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Meta-analysis

Network Meta-analysis of Trials Comparing Intravascular Ultrasound, Optical Coherence Tomography, and Angiography-Guided Technique for Drug-Eluting Stent Implantation

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ABSTRACT

Background: The current advances in coronary imaging with the introduction of intravascular ultrasound (IVUS), and more recently, optical coherence tomography (OCT) have overcome the limitations of coronary angiography.

Objective: This study aimed to conduct a comprehensive network meta-analysis of randomized clinical trials to report clinical outcomes among patients undergoing drug-eluting stent (DES) implantation either by IVUS- or OCT-guided technique or angiography alone.

Methods: PubMed/MEDLINE and EMBASE databases were searched systematically for all relevant published randomized clinical trials from the inception of the respective database to October 15th, 2021. The outcomes of interest assessed in this meta-analysis were major adverse cardiac events, myocardial infarction, target vessel revascularization, all-cause mortality, and cardiovascular mortality. All the endpoints were expressed as odds ratio (OR) with 95% CI. The network diagrams were computed using the OR as an effective measure. All statistical analyses were carried out in R statistical software version 4.0.3.

Results: A total of 14 randomized clinical trials were included in our meta-analysis. In patient undergoing DES implantation, angiography alone was associated with higher odds of major adverse cardiac events (OR, 1.62; 95% CI, 1.17-2.24), target vessel revascularization (OR, 1.60; 95% CI, 1.21-2.13) and cardiovascular mortality (OR, 1.97; 95% CI, 1.25-3.11). However, OCT demonstrated similar odds of major adverse cardiac events, cardiovascular mortality, and target vessel revascularization compared with IVUS. The odds of myocardial infarction and all-cause mortality were similar among all the 3 groups.

Conclusions: Although angiography alone was associated with worse outcomes than IVUS in a patient undergoing DES implantation, no difference in outcome was noted between patients undergoing DES implantation with OCT compared with IVUS. Advanced intracoronary imaging use should be encouraged to prevent excess mortality and morbidity.

Introduction

Coronary angiography has historically been used as the gold standard imaging technique to guide catheter-based coronary interventions.[1] The major downside of using coronary angiography alone is that it essentially is a real-time lumenogram that provides a 2-dimensional knowledge of a complex 3-dimensional lumen structure and lesion pathology.[1] However, the current advances in coronary imaging with the introduction of intravascular ultrasound (IVUS), and more recently, optical coherence tomography (OCT) have overcome these limitations of coronary

Abbreviations: DES, drug-eluting stents; IVUS, intravascular ultrasound; MACE, major adverse cardiovascular events; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; TVR, target vessel revascularization.

Keywords: angiogram; intravascular ultrasound; mortality; optical coherence tomography; target vessel revascularization.

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angiography. IVUS and OCT provide a detailed 3-dimensional tomographic visualization of the luminal anatomy, plaque pathology, and stent morphology, and are increasingly utilized to guide coronary interventions.[2] The greyscale IVUS provides a greater depth of tissue penetration compared with OCT, which has limited tissue penetration but provides images faster with a higher axial resolution and better visualization of finer details.[3]

An optimal stenting technique is imperative to minimize procedural complications and stent restenosis.[4,5] Several observational studies, randomized clinical trials (RCTs), and meta-analyses demonstrated a better overall reduction in major adverse cardiovascular events (MACE), with a reduction in target vessel revascularization (TVR) among IVUS-guided drug-eluting stent (DES) implantation as compared with angiographic techniques.[6-9] The superior ability of OCT compared with an angiogram to provide precise coronary lumen measurements has also been delineated by several studies.[10-12] However, a large number of studies are underpowered. All studies to date have compared IVUS- and OCT-guided percutaneous coronary intervention (PCI) to angiography-guided PCI, but large-scale studies with direct head-to-head comparison between IVUS and OCT are lacking. Finally, the most recent consensus document from the European Association of Percutaneous Coronary Interventions was recently published using articles only up to 2016.[13] Few RCTs have been published on this topic with new information since then. This study aimed to conduct a comprehensive network meta-analysis of RCTs to analyze clinical outcomes among patients undergoing DES implantation either by IVUS- or OCT-guided technique or angiography alone using the most recently available RCTs.

Methods

The present systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[14]

Data source and search strategy

A detailed search strategy was developed without language-based restrictions for PubMed/MEDLINE and EMBASE databases to search for all relevant published RCTs from the inception of the respective database to October 15th, 2021. The following search terms and their variations were utilized— “drug eluting stents,” “optical coherence tomography,” “intravascular ultrasound,” “angiography,” and “randomized clinical trials.” The detailed search strategy used for each database is provided in Supplemental Table S1. The systematic search was conducted by 2 investigators (A.K. and M.S.) independently and in tandem. The electronic search was further supplemented with a manual bibliographic search of all pertinent articles. All the observational studies, editorials, case reports, reviews, conference abstracts, and commentaries were excluded from our analysis.

Eligibility criteria and study selection

All trials were eligible for inclusion if they were RCTs that compared the outcomes among patients undergoing DES implantation either by IVUS-guided technique or OCT versus angiography alone and included more than 100 participants. No restrictions based on follow-up time were imposed—the longest available follow-up duration was included in this analysis.

The study selection was made in 2 stages. In the first stage, 2 investigators (A.K and M.S.) screened all the titles and abstracts of the retrieved articles after checking for duplicates. Secondly, the potentially eligible articles from stage one of the study selection were subjected to a full-text review by the same 2 investigators (A.K. and M.S.) to select studies in accordance with the inclusion criteria.

Data extraction and quality assessment

The data extraction was performed based on a predefined standardized data extraction form. Two investigators (M.S. and A.K.) performed the data extraction of the following data from each article: study characteristics, participant baseline characteristics, intervention type, follow-up duration, event rates, and sample size of outcomes. In addition, the data of the longest available follow-up were extracted, and the data extracted were based on the intention-to-treat principle.

The Cochrane Risk of Bias version 2 (RoB 2) form was employed to assess the associated bias with each trial.[15] The trials were assessed and scored on individual domains such as random sequence generation, allocation concealment, selective reporting, blinding of participants, personnel, and outcome assessors, incomplete outcome data, and other potential sources of bias. Two investigators (A.K and M.S.) independently assessed the risk of bias in the included trials and allotted a high, low, or unclear score to the respective domains. Discussion with other authors resolved disagreements at any stage until a mutual consensus was reached.

Outcomes

The outcomes of interest assessed in this meta-analysis were MACE, myocardial infarction (MI), TVR, all-cause mortality, and cardiovascular mortality. MACE was defined in accordance with the definition used in individual studies.

Data synthesis and analysis

The baseline characteristics data were summarized from all the studies and expressed as weighted means and percentages. The data for the pooled primary and secondary endpoints were expressed as odds ratio (OR) with 95% CI. The data were assessed for heterogeneity using Higgins I^2 statistics. Statistical significance was set at a significance level using a *P* value <.05. The network diagrams were computed with nodes representing the sample size of the particular technique under consideration, edges representing the number of studies with the comparison, and the color of the node representing the risk of bias of the studies with the technique under consideration. The OR was used as an effective measure in the present analysis. A random-effects model was used to compute direct and indirect evidence across technique comparisons. Further consistency of our network model was assessed using node splitting. “netmeta” package in R was used for all statistical analysis. R version 4.0.3 was used for the present analysis.

Results

The systematic search for the present meta-analysis yielded 965 articles after checking for duplicates and manual bibliographic search. A total of 14 RCTs were included after the detailed screening, comprising 6816 patients (Figure 1).[12,15–27] IVUS was used as a control group in our present meta-analysis, IVUS compared with OCT (3 studies), IVUS compared with angiography (11 studies), and OCT compared with angiography (4 studies). Two of the RCTs were 3-arm studies that compared all the 3 techniques of PCI. Figure 2 represents a network plot of included studies. The mean age of patients ranged from 57 to 76.5 years, and the percentage of males ranged from 54.7% to 87%. The baseline characteristics, including the prevalence of comorbidities such as hypertension, diabetes, etc., and coronaries involved in each RCT are detailed in Table 1. All the included studies were found to have a low risk of bias based on the RoB 2 form (Supplemental Table S2).

MACE

Major adverse cardiovascular events (MACE) were reported in 11 out of 14 studies. Angiography was associated with higher odds of MACE as

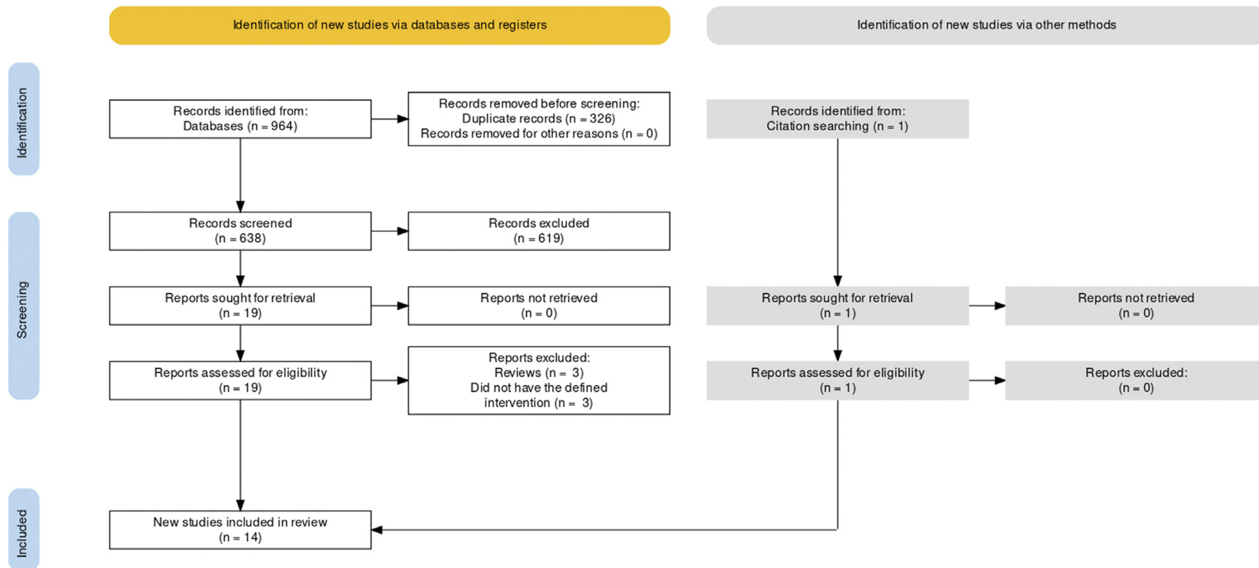


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicting systematic inclusion of studies in the current network meta-analysis.

compared with IVUS (OR, 1.64; 95% CI, 1.30-2.07), whereas OCT had similar odds of MACE compared with IVUS (OR, 1.31; 95% CI, 0.81-2.11) (Figure 3A). Node-splitting reported agreement between the direct and indirect evidence, and hence, robustness of the results (Figure 4A).

MI

Eleven out of 14 studies reported MI as an endpoint. Angiography compared with IVUS demonstrated no difference in the odds of MI (OR, 1.18; 95% CI, 0.81-1.73); and also, OCT compared with IVUS demonstrated no difference in the odds of MI (OR, 0.93; 95% CI, 0.42-2.06) (Figure 3B). Node-splitting reported agreement between the direct and indirect evidence, hence, the robustness of the results (Figure 4B).

TVR

Target vessel revascularization resulted in 9 of 14 studies. The angiography group demonstrated higher odds of TVR compared with IVUS

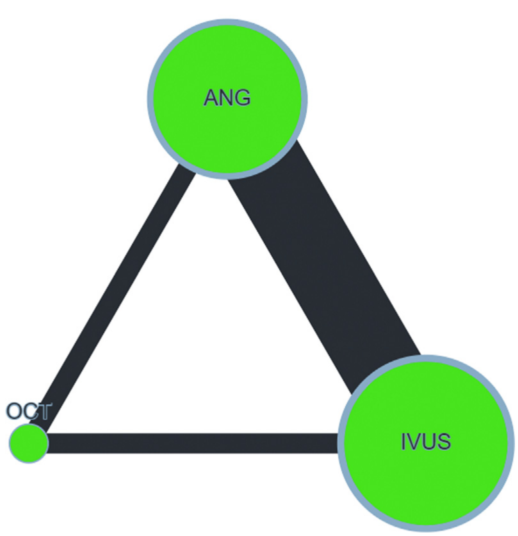


Figure 2. Network plot of studies included in the present meta-analysis. ANG, angiography; IVUS, intravascular ultrasound; OCT, optical coherence tomography.

(OR, 1.61; 95% CI, 1.21-2.14); whereas the OCT group demonstrated no difference in the odds of TVR compared with IVUS (OR, 1.33; 95% CI, 0.75-2.37) (Figure 3C). Node-splitting reported agreement between the direct and indirect evidence, hence, the robustness of the results (Figure 4C).

All-cause mortality

The all-cause mortality was reported in 11 out of 14 studies. The all-cause mortality endpoint was similar between angiography compared with IVUS (OR, 0.97; 95% CI, 0.70-1.35), and also similar between OCT and IVUS (OR, 2.55; 95% CI, 0.74-8.81) (Figure 3D). Node-splitting reported agreement between the direct and indirect evidence, hence, the robustness of the results (Figure 4D).

Cardiovascular mortality

Cardiovascular mortality was reported in 10 of 14 studies. Angiography, when compared with IVUS, demonstrated higher odds of cardiovascular mortality (OR, 1.97; 95% CI, 1.25-3.11). However, the odds of cardiovascular mortality when OCT was compared with IVUS demonstrated no difference (OR, 1.19; 95% CI, 0.20-7.20) (Figure 3E). Node-splitting reported agreement between the direct and indirect evidence, hence, the robustness of the results (Figure 4E).

Discussion

The present network meta-analysis of RCTs compared the outcomes among patients undergoing DES implantation either by IVUS- or OCT-guided technique or angiography alone. From the 14 RCTs that were included in our meta-analysis, we found: (1) angiography alone was associated with higher odds of MACE compared with IVUS, whereas OCT had similar odds of MACE compared with IVUS; (2) the odds of MI were similar among angiography and OCT compared with IVUS; (3) the odds of TVR were higher among angiography participants compared with IVUS; however, odds of TVR were similar among OCT participants compared with IVUS; (4) the incidence of all-cause mortality was similar among all the 3 groups; (5) angiography alone was associated with higher odds of cardiovascular mortality as compared with IVUS

Table 1. Baseline characteristics.

Study Name	HOME DES IVUS[17]		AVIO[18]		RESET[19]		CTO-IVUS[20]		Tan et al[21]	
Year	2010		2012		2013		2015		2015	
Study design	Single-center, prospective, randomized		Randomized, multicenter, open-labeled		Prospective, randomized, open-labeled, multicenter, noninferiority trial		Prospective, multicenter, randomized		Single-center, open-labeled, randomized	
Region	Czech Republic		International		South Korea, United States		Korea		China	
Recruitment period	Jan 2004 – Dec 2005		May 2008 – Jul 2011				Mar 2012 – Aug 2013		Oct 2009 – Sep 2012	
Follow-up	18 months		2 years		1 year (Intention-to-treat basis)		1 year		2 years	
Comparison	Angio	IVUS	IVUS	Angio	IVUS	Angio	IVUS	Angio	Angio	IVUS
Sample size	105	105	142	142	269	274	201	201	62	61
Baseline characteristics										
Age, y	60.2 ± 11	59.4 ± 13	63.9 ± 10.1	63.6 ±11.0	62.8 ± 9.3	64.3 ± 8.7	61.0 ± 11.1	61.4 ± 10.1	75.85 ± 3.49	76.54 ± 4.95
Male	75 (71)	77 (73)	117 (82)	109 (77)	177 (65.8)	150 (54.7)	162 (80.6)	162 (80.6)	43 (70)	38 (62)
Comorbidities										
Hypertension	75 (71)	70 (67)	100 (70.4)	95 (66.9)	165 (61.3)	178 (65.8)	126 (62.7)	128 (63.7)	29 (46.8)	25 (41.0)
Dyslipidemia	69 (66)	66 (63)	100 (70.4)	109 (76.8)	165 (61.3)	165 (61.7)				
Diabetes mellitus	47 (45)	44 (42)	34 (23.9)	38 (26.8)	85 (31.6)	82 (29.9)	70 (34.8)	68 (33.8)	18 (29.5)	21 (34.4)
Current smoker	37 (35)	42 (40)	49 (34.5)	44 (31.0)	58 (21.6)	47 (17.2)	71 (35.3)	69 (34.3)	29 (46.8)	27 (44.3)
Ischemic stroke									9 (14.8)	8 (13.1)
Prior cardiac history										
Prior MI	34 (32)	39 (37)			3 (1.1)	8 (2.9)	16 (8.0)	16 (8.0)	13 (21.0)	10 (16.4)
Prior PCI	15 (14)	18 (17)					31 (15.4)	32 (15.9)		
Prior CABG	11 (10)	15 (14)					3 (1.5)	5 (2.5)		
Clinical presentation										
Stable angina	42 (40)	40 (38)			143 (53.2)	141 (51.5)			21 (34)	18 (30)
Unstable angina	41 (39)	45 (43)	42 (29.6)	37 (26.1)	102 (37.9)	106 (38.7)			41 (66)	43 (71)
Acute MI	22 (21)	31 (29)			24 (8.9)	27 (9.9)				
NSTEMI										
Silent ischemia										

Study Name	AIR-CTO[22]		OPINION[12]		DOCTORS[15]		ROBUST sub-analysis[23]		Liu et al[24]	
Year	2015		2016		2016		2018		2019	
Study design	Randomized, multicenter		Multicenter, prospective, randomized, controlled, open-labeled, parallel, noninferiority trial		Multicenter, randomized, prospective		Multicenter, randomized, open-labeled		Randomized, open-labeled, single-blind	
Region	China		Japan		France				China	
Recruitment period	Oct 2010 – Nov 2011		Jun 2013 – Dec 2015		Sep 2013 – Dec 2015		Feb 2011 – Oct 2012		Dec 2010 – Dec 2015	
Follow-up	2 years		1 year		6 months		9 months		1 year	
Comparison	IVUS	Angio	OCT	IVUS	Angio	IVUS	OCT	Angio	IVUS	Angio
Sample size	115	115	412	405	120	120	105	96	167	169
Baseline characteristics										
Age, y	67 ±10	66 ± 11	69 ± 9	68 ± 9	60.2 ± 11.3	60.8 ± 11.5	57 (46-70)	59 (47-72)	65.3 ± 10.6	64.9 ± 11.2
Male	102 (88.7)	92 (80.0)	315 (76.5)	322 (79.5)	91 (75.8)	95 (79.2)	87 (83)	84 (87)	106 (63.5)	108 (63.9)
Comorbidities										
Hypertension	86 (74.8)	81 (70.4)	315 (76.5)	299 (73.8)	50 (41.7)	67 (55.8)	53 (50)	50 (52)	116 (69.5)	122 (72.2)
Dyslipidemia	25 (21.9)	32 (27.8)	316 (76.7)	321 (79.3)	56 (46.7)	59 (49.2)			63 (37.7)	64 (37.9)
Diabetes mellitus	34 (29.6)	31 (27.0)	169 (41.0)	165 (40.7)	19 (15.8)	26 (21.7)	18 (17)	25 (26)	56 (33.5)	52 (30.8)
Current smoker	45 (39.1)	45 (39.1)	67 (16.3)	73 (18.0)	51 (42.5)	47 (39.2)	67 (64)	57 (59)	62 (37.1)	60 (35.5)
Ischemic stroke	0	4 (3.5)							5 (3.0)	4 (2.4)
Prior cardiac history										
Prior MI	24 (20.9)	35 (30.4)	70 (17.0)	61 (15.1)			1 (1)	6 (6)	29 (17.4)	24 (14.2)
Prior PCI	23 (20.0)	24 (20.9)	140 (34.0)	140 (34.6)			4 (4)	3 (4)	33 (19.8)	28 (16.6)
Prior CABG	3 (2.6)	5 (4.3)	7 (1.7)	9 (2.2)			0	0	2 (1.2)	2 (1.2)
Clinical presentation										
Stable angina	82 (71.3)	87 (75.7)	363 (88.1)	352 (86.9)					20 (12.0)	18 (10.7)
Unstable angina	10 (8.7)	11 (9.6)	48 (11.7)	53 (13.1)	9 (7.5)	10 (8.3)			127 (76.0)	126 (74.6)
Acute MI	23 (20.0)	17 (14.8)							17 (10.2)	21 (12.4)
NSTEMI										
Silent ischemia										

Study Name	IVUS-XPL[25]		ULTIMATE[16]		ILUMIEN III: OPTIMIZE PCI[26]			iSIGHT[27]		
Year	2020		2021		2021			2021		
Study design	Randomized, multicenter		Multicenter, prospective, randomized		Randomized, single-blinded, open-labeled			Prospective, randomized, active-controlled, noninferiority, single-center trial		
Region	South Korea		China, United States		8 countries			Brazil		
Recruitment period	Oct 2010 – Jul 2014		Aug 2014 – Oct 2020		May 2015 – Apr 2016			Jan 2015 – Dec 2016		
Follow-up	5 year		3 year		1 year			1 year		
Comparison	IVUS	Angio	IVUS	Angio	OCT	IVUS	Angio	OCT	IVUS	Angio
Sample size	700	700	724	724	153	136	142	51	51	49
Baseline characteristics										
Age, y	64 ± 9	64 ± 9	65.2 ± 10.9	65.9 ± 9.8	66 (59-72)	66 (61-73)	67 (56-75)	59.92 ± 8.92	59.32 ± 10.37	58.59 ± 10.2
Male	483 (69)	481 (69)	535 (73.9)	530 (73.2)	106 (69)	101 (74)	104 (73)	31 (60.8)	36 (72.0)	38 (77.5)
Comorbidities										
Hypertension	454 (65)	444 (63)	512 (70.7)	521 (72.0)	119 (78)	106 (78)	107 (75)	46 (90.2)	42 (84)	39 (79.6)
Dyslipidemia	471 (67)	458 (65)	389 (53.7)	400 (55.2)	112 (73)	102 (75)	109 (77)	36 (70.6)	30 (60)	28 (57.2)
Diabetes mellitus	250 (36)	256 (37)	217 (30.0)	226 (31.2)	50 (33)	49 (36)	40 (28)	17 (33.3)	20 (40)	22 (44.9)
Current smoker	155 (22)	181 (26)	253 (34.9)	228 (31.5)	26 (17)	18 (13)	33 (23)	17 (33.3)	14 (28)	14 (28.6)
Ischemic stroke			85 (11.7)	85 (11.7)						
Prior cardiac history										
Prior MI	34 (5)	29 (4)	67 (9.3)	86 (11.9)	35 (22)	29 (20)	32 (22)			
Prior PCI	76 (11)	69 (10)	126 (17.4)	144 (19.9)	11 (7)	8 (5)	15 (10)			
Prior CABG	20 (3)	16 (2)	10 (1.4)	8 (1.1)	3 (2)	11 (8)	8 (5)			
Clinical presentation										
Stable angina	358 (51)	356 (51)	512 (70.7)	521 (72.0)	52 (34)	48 (35)	50 (36)	22 (43.1)	18 (36)	21 (42.9)
Unstable angina	242 (35)	226 (32)	389 (53.7)	400 (55.2)	25 (16)	33 (23)	27 (18)	20 (39.2)	22 (44)	16 (32.6)
Acute MI	100 (14)	118 (17)	217 (30.0)	226 (31.2)				9 (17.7)	10 (20.0)	12 (24.5)
NSTEMI			253 (34.9)	228 (31.5)						
Silent ischemia			85 (11.7)	85 (11.7)						

(*continued on next page*)

Table 1 (*continued*)

Study Name	HOME DES IVUS[17]		AVIO[18]		RESET[19]		CTO-IVUS[20]		Tan et al[21]		AIR-CTO[22]		OPINION[12]		DOCTORS[15]		ROBUST sub-analysis[23]		Liu et al[24]		IVUS-XPL[25]		ULTIMATE[16]		ILUMIEN III: OPTIMIZE PCI[26]			iSIGHT[27]		
Coronaries involved																														
Right coronary	25 (24)	31 (29)			61 (22.7)	54 (19.7)	88 (43.8)	75 (37.3)			40 (34.8)	53 (46.1)	102 (24.8)	117 (28.9)	32 (26.7)	38 (31.6)	50 (48)	50 (52)	104 (62.3)	98 (58.0)					22 (14.3)	22 (16.1)	23 (16.1)	20 (39.2)	19 (37.3)	26 (49.1)
LAD	57 (54)	59 (56)			167 (62.1)	185 (67.5)	84 (41.8)	94 (46.8)			51 (44.3)	42 (36.5)	223 (54.1)	197 (48.6)	60 (50.0)	56 (46.7)	41 (39)	31 (32)	93 (55.7)	89 (52.7)	455 (65)	419 (60)			52 (33.9)	50 (36.7)	57 (40.1)	19 (37.3)	22 (43.1)	20 (37.7)
LCx					41 (15.2)	35 (12.8)	29 (14.4)	32 (15.9)			24 (20.9)	17 (14.8)	84 (20.4)	87 (21.5)	28 (23.3)	26 (21.7)	17 (16)	11 (12)	74 (44.3)	84 (49.7)	96 (14)	108 (15)			27 (17.6)	27 (19.8)	20 (14.0)	12 (23.5)	10 (19.6)	7 (13.2)
RCx	16 (15)	12 (11)																			149 (21)	173 (25)								
LM	4 (4)	3 (3)																												
Multivessel											98 (85.2)	95 (82.6)			32 (26.6)	42 (35)	13 (12)	9 (9)	138 (82.6)	143 (84.6)			381 (52.6)	414 (57.2)						

Values are mean ± SD or n (%) unless otherwise noted.

CABG, coronary artery bypass grafting; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCx, left circumflex artery; LM, left main coronary artery; MI, myocardial infarction; NSTEMI, non ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; RCT, randomized clinical trial; RCx, right circumflex artery.

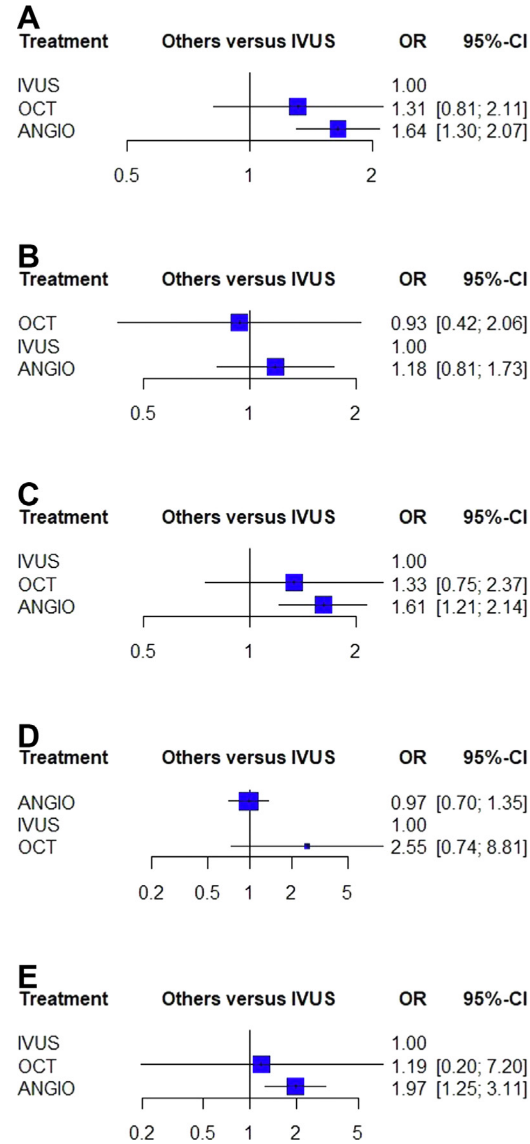


Figure 3. Forest plot for optical coherence tomography and angiography with intravascular ultrasound as the comparison. (**A**) Major adverse cardiac events, (**B**) myocardial infarction, (**C**) target vessel revascularization, (**D**) all-cause mortality, and (**E**) cardiovascular mortality. Angio, angiography; IVUS, intravascular ultrasound; OCT, optical coherence tomography; OR, odds ratio.

(Central Illustration). Our study provides more comprehensive data on the comparative analysis of various intervention types among patients undergoing DES implantation and their effect on clinical outcomes.

Percutaneous coronary intervention is the cornerstone treatment for acute coronary syndromes, which has traditionally utilized conventional angiography alone for stent implantation.[15] However, the advent of IVUS- and OCT-guided techniques in the modern era have optimized stent implantation with the provision of detailed 3-dimensional tomographic luminal and plaque views.[28] These advancements have overcome the inherent limitations of coronary lumenogram. IVUS and OCT are intravascular imaging modalities that provide an enhanced knowledge of the plaque burden and anatomical intricacies, which can facilitate optimal stent sizing, optimize stent expansion, and monitor immediate and late postprocedural outcomes.[29] Although OCT provides faster images with a higher resolution, facilitating better measurements, it has lower tissue penetration and requires blood clearance because of back-scattering from the blood, which occludes vessel imaging.[30] Conversely, IVUS has deeper tissue penetration, which provides full-thickness vessel wall imaging.[31]

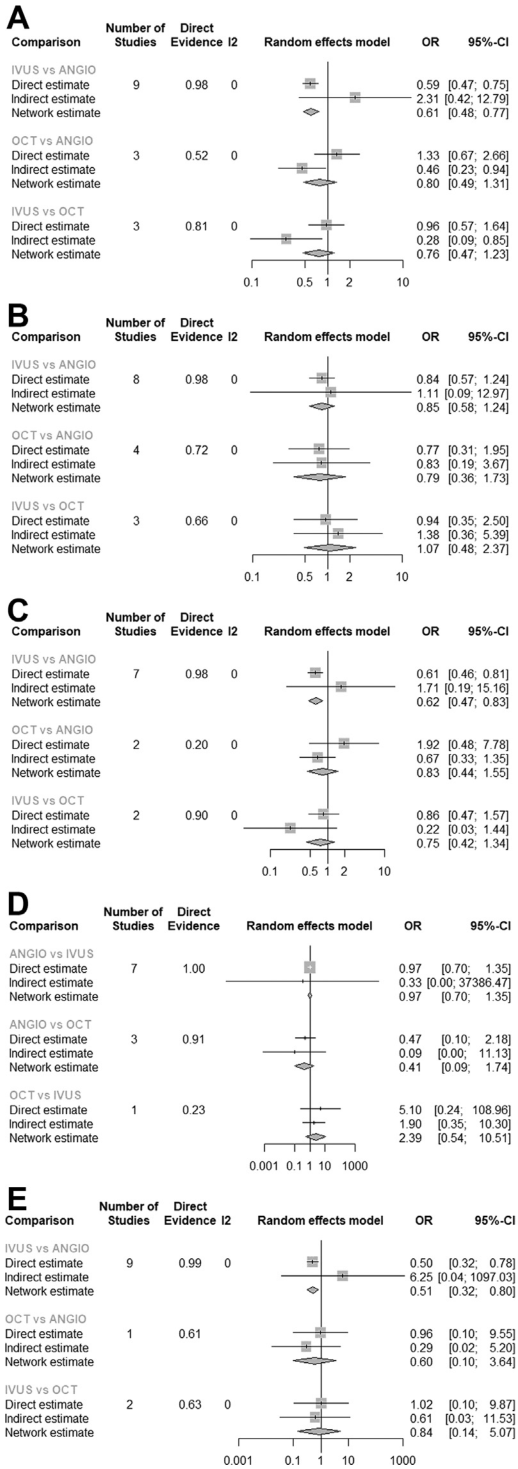
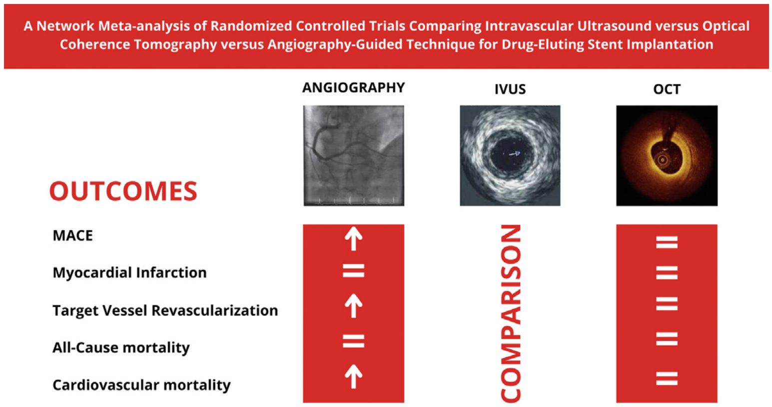


Figure 4. Forest plot comparing direct and indirect evidence. (**A**) Major adverse cardiac events, (**B**) myocardial infarction, (**C**) target vessel revascularization, (**D**) all-cause mortality, and (**E**) cardiovascular mortality. The column "Direct Evidence" reports the percentage of the final evidence derived from the direct evidence in the network model. Angio, angiography; IVUS, intravascular ultrasound; OCT, optical coherence tomography; OR, odds ratio.

In this meta-analysis of 14 RCTs, we found that the incidence of MACE, MI, TVR, all-cause mortality, and cardiovascular mortality was similar among IVUS-guided PCI participants compared with OCT-guided PCI participants. The results of our study are in congruence with former studies that reported similar rates of cardiac death, MI, TVR, and stent thrombosis in the OCT-guided PCI group as compared with the IVUS-guided PCI group.[12,32] This can be attributed to the enhanced understanding of the coronary lumen and lesion with superior imaging quality by guiding decision-making and stent optimization.[33] However, several former studies have delineated that OCT-guided PCI rendered a smaller stent sizing compared with the IVUS-guided technique.[34,35] The smaller stent sizing in the OCT-guided group directly translated to a smaller mean stent area and smaller mean stent expansion area than in the IVUS-guided group. The difference in stent sizing can be explained by the inability of OCT to penetrate the far-field area, which in turn affects its ability to visualize the external elastic membrane and hence, affects true vessel sizing.[33] In contrast to the smaller sizing in OCT, IVUS can overestimate the linear dimensions, leading to achieving larger poststent dimensions.[33,34] To overcome the low tissue penetration limitation of OCT in lipid-rich lesions, the authors of the ILUMIEN III, a prospective, multicenter RCT, designed a novel OCT protocol to evaluate OCT-based stent sizing.[28] The authors used reference segments proximal and distal to the diseased segment to determine the external elastic lamina-based sizing and found that this strategy was noninferior to that obtained with IVUS-guided stent implantation for both acute and long-term outcomes.[28] These results were similar to the OPtical frequency domain imaging vs. INtravascular ultrasound in percutaneous coronary InterventiON (OPINION trial), which demonstrated that OCT-guided PCI was noninferior to that of IVUS-guided PCI.[12] The recently developed optical frequency domain imaging, a type of OCT, combines the benefits of both time domain OCT and IVUS in terms of resolution and tissue volume.[36]

Our study demonstrated that angiography-alone PCI was associated with higher odds of MACE, cardiovascular mortality, and TVR than IVUS-guided DES stent implantation. Our study supports the data from former studies that have demonstrated an overall reduction in the composite of MACE and TVR with IVUS compared with an angiogram.[6,7,37,38] Although the growing body of evidence favors IVUS-guided PCI compared with traditional angiography-guided PCI in DES stent implantation, these imaging modalities are still underutilized. The utilization of intravascular imaging in the United States during coronary angiography was only 2.8% of the overall cases and only 4.8% of the PCI.[39] The underutilization of these modalities can be attributed to device availability, perceived cost constraints, practice methods, time limitations, operator comfort, and experience.[39] A cost-effectiveness analysis using IVUS-guided PCI for DES stent implantation in Italian health care demonstrated a negative incremental cost-effectiveness ratio per quality-adjusted life years.[40] In the large-scale Assessment of Dual AntiPlatelet Therapy with Drug-Eluting Stents (ADAPT-DES) study, the benefits of IVUS-guided DES implantation compared with angiography alone were extended to 2 years, with a reduction in the number needed to treat with IVUS guidance to prevent 1 MACE from 64 at 1 year to 41 at 2 years.[41] Thus, the IVUS technique provides greater cost-effectiveness by preventing repeated procedural requirements, especially in those with a higher risk of restenosis than the general population.[40] Additionally, based on the results of the ULTIMATE trial, IVUS-defined suboptimal procedure had a higher rate of primary outcomes, which were similar to the angiographic group.[16] Similar results with respect to higher primary outcomes with suboptimal optimization compared with adequate optimization were noted in the IVUS-XPL study, though the definitions used in the 2 aforementioned studies were different.[6] This highlights IVUS-guided procedural optimization as one of the key components in improving outcomes rather than using IVUS instead of angiography.

Intravascular imaging modalities have aided significantly in physician decision-making and procedural techniques. The use of IVUS or OCT should be encouraged for the analysis of in-stent restenosis or stent thrombosis to identify the etiology of the complication,



Central Illustration. A summary of the findings of the network meta-analysis, with the left column listing outcomes and the right three columns describing respective outcomes with angiography and optical coherence tomography in comparison with intravascular ultrasound. IVUS, intravascular ultrasound; OCT, optical coherence tomography.

additionally in patients with complex coronary artery lesions. Further, imaging modalities, particularly IVUS, have also been shown to be beneficial in left main disease subsets, which are otherwise not a candidate for surgery.[42,43] OCT has proved as a promising imaging modality with its high-resolution plaque imaging and stent optimization.[15] Although OCT requires a longer procedural and fluoroscopy timing and requirement of a greater dose of contrast media and radiation, the Does Optical Coherence Tomography Optimize Results of Stenting (DOCTORS) trial demonstrated no increase in periprocedural MI or acute kidney injury.[15] In fact, the most recently published consensus document recommends the use of IVUS-guided PCI to reduce the use of contrast. The development of fully automated software to analyze pre- and poststent assessments can help overcome this limitation. The use of advanced imaging to evaluate the left main disease should be encouraged because there are significant challenges in angiographic evaluation and procedural complexities. Therefore, the anticipated multicenter trial ILUMIEN IV (optical coherence tomography-guided coronary stent implantation compared with angiography) may provide further insight and details regarding the post PCI lumen dimensions and long-term clinical outcomes of OCT-guided versus angiography-guided PCI among patients with complex coronary lesions and/or diabetes.[44] Additionally, the development of hybrid imaging equipment with a combination of OCT and IVUS in a single catheter is underway.[45]

Limitations

The results of our study should be interpreted with caution as the present study has the following limitations. First, our study is a study-level meta-analysis, and analysis of patient-level data can provide more conclusive results. Secondly, the studies included in our analysis had a mixture of lesion locations and multivessel PCI, which can directly affect the postprocedural outcomes. Third, the studies included in our analysis deployed both first-generation and second-generation DES, which can also play an important role in clinical outcomes. Fourth, a cost-based analysis was not performed in any of our included studies, which is vital in determining the mode of imaging that can be used. Fifth, definitions for MI, TVR, and MACE were different in included articles that may affect outcomes; however, this was the same for both the groups in that particular RCT. Operator experience in using these imaging modalities can play a major role in their final outcome and has not been accounted for in the present analysis. Finally, the number of studies comparing IVUS with OCT is few and would benefit from further studies in the future, along with long-term outcomes and outcomes in subgroups such as the acute coronary syndrome presentation group.

Conclusion

In conclusion, while angiography was associated with worse outcomes than IVUS in a patient undergoing DES implantation, no difference in outcome was noted between patients undergoing DES implantation with OCT compared with IVUS. Therefore, intracoronary imaging should be encouraged to reduce cardiovascular outcomes in patients undergoing PCI-DES.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics statement

This study deemed exempt from the institutional review board approval as we utilized data publicy available in published literature.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography C Interventions* at https://doi.org/10.1016/j.jscai.2022.100507.

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