Intravascular Ultrasound for Guidance and Optimization of Percutaneous Coronary Intervention

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KEYWORDS

• Intravascular ultrasound • Percutaneous coronary intervention • Drug-eluting stent
• Major adverse cardiac events • Minimum lumen diameter • Minimum lumen area • Planimetry

KEY POINTS

- Conventional angiography provides a 2-dimensional silhouette that delivers a suboptimal assessment of true physiologic coronary artery stenosis.
- Intravascular ultrasound allows visualization of the trilaminar coronary vasculature, permitting better delineation of the quantity and quality of plaque burden.
- Clinical outcomes with intravascular ultrasound-guided interventions have revealed improved results, especially for complex and long coronary artery lesions.
- Parameters measured by intravascular ultrasound show modest correlation with other investigatory modalities.
- The use of intravascular ultrasound during routine percutaneous coronary intervention is not widely adopted, which may be in part due to equipment costs and increased procedural times.

BACKGROUND

Coronary angiography with percutaneous coronary intervention (PCI) is considered the reference standard for management of symptomatic stable coronary artery disease refractory to optimal medical management, and acute coronary syndromes.[1,2] Although conventional angiography has been used as the predominant technique to define the coronary anatomy and guide PCI, several shortcomings of this modality hinder achieving optimal results. Questions about the accuracy of coronary angiography dates to the 1970s, when researchers investigated discrepancies between a coronary lesion's appearance on angiography compared with its true physiologic effects on the myocardium.[3,4] Conventional angiography is limited by a 2-dimensional projection of the arterial lumen as well as complexity of coronary lesions, such as tortuosity or overlap of structures.[5,6] Studies have shown that there is a large degree of

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interobserver and intraobserver variability in assessing the degree of coronary stenosis.[7–9] The conventional methodology of quantifying stenotic lesions via their angiographic appearance relies heavily on the surrounding "nondiseased" lumen, which serves as the reference segment. However, because of diffuse involvement of the atherosclerotic disease process, a reference "nondiseased" segment is often unavailable.[10,11] The 2-dimensional planar silhouette during angiography in conjunction with a diffuse and symmetrically diseased artery poses a challenge for true physiologic assessment of a stenotic coronary lesion. Furthermore, this suboptimal visualization of stenotic lesions is compounded when PCI is performed under angiographic guidance. Conventional angiographic guidance may prohibit accurate deployment of balloons and sizing of stents, which may result in downstream complications, such as in-stent restenosis (ISR) or late stent thrombosis.[12–14] Because of the need for better visualization and improved understanding of the anatomic alterations that occur during PCI, intravascular ultrasound (IVUS) emerged as a valuable adjunct to conventional angiography.

ADVANTAGES OF INTRAVASCULAR ULTRASOUND

The use of IVUS as an adjunct imaging modality offers several advantages over conventional angiography. Compared with the 2-dimensional luminal silhouette created during angiography, IVUS offers visualization of the full circumference of the vessel wall. This improved visualization offers better characterization of coronary plaque via accurate assessment of the severity, length, morphology, and composition of the plaque. The direct cross-sectional view of the arterial wall produced by this technology provides higher sensitivity in detection of coronary artery disease. IVUS allows the operator to reliably detect complex coronary lesions, dissections, small thrombi, positive arterial wall remodeling during early atherosclerosis, and even diffuse advanced disease within the vessel wall that are otherwise challenging to detect only under angiographic guidance.[15]

In addition, IVUS offers more precise stent deployment during PCI by ensuring proper expansion, length, and apposition of the stent. Multiple studies have demonstrated the importance of these measures during PCI. Two major predictors of ISR and stent thrombosis include stent underexpansion and "geographic miss."[16,17] Smaller intrastent minimum lumen area (MLA) results from stent-underexpansion, whereas the concept of "geographic miss" refers to residual plaque edge that remains uncovered after stent deployment. Multiple analyses have shown that adjunctive use of IVUS during PCI resulted in larger stent sizes, greater final angiographic minimum lumen diameter (MLD), and larger minimum stent area.[18,19] When compared with dilation under angiographic guidance, the use of IVUS resulted in additional stent postdilation in as high as 80% of the cases.[20] All of these findings may be attributed to more accurate assessment of stent geometry, as visualized under IVUS guidance. IVUS-guided PCI has also been shown to use less contrast during stent deployment, which is advantageous in patients with renal insufficiency and in prevention of contrast-induced nephropathy.[21,22] Finally, perhaps one of the major benefits of IVUS-guided stenting is that the enhanced information from IVUS imaging may convince the operator that the result is already optimal, and that more intervention is no longer necessary. As the saying goes, "The enemy of 'good' is 'better'"; problems of inappropriate intervention may be averted by using IVUS imaging.

TECHNIQUE AND BASIC MEASUREMENTS

The IVUS catheter diameter ranges from 2.6 to 3.5 French with a miniaturized ultrasound transducer at its end, which is advanced over a guidewire and positioned to analyze the target lesion. High ultrasound frequencies, usually between 20 and 60 MHz, are used to provide grayscale images from the backscatter amplitude of the signal as the transducer rotates at 1800 rpm. Instead of a mechanically rotating transducer, images can be obtained with a synthetic aperture, but the image quality is not equal to the mechanically rotating transducer devices. Standard catheter delivery technique is used for IVUS examination, whereby the target coronary artery is cannulated, the IVUS probe is slowly advanced over the guidewire, and motorized or manual pullback is performed to record the desired segment.[23]

A normal arterial appearance is generated as a result of an abrupt change in acoustic impedance at the tissue interface within the trilaminar vessel wall. The first interface observed is at the border between blood and the leading edge of intima that appears bright. The second interface occurs at the external elastic membrane (EEM), which comprises the junction between media and adventitia. The muscle layer of the tunica media has a sonolucent appearance, whereas the outer adventitia layer appears bright or white on a grayscale image (Fig. 1).

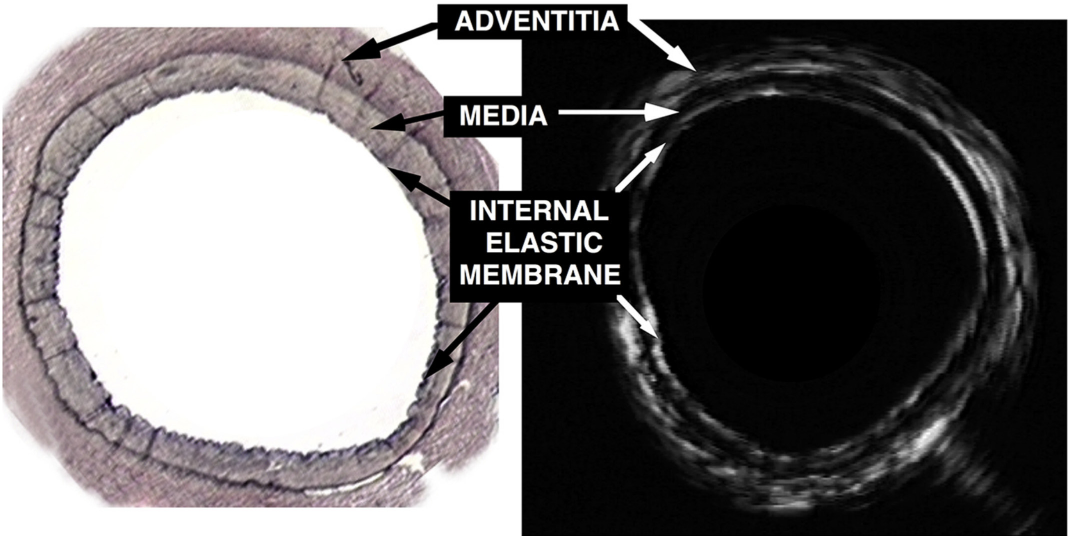

Fig. 1. IVUS image morphology of a nondiseased coronary artery (*right*) compared with its histologic cross-section (*left*). The 3 layers of the coronary artery are illustrated. The interface between the lumen and internal elastic membrane (inner layer) is the location of potential atherosclerosis. The dark sonolucent middle layer is the media, which outlines the size of the vessel in a nondiseased state. The outermost layer is the adventitia.

Planimetry is used to measure the atheroma area by subtracting the lumen area outlined by the intimal leading edge from the area surrounded by the EEM. The ratio between the plaque area measurement at the proximal reference area compared with the plaque area at the tightest lesion determines the significance of the stenosis. In general, 60% lumen area stenosis via IVUS measurements is considered significant.[24] Another measurement commonly performed is known as the MLA, which is an absolute value of the lumen area rather than a ratio compared with a reference segment. This measurement is made at the narrowest point in the epicardial vessel. Generally, MLA less than 4.0 mm^2 in the proximal epicardial vessels and less than 6.0 mm^2 in the left main vessel are considered significant.[25,26] A third measure of atheroma severity is the plaque burden. The plaque burden compares the total atheroma area at an individual cross-section divided by the total vessel area defined as the area subtended by the EEM. Studies have shown that total plaque burden and MLA are predictors of future clinical events.[27]

OPTIMIZATION OF STENT IMPLANTATION

The process of optimizing stent implantation begins during the preimplantation stage and continues during stent deployment as well as postimplantation. Before stent deployment, IVUS can be used to assess the lesion and surrounding anatomy, to create precise measurements of the reference segment, which further guides device selection and sizing of balloons and stents.[28] IVUS grayscale can also reveal important characteristics of the type of tissue that constitutes the atherosclerotic plaque (Fig. 2). IVUS is very sensitive to the presence of calcium and can reveal the relative hardness of a lesion, which may influence the choice of device, such as rotational atherectomy. During the stent deployment stage, IVUS guidance can assist with predilation, proper positioning of the balloon in relation to stent struts, and proper deployment of stents, thereby minimizing stent underexpansion or incomplete stent apposition. Last, after stent implantation, IVUS can aid in uncovering and treating complications, such as stent edge dissections, geographic mismatch, or plaque protrusion through the stent.

Several studies have evaluated the use of IVUS guidance on stent implantation, but definite guidelines regarding IVUS-guided stent optimization are lacking. Hence, stent optimization is often left to the discretion of the individual operator,[29] although generalized optimization criteria exist based on previous trials. For example, $(EEM^{ref}{}_{proximal} + EEM^{ref}{}_{distal})/2$ or $EEM^{ref}{}_{distal}$ are 2 of the most common computations used to estimate the balloon diameter.[30,31] Similarly, IVUS criteria for optimal stent implantation, first established by the Multicenter Ultrasound Stenting In Coronaries Study investigators, includes MLA greater than 80% of the average reference lumen

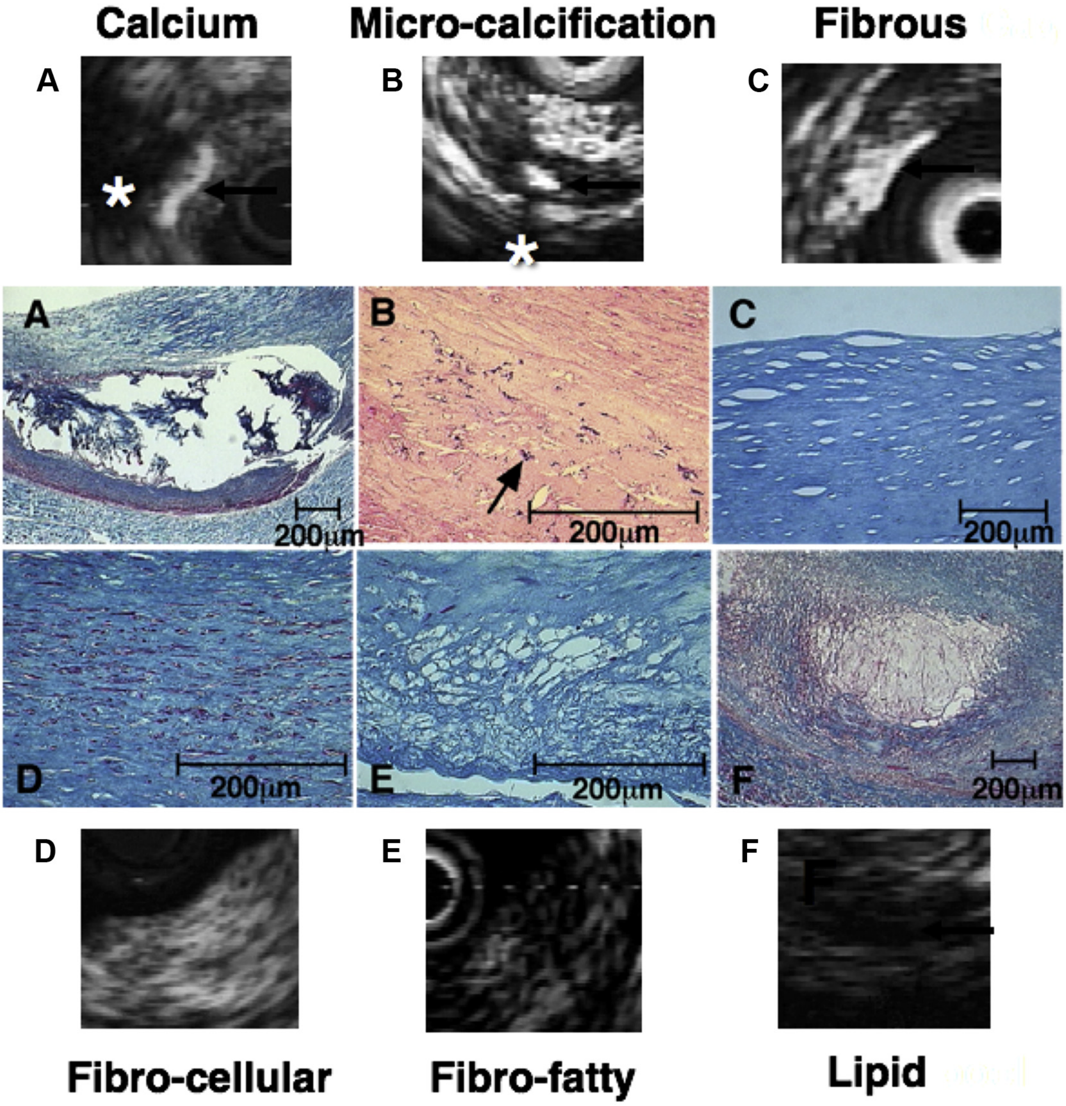

Fig. 2. Tissue characterization by IVUS compared with the corresponding hematoxylin and eosin histopathology. IVUS can be useful in detecting plaques of different morphologies, including plaque consisting of calcium (*A*), microcalcification (*B*), fibrous (*C*), fibrocellular (*D*), fibrofatty (*E*), and lipid-rich (*F*) material. Calcium deposits (*black arrows*) with IVUS appear as echogenic superficial reflections followed by an acoustic shadow (*asterisks*), both of which prevent thickness assessment.

area or greater than 90% of lumen area of the reference segment with the lowest lumen area.[32] By using the motorized transducer pullback method on IVUS, the distance between the distal and proximal landing zone can be measured, which estimates the optimal length for the stent to be deployed.[29] Complete stent apposition, minimal stent area (MSA) >90% of mean MLA^{ref}, or greater than 100% minimum MLA^{ref} is usually considered one of many acceptable criteria for optimal stent expansion.[32] Evaluation of IVUS-guided stent expansion in the era of bare-metal stents (BMS) was evaluated by Fitzgerald and colleagues[33] in the Can Routine Ultrasound Influence Stent Expansion study. The findings of this multicentered, randomized controlled trial showed that as compared with coronary angiography, addition of IVUS guidance was associated with larger MLD and MSA, which translated into clinically and statistically significant lower rates of target vessel revascularization (TVR). Gil and colleagues[34] showed similar findings in their multicenter, randomized, prospective trial, which demonstrated that, compared with angiographic guidance, IVUS-guided stent implantation resulted in the greatest lumen gain

(MLD) along with significant reduction in composite major adverse cardiac events (MACE). Robust evidence regarding superior stent expansion and apposition with IVUS optimization has been presented by other researchers as well.[35,36]

INTRAVASCULAR ULTRASOUND GUIDANCE DURING BARE-METAL AND DRUG-ELUTING STENT IMPLANTATION

During the era of BMS, the use of IVUS was first studied by Nakamura and colleagues. Although not powered for hard clinical endpoints, the investigators found that IVUS guidance resulted in larger minimum luminal diameter (MLD) during the index procedure and reduction in restenosis rates during the 6-month follow-up period.[20,37] In addition, by maximizing the lumen cross-sectional area, there was significantly less acute stent thrombosis such that the extended use of anticoagulation was no longer necessary. The lower incidence of acute stent thrombosis and freedom from extended use of anticoagulation revolutionized coronary artery stenting and lead to its general acceptance. Similar findings were suggested by a large meta-analysis of 8 randomized trials that demonstrated IVUS-guided BMS implantation was associated with lower rates of MACE.[38]

With the widespread use of drug-eluting stents (DES), which have a lower rate of restenosis compared with BMS,[39,40] there was concern that the use of IVUS guidance during PCI in the DES era would reap no additional benefit. These initial speculations were met with mixed results from several randomized controlled trials (Table 1). Jakabcin and colleagues[41] conducted a trial consisting of 210 patients who were randomized to DES implantation with or without IVUS guidance. At an 18-month follow-up, the investigators found that there was no significant difference in MACE or stent thrombosis between the 2 groups. A prospective, randomized trial of IVUS-guided compared with angiography-guided stent implantation in complex coronary lesions (AVIO) trial by Chieffo and colleagues[42] was a larger trial consisting of 284 patients with primary endpoint being improvement in postprocedure MLD. Secondary endpoints of this study were outcomes of MACE, TLR, TVR, myocardial infarction (MI), and stent thrombosis. The study demonstrated a benefit with IVUS guidance in regards to the primary outcome. However, no statistically significant difference was appreciated in the secondary outcomes, including MACE. The Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions (IVUS-XPL) was the largest, randomized, multicenter trial on this topic.[43] This trial enrolled 1400 patients with long coronary lesions, defined as ≥28 mm in length. At 1-year follow-up, IVUS guidance was superior to angiographic guidance in terms of TLR (2.5% vs 5.0%; hazard ratio [HR] = 0.51; confidence interval [CI] = 0.28–0.91; *P* = .02), whereas there was no significant difference in cardiac death and MI.

The Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents (ADAPT-DES) was a large study of ∼8600 patients who received second-generation DES. ADAPT-DES was a prospective, multicenter, nonrandomized trial wherein the investigators performed a propensity-adjusted analysis to assess the relationship between IVUS use and clinical outcomes at 1-year follow-up. ADAPT-DES demonstrated superiority of IVUS-guided PCI compared with conventional angiography; the IVUS group demonstrated a significantly lower risk of stent thrombosis (0.6% vs 1.0%; HR = 0.40, CI = 0.21–0.73, *P* = .003), MI (2.5% vs 3.7%, HR = 0.66, CI = 0.49–0.88, *P* = .004), and composite MACE (3.1% vs 4.7%, HR = 0.70, CI = 0.55–0.88, *P* = .002) (Fig. 3).[44] The investigators noted that risk reduction was significant in all groups but was remarkably apparent in the patients with complex lesions or acute coronary syndrome presentation. The use of IVUS resulted in additional optimization during PCI as larger-sized stents/balloons, higher inflation pressures, and longer stents were used. Additional postdilation was also performed during PCI under IVUS guidance. Although favorable outcomes were applauded, critics noted the observational nature of the study along with the decision to use IVUS being left to the operator's discretion, thereby potentiating unmeasured confounders.

ADAPT-DES was followed by several well-conducted meta-analyses, which have brought further clarity to this subject by showing improvement in MLD and restenosis rates with IVUS-guided DES PCI[18,19,45,46] (Table 2). Elgendy and colleagues[47] conducted a meta-analysis of 7 randomized trials with 3200 patients treated with first- or second-generation DES. At a 15-month mean follow-up, patients in the IVUS-guided group experienced a significant reduction in risk of MACE (6.5% vs 10.3%; odds ratio = 0.60; CI = 0.46–0.77; *P*<.0001) because of reduction in TLR (4.1% vs 6.6%; *P*<.0001), whereas only a marginal reduction was seen in stent thrombosis (0.6% vs 1.3%; *P* = .04) and cardiovascular mortality (0.5% vs 1.2%; *P* = .05). In a patient level analysis of

Table 1
Randomized clinical trials comparing drug-eluting stent implantation with intravascular ultrasound guidance versus conventional angiographic guidance

Reference, Year	Design	Lesion Type	DES Type	1-y Outcome	MACE Definition	Follow-up (mo)	Results
Zhang et al,[46] 2015	Single center	Small lesion[a]	Second generation	Postprocedure in lesion MLD	Cardiac death, MI, or TVR	12	Significant reduction in MACE with IVUS
IVUS-XPL4,[43] 2015	Multicenter	Long coronary lesions	Second generation	MACE	Cardiac death, TLR-related MI, or TLR	12	MACE was lower in IVUS-guided group
CTO-IVUS,[53] 2015	Multicenter	CTOs	Second generation	Cardiac death	Cardiac death, MI, or TVR	12	No significant difference in cardiac death between the 2 groups
AIR-CTO,[54] 2015	Multicenter	CTOs	First/second generation[e]	In-stent LLL	Death, MI, TLR, or ST	12	In-stent LLL was significantly lower in the IVUS-guided group
Tan et al,[61] 2015	Single center	Unprotected left main coronary lesions	First generation	MACE	Cardiac death, MI, or TLR	24	IVUS-guided group had significantly lower rate of MACE
RESET,[80] 2013	Multicenter	Long coronary lesions[b]	Second generation	MACE	Cardiac death, MI, ST, or TVR	12	No statistically significant differences between rates of MACE between the 2 groups
AVIO,[42] 2013	Multicenter	Complex lesions[c]	First generation	Postprocedure in lesion MLD	Cardiac death, MI, or TVR	24	Statistically significant benefit in postprocedure MLD was seen with IVUS guidance
HOME DES IVUS,[41] 2010	Single center	Complex coronary lesion or complex patients' characteristics[d]	First generation	MACE	Death, MI, TLR	18	No significant difference between both groups in terms of MACE

Abbreviations: CTO, chronic total occlusion; LLL, late lumen loss; ST, stent thrombosis; TLR, target lesion revascularization.

[a] Small vessel (diameter 2.25–2.75 mm).

[b] Implanted stent greater than 28 mm in length.

[c] Bifurcations, long lesions, CTOs, or small vessels.

[d] Lesion type B2 and C according to the American Heart Association, proximal left anterior descending artery, left main disease, reference vessel diameter less than 2.5 mm, lesion length greater than 20 mm, ISR, insulin-dependent diabetes mellitus, and acute coronary syndrome.

[e] 76% first generation, and 24% second generation.

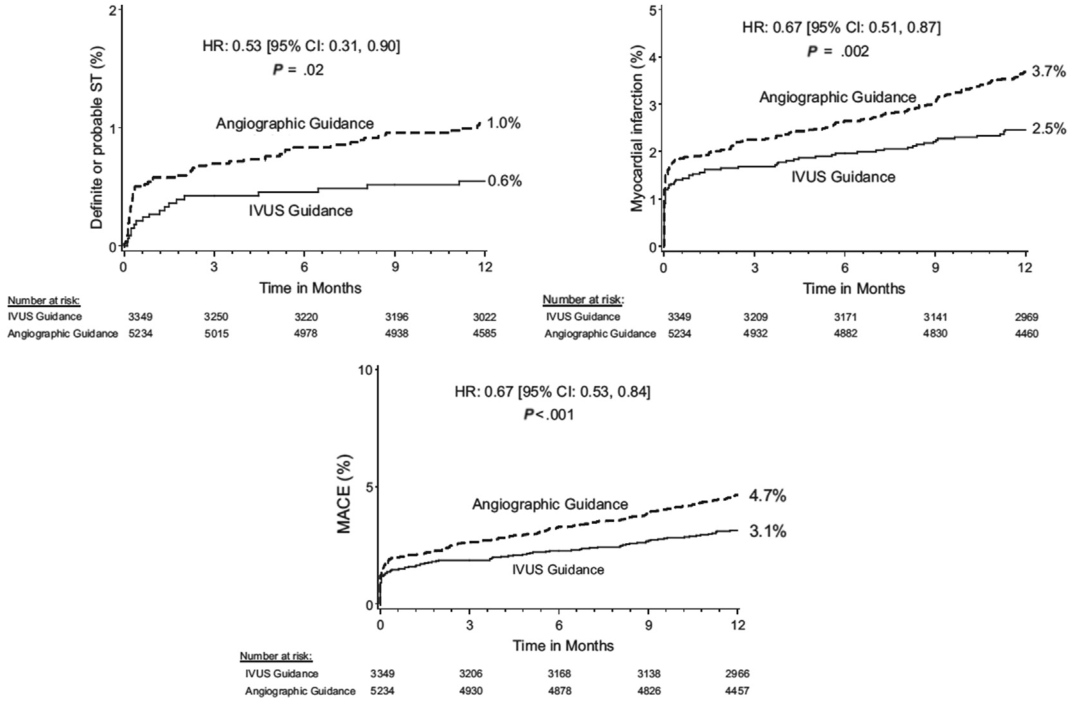

Fig. 3. IVUS versus angiographic guidance: time-to-event curves for stent thrombosis (*top left*), MI (*top right*), and MACE (*bottom*) within 1-year follow-up period. (*From* Witzenbichler B, Maehara A, Weisz G, et al. Relationship between intravascular ultrasound guidance and clinical outcomes after drug-eluting stents: the assessment of dual antiplatelet therapy with drug-eluting stents (ADAPT-DES) study. Circulation 2014;129:468; with permission.)

3 randomized controlled trials including 2345 patients who underwent second-generation DES implantation,[48] use of IVUS was associated with a reduction in risk of composite cardiac death, MI, and stent thrombosis when compared with conventional angiography (0.4% vs 1.2%, P = .04). The risk reduction in MI remained even at 1-year follow-up. A meta-regression analysis of 14 randomized trials showed that benefit of IVUS guidance was enhanced for longer lesions. For every 10-mm increase in lesion length, IVUS-guided PCI resulted in a 19% decrease in MACE.[49]

INTRAVASCULAR ULTRASOUND GUIDANCE DURING PERCUTANEOUS CORONARY INTERVENTION OF CHRONIC TOTAL OCCLUSION

Several studies have investigated the role of IVUS during CTO interventions. IVUS-guided imaging via a side branch may visualize the entry site of the occluded cap, which may facilitate the CTO recanalization process.[50–52] The influence of IVUS guidance on clinical endpoints was first tested by researchers of The Chronic Total Occlusion Intervention with Drug-eluting Stents (CTO-IVUS) trial.[53] CTO-IVUS was a multicenter, prospective, randomized controlled trial that compared CTO patients who underwent angiography-guided intervention versus IVUS-guided intervention after successful guidewire crossing. The primary endpoint was cardiac death, and the secondary endpoint was MACE, consisting of cardiac death, MI, and TVR. During the 12-month follow-up period, there was a significant reduction in MACE in the IVUS-guidance group compared with the angiography-guidance cohort (2.6% vs 7.1%, P = .035). Another large randomized controlled trial, The Angiographic and Clinical Comparisons of Intravascular Ultrasound Versus Angiography-Guided-Drug-Eluting Stent Implantation for Patients with Chronic Total Occlusion Lesions (AIR-CTO), was recently published.[54] Researchers evaluated differences in LLL after CTO intervention via angiography-guided versus IVUS-guided approach. The results of this trial were in line with lower rates of LLL, ISR, and stent thrombosis with an IVUS-guided approach compared with patients who underwent CTO PCI under conventional angiography guidance. Unfortunately, because of the small number of patients enrolled, improvement in these parameters did not translate to hard clinical outcomes, such as a reduction in MACE. Interpretation of

Table 2
Meta-analyses comparing stent implantation with intravascular ultrasound guidance versus conventional angiographic guidance

References	Patients	Studies	Stent Type	MACE	All-Cause Mortality	MI	ST	TLR	TVR
Bavishi et al,[78] 2017	3276	8 RCTs	DES	0.64 (0.51–0.80) *P* = .001	0.51 (0.23–1.12) *P* = .09	0.90 (0.58–1.41) *P* = .70	0.57 (0.26–1.23) *P* = .15	0.62 (0.45–0.86) *P* = .004	0.60 (0.42–0.87) *P* = .007
Elgendy et al,[47] 2016	3192	7 RCTs	DES	0.59 (0.46–0.76) *P*<.001	0.46 (0.21–1.00) *P* = .05	0.58 (0.030–1.11) *P* = .06	0.49 (0.24–0.99) *P* = .04	0.60 (0.43–0.84) *P* = .003	0.61 (0.41–0.91) *P* = .02
Shin et al,[48] 2016	2345	3[a] RCTs	DES	0.36 (0.13–0.99) *P* = .04	0.38 (0.10–1.42) *P* = .134	NR *P* = .026	0.50 (0.13–2.01) *P* = .320	0.61 (0.40–0.93) *P* = .02	NR
Steinvil et al,[79] 2016	31,283	7 RCTs and 18 observational	DES	0.76 (0.70–0.82) *P*<.001	0.62 (0.54–0.72) *P*<.001	0.67 (0.56–0.80) *P*<.001	0.58 (0.47–0.73) *P*<.001	0.77 (0.67–0.89) *P* = .005	0.85 (0.76–0.95) *P* = .005
Parise et al,[38] 2011	2193	7 RCTs	BMS	0.69 (0.49–0.97) *P* = .03	1.48 (0.81–2.69) *P* = .18	0.67 (0.34–1.34) *P* = .51	NR	0.66 (0.48–0.91) *P* = .004	NR

Data presented as relative risk of events and 95% confidence intervals after IVUS-guided versus conventional angiographic guided.
P value <.05 is significant.
Abbreviations: NR, not reported; RCTs, randomized control trials; ST, stent thrombosis.
[a] Patient level analysis.

the CTO anatomy and how to use IVUS to optimize the intervention requires experience and dedicated training. Along with this, future larger trials are needed to better determine the clinical outcomes with IVUS-guided PCI of CTO lesions.[55]

INTRAVASCULAR ULTRASOUND DURING LEFT MAIN CORONARY ARTERY INTERVENTIONS

Visualization and assessment of the left main coronary artery (LMCA) often present a unique challenge for several reasons. The LMCA may be a short vessel, which does not provide the observer with a normal segment for comparison. The aortic cusp may obscure visualization of the LMCA ostium under conventional angiography, and delineation of the distal LMCA is often hindered by the downstream bifurcation or trifurcation.[56] Thus, the addition of IVUS to conventional angiography for LMCA assessment has been studied with interest. The Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) and Coronary Artery Bypass Grafting versus Drug Eluting Stent Percutaneous Coronary Angioplasty in the Treatment of Unprotected Left Main Stenosis (NOBLE) were 2 randomized trials that compared PCI using DES to coronary artery bypass surgery (CABG) for LMCA revascularization.[57,58] Although EXCEL found PCI and CABG to be comparable, the results of NOBLE favored CABG. The difference in outcomes of these trials may partially be explained by more frequent use of IVUS in the EXCEL trial, suggesting that IVUS-guided LMCA intervention may be superior to conventional angiography alone.[59] This speculation is supported by 2 midsize propensity-matched analyses, which were conducted in Spain and Korea.[26,60] These studies showed better outcomes with IVUS-guided unprotected LMCA PCI compared with conventional angiography. Superiority of IVUS-guided unprotected LMCA intervention was further confirmed by a small randomized trial by Tan and colleagues.[61] This study showed that the incidence of TLR was lower in the IVUS-guided unprotected LMCA PCI group and that IVUS guidance was an independent factor in survival free of MACE at a 2-year follow-up.

ROLE OF INTRAVASCULAR ULTRASOUND IN BIORESORBABLE VASCULAR SCAFFOLDS

Concern over the safety and efficacy of the ABSORB Bioresorbable Vascular Scaffold (BVS) system has lingered since its inception. During initial analysis, the vascular response to the implantation of BVS was studied in detail via serial IVUS examinations, which showed stable findings and low rates of MACE.[62] However, data on long-term outcomes have revealed increased risk of adverse events and have shown statistically significant higher rates of MI and scaffold thrombosis.[63] In light of these negative findings, a warning was issued by the US Food and Drug Administration about these first-generation devices. Researchers have inquired as to whether this association with adverse outcomes may be attributed to the design and material of first-generation BVS or whether factors such as improper sizing, lesion preparation, or procedure optimization are to blame for device failure. To evaluate this further, Stone and colleagues[64] conducted an analysis after accounting for baseline patient and lesion characteristics. At 3-year follow-up, vessel sizing and operator technique were strongly associated with BVS-related clinical outcomes, despite accounting for other variables. The investigators demonstrated that aggressive predilation was associated with freedom from scaffold thrombosis, whereas optimal postdilation was associated with freedom from target lesion failure. These data underscore the importance of an optimal implantation strategy for BVS. The effect of optimal implantation technique on outcomes with BVS was further evaluated by another group of researchers, who showed that the risk of scaffold thrombosis is significantly lowered with an aggressive implantation strategy that included a low threshold for IVUS use.[65] In this prospective, 2-center, observational study of 264 patients with 400 lesions treated with BVS, IVUS was used in 86% of interventions. At 2-year follow-up, definite or probable scaffold thrombosis occurred in only 3 patients. Hence, BVS intervention requires specific implantation techniques, which is facilitated by IVUS. To ensure proper tissue coverage with the scaffolds, IVUS guidance can aid aggressive predilation, proper apposition, and adequate postdilation during BVS implantation.

INTRAVASCULAR ULTRASOUND AND OTHER INTRACORONARY IMAGING TECHNIQUES

Another modality that has gained interest in augmenting PCI is fractional flow reserve (FFR). This technology relies on a physiologic rather than visual assessment of coronary stenosis. Studies have demonstrated improvement in clinical outcomes and a reduction in MACE with FFR-guided PCI as compared with conventional angiography.[66] How FFR compares with IVUS-guided PCI also has been investigated. Correlation between FFR findings and IVUS parameters was found to be vessel dependent and particularly limited to small vessels with ischemic lesions.[67] When evaluating LMCA disease, Jasti and colleagues[68] demonstrated a strong correlation between IVUS parameters (MLD, MLA, area stenosis, and cross-sectional narrowing) and FFR's physiologic calculation. Based on their analysis, the investigators concluded that MLA of 5.8 mm^2 and MLD of 2.8 mm had the strongest correlation with FFR parameters consistent with physiologically significant stenosis. Similarly, for non-LMCA lesions, moderate correlation was found between FFR of less than 0.8 and MLA noted on IVUS.[69] A perfect correlation between these 2 modalities is not feasible given the need for different cutoff values depending on location of the lesion and amount of myocardium served by that particular vessel.[70]

LIMITATIONS OF INTRAVASCULAR ULTRASOUND

Although IVUS can be very useful in tissue characterization and defining anatomy, it has shortcomings. Compared with newer imaging modalities, such as optical coherence tomography (OCT), IVUS remains inferior in the detection of intracoronary thrombus. Similar echotextures on IVUS may represent different tissue components. For example, a sonolucent structure may represent a lipid-rich atheroma, but an intracoronary thrombus may also carry a similar hypoechoic appearance. In addition, artifacts can have an undesirable effect on ultrasound images, creating significant distortions in image quality.[71] Last, IVUS solely provides a visual assessment of the coronary anatomy, compared with FFR, which provides a physiologic evaluation.

TRENDS AND COST-EFFECTIVENESS OF INTRAVASCULAR ULTRASOUND USE

The rate of IVUS use with PCIs is low in the United States and other countries. A one-year analysis of the National Cardiovascular Data Registry reported rates as low as 20%, which has remained unchanged over the years.[72,73] In a 7-year analysis of the national inpatient sample, Elgendy and colleagues found the rate of IVUS use to be <9% during inpatient PCIs.[74] On the other hand, IVUS is used in a large percentage of catheterization procedures in Japan. It is hypothesized that the lack of widespread use of IVUS may be due to the cost of equipment, increased procedural time, and the perception of not needing IVUS to obtain good angiographic results.[75] Alberti and colleagues[76] modeled the economic impact of IVUS and found it to be a fairly robust and economic strategy. The investigators reported the highest cost-effectiveness of IVUS would be in patients with at higher risk of restenosis (eg, diabetes, renal insufficiency, or those presenting with an acute coronary syndrome). Although the economic benefits of IVUS decrease after the first year, the benefits persist during longer follow-up.[19] It is important to note that based on the economic analysis, the incremental cost added by IVUS remained well within the Italian population's willingness-to-pay threshold. Finally, the economic analysis of IVUS was also assessed by researchers from Denmark who reported improved clinical outcomes as well as better cost-effectiveness with the use of IVUS in their single-center, prospective randomized trial.[77]

SUMMARY

Over the last 2 decades, there has been accumulating evidence to support the routine use of IVUS for PCI interventions, even in the era of second-generation DES. This benefit has been consistently confirmed in observational and randomized trials. Moreover, there is evidence to suggest a greater improvement in clinical outcomes when IVUS is used to guide complex PCIs (LMCA intervention, complicated coronary anatomy, longer lesions, or CTOs). In addition, studies have demonstrated that an IVUS-guided PCI approach appears cost-effective. Although fairly robust data demonstrate improvement in clinical and angiographic outcomes with IVUS-guided interventions, most operators are reluctant to adopt the regular use of IVUS during PCI, because of the perceived increase in procedural time, lack of operator expertise, and lack of conviction of the need for IVUS use.

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