folia medica

Folia Medica 67(2)
DOI: 10.3897/folmed.67.e141763

Review

Coronary artery disease with heavily calcified lesions – literature review of novel therapeutic methods

Tomasz Furgoł[1], Karolina Karska[2], Michał Miciak[2], Joanna Jureczko[3], Konrad Gigoń[1]
Marcin Jezierzański[1], Paweł Jureczko[4]

1 *Faculty of Medicine, Medical University of Silesia, Zabrze, Poland*
2 *Faculty of Medicine, Wroclaw Medical University, Wroclaw, Poland*
3 *Faculty of Medicine, Academy of Silesia, Katowice, Poland*
4 *Department of Theoretical and Applied Mechanics, Faculty of Mechanical Engineering, Silesian University of Technology, Gliwice, Poland*

Corresponding author: Tomasz Furgoł, Faculty of Medicine, Medical University of Silesia in Katowice, Zabrze, Poland; Email: tomekfurgo@gmail.com

Received: 13 November 2024 ♦ **Accepted:** 11 February 2025 ♦ **Published:** 21 March 2025

Citation: Furgoł T, Karska K, Miciak M, Jureczko J, Gigoń K, Jezierzański M, Jureczko P. Coronary artery disease with heavily calcified lesions – literature review of novel therapeutic methods. Folia Med (Plovdiv) 2025;67(2):e141763. doi: 10.3897/folmed.67.e141763.

Abstract

Coronary artery disease and atherosclerosis are a very significant and widespread problem in modern medicine. The development of current diagnostics and treatment of atherosclerotic lesions is moving towards minimally invasive methods. The purpose of this article is to present selected novel methods of treating coronary atherosclerosis, comparing their effectiveness, indications, contraindications, and possible complications. A literature review of selected treatment methods for calcified atherosclerotic lesions was conducted in the online databases of PubMed, PubMed Central, Google Scholar, and NCBI. It includes original and review papers. The main language of the articles was English. The search used keywords such as "coronary artery disease," "calcified atherosclerotic lesions," "rotational atherectomy," "intravascular lithotripsy," and "RotaTripsy," as well as related phrases. After analyzing the abstracts, the papers that most closely matched the stated topic were selected. Atherosclerosis is the leading cause of coronary heart disease incidence. Several risk factors, both non-modifiable and modifiable, predispose to its occurrence. Heavily calcified atherosclerotic plaques are associated with a higher risk of coronary artery disease consequences. Currently, methods such as CT coronary angiography and optical coherence tomography are used for diagnosis. Endovascular therapies are now recommended for the treatment of atherosclerosis with heavily calcified plaques. Rotational atherectomy, intravascular lithotripsy and RotaTripsy are promising methods for treating high-grade atherosclerosis with calcified deposits. However, especially in the case of RotaTripsy, further clinical studies are required to better evaluate the efficacy of this novel method.

Keywords

atherothrombosis, coronary artery disease, intravascular lithotripsy, rotational atherectomy, rotatripsy, orbital atherectomy

Introduction

Heavily calcified coronary lesions, a major manifestation of coronary artery disease (CAD), pose a significant challenge in the field of interventional cardiology. They can hinder device delivery, lead to suboptimal stent expansion and malposition, prolong procedural time, and increase the risk of complications during percutaneous coronary intervention (PCI). Understanding the epidemiology, pathophysiology, symptoms, diagnosis, and prognosis associated with these lesions is crucial for effective management. The development of heavily calcified coronary lesions involves the accumulation of calcium deposits within the arterial walls, which reduces vessel elasticity and compliance, contributing to atherosclerosis and coronary artery narrowing. In recent years, there has been significant advancement in both diagnostic and therapeutic methods aimed at detecting and treating arterial calcification diseases using minimally invasive techniques. The aim of this paper is to review selected therapeutic methods in interventional cardiology, their efficacy, and potential complications.

Etiology of coronary lesions

The modifiable risk factors for atherothrombosis, a major contribution to CAD and subsequently, acute coronary syndromes (ACS), were initially identified in the INTERHEART study and show partial overlap with those documented in the MESA study.[1,2] These factors include age, male sex, white race, and traditional cardiovascular risk factors such as hypertension, body mass index, diabetes mellitus, glucose levels, family history of heart attack, and the occurrence and development of coronary artery calcium (CAC).[2,3] A risk calculator available on the MESA website estimates the 10-year risk of CAD by incorporating MESA risk factors alongside CAC, which is quantified through computed tomography (CT) using the Agatson scoring method.[2,4] Examples of modifiable and non-modifiable risk factors for ACS are presented in **Table 1**.

Pathophysiology of coronary lesions

The division of arterial calcification into two primary types, medial and intimal, remains significant in tailoring modification strategies. Calcific atherosclerosis is primarily present in the intima. Various theories exist regarding the formation and progression of calcification; however, the full mechanism behind the advancement of CAC still remains unclear. Vascular calcification was formerly considered an inert and degenerative process, but it is now understood that it can be both active and passive.[5] In recent years, the theory of active calcification has emerged as a major model of vascular mineralization and atherosclerosis.[6] According to this theory, pro-atherogenic stimuli facilitate the phenotypic conversion of vascular smooth muscles cells (VSMCs) into osteoblast-like cells. Factors such as hypercalcemia, hyperphosphatemia, tumor necrosis factor-α and platelet-derived growth factor-BB can stimulate VSMCs to secrete exosomal forms, such as matrix vesicles, which serve as the driving force behind calcium precipitation.[7] Inflammation most likely precedes calcification and plays a major role in its progression.[6,8] The passive theory of calcification is based on Urry's charge neutralization hypothesis.[9] Elevated phosphate ion levels correlate with tissue-nonspecific alkaline phosphatase (TNAP), which hydrolyzes pyrophosphatase (PPi) into inorganic phosphatase (Pi), thereby promoting calcification.[10] Li et al. and Tani et al. explored the connection between TNAP and CAC; however, further studies are needed due to TNAP's pleiotropic functions.[11-13] For many years, atherosclerotic plaques have been classified into two dominant phenotypes: stable plaques, characterized by the progression of extensive calcifications, and unstable (vulnerable) plaques, which contain characteristic microcalcifications. However, recent studies have questioned this paradigm. In their chapter of the book, Cardoso L. and Weinbaum S. argue that when microcalcifications are present in the cap of a stable plaque, the plaque may become vulnerable due to a localized increase in stress, which could surpass the rupture threshold.[5] Chronic total occlusions, which represent the stable plaque type, often require calcium modification before stent positioning.[14-16] A simplified pathophysiology of coronary lesions is presented in **Fig. 1**.

Table 1. Examples of modifiable and non-modifiable risk factors for coronary artery disease

Modifiable risk factors	Non-modifiable risk factors
Arterial hypertension	Sex (male)
Hypercholesterolemia	Age (>55 male, >60 female)
Diabetes mellitus	Premature menopause
Obesity	Family history of myocardial infarction
High body mass index (BMI)	Family history of hypertension
Waist-to-hip circumference ratio	
Dietary patterns	
Low physical activity	
Smoking	
Excessive alcohol consumption	
Metabolic syndrome	
Stress	

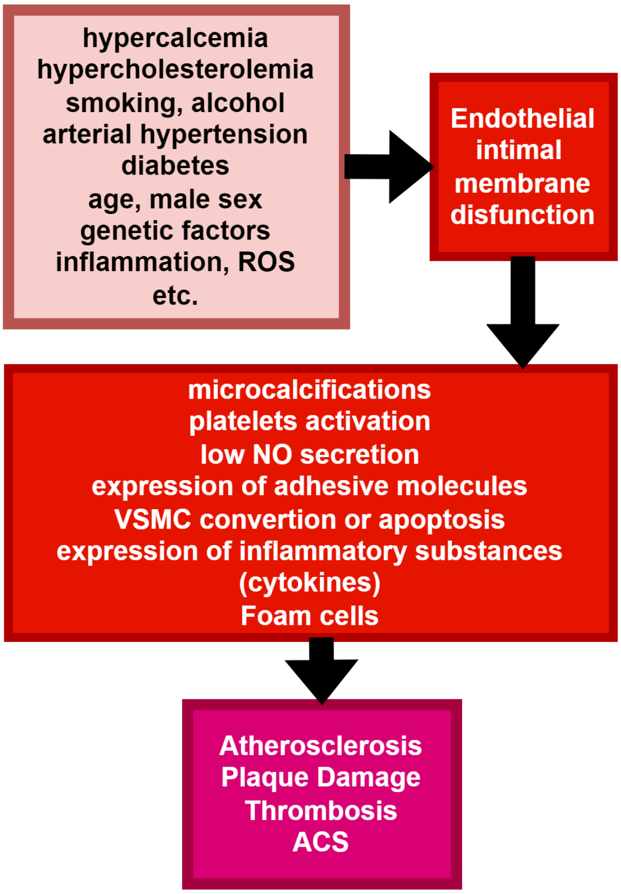

Figure 1. Pathophysiology of coronary lesions. ROS: reactive oxygen species; NO: nitric oxide; VSMC: vascular smooth muscle cell; ACS: acute coronary syndrome.

Review methods

The review is based on scientific publications retrieved from the PubMed, PubMed Central, Google Scholar, and NCBI databases. The reviewed articles are primarily in English and Polish. After an initial evaluation of the article abstracts, meta-analyses and reviews that best aligned with the stated topic and reflected current medical knowledge were selected. Finally, 62 articles were analyzed.

Diagnostic methods for CAD

Coronary computed tomography angiography (CCTA) is the most important non-invasive imaging technique for detecting calcium. When compared to grayscale intravascular ultrasound (IVUS) or optical coherence tomography (OCT) – the gold standards for detecting coronary calcium – coronary angiography has low to moderate sensitivity.[17] However, its positive predictive value is very high.[18] The SCOT-HEART (*Scottish Computed Tomography of the HEART*) trial demonstrated a significantly lower incidence of the combined endpoint of cardiovascular death or non-fatal myocardial infarction (2.3% vs. 3.9% during a five-year follow-up) among patients who underwent CCTA along with routine testing. In a multicenter study by Williams et al., images from 1769 patients who underwent CCTA during the SCOT-HEART multicenter randomized controlled trial were used for the CACS-DRS (*Coronary Artery Calcium Data and Reporting System*) evaluation together with CAC-RADS (*Coronary Artery Disease-Reporting and Data System*) score.[19] Calcium in CCTA and in the CACS-DRS is detected as an area of hyperattenuation, defined as a region of at least 1 mm^2 with >130 Hounsfield units or ≥3 adjacent pixels using the Agatston method.[20] The CAD-RADS score evaluates lesion severity and was upgraded to CAC-RADS 2.0 due to advancements in CT technology, recent clinical trials, and updated guidelines. [21] The study results indicated that the risk of experiencing fatal and non-fatal myocardial infarctions increased with higher scores on both of the aforementioned metrics.[19] Using OCT, it is possible and effective to plan revascularization and predict the necessity and efficacy of devices for managing calcified lesions.[20] The OCT-based calcium scoring system suggests that lesions with calcium pools having a maximum angle of >180°, a maximum thickness of >0.5 mm, and a maximum length of >5 mm may be more susceptible to stent underexpansion.[21,22] Together with IVUS, it provides a thorough assessment of cross-sectional calcium distribution.[20] In the ESC 2022 *Guidelines for the Management of ACS*, IVUS received a Class IIb recommendation, particularly for cases involving an uncertain culprit lesion.[23] The results from a study conducted in 2024 represent the most contemporary systematic review and meta-analysis of intravascular imaging-guided PCI. The findings suggest that the use of OCT or IVUS is associated with a reduced incidence of major adverse cardiac events (MACE), cardiac death, stent thrombosis, target-lesion revascularization, and target-vessel revascularization.[24] OCT is a high resolution imaging technique (10 times greater than IVUS) that enables quantitative evaluations of calcified plaques. It measures calcium angle, area, depth, volume and thickness, and also detects microcalcifications.[8,22,25,26] Additionally, while OCT provides a clearer depiction of calcium disruption, its limited penetration may cause it to overlook deep calcifications.[8] IVUS, due to its deeper ultrasound penetration, can semiquantitatively measure calcium deposit length and angle.[8,18] According to the 2021 *ACC/AHA/SCAI Guideline for Coronary Artery Revascularization*, if intravascular imaging reveals calcium accumulation greater than 500 μm or calcium involving a vessel arc of more than 270°, lesion modification will be required to facilitate stent placement.[27] However, eccentric calcification (occupying <180° of the vessel's cross-section) has been associated with a higher risk of complications during stent placement, compared to concentric calcium (occupying >180° of the vessel's cross-section).[28,29] The pooled analysis from disrupt CAD studies also suggests that coronary intravascular lithotripsy (IVL) is a feasible front-line tool for eccentric CAC, facilitating stent delivery. While eccentric calcification allows non-calcified areas to

Folia Medica

expand for stent placement, it may also increase the risk of vessel perforation.[30] However, the role of atherectomy in modifying eccentric calcium remains unclear and requires further research. For atherectomy to have a direct ablative effect, it must make contact with the calcified segment.[20]

Rotational atherectomy

Rotational Atherectomy (RA), also called rotablation, is a procedure developed more than three decades ago by David Auth. These procedures are performed using the RotaPro system, manufactured by Boston Scientific. RA is a highly effective technique designed to modify the size of atherosclerotic plaques, widen the lumen of occluded arteries, and reduce the hardness of the modified lesion.[31] These modifications are achieved using a single high-speed (140,000–180,000 rpm – *rotation per minute*) elliptical drill (boron) with diamond fines (20-30 μm) on its surface. The drill operates on the principle of “differential cutting” (preferential cutting), meaning it preferentially ablates hard and inflexible structures such as plaque while sparing soft tissues. These ablations break down the atherosclerotic plaque to particles smaller than 10 μm, allowing them to flow freely through the coronary microcirculation without causing secondary embolism with plaque material.[32] The RA system is guided by a steel guidewire (RotaWire), and is powered by compressed air or nitrogen. Its speed is controlled by a console that also contains the motor. The control mechanism is located on the drill advancement device (advancer). The system also includes a specialized tube, which delivers a flushing solution containing heparinized saline and Rotaglide lubricant (a composition of egg whites and olive oil) to the ablation site. When necessary, the vasodilators can also be added. The fluid serves to lubricate the system, dissipate temperature, and prevent a sudden drop in drill speed.[23]

Indications and contraindications for RA

The primary indication for RA is the presence of severely calcified atherosclerotic lesions, particularly those whose hardness and size prevent balloon angioplasty and proper drug-eluting stent (DES) deployment. However, in such cases, rotablation is considered an additional procedure to facilitate those techniques by modifying the plaque and minimizing the risk of late lumen loss or other major cardiovascular events, such as myocardial infarction, target vessel revascularization, and target lesion revascularization.[33] The ROTAXUS study suggests that RA alone has a high restenosis rate. The combined use of RA and DES appears to be the most effective strategy. However, this study did not demonstrate a significant advantage of RA + DES over DES implementation without prior RA. Additionally, more than half of the study group had moderate atherosclerotic plaques, suggesting that RA may yield better outcomes in patients with severely calcified lesions. This subgroup may have the most favorable results from RA + DES combination therapy.[34] Contraindications for RA are categorized as absolute and relative. Absolute contraindications include atherosclerotic lesions in venous bypass grafts, the presence of thrombi, and angiographic findings suggesting a dissection in the occluded vessel. Relative contraindications include severe left ventricular failure (ejection fraction <30%), severe lesions involving up to three coronary vessels, severe unprotected left main coronary artery (LMCA) occlusion, atherosclerotic lesions >25 mm in length, and atherosclerotic lesions in tortuous coronary segments with an angulation >45°.[32]

Complications of RA

Complications associated with the rotablation procedure largely overlap with those seen in other PCI procedures. The use of an intravascular catheter, which facilitates the use of boron, carries some mild complications. These are usually in the form of local injuries resulting from the femoral artery puncture, such as hematomas or pseudoaneurysms. Life-threatening complications include perioperative events, although these are less common. They may involve cardiac arrhythmias, conduction blocks requiring temporary pacing, tamponade, myocardial infarction, or stroke, which can lead to death during the procedure. There are also a number of complications related to the insertion of the catheter with the boron, including vessel perforation or dissection, stuck drill, and slow-reflow/no-reflow. The incidence of perioperative complications is approximately 7%.[32] Slow-reflow/no-reflow phenomena are among the most common complications in this group of patients, with an incidence ranging from 3% to 27% of cases.[34] Over the past thirty years of RA, studies have demonstrated and refined techniques aimed at minimizing the aforementioned perioperative complications. Some of the most relevant studies include the randomized CARAT (*Coronary Angioplasty and Rotablator Atherectomy Trial*) and STRATAS (*Study to Determine Rotablator and Transluminal Angioplasty Strategy*), both published in 2001. Based on their results, it was determined that using a boron with a diameter of less than 0.7 relative to the diameter of the vessel lumen was most advisable. It was shown that using drills with a ratio exceeding this value did not yield better procedural outcomes than those performed with smaller drills. In contrast, the risk of perioperative complications increased with larger drill diameter.[35] It is optimal to gradually modify the plaque by using short ablation attempts (15-20 seconds), keeping the boron speed in the range of 140,000 to 150,000 rpm, and avoiding rapid decelerations greater than 5000 rpm. These measures help prevent thermal damage and platelet aggregation, as well as mechanical complications such as vessel perforation and drill entrapment. Additionally, it is advisable to use a flushing mixture to ensure adequate cooling and prevent friction. The use of vasodilators contributes to the prevention of slow-reflow/no-reflow phenomena. Pharmacotherapy with IIb/IIIa receptor antagonists or adenosine is also employed to prevent complications such as angina and myocardial infarction.[32,36] In exceptional cases, it may also be advisable to treat transient bradycardia with atropine or temporary cardiac pacing to prevent bradyarrhythmia during procedures on the right coronary artery. In high-risk procedures, mechanical circulatory support such as the Impella device, may also be necessary.[31,32]

Orbital atherectomy

Orbital Atherectomy (OA) is a method used to facilitate PCI and peripheral endovascular procedures. The goal of this technique is to damage and alter the compliance of calcified plaques, making balloon inflation and stent deployment easier. For performing OA, appropriate equipment is necessary, called the Orbital Atherectomy System (OAS), which includes the following: a coronary atherectomy device, an atherectomy pump, a coronary guidewire of at least 6 French, and a lubricant and saline solution.[38] After obtaining vascular access, the calcified lesion is localized using angiography or IVUS. Then, the guidewire and atherectomy device equipped with a rotating drill are introduced through the vascular access. The procedure involves 30-second passes with the rotating device at a speed of 80,000-120,000 rpm through the calcified lesion, with a maximum speed of 1 mm/s. The maximum duration for using a single device is five minutes. After this time, the result of the procedure is assessed using a balloon. If full expansion is not achieved, OA may be repeated before stent implantation.[39-41]

Indications and contraindications for OA

The FDA (Food and Drug Administration) has approved the OA system for the treatment of advanced calcifications in coronary arteries. The decision to use OA depends on the thickness and grade of calcification. Studies indicate that atherosclerotic lesions with a calcium layer thinner than 0.24 mm can be effectively treated before stent implantation. Research also shows that the use of OA for treating calcified lesions with a Calcium Score of at least 4 points increases the chance of successful stent placement.[39,40,47] OA is contraindicated in situations where the guidewire insertion could damage the vessel or where insertion is impossible due to the presence of a thrombus or the consistency and size of the calcification. If the lesion is located in a transplanted organ or stent, or if only one coronary artery is patent (in cases of multi-vessel disease), or if the coronary artery is dissected, the procedure is contraindicated. OA is also not performed in pregnant women or children. Special caution should be exercised when performing the procedure in patients with an ejection fraction <25%, when treating lesions in the right coronary artery or left circumflex artery (due to the increased risk of heart block), and when the coronary vessels are tortuous.[37,39]

Complications of OA

The first clinical studies investigating OA were the ORBIT I and ORBIT II trials. ORBIT I was a non-randomized study involving 50 patients. This study assessed the safety and efficacy of OA in the treatment of de novo heavily calcified lesions. The results of this study indicated a procedural success rate of 94%.[40,42] The ORBIT II trial was a multicenter, prospective, open-label study involving 443 patients. This study focused on evaluating complications following the use of OA, specifically MACE. After the use of OA, 89.6% of patients did not experience MACE during the 30-day period (95% CI: 86.7%–92.55%). The incidence of MACE during hospitalization, one year, and three years after the procedure was 9.8%, 16.4%, and 23.5%, respectively.[42-44] The results of ORBIT II showed that MACE occurred less frequently three years after OA, compared to the two-year results of the previously mentioned ROTAXUS study. Based on these results, OA received FDA approval in 2013.[44,45] In 2018, a study was conducted to analyze the incidence of MACE in patients not included in the ORBIT II study – specifically, patients with LMCA disease and those with an ejection fraction of <25%. The results of this study indicated that one year after the OA procedure, 87.3% of patients did not experience MACE or cerebrovascular incidents.[46]

Intravascular lithotripsy

Intravascular Lithotripsy (IVL) is a new technology that delivers ultrasound waves at a specific frequency to the atherosclerotic vessel wall, causing the atherosclerotic plaque to vibrate and break down. The IVL device consists of several key components that enable precise and effective treatment. At its core, there is a portable generator with a rechargeable battery, which generates the electrical impulses that power the ultrasound wave emitters. A cable connects the generator to the control button, allowing manual operation of the IVL process. The central component of the device is the balloon catheter, which contains a core that emits ultrasound waves. This core, located inside the balloon, is the crucial element that converts electrical impulses into ultrasound waves. During the IVL procedure, the balloon catheter is inserted into the affected atherosclerotic blood vessel, where it facilitates the targeted disruption of calcified plaques. Using a plastic guidewire, the balloon catheter is precisely positioned at the intervention site. Inside the balloon, two ultrasound wave emitters respond to electrical impulses from a generator. These emitters cause the fluid inside the balloon to vaporize, leading to rapid expansion and contraction of microbubbles. This process generates an acoustic pressure wave with an intensity approaching 50 atmospheres, transferring mechanical energy to the vessel walls. The mechanism helps disrupt atherosclerotic plaques and restore normal blood flow. The IVL device offers various size and technical options. The balloons are available in diameters ranging from 2.5 mm to 4 mm, allowing precise adjustment to different vessel sizes. The standard catheter length is 12 mm, ensuring adequate penetration and effectiveness within the vessel.[49]

Indications and contraindications for IVL

In the treatment of coronary lesions, the effectiveness of different methods can vary depending on the lesion's characteristics and location. The main indication for IVL is the presence of heavily CAC lesions that are difficult to treat effectively with standard intervention methods. Heavily calcified lesions can hinder high-pressure balloon expansion and make balloon catheter insertion challenging. In such cases, the vessel lumen can be prepared using aforementioned rotablation. This method is also effective for treating restenosis after stenting, especially when combined with IVL.[50,51] RA can, though, prepare the vessel for IVL catheter insertion. However, certain factors may prevent successful IVL, including tortuous vessels, critical vessel stenosis, multiple stented areas, or an unfavorable atherosclerotic plaque shape. In these cases, inserting and positioning the lithotripsy balloon may be difficult or even impossible. To minimize the risk of complications and adequately evaluate the patient before IVL, vascular imaging is recommended. OCT provides a detailed evaluation of vascular lesions before the planned intervention, helping clinicians select the optimal treatment strategy for each patient.[52]

Complications of IVL

Rarely, serious complications such as MACE, can occur after IVL on coronary vessels. In a study conducted on a large group of 308 patients, 14 cases of MACE were recorded.[53,54] Additionally, 6 cases of mild vessel dissection (types A-C) were observed, while severe dissection (types D-F) was not reported. Vascular dissection can occur due to the rupture of the lithotripsy balloon when excessive pressure is applied under unfavorable vascular conditions. [55] A retrospective study by Wilson et al. indicates that IVL procedures may be associated with a high incidence of arrhythmias, especially in patients with a low heart rate before the procedure. The study results showed that an imposed ventricular rhythm occurred in 77.8% of cases during IVL. Patients with a pre-procedure heart rate below 65 BPM were 16 times more likely to experience arrhythmias during the intervention.[56]

RotaTripsy

Treating coronary lesions with a high calcium content (CLHCC) can be challenging. Preparation for stent placement in CLHCC is often a multi-step process, as balloon angioplasty alone is usually ineffective. The presence of coronary calcification is associated with poorer post-PCI outcomes, primarily due to inadequate stent expansion and misplacement. This can lead to an increased risk of stent thrombosis or restenosis. Both RA and IVL have significantly improved treatment efficacy in patients with this condition.[57] For effective treatment of heavily calcified lesions, a combined approach using the aforementioned tools – RotaTripsy – is increasingly required. Buono et al. published a paper evaluating the effectiveness and safety of the RotaTripsy method in 34 patients with CLHCC in the coronary arteries. The study population consisted primarily of men around 75 years old with multiple comorbidities. In 97% of cases, RotaTripsy was used to treat de novo lesions. The right coronary artery was the most frequently affected vessel, with calcium deposits present in 50% of patients. Procedural success was achieved in all patients, with no significant in-hospital complications. There were no in-hospital deaths, target-vessel myocardial infarctions (TV-MI) or complications requiring urgent cardiac surgery. However, the researchers observed several serious complications occurring later after the procedure. The most common complication was coronary artery perforation, which can potentially lead to cardiac tamponade. One patient developed a retroperitoneal hematoma related to the femoral artery access site. Within an average follow-up period of up to one year, 9% of patients died, with one death attributed to cardiovascular complications. Additionally, two patients developed TV-MI during this period.[58] Gonzálvez-García et al. described seven cases of patients treated with the RotaTripsy technique. The study demonstrated the effectiveness of this method. The patients were all men, with an average age of 76 years. Six of them had lesions in the left anterior descending artery, a branch of the LMCA. Initially, RA was performed to modify the lesion and facilitate passage of the balloon catheter.[59] However, despite RA, it failed to dilate the sites with heavily calcified lesions. Subsequently, IVL was performed, effectively breaking up the calcified inner and middle membranes, allowing successful balloon dilation, followed by the implantation of a DES. One patient developed an Ellis III-type coronary perforation, likely due to an excessively large or ill-fitting stent rather than the technique used. The complication was successfully treated with the implantation of a covered coronary stent. The study suggests that the RotaTripsy technique may be beneficial in treating severe stenosis with both peripheral and deep calcium clusters in coronary vessels. Despite the higher cost of the procedure, the combined method is considered worthy of consideration due to the lower risk of adverse events associated with underexpanded stents.[60] However, patients with implanted stents may develop restenosis and calcification at the implant sites.[61] Chen et al. presented the first reported case of a patient undergoing RotaTripsy for the treatment of severely calcified neoatherosclerosis. In a 61-year-old man who had previously undergone coronary artery bypass grafting (CABG) and multiple PCI in the right coronary artery, coronary angiography revealed in-stent restenosis (ISR) in a DES implanted in the artery. Calcification within the restenotic region was also confirmed by OCT. In this patient, a combined approach using RA and IVL allowed for the successful placement of a new DES. A 1.5 mm boron and 4×12 mm balloon were used, achieving low-pressure acute luminal gain. The use of RotaTripsy in the treatment of ISR remains a controversial topic. However, in this case, the combined approach yielded successful results. Excimer laser coronary atherectomy has been proposed as an alternative to RotaTripsy in ISR treatment. Unfortunately, this method has limitations, including intracoronary bubble formation and a higher risk of perioperative myocardial infarction, but this discussion is beyond the scope of this study.[62]

Conclusion

Coronary artery disease with heavily calcified lesions presents a significant clinical challenge, necessitating accurate diagnosis and targeted treatment. Modern endovascular techniques such as RA, OA, IVL, and RotaTripsy have demonstrated effectiveness in removing calcium deposits and preparing coronary vessels for DES implantation. These methods show promising results with low complication rates, though complications are not entirely absent. Further randomized controlled studies involving larger patient cohorts, including those with multi-vessel disease, are required to comprehensively evaluate the long-term outcomes of these techniques, assess their comparison, and establish standardized guidelines for their application.

Conflict of Interest

None to declare.

Funding

The authors have no additional funding to report.

Acknowledgements

All authors are grateful to staff members who contributed to this study

References

1. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364(9438):937–52. doi: 10.1016/S0140-6736(04)17018-9
2. McClelland RL, Jorgensen NW, Budoff M, et al. 10-year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNR (Heinz Nixdorf Recall) study and the DHS (Dallas Heart Study). J Am Coll Cardiol 2015; 66(15):1643–53. doi: 10.1016/j.jacc.2015.08.035
3. Kronmal RA, McClelland RL, Detrano R, et al. Risk factors for the progression of coronary artery calcification in asymptomatic subjects: results from the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation 2007; 115(21):2722–30. doi: 10.1161/circulationaha.106.674143
4. Blaha MJ, Naazie IN, Cainzos-Achirica M, et al. Derivation of a coronary age calculator using traditional risk factors and coronary artery calcium: the multi-ethnic study of atherosclerosis. J Am Heart Assoc 2021; 10(6):e019351. doi: 10.1161/JAHA.120.019351
5. Cardoso L, Weinbaum S. Microcalcifications, their genesis, growth, and biomechanical stability in fibrous cap rupture. Adv Exp Med Biol 2018; 1097:129–155. doi: 10.1007/978-3-319-96445-4_7
6. Demer LL, Tintut Y. Vascular calcification: pathobiology of a multifaceted disease. Circulation 2008; 117(22):2938–48. doi: 10.1161/circulationaha.107.743161
7. Kapustin AN, Chatrou ML, Drozdov I, et al. Vascular smooth muscle cell calcification is mediated by regulated exosome secretion. Circ Res 2015; 116(8):1312–23. doi: 10.1161/circresaha.116.305012
8. Sorini Dini C, Nardi G, Ristalli F, et al. Contemporary approach to heavily calcified coronary lesions. Interv Cardiol 2019; 14(3):154–163. doi: 10.15420/icr.2019.19.R1
9. Urry DW. Neutral sites for calcium ion binding to elastin and collagen: a charge neutralization theory for calcification and its relationship to atherosclerosis. Proc Natl Acad Sci USA 1971; 68(4):810–4. doi: 10.1073/pnas.68.4.810
10. Sheen CR, Kuss P, Narisawa S, et al. Pathophysiological role of vascular smooth muscle alkaline phosphatase in medial artery calcification. J Bone Miner Res 2015; 30(5):824-36. doi: 10.1002/jbmr.2420
11. Li Q, Huang J, Pinkerton AB, et al. Inhibition of tissue-nonspecific alkaline phosphatase attenuates ectopic mineralization in the Abcc6-/- mouse model of PXE but not in the Enpp1 mutant mouse models of GACI. J Invest Dermatol 2019; 139(2):360–368. doi: 10.1016/j.jid.2018.07.030
12. Tani T, Fujiwara M, Orimo H, et al. Inhibition of tissue-nonspecific alkaline phosphatase protects against medial arterial calcification and improves survival probability in the CKD-MBD mouse model. J Pathol 2020; 250(1):30–41. doi: 10.1002/path.5346
13. Goettsch C, Strzelecka-Kiliszek A, Bessueille L, et al. TNAP as a therapeutic target for cardiovascular calcification: a discussion of its pleiotropic functions in the body. Cardiovasc Res 2022; 118(1):84–96. doi: 10.1093/cvr/cvaa299
14. Brunner FJ, Moritz Becher P, Remmel M, et al. Percutaneous coronary interventions using calcium modification and intravascular imaging: temporal trends over the last decade. JACC Cardiovasc Interv 2024; 17(20):2450–2. doi: 10.1016/j.jcin.2024.06.030
15. Kostantinis S, Rempakos A, Simsek B, et al. Temporal trends of calcium modification therapies in chronic total occlusion percutaneous coronary intervention. JACC Cardiovasc Interv 2023; 16(19):2475–7.
16. Jurado-Román A, Gómez-Menchero A, Gonzalo N, et al. Plaque modification techniques to treat calcified coronary lesions. Position paper from the ACI-SEC. REC Interv Cardiol 2023; 5:46–61. doi: 10.24875/recice.m22000345
17. Kolodgie FD, Burke AP, Wight TN, et al. The accumulation of specific types of proteoglycans in eroded plaques: a role in coronary thrombosis in the absence of rupture. Curr Opin Lipidol 2004; 15(5):575–82. doi: 10.1097/00041433-200410000-00012
18. Mintz GS. Intravascular imaging of coronary calcification and its clinical implications. JACC Cardiovasc Imaging 2015; 8(4):461–71. doi: 10.1016/j.jcmg.2015.02.003

19. Williams MC, Moss A, Dweck M, et al. Standardized reporting systems for computed tomography coronary angiography and calcium scoring: A real-world validation of CAD-RADS and CAC-DRS in patients with stable chest pain. J Cardiovasc Comput Tomogr 2020; 14(1):3–11. doi: 10.1016/j.jcct.2019.07.010
20. Mehanna E, Abbott JD, Bezerra HG. Optimizing percutaneous coronary intervention in calcified lesions: insights from optical coherence tomography of atherectomy. Circ Cardiovasc Interv 2018; 11(5):e006813. doi: 10.1161/CIRCINTERVENTIONS.118.006813
21. Fujino A, Mintz GS, Matsumura M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. EuroIntervention 2018; 13(18):e2182–e9. doi: 10.4244/EIJ-D-17-00962
22. Räber L, Mintz GS, Koskinas KC, et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. EuroIntervention 2018; 14(6):656–677. doi: 10.4244/EIJY18M06_01
23. Cury RC, Leipsic J, Abbara S, et al. CAD-RADS™ 2.0 - 2022 coronary artery disease-reporting and data system: an expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the American College of Radiology (ACR), and the North America Society of Cardiovascular Imaging (NASCI). JACC Cardiovasc Imaging 2022; 15(11):1974–2001. doi: 10.1016/j.jcmg.2022.07.002
24. Sreenivasan J, Reddy RK, Jamil Y, et al. Intravascular imaging-guided versus angiography-guided percutaneous coronary intervention: a systematic review and meta-analysis of randomized trials. J Am Heart Assoc 2024; 13(2):e031111. doi: 10.1161/JAHA.123.031111
25. Kubo T, Akasaka T, Shite J, et al. OCT compared with IVUS in a coronary lesion assessment: the OPUS-CLASS study. JACC Cardiovasc Imaging 2013; 6(10):1095–1104. doi: 10.1016/j.jcmg.2013.04.014
26. Vancheri F, Longo G, Vancheri S, et al. Coronary artery microcalcification: imaging and clinical implications. Diagnostics (Basel) 2019; 9(4):125. doi: 10.3390/diagnostics9040125
27. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. Circulation 2022; 145(3):e4-e17. doi: 10.1161/CIR.0000000000001039
28. Hoffmann R, Mintz GS, Popma JJ, et al. Treatment of calcified coronary lesions with Palmaz-Schatz stents. An intravascular ultrasound study. Eur Heart J 1998; 19(8):1224–31. doi: 10.1053/euhj.1998.1028
29. Ali ZA, Kereiakes DJ, Hill JM, et al. Impact of calcium eccentricity on the safety and effectiveness of coronary intravascular lithotripsy: pooled analysis from the disrupt CAD studies. Circ Cardiovasc Interv 2023; 16(10):e012898. doi: 10.1161/circinterventions.123.012898
30. Mattesini A, Nardi G, Martellini A, et al. Intravascular imaging to guide lithotripsy in concentric and eccentric calcific coronary lesions. Cardiovasc Revasc Med 2020; 21(9):1099–1105. doi: 10.1016/j.carrev.2020.04.016
31. Sharma SK, Tomey MI, Teirstein PS, et al. North American expert review of rotational atherectomy. Circ Cardiovasc Interv 2019; 12(5):e007448. doi: 10.1161/circinterventions.118.007448
32. Dobrzycki S, Reczuch K, Legutko J, et al. Rotational atherectomy in everyday clinical practice. Association of Cardiovascular Interventions of the Polish Society of Cardiology (Asocjacja Interwencji Sercowo-Naczyniowych Polskiego Towarzystwa Kardiologicznego — AISN PTK): Expert opinion. Kardiol Pol 2018; 76(11):1576–84. doi: 10.5603/kp.2018.0225
33. Sousa-Uva M, Neumann FJ, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2018; 55(1):4–90. doi: 10.1093/ejcts/ezy289
34. Sakakura K, Funayama H, Taniguchi Y, et al. The incidence of slow flow after rotational atherectomy of calcified coronary arteries: A randomized study of low speed versus high speed. Cathet Cardio Intervent 2016; 89(5):832–40. doi: 10.1002/ccd.26698
35. Whitlow PL, Bass TA, Kipperman RM, et al. Results of the study to determine rotablator and transluminal angioplasty strategy (STRATAS). Am J Card 2001; 87(6):699–705. doi: 10.1016/s0002-9149(00)01486-7
36. Tomey MI, Kini AS, Sharma SK. Current status of rotational atherectomy. JACC Cardiovasc Interv 2014; 7(4):345–53. doi: 10.1016/j.jcin.2013.12.196
37. Chambers JW, Diage T. Evaluation of the Diamondback 360 Coronary Orbital Atherectomy System for treating de novo, severely calcified lesions. Expert Rev Med Devices 2014; 11(5):457–66. doi: 10.1586/17434440.2014.929493
38. Lee MS, Nguyen H, Philipson D, et al. "Single-operator" technique for advancing the orbital atherectomy device. J Invasive Cardiol 2017; 29(3):92–5. PMID: 28255104.
39. Shlofmitz E, Martinsen BJ, Lee M, et al. Orbital atherectomy for the treatment of severely calcified coronary lesions: evidence, technique, and best practices. Expert Rev Med Devices 2017; 14(11):867–79. doi: 10.1080/17434440.2017.1384695
40. Shlofmitz E, Shlofmitz R, Lee MS. Orbital atherectomy: a comprehensive review. Interv Cardiol Clin 2019; 8(2):161–71. doi: 10.1016/j.iccl.2018.11.006
41. Sotomi Y, Shlofmitz RA, Colombo A, et al. Patient selection and procedural considerations for coronary orbital atherectomy system. Interv Cardiol 2016; 11(1):33–38. doi: 10.15420/icr.2015:19:2
42. Parikh K, Chandra P, Choksi N, et al. Safety and feasibility of orbital atherectomy for the treatment of calcified coronary lesions: the ORBIT I trial. Catheter Cardiovasc Interv 2013; 81(7):1134–9. doi: 10.1002/ccd.24700
43. Lee M, Généreux P, Shlofmitz R, et al. Orbital atherectomy for treating de novo, severely calcified coronary lesions: 3-year results of the pivotal ORBIT II trial. Cardiovasc Revasc Med 2017; 18(4):261–4. doi: 10.1016/j.carrev.2017.01.011
44. Généreux P, Lee AC, Kim CY, et al. Orbital atherectomy for treating de novo severely calcified coronary narrowing (1-year results from the pivotal ORBIT II Trial). Am J Cardiol 2015; 115(12):1685–90. doi: 10.1016/j.amjcard.2015.03.009
45. 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(4):691–700. doi: 10.1002/ccd.26290
46. Lee MS, Shlofmitz E, Goldberg A, et al. Multicenter registry of real-world patients with severely calcified coronary lesions undergoing orbital atherectomy: 1-year outcomes. J Invasive Cardiol 2018; 30(4):121–4.
47. Fujino A, Mintz GS, Lee T, et al. Predictors of calcium fracture derived from balloon angioplasty and its effect on stent expansion assessed by optical coherence tomography. JACC Cardiovasc Interv 2018; 11(10):1015–17. doi: 10.1016/j.jcin.2018.02.004

48. Honton B, Monsegu J. Best practice in intravascular lithotripsy. Interv Cardiol 2022; 17:e02. doi: 10.15420/icr.2021.14
49. Wong B, El-Jack S, Newcombe R, et al. Shockwave intravascular lithotripsy for calcified coronary lesions: First real-world experience. J Invasive Cardiol 2019; 31(3):46–48. doi: 10.1016/j.hlc.2019.05.022
50. Venuti G, D'Agosta G, Tamburino C, et al. Coronary lithotripsy for failed rotational atherectomy, cutting balloon, scoring balloon, and ultra-high-pressure non-compliant balloon Catheter. Cardiovasc Interv 2019; 94(3):E111–115. doi: 10.1002/ccd.28287
51. Tovar Forero MN, Wilschut J, Van Mieghem NM, et al. Coronary lithoplasty: a novel treatment for stent underexpansion. Eur Heart J 2019; 40(2):221. doi: 10.1093/eurheartj/ehy593
52. Jurado-Román A, Gonzálvez A, Galeote G, et al. RotaTripsy: combination of rotational atherectomy and intravascular lithotripsy for the treatment of severely calcified lesions. JACC Cardiovasc Interv 2019; 12(15):e127–e9. doi: 10.1016/j.jcin.2019.03.036
53. 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 Interv 2019; 12(10):e008434. doi: 10.1161/circinterventions.119.008434
54. Brinton TJ, Ali ZA, Hill JM, et al. Feasibility of shockwave coronary intravascular lithotripsy for the treatment of calcified coronary stenoses. Circulation 2019; 139(6):834–36. doi: 10.1161/circulationaha.118.036531
55. Soriano F, Veas N, Piccinelli E, et al. Coronary dissection due to intravascular lithoplasty balloon rupture. EuroIntervention 2019; 15(6):E558–9. doi: 10.4244/EIJ-D-19-00383
56. Wilson SJ, Spratt JC, Hill J, et al. Coronary intravascular lithotripsy is associated with a high incidence of 'shocktopics' and asynchronous cardiac pacing. EuroIntervention 2019; 15(16):1429–35. doi: 10.4244/EIJ-D-19-00484
57. Aziz A, Bhatia G, Pitt M, et al. Intravascular lithotripsy in calcified-coronary lesions: A real-world observational, European multicenter study. Catheter Cardiovasc Interv 2021; 98(2):225–35. doi: 10.1002/ccd.29263
58. Buono A, Basavarajaiah S, Choudhury A, et al. "RotaTripsy" for severe calcified coronary artery lesions: insights from a real-world multicenter cohort. Cardiovasc Revasc Med 2022; 37:78–81. doi: 10.1016/j.carrev.2021.06.132
59. Gonzálvez-García A, Jiménez-Valero S, Galeote G, et al. "RotaTripsy": combination of rotational atherectomy and intravascular lithotripsy in heavily calcified coronary lesions: a case series. Cardiovasc Revasc Med 2022; 35:179–184. doi: 10.1016/j.carrev.2021.04.011
60. Ielasi A, Loffi M, De Blasio G, et al. "Rota-Tripsy": a successful combined approach for the treatment of a long and heavily calcified coronary lesion. Cardiovasc Revasc Med 2020; 21(11S):152–4. doi: 10.1016/j.carrev.2019.12.023
61. 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(8):897–906. doi: 10.1016/j.jcmg.2017.05.012
62. Chen G, Zrenner B, Pyxaras SA. Combined rotational atherectomy and intravascular lithotripsy for the treatment of severely calcified in-stent neoatherosclerosis: a mini-review. Cardiovasc Revasc Med 2019; 20(9):819–21. doi: 10.1016/j.carrev.2018.10.007