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Review

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Clinical outcomes with intravascular ultrasound guidance of percutaneous coronary interventions: a targeted literature review of randomized controlled trials

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Abstract

The use of intravascular ultrasound (IVUS) to guide and optimize percutaneous coronary intervention (PCI) has been subject to robust clinical investigation for the last three decades. In this narrative review, we summarize the major clinical outcomes of the randomized controlled trials evaluating the potential benefit of IVUS-guided PCI, compared with either angiography alone or other coronary imaging and physiology technologies. These studies, spanning decades and continents, provide the most rigorous evidence base that clinicians can use to guide real-world decision making regarding the utility of IVUS guidance during PCI in contemporary clinical practice.

Keywords: Intravascular ultrasound (IVUS), percutaneous coronary intervention (PCI), coronary artery disease (CAD)

INTRODUCTION

Intravascular ultrasound (IVUS) is a catheter-based intracoronary imaging technology that produces live, cross-sectional, 360-degree images of the lumen and vascular anatomy of a coronary artery[1]. Over the last thirty years, this technology has been used in a broad array of clinical and research scenarios to assess

coronary anatomy and pathology with micron-level resolution[2]. Among the most important identified uses for IVUS is its role in the optimization of percutaneous coronary interventions (PCI) [Table 1][4]. IVUS-guided PCI refers specifically to the use of IVUS during coronary interventions to systematically characterize lesion pathology and guide procedural decision making including lesion preparation, stent choice and delivery, and post-stenting optimization[5].

Evidence for improved procedural and clinical outcomes with IVUS-guided PCI has emerged from real-world observational studies, clinical trials, and meta-analyses of pooled trial data. In this targeted narrative review, we summarize and discuss the individual randomized controlled trials (RCTs) that compare clinical endpoints in IVUS-guided *vs.* angiography-only PCI in the drug-eluting stent (DES) era. A total of twelve English-language RCTs evaluating IVUS guidance *vs.* angiography alone in PCI were identified. Two of these studies separately published long-term outcomes that were also included. Additionally, four studies comparing IVUS guidance *vs.* alternative intracoronary imaging or coronary physiology techniques were identified and are briefly discussed separately.

The studies comparing IVUS guidance and angiography alone are grouped according to anatomic criteria that were used for patient selection in the individual trials. Though there is certainly imprecision and overlap within these divisions, the goal of grouping studies in this manner is to allow readers to better identify the evidence that most clearly applies to their own real-world patients and procedures.

An important aspect of the studies included in this review is that some individual trials failed to show an advantage of IVUS guidance. In addition, the effect of IVUS in individual trials is largely, although not exclusively, limited to vessel- and stent-related outcomes such as target vessel and target lesion revascularization. We conclude this review with a discussion of these issues and a brief description of major pooled analyses demonstrating the superiority of IVUS-guided PCI.

IVUS-GUIDED *VS.* ANGIOGRAPHY-GUIDED PCI: DRUG-ELUTING STENT ERA

In the DES era, studies evaluating clinical outcomes with IVUS-guided PCI expanded beyond stable coronary artery disease to include patients with a greater degree of clinical and anatomic complexity, in whom a greater degree of benefits from technical optimization might be expected. Eleven trials are included, with the separately published long-term outcomes of two larger trials also described [Table 2]. Studies are grouped according to the anatomic specifications required for inclusion, with unselected patients herein referring to those with any lesion complexity (as opposed to any clinical syndrome as above). All trials included clinically unselected patients (those with stable coronary disease or acute coronary syndromes) unless otherwise described.

All-comer patients

An early trial of IVUS- *vs.* angiography-guided PCI in procedures utilizing drug-eluting stents (DES) was the HOME-DES-IVUS study, a 2010 single-center RCT completed in the Czech Republic[6]. Of note, though the intention of the study design was for the inclusion of all-comers, due to insurance restrictions at the performing center, patients were required to meet either angiographic or clinical complexity criteria to be eligible for DES implantation and, therefore, to be included in this study. Inclusion criteria were American Heart Association lesion type B2 and C, left main disease, reference vessel diameter < 2.5 mm, lesion length > 20 mm, in-stent restenosis, insulin-dependent diabetes mellitus, and acute coronary syndrome. Among the 210 patients included in the study, no between-group differences in event rates of either MACE [defined as death, myocardial infarction (MI), or target lesion revascularization (TLR)] or late stent thrombosis (ST) were observed at 18 months.

Table 1. Advantages and disadvantages of intravascular imaging in coronary lesion assessment and percutaneous coronary intervention

Advantages	• Improved lesion characterization (plaque composition, morphology) • Ability to diagnose mechanisms of stent thrombosis and in-stent restenosis • Improved precision in pre-intervention planning (lesion length, vessel diameter) • Improved post-intervention optimization (assessment of stent expansion and apposition, identification of edge dissections) • Decreased radiation exposure
Disadvantages	• Increased procedural cost and duration • Risk of iatrogenic coronary spasm or dissection • No direct physiologic assessment • Reliance on manual image analysis
Guideline recommendations for clinical use*	• Defining lesion severity in patients with intermediate stenosis of the left main coronary artery (Class 2a, LOE B-NR) • Procedural guidance in patients undergoing coronary stent implantation (Class 2a, LOE B-R) • Determining the mechanism of stent failure (Class 2a, LOE C-LD)

*2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines[3].

IVUS guidance has also been used in the setting of chronic kidney disease to reduce contrast administration and the risk of acute kidney injury during PCI. The 2014 MOZART study, a single-center study completed in Brazil, demonstrated decreased contrast administration (20 *vs.* 64.5 mL, $P < 0.001$) with IVUS guidance vs angiography alone in 83 patients at high risk of contrast-induced nephropathy undergoing PCI with DES[7]. No difference was detected in clinical outcomes including MACE (defined as death, acute MI, unplanned revascularization, or ST) or worsening renal impairment during index hospitalization or at four months, though analysis is likely limited by the small study size and relatively short follow-up.

Only one study specifically evaluating the role of IVUS guidance in exclusively acute coronary syndromes or acute myocardial infarction was identified[8]. In this 2015 single-center study from China, the study authors randomized 80 patients with ST-elevated myocardial infarction and high thrombus burden upon initial angiographic assessment to either IVUS- or angiography-guided PCI. Interestingly, there was no difference in clinical outcomes (MACE, defined as cardiac death, recurrent MI, TVR, and intractable myocardial ischemia) between groups at twelve months despite the IVUS group using less or even no stents depending on IVUS-based assessment of lesion risk. While the authors concluded that IVUS guidance improved the identification of patients for whom stent implantation could be avoided, the trial was not designed specifically to examine that question and was likely significantly underpowered to show any differences between IVUS guidance and angiographic guidance.

More recently, the 2018 ULTIMATE trial compared IVUS- *vs.* angiography-guided revascularization using DES in 1,448 unselected patients across eight sites in China[9,10]. In this large study, spanning both one- and three-year analyses, the IVUS-guided group was found to have a statistically significant reduced risk of the composite outcome of target vessel failure (TVF; defined as cardiac death, target-vessel myocardial infarction (MI), or clinically driven target-vessel revascularization (TVR)) (One-year HR 0.53, $P = 0.02$; three-year HR 0.60, $P = 0.01$). This outcome was largely due to a reduction in clinically driven TVR at both time points. At three years, there was also a significantly reduced rate of definite or probable ST in the IVUS group (HR 0.12, $P = 0.02$). There was no difference in cardiac death or overall death at any time point during this study.

Complex lesions

Several studies investigating the potential benefit of IVUS-guided PCI have enrolled patients with pre-defined anatomic complexity. Given the higher procedural and post-procedural risk of revascularization

Table 2. Randomized controlled trials of intravascular ultrasound-guided percutaneous coronary intervention compared with angiography alone in the drug-eluting stent era

Name or first author	Year of publication	Design	Size	Primary endpoint	Clinical outcomes
Unselected patients					
HOME-DES-IVUS	2010	Single center. 1:1 randomization of clinically unselected meeting insurance criteria for intravascular ultrasound (IVUS) (complex coronary lesions or patient characteristics)	210	Incidence of MACE at 18 months, defined as death, MI, and TLR; late stent thrombosis (ST)	No significant difference in event rates between study groups
MOZART	2014	Single center. Block randomization of clinically unselected patients scheduled for PCI with known risk of contrast-induced acute kidney injury. Guidelines provided to reduce contrast use in both arms with further specific guidance for reducing contrast with IVUS	83	Primary: volume of contrast used intraprocedurally Secondary: In-hospital and four-month MACE (death, acute MI, unplanned revascularization, ST) and evidence of renal impairment	Less total contrast used in the IVUS group. No significant difference in event rates during hospitalization or at four months
Wang	2015	Single center. 1:1 consecutive randomization of patients with ST-elevation MI and high angiographic thrombus burden. IVUS group divided into low/high-risk based on IVUS findings with prespecified criteria to decrease DES implantation in low risk	80	MACE rates (defined as cardiac death, recurrent MI, TVR, and intractable myocardial ischemia) at 1, 3, 6, and 12 months	Decreased number of stents placed in the IVUS group. No difference in MACE rates at 12 months
ULTIMATE (1-year)	2018	Multicenter. 1:1 randomization of clinically unselected patients with de novo coronary lesions. Chronic total occlusions, severe calcification, and inexperienced operators excluded	1,448	Incidence of target vessel failure (TVF) at 12 months (composite of cardiac death, target-vessel MI, clinically driven TVR)	Decreased incidence of composite endpoint in IVUS group (HR 0.53, $P = 0.02$). No significant difference in individual components of composite endpoint
ULTIMATE (3-year)	2021	Multicenter. 1:1 randomization of clinically unselected patients with de novo coronary lesions. Chronic total occlusions, severe calcification, and inexperienced operators excluded	1,448	Incidence of TVF at 3 years, defined as in ULTIMATE 1-year study Safety endpoint of definite or probable ST	Decreased incidence of composite endpoint in IVUS group (HR 0.60, $P = 0.01$) driven by a decrease in clinically-driven TVR. Lower incidence of definite/probable ST in IVUS group (HR 0.12, $P = 0.02$)
Complex lesions					
AVIO	2013	Multicenter. 1:1 randomization of patients with stable coronary disease or unstable angina with complex lesions (> 28 mm, CTO, bifurcation, < 2.5mm, four or more stents required)	284	Primary: in-lesion minimal lumen diameter Secondary: target lesion revascularization at 9 months; MACE (any MI, cardiac death, TVR) at 30 days, 6, 9, 12, and 24 months	No significant difference in event rates between study groups
RENOVATE	2023	Multicenter. 2:1 randomization of clinically unselected patients with complex coronary disease (bifurcation, CTO, unprotected left main, long lesions (> 38 mm stent), multivessel PCI, three+ stents, in-stent restenosis, severely calcified, ostial lesions)	1,639 (800 IVUS)	TVF (death from cardiac causes, target-vessel-related MI, or clinically-driven TVR)	Decreased incidence of primary endpoint (HR 0.64, $P = 0.008$). No difference in death from any cause, any MI, and any repeat revascularization
Chronic total occlusions					
AIR-CTO	2015	Multicenter. 1:1 randomization. Clinically unselected patients with at least one CTO randomized after initial lesion crossing to IVUS optimization or angiography alone	230	Primary: in-stent late lumen loss Secondary: all-cause death, cardiac death, MI, TLR, TVR Safety: definite/probable ST	No significant difference in clinical events (composite or individual components) at any time point, with the exception of decreased incidence of definite/probable ST at 2 years in IVUS group (no difference in overall STs)
CTO-IVUS	2015	Multicenter. 1:1 randomization stratified by center. Patients with	402	Occurrence of cardiac death	No significant difference in cardiac death. Decreased

		stable coronary artery disease with at least one CTO randomized after initial lesion crossing to IVUS optimization or angiography alone			incidence of overall MACE driven by decreased cardiac death or MI (HR 0.35, *P* = 0.035). No difference in TVR or all-cause mortality
Long lesions					
RESET	2013	Multicenter. Block randomization of patients with stable coronary disease and long coronary lesions (>28 mm). Revascularization with DES	543	MACE (cardiovascular death, MI, ST, TVR) at one year	No significant difference in event rates between study groups
IVUS-XPL (1-year)	2015	Multicenter. Block randomization of clinically unselected patients with long coronary lesions (> 28 mm)	1,400	MACE (cardiac death, target lesion-related MI, ischemia-driven TLR) at one year	Decreased incidence of MACE at one year (HR 0.48, *P* = 0.007), driven by decreased ischemia-driven TLR. No difference in definite or probable stent thrombosis
IVUS-XPL (5-year)	2020	Multicenter. Block randomization of clinically unselected patients with long coronary lesions (> 28 mm)	1,400	MACE (cardiac death, target lesion-related MI, ischemia-driven TLR) at one year	Decreased incidence of MACE at five years (HR 0.50, p = 0.001), driven by decreased ischemia-driven TLR. No difference in definite or probable stent thrombosis
Left main coronary artery disease					
Tan	2015	Single center. 1:1 randomization of consecutive patients aged > 70 with stable unprotected left main coronary artery disease (> 50% stenosis)	123	Primary efficacy: two-year incidence of MACE (death, non-fatal MI, TLR) Safety: ST	Decreased incidence of MACE at two years, driven by decreased rates of TLR (12.1% *vs.* 29.3%, *P* = 0.031). No significant difference in ST
Liu	2019	Single center. 1:1 randomization of consecutive patients with stable unprotected left main coronary artery disease (> 50% stenosis)	348	Primary efficacy: one-year incidence of MACE (cardiac death, MI, TVR) Safety: ST	Decreased incidence of MACE at one year, driven by decreased rate of cardiac death (13.2% *vs.* 21.9%, *P* = 0.031). No significant difference in ST

failure for these lesions, IVUS guidance is hypothesized to have a greater benefit in these patients compared with its use in patients with simple lesions. These studies are grouped by type of complex lesion and include studies covering any anatomically complex lesion (unselected), chronic total occlusions (CTOs), long lesions, or left main coronary artery lesions.

The AVIO trial was a 2013 multicenter international trial at 18 centers across Europe, comparing procedural and clinical outcomes in 284 patients with complex coronary disease who underwent IVUS- *vs.* angiography-guided PCI with DES[11]. Though there was a statistically significant increase in the primary study endpoint of minimal lumen diameter at the conclusion of the procedure in the IVUS group (2.70 *vs.* 2.51 mm, *P* = 0.0002), no reduction in MACE (defined as any MI, cardiac death, or TVR) was observed at any time point through 24 months in the total study population, nor was there a signal for benefit identified in any specific lesion-type subgroup.

The larger RENOVATE-COMPLEX-PCI trial published in 2023 compared intravascular imaging-guided PCI with angiography-guided PCI in 1,639 patients with anatomically complex coronary artery disease at 20 sites in South Korea[12]. Though the imaging group allowed either IVUS or Optical Coherence Tomography (OCT) guidance, the trial is included in this IVUS-focused review, given its size, recent publication, and importance to the field. Moreover, 73% of imaging-guided procedures in this study used IVUS (chosen at the operator's discretion). Overall, at a median 2.1-year follow-up, there was a significant

decrease in TVF (defined as a composite outcome of death from cardiac causes, target-vessel-related MI, or clinically driven TVR) with the use of either intravascular imaging modality compared with angiography alone (7.7% *vs.* 12.3%, $P = 0.008$). However, at three years, there was no difference in all-cause death, MI, or overall revascularization. Prespecified subgroup analyses from RENOVATE-COMPLEX-PCI investigated the outcomes in patients with specific lesions or clinical subtypes and demonstrated consistent significant benefits in CTO interventions, left main coronary artery interventions, and in patients presenting with acute coronary syndromes[13-15].

Chronic total occlusions

Two 2015 studies described the impact of IVUS guidance on PCI of CTOs. The AIR-CTO multicenter study performed in two centers in China evaluated lesion characteristics and clinical events two years after randomizing 230 patients to PCI with DES using IVUS optimization *vs.* angiographic guidance alone[16]. Though they were able to demonstrate a reduction in late lumen loss (primary endpoint, defined as minimal lumen diameter at one-year follow-up subtracted from minimal lumen diameter at the conclusion of index procedure) at one year with IVUS guidance (0.21 *vs.* 0.46 mm, $P = 0.025$), there was no significant difference in clinical events including all-cause death, cardiac death, MI, in-stent restenosis, TLR, or TVR. Conversely, the CTO-IVUS study, conducted in 20 centers across South Korea, enrolled 402 patients with stable coronary artery disease to compare IVUS with angiographic optimization after CTO PCI with DES. Here, the authors did show a reduction in both cardiac death and the composite MACE outcome (defined as cardiac death, MI, or TVR at 12 months; HR 0.35, $P = 0.035$), driven by decreased cardiac death and MI[17]. This difference may have been due to a larger sample size in the latter trial.

Long lesions

The utility of IVUS guidance for long lesions in the DES era was first assessed in the prespecified IVUS sub-study of the 2013 multicenter RESET study, which was conducted at 26 sites in South Korea and evaluated for differences in outcomes between PCI with DES of long lesions > 28 mm with IVUS guidance *vs.* angiography alone in 543 patients[18]. These investigators also did not demonstrate any differences in MACE (defined as cardiovascular death, MI, or TVR) at one year.

Conversely, the 2015 IVUS-XPL trial enrolled 1400 clinically unselected patients at 20 sites in South Korea with coronary lesions > 28 mm and also compared IVUS-guided PCI with DES *vs.* angiography alone. Here, there was a reduction in MACE (defined as cardiac death, target lesion-related MI, or ischemia-driven TLR) at both one-year (HR 0.48, $P = 0.007$) and five-year (HR 0.50, $P = 0.001$) follow-up[19,20]. The decrease in event rates observed in this study was driven at both time points by decreased ischemia-driven TLR, with no observed difference in cardiac death or MI.

Left main coronary artery PCI

The role of IVUS guidance in unprotected left main coronary artery stenting has been evaluated in two RCTs. Tan *et al.* demonstrated in their 2015 single-center study of 123 patients in China that IVUS guidance in unprotected left main coronary artery stenting in the elderly (age > 70) resulted in decreased MACE (defined as death, non-fatal MI, or TLR) at two years (13.1% *vs.* 29.3%, $P = 0.031$), driven by decreased target lesion revascularization[21]. Liu *et al.* also reported in their 2019 Chinese single-center study of 336 patients that IVUS guidance for unprotected left main coronary artery disease resulted in decreased incidence of MACE (defined as cardiac death, MI, and TVR) at 12 months (13.2% *vs.* 21.9%, $P = 0.031$), driven in this case by decreased cardiac death. All-cause mortality was not reported in this study, and there was no difference in TVR[22].

IVUS-GUIDED *VS.* ALTERNATIVE INTRACORONARY IMAGING OR PHYSIOLOGY-GUIDED PCI

IVUS guidance for PCI has also been compared with other technologies intended to optimize PCI outcomes, including Fractional Flow Reserve (FFR) and OCT. Though not intended to be a comprehensive review, four recent large-scale trials were identified and included [Table 3].

IVUS *vs.* physiology

Unlike IVUS, physiologic assessment using fractional flow reserve (FFR) or non-hyperemic pressure ratios (NHPR) such as instantaneous wave-free ratio (iFR) do not provide visual information about the anatomy of the coronary artery. Instead, FFR and NHPRs give functional information about the degree of ischemia of a coronary lesion and its physiologic significance. Intravascular imaging and physiologic assessments provide different and often complementary information regarding coronary anatomy and physiology.

The multinational FLAVOUR trial, published in 2022 from 18 centers in China and Korea, evaluated whether IVUS- or FFR-guidance for PCI yielded improved outcomes for angiographically intermediate lesions (40%-70% occlusion by visual estimation on coronary angiography) in 1,682 patients[23]. This study demonstrated no significant difference in the primary composite outcome of death, myocardial infarction, and revascularization at 24 months between study groups; however, fewer patients underwent PCI (44.4% *vs.* 65.3%, difference - 20.9% (95% confidence interval -25.7 to -16.1)) and fewer stents were placed per patient [0.6+/-0.9 *vs.* 0.9+/-1.0, difference - 0.3 (95% confidence interval -0.4 to -0.3)] in the patients assigned to the FFR arm compared with the IVUS arm. These data support the paradigm that physiology should be used to assess the indication for PCI, while intravascular imaging should be used to optimize the interventional result.

IVUS *vs.* OCT

OCT [historically termed optical frequency domain imaging (OFDI)] is a more recently developed light-based intracoronary imaging technology analogous to IVUS in that it also yields real-time, cross-sectional, 360-degree imaging using an intracoronary catheter. The differences in IVUS and OCT technologies and performance techniques have been previously described[24]; however, whether one technique yields superior clinical outcomes has been less well-defined.

To answer this question, the multinational ILUMIEN III: OPTIMIZE PCI trial, published in 2016, compared procedural success and 30-day clinical outcomes in IVUS guidance, OCT guidance, and angiography guidance in 450 patients at 29 hospitals in eight countries[25]. In this study, no significant difference was detected between any study group for either the primary procedural outcome (minimal stent area) or either procedural or 30-day MACE. Similarly, the 2017 OPINION trial, which enrolled 829 patients from 42 medical centers in Japan, demonstrated no difference in clinical outcomes (primary outcome TVF defined as cardiac death, target-vessel related MI, and ischemia-driven TVR) at one year when comparing IVUS *vs.* OCT guidance for PCI with DES[26]. These results were again replicated in the 2023 OCTIVUS trial, which enrolled 2,008 patients in nine centers in South Korea and demonstrated noninferiority of OCT guidance compared with IVUS guidance with respect to two-year MACE[27].

DISCUSSION

In this review, we have examined the English-language RCTs that have evaluated the potential benefit of IVUS guidance in the performance and optimization of PCI. These studies have evolved with PCI and IVUS technology, with the earliest studies including procedures limited to PTCA and BMS implantation, to

Table 3. Randomized controlled trials of intravascular ultrasound-guided percutaneous coronary intervention compared with alternative imaging or physiology assessments in the drug-eluting stent era

Name or first author	Year of publication	Design	Size	Primary endpoint	Clinical outcomes
Alternative intracoronary imaging/physiology					
ILLUMIEN III: OPTIMIZE PCI	2016	Multicenter. 1:1:1 randomization (IVUS guidance, Optical Coherence Tomography guidance, angiography guidance)	450	Primary efficacy: post-PCI minimum stent area (assessed by OCT) Primary safety: procedural MACE	No significant difference in post-PCI minimum stent area between groups. No significant in procedural or 30-day MACE between groups
OPINION	2017	Multicenter. 1:1 randomization of IVUS guidance *vs.* OCT guidance. Stable coronary disease or unstable angina only. Revascularization with second-generation DES	817	TVF (cardiac death, target-vessel related MI, ischemia-driven TVR)	No significant difference in rates of any primary or secondary outcomes between groups at 12 months
FLAVOUR	2022	Multicenter. 1:1 randomization of patients with suspected ischemic heart disease and angiographically intermediate lesions (40%-70% stenosis) to IVUS guidance *vs.* FFR guidance	1,682	Composite of death from any cause, MI, or any revascularization	No significant difference in event rates or patient-reported symptoms (SAQ score) at 24 months between groups
OCTIVUS	2023	Multicenter. 1:1 randomization of patients undergoing PCI to IVUS guidance *vs.* OCT guidance	2,008	Composite of death from cardiac causes, target vessel-related MI, or ischemia-driven TVR at 1 year	No significant difference in event rates between study groups

modern studies now using second- and third-generation DES. Over this same period, medical therapy for coronary artery disease and the medical field's understanding of best practices for the treatment of coronary artery disease have similarly matured.

Other authors have argued that on the basis of the trials included in this review, as well as meta-analyses and registry data, intravascular imaging during PCI constitutes a fundamental aspect of optimal invasive management of coronary artery disease[1,2,4,5]. This perspective is supported in both American and European guidelines on myocardial revascularization, which each give a class 2a recommendation to IVUS guidance in PCI in their most recent iterations[3,28].

An appraisal of the RCT evidence for these recommendations is not unequivocally positive; many early studies in this space showed no improvement in clinical outcomes with IVUS usage. However, these studies were generally smaller and potentially underpowered to detect small but clinically significant differences. It is important to note that the evolution of PCI devices and drugs has resulted in a steady decrease in procedural adverse events and an improvement in short- and long-term clinical outcomes; therefore, larger trials were needed to demonstrate the benefit of intravascular imaging. Moreover, since these trials cannot be blinded to investigators, the Hawthorne effect (whereby the investigators perform more optimized PCI in patients randomized to the angiography-guided arm simply because they are participating in a randomized trial) likely narrows the difference between the two randomized strategies. Nevertheless, recent large-scale trials have more consistently shown decreased incidence of MACE with the addition of IVUS to PCI, particularly among patients with complex coronary artery disease where event rates are higher. Though the benefit in individual trials has been typically limited to reducing target-vessel events, several meta-analyses of DES-era RCTs comparing IVUS-guided with angiography-only PCI have demonstrated a reduction in cardiovascular mortality[29-32].

Recent studies of clinical outcomes with other intravascular imaging modalities in similar contemporary patient populations have shown discordant results. The 2023 ILUMIEN-IV trial, which assessed clinical outcomes using OCT-guided PCI compared with angiography alone in 2,487 medically or anatomically complex patients at 80 sites in 18 countries, showed no reduction in TVF at two years[33]. This failure to detect differences was attributed to low event rates during the study period (as well as the possible impact of the COVID pandemic). The simultaneously published OCTOBER trial randomized 1,201 patients in 38 European centers with complex bifurcation lesions to either OCT-guided revascularization *vs.* angiography, but in this study, a significant reduction in MACE (death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization; HR 0.7, $P = 0.035$) at two years was observed[34].

Notwithstanding inter-trial variability, the overall body of evidence continues to support a role for intravascular imaging-guided PCI in select patients with appropriate clinical or anatomic complexity. Most recently, a network meta-analysis of more than 15,000 patients in 22 RCTs comparing imaging-guided *vs.* angiography-only PCI in the DES era demonstrated for the first time a reduction in all-cause mortality in patients treated with intravascular imaging guidance[35]. This meta-analysis, as well as the others referenced above, strongly supports a significant clinical advantage of using these technologies to improve PCI outcomes in appropriately selected patients.

Limitations

This review is, by its nature, limited in scope and depth. The focus is on summarizing the primary clinical outcomes of the included studies, in order to provide the practicing clinician with a foundational knowledge of the evidence. This review is not meant to serve as an in-depth analysis of the methodology or results of the included studies. It also does not thoroughly describe procedural outcomes included in the studies, though we acknowledge that the degree and frequency of procedural improvement likely impact the overall clinical benefit observed. Readers are encouraged to use this review as a starting point for understanding this body of literature and as a reference for further reading and evaluation.

Looking forward, a number of ongoing trials aim to further refine the practice scenarios in which IVUS guidance will yield clinical benefits, including trials investigating IVUS guidance in ST-elevation myocardial infarctions, unprotected left main coronary artery disease, complex coronary artery disease, and bifurcation lesions[36-40]. Other areas of future focus should also include improved uptake and delivery of IVUS-guided PCI, including ensuring appropriate integration of IVUS into routine workflow (i.e., with angiographic co-registration for ease of use), comprehensive training with IVUS modalities during and after interventional fellowship, and appropriate reimbursement for IVUS-guided PCI.

DECLARATIONS

Authors' contributions

Study conception and design: Rao SV, Razzouk L
Data collection: Flattery E
Analysis and interpretation of results: Flattery E, Razzouk L, Rao SV
Draft manuscript preparation: Flattery E, Razzouk L, Rao SV
All authors reviewed the results and approved the final version of the manuscript.

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All authors declare that there are no conflicts of interest.

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