Reviews

Current role of intravascular imaging in percutaneous treatment of calcified coronary lesions

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Abstract

Percutaneous treatment of calcified coronary lesions is still a challenge in modern interventional cardiology practice. Coronary angiography is limited to the precise and quantitative assessment of calcium in coronary arteries. Intracoronary imaging (ICI) modalities, including optical coherence tomography (OCT) and intravascular ultrasound (IVUS), produce a very detailed image of calcifications and could help in proper percutaneous treatment. Intracoronary imaging indicates the need to use additional tools and improves the final effect of an intervention. Drawing on the already published literature, the authors focused on the qualification of patients to the procedure, conduct and result of interventional procedures involving calcified lesions supported by ICI. The article shows the advantages and disadvantages of both ICI methods in general and especially in calcified lesions. Currently available tools dedicated to dealing with coronary calcium and helping to meet optimal stent implantation criteria are also described. This article reviews the data on ICI implementation in daily clinical practice to improve the results of percutaneous interventions, and indicates further directions.

Key words: coronary artery disease, percutaneous coronary intervention, coronary stenosis

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Background

Coronary artery disease (CAD) is one of the most common conditions in the current population. Coronary atheroma is composed of lipid-rich and calcified lesions. Detection and appropriate modification of coronary artery calcification (CAC) remain one of the last unmet clinical needs in interventional cardiology. Coronary artery calcification is a frequent problem encountered during percutaneous coronary intervention (PCI) in various patient populations.[1] Among the 8,582 patients included in the multicenter ADAPT-DES study focused on the drug-eluting stent (DES), calcifications were present in 30.8% of patients,[2] and similar frequency was reported in many other publications.[3] Age, hypertension, hyperlipidemia, nicotinism, insulin-dependent diabetes mellitus, hemodialysis, and peripheral artery disease were independent predictors of coronary calcification.[2]

Coronary artery calcification may lead to unsatisfying results of stent implantation, causing its underexpansion,[4] assymetry[5] and inappropriate struts apposition[6] despite using special tools for calcium modification. Even nowadays the treatment of this population is very difficult, as was reported in a meta-analysis[7] of 2,361 patients with new-generation DES. Patients with moderate/severe calcifications had higher rate of target-lesion failure (13.5% vs 8.4%; $p = 0.003$) and stent thrombosis (2.1% vs 0.2%; $p < 0.0001$). Bourantas et al.[8] found a lower rate of complete revascularization (48% vs 55.6%; $p < 0.001$) among 6,269 patients with severe calcifications. Moreover, patients with severe calcifications had a higher mortality rate compared to those without calcifications (10.8% vs 4.4%; $p < 0.001$). Another large meta-analysis[3] of 18 randomized DES trials confirmed worse PCI outcomes for moderately/severely calcified coronary lesions. The 5-years risk of a composite endpoint including death, myocardial infarction, revascularization (adjusted HR: 1.12; 95% CI: 1.05–1.20), target lesion failure (adjusted HR: 1.21; 95% CI: 1.09–1.34), as well as death, myocardial infarction, and ischemia-driven target lesion revascularization was higher in patients with severe CAC.

As technology has advanced, interventional cardiology has been equipped with advanced tools for detecting and assessing CAC and thus for planning interventions in CAC such as intracoronary imaging (ICI). Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are nowadays widely employed in catheterization laboratories. Intracoronary imaging helps to assess the burden of CAC and choose appropriate treatment strategy at a time when multiple dedicated calcium management tools are available. This article presents how ICI facilitates the management of CAC during PCI.

Objectives

The aim of this review was to provide comprehensive information about the use of ICI in percutaneous treatment of calcified coronary lesions.

Formation and histology of coronary calcifications

The process of calcium formation is not fully understood and involves multiple factors and cells. Nowadays, arterial mineralization process is considered to be the main driver of lesion calcification. The loss of function of osteopontin, fetuin, gamma-carboxyglutamic acid and Gia protein, which inhibits mineralization and the induction of osteogenesis by osteoblast-like cells, is the beginning of CAC formation.[9] Vascular smooth muscle cells are induced to an osteoblastic phenotype. Residual pericytes and circulating stem cells are activated to osteochondrogenic phenotype. Furthermore, the process is associated with oxidative stress, inflammation and lipids. There are 2 types of CAC: intimal (also called: vascular, atherosclerotic) and medial. In the 1st type, the intima thickens as a response to the following clinical risk factors: advanced age, diabetes mellitus, dyslipidemia, hypertension, male sex, nicotinism, and hyperphosphatemia. The 2nd type is connected with the thickening of the medial layer of the artery, and is more common in patients of advanced age with diabetes mellitus, lower glomerular filtration rate, hypercalcemia, hyperphosphatemia, and long duration of dialysis.[10] An analysis of 902 histological cross-sections from 44 cadavers revealed 4 types of calcifications – superficial (158 (18%)), deep intimal (20 (13%)), scattered (30 (19%)), and calcified nodules (CN) (3 (2%)).[11] Chronic coronary syndrome is connected with extensive calcium formation.[12] Statin therapy reduces fibrofatty tissue volume, but promotes the increase of calcium volume in atherosclerotic plaques.[13] However, about 5% of cases of acute coronary syndrome (ACS) are caused by eruptive CN. This mechanism was described by Torii et al., who suggested that fragmentation of the necrotic core causes CN disruption and formation of thrombosis.[14]

Intracoronary imaging

General information

Both IVUS and OCT probes are monorail catheters inserted into the coronary vessels using a conventional 0.014" guidewire. Optical coherence tomography uses near-infrared light waves (wavelength of approx. 1,300 nm), whereas IVUS imaging relies on emission and detection of 20–60 MHz sound waves bouncing back from the artery wall. Multiple advantages and disadvantages of different ICI modalities result from their physical principles (Table 1).[15–17]

Intracoronary imaging for PCI in general

Traditional coronary angiography (CA) is a standard for lesions assessment and PCI guidance. Unfortunately, the 2-dimensional lumenogram has too many limitations to give appropriate insight into 3-dimensional (3D) structures.

Table 1. Advantages and disadvantages of OCT and IVUS

ICI	Advantages	Disadvantages
OCT	• high resolution (axial 12–15 µm; lateral 20–40 µm) • better tissue characterization (more details visualized: malapposition, dissection, thrombus, tissue protrusion) • easier to interpretate • calcium thickness assessment possible • long and fast pull-back	• flushing required (poor flushing interrupts/impedes image interpretation), low likelihood of dissection, hematoma • additional contrast injection • low penetration (1.0–2.5 mm) • difficult probe delivery in complex lesions • less research data in comparison with IVUS
IVUS	• deep penetration (>5 mm: to adventitia) • flushing is not necessary: lower likelihood of dissection, hematoma • long and fast pull-back • more research data in comparison with OCT	• inferior resolution (axial – 100–300 µm, up to 22 µm (60 MHz); lateral 150–300 µm, 50–140 µm) • worse detection of tissue details • limited tissue interpretation • calcium thickness assessment impossible • difficult probe delivery in complex lesions

ICI – intracoronary imaging; IVUS – intravascular ultrasound; OCT – optical coherence tomography.

Technological progress has provided modern cardiology new, immensely helpful and accurate tools to meet current requirements. Intracoronary imaging has become a method that broadens insight into plaque morphology, often changing clinical decisions during percutaneous procedures. Intravascular ultrasound and OCT are increasingly popular instruments used in catheter laboratories worldwide. Other ICI methods, i.e., near-infrared spectroscopy or virtual-histology IVUS, are dedicated to evaluate lipid-rich plaques and are therefore not described in this article.

A meta-analysis conducted by Darmoch et al.[18] clearly showed the superiority of IVUS-guided compared to CA-guided PCIs in the reduction of cardiovascular death (risk ratio (RR): 0.63; 95% CI: 0.54–0.73), myocardial infarction (RR: 0.71; 95% CI: 0.58–0.86), target lesion revascularization (RR: 0.81; 95% CI: 0.70–0.94), and stent thrombosis (RR: 0.57; 95% CI: 0.41–0.79). Three-year results from the ULTIMATE trial[19] (CA vs IVUS-guided PCI) demonstrated a lower rate of target vessel failure (47 vs 76; $p = 0.01$) and stent thrombosis (0.1% vs 1.1%; $p = 0.02$) in the IVUS group. Procedural data presented possible explanation for the difference in 3-year outcomes.[20] Patients in the IVUS-guided group received longer (49.99 ±25.10 mm vs 47.38 ±22.42 mm; $p = 0.02$) and larger (3.14 ±0.51 mm vs 2.97 ±0.48 mm; $p < 0.001$) stents, and post-dilatation, larger non-compliant balloon catheters (3.73 ±0.56 mm vs 3.51 ±0.53 mm; $p < 0.001$) were used at higher pressures (19.7 ±3.7 atm vs 19.0 ±3.7 atm; $p < 0.001$). Same as with IVUS-guided PCI, studies on OCT-guided PCI demonstrated superiority in relation to CA-guidance alone.

Kuku et al.,[21] in their meta-analysis, showed results from 1,753 percutaneous procedures and found lower rates of MACE (odds ratio (OR): 0.70 (0.49, 1.00) $p = 0.05$) and cardiac deaths (OR: 0.40 (0.18, 0.90) $p = 0.03$). Furthermore, they compared results from OCT and IVUS-guided PCIs, and did not conclude that either method is superior.

A large observational study on Pan-London PCI cohort[22] included 87,166 patients who underwent CA-guided PCI (75,046; 86.1%), IVUS (10,539; 12.6%) and OCT (1,149;1.3%). All-cause mortality was established as primary endpoint at median follow up of 4.8 years. The results clearly showed the superiority of OCT guidance in terms of lowering incidence rate of the primary endpoint (7.7%) compared with IVUS (12.2%) or CA (15.7%; $p < 0.0001$) in general, as well as in chronic ($p < 0.0001$) and acute coronary syndrome patients ($p < 0.0024$). Procedural details revealed that the group of OCT patients had longer and bigger stents (25.8 ±13.9 mm; 3.48 ±2.43) than the IVUS group (23.5 ±13.5 mm; 3.59 ±3.46) and the CA group (21.0 ±11.9 mm; 3.20 ±3.23).

A detailed analysis of various aspects imaged using different modalities presents a possible mechanism for their advantages and disadvantages. The OPUS-CLASS study[23] proved the accuracy of the intracoronary OCT diameter measurements, which were equal to the phantom diameters. A large, prospective, 3-arm, single-blinded, multicenter ILUMIEN III trial[24] was designed to establish whether OCT-guidance has any advantage in terms of minimal stent area (MSA) achieved during PCI over the IVUS and/or CA guidance. A total of 450 patients were randomly allocated to the OCT (158 (35%)), IVUS (146 (32%)) and CA-alone (146 (32%)) groups, and the results did not demonstrate OCT to be superior to IVUS. However, post-PCI findings showed lower rate of untreated major dissections (OCT 14% vs IVUS 26% vs CA 19%; for OCT vs IVUS $p = 0.009$, for OCT vs CA $p = 0.25$) and major malappositions (OCT 11% vs IVUS 21% vs CA 31%; for OCT vs IVUS $p = 0.02$, for OCT vs CA $p < 0.0001$) among OCT-group patients in comparison to IVUS and CA patients. Twelve-month observation of the ILUMIEN III trial population[25] did not show significant clinical results.

Recently published ILUMIEN IV trial[26] indicated larger MSA in OCT-guided PCI group in comparison to angiography guidance group (5.72 ±2.04 mm^2 vs 5.36 ±1.87 mm^2; 95% CI 0.21–0.51; $p < 0.001$). There was no difference in incidence of target-vessel failure at 2 years observation in both groups.

Intracoronary imaging for calcified lesions

Intracoronary imaging presents CAC in a distinct way due to its physical principles. Optical coherence tomography depicts a calcified plaque as a sharp, well-demarcated, bordered, signal-poor region (Fig. 1), and CN as a protruding area of calcium, which could be connected to an overlying thrombus and/or fibrous cap disruption (Fig. 2).[27] Intravascular ultrasound, on the other hand, shows CAC as a bright echo with shadowing caused by impermeability of ultrasounds through calcium. Due to the good penetration of ultrasounds, the leading edge of the acoustic shadow in the shallow half (superficial CAC) (Fig. 1,3), as well as in the deeper half of the vessel (deep CAC), can be detected (Fig. 4).[28] In comparison with CA, IVUS detects calcium more often (38% vs 73%; $p < 0.0001$).[29] Greater arc, length, as well as superficial location, concordant distribution (CAC within 45° to the max. plaque thickness) were associated with better detection of CAC in CA. Another study, published by Wang et al.,[30] confirmed the superiority of IVUS in terms of calcium detection (82.7% (364 of 440)) in relation to CA (40.2% (177 of 440)) and OCT (76.8% (338)). Coronary angiography has a high specificity in identifying OCT CAC of 95.1% and IVUS CAC of 98.7%, but low sensitivity – 50.9% and 48.4%, respectively. A detailed analysis clarifies why 26 calcified lesions were detected only with IVUS in this study: plaque attenuation in 15 superficial CACs concealed the morphology in OCT, and 11 were located too deep for OCT penetration. Furthermore, the researchers presented values that predict visible calcification of CA: 110° maximum calcium

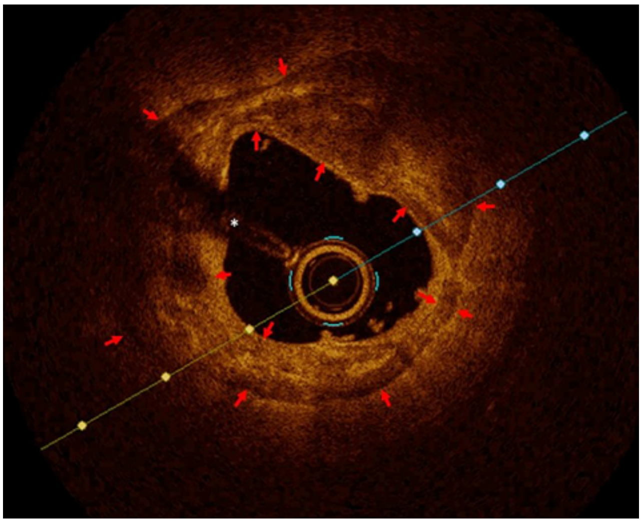

Fig. 1. Coronary calcification – sharp, well-demarcated, bordered, signal-poor region, superficial, 360° (red arrows), wire artifact (white asterisk) – optical coherence tomography

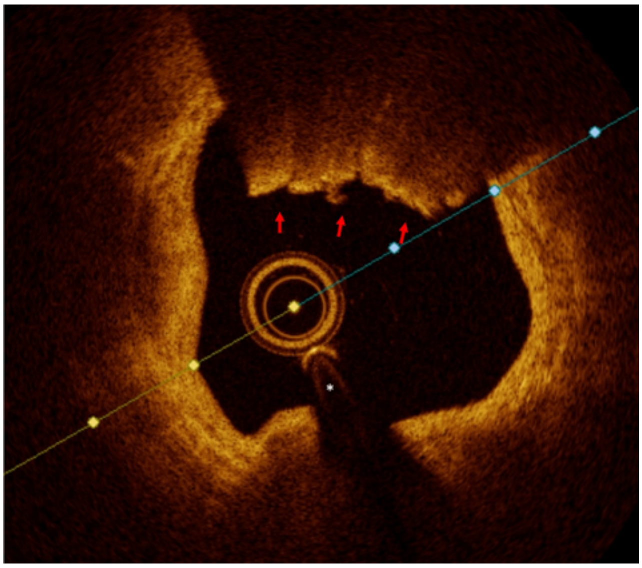

Fig. 2. Protruding calcified nodule (red arrow), wire artifact (white asterisk) – optical coherence tomography

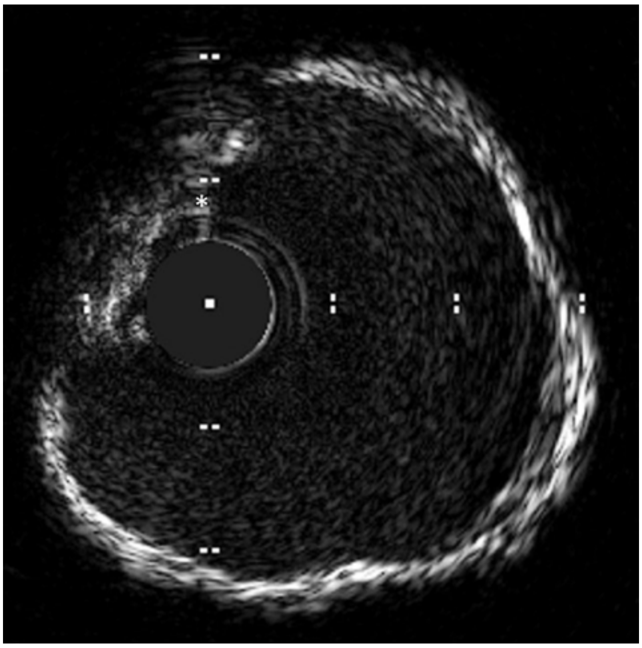

Fig. 3. Superficial, 360° calcification, wire artifact (white asterisk) – intravascular ultrasound

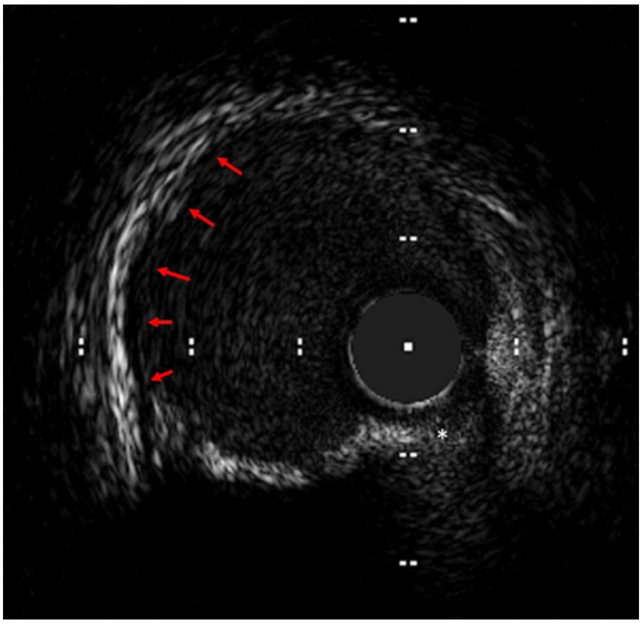

Fig. 4. Deep calcification (red arrows), wire artifact (white asterisk) – intravascular ultrasound

angle in IVUS (area under curve (AUC): 0.80, 95% CI: 0.76–0.83; $p < 0.0001$) and for OCT, calcium angle of 101° (AUC: 0.78, 95% CI: 0.73–0.81; $p < 0.0001$), 4.0 mm length (AUC: 0.81, 95% CI: 0.77–0.84; $p < 0.0001$), and 0.57 mm thickness (AUC: 0.80, 95% CI: 0.76–0.84; $p < 0.0001$). Mintz et al.[29] classified CAC visible in CA as non/mild, moderate (radiopacities visible only during cardiac motion) or severe (radiopacities on both sides of the vessel, visible without cardiac motion), and IVUS CAC intensity was correlated with this classification.

The next step for the proper treatment of a calcified lesion is adequate evaluation of its burden. Intravascular ultrasound, due to impermeability of ultrasounds through calcium, cannot image more than its proximal border, causing an underestimation of the calcium area in relation to histology and OCT.[31] There was a strong correlation between the lumen and the arc of calcification measured using OCT, IVUS and histology. The accuracy of OCT assessment of CAC was also investigated on cadaveric coronary arteries in a more recent study by Mehanna et al.,[32] in which 1,285 cryo-images were compared with 257 OCT images. The study results prove a high agreement between both methods. Mean calcium depth (0.25 ±0.09 mm vs 0.26 ±0.12 mm; $p = 0.742$; $R = 0.90$) and mean calcium angle (35.33 ±21.86° vs 39.68 ±26.61°; $p = 0.207$; $R = 0.90$) were similar. There was a limitation in the evaluation of calcium volume only in the case of inability to visualize its distal border, which required trace interpolation and turned out to under-report CAC volume (3.11 ±2.14 vs 4.58 ±3.39 mm; $p = 0.001$). Intracoronary imaging is very helpful to plan PCI, but OCT and IVUS probes in particularly severely calcified, tight and tortuous lesions can be uncrossable before initial preparation.

Dedicated tools for the treatment of calcifications

Modern interventional cardiology has several instruments for treating coronary calcifications. These range from "gentle" devices such as the non-compliant high and very-high pressure balloon catheters, through scoring balloon (SB)/cutting balloon (CB), to more aggressive methods such as rotational/orbital atherectomy (OA) and intravascular lithotripsy (IVL). Non-compliant balloon catheters were designed to avoid the uncontrolled expansion of the well-known semi-compliant ones, which may lead to vessel dissection and/or perforation, especially in calcified lesions, due to easier expansion in lower resistance regions. Higher pressures can be used with the non-compliant catheters with rated burst pressure (usually about 20 atm). Special, ultra-high-pressure non-compliant balloons have a rated burst pressure of 35 atm; it is effective and safe in treatment of severely calcified lesions, which was demonstrated in OCT multicenter registry.[33] There is always a safety concern when using high pressure so as not to damage the vessel. Plenty of lesions remain resistant to high pressure inflations. The next step and more aggressive tools are SB and CB. The former is an encased spiral with wires on the balloon, while the latter is longitudinally covered with 3 or 4 blades, which are designed to damage coronary calcium and allow full balloon expansion before stent implantation. Cutting balloons have worse deliverability due to their larger crossing profile and low vulnerability of blades, especially in tight lesions, sometimes located distally and/or in angulated vessels. Both types have proven effective in better stent expansion.[34,35] Nevertheless, everyday practice shows that even these tools are insufficient when dealing with severe CAC.

The next step in the treatment of CAC is atherectomy. Currently, there are 2 methods available: rotational and orbital atherectomy. Rotational atherectomy (RA) has been known since 1988. This method uses olive-shape diamond coated burr between 1.25 and 2.5 mm in size. The procedure is conducted in burr runs, which can last up to 30 s, when the burr is gently moved forward-backward (pecking motion) on a RotaWire (Boston Scientific, Boston, USA) to modify calcium. The technique employs the new RotaPRO system (Boston Scientific), as opposed to the previous ROTABLATOR system (Boston Scientific). The new system is easier to use and more operator-friendly. The technique can be used in both stable CAD and ACS.[36,37] European,[38] North American[39] and Japanese[40] consensus documents describe how to safely and effectively use this tool. Two large, randomized trials assessing RA before stent implantation strategy were conducted. The PREPARE-CALC study[41] compared RA with the cutting and scoring balloons, whereas the ROTAXUS study[42] compared RA with the standard therapy. Both trials proved the safety and feasibility of RA, as well as higher strategy success. Rotablation leaves behind specific calcium modifications such as semicircular marks in the exact size of the burr used (Fig. 5), sometimes combined with white thrombi (Fig. 6), fractures (Fig. 7,8) and dissections (Fig. 9). Combination of RA and CB results in better acute lumen gain and stent expansion compared to RA or SB/CB alone.[43]

Still under development, the OA technique introduced in 2013 uses a 1.25 mm diamond-coated crown mounted eccentrically and proximally to the tip of the shaft. Depending on the speed of the crown, it can be used in the treatment of vessels from 2.5 to 4 mm. In contrast to RA, OA provides bidirectional atherectomy. This method, like RA, ensures good PCI outcomes and procedure safety.[44] Rotablation and OA have never been directly compared in a reliable multicenter trial, so there is no way of knowing which atherectomy type is better or which exact type of lesion is better for which method. One small, nonrandomized study[45] compared 30 RA and 30 OA PCIs and showed a trend toward more frequent calcium modification with OA, especially in larger vessels, but it did not affect OCT results for the procedure.

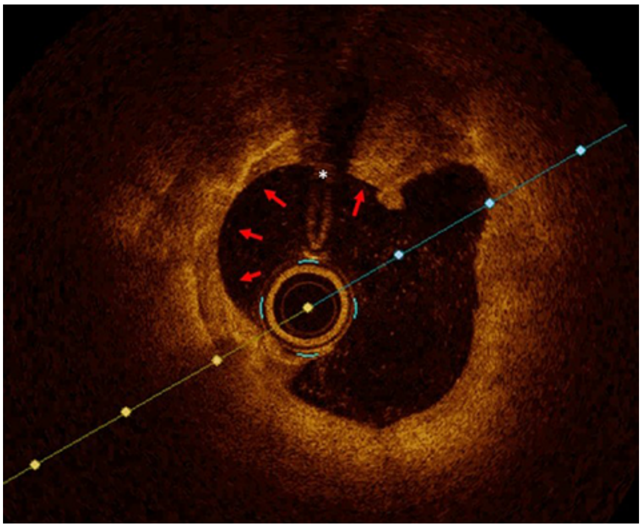

Fig. 5. Burr mark (red arrows) after 1.75 rotational atherectomy, wire artifact (white asterisk) – optical coherence tomography

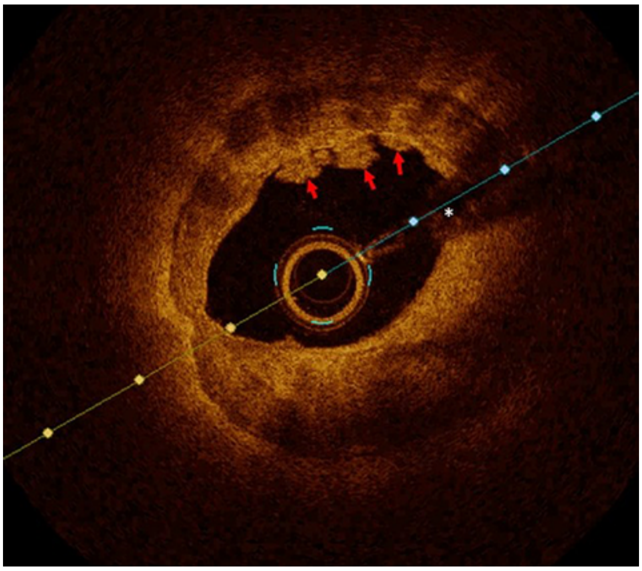

Fig. 6. White thrombi (red arrows) after rotational atherectomy, wire artifact (white asterisk) – optical coherence tomography

The latest tool invented for dealing with CAC uses a well-known technique for treating nephrolithiasis. The Shockwave Intravascular Lithotripsy System (Shockwave Medical, Fremont, USA) employs ultrasounds to deliver sonic pressure waves that crush calcium located even in the deep layer of the artery. The crossing profile of IVL balloon catheters ranges from 0.043 to 0.046 inches (depending on the diameter – from 2.5 to 4.0 mm), which makes it useful in larger vessels. Its high efficacy and safety were shown in the Disrupt CAD III study.[46] Delivery of IVL catheter to tight as well as tortuous lesions is demanding and sometimes even unreachable. It could potentially be used to treat stent underexpansion[47] and stent restenosis associated with the formation of calcified plaque (Fig. 10).

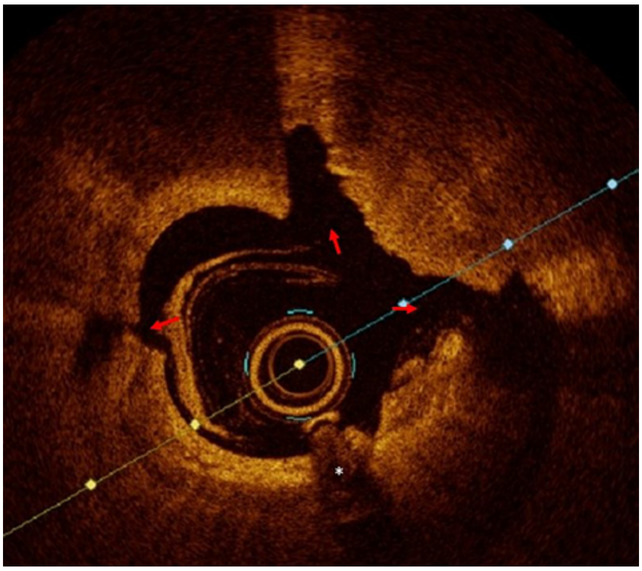

Fig. 7. Calcification fractures (red arrows), wire artifact (white asterisk) – optical coherence tomography

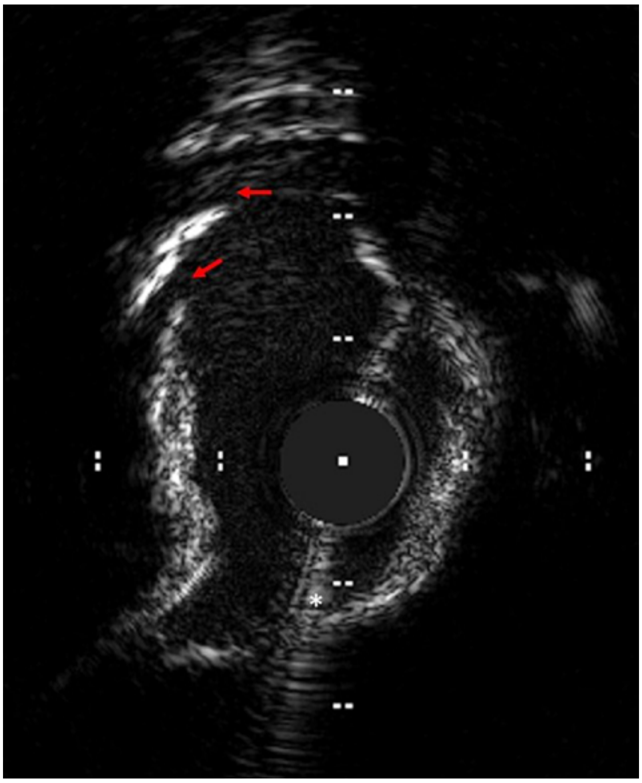

Fig. 8. Calcification fractures (red arrows), wire artifact (white asterisk) – intravascular ultrasound

There is one more tool, i.e., coronary laser atherectomy catheter, which is sometimes considered for the treatment of CAC. It is rather helpful in the delivery of RA, OA and IVL[48] catheters, especially in tight stenoses, when wires cannot pass beyond the lesion. The manufacturer of the device predicts that it will be able to deal with moderately calcified stenoses.

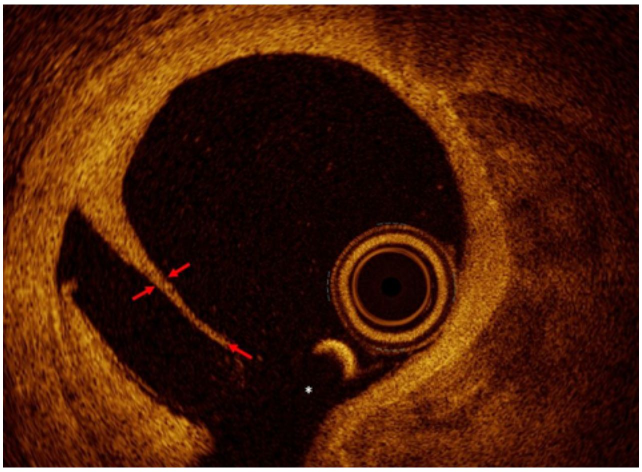

Fig. 9. Dissection flap (red arrows), wire artifact (white asterisk)

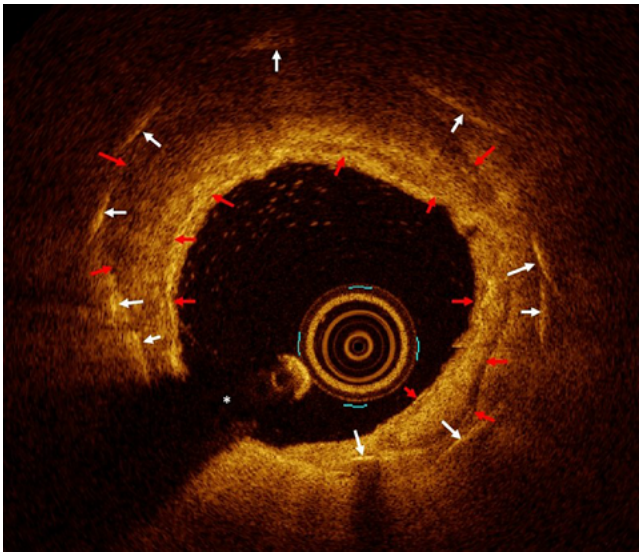

Fig. 10. Calcified in-stent restenosis (red arrows), stent struts (white arrows), wire artifact (white asterisk) – optical coherence tomography

Percutaneous coronary intervention of calcified coronary lesions supported by ICI

Intracoronary imaging modalities provide a lot of data, which help to optimize percutaneous interventions. Calcium burden, its localization and diameters influence the final effect of PCI. Many papers demonstrated worse results of CAC procedures with higher rate of stent underexpansion,[4] stent apposition,[6] target vessel failure, stent thrombosis,[7] incomplete revascularization, mortality,[8] and major adverse cardiac events (MACE).[3] A recently published European consensus statement for heavily calcified coronary stenoses management,[38] as well as a document issued by the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) on RA,[40] and the North American Expert Review of Rotational Atherectomy,[39] clearly advise to use ICI during PCI of calcified lesions. The researchers were looking for specific calcium parameters that lead to worse outcomes. Henneke et al.[49] already in 1999 presented such a parameter, stent asymmetry, among patients with >180° IVUS calcium angle, in comparison with non-calcified lesions ($p < 0.05$). Another ultrasound-based study has shown less frequent proper stent apposition and higher rate of periprocedural non-Q-wave myocardial infarct among ≥270° angle calcified lesions than among <270° angle calcium lesions.[50] The next paper, published in 2014, using OCT measurements, pointed to the arc and area of the calcification as a predictor of stent expansion.[51] Patients with a greater arc of calcium had lower percentage of predicted minimal stent diameter and area (respectively, $r = -0.37$, $p < 0.01$; and $r = -0.33$, $p < 0.02$). Larger calcium area turned out to affect only the predicted minimal stent diameter ($r = -0.38$, $p < 0.01$), but not the minimal stent area ($r = -0.26$, $p = 0.07$). Lesions with >90° arc and >1.58 mm^2 calcium area had lower minimal stent diameter on the final OCT.

An innovative approach to assessing lesion calcium burden was introduced by Fujino et al.[52] The authors established OCT-based scale regarding 3 parameters: the arc of calcium, its length and thickness. A lesion is scored as follows: 2 points for >180° arc and 1 for >5 mm length, and one for ≥0.5 mm thickness of calcium. An analysis showed that the 4-point lesions indicate the worst stent expansion and seem to require specific plaque modification before stent implantation. Zhang et al.[53] published an IVUS-based scoring system for predicting stent underexpansion. The scale awarded 1 point for each >5 mm length of >270° calcium, the presence of CN and <3.5 mm vessel diameter. The cutoff that predicts underexpansion was 2 points, so ≥2 point lesions should be considered for preparation with dedicated devices for calcium modification. The abovementioned studies are in line with conclusions made by Wang et al.,[30] according to which minor calcifications did not affect the final stent expansion during PCI, and only major calcium burden requires additional tools to improve PCI outcomes.

Lesions that require additional tools have been described, but it is also important to know what can be achieved using them. Maejima et al.[54] assessed OCT images after rotablation and inflation of balloon catheter in 37 calcified coronary lesions. Results showed better stent expansion when OCT imaging revealed the presence of calcium fractures before stenting. Lesions with calcium fractures achieved greater stent cross-sectional area (7.38 ±1.92 mm^2 vs 7.13 ±1.68 mm^2; $p = 0.035$) and lumen gain (3.89 ±1.53 mm^2 vs 3.40 ±1.46 mm^2; $p < 0.001$). According to this study, the optimal calcium arc and thickness for predicting formation of fractures is 227° and 0.67 mm, respectively. The group of lesions with OCT fractures had thinner calcium (0.53 ±0.28 mm vs 1.02 ±0.42 mm; $p < 0.001$) with a larger arc (360°, interquartile range (IQR): 246–360° vs 147°, IQR: 118–199°; $p < 0.001$), which was also affirmed by Fujino et al.[52] An OCT-based study[55] on a new tool, IVL device, dedicated to calcified lesions, confirmed the link between calcium burden and fracture formation. Another paper[56] indicated better stent expansion (minimal stent area of 5.02 ±1.43 mm^2 vs 4.33 ±1.22 mm^2; p = 0.047) when OCT calcium fractures were achieved. Moreover, it showed smaller angiographic diameter stenosis (19 ±27% vs 38 ±38%; p = 0.030), lower frequency of binary restenosis (14% vs 41%; p = 0.024) and ischemia-driven target lesion revascularization (7% vs 28%; p = 0.046) at 10-month follow-up in the group with primary fracture formation. Kobayashi et al.[57] similarly demonstrated that greater calcium damage resulted in better stent expansion. The formation of dissections was a predictor of greater MSA when RA was performed. Moreover, the minimal thickness of CAC in multivariable analysis turned out to be crucial for larger final MSA.

Furthermore, ICI provides other data to optimize PCI in calcified lesions. Intravascular ultrasound might help in the choice of the RotaWire: extra support or floppy in preparation for the rotablation.[58] Unlike angiography alone, the IVUS probe can show the precise position of the wire and its contact with the vessel structures. It is particularly helpful when dealing with angulated lesions. The fibrofatty and/or necrotic core component of the target plaque imaged by IVUS before intervention[59] and ineffective probe delivery through CAC[60] determine a higher probability of slow/no flow during PCI. Intracoronary imaging provides a lot of useful data about the treated vessel such as plaque morphology, calcium burden and vessel diameters, determining the intervention strategy and often identifying the need to change it during the procedure. Especially with regard to CAC, as one of the most complex problems in CAD treatment, there are benefits to the use of ICI. Roy et al.[61] showed that during IVUS-guided PCI with DES implantation, operators choose RA and CB more often than during CA-guided PCI alone. Moreover, ICI-guided RA PCI lowers 1-year MACE compared with CA-guided PCI (28.9 vs 4.3%; OR: 9.06, 95% CI: 3.82–21.52; p < 0.001), which is driven by the reduction of all-cause death (OR: 8.19, 95% CI: 2.15–31.18; p = 0.002), myocardial infarction (OR: 6.13, 95% CI: 2.05–18.3; p = 0.001) and target vessel revascularization (OR: 3.67, 95% CI: 1.13–11.96; p = 0.031). Procedural data analysis shows that ICI guidance increases the number of burrs used (1.210 ±0.42 vs 1.070 ±0.31; p = 0.005) and the final diameter (1.50 mm (1.50–1.75) vs 1.50 mm (1.25–1.50); p = 0.001), as well as the length of the implanted stent (38.0 mm (30.0–53.7) vs 33.0 mm (22.0–49.0); p = 0.004) and its diameter 3.00 mm (3.00–3.50) vs. 2.75 mm (2.50–3.50); p < 0.001).[62]

Interventional cardiologists have multiple parameters to consider during CAC PCI, which are summarized in Table 2. Two studies on OCT vs IVUS-guided RA PCI showed better results using the former modality. Kobayashi et al.[63] analyzed 88 RA PCI, and the percentage of stent expansion was established as the primary endpoint. The OCT group achieved significantly better expansion (83 ±15% vs 72 ±16%; p = 0.0004) and outcomes due to frequent burr upsizing (55% vs 32%; p = 0.001), larger final burr (1.75 mm (1.50–1.75) vs 1.50 mm (1.50–1.75); p < 0.001) and more burrs used (2.0 mm (1.00–2.00) vs 2.0 mm (1.00–2.00); p < 0.001). Another smaller but also valuable study[64] compared 18 OCT and IVUS images taken after stent implantation in lesions requiring RA PCI. The results indicated better detection of stent malapposition and its extent (20% vs 6%; p < 0.001) in the OCT group, which led to additional post-dilatation and better final MSA (8.15 ±1.90 vs 7.30 ±1.62 mm^2; p < 0.05). In conclusion, the authors want to point to OCT as a method supported by literature for guiding PCI of calcified lesions, because it shows more details of the calcified plaque, has the above-mentioned scale established to predict the need to use an additional tool dedicated to calcified lesions, and better assesses results of such an intervention. Figure 11 presents a practical algorithm for the treatment of calcified lesions based on ICI.

Imaging-guided optimal stent implantation

Optimal stent implantation is the final step of PCI, and its outcome affects the patient's further prognosis. Intracoronary imaging provides very precise data about stent deployment and related complications. The European Intracoronary Imaging Consensus[17] established several points which should be assessed before and after stent implantation. When preparing for deployment, the operator

Table 2. Deciding parameters visualized with OCT and IVUS during CAC PCI

ICI	Primary imaging	Imaging before stent implantation
OCT	• calcium length ≥5 mm, arc ≥180° and thickness ≥0.5 mm: qualification for calcium modification tools, atherectomy or IVL • probe uncrossable lesion and/or fibrofatty/necrotic core component: slow/no flow suspected • determination of wire bias before atherectomy	calcium fractures, dissections: predicts good stent expansion
IVUS	• ≥2 of >5 mm calcium length, arc >270°, presence of CN, <3.5 mm vessel diameter >qualification for calcium modification tools, atherectomy or IVL • probe uncrossable lesion and/or fibrofatty/necrotic core component: slow/no flow suspected • determination of wire bias before atherectomy	calcium fractures, dissections: predicts good stent expansion

ICI – intracoronary imaging; OCT – optical coherence tomography; IVUS – intravascular ultrasound; CAC – coronary artery calcification; PCI – percutaneous coronary intervention; IVL – intravascular lithotripsy.

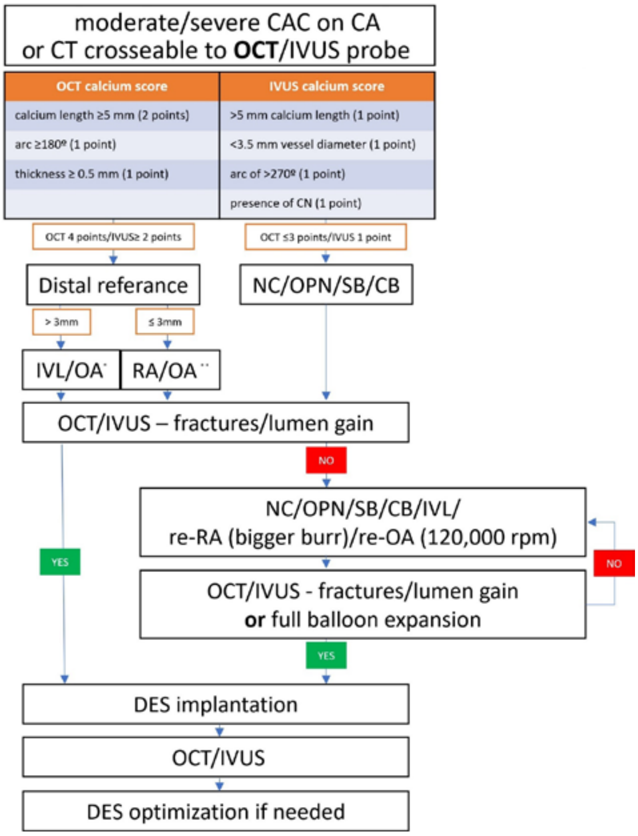

Fig. 11. Practical algorithm for the treatment of calcified lesions based on intracoronary imaging

CA – coronary angiography; CAC – coronary artery calcification; CB – cutting balloon; CN – calcified nodule; CT – computed tomography; DES – drog eluted stent; JVL – intravascular lithotripsy; IVUS – intramuscular ultrasound; NC – non-compliant balloon; OA – orbital atherectomy; OCT – optical coherence tomography; OPN – ultra-high-pressure non-compliant balloon; RA – rotational atherectomy; SB – scoring balloon; * 120,000 rpm; ** 80,000 rpm

ought to choose a proper landing zone. It cannot be located in a lipid-rich region, and the plaque burden cannot exceed 50%. Stent diameter sizing should depend on the distal reference measured with an external elastic membrane (EEM) or, if it cannot be sufficiently visualized (<180% of the EEM is invisible), a lumen-based diameter should be used. Stent size is selected based on the diameter of the EEM with rounding down to the nearest 0.25 mm or rounding up if only the lumen-based approach is viable. In cases of CAC and advanced atherosclerotic lesions, the EEM-based approach is usually not possible. Optimal stent deployment should provide >80% expansion (MSA/average reference lumen area) with MSA >5.5 mm^2 (on OCT) or >4.5 mm^2 (on IVUS) in a location other than the left main. Important aspects that were found to require further optimization are acute malapposition of the stent struts (exceeding >0.4 mm axially and > 1 mm in length), late-acquired malapposition, tissue prolapse (especially in ACS lesions), and dissection localized on the distal stent edge (>60° and >2 mm longitudinally with the involvement of media), which could be associated with local hematoma formation. The criteria for proper stent implantation differ depending on the ICI modality. Based on the ULTIMATE trial,[20] the optimal IVUS image after stent deployment should meet the following criteria: >5.0 mm^2 of the minimal lumen area (MLA) or 90% of the distal reference MLA, <50% plaque burden proximally and distally to the stent, and no stent edge dissection longer than 3 mm, including the media layer. In OCT, on the other hand, optimal stent implantation depends on the ILUMIEN IV trial[26] and involves: ≥90% stent expansion in both proximal and distal parts, ≥270° visibility of the vessel EEL at both reference sites, no more than 10% intra-stent plaque protrusion/thrombus (protrusion area/stent area), stent edge dissection (≥60 degrees of the circumference of the vessel and ≥3 mm length), and ≥200 µm stent malaposition associated with unacceptable stent expansion. Obtaining a perfect image after PCI, especially in the case of severely calcified lesions, is usually extremely difficult, and additional post-dilatations to achieve the ideal image can result in vessel dissection and/or perforation. Operators should consider the possible losses and gains associated with attempting to achieve an excellent image.

Limitations

This review has some limitations. There is a lack of randomized studies that compare the results of CAC PCI based on OCT compared to IVUS, a shortage of randomized trials comparing dedicated methods to treat CAC head-to-head, and limited data on the exact goal of CAC preparation before stent implantation.

Conclusions

To sum up, ICI is a very safe and helpful tool during percutaneous treatment of calcified coronary lesions. Intracoronary imaging, and particularly OCT, can identify lesions requiring the use of additional tools dedicated to treating calcifications. During the procedure, ICI indicates the need for further calcium modifications. Moreover, even if an acceptable angiographic result of stenting is achieved, ICI often shows abnormalities requiring further improvement. However, imaging modalities are not free from limitations and lesions can still be over- or underestimated. Further studies are needed to improve imaging capabilities, especially IVUS precision and OCT penetration. Intravascular ultrasound provides good insight into deep structures of the vessel, but cannot show calcium parameters. Optical coherence tomography accurately shows structures, but only those localized not too deep, so it can be problematic to image large vessels, especially the left main stem. Efforts continue to combine OCT and IVUS to take advantage of the strengths of both methods. Further research is needed to advance coronary calcium imaging to improve PCI outcomes. The human factor in the assessment of obtained images certainly has an impact on the course of treatment. This is the place for artificial intelligence, which will assist us in interpretation and decision making in the future. Furthermore, the combination of imaging and physiological measurements of stenosis will bring percutaneous treatment of CAC to the next level. The course of intervention, the choice of appropriate tools, and the combination of available techniques for dealing with calcium are still not fully explored. This is a major area for future research. In particular, calcium resistance during primary intervention remains a difficult problem for interventional cardiologists, and this topic requires further research.

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