TEXAS
CHAPTER

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The Role of Intracoronary Imaging:
Including IVUS and OCT, in Guiding Coronary Interventions: A Review of the Recent Trials and the Latest Metanalysis Outcomes.

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Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide. When indicated, percutaneous coronary intervention (PCI) has become the cornerstone of the management of patients with symptomatic CAD. Traditionally, PCI is performed based on angiographic guidance; however, optimizing PCI outcomes requires precise visualization of coronary anatomy and intracoronary pathologies. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have emerged as advanced intracoronary imaging technologies to identify plaque morphologies and plan and guide PCIs. These Imaging modalities have revolutionized the interventional cardiology field. These advanced technologies have improved diagnostic accuracy and patient outcomes.

There are two main types of IVUS systems: mechanical (One ultrasound unit works as both an emitting and a receiving ultrasound wave unit) and electronic, which uses a multi-phased array (works simultaneously transmitting ultrasound waves by one set of elements and receiving by a second set). Both types are commercially available from different manufacturers. Regardless of the type, the IVUS system utilizes different operating frequencies (based on the manufacturer, which impact the image resolution) emitted at the catheter tip covering 360 degrees, creating an axial imaging of the vessel being assessed.

On the other hand, optical coherence tomography (OCT) uses near-infrared light to produce high-resolution images of coronary arteries. It has a similar

concept to IVUS; however, OCT has ten times the resolution and uses light instead of ultrasound.

Furthermore, a commercially available catheter has both IVUS and OCT.

Despite the difference in the design and image characteristics, both imaging modalities play an essential role in guiding the PCIs, as proven by the data from clinical trials and metanalyses (figure). They have multiple roles, starting with Pre-PCI Assessment by providing critical information on plaque burden and distribution or assessing in-stent restenosis. Then, planning the PCI by assessing the need for plaque modifications, assessing the result of plaque modifications, and selecting appropriate stent size and length. Imaging is used in post-PCI evaluation by assessing stent expansion, apposition, and check for stent edge dissection to take immediate, appropriate corrective measure if needed.

Many studies and analyses have evaluated the outcomes of intravascular imaging (Figure 3); however, we will briefly summarize the findings of the most recent trials and the latest meta-analysis.

The CTO-IVUS[1] (Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation) randomized trial (published in 2015) Included 402 patients with a chronic total occlusion (CTO) randomized at 1:1 to the IVUS-guided group (201 patients), versus Angiography-guided CTO intervention with secondary randomization to receive resolute zotarolimus-eluting stents or Nobori biolimus-eluting stents. The primary and secondary endpoints were cardiac death and a major adverse cardiac event (MACE) defined as the composite of cardiac death, myocardial infarction, or target vessel revascularization, respectively. The result of this study showed that IVUS-guided CTO intervention did not significantly reduce cardiac mortality at 12 months follow-up; however, it demonstrated that IVUS-guided CTO intervention might improve the major adverse cardiac event rate after a new

generation drug-eluting stent implantation when compared to angiography guided CTO at 12-month follow-up.

The IVUS-XPL[2] (Effect of Intravascular Ultrasound–Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation), a randomized trial (published in 2015), included 1400 patients randomized at 1:1 to IVUS-guided stent implantation (700 patients), or angiography-guided stent implantation (700 patients). The primary outcome was the composite of major adverse cardiac events, including cardiac death, target lesion-related myocardial infarction, or ischemia-driven target lesion revascularization. In this trial, the enrolled patients had a longer lesion with stent implantation of > 28 mm. This trial showed that IVUS-guided everolimus-eluting stent implantation resulted in a significantly lower rate of major adverse cardiac events at 1 year compared to angiography-guided stent implantation.

The ILUMIEN III[3]:OPTIMIZE PCI (Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation) (Published in 2016) was a prospective, three-arms, single-blind randomized trial included 450 patients randomized at 1:1:1 with 158 patient in the OCT-guided PCI arm, 146 patient in the IVUS-guided PCI arm, and 146 patient in the Angiography-guided PCI arm. The clinical endpoints of this trial were target lesion failure, a composite of cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization and major adverse cardiac event, a composite of death, myocardial infarction, stent thrombosis, or repeat revascularization. This trial was reported to be underpowered, and the result showed that OCT-guided PCI did not impact the clinical outcome compared to IVUS-guided or Angiography-guided PCI at 12 months follow-up. This trial has led the foundation to the ILUMIEN IV randomized trial, though. The latter will be discussed later.

The OPINION[4] (Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention) trial included 829 patients randomized to receive OCT-guided PCI (414) or IVUS-guided PCI (415). The primary endpoint was TVF at 12 months after the PCI. The major secondary

endpoint was angiographic binary restenosis at 8 months. The result of this trial showed similar clinical outcomes between OCT-guided and IVUS-guided PCI; however, OCT provided superior imaging resolution.

The ULTIMATE[5] (Intravascular Ultrasound Guided Drug-Eluting Stents Implantation in "All-Comers" Coronary Lesions) randomized trial (published in 2018 and 2020 for 12 months and 26 months respectively) included 1448 patients randomized 1:1 to IVUS guided PCI arm and angiographic guided PCI arm. The primary endpoint was the risk for target vessel failure (TVF) at 3 years. The safety endpoint was definite or probable stent thrombosis. were The result from this trial showed that IVUS-guided PCI with DES implantation significantly improved clinical outcomes in all-comers, particularly for patients who had an IVUS-defined optimal procedure (defined as the stented segment should have a minimum luminal area (MLA)more than 5.0 mm^2 or 90% of the MLA at the distal reference segments, at 5 mm proximal or distal plaque burden from the stent is less than <50%; and no media dissection with length more than 3 mm at the stent edge.

The iSIGHT[6] (Optical coherence tomography versus intravascular ultrasound and angiography to guide percutaneous coronary interventions) randomized trial (published 2021) Included 151 patients with a total of 156 lesions randomized at 1:1:1 to OCT-guided PCI (51 patients and 51 lesions), IVUS-guided PCI (51 patients, 52 lesions), or Angiography-guided PCI (49 patients, and 53 lesions). The primary endpoint was non-inferiority. The post-procedure stent expansion defined as the minimal stent area divided by the average luminal area of the distal and proximal reference is in the OCT versus IVUS arms. The secondary endpoints were superiority testing of stent expansion among the trial arms and compared region of the mean and minimal stent areas, mean and minimum in-stent lumen areas, stent eccentricity, mean and minimum stent diameters, plaque prolapse area, incomplete stent apposition, stent edge dissection, and the circumferential arc of visible external elastic membrane (EEM) at the vessel references. The result of this study showed

that OCT-guided PCI using a dedicated EEM-paste sizing strategy was inferior to that achieved with IVUS-guided PCI strategy and superior to angiographic-guided PCI strategy.

The RENOVATE-COMPLEX-PCI[7] (Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention) trial Included 1639 patients randomization at 2:1, with 1092 assigned to undergo intravascular imaging–guided PCI(the choice of IVUS or OCT was left at the discretion of the operator with reported 74.5% and 25.5% utilization of IVUS and OCT respectively) and 547 assigned to undergo angiography-guided PCI for a median follow-up of 2.1 years. The primary end-point was a composite of death from cardiac causes, target-vessel–related myocardial infarction, or clinically driven target-vessel revascularization. The result from this study showed that imaging-guided PCI was associated with a lower risk of the primary endpoints.

The OCTOBER[8] (OCT or angiography guidance for PCI in complex bifurcation lesions) trial (published in 2023) Included 1201 patients with complex bifurcation lesions randomized at 1:1 to OCT-guided PCI (600 patients) or angiography-guided PCI (6001 patient's). The primary endpoint was a composite of MACE defined as death from a cardiac cause, target lesion myocardial infarction, or ischemia-driven target lesion revascularization at a median follow-up of 2 years. The result of this study showed that in bifurcation lesions, OCT-guided PCI was associated with a lower incidence of mc compared to angiography-guided PCI at 2 years.

The ILUMIEN IV[9] (Optical Coherence Tomography–Guided versus Angiography-Guided PCI) randomized trial (published in 2023) included 2487 patients randomized with 1233 patients assigned to undergo OCT-guided PCI and 1254 to undergo angiography-guided PCI. The primary endpoints were the minimum stent area after PCI, assessed with OCT and TVF at 2 years. This trial showed that OCT-guided PCI resulted in a larger minimum stent area than angiography guidance, but there was no

apparent between-group difference in the percentage of patients with target-vessel failure at 2 years. One can interpret this study as OCT, which may not be better than angiographically guided PCI; however, this is not necessarily true. Reviewing the trial design showed that it was mandated to place an additional drug-eluting stent (DES) if there was untreated a proximal or distal reference segment disease that has a focal MLA <4.5mm2, and it was recommended that an additional DES be placed if a major dissection defined as >3 mm in length, and ≥60 degree of the vessel diameter but did not mandate the dissection to extend to the media of the vessel. These points have led to more stent deployment and may better explain the discrepancy in the result of this trial from the prior ones.

The OCTIVUS[10] (Optical Coherence Tomography–Guided or Intravascular Ultrasound–Guided Percutaneous Coronary Intervention) randomized trial (published in 2023) included 2008 patients in a 1:1 ratio with 1005 patients in the OCT-guided PCI, and 1003 patients in the IVUS-guided PCI. The primary endpoint was a composite of death from cardiac causes, target vessel-related myocardial infarction, or ischemia-driven target vessel revascularization at 1 year that was powered for non-inferiority. The result of this trial concluded that OCT-guided PCI was done anterior to IVUS-guided PCI with respect to the primary endpoint at 1 year.

The GUIDE-DES[11](Quantitative Coronary Angiography vs Intravascular Ultrasonography to Guide Drug-Eluting Stent Implantation) randomized trial (published in 2024) included 1528 patients randomized in a one-to-one ratio to quantitative Angiography-guided (QCA)-PCI (763 patients), or IVUS-guided PCI (765 patients). The primary endpoint was target lesion failure, defined as a composite of cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization at 12 months. The result of this trial concluded that Q Ca-guided PCI had similar rates of target lesion failure at 12 months. However, due to the lower-than-expected rates of target lesion failure in this trial, one should be careful during the interpretation of this trial.

Lastly, the most recent meta-analysis was performed by G Stone et al[12] and published in the Lancet in 2024. This is the largest meta-analysis to date regarding intravascular imaging. In this analysis, 22 trials were included, including the above-mentioned ones + older trials. In his meta-analysis, G.Stone and his co-authors included a total of 15,964 patients with a weighted mean duration of follow-up at 24.7 months. This analysis is distinct from prior meta-analyses, which showed a reduction in the risks of composite adverse events with IVUS-guided PCI compared with angiography-guided PCI, but those analyses were underpowered to show a reduction in all-cause death or all myocardial infarction with intravascular guided-PCI, and only evaluated IVUS but not the OCT. The results of this meta-analysis showed that intravascular imaging-guided PCI resulted in a decreased risk of target lesion failure driven by reductions in the risk of cardiac death, target vessel myocardial infarction, and target lesion revascularization. Furthermore, intravascular imaging-guided PCI also reduced the risk of stent thrombosis, old myocardial infarction, and all-cause death with similar outcomes for OCT-guided PCI and IVUS-guided PCI.

Why Is This Important?

Based on the above-mentioned trials and the latest meta-analysis, intravascular guidance during PCI, whether simple, complex, or even CTO, has proven superior to angiography-guided PCI, and therefore, its utilization is essential to improve PCI short and long-term outcomes. Regardless of the imaging modality, intravascular imaging guidance offers complementary strengths that enhance the safety and efficacy of coronary interventions and reduce the risk of myocardial infarction, repeat revascularization, and stent thrombosis. Despite the above-mentioned facts, and although, the utilization of intravascular imaging is expanding, it is not yet at goal in the United States. Future research should focus on further integrating these technologies into clinical practice and exploring their combined use to optimize patient outcomes.

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Figure 3 shows the hierarchy of evidence of the studies that were performed to evaluate the intravascular imaging-guided intervention from lowest to highest (top to bottom).

Observational Studies
- SCAAR LM registry - Andeli et al. 2017 (IVUS)
- DEFINITION registry - Chen et al. 2018 (IVUS)
- ADAPT-DES 2-yr folow up - Maehara et al. 2018 (IVUS)
- Samsung MC Registry - Choi et al. 2019 (IVUS)

Large meta-analyses
- Outcomes after IVUS- Ahn et al. 2014 (IVUS)
- Long-term outcomes of stenting- Mentias et al. 2020 (IVUS)
- IVUS in STEMI- Megaly et al. 2020 (IVUS)
- Intravascular imaging in PCI- Fazel et al. 2023 (IVUS)

Large randomized controlled trials
- CTO-IVUS- Kim, Shin, Hong et al. 2015 (IVUS)
- IVUS-XPL- Hong et al. 2015 (IVUS)
- ILUMIEN III- Ali et al. 2016 (OCT)
- ULTIMATE 3-year outcomes- Zhang et al. 2020 (IVUS)
- iSIGHT- Chamie et al. 2021 (OCT and IVUS)
- RENOVATE-COMPLEX-PCI- Lee et al. 2023 (IVUS)
- OCTOBER- Holm et al. 2023 (OCT)
- ILUMIEN IV- Ali et al. 2023 (OCT)
- OCTIVUS- Kang et al. 2023 (OCT and IVUS)
- GUIDE-DES- Lee et al. 2024

Meta-analyses of randomized controlled trials
- Meta analysis of 7 studies- Elgendy et al. 2016 (IVUS)
- Meta analysis of 3 studies- Shin et al. 2016 (IVUS)
- Meta analysis of 10 studies- Malik et al. 2020 (IVUS)
- Meta analysis of 11 studies- Elgendy et al. 2020 (IVUS)
- Meta analysis of 19 studies- Darmoch et al. 2020 (IVUS)
- Meta analysis of 22 studies- Stone et al. 2024 (OCT and IVUS)