consistent long-term benefits in terms of restenosis and cardiac events. The ROTAXUS study randomized 240 patients with moderately-to-severely calcified coronary lesions to RA plus stenting or stenting alone. The study showed higher procedural success rates in the RA group (92.5% vs 83.3%; $P = .03$) and higher luminal gain, but also higher luminal loss at 9 months, with no effect on restenosis.⁷ Recently, the PREPARE-CALC study randomized 200 patients with severely calcified coronary lesions to RA or modified (cutting/scoring) balloon. In terms of procedural success, RA was superior (98% vs 81%; $P = .0001$) and was not associated with greater luminal loss at 9 months. Complication rates were similar for the 2 groups.⁸ However, RA is not a risk-free technique, even in the hands of experts, and the complications described include dissection, no/slow flow, vasospasm, and cardiac tamponade or perforation. Furthermore, this technique requires a learning curve for interventional cardiologists.

Other, less commonly used coronary plaque debulking techniques are orbital atherectomy and coronary laser. The ORBIT II⁹ multicenter study included 443 patients with severely calcified coronary lesions treated by orbital atherectomy. The study results were good in terms of device success (98.6% of patients with residual stenosis $< 50\%$). At 2 years of follow-up, the rates for

SEE RELATED CONTENT:

<https://doi.org/10.1016/j.rec.2020.02.010>

* Corresponding author: Unidad de Hemodinámica, Hospital Regional Universitario de Málaga, Avda. Carlos Haya s/n, 29010 Málaga, Spain.

E-mail address: cristobalurbano@gmail.com (C.A. Urbano-Carrillo).

<https://doi.org/10.1016/j.rec.2020.05.041>

1885-5857/© 2020 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

major cardiovascular events and need for target lesion revascularization were 19.4% and 6.2%, respectively.⁹ The patient subgroup treated with first-generation drug-eluting stents in the ORBIT II study (17.2%; n = 74) were found to have fewer events than patients in the ROTAXUS study (29.4%; n = 120). The incidence of no/slow flow described with this technique was also lower, due to the smaller size of particles produced during ablation. Coronary laser was introduced more than 2 decades ago as an alternative to balloon angioplasty and is based on atherosclerotic plaque photoablation. Although the procedural success of this technique has been reported to be 93%, it is rarely used as an initial strategy; nevertheless, it is an option when a microcatheter cannot be advanced or the atherectomy-specific guide wire cannot cross the lesion.⁶

Coronary intravascular lithotripsy (IVL) is a new and promising method for the treatment of severely calcified coronary lesions that was approved in 2017; the initial experience in Spain was reported in 2019.¹⁰ This technique is based on the principles of lithotripsy, which has been used to break up renal calculi for more than 30 years. Pulsatile mechanical energy is applied to selectively crack calcium, while also preserving soft tissue. Unlike other techniques, calcium fragments from IVL are left in situ, thus lowering the likelihood of distal embolization. The IVL system (Shockwave Medical Inc; United States) has 3 components: a power generator programmed to supply a fixed number of balloon pulses, a connector cable between the generator and catheter, and a single-use sterile catheter with a semi-compliant balloon with 3 emitters. These emitters convert electrical power into sonic pressure waves (1 pulse/s for up to 80 pulses per catheter). The balloons are available in sizes of 2.5 to 4.0 mm, with a single length of 12 mm. Following balloon expansion at 4 atm, pulsatile energy is emitted for 10 s and the balloon is then expanded at 6 atm. Balloons for IVL are compatible with 5 and 6 Fr guide catheters, are suitable for patients with small radial arteries, and can be used with conventional 0.014-inch angioplasty guidewires. Because the crossing profile is larger than with a conventional balloon, predilation may sometimes be necessary.¹¹ Fortunately, the technique requires no learning curve and, according to various series, has a low incidence of complications.

The Disrupt CAD I study was the first to assess the safety and efficacy of the system, and included 60 patients with heavily calcified coronary lesions who underwent IVL prior to drug-eluting stent implantation. The primary endpoint (residual stenosis < 50% after device use with no hospital events) was reached in 98.5% of patients with a luminal gain of 1.7 ± 0.6 mm. Predilation was performed in 37% of cases. There were no serious complications, such as residual dissections, perforations, or no-reflow phenomena. After 6 months of follow-up, the rate of major adverse cardiac events was 8.3%, with 3 non-Q-wave myocardial infarctions and 2 cardiac deaths.¹² A study conducted by Ali et al.¹³ used OCT in 31 patients and described the mechanism of action. Calcified plaque fractures were observed in 42.9% of lesions, and multiple circumferential cracks were seen in the same transversal area in 25% of cases, with a higher incidence in more severely calcified plaques, allowing acute luminal gain regardless of the degree of calcification. Four coronary dissections were observed, and all cases were successfully treated by stent implantation, with no other complications seen during the study.

The Disrupt CAD II study included 120 patients at 15 hospitals by April 2019. Among these patients, 94.2% of lesions were classified as severely calcified on angiography. All cases were treated by IVL with no incidents, with a predilation rate of 34%. Acute luminal gain was 1.67 ± 0.49 mm. The primary endpoint, defined as in-hospital major adverse cardiac events (cardiac death, myocardial infarction, or need for revascularization), was reached in 5.8% of patients, with 7 cases of asymptomatic non-Q-wave

myocardial infarction, yielding a clinical success rate of 94.2%. Angiographic success (defined as successful stent delivery with residual stenosis < 50% and no severe complications) was 100%. A total of 47 patients underwent OCT, and fracture of the calcified area was observed in 78.7% of lesions, with 3.4 ± 2.6 fractures per lesion. No serious complications were reported.¹⁴ The Disrupt CAD I and II studies showed, therefore, that IVL is a safe and effective technique for disrupting this type of lesion. The Disrupt CAD III study is currently underway, has a similar design, and will include 392 patients (NCT03595176).

In view of the safety and efficacy results obtained with IVL, the technique is now being used in other, more heterogeneous and challenging situations, such as acute coronary syndrome, distal lesions of the left coronary trunk, and chronic occlusions, with good initial success in isolated cases or small case series. The technique can also be used to treat stent underexpansion. Until now, undilatable lesions in segments with a previously implanted stent had been treated by cutting balloon or atherectomy, with unpredictable results and a risk of complications and stent damage. The effectiveness of these techniques was limited by the presence of metal struts and deep calcium. An added benefit of IVL is that the waves emitted extend beyond superficial layers and can break up deep calcium. There are clinical reports of the successful use of IVL in this context, with no complications.¹¹ Additionally, underexpanded stents have a very high risk of thrombosis and restenosis, and there are very few treatment options in this situation. In the context of stent underexpansion, IVL achieved a success rate of 64.7% in an arm of the recently published multicenter study by Aksoy et al.¹⁵ among patients with virtually no other therapeutic options.

In a recent article published in *Revista Española de Cardiología*, Cubero-Gallego et al.¹⁶ reported the data from the largest clinical multicenter registry with unselected, high-risk patients treated by IVL. The cases included were obviously technically complex, as 61% of lesions were classified as type C, mean Syntax score was 23, and 75% required predilation with a noncompliant balloon, cutting balloon, or RA prior to IVL balloon use. Although the navigability of the currently marketed device is certainly limited, the authors show that these predilation techniques with support from guide catheter extensions (used in 16.7%) have been used to achieve technical success in 98% of cases, indicating the feasibility of the procedure in an unselected high-risk population when various techniques are combined. Future design improvements related to the navigability of the IVL device may further facilitate the procedure, which requires no specific learning curve of its own beyond the use of the control panel-power source. The safety of the procedure is another key point confirmed by the study conducted by Cubero-Gallego et al. In this study, the only procedure-related acute events were 2 post-IVL dissections, both resolved by stenting, and 1 myocardial infarction secondary to stent thrombosis 48 hours after the procedure, treated by postdilation. Most notably, there were no reports of any no/slow flow phenomena, and we agree with the authors that the IVL mechanism could lead to calcium fragments remaining in situ, thus lowering the possibility of particle embolization compared with ablation techniques. Moreover, the short-term follow-up results are very positive in terms of clinical outcomes and luminal gain, but should ideally be confirmed by long-term follow-up of the series. Therefore, this study confirms that IVL is emerging as a safe and reliable technique for treating calcified lesions, with the huge advantage that it is technically simple and can be combined with other plaque debulking techniques for patients in routine clinical practice.

Beyond the technical aspects, calcium in coronary disease still suggests a poor prognosis that should be approached from all therapeutic angles available, and any advances should be

welcomed after analysis of the clinical outcomes and cost-efficiency of the techniques. Until effective gene and molecular therapies are available, we should continue to offer interventional cardiology procedures to patients who, prior to the development of plaque debulking techniques and intravascular imaging techniques, had no options apart from drug therapy. Therefore, we consider that IVL is a useful tool for clinicians encountering this situation on a daily basis.

CONFLICTS OF INTEREST

None declared.

REFERENCES

- Copeland-Halperin RS, Baber U, Aquino M, et al. Prevalence, correlates, and impact of coronary calcification on adverse events following PCI with newer-generation DES: findings from a large multi-ethnic registry. *Catheter Cardiovasc Interv.* 2018;91:859–866.
- 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.
- Wang X, Matsumura M, Mintz GS, et al. In vivo calcium detection by comparing optical coherence tomography, intravascular ultrasound and angiography. *Am J Coll Cardiol Imaging.* 2017;10:869–879.
- Zeng Y, Tateishi H, Cavalcante R, et al. Serial assessment of tissue precursors and progression of coronary calcification analysed by fusion of IVUS and OCT: 5-year follow-up of scaffolded and nonscaffolded arteries. *JACC Cardiovasc Imaging.* 2017;10:1151–1161.
- Fujino A, Mintz GS, Matsumura M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. *EuroIntervention.* 2018;13:e2181–e2189.
- DeMaria GL, Scarsini R, Banning AP. Management of calcific coronary artery lesions: is it time to change our interventional therapeutic approach? *JACC Cardiovasc Interv.* 2019;12:1465–1478.
- De Waha S, Allali A, Büttner HJ, et al. Rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: Two-year clinical outcome of the randomized ROTAXUS trial. *Catheter Cardiovasc Interv.* 2016;87:691–700.
- 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.
- Généreux P, Bettinger N, Redfors B, et al. Two-year outcomes after treatment of severely calcified coronary lesions with the orbital atherectomy system and the impact of stent types: insight from the ORBIT II trial. *Catheter Cardiovasc Interv.* 2016;88:369–377.
- Rodríguez Costoya I, Tizón Marcos H, Vaquerizo Montilla B, Salvatella Giral N, Martí Almor J, Millán Segovia R. Litoplastia coronaria: experiencia inicial en lesiones calcificadas. *Rev Esp Cardiol.* 2019;72:788–790.
- Forero MNT, Daemen J. The coronary intravascular lithotripsy system. *Interv Cardiol.* 2019;14:174–181.
- Brinton TJ, Ali ZA, Hill JM, et al. Feasibility of shockwave coronary intravascular lithotripsy for the treatment of calcified coronary stenosis. *Circulation.* 2019;139:834–836.
- 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.
- 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. <http://doi.org/https://doi.org/10.1161/CIRCINTERVENTIONS.119.008434>.
- Aksoy A, Salazar C, Becher MU, et al. Intravascular lithotripsy in calcified coronary lesions: a prospective, observational, multicentre registry. *Circ Cardiovasc Interv.* 2019. <https://doi.org/10.1161/CIRCINTERVENTIONS.119.008154>.
- Cubero-Gallego H, Millán R, Fuertes M, et al. Coronary lithoplasty for calcified lesions: real-world multicenter registry. *Rev Esp Cardiol.* 2020;73:1003–1010.