EuroIntervention

Is there still a role for intravascular ultrasound in the current practice era?

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Abstract

Although coronary angiogram is considered the gold standard for coronary assessment, it consistently underestimates vessel size/lesion severity, and usually misses heavy calcified plaques. Intravascular ultrasound (IVUS) technology accurately determines vessel size/lesion severity and allows a detailed plaque composition evaluation. The role of IVUS guidance after bare metal stent implantation has been explored in various trials; however, no study has tested how the pre-procedural use of IVUS might impact intervention strategy and clinical outcome. Limited studies have specifically addressed the utility of IVUS after drug-eluting stent implantation. Based on the published evidence and on our clinical experience, we support a more liberal use of IVUS, especially when approaching complex coronary lesions, and resulting in an optimal interventional result that might impact clinical outcome.

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Introduction

Although the benefit of drug-eluting stents (DES) in the treatment of native coronary artery lesions has been widely demonstrated in multiple clinical trials, concern remains regarding the risk of late stent thrombosis. Intravascular ultrasound (IVUS) technology is proven to be superior to coronary angiography for assessment of vessel size, plaque composition, calcium content and lesion severity.[1,2] The role of IVUS guidance after bare metal stent (BMS) implantation has been explored by various trials; however, no study has tested how the preprocedural use of IVUS might impact intervention strategy and clinical outcomes. Limited studies have specifically addressed the utility of IVUS after DES implantation. In this review, we examine the role of IVUS guidance for percutaneous coronary intervention (PCI) in the current practice era in view of the latest clinical evidence.

Evaluation of intermediate coronary lesions

Intermediate coronary lesions identified by angiography (40-70% angiographic stenosis) represent a challenge for revascularisation decisions. Coronary angiography, considered the standard for coronary evaluation, consistently and significantly underestimates lumen diameter when compared to IVUS measurements (Figure 1). Intermediate coronary lesions can be evaluated either anatomically by assessing the stenosis severity using IVUS, or physiologically by measuring the haemodynamic significance of a lesion using the coronary pressure wire-derived fractional flow reserve (FFR). Although anatomic evaluation does not provide direct estimation of haemodynamic significance of a coronary lesion, a combination of a minimal lumen area (MLA) <3.0-4.0 mm^2 and percentage area stenosis >60-70% has demonstrated good correlation with a FFR value <0.75.[3,4] Validated FFR data have shown that deferring interventions in lesions with intermediate severity – considered not haemodynamically significant (FFR>0.8) – have favourable clinical prognosis.[5] Similarly, Abizaid et al reported the clinical outcomes of 300 patients (357 intermediate native artery lesions) in whom intervention was deferred based on IVUS findings.[6] In 248 lesions with a MLA >4.0 mm^2, the rate of the composite endpoint was only 4.4%, driven primary by target lesion revascularisation (TLR) (2.8%) (Figure 2). As a result IVUS imaging appears to be an acceptable alternative to physiological assessment in patients presenting with intermediate coronary lesion.[6] The lack of randomised clinical trials comparing FFR to IVUS does not allow us to declare superiority of any of those technologies. However, IVUS and FFR should be considered complementary techniques that provide valuable, yet different information.

IVUS guidance for complex PCI

The results from different randomised clinical trials have demonstrated that routine IVUS guidance compared to angiography guidance for BMS placement decreases the rate of target vessel revascularisation (TVR) by optimising the stent's features after deployment.[7-10] Following the introduction of DES and the

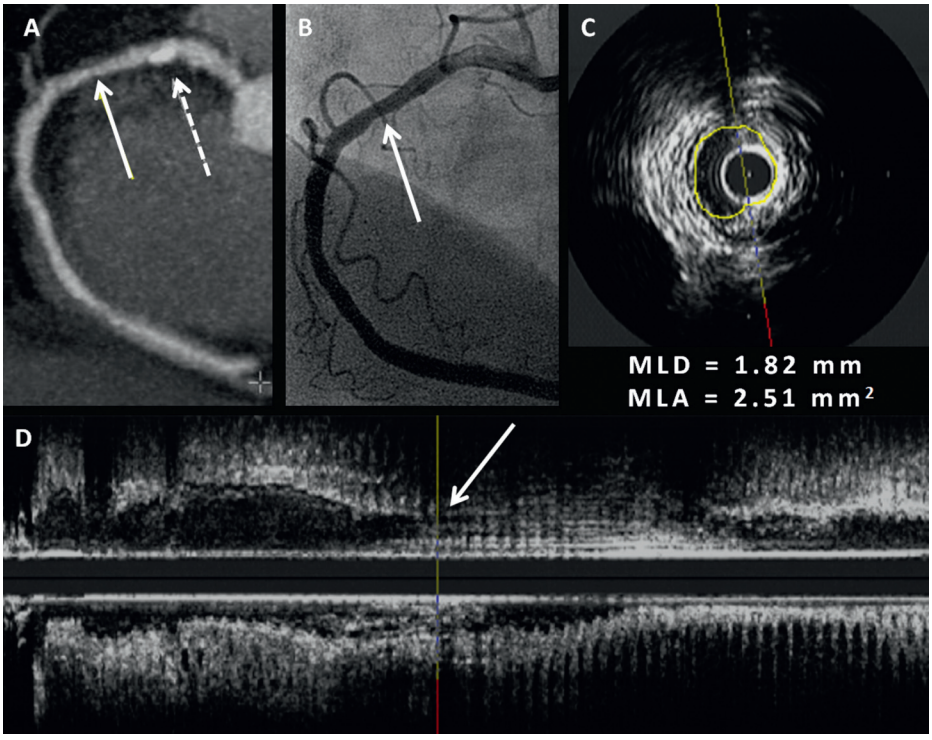

Figure 1. A. Multiplanar cardiac CT reconstruction showing the presence of a moderate stenosis caused by a non-calcified plaque (straight arrow), and a severely calcified lesion more proximal (dashed arrow) involving the proximal RCA. B. Angiography of same vessel showing the presence of a 30% stenotic lesion in the proximal RCA. C. Cross-sectional IVUS view of the pointed lesion (straight arrows) showing the presence of a mixed plaque that determines a severe stenotic lesion. D. Long IVUS run view of the RCA. CT: computed tomography; RCA: right coronary artery; MLA: minimum lumen area; MLD: minimum lumen diameter

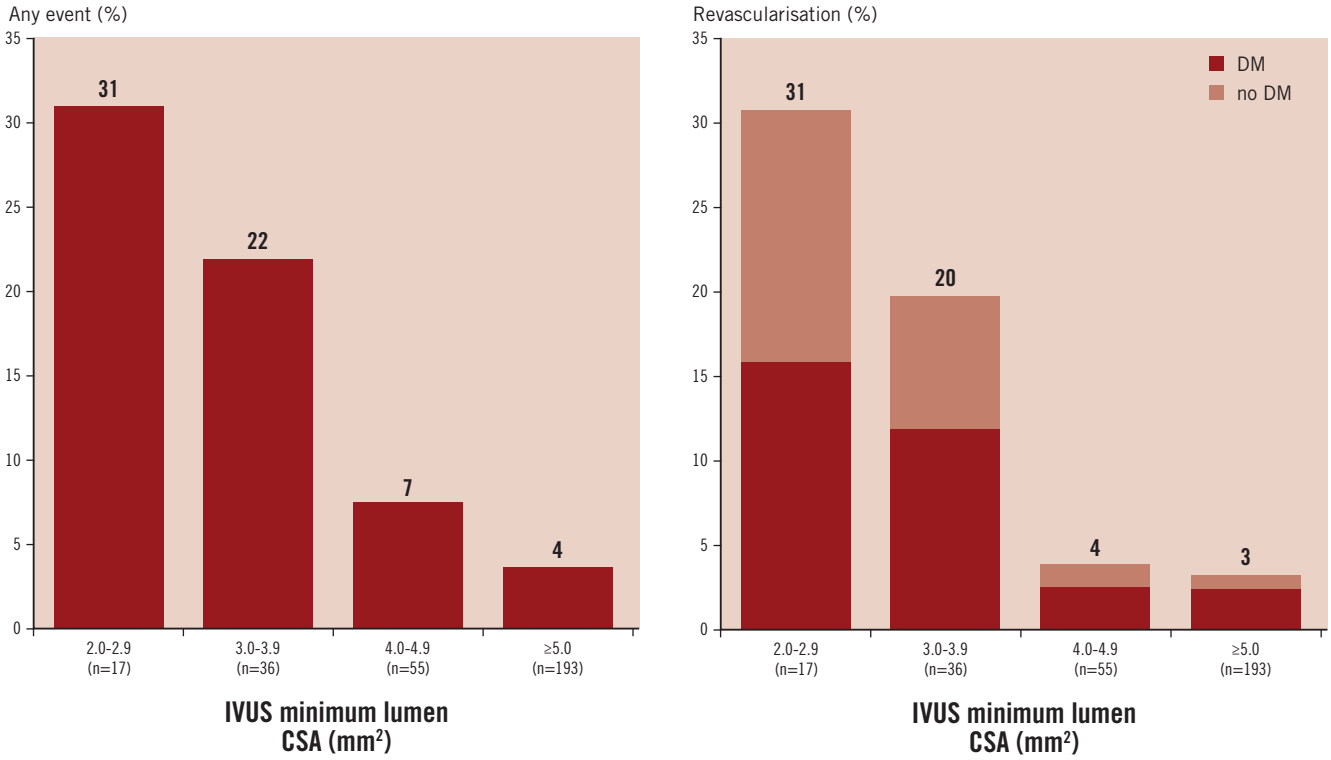

Figure 2. The occurrence of any event (death, MI, or revascularisation) decreased with increasing minimum lumen CSA and was similar in diabetics and nondiabetics. Target lesion revascularisation decreased with increasing minimum lumen CSA, but it was lower in nondiabetic than diabetic patients. DM indicates diabetes mellitus.[6]

subsequent decrease in the rate of in-stent restenosis (ISR), it has been suggested that the benefit related to IVUS guidance may be minimised. However, DES underexpansion is an important predictor for further stent failure and stent thrombosis (ST),[11,12] an issue of major concern after DES implantation. No study, however, has tested how the preprocedural use of IVUS might modify the intervention strategy, particularly when approaching complex coronary lesions, such as left main coronary artery (LMCA) stenosis, ostial lesions of large vessels, bifurcated lesions involving a large branch, undilatable lesions (heavily calcified plaques), degenerated saphenous vein grafts (SVG), or diffuse ISR. Additionally, no information is available on how IVUS guidance may impact the outcomes for these particular situations. Interestingly, Roy et al reported for first time in a retrospective propensity score matched population the potential benefit of routine IVUS guided implantation of DES, showing a significant decrease in the rate of acute ST.[13] Additionally, the recent results of the Revascularisation for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularisation (MAIN-COMPARE) registry showed a significant benefit with routine IVUS use for left main stenting.[14] Therefore, we advocate routine pre- and post-intervention IVUS guidance when approaching a complex coronary lesion.

Left main coronary disease

Left main coronary artery (LMCA) lesions are difficult to assess and characterise by angiography. In fact, the reliability of quantitative coronary angiography on the LMCA is worse than on any other coronary territories.[15] Therefore, IVUS appears to be a very useful tool for accurate assessment of the LMCA when the angiographic interpretation is ambiguous (Figure 3). Indeed, the MAIN-COMPARE registry reported that IVUS-guided stenting may reduce long-term mortality when compared to conventional angiography-guided stenting for unprotected LMCA stenosis.[14] In particular, in 145 matched pairs of patients receiving DES, the 3-year incidence of mortality was lower with IVUS guidance when compared to angiography guidance (4.7% versus 16.0%, log-rank p=0.048).[14] Clinical studies support that a minimum lumen diameter (MLD) <2.8 mm and/or a MLA <5.9 mm^2 predict haemodynamically significant LMCA lesions, with sensitivity and specificity above 90%[16] and adequately correlate with long-term clinical outcome as well.[17] From a practical point of view, we advise using a MLA of 6.0 mm^2 as a cut-off value for revascularisation decisions and routine use of IVUS guidance for PCI on LMCA.

Ostial lesions

IVUS can easily differentiate between true ostial lesions where the MLA and the maximum plaque burden are located at the ostium, and "pseudo-ostial" lesions, wherein it is possible to identify a proximal reference segment (Figure 4). We highly recommend the use of IVUS for all ostial lesions. Severe, concentric calcification is frequent in this location, especially when the lesion is aorto-ostial; and these lesions should never be stented without prior effective plaque dilation.

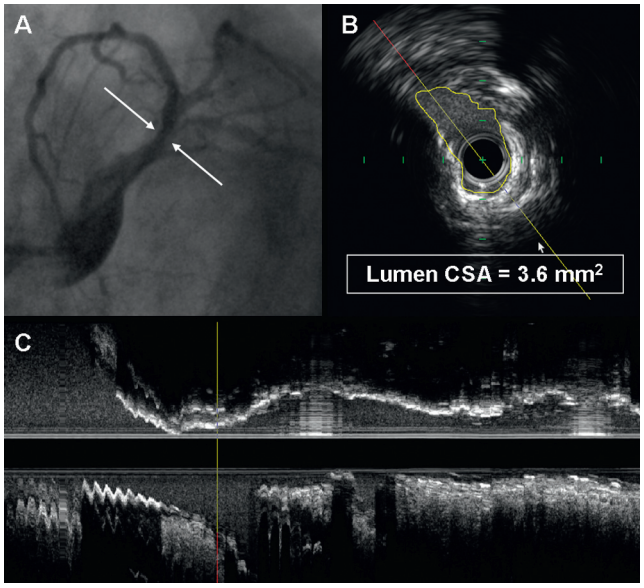

Figure 3. A. Coronary angiogram showing the presence of a hazy lesion involving the distal left main that determines as moderate stenosis (40%). B and C. IVUS imaging showing the presence of a severely calcified lesion that determines a severe stenosis (minimal cross sectional area of 3.6 mm²).

Bifurcation lesions

We also recommend IVUS use in most bifurcations to obtain images of both branches. The involvement of the side branch has been shown to increase the risk for side branch occlusion and myocardial infarction.[18] In an IVUS retrospective series of 81 bifurcated lesions undergoing PCI, Furukawa et al reported that the presence of plaque involving the side branch ostium was associated with side branch occlusion in 35% of cases vs 8% when the side branch was not involved (p=0.003).[19] Also it showed that angiography frequently failed to predict the extent of branch ostial involvement.[19] IVUS findings often lead to plaque modification with device before stenting the main branch (Figure 5).

Undilatable lesions

Severely calcified coronary lesions are frequently missed by angiography and their treatment using balloon angioplasty has been associated with decreased angiographic success and increased complications.[20] Stenting in these cases results in an unexpanded stent and higher rates of restenosis and thrombosis. Despite an apparently well inflated balloon, lesions with concentric calcium remain undilatable and should not be stented until well prepared by the use of atherectomy. Furthermore, the presence of long severely calcified coronaries might contraindicate PCI, preferring surgical revascularisation when feasible.

Saphenous vein grafts

Conventional angiography underestimates the severity of vein graft remodelling and athermanous plaque development compared to IVUS.[21] Morphologically, vein graft atherosclerosis tends to be diffuse, concentric, and friable, with a poorly developed or absent

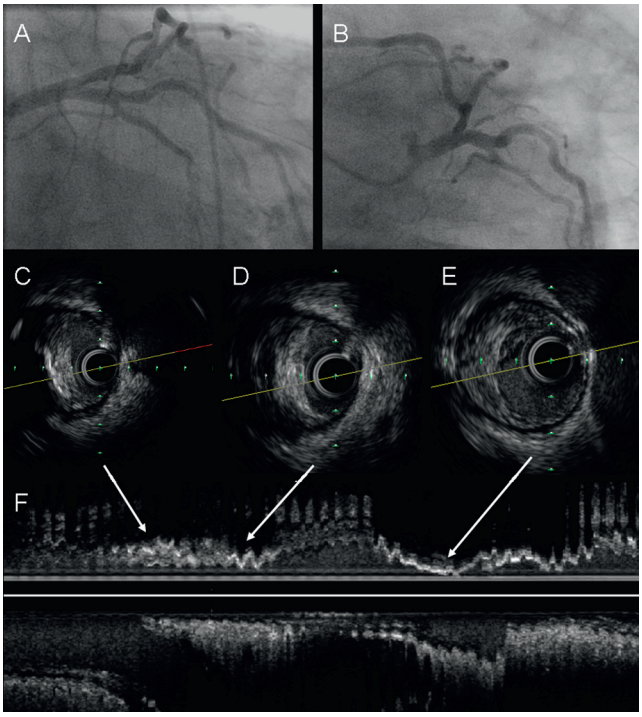

Figure 4. A sixty-five-year-old woman presenting with progressive shortness of breath and chest pain. Coronary angiogram showed the presence of mild disease involving the proximal left anterior descending artery (LAD) segment (A and B). IVUS imaging of the LAD showed the presence of an excentric, mixed plaque that determined a severe stenosis in the proximal segment (C and D) and a more distal, soft plaque (E), also missed by the angiography.

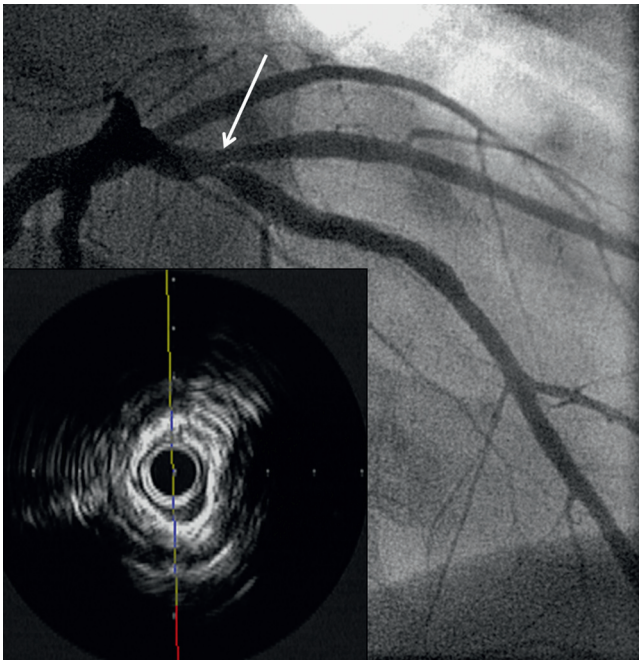

Figure 5. Coronary angiogram showing the presence of a lesion right after the origin of a large diagonal branch of the left anterior descending artery. IVUS imaging of the diagonal branch showed extensive compromise of the ostium, with unsuspected severe concentric calcium.

fibrous cap and little evidence of calcification. As a result, PCI of degenerative SVG represents a clinical dilemma since it is associated with a higher risk of distal embolisation, subsequent myocardial infarction (MI), and late cardiac events when compared to native vessel PCI.[22] Based on our published experience, we recommend a direct and undersized stenting approach with DES each time SVG PCI is performed.[23,24] In a clinical experience of 209 treated SVG, we observed that the undersized stenting approach, defined as stent size <89% of the reference lumen, was associated with a reduction in frequency of postprocedural CK-MB elevation, significantly less plaque prolapse shown by IVUS, and no increase in the rate of 1-year TLR.[24] Nonetheless, IVUS should not be used before stenting in extremely degenerated grafts. If the lesion is distally located in a vein graft, IVUS can be used proximally to assess vessel size. We recommend assessing the result after stenting by using IVUS. Lack of apposition of these undersized stents is frequent and not associated with adverse events.[24]

In-stent restenosis

IVUS is an essential tool in the evaluation of patients with ISR. We have demonstrated that 24% of patients referred for treatment of ISR did not have restenosis but had mechanical problems instead – most often under-expanded stents.[25] Additionally, when IVUS is performed before treatment of ISR it allows for an accurate assessment of the hyperplasia extent and the reference vessel. When approaching a BMS failure, after exclusion of a mechanical problem, DES implantation has become the standard recommended therapy; however, drug-coated balloons are under evaluation and seem to be a very attractive alternative to DES. In the case of DES failure the therapeutic approach represents a major dilemma since no evidence allows for recommendation of any particular treatment. Nevertheless, we believe that IVUS guidance will help to better therapy selection based on the possible underlying mechanism. When the ISR pattern appears focal (<10-20 mm) the more logical approach would be to perform high pressure balloon dilatation, ensuring the result by using IVUS. The implantation of a second DES, a technique commonly known as the "stent sandwich", has been used to treat DES restenosis despite the lack of clinical evidence. A double layer of non-resorbable polymer and sent strut overlap may delay stent endothelisation, the predominant aetiology implicated by late ST.[26] When dealing with diffuse DES restenosis (>20 mm) demonstrated by IVUS – large amount of neointimal hyperplasia that implies an exaggerated neointimal response to stenting – a different treatment modality such as brachytherapy, drug-coated balloon, or surgical revascularisation appears to be more attractive, depending on the local experience.

Optimising the post-procedural result

The role of IVUS in the optimisation of stent implantation has been established when IVUS observations revealed that incomplete stent apposition significantly contributes to early ST occurrence.[27] These observations lead to widespread adoption of high-pressure balloon post-dilatation after stent deployment. The results of several trials support the routine use of IVUS to ensure good stent expansion and apposition when using BMS.[7-10] However, with the emergence of DES and the significant decreases in late loss, various authors have suggested that routine IVUS guidance after DES deployment is not required. Nevertheless, incomplete stent expansion, procedural or acquired stent malapposition, and smaller minimum stent area after DES implantation measured by IVUS are reported to correlate with restenosis[11] and ST.[12] Additionally, using the traditional criteria for adequate stent expansion, defined per the Multicentre Ultrasound Stenting in Coronaries (MUSIC) study – final stent cross sectional area (CSA) >80% of the reference CSA (or >90% if reference CSA area was <9 mm^2)[28] – we reported significantly higher rates of stent underexpansion with sirolimus-eluting stents (SES) and paclitaxel-eluting stents at conventional delivery pressures.[29,30] Interestingly, Sera et al in a series of 28 lesions treated with SES, recently reported that the optimisation of the final minimum stent CSA using IVUS might contribute to complete neointimal coverage after SES implantation.[31] In view of this evidence, we support a more liberal use of IVUS to ensure an appropriate result after stent deployment, especially regarding the concerns raised when approaching complex coronary lesions or in patients who are theoretically at higher risk of ST.

Differential diagnosis of coronary artery disease

Conventional angiography depicts coronary anatomy from a planar two-dimensional silhouette of the lumen. Therefore when using only angiography, a variety of coronary conditions are misinterpreted as "normal" when in fact they are not. In this context, IVUS use might add important prognostic information and guide the appropriate therapy, as described for the following situations:

Myocardial infarction with "normal" angiography

The typical pathological process underlying MI is ruptured plaque and thrombus formation and/or lumen compromise, usually identified by angiography as complex coronary lesions. Nevertheless, some conditions may present clinically as MI with apparently normal coronaries on angiogram, such as spontaneous dissections, coronary spasm – especially related to the cocaine abuse – and "silent" ruptured plaques, conditions that are better recognised and differentiated by IVUS.

Angiographic filling defects

Although most of the angiographic filling defects correspond to thrombi, a percentage of them are represented by different calcified plaques patterns. In a retrospective analysis of 78 angiographic filling defects, 48 (61.5%) had IVUS evidence of thrombus and 30 did not (38.5%).[32] Thirteen (16.7%) were calcified plaques on IVUS not seen angiographically. Additionally, of the 48 IVUS thrombus-containing lesions, nine (18.8%) showed thrombus superimposed on calcified plaque.

Angiographic haziness

Angiographic hazy lesions can represent the full spectrum of morphologies, including calcium, thrombus, dissections, and large plaque burden with positive remodelling.

Therefore, we propose a more liberal use of IVUS for patients presenting with ambiguous angiographic coronary lesions and/or who are undergoing potentially complex interventions to improve diagnostic accuracy and appropriate guidance.

Post-intervention complications

The rate of persistent angiographic haziness proximal or distal to the stent has seen to be is about 15% after high-pressure stent deployment. Stent edge dissection is the most common reason; however other conditions such as thrombus, calcification or material prolapse could be distinguished by IVUS and further treated if necessary. Stent edge dissection is a frequent phenomenon detected by IVUS and does not necessarily proscribe an adverse prognosis. Indeed, Nishida et al reported the results of 124 consecutive native coronary lesions with angiographic non-obstructive residual dissection in 97 patients compared with 124 lesions in 100 matched patients without residual dissection.[33] They observed that most non-flow-limiting residual dissections that occur after successful PCI have a good long-term prognosis and do not need additional stenting. More importantly, IVUS examination identified an area stenosis >60% at the site of dissection to be the best threshold for distinguishing patients who had in-hospital major adverse cardiac event.[33] Therefore, we encourage IVUS guidance for complications encountered after PCI, especially to prevent unnecessary deployments of additional stents.

Conclusions

As a result of our clinical experience and the evidence provided, we strongly support the use of IVUS. Routine use of IVUS, especially when approaching complex coronary lesions, allows for better definition of the nature of the disease, thereby leading to a more tailored and focused therapeutic strategy resulting in optimal interventional result. As new therapies become available – where efficacy is the main objective, but safety is the major concern – we do believe that IVUS has still a major role in the current PCI practice era.

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