Advances in Cardiac Research

REVIEW

How Does Intravascular Imaging Assist Interventional Cardiologists?

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Abstract

In recent years, intravascular (IV) imaging has gained significant prominence in the field of interventional cardiology. Randomized controlled trials (RCT) have demonstrated the benefits of routine IV imaging in cardiovascular outcomes. IV imaging aids in the assessment of lesion morphology prior to the intervention, facilitates the selection of appropriate tools for lesion preparation, enables prediction and preparation for potential complications during the procedure, determines optimal stent size and length, assists in the post-percutaneous coronary intervention optimization of stent position, and helps address issues such as lesion coating, edge dissection, stent fracture, and malapposition that are not easily identifiable through conventional angiography. This review aims to provide a comprehensive summary of the expanding applications of IV imaging in interventional cardiology and highlight its significance in facilitating the work of operators during procedures.

Keywords: intravascular ultrasound, optical coherence tomography, percutaneous coronary intervention optimization

Introduction

Percutaneous coronary intervention (PCI) remains the preferred primary treatment approach for appropriate patients with acute and chronic coronary syndromes. Recent data has demonstrated that PCI is equivalent to coronary artery bypass grafting (CABG) in terms of cardiovascular outcomes, particularly in complex lesion subgroups.[1] Complex lesions, such as those in the left main coronary artery (LMCA), main branch ostia, and heavily calcified lesions, pose a higher risk of complications during the procedure. Intravascular imaging (IV) has emerged as a valuable tool in optimizing procedures for these patient groups and significantly reducing the risk of complications. Guidelines recommend the use of IV imaging, especially in LMCA and complex lesion subgroups (Class IIa, level of evidence B).[2]

Despite its extensive utilization, especially in Far Eastern countries like Japan where it is employed in up to 95% of cases, IV imaging remains underutilized in comparison to the expectations in the USA and Europe. Several factors contribute to this situation, including limited coverage by local health insurance, increased procedure duration and associated costs, and a shortage of adequately trained operators. IV imaging plays a crucial role in various aspects of PCI procedures.

Interventional cardiology utilizes two main types of IV imaging: IV ultrasound (IVUS) and optical coherence tomography (OCT). Each modality has its advantages and disadvantages. OCT provides superior information on calcium thickness, plaque morphology, thrombus evaluation, and the determination of instent restenosis causes. On the other hand, IVUS, with its better tissue penetration, offers more accurate evaluation in larger vessels like the LMCA and does not require the use of contrast agents that can affect the patient's creatinine levels. IVUS also provides safer evaluation in patients with dissection and vascular injuries. Recent publications have demonstrated the safe use of OCT in LMCA evaluation with newly developed OCT systems.[3] Both IVUS and OCT can be used independently in appropriate patient groups, or they can be employed simultaneously for specific lesion types, particularly in Far Eastern countries with well-developed healthcare systems.

Intravascular Imaging for Plaque Morphologies and Lesion Types: Methods and Advantages

Plaque morphologies

Although atherosclerosis and normal area evaluation can be performed when the intimal thickness exceeds 0.3 mm, it is still not always easy to distinguish between normal and abnormal.[4] In such cases, numerical assessment of plaque burden, achieved by proportioning the combined plaque and media thickness to the entire vessel area, is more reliable, particularly with IVUS.[5] Until the plaque burden exceeds 40%, the vascular lumen area remains relatively constant due to positive and negative remodeling mechanisms.[6]

Soft Plaque

Soft plaque is characterized by low echogenicity and does not directly describe plaque morphology. It predominantly consists of lipid-derived structures and varying amounts of fibrous tissue, often containing a lipid necrotic core that further weakens acoustic signals (Figure 1a and Figure 2). [7,8]

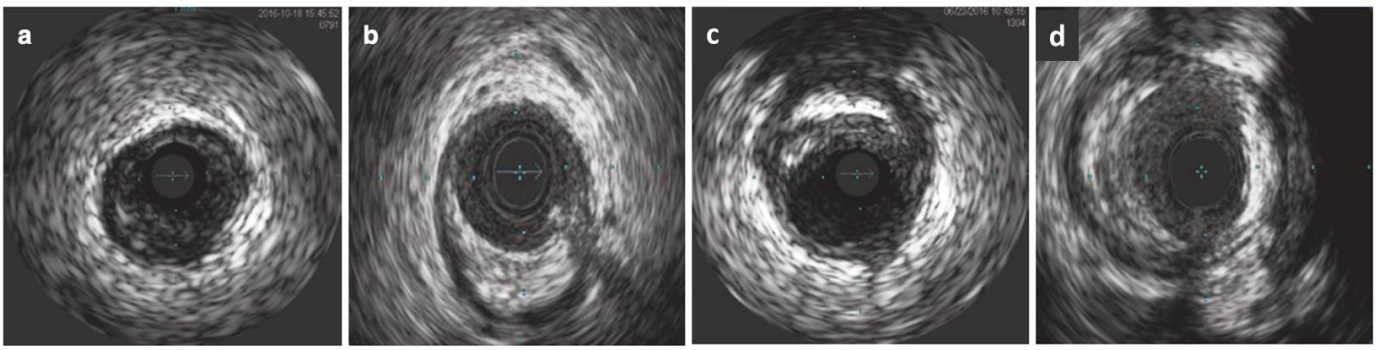

Figure 1. Plaque types of different morphologies in intravascular ultrasound. Reproduced with permission.[7]

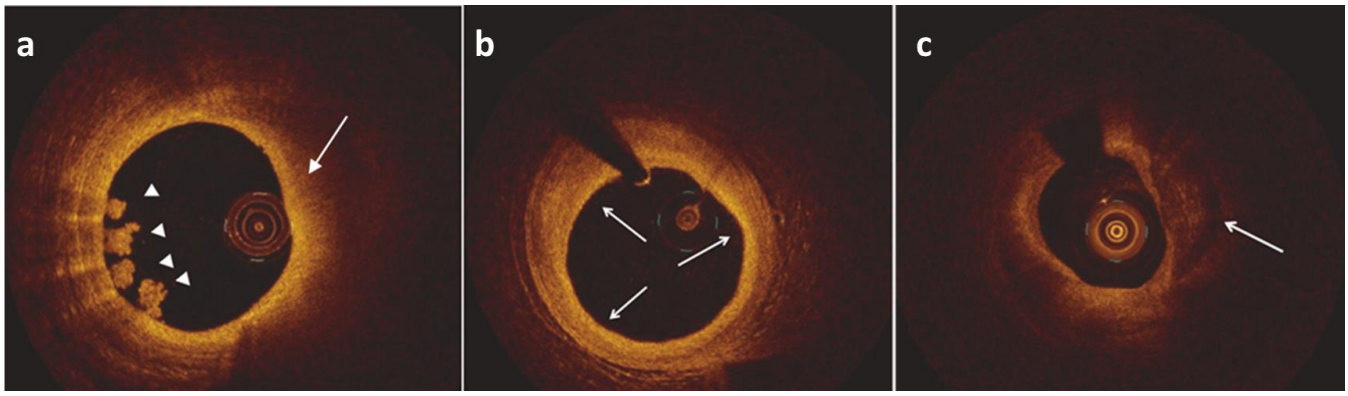

Figure 2. Different plaque morphologies in optical coherence tomography; a) thin fibrous cap and soft plaque with high attenuation (arrow), white thrombi (arrowheads); b) fibrous plaque; c) very well separated calcific area (arrow). Reproduced with permission.[8]

Fibrous plaque

Fibrous plaque exhibits echogenicity higher than soft plaque but lower than calcified lesions. It does not create an acoustic shadow and appears approximately as bright as or brighter than the vascular adventitia. In some cases, dense fibrous plaques may be mistaken for calcific plaques due to acoustic shadowing. Dense fibrous plaques are typically rubber-like and exhibit poor response to standard non-compliant balloons (NCB). While modification methods like cutting-scoring balloons are often sufficient, in rare cases, upgrading the plaque modification with techniques like rotablation may be necessary (Figure 1b and Figure 2). [7,8]

Calcific plaque

Calcific plaques appear hyperechoic as they cause acoustic shadowing by impeding the passage of IVUS waves. Although the exact composition cannot be assessed by IVUS due to acoustic shadowing, superficial calcification refers to calcification near the lumen, while deep calcification refers to calcification near the external elastic lamina (EEL). OCT is the preferred method for evaluating calcification, providing crucial information to operators regarding thickness, depth, angle, and extent before the procedure (Figure 1c and Figure 2). [7,8]

Mixed plaque

Mixed plaque is characterized by the absence of a specific dominant echogenous element. It can exhibit a combination of fibrocalcific or fibrofatty components (Figure 1d).[7]

Management of Vulnerable Plaque with Intravascular Imaging

Vulnerable plaque, although initially considered as a soft plaque, possesses unique characteristics and appearances. While there is no definitive definition of plaque vulnerability in IVUS, vulnerable plaques can be identified by the presence of thin, poorly formed fibrous caps accompanied by hypoechoic plaques. Attenuated plaques, characterized by deep attenuation and hypoechoic appearance, were found in 78% of patients with acute coronary syndrome in the HORIZON-AMI study. These plaques are often associated with TIMI 2 flow, angiographic thrombus, positive remodeling, and plaque rupture.[9]

In OCT, the definition of vulnerable plaque has been standardized, and studies have demonstrated its effectiveness in predicting cardiovascular outcomes. According to these studies, plaques with a fibrous cap thickness less than <75 μm, a lipid arc encompassing 180 degrees or more, and the presence of macrophages detectable by OCT are considered high-risk features (Figure 3). Additionally, if the minimal lumen area (MLA) in the left anterior descending artery (LAD) is less than <3.5 mm^2, it further indicates high-risk plaque. Plaques exhibiting these high-risk features progress rapidly within one year and are associated with an increased risk of cardiac death and myocardial infarction compared to plaques lacking these features (Figure 3).[10]

Furthermore, several studies have demonstrated that vulnerable plaques in nonobstructive angiographic images

within Acute Coronary Syndrome (ACS) subsets can manifest in three distinct morphological appearances when assessed using IV imaging[11]

1. Plaque rupture: This is characterized by a view of the cavity associated with the lumen, indicating a breach in the fibrous cap (Figure 4a).
2. Plaque erosion: In this scenario, an irregular view of the plaque surface is observed, indicating erosion without a distinct rupture (Figure 4b).
3. Calcified nodule: These plaques exhibit irregular looking calcific hyperechogenic areas with a convex protrusion towards the lumen, representing a distinctive calcified nodule (Figure 4c).

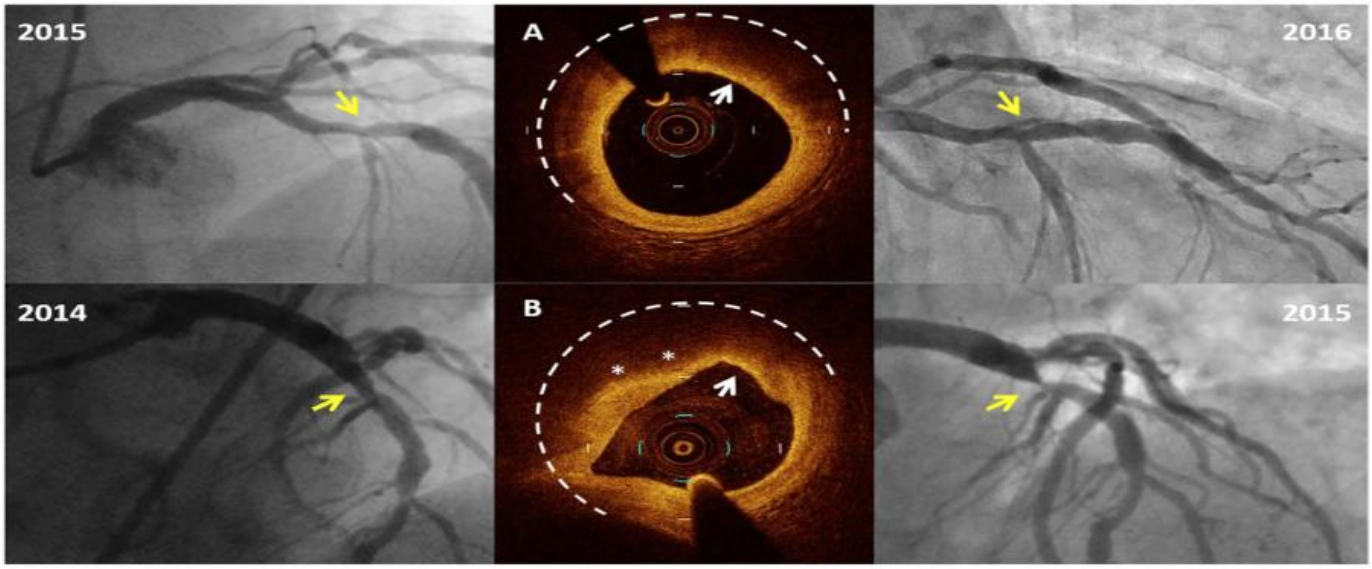

Figure 3. In the image provided above, a lesion that does not meet all the high-risk criteria does not exhibit any progression on angiography after one year (dashed lines show a lipid arc of 200^0, and the arrow shows a thin fibrous cap diameter of 60 μm). In the image below, it is evident that a vulnerable plaque displaying all the high-risk criteria results in an acute coronary syndrome event within one year (dashed lines show 206^0 lipid arc; asterixis show macrophage infiltration; arrow shows a thin fibrous cap of 50 μm. LAD-MLA:2.64) Reproduced with permission.[10]

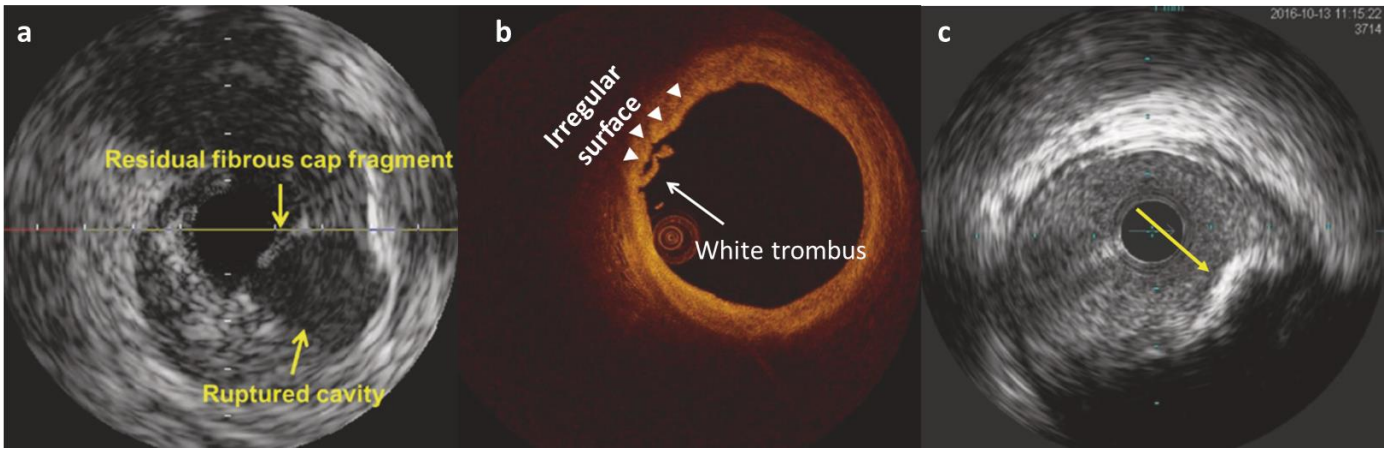

Figure 4. Representative intravascular images depict (a) plaque rupture, (b) plaque erosion and (c) calcified nodule. Reproduced with permission.[7]

In patients presenting with ACS and elevated troponin levels, the presence of a nonobstructive lesion observed on coronary angiography, along with the identification of certain conditions through IV imaging, necessitates intervention in these lesions to prevent subsequent events.

Furthermore, when IV imaging reveals an attenuated plaque, the operator, being aware of the increased risk of major vessel obstruction and slow-no flow phenomena associated with such plaques, may opt to place distal protection devices or keep no-reflow medication readily available near the operation table before initiating PCI. This preliminary information proves invaluable in preventing complications that may arise during the procedure. Likewise, in cases where a calcific nodule is observed within a lesion, IV imaging plays a critical role in minimizing the risk of vascular rupture during high-pressure balloon inflation. By facilitating the fracture of the calcific nodule through techniques like orbital atherectomy or intravascular lithotripsy (IVL), IV imaging ensures the adequate expansion of the stent and subsequently reduces the risk of subsequent events. Studies have demonstrated an increased risk of stent restenosis in calcific lesions where stent expansion is inadequate.[12] Overall, the utilization of IV imaging not only aids in guiding interventions but also serves to mitigate complications and improve outcomes during coronary procedures.

Management of calcific lesions using intravascular imaging

Calcifications within a lesion can manifest in three ways: superficial, deep, or as calcified nodules. While deep calcifications often respond well to balloon expansion, addressing severe superficial calcifications requires the use of atherectomy tools to ensure proper stent expansion and minimize complications.

For instance, in cases of severe circular thick superficial calcifications, it is beneficial to perform calcium modification using a rotablation prior to stenting in order to achieve optimal stent apposition. However, when dealing with localized superficial calcifications or calcified nodules, it is more prudent to utilize orbital atherectomy with wire bias. This approach reduces the risk of deep vascular damage that could potentially result in rupture within noncalcified areas. Additionally, using non-compliant or optimal pressure NCBs in such lesions may increase the risk of vascular rupture. Certain expert opinions, observational studies, and cases suggest that IVL is more effective in managing deep calcifications that do not have a superficial connection.[13,14]

After employing methods to reduce calcification, reassessing the lesion using IV imaging allows us to determine the effectiveness of the calcification modification (Figure 5). This evaluation helps us determine whether sufficient fractures have occurred or if additional debulking is necessary. Furthermore, IV imaging provides valuable information to the operator in assessing the presence of vascular injury that may pose a risk during subsequent balloon interventions (Figure 6).

Moreover, evaluating stent expansion following the PCI procedure aids in reducing and predicting the risk of post-procedural events. It allows for an assessment of appropriate stent apposition throughout the entire segment, as insufficient stent expansion in calcified regions significantly increases the risk of stent restenosis.[12]

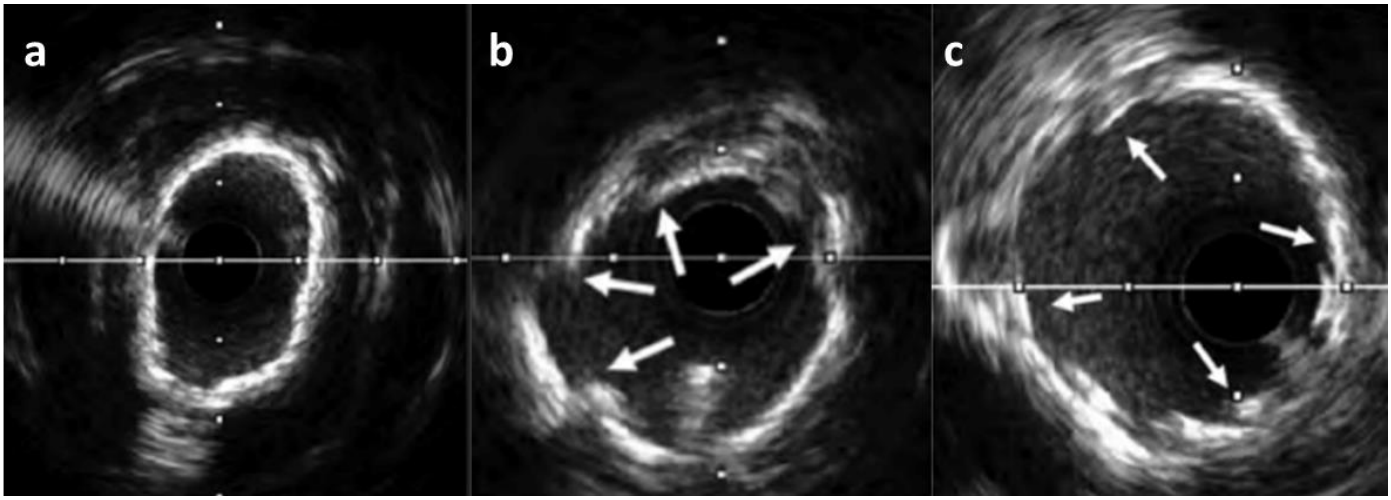

Figure 5. Angiographic images demonstrating different aspects of calcification and stent apposition. (a) Superficial circular calcification. (b) Fractures in the calcium after the use of intravascular lithotripsy. (c) Illustration of good stent apposition. Reproduced with permission.[15]

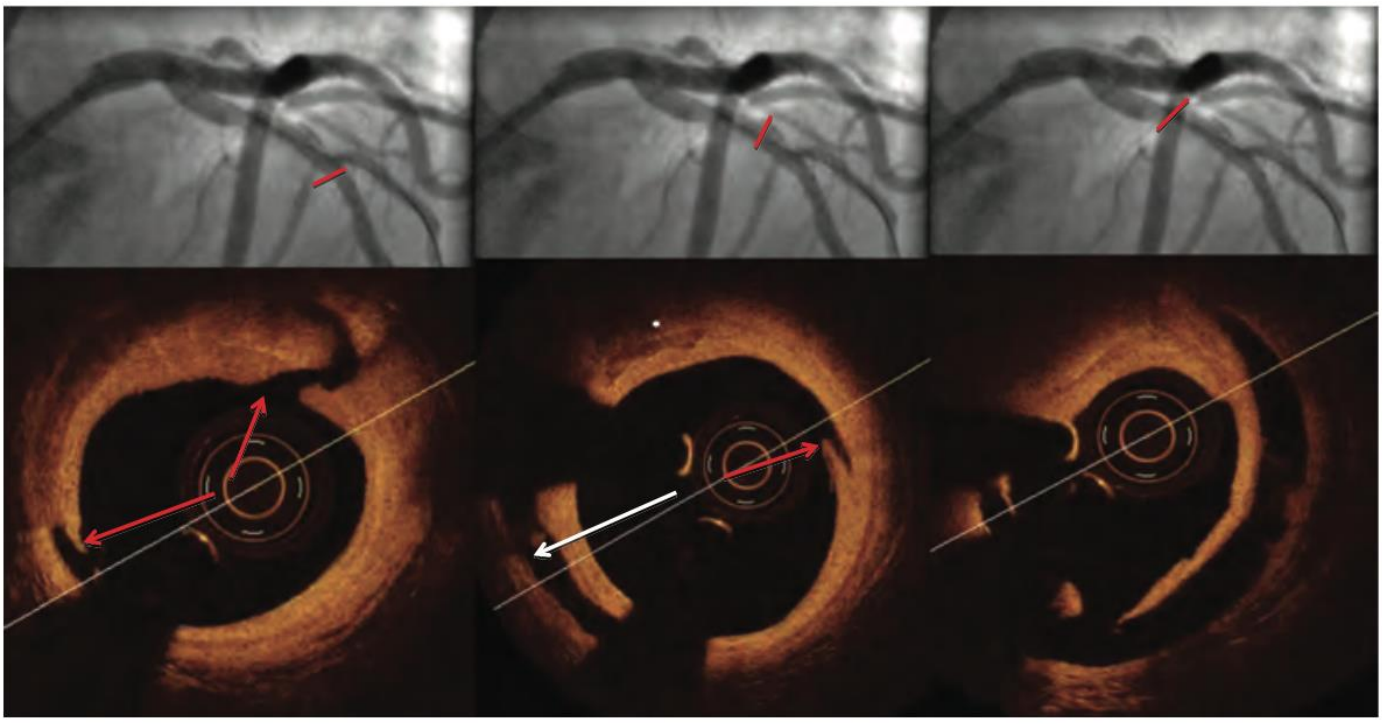

Figure 6: Angiographic and optical coherence tomography images showing a cross-sectional view of a fibrocalcific lesion in the left anterior descending artery, from distal to proximal. The figure highlights complete and incomplete plaque ruptures indicated by red arrows, along with the presence of an intramural hematoma marked by a white arrow. The lesions were observed after the use of a scoring balloon. Reproduced with permission.[16].

Intravascular Imaging-Guided Management of Bifurcation Lesions

Observational studies have demonstrated that the utilization of IV imaging in bifurcation procedures leads to a reduction in stent usage and decreased mortality rates and combined end points at the 3-year follow-up.[17]

Longitudinal frames obtained from IV imaging allow for the evaluation of side branch localization, diameter, exit angle, lesion length, plaque morphology, and calcium extension. Furthermore, IV imaging aids in predicting the risk of side branch occlusion during provisional stenting.[18] In bifurcation lesions involving a 0:0:1 subset, the procedure can be concluded with the use of a drug-coated balloon (DCB) if the side branch exhibits sufficient lesion enlargement and lacks any dissection. Similarly, employing DCB for the side branch and provisional stenting for the main branch has been shown to reduce the number of stents required in bifurcation lesions when guided by IV imaging. Notably, a Korean study demonstrated the safety of omitting the kissing balloon technique (KBT) in LAD to LMCA crossover stenting when IV imaging and coronary physiologic assessment were employed. In such cases, the fractional flow reserve (FFR) value was found to be the most critical factor determining side branch ostial restenosis. Cirfumflex coronary artery (CX) ostium restenosis risk was significantly elevated by 5 times when the FFR of CX was less than 0.80, even if kissing balloons were utilized and appropriate angiographic imaging was obtained.[19] Additionally, IV imaging provides invaluable information to the operator regarding the distribution of stent struts at the side branch ostium. It assists in identifying conditions such as wire progression between stent struts, which may hinder the advancement of the balloon or stent into the side branch. By reducing unnecessary effort and potential complications, IV imaging helps decrease procedure time contrary to common assumptions.

The Role of Intravasvular Imaging in Chronic Total Occlusions

Chronic Total Occlusion (CTO) lesions predominantly manifest as severe calcific lesions. In these challenging cases, IVUS emerges as a crucial tool, offering extensive support to CTO operators. IVUS plays a pivotal role in visualizing calcification at the proximal cap, facilitating precise puncture and guiding intraluminal progression, notably through techniques like IVUS-guided wiring reentry (Figure 7).

Experienced CTO operators emphasize that while the retrograde approach rate in CTO is diminishing, IVUS guidance is associated with increased intraplaque progression and improved success of side branch access within the CTO segment. As the collective experience in this domain expands, further observational studies and registry data are expected to provide us with clearer and more comprehensive insights.

Moreover, although pre- and post-stent evaluations following IVUS-guided CTO opening may not demonstrate apparent superiority over conventional angiography, a randomized controlled trial (RCT) revealed a significant finding. The group utilizing IV imaging exhibited lower rates of late lumen loss, indicating a potential benefit in terms of long-term outcomes.[20]

Management of In-Stent Restenosis

IV imaging guidelines are recommended IV imaging to define the pathophysiology of instent restenosis. IVUS imaging is particularly effective in identifying neointimal hyperplasia, stent under-expansion, and fractures. On the other hand, OCT imaging excels in identifying in-stent restenosis by offering detailed visualization of plaque morphology and detecting complications that may have occurred within the plaque. Angiographically, restenosis can manifest as focal, diffuse, involving stent edges, or even occlusive. In OCT imaging, four distinct plaque morphologies are observed: homogeneous, heterogeneous, layered, and attenuated plaque[22] (Figure 8);

1- The heterogeneous pattern features areas with low density and high attenuation on the luminal side, and high density and low attenuation on the abluminal side of the stents. Although not well-defined histologically, this appearance is believed to result from the presence of fibrin, organized thrombus, proteoglycan structures, and areas of inflammation, indicating early atherosclerotic changes (Figure 8b)[23],

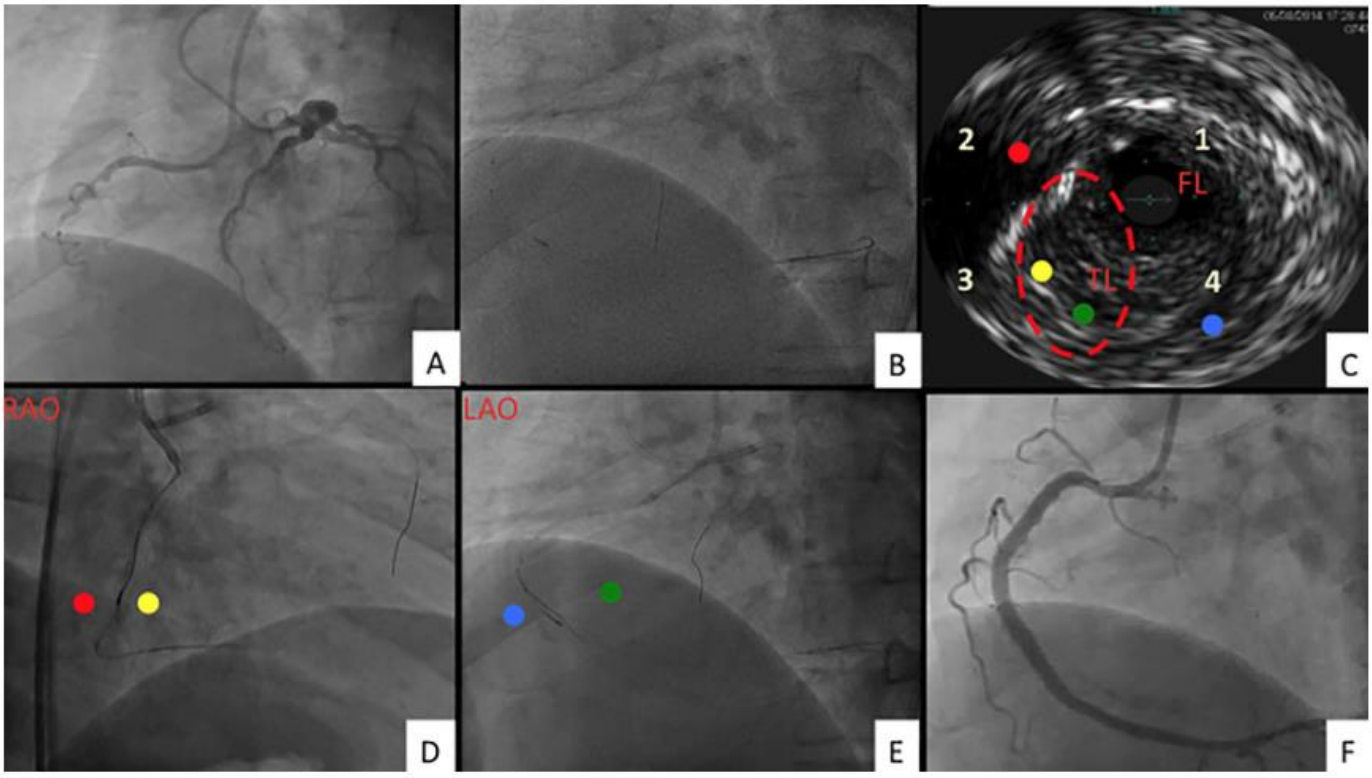

Figure 7. Wire navigation method with intravascular ultrasound (IVUS) guidance. The figure demonstrates the process of navigating the wire within the vessel. Utilizing IVUS imaging, the vessel is divided into four quadrants to identify the true lumen. Two different perpendicular angiographic images are correlated with IVUS images to guide the direction of a second wire towards the true lumen. Reproduced with permission.[21]

2- The layered pattern is characterized by high-density, low-attenuation areas on the luminal face and low-density, high attenuation in the region facing the stent (Figure 8c)[23],

3- The attenuated pattern represents plaque formation with high attenuation, indicating a higher content of lipid core (Figure 8d).[22]

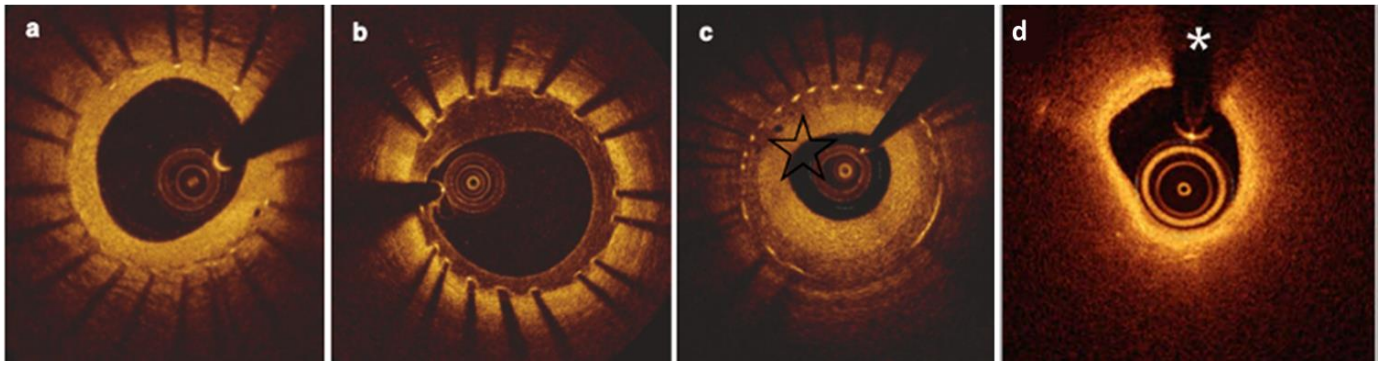

Figure 8. Illustrates homogeneous (a), heterogeneous (b), layered (c) and attenuated plaque (d) respectively. Reproduced with permission.[22,23]

In an OCT observational study based on prospective data, the most common plaque type associated with cardiovascular events was found to be heterogeneous plaque, accounting for 13.7% of cases. Conversely, homogeneous plaques had the lowest risk with only 2.9%. Notably, heterogeneous plaques were significantly associated with major adverse cardiovascular events (MACE), regardless of other contributing factors.[24]

Neo-atherosclerosis refers to the presence of a lipid layer containing foamy macrophages, calcification, and/or necrotic core within the neointima. It is a significant cause of late stent failure in drug-eluting stents (DES), leading to clinical events such as plaque rupture and thrombosis. Neo-atherosclerosis tends to occur earlier in patients with classical risk factors and DES compared to bare-metal stents (BMS). Therefore, strict control of risk factors and close follow-up are essential in nonobstructive cases with neo-atherosclerosis.[25]

In the context of restenosis at stent edges, two important causes are edge dissections and geographical miss. While IVUS may not always successfully demonstrate edge dissections, OCT provides highly detailed information in this regard (Figure 9).[26] Geographical miss, which can lead to edge dissection, poses a challenge in OCT due to the limited visualization of the EEM, especially in cases of attenuated plaque. Positive vessel remodeling can occur until the plaque burden reaches up to 40%. In preventing geographical miss, IVUS offers better resolution compared to OCT.[6]

Late-stage stent thrombosis can be attributed to two primary mechanisms. Firstly, it may result from the lack of proper tissue coating, which includes inadequate stent endothelialization (Figure 9, b), persistent malposition, or acquired malposition.[27,28] Secondly, neo-atherosclerosis also plays a role in late-stage stent thrombosis.[28,29]

Therefore, if the underlying cause of instent restenosis or late thrombosis cannot be determined through conventional angiography, intervening in these lesions may lead to a detrimental cycle, increasing the risk of recurrent instent restenosis and thrombosis in the future.

In order to unravel the mechanisms of instent restenosis or thrombosis using OCT, a comprehensive evaluation of stent expansion and apposition, plaque morphology, stent strut coverage, stent structure and alignment, and stent edges is crucial.[28]

Unveiling Post-Percutaneous Coronary Intervention Management: Intravascular Imaging beyond Conventional Angiography

Malaposition

Considering that almost only DES's are used in PCI today and strut thicknesses are reduced to 80-90 μm, the clinical important malaposition is defined as where malaposed segments longitudinal length is longer than 1 mm and struts are >400 μm far from the endothelium. Although the clinical evidence of persistent malaposition is contradictory[31], acquired malaposition has clinical impacts on late phase instent thrombosis. When the thrombus buried behind the stent melts with antiplatelet treatment in the following time this will cause late-term acquired malaposition, or the vessel undergoing negative remodeling in the chronic process returns to its normal state after stenting over time, or because of the positive remodeling, again acquired malaposition will occur. Another condition is that in some people, hypersensitivity or cytotoxic DES drugs can cause aneurysmal dilatation in the intima and can cause acquired malaposition. All of these conditions increase the risk of late stent thrombosis and restenosis in patients (Figure 9, c and d).[28]

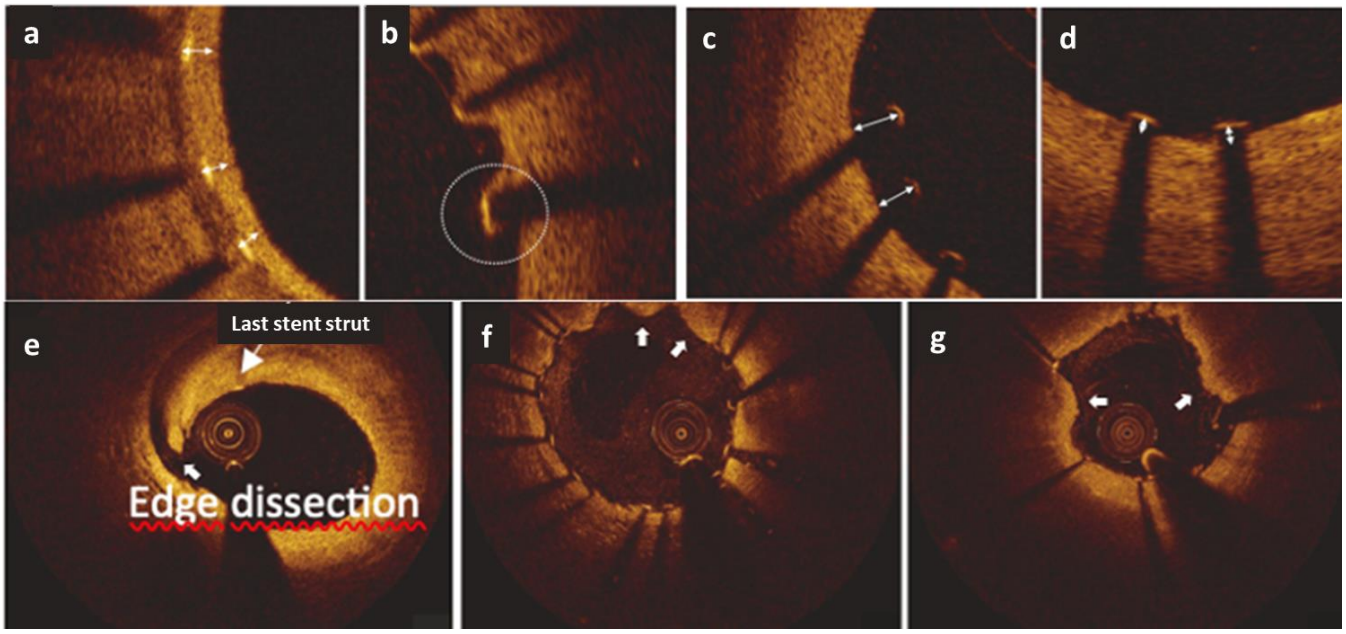

Figure 9. Depicts (a) normal stent coverage, (b) insufficient strut coverage, (c and d) different segments of stent malapposition, (e) edge dissection, (f and g) tissue prolapse. Reproduced with permission.[30]

Stent under-expansion

Stent under-expansion is an important parameter that increases instent restenosis and thrombosis.[32] (Although it is thought as malapposition, it is actually a parameter that indicates the status of the stent reaching the target diameter. Incomplete stent expansion is one of the most common causes of stent restenosis, especially in areas with dense plaque burden and calcific lesions.[33]

Edge Dissections

Clinically significant edge dissections have 2 features which are longer than >2 mm length, more than 60^0 degree in circular images and not limited by intima which may necessitate additional stent therapy (Figure 9, e).[26]

Tissue Protrusion

The clinical significance of tissue protrusion has not been established in studies examining clinical endpoints. However, if the protrusion disrupts flow or fails to reach the target MLA, additional angioplasty is recommended (Figure 9, f and g).

Stent Fracture

It is an interruption between the struts of the stent or the appearance of fewer stent struts in the suspicious area than in the area with a normal stent. IVUS and OCT both are good at stent fracture identification. Especially in bifurcation procedures or when the wire is lost and sent through the intrastent again, conventional angiography can never be sure whether the wire goes abluminal or not, especially in cases where the appropriate proximal optimization technique procedure is not performed. IV imaging is the most appropriate tool to prevent complications that may occur in the acute and chronic process by providing unique information especially in these cases.

CONCLUSION

IV imaging has demonstrated its clinical benefits in various lesion subsets through recent studies, leading to increased utilization in interventional cardiology over the past decade. It serves as the interventional cardiologist's eyes within the coronary vessels during procedures, influencing decision-

making and reducing the risk of complications. IV imaging plays a vital role in achieving long-term success in cases, empowering the operator to navigate procedures based on a clear understanding of the lesion using IV imaging.

Author Contributions

All authors have contributed to the content of this manuscript and reviewed the final version.

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