Treatment Procedures for Calcified Coronary Artery Lesions: A Juxtaposing Review of Intravascular Lithotripsy and Rotational Atherectomy

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Systematic Review

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Abstract

The calcium content in the coronary artery is one of the most important factors that influence coronary events. High calcium levels lead to excessive calcification in coronary vessels and are more difficult to treat with percutaneous intervention (PCI). Treatment for complex lesions is performed by intravascular lithotripsy (IVL) system consisting of balloon catheters within which electrical energy is being transformed into mechanical energy. IVL technology discharges soundwaves that transmit to the neighbouring tissue leading to improvement in vascular compliance and the destruction of both superficial and visceral calcium deposits. Consequently, coronary artery calcification (CAC) treatment becomes more effective, more practical, and plays a role in reducing lesion complexity. Types of lesions studied for the IVL system comprise of calcified coronary arteries and peripheral vascular lesions. This article evaluates the role of the IVL system in treating coronary arteries calcification, its benefits, and drawbacks compared to other techniques. According to clinical trials in intravascular lithotripsy and rotational atherectomy, the former was deemed more secure, primarily by reducing the risk of embolization by atheroma. Interpreting the studies included in this review, IVL appears to have superior results in acute lumen gain, success rate, and improvement in stenosis residue, while rotational atherectomy (RA) delivers lesser in-hospital major adverse cardiovascular events (MACE) and provides better approach in the presence of lesion crossings. Additional extensive researches and clinical data are needed to substantiate the efficiency and safety of IVL technology.

Introduction

Calcification is caused by an increase in the calcium content in the body, and it is most commonly found in the bones of the body and can also be found in the soft tissues making it hard. There are two types of calcifications, the first type is diffuse (metastatic) calcification and this calcification is related to hypercalcemia and occurs in healthy tissues. The second type is dystrophic calcification, which is associated with normal calcium levels and occur in the affected tissues. Factors that increase calcium deposition in the arteries include injury, repair, and inflammation of blood vessels. Vascular calcification is a serious condition that occurs due to the pathological deposition of calcium salts in the vessels. It is more common in the elderly and those with diabetes, valvular heart disease, kidney failure, and dyslipidemia. This classification is associated with cardiovascular diseases such as heart failure, cardiomyopathy, hypertension, ischemia, and heart attack.¹,²

Vascular calcification occurs most commonly with cardiovascular disease. It is essential to know the difference between the classification of coronary and peripheral vessels.³ Lower extremities peripheral artery calcification occurs through osteoblast-like cells in the presence of high levels of phosphate, calcium, and parathyroid hormone.³ Coronary calcification occurs due to a deformation of the calcium deposition induced by chondrocytes in the presence of inflammatory agents such as cytokines. Calcium deposits in coronary vessels cannot be changed with medical treatment.⁴
The cornerstone of treatment is lifestyle modification that plays a role in reducing and slowing the progression of calcifications in the coronary vessels. Adjustment includes weight loss, stopping smoking and drinking alcohol, and good control of blood pressure level, blood sugar level, and body fat percentages. Additional intervention may well be required for complex arterial calcification such as stenting or coronary bypass. Complex calcified, fibrotic coronary artery stenosis is considered a very difficult condition for the percutaneous procedure (PCI) and it is a case in which surgical revascularization is required because calcified arteries are so rigid, stents are difficult to replace inside. Many surgical methods for treating calcified coronary artery lesions, including excimer lasers, high-pressure balloons, orbital cutting balloons, as well as RA devices. The devices are more prone to complications such as embolization, perforation, and dissection. Moreover, the success rate decreases with severe calcifications, and restenosis accelerates when tissue is damaged. To date, specialized balloon techniques or atherectomy are no better than high-pressure balloons to improve clinical outcomes.

The intravascular lithotripsy (IVL) approach translates electrical energy into mechanical energy in the period of low-pressure balloon inflation. For plaque modification, this technology relies on sound waves in preference over immediate damage to vascular tissue. While the balloon catheter promotes vessel compliance with the lowest amount of soft tissue damage, it sends sound waves to adjacent tissues and securely disrupt both superficial and visceral calcium deposits. This article studies the lithotripsy's shock wave for coronary artery calcification and the benefits and drawbacks of other techniques such as hyperbaric balloons and rotary atherectomy devices.

Review

Method

Various methods have been used to maintain a high-quality review. Databases such as Google Scholar and PubMed were thoroughly searched. Keywords like coronary lithotripsy, CAD, calcified plaque, and coronary calcification were applied. Related studies to the main object and review articles were included. Included persons consisted of men and women between the ages of 18 and 80, excluding adolescents and children. All studies incorporated are published in English. This investigation procedure revealed 35 appraised articles.

Discussion

A coronary calcium level is a tool used to predict the condition of coronary arteries in patients with symptoms or not. Depend on the Multi-Ethnic Study of Arteriosclerosis study, coronary calcium content is the best marker for determining cardiovascular disease associated with atherosclerosis. Risks of calcium deposition have the same effect on all ages, genders, and races. CT coronary angiography is a non-invasive imaging procedure applied to identify the deposit of calcium and considered the most useful technique for diagnosis the coronary calcification, it scans can measure calcium levels and evaluate the
prognosis.\textsuperscript{4,12} Four markers indicating the severity of atherosclerotic plaques are the paper ring marker, low CT attenuation, incomplete, patchy calcification, and remodelling. Unstable plaques and acute coronary syndrome are associated with patchy calcification diagnosed by CCTA. CCTA is an important tool for performing PCI by identifying a calcified calcium lesion in coronary vessels. The collaboration between PCI with Taxus Score and Cardiac Surgery (SYNTAX) is a process aimed to assess the severity of coronary artery disease, the location of the lesions, and their complexity are the main factors that increase the severity.\textsuperscript{13,14,15,16}

### Interventions For Calcified Coronary Artery Disease

The occurrence of critical coronary calcification in PCI cases is presently projected to reach between 18\% and 26\%, but is likely to increase, in conjunction with the continuous aging of the population. Because viscerally calcified coronary lesions are considered difficult in dilation, it is intricate to discharge and insert stents adequately, and these facts remain a hindrance to deployment of percutaneous coronary intervention (PCI). The involvement of calcified plaques negatively affects stent-crossing, influencing drug delivery and elution by disrupting the drug polymers from the coating, and limiting stent position and expansion. This leads to higher rates of sub-optimal long-term treatment response and periprocedural sequelae. Although varied adjuvant procedural devices have been advocated to improve the efficacy of this particular circumstance, the percutaneous strategy to coronary artery calcifications has managed to stay a constant challenge. Reductions in peri-procedural complications and enhanced procedural effectiveness have been seen in more equipped methods such as balloon cutting and scoring, accurate and more efficient RA, OA, non-compliant balloons (NC balloons), and IVL. Rotational atherectomy is the most common methodology used for the treatment of calcified coronary lesions. Even then, new devices and technologies have opened up into further application in clinicians' practice and, in combination with improved intravascular method of imaging, are potential to spearhead a change in algorithms approach the for the treatment of calcified coronary lesions. NC balloons are the main choice in mild and moderate calcified stenosis due to their increased inflation resistance; they induce homogenous expansion of the balloon and exert stronger force in the focal section of the coronary vessel. However, by imposing considerable pressure on the sides, they could trigger coronary dissection or perforation.\textsuperscript{18,19}

Microsurgical blades attached to the exterior cutting balloons, rendering them effective to create discreet incisions in the targeted coronary sections during balloon inflation, triggering an immediate alteration of the luminal calcium. Mentioned methods are easy to use to establish a partial modification of the plaque. However, a randomized trial demonstrated that traditional balloon angioplasty or balloon cutting approaches had success performance comparable to non-dilatable calcified coronary artery lesions.\textsuperscript{9} Balloons that are semi-compliant, such as score balloons, are ringed by scoring elements that allow the focal deployment of force during inflation with a decreased incidence of balloon displacement. While the indication of balloon scoring and balloon cutting are identical, balloon scoring has a higher consistency profile than balloon cutting due to its dynamism, fewer vessel exterior trauma, and a benign likelihood of
The technique involved in atherectomy procedure is built on the foundation of manipulating plaque microstructure and adherence, triggering calcium deposit disintegration. Rotational atherectomy is an intricate technique that utilizes a burr with diamond tip. The calcium plaque is adequately fractured by the fast-moving rotation, causing the plaques to disintegrate. Utilising techniques similar to kidney stone lithotripsy, IVL is a new approach that destabilizes coronary artery calcifications by releasing potent acoustic shock waves using the balloon. This strategy is providing new hope considering its ability to operate on superficial and visceral calcium plaques and captured disintegrated calcium, which mitigates embolization in the distal vessel wall. IVL is the most accepted approach to be performed to the plaques beneath the struts of the stents, considering its ultrasound-based performance that is not inhibited by the existence of stents.\(^\text{22}\)

**The Shock-wave Lithotripsy Technique**

The IVL system consists of a connecting cable, compatible with six Fr which allows the manually controlled connection of rapidly exchanging electrical pulses, a portable generator, a semi-compliant balloon catheter to be used for standard angioplasty practice over a 0.014-inch guidewire. An IVL catheter is implanted over the calcified lesion using tape-specific angiography. When the incorporated balloon is expanded by mixed saline and contrast solution to a nominal pressure of 4 standard atmosphere (atm), fluids in the middle of the opposite balloon serves as a coupler to allow for transmission of efficient balloon energy, sound pressure waves in the vessel wall to reach the plaque. Although other treatments cannot distinguish soft tissue and calcium, acoustic pressure waves are able to disseminate through the soft tissue, altering both medial and intimal calcium plaques. The generator generates 3 kW of energy, which flows once per second through the catheter cables and connection to the emitters for lithotripsy. A concentrated field effect is generated with the emitters along the balloon's extent. Inside the emitter, a small emission of electrics evaporates the balloon, forming an inflating bubble rapidly, creating a sound pressure wave before disintegrating in microseconds. Once the waves affect calcium at about 50 atm, the waves generate a set of small fractures. The balloon is inflated to nominal pressure at 10 pulses, which increases the balloon's compliance. IVL can improve clinical outcomes by simplifying severe, calcified lesions that are difficult to treat.\(^\text{4}\)

**The IVL Procedure Indications**

Indications for The Shock Wave Lithotripsy System involved conditions such as a cute coronary syndrome, left main artery calcification and arterial occlusion. Calcified lesions treated with balloon dilation with lithotripsy include coronary, femoral, iliac, iliac-femoral and renal arterial lesions. The method should not be used if a 0.014-inch guidewire cannot be passed over the lesion. Medium balloon inflation is recommended for this technique, and the doctor must prepare treatment to prevent blood clots if they occur. The unique risks of the device include device malfunction or failure, sensitivity toward catheter materials, excessive heat at target sites, an asymmetric heart rhythm, and effects on the heart rhythm that causes shock. Standard angioplasty complications include sensitivity to radiological
contrast media, arterial bypass surgery, high or low blood pressure, stent placement, infection, kidney failure, vascular complications, organ rupture, bleeding, and death.\textsuperscript{12}

**Rotational Atherectomy**

Rotational atherectomy (RA) is an alternative technique that works by eliminating mechanically complex calcified lesions by widening the vascular lumen by removing atherosclerotic plaques and reducing plaque stiffness that becomes easy to expand.\textsuperscript{23} The system consists of three micro-transformers including a nickel-coated oval top covered with a microscopic diamond crystal with a diameter of 1.25 to 2.50 mm, a control device, a connecting handle, and an optimizer capable of transmitting high speed to the hatch, also coupled with a gas turbine.\textsuperscript{23} RA was most commonly used before stenting, as confirmed by the Society's Guidelines for Cardiovascular Angiography and Interventions (Class C Recommendation, Level IIa Guide) in 2011.\textsuperscript{25} Common complications of RA include slow or no flow, lumps entrapment, transient atrioventricular masses, and coronary perforation, the flow problem should be addressed by vasodilators within the coronary vessels such as adenosine, nitroprusside, and nicorandil.\textsuperscript{26} Other rare complications are distal emboli and the phenomenon of non-contractility. Contraindications for RA include dissection, thrombosis, and stenosis of the saphenous vein.\textsuperscript{27} The limiting factors for RA are difficulty cutting and incising. The decision of an algorithm is to establish the most appropriate approach which corresponds to settings to direct interventional cardiology.\textsuperscript{4}

**Clinical results of IVL for Disrupt Peripheral Arterial Disease (PAD I / II & III)**

Peripheral arterial disease I / II is a long-term study that records only severe calcified lesions and includes patients with 85% complicated vascular calcifications. The result is a 100% success rate for IVL catheters. The acute lumen gain after IVL angiography was 2.9 mm and residual stenosis was reduced by 24% after drug-filled stent implantation. PAD III is a planned, non-randomized, one-arm study to evaluate the efficacy and safety of the IVL regimen in patients being treated for calcified lower extremity lesions. A 100% success rate was achieved with IVL catheterization for patients. The most prominent limiting factor in the PAD III study was the single-arm, observational study with no control group. The PAD III study is the most comprehensive application of IVL in daily clinical training. Compared to previous IVL studies, IVL for peripheral calcified lesions in lower extremities continued to show more safety and effective results.\textsuperscript{28}

**Table 1.** A comparison table of studies of endovascular lithotripsy with a study of rotational atherectomy
|                  | Single-arm Multi-center | Disrupt CAD I | Disrupt CAD II | Disrupt PAD I/II | Disrupt PAD III (RCT) | ROTAXUS |
|------------------|-------------------------|--------------|---------------|-----------------|-----------------------|---------|
| Number of patients and sites | 60 patients, 7 sites | 120 patients, 15 sites | PAD I: 35 patients, 3 sites, PAD II: 60 patients, 8 sites | 400 patients at 54 sites | 240 patients |
| Inclusion criteria | - RVD 2.5-4.0 mm - Stenosis >50% - De novo moderate/severe calcific coronary lesions | - RVD 2.5-4.0 mm - Diameter stenosis ≥50% - Severe calcification - Stabilized acute coronary syndrome - Lesion length ≤32 mm | - RVD 3.5-7.0 mm - SFA/popliteal lesions >70% stenosis - Moderate to severe calcification - Intermittent claudication (Rutherford Class 2-4) - ABI<0.9 - Lesion length <150 mm | - RVD 4.0-7.0 mm - Stenosis ≥70% - Moderate and severe calcification - Intermittent claudication (Rutherford 2-4) - Femoropopliteal arteries - Lesion length ≤18 cm occlusive or ≤10 cm CTO | - RVD 3.25 mm - Mean diameter stenosis by visual estimate 83.02 - Severe calcification - Stable coronary artery disease - Angina II to IV - Lesion length ≤32 mm |
| Procedural success | 98.3% | 100% | 100% | 100% | 92.5% |
| Clinical success | 95% | 95.7% | 98.9% | - | 91.9% |
| Acute gain | 1.7mm | 1.6mm | PAD I - 2.9mm PAD II - 3.0mm | 3.4-mm | 1.56mm |
| 30-day MACE | 5.0% | 4.3 | PAD I - 0% PAD II - 1.7% | - | 5% |
| 6-month MACE | 8.3% | - | PAD I - 0% PAD II - 1.1% | - | - |
| 9-month MACE | - | - | - | - | 24.2% |

Note: PAD = peripheral arterial disease; CAD = coronary artery disease; RCT = randomized controlled trial; ROTAXUS = rotational atherectomy before using a paclitaxel coronary artery absorbent stent; RVD = reference vessel; MACE = major adverse cardiovascular events; ABI = ankle brachial index.
Clinical results of Disrupt Coronary Artery Disease (CAD I & II)

CAD I was the first single-arm study to evaluate the effective and integrity of coronary IVL for treating coronary arteries calcification. We included 60 cases with severe or moderate calcified lesion of coronary vessels. The success rate of IVL for CAD I is 98.3%, and it can increase the lumen vessel size by 1.7 mm and reduce the stenosis by 13.3% without cardiac complications. Cardiac complication rates of 5-8% have been reported at one and six months, including three cardiac infarctions and cardiac deaths, and the absence of perforation of blood vessels, which is an important benefit of IVL. CAD II, a prospective one-arm study, was performed in 15 hospitals in 9 countries. It included 120 patients with severe calcified coronary vessels. A 100% success rate has been achieved for IVL catheters. After IVL angiography, the volume of the vessel lumen increased by 0.83 mm and after the drug-filled stent was replaced, the stenosis decreased by 7.8%. Therefore, IVL is a safe method with a high success rate. In conclusion, CAD I exhibited the advantages of IV treatment for severe calcified coronary lesions and CAD II tried to determine the safety and efficacy of the IVL method.29

Clinical results of RA & ROTAXUS

The study used 240 patients with calcified lesions who underwent a rotational atherectomy before using a paclitaxel coronary artery absorbent stent (TAXUS) to treat complicated coronary artery disease. This comparison showed more success rates in the RA group (92.5% versus 83.3%; p = 0.03) with more advantageous acute lumen acquisition, but after nine months the late lumen loss was significantly higher. Although the study obtained 5% as a result of 30-day MACE, MACE in 9-month duration was 24.2%, which is significantly greater than anticipated.30 However, AR is a gold standard technique for creating highly calcified lesions in front of the stent, specifically when the balloon device fails to pass through the lesions. In centres with high-volume, the technique is restricted to experienced operators. Merely 1% to 3% of PCIs are used in Europe, apparently due to the potential complexity and costs that cannot be overlooked or the low employment for insurance.31

When comparing the latest CAD II disorder with ROTAXUS, 120 patients versus 240 patients were included. Successful application and administration of IVL catheters in patients were accomplished 100%, whereas 92.5% occurred in RA. The increase of acute lumen after IVL angiography was 1.63 compared to acute lumen gains of 1.56 in RA and after placement of the damaged stent, the IVL residual stenosis was 7.8% versus 10.79% in RA. The clinical success rate for IVL is 95.7% versus 91.9% for RA. CAD II showed 5.8% in hospital and 4.3% after 30 days of MACE versus 4.3% in hospital and 24.2% after 9 months of MACE in RA.12,28,30 The main interpretations of these studies include: first, the IVL catheter, which crosses the lesion and provides therapy in all cases, is a valuable tool for modifying CAC plaques. Secondly, the IVL was very effective. The stenosis reduced the heavily calcified coronaries with an acute increase of 1.6 mm to a residual value of <8% and facilitated stent delivery in the entire cases. Third, in-hospital MACE was lower in the ROTAXUS study, but long-term MACE was significantly higher than in IVL studies. Therefore, IVL was reasonably more benign with null reports of type D dissections through F, sudden occlusion, perforations, or no reflux or slow flow. Fourth, the mechanism of action of IVL has been
shown to be intraplaque calcium alteration by fracture, thus modifying vascular compliance and facilitating stent expansion.\textsuperscript{32} The 30-day MACE was the same between the ROTAXUS and CAD I studies, but comparing the long-term results, the CAD I study showed an 8.3% MACE after six months, while the ROTAXUS showed a MACE of nine months showed 24.2%. This indicates the fact that IVL may have a lower long-term MACE than the RA procedure.

The advantages of intravascular lithotripsy over atherectomy are thusly: First, contrasted with atherectomy, no distinct training is of prerequisite in IVL because the apparatus is being carried in a similar way to an average, catheter-based PCI. Second, because IVL therapy is based on balloon, the possible risk of atheromatous embolization may be lower than with free-standing debulking machines. Third, with IVL, the energy is evenly distributed on the lithotripsy emitter. Therefore, regardless of its circumferential position, it is not subject to a guidewire during plate modification, which relates to stock. Fourth, IVL delivers ultrashort circumferential pulses with high energy, which leads to effective modification for atheroma through its compressive and decompressive components.\textsuperscript{33,34} Fifth, lateral branch protection using a guidewire using IVL can be performed without problems without the risk of pinching or severing the wire as can happen with orbital or rotational atherectomy. Finally, the IVL is performed by inflating the balloon with minimal air pressure, and thus it is made safe by reducing injury to the blood vessels.

Table 2. A comparison table of circulatory atherectomy and endovascular lithotripsy in acute coronary calcification
### Circulatory Atherectomy vs. Intravascular Lithotripsy

|                          | Circulatory Atherectomy                                      | Intravascular Lithotripsy                                      |
|--------------------------|----------------------------------------------------------------|----------------------------------------------------------------|
| Guidewire Size           | 0.09-inch proprietary wire                                    | 0.014-inch wire of choice                                      |
| Wire bias                | Modification of calcium that is wire-bias dependent            | Balloon inflation disregards wire bias, supporting circumferential modification of calcium |
| Lesion crossing          | Chosen as the first line for balloon uncrossable lesions       | Superior profile for crossing than contemporary balloons       |
| Side branch guard        | The wire of side branch has to be removed during atherectomy   | No contact with the wire of side branch                        |
| Perforation              | Acknowledged risk for atherectomy, greater risk in tortuous vessel | No documented perforations                                     |
| Distal embolization      | Atherectomy working by releasing atherosclerotic debris        | Hypothetically imposed the same risk as contemporary angioplasty balloon |
| Plaque ablation          | Relied on designated burr size.                               | No plaque ablation                                             |
| Bradyarrhythmia          | Dominant coronary atherectomy requires temporary pacemaker as the standard of care | No documented arrhythmia                                       |
| Effect of deep calcium   | Atherectomy influences only superficial calcium                | Hypothetically alters visceral calcium                          |

In understanding abovementioned studies, IVUS appears to be better on parameters such as clinical success rate, procedural success rate, acute lumen gain, and less residual stenosis, with the exception of hospital clubs, which were better in RA. Nevertheless, RA MACE in nine-month duration was soaring in comparison with former IVL studies such as CAD I. In anticipation of the long-term outcomes of the current DISRUPT CAD II and further studies, better results can be compared. CAD I & II have demonstrated the effective of IVL in modifying these injuries. IVL is a new treatment method for complex CAC. However, when the lesion is difficult to treat with balloon catheters, approaching atherectomy remains the principal therapy. This study contains a number of limiting factors, including modest size in sample without continuous update by follow-up. MACE has also not been tested regularly, and moreover, the study has not yet been conducted to demonstrate IVL results with different stents.

## Conclusion

Intravascular lithotripsy (IVL) of coronary artery is a hopefully modern method of treating calcified coronary artery. IVL before stent placement has a greater success rate and fewer complications than rotational atherectomy. Clinically, despite these encouraging facts, intravascular lithotripsy of calcified coronary arteries is underutilized due to the cost and the high-risk effects of cardiac rhythm. Randomized controlled trials are needed to evaluate the benefit over other currently available calcium-modifying
devices. RotaTripsy devices, a combination of RA and IVL, can be used if treatment fails or is not completed. Long-term clinical data research is needed to ensure the efficacy this technique, while carefully considering its effects on vascular healing outcomes and heart rhythm. This will build more information on the safe use of these innovative technologies.

**Declarations**

**Funding**

None.

**Conflict of Interest**

The author declares there is no conflict of interest regarding all aspect of the study.

**Author Contribution**

PHW is responsible for the study from the literature search, data gathering, data analysis, until reporting the results of the study by a narrative form of literature review.

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