The outcomes of intravascular ultrasound-guided drug-eluting stent implantation among patients with complex coronary lesions: a comprehensive meta-analysis of 15 clinical trials and 8,084 patients

Zhong-Guo Fan¹, Xiao-Fei Gao^{1,2}, Xiao-Bo Li^{1,2}, Ming-Xue Shao^{1,2}, Ya-Li Gao¹, Shao-Liang Chen^{1,2}, Nai-Liang Tian^{1,2}

¹Department of Cardiology, Nanjing First Hospital, Nanjing Medical University: Nanjing-People's Republic of China ²Department of Cardiology, Nanjing Heart Center; Nanjing-People's Republic of China

Abstract

Objective: The effects of intravascular ultrasound (IVUS)-quided drug-eluting stent (DES) implantation in patients with complex coronary artery lesions remains to be controversial. This study sought to evaluate the outcomes of IVUS guidance in these patients.

Methods: The EMBASE, Medline, and other internet sources were searched for relevant articles. The primary endpoint was major adverse cardiac events (MACE), including all-cause mortality, myocardial infarction (MI), and target-vessel revascularization (TVR). The incidence of definite/probable stent thrombosis (ST) was analyzed as the safety endpoint.

Results: Fifteen clinical trials involving 8.084 patients were analyzed. MACE risk was significantly decreased following IVUS-quided DES implantation compared with coronary angiography (CAG) guidance (odds ratio [OR] 0.63, 95% confidence intervals [CI]: 0.53–0.73, p<0.001), which might mainly result from the lower all-cause mortality risk (OR 0.52, 95% CI: 0.40–0.67, p<0.001), MI (OR 0.70, 95% CI: 0.56–0.86, p=0.001), and TVR (OR 0.53, 95% CI: 0.40–0.70, p<0.001). The subgroup analyses indicated better outcomes of IVUS guidance in DES implantation for these patients with left main disease or bifurcation lesions.

Conclusion: IVUS guidance in DES implantation is associated with a significant reduction in MACE risk in patients with complex lesions, particularly those with left main disease or bifurcation lesions. More large and powerful randomized trials are still warranted to guide stenting decision making. (Anatol J Cardiol 2017; 17: 258-68)

Keywords: intravascular ultrasound, drug-eluting stent, complex lesions, meta-analysis

Introduction

In the new era of drug-eluting stents (DES), the improved stenting outcomes that have been reported mainly appear as decreased incidence of repeat revascularization compared to the bare-metal stents (1). To our knowledge, the successful procedure of stent implantation is considered to strengthen these beneficial effects, which are usually assessed according to the expansion and apposition of implanted stents.

Intravascular ultrasound (IVUS) guidance in DES implantation is an essential technique for prevention of stent malapposition because of its high resolution of evaluating lesion severity, optimizing stent implantation (2, 3). In recent years, several large observational clinical trials (Obs) (4, 5) have indicated the benefits of IVUS guidance in terms of a lower rate of major adverse cardiac events (MACE) than angiography guidance, as well as these recent comprehensive meta-analyses (6-8). However, a study by Park et al. (9) analyzing the data from the EXCELLENT trial (the Efficacy of Xience/Promus versus Cypher in rEducing Late Loss after stENTing) indicated no significant advantages of IVUS guidance, and another one recent observational trial (10) also showed doubt about the efficacy of IVUS guidance in DES implantation. In addition, the efficacy of IVUS guidance in patients with complex coronary lesions undergoing DES implantation still remains controversial. A large randomized controlled trial (RCT) conducted by Kim et al. (11) showed only limited or no benefits of IVUS guidance on prevention of MACE in patients with long coronary artery stenosis, whereas another one recent large RCT (12) indicated contrasting results. These conflicting data from several other recent RCTs (13, 14) and Obs (15-17) focusing on different coronary lesions have also raised questions regarding the usage of IVUS guidance. Moreover, only one meta-analysis recently published by Zhang et al. (18) pointed out that IVUS guidance would mostly benefit patients with complex

Address for correspondence: Nai-Liang Tian, Department of Cardiology, Nanjing First Hospital Nanjing Medical University; No. 68 Changle Road, 210006 Nanjing-People's Republic of China Phone-Fax: +86-25-52208048 E-mail: tiannailiang@163.com Accepted Date: 21.12.2016 Available Online Date: 22.03.2017 ©Copyright 2017 by Turkish Society of Cardiology - Available online at www.anatoljcardiol.com



coronary lesions or acute coronary syndromes (ACS) receiving DES implantation, although in which most of the enrolled clinical trials were retrospective or small scale. Furthermore, the absence of more precise subgroups depending on different coronary lesions would not allow them to identify specific patient populations. Therefore, we performed this comprehensive metaanalysis involving as many related clinical trials as possible to represent the largest analysis comparing efficacy and safety between IVUS guidance and angiography guidance in DES implantation for patients with complex coronary artery lesions and tried to identify the specific patient populations who would truly benefit from the technique.

Methods

Literature search

The EMBASE, Medline, and the Cochrane Controlled Trials Registry, as well as several other internet sources were searched for clinical trials comparing outcomes following IVUS guidance with coronary angiography guidance (described as the CAG group) in patients with complex coronary artery lesions [defined as long coronary artery lesions, chronic total occlusion (CTO) lesions, unprotected left main (LM) lesions, bifurcation lesions, multiple overlapping stents, or the composite of all these abovementioned lesions] receiving DES implantation from their date of inception until March 2016. The combinations of several relevant key words were used to make sure all relevant studies were included, including "intravascular ultrasound," "IVUS," "IVUS-guided," "angiography," "angiography-guided," "chronic total occlusion," "left main," "bifurcation," "long lesions," "drug-eluting stent," or "DES." All potentially relevant citations and references from published reviews or meta-analyses were subsequently screened for eligibility.

Inclusion and exclusion criteria

All included studies fulfilled the following criteria: (1) adult patients (age 18–90 years) undergoing percutaneous coronary intervention (PCI) with DES for complex coronary artery lesions as defined previously; and (2) clinical trials comparing the IVUS guidance and CAG guidance groups. The exclusion criteria were as follows: (1) non-human or ongoing studies; (2) non-English language studies; (3) duplicated studies, or different studies using the same sample; and (4) patients implanted with both of bare-metal stents and DES, whereas the relevant data of DES were not provided.

Data extraction, synthesis, and quality assessment

Two independent investigators (FZG and GXF) reviewed all relevant articles for assessing their eligibility, using standardized data-abstraction forms. The third investigator (LXB) resolved disagreements. The following data were extracted from each included study: the name or the first author of the trial, publication year, baseline demographics, characteristics of lesions, details of PCI procedure, and clinical outcomes during follow-up. All the included studies were divided into five subgroups according to the different types of coronary artery lesions, described as follows: long lesion, CTO, unprotected left main, bifurcation, and complex lesions subgroups (specific type of complex coronary lesions could not be distinguished from original study). On the other hand, we also performed a further analysis of propensitymatched and randomized studies. The quality of all retrieved studies were assessed in according to the Newcastle–Ottawa Scale (NOS) (19) and the Jadad score (20) for the cohorts and randomized studies respectively.

Study endpoints

The primary endpoint of this study was incidence of MACE, including all-cause mortality [cardiac death instead in four trials (12, 14, 21, 22)], myocardial infarction (MI; included both of Q-wave MI and non-Q-wave MI), and target-vessel revascularization (TVR). The safety endpoint was definite/probable stent thrombosis (ST), according to the definition of the Academic Research Consortium (23). The definitions of the clinical endpoints varied slightly among these included trials, but the studies generally followed standardized definitions.

Statistical analysis

We performed the present meta-analysis in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statements (24). All statistical analyses were performed with STATA 12.0 (StataCorp LP, College Station, TX, USA). All endpoints were treated as dichotomous variables, expressed with odds ratios (ORs) and 95% confidence intervals (CIs). Statistical heterogeneity among the included studies was measured using the Cochrane's Q test and the *l*² statistic. When the p value of Q test was <0.10 and/or the l^2 was \geq 50%, significant heterogeneity was considered and a random-effects model would be selected. If not, the fixed-effects model with the Mantel-Haenszel method was used instead. We examined publication bias via the Egger's test (p<0.1 for significant asymmetry) (25). The sensitivity analyses (exclude one study at a time) were performed to assess the stability of the overall treatment effects. All p values were two-tailed, and p values <0.05 were considered statistically significant.

Results

Eligible studies and patient characteristics

After screening 456 initial articles using the electronic databases and another 10 articles through several other internet sources, 15 clinical trials were finally identified, including six RCTs (11–14, 26, 27) and nine Obs (15–17, 21, 22, 28–31; Fig. 1). In the 15 enrolled articles, there were two for long lesions (11, 12), three for CTO lesions (13, 15, 27), four for unprotected LM disease (16, 22, 28, 31), three for bifurcation lesions (17, 29, 30), and three for combined complex lesions (14, 21, 26). In addition, seven clini-

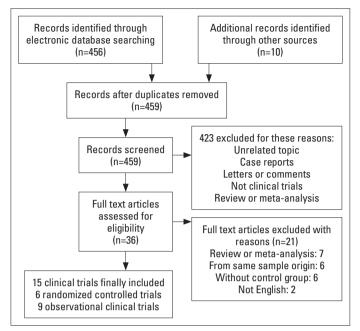


Figure 1. A flow chart of depicting the selection of the studies included in this meta-analysis

cal trials performed sub-analysis following the propensity score matching (15–17, 22, 29–31). The baseline characteristics and lesion or procedural characteristics of the included studies were summarized in Tables 1–3. The follow-up time of included studies ranged 1–4 years, and the qualities of these studies were good.

MACE

As depicted in Figure 2, the significant reduction in the overall MACE risk was observed related to IVUS guidance (OR 0.63, 95% CI: 0.53–0.73, p<0.001; l^2 =11.6%, p=0.326; Fig. 2a), which was mainly because of the decreased risk from the subgroups of long lesions (OR 0.51, 95% CI: 0.33–0.80, p=0.003; l^2 =0.0%, p=0.631) and unprotected LM (OR 0.57, 95% CI: 0.45–0.72, p<0.001; l^2 =9.1%, p=0.347). The Egger's test did not suggest publication bias (p=0.464), and the sensitivity analysis demonstrated that the beneficial efficacy of IVUS guidance in DES implantation was always observed by omitting a single study at a time.

All-cause mortality

A significant lower incidence of all-cause mortality rate was observed in the IVUS guidance group than in the CAG guidance group (OR 0.52, 95% CI: 0.40–0.67, p<0.001; l^2 =0.0%, p=0.768; Fig. 2b), as well as in the unprotected left main subgroup (OR 0.46, 95% CI: 0.32–0.65, p<0.001; l^2 =0.0%, p=0.405) and the bifurcation lesions subgroup (OR 0.44, 95% CI: 0.24–0.81, p=0.008; l^2 =0.0%, p=0.403). No publication bias was found examined by the Egger's test (p=0.281) and the stability of results were proved by the sensitivity analysis.

MI

The impact of IVUS guidance on the reduction in MI risk differed significantly from angiography guidance (OR 0.70, 95% CI: 0.56–0.86, p=0.001; l^2 =10.2%, p=0.343; Fig. 2c); this difference can probably be attributed to the subgroups of unprotected LM disease (OR 0.67, 95% CI: 0.50–0.89, p=0.006; l^2 =0.0%, p=0.726) and bifurcation lesions (OR 0.46, 95% CI: 0.25–0.81, p=0.008; l^2 =0.0%, p=0.548). No publication bias was observed (p=0.204). The sensitivity analysis demonstrated these superior effects of IVUS guidance.

TVR and target-lesion revascularization

As shown in Figure 2d, TVR incidence was lower in the IVUS guidance group than in the CAG group (OR 0.53, 95% CI: 0.40– 0.70, p<0.001; l^2 =11.2%, p=0.343); a similar result of decreased TLR risk could also be acquired (OR 0.69, 95% CI: 0.50–0.94, p=0.019; l^2 =52.3%, p=0.017, Fig. 2e). In addition, the results from analyses of different subroups also showed decreased TVR risk related to IVUS guidance in patients with CTO (OR 0.49, 95% CI: 0.26–0.91, p=0.025; l^2 =0.0%, p=0.625) and bifurcation lesions (OR 0.62, 95% CI: 0.39–1.00, p=0.049), as well as found in the subgroup of long lesions (OR 0.50, 95% CI: 0.28–0.91, p=0.024) with respect to the lower TLR risk. Egger's test indicated no publication bias (p=0.575, 0.147, for TVR and TLR respectively). The sensitivity analysis confirmed the stability of results.

Definite/probable ST

IVUS guidance was associated with the lower incidence of definite/probable ST (OR 0.31, 95% CI: 0.20–0.50, p<0.001, Fig. 2f) without any heterogeneity (l^2 =0.0%, p=0.787), and a decreased risk of ST pertaining to IVUS guidance was also observed in the subgroups of CTO (OR 0.26, 95% CI: 0.08–0.80, p=0.019; l^2 =0.0%, p=0.679), unprotected LM disease (OR 0.25, 95% CI: 0.09–0.65, p=0.019; l^2 =0.0%, p=0.839), and bifurcation lesions (OR 0.21, 95% CI: 0.09–0.48, p<0.001; l^2 =0.0%, p=0.807). No evidence of publication bias was found determined by the Egger's test (p=0.424).

Outcomes of propensity-matched and randomized trials

Seven propensity-matched studies and six RCTs enrolling 6.573 patients were repeatedly analyzed and subgroup analyses indicated different results as follows: (1) IVUS-guided DES implantation was associated with decreased MACE risk in patients with long lesions (OR 0.51, 95% CI: 0.33-0.80, p=0.003, Fig. 3a) and unprotected LM disease (OR 0.65, 95% CI: 0.51–0.82, p<0.001); (2) all-cause mortality rates were found among patients with unprotected LM disease (OR 0.48, 95% CI: 0.33-0.69, p<0.001, Fig. 3b) and bifurcation lesions (OR 0.35, 95% CI: 0.16–0.75, p=0.007); (3) IVUS guidance was associated with a lower incidence of MI in patents with bifurcation lesions (OR 0.31, 95% CI: 0.13-0.75, p=0.009, Fig. 3c); (4) significant reduction in TVR risk was observed in patients with CTO lesions (OR 0.49, 95% CI: 0.26-0.92, p=0.025, Fig. 3d), whereas no significant difference was observed pertaining to TLR (TLR: OR 0.79, 95% CI: 0.61-1.01, p=0.058, Fig. 3e); (5) decreased ST incidence was observed in patients with CTO (OR 0.25, 95% CI: 0.08-0.76, p=0.015, Fig. 3f), LM disease (OR 0.22, 95% CI: 0.08–0.67, p=0.008), and bifurcation lesions (OR 0.22, 95% CI: 0.07-0.63, p=0.005).

Table 1. The baseline characteristics of the included trials	acteristics of the in	ncluded trials						
Study	Design	Enrolled patients	Patients (N) IVUS/Control	Age, years IVUS/Control	Male, n IVUS/Control	LVEF, % IVUS/Control	Follow-up	Study quality
RESET trial (2013)	RCT	Patients with long lesions	269/274	62.8/64.3	177/150	55.3/54.0	1 year	5*
IVUS-XPL trial (2016)	RCT	Patients with long lesions	700/700	64/64	483/481	62.9/62.4	1 year	5*
CT0-IVUS trial (2015)	RCT	Patients with CTO	201/201	61.0/61.4	162/162	56.9/56.7	1 year	5*
Tian et al. (2015)	RCT	Patients with CTO	115/115	67/66	102/92	55/56	2 years	4*
Hong et al. (2014)	Observational	Patients with CTO	206/328	62/63	159/234	NA	2 years	6
Agostoni et al. (2005)	Observational	Patients with unprotected LM	24/34	62/64	15/25	52/44	14 months	7
Hernandez et al. (2014)	Observational	Patients with unprotected LM	505/505	66.1/66.9	404/397	54.9/55.3	3 years	8
Park et al. (2009)	Observational	Patients with unprotected LM	145/145	64.21/64.99	102/102	60.18/61.17	3 years	6
Gao et al. (2014)	Observational	Patients with unprotected LM	337/679	66.0/67.1	274/526	58.7/56.7	1 year	6
Kim et al. (2010)	Observational	Patients with bifurcation	308/112	~59/60	~73%/72%	$\sim 60/59$	4 years	œ
Kim et al. (2011)	Observational	Patients with bifurcation	487/487	62.0/61.8	324/326	60.1/58.8	3 years	6
Chen et al. (2013)	Observational	Patients with bifurcation	324/304	63.4/64.5	261/227	60.9/59.8	1 year	8
Jakabcin et al. (2010)	RCT	Patients with complex lesions	105/105	59.4/60.2	77/75	NA	18 months	4*
AVIO trial (2013)	RCT	Patients with complex lesions	142/142	63.9/63.6	117/109	55.3/55.9	2 years	4*
Ahn et al. (2013)	Observational	Patients with complex lesions	49/36	65/65	30/22	54/56	2 years	7
CTO - chronic total occlusion; IVUS - intravascular ultrasound; LM - left assessed by the Newcastle-Ottawa Scale and the max score = 9; *-Th-	US - intravascular ultras wa Scale and the max :	CTO - chronic total occlusion; IVUS - intravascular ultrasound; LM - left main disease; LVEF - left ventricular ejection fraction; NA - not available; RCT - randomized controlled trials. Notes-The qualities of observational trials were assessed by the Jadad score of the max score = 9; *-The qualities of included randomized trials were assessed by the Jadad score	ntricular ejection fractio nized trials were asses	n; NA - not available; F sed by the Jadad score	CT - randomized contro	olled trials. Notes-The	qualities of observa	ational trials were
Table 2. The characteristics of the past medical histories	s of the past medic	cal histories among the included trials	trials					
Study	Hypertension, n	nsion, n Diabetes, n	Dyslipidemia,	Dyslipidemia, n	Smoker, n	Prior MI, n	Al, n	Prior PCI, n

Study	Hypertension, n IVUS/Control	Diabetes, n IVUS/Control	Dyslipidemia, n IVUS/Control	Smoker, n IVUS/Control	Prior MI, n IVUS/Control	Prior PCI, n IVUS/Control
RESET trial (2013)	NA	85/82	165/165	58/47	3/8	NA
IVUS-XPL trial (2016)	454/444	250/256	471/458	155/181	34/29	76/69
CT0-IVUS trial (2015)	126/128	70/68	NA	71/69	16/16	31/32
Tian et al. (2015)	86/81	34/31	25/32	45/45	24/35	NA
Hong et al. (2014)	118/224	62/124	89/116	58/93	24/29	44/62
Agostoni et al. (2005)	14/20	9/10	15/23	4/7	9/17	12/7
Hernandez et al. (2014)	342/325	183/175	314/284	148/161	122/130	111/107
Park et al. (2009)	86/85	49/49	42/44	28/30	10/11	38/38
Gao et al. (2014)	244/489	109/232	228/487	111/230	60/123	60/119
Kim et al. (2010)	~43%/46%	~20%/22%	$\sim 28 \%/35 \%$	~36%/36%	NA	$\sim 10\%/7\%$
Kim et al. (2011)	292/284	155/162	168/170	106/111	42/39	NA
Chen et al. (2013)	216/185	60/54	108/107	147/154	50/35	57/51
Jakabcin et al. (2010)	70/75	44/47	69/99	42/37	39/34	18/15
AVIO trial (2013)	100/95	34/38	100/109	49/44	NA	NA
Ahn et al. (2013)	25/20	13/11	14/9	16/14	2/2	1/3
IVUS - intravascular ultrasound; MI - myocardial infarction; NA - not available; PCI - percutaneous coronary intervention	myocardial infarction; NA - not avail	able; PCI - percutaneous corona	ry intervention			

RESET trial (2013) 0/0 RESET trial (2013) 0/0 IVUS-XPL trial (2016) 0/0 CTO-IVUS trial (2015) 0/0 Tian et al. (2015) 0/0 Hong et al. (2014) 6/4 Agostoni et al. (2005) 24/34 Hernandez et al. (2014) 505/505 Park et al. (2014) 505/505 Fark et al. (2019) 145/145 Gao et al. (2014) 337/679 Kim et al. (2013) 17/19 Chen et al. (2013) 137/83 Lakabrin et al. (2013) 337/679	LAU, n 167/185 455/419 84/94 51/42 91/123 0/0 NA NA NA NA NA NA 129/186 404/402 129/186	LCX, n 41/35 96/108 96/108 29/32 29/32 29/32 29/32 0/0 NA NA NA NA S3/63 63/63 NA	RCA. n 61/54 149/173 88/75 88/75 40/53 NA 0/0 NA 75/80 146/369 NA 75/80 14/9 14/9 30/75	#Lesion length, mm 29.6/30.6 34.7/35.2 36.3/35.5 29.0/30.59 26.6/27.0 7.47/7.33 NA NA NA NA NA NA NA NA NA NA NA NA NA	#Stent length, mm 32.4/32.3 39.3/39.2 43.6/41.5 55/52 43.6/41.5 55/52 44.6/36.9 27/23 16.0/16.8 35.16/35.63 35.16/35.63 35.4/33.3 −34/26 NA NA 232.67/30.53 23.67/30.53	#Stent number, n NA 1.3/1.3 NA 1.3/1.5 1.3/1.4 1.5/1.4 NA 1.5/1.4 1.5/1.4 1.5/1.4 1.2/1.24 1.5/1.24 1.5/1.2 1.3/1.2 1.3/1.20	#Stent diameter, mm NA NA 2.91/2.85 3.05/2.86 3.05/2.83 3.2/3.2 3.2/3.2 3.2/3.4 NA NA NA NA	Types of DES Zotarolimus/Everolimus Everolimus Zotarolimus/Nobori Biolimus First and second-generation Zotarolimus/Everolimus Rirolimus/Paclitaxel Sirolimus/Paclitaxel Sirolimus/Paclitaxel NA Taxus/Cvnher
	NA	NA	NA	27.4/25.5	23.9/23.2	NA	2.95/2.86	AN
Ahn et al. (2013) 0/0	29/16	6/2	14/18	68/60	74/66	2.8/2.2	3.00/2.87	Sirolimus/Paclitaxel/Everolimus /Zotarolimus

Table 3. Angiographic and procedural characteristics

Discussion

100

The major finding of this comprehensive meta-analysis was that IVUS guidance in DES implantation was associated with a 37% reduction in MACE risk and a 48% reduction in all-cause mortality risk compared with CAG guidance. In addition, IVUS guidance could also decrease the incidence of MI, TVR, TLR, and ST. The data from RCTs and the propensity-matched subgroups were repeatedly analyzed, which demonstrated broadly similar clinical outcomes; however, no statistically significant difference was observed pertaining to TLR risk. The subgroup analyses indicated that IVUS-guided DES implantation seemed to have more beneficial effects on patients with left main disease or bifurcation lesions.

IVUS plays a key role in the procedure of stent implantation, because not only much more accurate details of the PCI procedure could be provided to evaluate lesion severity and to optimize stent implantation, but also being helpful to detect these complications following the procedure earlier. These positive effects were thought to improve the clinical outcomes among patients undergoing stent implantation in the DES era, which were evaluated by several recent observational trials (4, 5) and metaanalyses (6-8). In contrast, another one large observational trial (9) indicated modest or no benefits of IVUS guidance in terms of the increased MACE risk (5.5% vs. 3.9%, p=0.148, for IVUS auidance vs. angiography auidance). In addition, Singh et al. (10) cautiously pointed out that IVUS guidance was associated with lower in-hospital mortality risk at the cost of expensive care fee and increased incidence of vascular complications (10). Who could benefit mostly from IVUS guidance after costing a large number of treatment fee? It is such an important question which can not be ignored, especially in these developping countries. As a result, identifying such specific patient populations is absolutely necessary. The large randomized IVUS-XPL (IVUS-Xience Prime stent for long coronary lesions) trial (12) had reported lower MACE risk with respect to IVUS guidance during DES implantation for patients with long artery lesions than angiography guidance (2.9% vs. 5.8%, p=0.007), whereas another one large randomized trial called the RESET trial (Real Safety and Efficacy Trial) (11) indicated a contrast result (4.5% vs. 7.3%, p=0.16, for IVUS guidance vs. angiography guidance). Several other cohort studies (15-17) enrolling large numbers of patients with different complex coronary artery lesions were also conducted to determine if some special patients can benefit mostly from the technique; however, final results were controversial, which called the usage of IVUS guidance in DES implantation for such patients into question. There were few meta-analyses except for one pubished by Zhang et al. (18) focused on this topic. However, most of the included data in this meta-analysis were based on observational trials, and there were no enough precise subgroups according to the various coronary artery lesions. So far, there had been no sufficient evidence to support the benefits of IVUS guidance in patients with complex coronary artery lesions.

Sharp MALE OR (95%, C) Weight % Partial Feature F	0. 1		14405		0. 1	AU	
BEST Time (2013) BEST Time (2013) BEST Time (2013) BEST Time (2014) BEST Time (2	Study ID		MACE	OR (95% CI) Weight %	Study ID	All-cause mortality	OR (95% CI) Weight %
NUS XPL (2016) 0.47 (27, 08) 7.24 Statual (+squared-0.05, A-0.30) 0.47 (27, 08) 7.24 Statual (+squared-1.05, A-0.31) 0.47 (27, 08) 7.24 Statual (+squared-1.05, A-0.31) 0.47 (27, 08) 7.24 Statual (+squared-1.05, A-0.32) 0.48 (27, 08) 7.24 Statual (+squared-1.05, A-0.32) 0.58 (0.7, 10.15) Statual (+squared-1.05, A-0.32) 0.58 (0.7, 10.15) For importation (Internation (Int							
Subtractil (segured-d.0%, P-0.42) Subtractil (segu			• • •			•	
For C10 C10-VUS C10-VUS (1) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2		D 0 001)					
CTO-NUSS manual regularizations of CTO-NUSS Train (2015) Train et al (2015) CTO-NUSS Train (2015) CTO-NUSS Trai	Subtotal (I-squared=0.0%,	P=0.631)		0.51 (0.33, 0.80) 11.62	Subtotal (1-squared=0.0%, F=0.422)		0.00 (0.20, 2.03) 5.07
Tate of al (2016) Operating (2016) Operating (2016) Operating (2016) Subtrail (-squared-28, W, PA, 257) Operating (2014) Operating (2014) Operating (2014) Approximation (2014) Operating (2014) Operating (2014) Operating (2014) Approximation (2014) Operating (2014) Operating (2014) Operating (2014) Gene (2017) Operating (2014) Operating (2014) Operating (2014) Gene (2017) Operating (2014) Operating (2014) Operating (2014) Autor (2013)							0.66 (0.11 / 01) 2.20
inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201 k2) inong et al (2014) 0.20 (201, 1201 k2) 0.20 (201, 1201			•				
Subtical (I-squared-28, 8/, P.42, 257) 0.28 (0.44, 118) 14.65 Subtical (I-squared-28, 8/, P.42, 257) 0.28 (0.31, 13, 117) For emprotenced (M) 0.28 (0.24, 118) 14.65 0.58 (0.21, 0.21) 0.58 (0.21, 0.21) 0.58 (0.21, 0.21) Gase at (2014) 0.28 (0.21, 0.21) 0.58 (0.21, 0.18) 19.80 0.58 (0.21, 0.18) 19.80 0.58 (0.21, 0.18) 19.80 Subtical (I-squared-0.15, P.0.4050) 0.59 (0.53, 118) 15.17 0.53 (0.54, 118) 19.27 10.25 (0.56, 118) 12.17 0.53 (0.54, 118) 12.17 0.53 (0.54, 118) 12.17 Chem et al (2013) 0.29 (0.54, 118) 12.12 0.29 (0.56, 118) 12.12 0.53 (0.54, 10.27, 112.66 0.57 (0.52, 113.86 Markatin et al (2010) 0.59 (0.54, 118) 12.12 0.59 (0.56, 118) 12.12 0.59 (0.56, 118) 12.12 0.59 (0.56, 118) 12.12 Ann et al (2013) 0.59 (0.52, 0.51) 1000 0.59 (0.52, 0.51) 1000 0.59 (0.56, 0.118) 12.12 0.59 (0.56, 0.118) 12.12 Ann et al (2013) 0.59 (0.52, 0.51) 1000 0.59 (0.52, 0.51) 1000 0.59 (0.52, 0.51) 1000 Ann et al (2013) 0.59 (0.52, 0.51) 1000 0.59 (0.52, 0.51) 1000 0.59 (0.51, 0.57) 1000 Ann et al (2013) 0.59 (0.52, 0.118) 10.52 0.59 (0.50, 0.59) 110.50 0.59 (0.51, 0.59) 1000 <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>							
For unprotected LM Apprint at (2005) and rat (2014) 0.55 0.07.1501 65 0.06.02.501145 0.66 002.501145 0.66 002.501145 0.66 002.501145 0.66 002.501145 0.66 002.501145 0.67 0.02.510.02.12015 The unprotected LM Prix at (2005) Drive static constraints (2006) Drive static const		<i>P</i> =0 257)	$\langle \rangle$				
Provide variance reconsider cell (2014) Gas et al (2014) Gas (0.52, 0.23, 0.03, 0.03, 2.02, 0.03, 0.03, 2.02, 0.03,		,,	-		For upprotected I M		
Appendix No. (2007)				0.05 (0.07, 1.00) 0.00		_	0.53 (0.34, 0.80) 39.82
Gao et al (2014) Park et al (2009) 0.48 (0.22, 0.641 164 46 (0.52, 0.043) 0.043 (0.57 (0.48, 0.22) 4037) Subtrail (F-quared-0.15, P-0, 4.65) 0.44 (0.22, 0.657, 56.66) Subtrail (F-quared-0.15, P-0, 4.65) 0.57 (0.48, 0.22) 4037 0.57 (0.48, 0.22) 4037 0.57 (0.48, 0.22) 4037 Chen et al (2011) 0.57 (0.48, 0.22) 1158 123 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 For complex leader-0.056, P-0, 4.050 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 For complex leader-0.056, P-0, 4.030 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 For complex leader-0.056, P-0, 4.030 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 Ahor tal (2013) 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.21) 1158 26 0.57 (0.48, 0.22) 1158 0.57 (0.48, 0.22) 1158 0.57 (0.48, 0.22) 1158 Complex leader-0.158, P-0.000 0.57 (0.28, 0.60) 1133 0.57 (0.28, 0.60) 1133 0.57 (0.28, 0.60) 1133 0.57 (0.28, 0.60) 1133 Complex leader-0.158, P-0.000 0.57 (0.28, 0.60) 1123 0			· · · · ·		Park et al (2009)	•	
Prick tel (2009) Bolto 40 (03), 104 (03) For biffer ation For complex lesions Subtral II-squared=0.05, P-0.400) For complex lesions Subtral II-squared=0.05, P-0.400) For complex lesions Subtral II-squared=0.05, P-0.400) Bolto 40 (23, 104) 208 For complex lesions Subtral II-squared=0.05, P-0.400) Bolto 40 (23, 104) 208 Subtral II-squared=0.05, P-0.400) Bolto 40 (24, 104) 418 Subtral II-squared=0.05, P-0.400) Bolto 41 (24, 104) 400 Subtral II-squared=0.05, P-0.4000 Subtral II-squared							
For bifurcation 0.76 (0.5.0, 15) 12 17 Chen et al (2013) 0.76 (0.5.0, 15) 12 17 Subtral (1-squared-0.0%, P-0.304) 0.75 (0.5.1, 103) 2.18 And real (2013) 0.91 (0.4, 2.11) 3.6 Availabilities					Subtotal (I-squared=0.0%, <i>P</i> =0.405)	\sim	0.46 (0.32, 0.65) 56.66
Problem 276 (0.50, 0.15) 12.17 (0.00, 0.21) 4.0, 0.22) 4.02 (0.00, 0.21) 4.02 (0.00, 0.02) 4.02 (0.00, 0.21) 4	Subtotal (I-squared=9.1%,	P=0.347)	\diamond	0.57 (0.45, 0.72) 40.97	For bifurcation		
Chen et al (2013) Chen et al (2014) Subtotal (I squared-0.0%, P-0.904) For complex lesions Jancen et al (2010) Control (2	Faa bifaan af aa						
Kim et al (2011) 0.73 (0.44, 119.8.66 Corr complex lesions 0.75 (0.54, 1.03.210) Subbtal (I-squared-0.0%, P-0.040) 0.75 (0.54, 1.03.210) And corr and constraints 0.91 (0.40, 2.119.8.66 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.8.66 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.91 (0.40, 2.119.1.26 0.75 (0.54, 1.03.210) 0.95 (0.28, 1.18) 11.22 0.75 (0.54, 1.03.210) 0.55 (0.28, 1.18) 11.22 0.75 (0.54, 1.03.210) 0.55 (0.28, 1.18) 11.22 0.75 (0.54, 1.03.210) 0.55 (0.28, 1.03.210) 0.75 (0.54, 1.03.210) 0.55 (0.28, 0.29) 0.75 (0.54, 1.02.210) 0.53 (0.53, 0.73) 100.00 0.75 (0.54, 1.02.210) 0.55 (0.28, 0.29) 0.75 (0.54, 1.02.210) 0.75 (0.01, 1.18) 1.56 0.75 (0.02, 1.22) 0.50 (0.01, 1.18) 1.56 0.56 (0.03, 1.41) 12.71 0.56 (0			•	0.76 (0.50, 1.15) 12.17		• •	
Subtool (1 squared-0.0%, P-0.904) 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.54, 1.03) 21.03 0.75 (0.25, 2.61)							
For complex lesions subschier et al (2010) AVID Trial (2013) AVID Trial (2013) AVID Trial (2013) AVID Trial (2013) Ann et al (2014) Bolton al (1-squared-0.0%, P-0.025) For long lesions RESET Trial (2013) Ann et al (2014) Bolton al (1-squared-0.0%, P-0.025) For complex lesions RESET Trial (2014) Ann et al (2015) For unprotected LM Hermanadez et al (2014) Ann et al (2014) Bolton al (1-squared-0.0%, P-0.025) For unprotected LM Hermanadez et al (2014) Bolton al (1-squared-0.0%, P-0.025) For unprotected LM Hermanadez et al (2014) Bolton al (1-squared-0.0%, P-0.025) For complex lesions Reset Trial (2014) Bolton al (1-squared-0.0%, P-0.025) For unprotected LM Hermanadez et al (2014) Bolton al (1-squared-0.0%, P-0.025) For complex lesions Attion at (2015) For complex lesions Attion at (2016) Bolton al (1-squared-0.0%, P-0.025) For complex lesions Attion at (2016) Bolton at (1-squared-0.0%, P-0.025) For complex lesions Attion at (2016) Bolton at (2016) Bolton at (2017) Bolton at (2017) Bolton at (2017) Bolton at (2016) Bolton at (2017) Bol		P=0.904)	$\langle \rangle$		Subtotal (1-Squareu=0.0 %, F=0.403)		0.44 (0.24, 0.01) 13.40
Jakabatia (1 squared-10 %, P-0.32) Altor Trai (2013) Ant of 1 (2013) Ant of 1 (2013) Correct (1 squared-11 5%, P-0.326) NOTE: Weights are from random effects analysis Correct (1 squared-20 %, P-0.516) Or erail (1 squared-20 %, P-0.516) Description (1 squared-20 %, P-0.526) Train et al (2014) Subtotal (1 squared-20 %, P-0.526) Description (1 squared-30 %, P							
AlvD Trail [2013] Ahn et al [2013] Subtrail (1-squared-0.0%, P-0.521) Orall (1-squared-0.0%, P-0.521) Orall (1-squared-0.0%, P-0.521) Orall (1-squared-0.0%, P-0.521) Ahn et al [2013] Ahn et al [2014] Ahn et al [2015] Ahn et al [2015] Ahn et al [2015] Ahn et al [2016] Ahn et al [2017] Ahn et al [2016] Ahn et al [2016] Ahn et al [2016] Ahn et al [2017] Ahn et al [2016] Ahn et al [2016] Ahn et al [2017] Ahn et al [2016] Ahn et al [2016] Ahn et al [2017] Ahn et al [2017] Ahn et al [2016] Ahn et al [2017] Ahn et al [2017] Ahn et al [2018] Ahn et al [2018] Ah			•	0.01/0.40.2.11\2.46		•	
Ahn et al (2013) 							
Subtrail (I-squared-31.58, P-0.090) 0.55 (0.28, 1.18) 11.72 0.83 (0.53, 0.73) 100.00 OTE: Weights are from random effects analysis 0.517 1.3 a 0.517 1.33 For long lesions Favors NUS Favors non-IVUS Study Myocardial infarction 0.61 (0.31, 1.41) 12.71 10 0.71 (0.22, 1.82) 0.71 (0.22, 1.82) For long lesions 0.23 (0.01, 4.22) 0.50 0.26 (0.01, 2.23) 0.03 Subtrail (I-squared-0.0%, P-40.256) 0.20 (0.01, 4.22) 0.50 0.50 (0.03, 2.24) 0.03 For long lesions 0.20 (0.01, 4.23) 0.50 0.26 (0.03, 2.24) 0.03 Subtrail (I-squared-0.0%, P-40.256) 0.20 (0.01, 4.23) 0.50 0.66 (0.31, 1.41) 12.71 For CTO CTO 0.20 (0.01, 4.23) 0.50 0.56 (0.31, 1.41) 12.71 Subtrail (I-squared-0.0%, P-40.256) 0.20 (0.01, 4.23) 0.50 0.49 (0.16, 1.45) 6.39 For uprotected LM 0.86 (0.33, 1.51) 1.59 0.26 (0.31, 1.61) 1.27 Herraganed-0.0%, P-40.250) 0.51 (0.22, 0.08) 15.7 0.51 (0.23, 0.08) 15.7 For infurcation 0.50 (0.22, 0.09) 18.20 0.51 (0.23, 1.00) 2.70 For complex lesions <t< td=""><td></td><td>$\leftarrow \bullet$</td><td></td><td></td><td></td><td></td><td></td></t<>		$\leftarrow \bullet$					
Diverall (L-squared=0.0%, P=0.28) OB3 (0.53, 0.73) 100.00 Overall (L-squared=0.0%, P=0.768) 0.52 (0.40, 0.67) 100.00 NDTE: Weights are from random effects analysis Obs (0.55, 0.73) 100.00 Overall (L-squared=0.0%, P=0.768) 0.52 (0.40, 0.67) 100.00 Study Myocardial infarction Infarction On (55% CI) Weight % Study Myocardial infarction On (55% CI) Weight % Fer EF Trail (2013) Operall (L-squared=0.0%, P=0.325) Operall (L-squared=0.0%, P=0.325) Operall (L-squared=0.0%, P=0.325) For CTO Operall (L-squared=0.0%, P=0.325) Operall (L-squared=0.0%, P=0.325) Operall (L-squared=0.0%, P=0.325) Operall (L-squared=0.0%, P=0.325) For CTO Operall (2014) Operall (L-squared=0.0%, P=0.325) Operal	Subtotal (I-squared=58.5%	5, <i>P</i> =0.090)	<				
NUTE: Weights are from random effects analysis Decomposition reades a A517 1 133 B Favors IVUS Favors non-IVUS Study Myocardial infarction DI (estors, ECI Trial (2013) TVR D For long lesions Ester Trial (2013) OR (95% CI) Weight % For long lesions Study TVR For complexions O 20 (001, 4.23: 0.50 0.23 (001, 8.18) 0.45 Subtratil (1-squared=0.0%, P=0.925) O 20 (001, 4.15) 0.50 0.29 (001, 4.15) 0.50 0.29 (001, 4.15) 0.50 0.29 (001, 4.15) 0.50 0.19 (0.57, 2.07) 11.25 Hong et al (2014) Study (D 20 (001, 4.15) 0.50 0.49 (0.16, 1.49) 6.83 0.33 (0.01, 8.18) 15.49 0.61 (0.25, 1.49) 15.21 For unprotected LM Hermandez et al (2014) Gao et al (2014) O 49 (0.16, 1.45) 6.39 0.61 (0.25, 0.48) 10.33 0.61 (0.25, 0.48) 10.37 For unprotected LM Hermandez et al (2014) Gao et al (2014) O 49 (0.25, 0.13) 0.48) 16.56 0.49 (0.25, 0.13) 0.48 16.56 0.49 (0.25, 0.13) 0.48 16.56 0.49 (0.25, 0.13) 0.40, 1.13 32 0.50 (0.25, 0.48) 10.37 0.44 (0.14, 1.39) 2.20 5 0.44 (0.14,		B 0 000)	<	0.00 /0.50, 0.70\ 100.00		\diamond	0 52 (0 40 0 67) 100 00
Favors IVUS Favors non-IVUS Favors non-IVUS Favors NUS Favors non-IVUS Study Myocardial infarction (D 0 08/95% CI) Weight % Study TVR Por long lesions RESET Trial (2013) 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 818: 0.45 Subtotal (I-squared=0.0%, P=0.825) 0.26 (0.03, 2.32) 0.95 Study TVR 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.67 (1.50, 0.81) 13.73 0.68 (0.32, 1.22) 1.38 0.50 (0.22, 0.23) 1.33 0.60 (0.22, 0.23) 1.33 0.60 (0.23, 1.22) 1.38 0.50 (0.24, 0.27) 12.75 0.50 (0.26, 0.31) 13.73 0.60 (0.23, 1.22) 1.38 0.50 (0.23, 1.22) 1.38 0			rsis	0.63 (0.53, 0.73) 100.00			0.32 (0.40, 0.07) 100.00
Favors IVUS Favors non-IVUS Favors non-IVUS Favors NUS Favors non-IVUS Study Myocardial infarction ID OR (95% CI) Weight % DO (001, 423: 050 Subtotal (I-squared=.0.0%, P=0.825) OR (95% CI) Weight % DO (001, 423: 050 CI (0.03, 2.32) 0.95 Study TVR OR (95% CI) Weight % For long lesions For CTO CTO-VUS Trial (2015) 0.20 (0.01, 423: 0.50 CI (0.03, 2.32) 0.95 Study TVR 0.66 (0.31, 141) 12.71 Subtotal (I-squared=.0.0%, P=0.450) 0.20 (0.01, 415) 0.50 I.40 (0.82, 200) 8.80 I.109 (157, CI) Trial (2015) 0.49 (0.16, 145) 6.59 I.109 (157, CI) Trial (2015) 0.49 (0.16, 145) 6.59 I.109 (157, CI) VISTRIA (2015) For curpotected LM Hernandez et al (2014) 0.68 (0.39, 1.18) 15.49 0.61 (0.25, 0.31) 13.73 0.50 (0.26, 0.96) 10.93 0.22 (0.09, 1.18) 2.20 I.100 (15, 1.49) 9.52 I.17 0.49 (0.16, 1.45) 6.59 I.17 (0.27, 0.27) 12.25 For curpotected LM Hernandez et al (2014) 0.50 (0.26, 0.96) 10.93 0.22 (0.09, 1.18) 2.20 I.110 (1.5, 0.250 (0.26, 0.96) 10.33 0.22 (0.09, 1.18) 2.20 I.110 (1.5, 0.250 (0.26, 0.96) 10.33 0.22 (0.09, 1.18) 2.20 I.110 (1.5, 0.26 (0.31, 1.16) 0.55 I.17 (0.27, 1.22) 8.00 Noteal (I-squared=.33.4%, P=0.223) 0.50 (0.26, 0.26) 10.57 0.22 (0.13, 0.48) 16.55 I.50 IIII (2013) I.110 (1.16) 0.50 (0.26, 0.26) 10.57 I.110 (1.16) 0.50 (0.26, 0.26	а	.0517	1	19.3	h .01	1	100
D OR (95% CI) Weight % For long lesions RESET Trial (2013) 0.20 (0.01, 4.23: 0.50 NUS-XPL (2016) 0.26 (0.03, 2.32) 0.56 (0.31, 1.41) Subtotal (I-squared=.0.%, P=0.425) 0.26 (0.03, 2.32) 0.56 (0.31, 1.41) For CTO 0.20 (0.01, 4.15) 0.50 For CTO 0.20 (0.01, 4.15) 0.50 Tian et al (2015) 0.20 (0.01, 4.15) 0.50 For uprotected LM 0.58 (0.39, 1.18) 1.40 (0.68, 2.90) Hemranadez et al (2014) 0.58 (0.39, 1.18) 15.49 Gao et al (2014) 0.58 (0.39, 0.18) 0.51 (0.41, 0.90) Subtotal (I-squared=0.0%, P=0.625) 0.57 (0.50, 0.89) 56.77 For complex lesions 0.50 (0.26, 0.66) 10.33 Subtotal (I-squared=-0.0%, P=0.548) 0.50 (0.26, 0.66) 10.33 For complex lesions 0.57 (0.27, 1.22) 8.00 Subtotal (I-squared=-3.3.4%, P=0.223) 0.27 (0.56, 0.86)100.00 0.57 (0.27, 1.22) Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 0.57 (0.27, 1.22) 0.53 (0.40, 0.70)100.00 VOT Tial (I-squared=-1.2%, P=0.343) 0.70 (0.56, 0.86)100.00 0.572 1.75 <td>u</td> <td>Favors IVUS</td> <td></td> <td>Favors non-IVUS</td> <td>Favors IVUS</td> <td></td> <td>Favors non-IVUS</td>	u	Favors IVUS		Favors non-IVUS	Favors IVUS		Favors non-IVUS
RESET Trial (2013) 0.20 (0.01, 4.22: 0.50 RESET Trial (2013) 0.66 (0.31, 1.41) 12.71 VUS-XPL (2016) 0.26 (0.03, 2.32) 0.95 For CTO 0.20 (0.01, 4.15) 0.50 Tian et al (2015) 0.20 (0.01, 4.15) 0.50 For CTO 1.09 (0.57, 2.07) 11.25 Subtotal (I-squared=0.0%, P=0.450) 1.17 (0.7, 1.87) 20.55 Horg et al (2014) 0.25 (0.13, 0.48) 16.56 For unprotected LM 0.66 (0.3, 1.18) 15.49 Gao et al (2014) 0.67 (0.50, 0.89) 56.77 For unprotected LM For bifurcation 0.50 (0.25, 0.96) 10.93 Subtotal (I-squared=0.0%, P=0.726) 0.24 (0.03, 2.21) 0.95 For bifurcation 0.50 (0.25, 0.86) 10.							
VUS-XPL (2016) 0.33 (0.01, 8.18) 0.45 0.36 (0.03, 2.32) 0.95 Subtotal (I-squared=0,%, P=0.825) 0.26 (0.03, 2.32) 0.95 0.66 (0.31, 1.41) 12.71 For CTO 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 0.57 (0.27) 11.25 Subtotal (I-squared=0,%, P=0.450) 1.71 (0.72, 1.87) 20.55 0.66 (0.39, 1.18) 15.49 0.66 (0.39, 1.18) 15.49 Gao et al (2014) 0.66 (0.39, 1.18) 15.49 0.66 (0.41, 0.90) 30.21 0.67 (0.50, 0.89) 56.77 For bifurcation 0.67 (0.50, 0.89) 56.77 0.50 (0.25, 0.66) 10.33 0.50 (0.25, 0.66) 10.33 Chen et al (2013) 0.50 (0.25, 0.66) 10.33 0.50 (0.25, 0.66) 10.33 0.50 (0.25, 0.86) 10.37 Subtotal (I-squared=0.34, %, P=0.223) 0.24 (0.03, 2.21) 0.55 - - For complex lesions 0.41 (0.52, 0.81) 13.73 0.50 (0.25, 0.86) 10.33 0.57 (0.27) 1.12 Subtotal (I-squared=3.34, %, P=0.223) 0.70 (0.55, 0.86) 10.00 - - Voor Trail (I-squared=1.02, %, P=0.343) 0.70 (0.55, 0.86) 10.00 - - Overall (I-squared=1.02, %, P=0.343) 0.70 (0.55, 0.86) 10.00 - - Overall (I-squared=1.2, %, P=0.343) 0.70 (0.55, 0.86) 10.00 - - - O		Ν	Myocardial infarct			TVR	OR (95% CI) Weight %
Subtotal (I-squared=0.0%, P=0.825) 0.26 (0.03, 2,32) 0.95 Subtotal (I-squared=.%, P=.) 0.49 (0.16, 1.49) 6.39 For CTO CTO-IVUS Trial (2015) 0.20 (0.01, 4.15) 0.50 For CTO CTO-IVUS Trial (2015) 0.49 (0.16, 1.49) 6.39 For CTO CTO-IVUS Trial (2014) 0.68 (0.39, 1.18) 15.49 0.68 (0.39, 1.18) 15.49 0.68 (0.39, 1.18) 15.49 Subtotal (I-squared=0.0%, P=0.450) 0.68 (0.39, 1.18) 15.49 0.68 (0.39, 1.18) 15.49 0.68 (0.39, 1.18) 15.49 For bifurcation 0.68 (0.39, 1.18) 15.49 0.67 (0.50, 0.89) 56.77 For unprotected LM Part et al (2013) 0.50 (0.26, 0.96) 10.93 . . For complex lesions 0.51 (0.25, 0.38) 11.37 Subtotal (I-squared=78.2%, P=0.032) 0.44 (0.14, 1.35) 27.05 Subtotal (I-squared=3.4%, P=0.548) 0.24 (0.03, 2.21) 0.95 . . For complex lesions 0.16 (0.25, 0.86) 10.93 . . Alm et al (2013) 0.24 (0.03, 2.21) 0.95 . . Subtotal (I-squared=3.4%, P=0.548) 0.70 (0.56, 0.86) 10.00 . . Mercogeneity between groups: P=0.103 0.70 (0.56, 0.86) 100.00 . . . Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86) 100.00 . .<	ID For long lesions	N	Myocardial infarct	OR (95% CI) Weight %	ID	TVR	OR (95% CI) Weight %
For CTO CTO-IVUS Trial (2015) Tian et al (2014) Subtotal (I-squared=0.0%, P=0.450) 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.20) 8.80 1.40 (0.68, 2.20) 8.80 1.40 (0.68, 2.20) 8.80 1.40 (0.68, 2.20) 8.80 1.40 (0.68, 2.20) 8.80 1.17 (0.72, 1.87) 20.55 For CTO CTO-IVUS Trial (2015) Tian et al (2014) Gao et al (2014) Gao et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, P=0.726) 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 13.38 For Umprotected LM Hernandez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, P=0.726) 0.58 (0.39, 1.18) 15.49 0.57 (0.25, 0.28) 95.77 For unprotected LM Gao et al (2014) Gao et al (2013) Subtotal (I-squared=0.0%, P=0.548) 0.50 (0.26, 0.68) 10.33 0.32 (0.09, 1.18) 2.380 0.57 (0.27, 1.22) 8.00 0.57 (0.27, 1.22) 8.00 NOTE: Weights are from random effects analysis 0.60 (0.29, 1.22) 13.85 0.60 (0.29, 1.22) 13.85	ID For long lesions RESET Trial (2013)	M 	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50	ID For long lesions	TVR	
CTO-IVUS Trial (2015) 0.20 (0.01, 4.15) 0.50 (0.28, 2.90) 8.80 Hong et al (2014) 1.40 (0.86, 2.90) 8.80 1.40 (0.86, 2.90) 8.80 Subtotal (I-squared=0.0%, P=0.450) 1.17 (0.72, 1.87) 20.55 Tian et al (2015) 0.49 (0.16, 1.45) 6.39 For unprotected LM 0.68 (0.39, 1.18) 15.49 0.61 (0.43, 0.90) 0.21 (0.43, 0.90) 0.26 (0.06, 1.17) 3.45 Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 Part et al (2009) 0.50 (0.26, 0.91) 9.38 For bifurcation 0.50 (0.26, 0.96) 10.93 0.21 (0.93, 2.21) 0.57 (0.50, 0.89) 56.77 For complex lesions 0.51 (0.26, 0.96) (1.93 0.22 (0.03, 2.21) 0.95 0.52 (0.32, 1.81) 2.57 (0.52, 0.28) 0.44 (0.14, 1.35) 27.05 For complex lesions 0.51 (0.26, 0.96) (1.93 0.52 (0.03, 1.18) 2.80 0.44 (0.14, 1.35) 27.02 VIO Trial (2013) 0.50 (0.26, 0.28) (1.18, 2.80 0.57 (0.27, 1.22) 0.52 0.52 (0.33, 1.00) 27.02 Subtotal (I-squared=1.02%, P=0.243) 0.57 (0.27, 1.22) 8.00 0.53 (0.40, 0.70)(10.00 0.53 (0.40, 0.70)(10.00 Vorall (I-	ID For long lesions RESET Trial (2013) IVUS-XPL (2016)	<	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 	ID For long lesions RESET Trial (2013)	TVR	0.66 (0.31, 1.41) 12.71
Tian et al (2015) 1.40 (0.68, 2.90) 8.80 C0 FOR MALCOLON 0.51 (0.10, 1.43) 0.53 Hong et al (2014) 1.09 (0.57, 2.07) 11.25 Tian et al (2015) 0.61 (0.25, 1.48) 0.53 For unprotected LM 0.68 (0.39, 1.18) 15.49 0.68 (0.39, 1.18) 15.49 0.51 (0.41, 0.90) 30.21 Gao et al (2014) 0.63 (0.43, 1.57) 11.07 0.65 (0.62, 0.91) 19.38 Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 Port et al (2013) Kim et al (2011) 0.50 (0.26, 0.96) 10.93 0.50 (0.26, 0.96) 10.93 0.50 (0.26, 0.96) 10.93 Subtotal (I-squared=0.0%, P=0.548) 0.50 (0.26, 0.96) 10.93 For bifurcation Chen et al (2010) 0.50 (0.26, 0.81) 13.73 0.50 (0.26, 0.84) 1.57 0.52 (0.33, 1.00) 27.02 Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 0.57 (0.27, 1.22) 8.00 Subtotal (I-squared=0.0%, P=0.032) 0.57 (0.27, 1.22) 8.00 For complex lesions Ahrie et al (2013) 0.57 (0.27, 1.22) 8.00 For complex lesions Ahrie et al (2013) 0.57 (0.27, 1.22) 8.00 Overall (I-squared=10.2%, P=0.334) 0.50 (0.29, 1.22) 13.85 0.53 (0.4	ID For long lesions RESET Trial (2013) IVUS-XPL (2016)	<	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 	ID For long lesions RESET Trial (2013)	TVR	0.66 (0.31, 1.41) 12.71
Hong et al (2014) 1.09 (0.57, 2.07) 11.25 In an et al (2015) 0.61 (0.25, 1.48) 9.53 Subtotal (I-squared=0.0%, P=0.450) 1.17 (0.72, 1.87) 20.55 Hong et al (2014) 0.26 (0.06, 1.17) 3.45 For unprotected LM 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.49 (0.26, 0.91) 19.38 Gao et al (2014) 0.63 (0.43, 1.57) 11.07 0.63 (0.43, 0.57) 0.67 (0.50, 0.89) 56.77 For bifurcation 0.67 (0.50, 0.89) 56.77 0.56 (0.25, 0.81) 13.73 0.25 (0.13, 0.48) 0.50 (0.26, 0.96) 0.80 (0.35, 1.86) 10.50 Subtotal (I-squared=0.0%, P=0.548) 0.50 (0.26, 0.96) 10.93 . . For bifurcation 0.44 (0.14, 1.35) 27.05 For complex lesions 0.32 (0.09, 1.18) 2.80 . . For complex lesions 0.62 (0.39, 1.00) 27.02 Jakabcin et al (2013) 0.24 (0.03, 2.21) 0.95 . . For complex lesions A/10 Trial (2013) 0.60 (0.29, 1.22) 13.85 Subtotal (I-squared=33.4%, P=0.23) 0.70 (0.56, 0.86)100.00 0.70 (0.56, 0.86)100.00 	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO	<	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.)	TVR	0.66 (0.31, 1.41) 12.71
Subtotal (I-squared=0.0%, P=0.450) 1.17 (0.72, 1.87) 20.55 Hong et al (2014) 0.26 (0.06, 1.17) 3.45 For unprotected LM 0.68 (0.33, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.43, 1.57) 11.01 Gao et al (2014) 0.61 (0.41, 0.90) 30.21 0.63 (0.43, 1.57) 11.01 0.63 (0.43, 1.57) 11.01 Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 Part et al (2009) 0.25 (0.13, 0.48) 16.56 For bifurcation 0.50 (0.26, 0.96) 10.93 0.50 (0.26, 0.96) 10.93 0.52 (0.32, 1.18) 2.80 Subtotal (I-squared=0.0%, P=0.548) 0.50 (0.26, 0.96) 10.93 0.52 (0.32, 1.18) 2.80 For complex lesions 0.52 (0.32, 1.18) 2.80 0.51 (0.02, 0.81) 13.73 Chen et al (2013) 0.62 (0.39, 1.00) 27.02 Ahn et al (2013) 0.22 (0.03, 1.18) 0.95 0.57 (0.27, 1.22) 8.00 Subtotal (I-squared=.%, P=.) 0.60 (0.29, 1.22) 13.85 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 0.57 (0.27, 1.22) 8.00 Subtotal (I-squared=1.2%, P=0.343) 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00 0.53 (0.40, 0.70)100.00 0.53 (0.40, 0.70)100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015)	<	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71
For unprotected LM 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 For unprotected LM Gao et al (2014) 0.83 (0.43, 157) 11.07 0.83 (0.43, 157) 11.07 Gao et al (2014) 0.25 (0.13, 0.48) 16.56 Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 0.67 (0.50, 0.89) 56.77 0.67 (0.50, 0.89) 56.77 0.67 (0.50, 0.89) 56.77 0.67 (0.50, 0.89) 56.77 0.80 (0.35, 1.86) 10.50 For bifurcation 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.50 (0.26, 0.96) 10.93 0.44 (0.14, 1.35) 27.05 Subtotal (I-squared=0.0%, P=0.548) 0.16 (0.25, 0.81) 13.73 0.50 (0.29, 1.22) 1.85 0.62 (0.39, 1.00) 27.02 For complex lesions 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.57 (0.27, 1.22) 8.00 0.60 (0.29, 1.22) 13.85 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0.27, 1.22) 8.00 0.70 (0.56, 0.86) 100.00 0.70 (0.56, 0.86) 100.00 0.572 0.60 (0.29, 1.22) 13.85 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86) 100.00 0.70 (0.56, 0.86) 100.00 0.572 0.53 (0.40, 0.70) 100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70) 100.00 0.53 (0.40, 0.70) 100.00 0.53 (0.40, 0.70) 100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015)	<	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.69 (0.16, 1.41) 12.71
Hernanadez et al (2014) 0.68 (0.39, 1.18) 15.49 . Gao et al (2014) 0.68 (0.39, 1.18) 15.49 . Part et al (2009) 0.83, (0.43, 1.57) 11.07 Gao et al (2014) 0.25 (0.13, 0.48) 16.56 Subtotal (I-squared=0.0%, P=0.726) 0.57 (0.50, 0.89) 56.77 Gao et al (2019) 0.80 (0.35, 1.86) 10.50 For bifurcation 0.50 (0.26, 0.96) 10.93 . . . Chen et al (2011) 0.50 (0.26, 0.81) 13.73 . For bifurcation 0.62 (0.39, 1.00) 27.02 Subtotal (I-squared=0.0%, P=0.548) 0.16 (0.22, 0.81) 13.73 For bifurcation 0.62 (0.39, 1.00) 27.02 For complex lesions 0.13 (0.01, 1.16) 0.96 . . . Allor trai (2013) 0.24 (0.03, 2.21) 0.95 . . . Subtotal (I-squared=33.4%, P=0.223) 0.57 (0.27, 1.22) 8.00 . . . Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014)	< ₽=0.825) ───── <	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.69 (0.16, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53
Gao et al (2014) 0.61 (0.41, 0.90) 30.21 For uprotected LM Part et al (2009) 0.83 (0.43, 1.57) 11.07 Gao et al (2014) 0.25 (0.13, 0.48) 16.56 Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 Part et al (2009) 0.80 (0.35, 1.86) 10.50 For bifurcation 0.50 (0.26, 0.96) 10.93 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.44 (0.14, 1.35) 27.05 Kim et al (2011) 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 For bifurcation Chen et al (2013) 0.62 (0.39, 1.00) 27.02 For complex lesions 0.32 (0.03, 2.21) 0.95 . For complex lesions 0.62 (0.39, 1.00) 27.02 Jakabcin et al (2013) 0.24 (0.03, 2.21) 0.95 . . For complex lesions 0.60 (0.29, 1.22) 13.85 Subtotal (I-squared=33.4%, P=0.223) 0.70 (0.56, 0.86) 100.00 . . For complex lesions AVIO Trial (2013) 0.60 (0.29, 1.22) 13.85 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86) 100.00 . . Overall (I-squared=11.2%, P=0.343) 0.53 (0.40, 0.70) 100.00 NOTE: Weights are from random effects analysis 01 1 100 . <td>ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%,</td> <td>< ₽=0.825) ───── <</td> <td>Myocardial infarct</td> <td>OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25</td> <td>ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i>=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014)</td> <td>TVR</td> <td>0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45</td>	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%,	< ₽=0.825) ───── <	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45
Subtotal (I-squared=0.0%, P=0.726) 0.67 (0.50, 0.89) 56.77 Part et al (2009) 0.80 (0.35, 1.86) 10.50 For bifurcation 0.50 (0.26, 0.96) 10.93 0.32 (0.99, 1.18) 2.80 0.50 bifurcation 0.44 (0.14, 1.35) 27.05 Kim et al (2011) 0.50 (0.26, 0.96) 10.93 - For bifurcation 0.44 (0.14, 1.35) 27.05 For complex lesions 0.16 (0.25, 0.81) 13.73 For bifurcation 0.62 (0.39, 1.00) 27.02 Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 - - AVID Trial (2013) 0.82 (0.34, 1.97) 6.08 - - Ahn et al (2013) 0.57 (0.27, 1.22) 8.00 - - Verall (I-squared=33.4%, P=0.223) 0.70 (0.56, 0.86) 100.00 - - Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86) 100.00 - - Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86) 100.00 - - NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70) 100.00 -	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM	< ₽=0.825) ───── <	Myocardial infarct	OR (95% CI) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.625)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45
For bifurcation Chen et al (2013) Kim et al (2011) 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 . 0.44 (0.14, 1.35) 27.05 For complex lesions Jakabcin et al (2010) AVIO Trial (2013) Ahn et al (2013) Subtotal (I-squared=33.4%, P=0.223) 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96 0.57 (0,27, 1.22) 8.00 . 0.62 (0.39, 1.00) 27.02 Heterogeneity between groups: P=0.103 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 . . Overall (I-squared=11.2%, P=0.343) 0.70 (0.56, 0.86)100.00 . . . Overall (I-squared=11.2%, P=0.343) 0.53 (0.40, 0.70)100.00 . .	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014)	< ₽=0.825) ───── <	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.625) For unprotected LM	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38
Chan et al (2013) 0.50 (0.26, 0.96) 10.93 Subtotal (I-squared=0.0%, P=0.548) 0.16 (0.25, 0.81) 13.73 For complex lesions 0.24 (0.03, 2.21) 0.95 Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 AVIO Trial (2013) 0.82 (0.34, 1.97) 6.08 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0.27, 1.22) 8.00 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009)	< P=0.825) ← P=0.450)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.625) For unprotected LM Gao et al (2014)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56
Kim et al (2011) 0.32 (0.09, 1.18) 2.80 Subtotal (I-squared=0.0%, P=0.548) 0.16 (0.25, 0.81) 13.73 For complex lesions 0.24 (0.03, 2.21) 0.95 Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 AVIO Trial (2013) 0.82 (0.34, 1.97) 6.08 Ahn et al (2013) 0.57 (0.27, 1.22) 8.00 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0.27, 1.22) 8.00 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)1100.00 0.70 (0.56, 0.86)1100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009)	< P=0.825) ← P=0.450)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.625) For unprotected LM Gao et al (2014) —	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50
Subtotal (1-squared=0.0%, P=0.548) 0.16 (0.25, 0.81) 13.73 Chen et al (2013) 0.62 (0.39, 1.00) 27.02 For complex lesions Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 . 0.62 (0.39, 1.00) 27.02 AVIO Trial (2013) 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96 . For complex lesions Subtotal (1-squared=33.4%, P=0.223) 0.57 (0,27, 1.22) 8.00 0.60 (0.29, 1.22) 13.85 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 0.70 (0.56, 0.86)100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%,	< P=0.825) ← P=0.450)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.625) For unprotected LM Gao et al (2014) —	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50
For complex lesions 0.062 (0.03, 1.00) 27.02 Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 AVIO Trial (2013) 0.82 (0.34, 1.97) 6.08 Ahn et al (2013) 0.13 (0.01, 1.16) 0.96 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0.27, 1.22) 8.00 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 NOTE: Weights are from random effects analysis 0.53 (0.40, 0.70)100.00	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013)	< P=0.825) ← P=0.450)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50
For complex resides Jakabcin et al (2010) AVIO Trial (2013) Ahn et al (2013) Subtotal (I-squared=33.4%, P=0.223) Heterogeneity between groups: P=0.103 Overall (I-squared=10.2%, P=0.343) 0.11 1 100	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011)	P=0.825) P=0.450) P=0.726)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05
Jakabcin et al (2010) 0.24 (0.03, 2.21) 0.95 AVIO Trial (2013) 0.82 (0.34, 1.97) 6.08 Ahn et al (2013) 0.13 (0.01, 1.16) 0.96 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0,27, 1.22) 8.00 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 - Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 - Utor tal (0.10, 0.1	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011)	P=0.825) P=0.450) P=0.726)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02
Ahn et al (2013) 0.13 (0.01, 1.16) 0.96 Subtotal (I-squared=33.4%, P=0.223) 0.57 (0,27, 1.22) 8.00 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86) 100.00 AVIO Trial (2013) 0.60 (0.29, 1.22) 13.85 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86) 100.00 0.70 (0.56, 0.86) 100.00 0.00 (0.29, 1.22) 13.85 More all (I-squared=11.2%, P=0.343) 0.53 (0.40, 0.70) 100.00 0.0572 1 17.5	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%,	P=0.825) P=0.450) P=0.726)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02
Subtotal (I-squared=33.4%, P=0.223) 0.57 (0,27, 1.22) 8.00 AVIO Intal (2015) 0.60 (0.29, 1.22) 10.80 Heterogeneity between groups: P=0.103 0.70 (0.56, 0.86)100.00 0.70 (0.56, 0.86)100.00 0.70 (0.56, 0.86)100.00 0.70 (0.56, 0.86)100.00 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 1 100 1 1 1	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2013) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2010)	P=0.825) P=0.450) P=0.726)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02
Heterogeneity between groups: P=0.103 Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 0.verall (I-squared=11.2%, P=0.343) 0.60 (0.29, 1.22) 13.85 Overall (I-squared=11.2%, P=0.343) 0.70 (0.56, 0.86)100.00 0.00 (0.29, 1.22) 13.85 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 1 100 1 1	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2019) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2010) AVIO Trial (2013)	P=0.825) P=0.450) P=0.726)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02
Overall (I-squared=10.2%, P=0.343) 0.70 (0.56, 0.86)100.00 Overall (I-squared=11.2%, P=0.343) 0.53 (0.40, 0.70)100.00 NOTE: Weights are from random effects analysis 1 100 1 17.5	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2013) Ahr et al (2013) Ahr et al (2013)	P=0.825) P=0.450) P=0.726) P=0.548)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02
c .01 1 100 d .0572 1 17.5	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2013) Ahn et al (2013) Subtotal (I-squared=33.4%	P=0.825) P=0.450) P=0.726) P=0.548) 5, P=0.223)	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.83, (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032) For bifurcation Chen et al (2013) Subtotal (I-squared=.%, P=.) For complex lessions AVIO Trial (2013)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02 0.60 (0.29, 1.22) 13.85
	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2010) AvIO Trial (2013) Subtotal (I-squared=33.4% Heterogeneity between gr	P=0.825) P=0.450) P=0.726) P=0.548) 5, P=0.223) oups: P=0.103	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96 0.57 (0,27, 1.22) 8.00	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032) For bifurcation Chen et al (2013) Subtotal (I-squared=.%, P=.) For complex lessions AVIO Trial (2013) Subtotal (I-squared=.%, P=.)	TVR	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02 0.60 (0.29, 1.22) 13.85 0.60 (0.29, 1.22) 13.85
	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Trian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2009) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2011) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2010) AvIO Trial (2013) Subtotal (I-squared=33.4% Heterogeneity between gr	P=0.825) P=0.450) P=0.726) P=0.548) 5, P=0.223) oups: P=0.103	Myocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23: 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96 0.57 (0,27, 1.22) 8.00	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032) For bifurcation Chen et al (2013) Subtotal (I-squared=.%, P=.) For complex lessions AVIO Trial (2013) Subtotal (I-squared=.%, P=.) Overall (I-squared=11.2%, P=0.343)		0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02 0.60 (0.29, 1.22) 13.85 0.60 (0.29, 1.22) 13.85
	ID For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, For unprotected LM Hernanadez et al (2014) Gao et al (2014) Part et al (2019) Subtotal (I-squared=0.0%, For bifurcation Chen et al (2013) Kim et al (2013) Subtotal (I-squared=0.0%, For complex lesions Jakabcin et al (2010) AVID Trial (2013) Ahn et al (2013) Subtotal (I-squared=33.4% Heterogeneity between gr Overall (I-squared=10.2%,	<i>P</i> =0.825) <i>P</i> =0.450) <i>P</i> =0.726) <i>P</i> =0.548) <i>p</i> =0.223) oups: <i>P</i> =0.103 <i>P</i> =0.343)	Vyocardial infarct	OR (95% Cl) Weight % 0.20 (0.01, 4.23; 0.50 0.33 (0.01, 8.18) 0.45 0.26 (0.03, 2,32) 0.95 0.20 (0.01, 4.15) 0.50 1.40 (0.68, 2.90) 8.80 1.09 (0.57, 2.07) 11.25 1.17 (0.72, 1.87) 20.55 0.68 (0.39, 1.18) 15.49 0.61 (0.41, 0.90) 30.21 0.63 (0.43, 1.57) 11.07 0.67 (0.50, 0.89) 56.77 0.50 (0.26, 0.96) 10.93 0.32 (0.09, 1.18) 2.80 0.16 (0.25, 0.81) 13.73 0.24 (0.03, 2.21) 0.95 0.82 (0.34, 1.97) 6.08 0.13 (0.01, 1.16) 0.96 0.57 (0.27, 1.22) 8.00 0.70 (0.56, 0.86)100.00	ID For long lesions RESET Trial (2013) Subtotal (I-squared=.%, P=.) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, P=0.625) For unprotected LM Gao et al (2014) Part et al (2009) Subtotal (I-squared=78.2%, P=0.032) For bifurcation Chen et al (2013) Subtotal (I-squared=.%, P=.) For complex lessions AVIO Trial (2013) Subtotal (I-squared=.%, P=.) Overall (I-squared=11.2%, P=0.343) NOTE: Weights are from random effects	analysis	0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.66 (0.31, 1.41) 12.71 0.49 (0.16, 1.45) 6.39 0.61 (0.25, 1.48) 9.53 0.26 (0.06, 1.17) 3.45 0.49 (0.26, 0.91) 19.38 0.25 (0.13, 0.48) 16.56 0.80 (0.35, 1.86) 10.50 0.44 (0.14, 1.35) 27.05 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02 0.62 (0.39, 1.00) 27.02 0.60 (0.29, 1.22) 13.85 0.53 (0.40, 0.70)100.00

Figure 2. Forest plots of the efficacy endpoints of the included trials. The odds ratios of MACE (a), all-cause mortality (b), myocardial infarction (c), target-vessel revascularization (d), target-lesion revascularization (e), and stent thrombosis (f) associated with IVUS guidance compared with angiography guidance

Notably, most adverse events related to the procedure were potentially considered to be because of the underexpansion and malapposition of implanted stents, which might influence the clinical outcomes. The optimal stent deployment were considered if the following criteria were met: good apposition (all stent struts posited to the vessel wall), optimal stent expansion (minimal area of stents \geq 5 mm²) or cross-sectional area (CSA) >90% of distal reference lumen CSA for small vessel/and no edge dissection (5-mm margins proximal and distal to the stent). IVUS guidance had a beneficial effect on decreasing strut malapposi-

Study ID	TLR	OR (95% CI) Weight %	Study ID	Stent thrombosis	OR (95% CI) Weigh	ıt %
For long lesions IVUS-XPL (2016) Subtotal (I-squared=.%, <i>P</i> =.)	*	0.50 (0.28, 0.91) 10.71 0.50 (0.28, 0.91) 10.71	For long lesions RESET Trial (2013) IVUS-XPL (2016) Subtotal (I-squared=0.0%, <i>P</i> =0.991)	•	1.00 (0.14, 7.12) 5	2.79 5.59 3.39
For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.642)		0.62 (0.20, 1.91) 5.27 0.64 (0.25, 1.63) 6.81 0.98 (0.55, 1.74) 11.00 0.83 (0.53, 1.30) 23.08	For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.679)	<u> </u>	0.36 (0.09, 1.39) 11 0.10 (0.01, 1.83) 2	2.44 1.77 2.62 5.83
For unprotected LM Henmandez et al (2014) Gao et al (2014) Subtotal (I-squared=92.6%, <i>P</i> =0.000)	+	1.24 (0.766, 2.01)12.320.23 (0.11, 0.49)8.740.55 (0.11, 2.82)21.06	For unprotected LM Hermandez et al (2014) Gao et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.839)	>	0.22 (0.05, 0.95) 10	8.10 0.02 8.11
For bifurcation Chen et al (2013) Kim et al (2010) Kim et al (2011) Subtotal (I-squared=0.0%, <i>P</i> =0.505)		0.61 (0.36, 1.01) 11.96 0.94 (0.39, 2.24) 7.37 0.91 (0.52, 1.62) 11.08 0.76 (0.53, 1.07) 30.42	For bifurcation Chen et al (2013) Kim et al (2010) Kim et al (2011) Subtotal (I-squared=0.0%, <i>P</i> =0.807)		0.27 (0.06, 1.22) 9 0.33 (0.04, 3.21) 4	3.44 9.50 1.48 2.42
For complex lession Jakabcin et al (2010) AVIO Trial (2013) Ahn et al (2013) Subtotal (I-squared=63.5%, <i>P</i> =0.065)		1.00 (0.31, 3.21) 5.08 0.74 (0.35, 1.59) 8.55 0.03 (0.00, 0.45) 1.10 0.51 (0.14, 1.82) 14.74	For complex lesions Jakabcin et al (2010) AVIO Trial (2013) Ahn et al (2013) Subtotal (I-squared=10.8%, P=0.326)	*	3.02 (0.12, 74.79) 2 0.17 (0.02, 1.56) 4	2.85 2.09 1.31 0.25
Overall (I-squared=52.3%, <i>P</i> =0.017) NOTE: Weights are from random effects ar	alysis	0.69 (0.50, 0.94) 100.00	Heterogeneity between groups: <i>P</i> =0.344 Oveerall (I-squared=0.0%, <i>P</i> =0.787)		0.31 (0.20, 0.50) 100	.00
e .002 Favors IVUS	1	500 Favors non-IVUS	f .0059 Favors IVUS	l 1 Favors non-I ^N	170 /US	

Figure 2. Forest plots of the efficacy endpoints of the included trials. The odds ratios of MACE (a), all-cause mortality (b), myocardial infarction (c), target-vessel revascularization (d), target-lesion revascularization (e), and stent thrombosis (f) associated with IVUS guidance compared with angiography guidance

tion risk and resulted in larger minimum luminal diameter (MLD), (14) which were thought to be more useful for the complex coronary artery lesions. The study from Park et al. (31) pointed out that IVUS-guided DES implantation might decrease the longterm mortality rate for unprotected LM coronary artery stenosis (4.7% vs. 16.0%, for IVUS guidance vs. angiography guidance) after analyzing the data of 145 matched pairs of patients. A recent large pooled analysis of four registries reported by Hernandez et al. (16) indicated an association of IVUS guidance during DES implantation with better 1-year outcomes in patients with LM disease, mainly derived from the lower incidence of all-cause mortality (7.4% vs. 13.0%, p=0.01) and ST (0.6% vs. 2.2%, p=0.04). On the other hand, Gao et al. (22) performed another one large cohort and stated several possible reasons to support the usage of IVUS guidance in patients with LM disease, including more accurate quantification of stent diameter or length as well as less late loss. Similarly, we found lower incidence of MACE composited of all-cause mortality, MI, and TVR pertaining to IVUS guidance, especially in patients with LM disease. These results might mostly benefit from IVUS guidance derived minimal area and fractional flow reserve, which facilitated detection of significant hemodynamically in this specific lesion subset of coronary disease (32). Indeed, these results from the over-mentioned registries were unavoidably affected by the unbalanced baseline characteristics and lesion or procedural details of the included patients. However, the repeated analyses of data from RCTs and propensity-matched subgroups in Obs were performed to decrease possible sources of bias, from which the results might confirm the beneficial efficacy of IVUS guidance partly. Thus, the recommendations for percutaneous revascularization of LM disease had been granted to a Class IIb level (33).

Since the "double kissing crush (DK Crush) with two stents" technique for bifurcation lesions was first reported by Chen et al. (34), the improved clinical outcomes had been observed mainly appeared as significant reduction in TLR and TVR risks. It should be noted that thrombosis might be thought as possible reason leading to repeat revascularization. There were many factors considered to be associated with incidence of ST, including the characteristics of lesions (anatomical), device, or techniques, resulting in more common usage of IVUS in this specific lesion subset (35, 36). One large observational trial conducted by Chen et al. (29) reported comparable very-late ST risk between the IVUS guidance group and the angiography guidance group in patients with bifurcation lesions (0.6% vs. 4.3%, p=0.003, for IVUS guidance and angiography guidance respectively); similar results were also reported by Kim et al. (30) In addition, bifurcation lesions are always a varied and complicated subset of coronary artery disease, meaning that they would be more possible to get advantages from imaging modality such as IVUS according to the clinical benefits described previously. The present meta-analysis indicated a lower incidence of ST following IVUS guidance, as well as other MACE involving all-cause mortality and MI, being similar as outcomes of these over-mentioned large observational tri-

OR (95% CI) Weight %

2.44

3.98

6 4 3

2.53

6.51 5 00

14.05

45 85

8.45

7.69

0.97

5.26

7.91

2 50

0.88 3.39

200

7.43

11.42

3.63

15.49

14 14

61.99

0.15 (0.02, 0.95)

0.60 (0.14, 2.51)

0.36 (0.11, 1.10)

0.66 (0.11, 4.01)

0.85 (0.28, 2.61) 0.66 (0.18, 2.37)

0.74 (0.35, 1.59)

0.53 (0.34, 0.80)

0.40 (0.15, 1.08)

0.32 (0.11, 0.89)

0.48 (0.33, 0.69)

0.09 (0.00, 1.59)

0.21 (0.06, 0.73)

0.58 (0.21, 1.61)

0.35 (0.16, 0.75)

1.51 (0.25, 9.26)

0.20 (0.01, 4.14) 0.89 (0.19, 4.22)

0.49 (0.37, 0.65) 100.00

Favors non-IVUS

OR (95% CI) Weight % 0.66 (0.31 1.41) 15.72 0.66 (0.31, 1.41) 15.72

0.49 (0.16, 1.45)

0.61 (0.25. 1.48)

0.24 (0.05, 1.16)

0.49 (0.26, 0.92) 22.49

0.32 (0.15, 0.67) 16.26 0.80 (0.35, 1.86) 12.70 0.50 (0.20, 1.21) 28.96

0.80 (0.38, 1.71) 15.49 0.80 (0.38, 1.71)

0.60 (0.29, 1.22) 17.34 0.60 (0.29, 1.22) 17.34 0.57 (0.42, 0.77) 100.00

19.7

Favors non-IVUS

CTO-IVUS Trail (2015) CTO-IVUS Trail (2015)	Study ID	MACE	OR (95% CI) We	ight %	Study ID	All-cause mortality
RESET True (2013) 0.47 (120, 120, 100) 0.47 (120, 120, 100) 0.4	For long lesions				For long lesions	
VUS XPL Trail (2016) 0, 47 (027, 0.28) 8.14 VUS XPL Trail (2016) VUS XPL Trail (2016) 0, 51 (0.25, 0.28) 8.14 VUS XPL Trail (2016) For CTD 0, 34 (0.12, 0.93) 8.14 For CTD CTD-VUS Trail (2015) 0, 34 (0.12, 0.93) 8.14 For CTD For CTD 0, 34 (0.12, 0.93) 8.14 For CTD CTD-VUS Trail (2015) 0, 34 (0.12, 0.93) 8.14 For CTD For CTD 0, 34 (0.12, 0.93) 8.14 For CTD For Unreaded 056, P-0.637) 0, 56 (0.4, 0.39) 1.93 Subtrail (1-squared-0.0%, P-0.520) For CTD 0, 57 (0.4, 1.19) 0, 57 (0.4, 1.19) 1.02 For CTD For Complex lesions 0, 57 (0.5, 0.71) 1.12 8.13 For CTD For CTD CTD-VUS Trail (2015) 0, 70 (0.5, 0.71) 1.12 1.12 For CTD For CTD CTD-VUS Trail (2016) 0, 70 (0.5, 0.71) 1.12 1.12 For CTD For CTD CTD-VUS Trail (2013) 0, 70 (0.5, 0.71) 1.12 1.12 For CTD For CTD CTD-VUS Trail (2015) 0, 70 (0.5, 0.71) 1.12 For CT		•	0 59 (0 28 1 24)	4 68		•
Subtool In-squared-20, %, P-0, 831) For CTO CTO-VUS Trial (2018) For CTO CTO-VUS Trial (2018) For compared-13, %, P-0, 820) For unprotected LM Hernandez et al (2014) Subtool II-squared-13, %, P-0, 827) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 827) For Unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 828) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 828) For unprotected LM Hernandez et al (2014) Subtool II-squared-20, %, P-0, 829) B Subtool II-squared-20, %, P-0, 829) Subtool II-squared-20, %, P-0, 829) B Tor Information Dore al (12010) Subtool II-squared-20, %, P-0, 829) B Subtool II-squared-20, %, P-0, 829) Subtool II-squared-20, %, P-0, 829) CTO-VUS Fini (2015) Subtool II-squared-20, %, P-0, 829) CTO-VUS Fini (2015) Subtool II-squared-20, %, P-0, 829) Subtool II-squared-20, %, P-0, 829) For Unprotected LM Soubtool II-squared-20,		•			IVUS-XPL Trial (2016)	
CTU-USE Trial (2015) 0.4 (0.12, 0.96) 2.35 Hong et al (2014) 0.82 (0.45, 1.52) 6.80 Monta et al (2014) 0.81 (0.42, 1.54) 5.90 Subtral (I-squared-0.0%, P-0.827) 0.81 (0.42, 1.54) 5.90 For unprotocted LM 0.81 (0.42, 1.54) 5.90 Gas et al (2014) 0.81 (0.42, 1.54) 5.90 Subtral (I-squared-0.0%, P-0.827) 0.81 (0.42, 1.13) 0.82 (0.45, 1.13) For unprotocted LM 0.81 (0.42, 1.13) 0.82 (0.45, 1.13) 0.82 (0.45, 1.13) Subtral (I-squared-0.0%, P-0.828) 0.81 (0.42, 1.13) 0.82 (0.45, 1.13) 0.82 (0.45, 1.13) For compacts balance 0.81 (0.42, 1.13) 0.82 (0.45, 1.13) 0.82 (0.45, 1.13) Subtral (I-squared-0.0%, P-0.828) 0.87 (0.57, 0.78) 10.00 For compacts balance 0.87 (0.57, 0.78) A 1.2 1.2 1.2 1.2 1.2 1.2 1.2 For compacts balance 0.87 (0.57, 0.78) 100.00 0.87 (0.57, 0.78) 100.00 0.65 1.2 For unprotocted LM 0.65 1.2 For unprotocted LM 0.65 1.2 For unprotocted LM 1.2 For unprotocted		>				
Tan at 2(216) Tan at 2(216) Tan at 2(216) Tan at 2(216) Tan at 2(216) Tan at 2(216) Subta [1-squared-0.15%, P-0.52) Tan at 2(216) Subta [1-squared-0.15%, P-0.52) Tan at 2(216) Subta [1-squared-0.0%, P-0.52) Tan at 2(217) Subta [1-squared-0.0%, P-0.52) Tan at 2(216) Subta [1-squared-0.0%, P-0.52) Tan at 2(217) Subta [1-squared-0.0%, P-0.52) Tan at 2(217) Subta [1-squared-0.0%, P-0.52) Tan at 2(216) Subta [1-squared-0.0%, P-0.52) Subta [1-squared-0.	For CTO					_
Hard en al 2000) Statutal (1-squared-10%, P-0.050) Statutal (1-squared-0.0%, P-0.050) Statutal (1-squared-0.0%, P-0.050) For complex lesions Statutal (1-squared-0.0%, P-0.050) Statutal (1-squared-0.0%, P-0.050) For complex lesions Statutal (1-squared-0.0%, P-0.050) For	CTO-IVUS Trial (2015) 🛛 < 🔹 🔹		0.34 (0.12, 0.96)	2.35		
bill (1) (1)	ïan et al (2015)	•	0.82 (0.45, 1.52)	6.80		
For unprotected LM termande ce al (2014) Sase of a (2014) Far et al (2019) Far et al (2013) Gen et al (2014) Subtral (I +squared-0.0%, P-0.657) For complex lesions Gen et al (2014) Gen et al (2013) Gen et al (2013) Gen et al (2014) Subtral (I +squared-0.0%, P-0.657) For complex lesions Gen et al (2013) Gen et al (2014) Subtral (I +squared-0.0%, P-0.258) For bine set al (2014) Gen et al (2014) Subtral (I +squared-0.0%, P-0.258) For complex lesions Gen et al (2014) Gen et al (2014) For complex lesions Gen et al (2014) Gen et al (2014) Subtral (I +squared-0.0%, P-0.258) For complex lesions Gen et al (2014) Gen et al (2014) For complex lesions Gen et al (2014) Gen et al (2014) For complex lesions Gen et al (2015) For complex lesions Gen et al (2014) For complex lesions Subtrotal (I-squared-5, P, A-0.527) For complex lesions Gen et						
of n/p/07082102101 0.89 (0.88, 0.89) 15.5 marker et al (2014) 0.89 (0.88, 0.89) 15.5 marker et al (2014) 0.89 (0.84, 0.93) 15.5 marker et al (2013) 0.89 (0.84, 0.73) 5.75 motion et al (2014) 0.89 (0.84, 0.73) 5.75 motion et al (2011) 0.99 (0.84, 1.73) 5.75 or nuplox leasions 0.91 (0.84, 2.11) 5.75 motion et al (2010) 0.73 (0.51, 2.12) 7.85 motion et al (2010) 0.73 (0.52, 1.17) 10.00 statch et al (2010) 0.73 (0.57, 0.78) 10.00 motion et al (2010) 0.73 (0.57, 0.78) 10.00 motion et al (2014) 0.67 (0.57, 0.78) 10.00 motion et al (2015) 0.67 (0.57, 0.78) 10.00 motion et al (2015) 0.67 (0.57, 0.78) 10.00 motion et al (2015) 0.73 (0.51, 0.22) 1.81 1.82 statch et al (2014) 0.67 (0.57, 0.78) 10.00 1.92 Motion et al (2015) 0.73 (0.01, 4.22) 0.85 1.92 1.92 motion et al (2016) 0.73 (0.01, 4.22) 0.85 1.92 1.9			0.71 (0.47, 1.07)	13.05	For unprotected I M	
Harmandez et al (2014) Bos et al (2015) Bos et al (2014) Bos et al (2014) Bos et al (2014) Bos et						_ —
Park et al (2009) Def (1.52, 0.22) 45.10 Def (1.52,						
Subtoal (I-squared=0.0%, P=0.897) orb furctation Chen et al (2011) Subtoal (I-squared=0.0%, P=0.897) For complex lesions Subtoal (I-squared=0.0%, P=0.55) Subtoal (I-squared=0.0%, P=0.55) Subtoal (I-squared=0.0%, P=0.55) Subtoal (I-squared=0.0%, P=0.680) Overal (I-squared=0.0%, P=0.683) Overal (I-squared=0.0%, P=0.682) Overal (I-squar					Gao et al (2014)	
For bifurcation Chen et al (2013) Subtoal (I-squared=0.0%, P=0.637) For complex lesions dachorin et al (2010) Subtoal (I-squared=0.0%, P=0.580) Our al (2010) AVIO Trial (2013) Subtoal (I-squared=0.0%, P=0.580) Our al (2010) AVIO Trial (2013) Subtoal (I-squared=0.0%, P=0.282) The servers IVUS Subtoal (I-squared=0.0%, P=0.282) The servers IVUS Subtoal (I-squared=0.0%, P=0.283) Over al (I-squared=0.0%, P=0.283) For OTO TO I-VUS Trial (2015) Trian et al (2016) Subtoal (I-squared=0.0%, P=0.283) For unprotected LM For long lesions Al (0.068, 2.29) 1.13 Subtoal (I-squared=0.0%, P=0.083) Subtoal (I-squared=0.0%, P=0.084) Subtoal (I-squared=0.0%, P=0.084) Sub		$\overline{\langle}$			Subtotal (I-squared=0.0%, P=0.628)	\diamond
Chen et al (2013) (mit et al (2011) Subtoal (I-squared=0.0%, P=0.837) 0.88 (046, 17.3) 5.75 (0.78 (0.53, 1.17) 16.01 Win Trai (2013) Subtoal (I-squared=0.0%, P=0.580) 0.91 (0.40, 2.11) 3.64 (0.57 (0.37, 12.21) 7.84 (0.57 (0.37, 0.78) 10.00 A 1.2 8.31 8.31 8.31 8.31 (1.5quared=0.0%, P=0.580) 9.67 (0.57, 0.78) 10.00 A 1.2 8.31 8.31 8.31 9.67 (0.57, 0.78) 10.00 B 1.2 8.31 9.20 (0.01, 4.23) 0.53 (0.00, 2.22) 1.10 1.10 Corr Cito	•		,			
Kim et al (2011) Subtal (I-squared=0.0%, P=0.637) For complex lesions databatin et al (2010) AVIO Tria (2013) Subtal (I-squared=0.0%, P=0.556) Corral (I-squared=0.0%, P=0			0.00/0.42	F 7F		
Subtotal (I-squared=18.9%, P=0.292) For complex lesions Jakabcin et al (2010) AVIO Trial (2013) AVIO Trial (2013) Derral (I-squared=0.0%, P=0.556) 0.67 (0.57, 0.78) 100.00 AVIO Trial (2013) Derral (I-squared=2.14%, P=0.259) Heterogeneity between groups: P=0.533 Dorral (I-squared=2.14%, P=0.259) Heterogeneity between groups: P=0.533 Dorral (I-squared=0.0%, P=0.355) Derral (I-squared=0.0%, P=0.553) Derral (I-squared=0.0%, P=0.55) Derral (I-squared=0.0%, P=0.55) Derral (I-squared=0.0%, P=0.55) Derral (I-squared=0.0%, P=0.52) Derral (I-square						
For complex lesions Jakabein et al (2010) AvrO Trial (2013) Subtotal (I-squared=0.0%, P-0.556) 0.91 (0.40, 2.11) 3.64 0.74 (0.46, 1.20) 11.01 0.67 (0.57, 0.78) 100.00 0.67 (0.57, 0.78) 100.00 0.67 (0.57, 0.78) 100.00 0.67 (0.57, 0.78) 100.00 Jakabein et al (2010) Jakabein et al (2014) Favors IVUS For complex lesions Jakabein et al (2014) For long lesions REST Trial (2015) For complex lesions Jakabein et al (2014) For unprotected LM Himandez et al (2014) For complex lesions Subtotal (I-squared=0.0%, P-0.924) Myoc ardial infarction 0.20 (0.01, 4.23) 0.83 0.26 (0.82, 222) 1.173 1.12 (0.88) 1.85 (0.33) 0.20 (0.01, 4.15) 0.83 1.00 (0.50, 2.02) 11.73 1.12 (0.88) 1.85 (0.33) 0.76 (0.58) (0.39) 1.18 (0.98) 0.06 (0.39, 1.18) 19.33 0.76 (0.56) 0.37 (10.00, 99) 4.30 0.31 (0.10, 0.99) 4.30 0.31 (0.10, 0.99						•
Jakabein et al (2010) Alakabein et al (2010) WVD Trial (2013) Subtotal (I-squared=0.0%, P=0.556) Dveral (I-squared=0.0%, P=0.580) Dveral (I-squared=0.0%, P=0.880) Dveral (I-squared=0.0%, P=0.712) Dveral (I-squared=0.0%, P=0.714) For complex lesions Subtotal (I-squared=0.0%, P=0.714) For complex lesions Subtotal (I-squared=0.0%, P=0.714) Dveral (I-squared=0.0%, P=0.742) Dveral (I-squared=0.0%, P=0.742) Dveral (I-squared=0.0%, P=0.7	subtotal (I-squared=0.0%, <i>P</i> =0.637)	\rightarrow	0.78 (0.53, 1.17)	16.01	Subtotal (I-squared=18.9%, P=0.292)	
AVIO Trai (2013) Subtotal (I-squared-0.0%, P-0.556) Overall (I-squared-0.0%, P-0.895) Overall (I-squared-0.0%, P-0.895) Overall (I-squared-0.0%, P-0.895) Overall (I-squared-0.0%, P-0.712) a 12 Favors IVUS Study Myocardial infarction ID OR (95% CI) Weight % Der long lesions RESET Trai (2013) Subtotal (I-squared-0.0%, P-0.825) Overall (I-squared-0.0%, P-0.912) Subtotal (I-squared-0.0%, P-0.925) Subtotal (I-squared-0.0%, P-0.926) Subtotal (I-squared-0.0%, P-0.927) Subtotal (I-s						
Subtotal (I-squared=0.0%, P=0.556) 0.47 (0.46, 1.20) 11.01 Betarogeneity between groups: P=0.530 0.67 (0.57, 0.78) 100.00 0.67 (0.57, 0.78) 100.00 0.68 (0.39, 1.81) 15.33 0.76 (0.56, 1.04) 58.91 0.76 (0.56, 1.04) 58.91 0.77 (0.48, 1.27) 2.577 0.76 (0.56, 1.04) 58.91 0.76 (0.56, 1.04) 58.91 0.77 (0.57, 1.137) 0.77 (0.57, 1.137) 0.76 (0.56, 1.04) 58.91 0.77 (0.57, 1.137) 0.77 (0.57, 1.77) 0.76 (0.56, 1.04) 58.91 0.77 (0.57, 1.77) 0.76 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.91 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.76 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.91 0.77 (0.57, 1.77) 0.76 (0.56, 1.04) 58.91 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.77 (0.57, 1.77) 0.77 (0.56, 1.04) 58.91 0.77 (0.56, 1.04) 58.						
Heterogeneity between groups: P=0.680 Overall (I-squared=0.0%, P=0.895) 0.67 (0.57, 0.78) 100.00 a12		$\langle \rangle$				
Overall (I-squared=0.0%, P=0.835) 0.67 (0.57, 0.78) 100.00 Overall (I-squared=0.0%, P=0.712) a 12 1 8.31 Favors IVUS Favors non-IVUS D Study Myocardial infarction 0.8 (95%, CI) Weight % ID 0.8 (95%, CI) Weight % ESET Trial (2013) 0.20 (0.01, 4.23) 0.63 VUS -KPL Trial (2016) 0.20 (0.01, 4.15) 0.63 Subtral (I-squared=0.0%, P=0.825) 0.20 (0.01, 4.15) 0.63 Trian et al (2014) 0.20 (0.01, 4.15) 0.63 Subtral (I-squared=0.0%, P=0.825) 0.20 (0.01, 4.15) 0.63 Trian et al (2014) 0.20 (0.01, 4.15) 0.63 Subtral (I-squared=0.0%, P=0.828) 1.12 (0.68, 1.85) 23.48 Por unprotected LM 0.80 (0.33, 1.18) 19.33 Himandez et al (2014) 0.83 (0.33, 1.57) 13.81 Subtral (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.31 For furgrated Log(0, P=0.883) 0.31 (0.10, 0.99) 4.30 Subtral (I-squared=0.0%, P=0.974) 0.24 (0.03, 2.21) 1.19 For complex lesions 0.26 (0.04, 1.77) 7.79 Subtral (I-squared=0.0%, P=0.487) 0.76 (0.56, 0.07) 100.00 C 0.76 (0.56, 0.07) 100.00 C 0.7	•		, .,			
Favors IVUS Favors non-IVUS Favors NUS Study Myocardial infarction OR (95% CI) Weight % Study Dr long lesions 0.20 (0.01, 4.23) 0.63 RESET Trial (2013) 0.20 (0.01, 4.23) 0.63 VUS XPL Trial (2016) 0.20 (0.01, 4.23) 0.63 For CTO 0.20 (0.01, 4.15) 0.63 Tone of al (2015) 0.20 (0.01, 4.15) 0.63 Hong et al (2014) 1.00 (0.50, 2.02) 11.73 Subtotal (I-squared=0.0%, P=0.424) 1.12, (0.68, 1.55) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Himmadez et al (2014) 0.58 (0.39, 1.18) 19.33 Subtotal (I-squared=0.0%, P=0.424) 0.76 (0.56, 1.04) 58.91 For improtected LM 0.58 (0.39, 1.18) 19.33 Himmadez et al (2014) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.424) 0.31 (0.10, 0.97) 7.79 Subtotal (I-squared=0.0%, P=0.315) 0.32 (0.03, 1.18)		\Diamond	0.67 (0.57, 0.78)	100.00		93
Favors IVUS Favors non-IVUS Favors NVUS Study Myocardial infarction 0R (95% CI) Weight % Study D 0R (95% CI) Weight % 10 For long lesions 0.20 (0.01, 4.23) 0.63 RESET Trial (2013) 0.20 (0.01, 4.23) 0.63 VUS -NPL Trial (2016) 0.20 (0.01, 4.23) 0.63 For CTO 0.20 (0.01, 4.15) 0.63 Tran et al (2015) 1.40 (0.68, 2.90) 10.83 Hong et al (2014) 0.68 (0.39, 1.18) 19.33 Subtotal (I-squared=0.0%, P=0.424) 1.12, (0.68, 1.55) 22.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Himandez et al (2014) 0.56 (0.50, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2013) 0.32 (0.09, 1.18) 5.50 Subtotal (I-squared=0.0%, P=0.974) 0.32 (0.03, 1.57) 7.79 For complex lesions 0.24 (0.03, 2.21) 1.19 Jakabain et al (2013) 0.76 (0.56, 0.97) 100.00 Subtotal (I-squared=0.0%, P=0.497) 0.76 (0.50, 0.97) 100.00 Orerall (I-squared=0.0%, P=0.497) 0.76 (0.50, 0.97) 100.00 Orerall (I-squared	- 10				L oos	
Study ID Myocardial infarction OR (95% CI) Weight % Study ID TVR For long lesions RESET Trial (2013) Subtrati (I-squared=0.0%, P=0.825) 0.20 (0.01, 4.23) 0.63 0.26 (0.03, 2.32) 1.19 0.26 (0.03, 2.32) 1.19 0.26 (0.03, 2.32) 1.19 0.26 (0.03, 2.32) 1.19 1.12, (0.68, 1.85) 2.34 1.12, (0.68, 1.85) 2.3.4 For LOT UNUS Trial (2015) Subtrati (I-squared=0.0%, P=0.424) For LOT UNUS Trial (2015) Tian et al (2014) Subtrati (I-squared=0.0%, P=0.424) For Unprotected LM Gao et al (2014) Subtrati (I-squared=0.0%, P=0.883) For unprotected LM Gao et al (2014) Subtrati (I-squared=0.0%, P=0.883) For unprotected LM Gao et al (2014) Subtrati (I-squared=0.0%, P=0.374) For Unprotected LM Gao et al (2011) Subtrati (I-squared=0.0%, P=0.315) For unprotected LM Gao et al (2010) Subtrati (I-squared=0.0%, P=0.315) For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.315) For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.315) For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.427) Cert di (I-squared=0.0%, P=0.315) For (0.66, 0.97) 100.00 For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.642) For complex lesions AVIO Trial (I-squared=0.0%, P=0.642) Cert di (I-squared=0.0%, P=0.437) For (0.66, 0.97) 100.00 For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.642) For complex lesions AVIO Trial (2013) Subtrati (I-squared=0.0%, P=0.642)	ч	I	Favors non-IV		Favors IVUS	I
For long lesions For long lesions RESET Trial (2013) 0.20 (0.01, 4.23) 0.63 IVUS-XPL Trial (2016) 0.26 (0.03, 2.32) 1.19 For CTO 0.20 (0.01, 4.15) 0.63 CTO-VUS Trial (2015) 0.20 (0.01, 4.15) 0.63 Tian et al (2014) 0.20 (0.01, 4.15) 0.63 Hong et al (2014) 0.050, 2.02 (1.17, 3) 1.12, (0.58, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 1.9, 33 0.64 (2014) Go et al (2014) 0.66 (0.39, 1.18) 1.9, 33 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.833) 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=61.1%, P=0.109) - For complex lesions 0.31 (0.10, 0.99) 4.30 0.32 (0.09, 1.18) 3.50 Subtotal (I-squared=0.0%, P=0.374) 0.31 (0.13, 0.75) 7.79 - - For complex lesions 0.24 (0.03, 2.21) 1.19 - - - Alkabcin et al (2013) 0.76 (0.56, 0.97) 100.00 - - - - Subtotal (I-squared=0.0%, P=0.315) 0.76 (0.60, 0.97) 0.76 (0.60, 0.97) 0.76 (0.6		Ayocardial infarctio		0/		TVR
RESET Trial (2013) 0.20 (0.01, 4.23) 0.63 IVUS-XPL Trial (2016) 0.33 (0.01, 8.18) 0.56 Subtratel (1-squared=0.0%, P=0.825) 0.26 (0.03, 2.32) 1.19 For CTO 0.20 (0.01, 4.15) 0.68 CTO-IVUS Trial (2015) 0.20 (0.01, 4.15) 0.68 Tian et al (2014) 0.068 (0.39, 1.18) 10.93 Subtratel (1-squared=0.0%, P=0.424) 1.02 (0.66, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Subtratel (1-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2013) 0.31 (0.13, 0.75) 7.79 Subtratel (1-squared=1.0%, P=0.315) 0.24 (0.03, 2.21) 1.19 Oxerall (1-squared=1.0%, P=0.4118 0.76 (0.66, 0.97) 100.00 Overall (1-squared=0.0%, P=0.497) 0.76 (0.66, 0.97) 100.00 C 0.1 1 100			UR (95% CI) VVe	ignt %		
IVUS-XPL Trial (2016) 0.33 (0.01, 8.18) 0.56 Subtotal (I-squared=0.0%, P=0.825) 0.26 (0.03, 2.32) 1.19 For CTO 0.20 (0.01, 4.15) 0.63 Tian et al (2015) 0.20 (0.01, 4.15) 0.63 Tian et al (2014) 0.20 (0.03, 2.22) 1.73 Subtotal (I-squared=0.0%, P=0.424) 1.40 (0.68, 2.90) 10.98 For unprotected LM 1.12, (0.68, 1.85) 23.34 Himandez et al (2014) 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.79 (0.49, 1.27) 25.77 Derk et al (2003) 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.374) 0.31 (0.10, 0.99) 4.30 For complex lesions 0.31 (0.10, 0.99) 4.30 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.76 (0.60, 0.97) 100.00 C 0.71 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.42) 0.76 (0.60, 0.97) 0.76 (0.60, 0.97) Overall (I	For long lesions				For long lesions	
Subtotal (I-squared=0.0%, P=0.825) 0.26 (0.03, 2.32) 1.19 For CTO 0.20 (0.01, 4.15) 0.68 (0.32, 2.32) 1.19 For CTO 0.20 (0.01, 4.15) 0.68 (0.32, 2.32) 1.19 Hong et al (2014) 1.00 (0.50, 2.02) 11.73 Subtotal (I-squared=0.0%, P=0.424) 0.68 (0.39, 1.18) 19.33 For unprotected LM 0.68 (0.39, 1.18) 19.33 Hirnandez et al (2014) 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For complex lesions 0.31 (0.10, 0.99) 4.30 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.76 (0.50, 0.97) 100 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.50, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.50, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis MU 1 100 0.508 1		•			RESET Trial (2013)	
Subtotal (I-squared=0.0%, P=0.825) For CTO CTO-IVUS Trial (2015) Tian et al (2015) Tian et al (2015) Tian et al (2014) Subtotal (I-squared=0.0%, P=0.424) For unprotected LM Himandez et al (2014) Gao et al (2014) Gao et al (2014) Chen et al (2013) Subtotal (I-squared=0.0%, P=0.883) Subtotal (I-squared=0.0%, P=0.883) Subtotal (I-squared=0.0%, P=0.883) Cro complex lesions Jakabein et al (2010) AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) Heterogeneity between groups: P=0.118 Overall (I-squared=0.0%, P=0.118 Ora (0.66, 0.67) 100.00 Cto (0.66, 0.97) 100.00 Cto (0.56, 0.97) 100.00 Cto (0.50, 0.97) 100.00 Cto (0.		•			Subtotal (I-squared = $\% P$ =)	
CTO-IVUS Trial (2015) 0.20 (0.01, 4.15) 0.63 Tian et al (2015) 1.40 (0.68, 2.90) 10.98 Hong et al (2014) 1.12, (0.68, 1.85) 23.34 Subtotal (I-squared=0.0%, P=0.424) 0.58 (0.39, 1.18) 19.33 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Subtotal (I-squared=0.0%, P=0.583) 0.76 (0.56, 1.04) 58.91 For inprotected LM 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For complex lesions 0.31 (0.10, 0.99) 4.30 Otatical (I-squared=0.0%, P=0.974) 0.24 (0.03, 2.21) 1.19 For complex lesions 0.24 (0.03, 2.21) 1.19 Jakabcin et al (2013) 0.24 (0.03, 2.21) 1.19 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 7.59 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 C 0.1 1 100	Subtotal (I-squared=0.0%, <i>P</i> =0.825)		0.26 (0.03, 2.32)	1.19		
Tian et al (2015) 1.40 (0.68, 2.90) 10.98 Hong et al (2014) 1.00 (0.50, 2.02) 11.73 Subtotal (I-squared=0.0%, $P=0.424$) 1.12, (0.68, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Subtotal (I-squared=0.0%, $P=0.883$) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2011) 0.31 (0.10, 0.99) 4.30 Jakabcin et al (2013) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=0.0%, $P=0.974$) 0.32 (0.09, 1.18) 3.50 For complex lesions 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=1.0%, $P=0.315$) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: $P=0.118$ 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, $P=0.642$) NOTE: Weights are from random effects analysis Overall (I-squared=0.0%, $P=0.642$) NOTE: Weights are from random effects analysis	For CTO					
Hong et al (2014) 1.00 (0.50, 2.02) 11.73 Subtotal (I-squared=0.0%, P=0.424) 1.12, (0.68, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Park et al (2009) 0.34 (0.43, 1.57) 13.81 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2010) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions - - Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.22 (0.34, 1.97) 7.59 Subtotal (I-squared=0.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 0.70 (0.31, 1.57) 8.78 Overall (I-squared=0.0%, P=0.642) - - - Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis - Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis -		•			CTO-IVUS Trial (2015)	
Hong et al (2014) 1.00 (0.50, 2.02) 11.73 Subtotal (I-squared=0.0%, P=0.424) 1.12, (0.68, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2011) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.10, 0.99) 4.30 For complex lesions 0.32 (0.09, 1.18) 3.50 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.70 (0.31, 1.57) 8.78 Vorrall (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis		÷ •			Tian et al (2015)	
Subtotal (I-squared=0.0%, P=0.424) 1.12, (0.08, 1.85) 23.34 For unprotected LM 0.68 (0.39, 1.18) 19.33 Gao et al (2014) 0.68 (0.39, 1.18) 19.33 Park et al (2009) 0.76 (0.56, 1.04) 58.91 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2011) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.24 (0.03, 2.21) 1.19 Subtotal (I-squared=.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00		•				
Hirnandez et al (2014) Gao et al (2014) Park et al (2009) Subtotal (I-squared=0.0%, P=0.883) For bifurcation Chen et al (2013) Subtotal (I-squared=0.0%, P=0.974) For complex lesions AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) Heterogeneity between groups: P=0.118 Overall (I-squared=1.0%, P=0.497) C 0.1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Subtotal (I-squared=0.0%, <i>P</i> =0.424)		1.12, (0.68, 1.85)	23.34		\sim
Gao et al (2014) 0.79 (0.49, 1.27) 25.77 Park et al (2009) 0.83 (0.43, 1.57) 13.81 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Kim et al (2011) 0.32 (0.09, 1.18) 3.50 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions 0.31 (0.13, 0.75) 7.79 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00						
Park et al (2009) 0.83 (0.43, 1.57) 13.81 Order (2014) Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 Park et al (2009) For bifurcation 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=61.1%, P=0.109) Kim et al (2011) 0.32 (0.09, 1.18) 3.50 Chen et al (2013) Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions 0.31 (0.13, 0.75) 7.79 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis MOTE: Weights are from random effects analysis 1		•			For unprotected LM	
Park et al (2009) 0.83 (0.43, 1.57) 13.81 Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.91 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2013) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.974) 0.32 (0.09, 1.18) 3.50 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions 0.31 (0.13, 0.75) 7.79 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) . . NOTE: Weights are from random effects analysis . d .0508 1					Gao et al (2014)	•
Subtotal (I-squared=0.0%, P=0.883) 0.76 (0.56, 1.04) 58.31 For bifurcation 0.31 (0.10, 0.99) 4.30 Chen et al (2013) 0.31 (0.10, 0.99) 4.30 Subtotal (I-squared=0.0%, P=0.974) 0.32 (0.09, 1.18) 3.50 Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 For complex lesions 0.24 (0.03, 2.21) 1.19 Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) . . NOTE: Weights are from random effects analysis 1		•				•
Chen et al (2013) 0.31 (0.10, 0.99) 4.30 For bifurcation Kim et al (2011) 0.32 (0.09, 1.18) 3.50 Chen et al (2013) Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=.%, P=.) For complex lesions 0.24 (0.03, 2.21) 1.19 Subtotal (I-squared=.%, P=.) AvIO Trial (2013) 0.24 (0.03, 1.157) 8.78 AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 · Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 · Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 · Overall (I-squared=0.0%, P=0.642) NOTE: Weights are from random effects analysis 1 1 100 I 0.0508 1	Subtotal (I-squared=0.0%, <i>P</i> =0.883)	$\langle \rangle$	0.76 (0.56, 1.04)	58.91		
Kim et al (2011) 0.32 (0.09, 1.18) 3.50 Chen et al (2013) Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=.%, P=.) For complex lesions 0.24 (0.03, 2.21) 1.19 Subtotal (I-squared=.%, P=.) AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 d .0508 1			0.04 /0.45 5 5 5 1		•	
Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=.%, P=.) For complex lesions 0.24 (0.03, 2.21) 1.19 Subtotal (I-squared=.%, P=.) AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Image: triangle of the term of the term of the term of ter	('hon of al (2013) -				For bifurcation	
Subtotal (I-squared=0.0%, P=0.974) 0.31 (0.13, 0.75) 7.79 Subtotal (I-squared=.%, P=.) For complex lesions 0.24 (0.03, 2.21) 1.19 For complex lesions Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 For complex lesions AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 AVIO Trial (2013) Subtotal (I-squared=1.0%, P=0.315) 0.76 (0.60, 0.97) 100.00 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) . . NOTE: Weights are from random effects analysis 1					Chen et al (2013)	
Jakabcin et al (2010) 0.24 (0.03, 2.21) 1.19 AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.70 (0.31, 1.57) 8.78 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Image: triangle of the squared decision of the squared decisi	Kim et al (2011) —			7.79		
AVIO Trial (2013) 0.82 (0.34, 1.97) 7.59 Subtotal (I-squared=1.0%, P=0.315) 0.70 (0.31, 1.57) 8.78 Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Image: Comparison of the squared of th	Kim et al (2011) —		0.31 (0.13, 0.75)			
Subtotal (I-squared=1.0%, P=0.315) 0.70 (0.31, 1.57) 8.78 Subtotal (I-squared=.%, P=.) Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) Overall (I-squared=0.0%, P=0.542) 0.76 (0.50, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642)	Kim et al (2011) — Subtotal (I-squared=0.0%, <i>P</i> =0.974) For complex lesions					
Heterogeneity between groups: P=0.118 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Image: Constraint of the squared state of the squared st	Kim et al (2011)		0.24 (0.03, 2.21)	1.19	For complex lesions	
Overall (I-squared=0.0%, P=0.497) 0.76 (0.60, 0.97) 100.00 Overall (I-squared=0.0%, P=0.642) C .01 1 100 I <tdi< td=""> I I <</tdi<>	Kim et al (2011) — Subtotal (I-squared=0.0%, <i>P</i> =0.974) For complex lesions Jakabcin et al (2010) ——— AVIO Trial (2013)		0.24 (0.03, 2.21) 0.82 (0.34, 1.97)	1.19 7.59	For complex lesions AVIO Trial (2013)	
C .01 1 100 d .0508 1	Kim et al (2011) — Subtotal (I-squared=0.0%, <i>P</i> =0.974) For complex lesions Jakabcin et al (2010) AVIO Trial (2013) Subtotal (I-squared=1.0%, <i>P</i> =0.315)		0.24 (0.03, 2.21) 0.82 (0.34, 1.97)	1.19 7.59	For complex lesions AVIO Trial (2013)	
C .01 1 100 d .0508 1	Kim et al (2011)		0.24 (0.03, 2.21) 0.82 (0.34, 1.97) 0.70 (0.31, 1.57)	1.19 7.59 8.78	For complex lesions AVIO Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.)	
	Kim et al (2011)		0.24 (0.03, 2.21) 0.82 (0.34, 1.97) 0.70 (0.31, 1.57)	1.19 7.59 8.78	For complex lesions AVIO Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) Overall (I-squared=0.0%, <i>P</i> =0.642)	cts analysis
Favors IVUS Favors non-IVUS Favors IVUS F	Kim et al (2011)		0.24 (0.03, 2.21) 0.82 (0.34, 1.97) 0.70 (0.31, 1.57) 0.76 (0.60, 0.97)	1.19 7.59 8.78 100.00	For complex lesions AVIO Trial (2013) Subtotal (I-squared=.%, <i>P</i> =.) Overall (I-squared=0.0%, <i>P</i> =0.642) NOTE: Weights are from radom effe	

Figure 3. Forest plots of the efficacy endpoints of the propensity-matched and randomized trials. The odds ratios of MACE (a), all-cause mortality (b), myocardial infarction (c), target-vessel revascularization (d), target-lesion revascularization (e), and stent thrombosis (f) associated with IVUS guidance compared with angiography guidance

als. The repeated analyses of propensity-matched groups were also performed with the goal of decreasing bias and proving the final results, which might be the significant favorable evidence of IVUS guidance on improving clinical outcomes in this subset of patient populations.

In fact, the other different complex coronary artery lesions such as CTO lesions, long lesions, or combined of all-overmentioned might just benefit partly from the IVUS guidance. A randomized trial conducted by Tian et al. (27) indicated that IVUS-guided stenting for the CTO lesions was associated with

Study ID	TLR	OR (95% CI) Weight %	Study Stent throu ID	nbosis OR (95% CI) Weight %
For long lesions IVUS-XPL Trial (2016) — Subtotal (I-squared=.%, <i>P</i> =.) —		0.50 (0.28, 0.91) 12.93 0.50 (0.28, 0.91) 12.93	For long lesions RESET Trial (2013) IVUS-XPL Trial (2016) Subtotal (I-squared=0.0%, <i>P</i> =0.991)	1.02 (0.06, 16.37) 3.63 1.00 (0.14, 7.12) 7.27 1.01 (0.20, 5.00) 10.90
For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.814)		0.62 (0.20, 1.91)4.360.64 (0.25, 1.63)6.180.86 (0.46, 1.60)12.110.75 (0.47, 1.21)22.66	For CTO CTO-IVUS Trial (2015) Tian et al (2015) Hong et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.580)	0.14 (0.01, 2.74) 3.17 0.36 (0.09, 1.39) 15.29 0.07 (0.00, 1.33) 3.37 0.25 (0.08, 0.76) 21.84
For unprotected LM Hernandez et al (2014) Gao et al (2014) Subtotal (I-squared=87.5%, <i>P</i> =0.005)		1.24 (0.76, 2.01)17.240.31 (0.14, 0.71)7.790.65 (0.17, 2.48)25.03	For unprotected LM Hernandez et al (2014) Gao et al (2014) Subtotal (I-squared=0.0%, <i>P</i> =0.604)	0.27 (0.07, 0.97)17.020.14 (0.02, 1.14)6.340.22 (0.08, 0.67)23.36
For bifurcation Chen et al (2013) Kim et al (2010) Kim et al (2011) Subtotal (I-squared=0.0%, <i>P</i> =0.853)		1.20 (0.52, 2.80) 7.36 0.90 (0.33, 2.54) 5.29 0.91 (0.52, 1.627 13.83 0.98 (0.64, 1.50) 26.48	For bifurcation Chen et al (2013) Kim et al (2010) Kim et al (2011) Subtotal (I-squared=0.0%, <i>P</i> =0.638)	0.09 (0.01, 0.74) 6.53 0.28 (0.06, 1.25) 12.15 - 0.33 (0.04, 3.21) 5.82 0.22 (0.07, 0.63) 24.50
For complex lesions Jakabcin et al (2010) AVIO Trial (2013) Subtotal (I-squared=0.0%, <i>P</i> =0.673)		1.00 (0.31, 3.21) 4.16 0.74 (0.35, 1.59) 8.74 0.81 (0.43, 1.53) 12.90	For complex lesions Jakabcin et al (2010) AVIO Trial (2013) Subtotal (I-squared=0.0%, <i>P</i> =0.386)	0.65 (0.18, 2.39) 16.69 3.02 (0.12, 74.79) 2.72 0.81 (0.24, 2.69) 19.41
Overall (I-squared=18.4%, <i>P</i> =0.269) NOTE: Weights are from random effects ana	Ivsis	0.79 (0.61, 1.01) 100.00	Heterogeneity between groups: <i>P</i> =0.257 Overall (I-squared=0.0%, <i>P</i> =0.685)	0.34 (0.20, 0.58) 100.00
e .139 Favors IV	1	7.2 s non-IVUS	f .00418 1 Favors IVUS	239 Favors non-IVUS

Figure 3. Forest plots of the efficacy endpoints of the propensity-matched and randomized trials. The odds ratios of MACE (a), all-cause mortality (b), myocardial infarction (c), target-vessel revascularization (d), target-lesion revascularization (e), and stent thrombosis (f) associated with IVUS guidance compared with angiography guidance

less late lumen loss and lower incidence of "in-true-lumen" stent restenosis, which might result from the advantages of IVUS guidance in optimizing stent expansion, edge dissection, and minimal stent area for such lesion subsets. However, these offered modest or no benefits in terms of decreasing the MACE incidence, there were more risk factors pertaining to the occurence of this lesion compared to other different lesions might be the possible reasons, such as more current smokers, high incidence of diabetes or poor compliance for antiplatelet treatment. On the other hand, Hong et al. (12) conducted the IVUS-XPL trial to evaluate the effects of IVUS guidance in patients with long coronary artery diseases. The largest randomized trial enrolled of 1,400 patients who were randomly assigned to two groups at a 1:1 ratio and demonstrated that IVUS guidance was associated with a significantly lower rate of the composite of MACE at 1 year (2.9% vs. 5.8%, p=0.07, for IVUS guidance vs. angiography guidance). In addition, Chieffo et al. (14) conducted one RCT focusing on combined complex lesions described the superiority of IVUS-guided DES implantation, whereas another RCT (26) reported a contrasting result, which is only small scale without enough powerty. Results from this present meta-analysis just indicated some limited benefits pertaining to IVUS guidance in DES implantation in these patients as well. As a result, possible reasons might be summarized as unbalanced baseline characteristics, uniform stenting procedure or different standards of decision making, and satisfaction for IVUS usage.

Several questions remained unsolved. First, there were not enough data to assess the efficacy of IVUS-guided PCI using different generations of DES because of varying drug coats or structures of implanted stents might lead to unsimilar outcomes. A second dilemma was considered as the absence of a cost-effectiveness analysis of IVUS just described by Zhang et al. (18), although these specific patient populations with left main disease or bifurcation lesions seemed to be associated with more feasible benefits.

Study limitations

This study has several limitations. First, this meta-analysis was performed without individual patient data, and the small sample size of several included RCTs also made the evaluation of IVUS guidance's efficacy easily influenced. Second, the un-avoidable involvement of several potential confounding factors, such as the time of procedure and details of DES implantation, including types of DES, techniques, and the choice of sheath with different sizes, did not allow us to explore the true effects of IVUS guidance on patients with complex coronary artery lesions, despite the repeated analyses of data from matched and randomized trials. Third, the insufficient analyses of these data from Quantitative Coronary Analysis among each included trial limited us studying specific benefits on stenting procedure. In addition, this meta-analysis was performed mainly focused on evaluating the effects of IVUS applied for different types of

coronary artery lesions instead of heart diseases; therefore, the subgroup analysis of high-risk patients with ACS should not be conducted. At last but not least, there was no strict duration of dual-antiplatelet treatment for these included patients though it was commonly thought as lasting for \geq 12 months.

Conclusion

IVUS-guided DES implantaion was seemed to improve the clinical outcomes in patients with complex coronary artery disease, particulaly in patients with left main disease or bifurcation lesions. However, powerful randomized clinical trials comparing IVUS guidance to angiography guidance in such patients with more precise subgroups focusing on different coronary lesions and types of implanted DES are still warranted to guide stenting decision making in the catheterization room.

Disclosures: The study was supported by the Jiangsu Provincial Special Program of Medical Science (BL2013001).

Acknowledgments: FZG and GXF were involved in the design, literature search, assessment of study quality, and both drafted the manuscript. Disagreements were resolved by LXB. FZG performed statistical analysis and critically revised the manuscript. SMX and GYL constructed the maps. CSL and TNL critically revised original study design and the manuscript. All authors contributed to the data analysis, drafting of the manuscript, and its critical revisions, and all authors agree to be accountable for all aspects of the work.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – N.T.; Design – Z. F., X.G.; Supervision – X. L.; Fundings- All authors; Materials – M.S., Y.G.; Data collection &/or processing – Z.F., X.G.; Analysis &/or interpretation – Z.F.; Literature search – Z.F., X.G.; Writing – Z.F.; Critical review – S.C., N.T.

References

- Stone GW, Moses JW, Ellis SG, Schofer J, Dawkins KD, Morice MC, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007; 356: 998-1008.
- Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Circulation 2014; 130: 2354-94.
- Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS guidelines on myocardial revascularization. EuroIntervention 2015; 10: 1024-94.
- Witzenbichler B, Maehara A, Weisz G, Neumann FJ, Rinaldi MJ, Metzger DC, 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: 463-70.

- Claessen BE, Mehran R, Mintz GS, Weisz G, Leon MB, Doğan O, et al. Impact of intravascular ultrasound imaging on early and late clinical outcomes following percutaneous coronary intervention with drug-eluting stents. JACC Cardiovasc Interv 2011; 4: 974-81.
- Ahn JM, Kang SJ, Yoon SH, Park HW, Kang SM, Lee JY, et al. Metaanalysis of outcomes after intravascular ultrasound-guided versus angiography-guided drug-eluting stent implantation in 26,503 patients enrolled in three randomized trials and 14 observational studies. Am J Cardiol 2014; 113: 1338-47.
- Jang JS, Song YJ, Kang W, Jin HY, Seo JS, Yang TH, et al. Intravascular ultrasound-guided implantation of drug-eluting stents to improve outcome: a meta-analysis. JACC Cardiovasc Interv 2014; 7: 233-43.
- Klersy C, Ferlini M, Raisaro A, Scotti V, Balduini A, Curti M, et al. Use of IVUS guided coronary stenting with drug eluting stent. Int J Cardiol 2013; 170: 54-63.
- 9. Park KW, Kang SH, Yang HM, Lee HY, Kang HJ, Cho YS, et al. Impact of intravascular ultrasound guidance in routine percutaneous coronary intervention for conventional lesions: data from the EX-CELLENT trial. Int J Cardiol 2013; 167: 721-6.
- Singh V, Badheka AO, Arora S, Panaich SS, Patel NJ, Patel N, et al. Comparison of inhospital mortality, length of hospitalization, costs, and vascular complications of percutaneous coronary interventions guided by ultrasound versus angiography. Am J Cardiol 2015; 115: 1357-66.
- Kim JS, Kang TS, Mintz GS, Park BE, Shin DH, Kim BK, et al. Randomized comparison of clinical outcomes between intravascular ultrasound and angiography-guided drug-eluting stent implantation for long coronary artery stenoses. JACC Cardiovasc Interv 2013; 6: 369-76.
- Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, et al. Effect of Intravascular Ultrasound-Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation: The IVUS-XPL Randomized Clinical Trial. JAMA 2015; 314: 2155-63.
- Kim BK, Shin DH, Hong MK, Park HS, Rha SW, Mintz GS, et al. Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study. Circ Cardiovasc Interv 2015; 8: e002592.
- Chieffo A, Latib A, Caussin C, Presbitero P, Galli S, Menozzi A, et al. A prospective, randomized trial of intravascular-ultrasound guided compared to angiography guided stent implantation in complex coronary lesions: the AVIO trial. Am Heart J 2013; 165: 65-72.
- Hong SJ, Kim BK, Shin DH, Kim JS, Hong MK, Gwon HC, et al. Usefulness of intravascular ultrasound guidance in percutaneous coronary intervention with second-generation drug-eluting stents for chronic total occlusions (from the Multicenter Korean-Chronic Total Occlusion Registry). Am J Cardiol 2014; 114: 534-40.
- 16. de la Torre Hernandez JM, Baz Alonso JA, Gomez Hospital JA, Alfonso Manterola F, Garcia Camarero T, Gimeno de Carlos F, et al. Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: pooled analysis at the patient-level of 4 registries. JACC Cardiovasc Interv 2014; 7: 244-54.
- Kim JS, Hong MK, Ko YG, Choi D, Yoon JH, Choi SH, et al. Impact of intravascular ultrasound guidance on long-term clinical outcomes in patients treated with drug-eluting stent for bifurcation lesions: data from a Korean multicenter bifurcation registry. Am Heart J 2011; 161: 180-7.

- Zhang YJ, Pang S, Chen XY, Bourantas CV, Pan DR, Dong SJ, et al. Comparison of intravascular ultrasound guided versus angiography guided drug eluting stent implantation: a systematic review and meta-analysis. BMC Cardiovasc Disord 2015; 15: 153.
- Biondi-Zoccai GG, Abbate A, Agostoni P, Testa L, Burzotta F, Lotrionte M, et al. Long-term benefits of an early invasive management in acute coronary syndromes depend on intracoronary stenting and aggressive antiplatelet treatment: a metaregression. Am Heart J 2005; 149: 504-11.
- Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1-12.
- Ahn SG, Yoon J, Sung JK, Lee JH, Lee JW, Youn YJ, et al. Intravascular ultrasound-guided percutaneous coronary intervention improves the clinical outcome in patients undergoing multiple overlapping drug-eluting stents implantation. Korean Circ J 2013; 43: 231-8.
- Gao XF, Kan J, Zhang YJ, Zhang JJ, Tian NL, Ye F, et al. Comparison of one-year clinical outcomes between intravascular ultrasoundguided versus angiography-guided implantation of drug-eluting stents for left main lesions: a single-center analysis of a 1,016-patient cohort. Patient Prefer Adherence 2014; 8: 1299-309.
- Laskey WK, Yancy CW, Maisel WH. Thrombosis in coronary drugeluting stents: report from the meeting of the Circulatory System Medical Devices Advisory Panel of the Food and Drug Administration Center for Devices and Radiologic Health, December 7-8, 2006. Circulation 2007; 115: 2352-7.
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009; 339: b2700.
- Egger M, Davey Smith G, Schneider M, Minder C. Bias in metaanalysis detected by a simple, graphical test. BMJ 1997; 315: 629-34.
- Jakabcin J, Spacek R, Bystron M, Kvasnak M, Jager J, Veselka J, et al. Long-term health outcome and mortality evaluation after invasive coronary treatment using drug eluting stents with or without the IVUS guidance. Randomized control trial. HOME DES IVUS. Catheter Cardiovasc Interv 2010; 75: 578-83.
- Tian NL, Gami SK, Ye F, Zhang JJ, Liu ZZ, Lin S, et al. Angiographic and clinical comparisons of intravascular ultrasound- versus angiography-guided drug-eluting stent implantation for patients with chronic total occlusion lesions: two-year results from a randomised AIR-CTO study. EuroIntervention 2015; 10: 1409-17.

- Agostoni P, Valgimigli M, Van Mieghem CA, Rodriguez-Granillo GA, Aoki J, Ong AT, et al. Comparison of early outcome of percutaneous coronary intervention for unprotected left main coronary artery disease in the drug-eluting stent era with versus without intravascular ultrasonic guidance. Am J Cardiol 2005; 95: 644-7.
- 29. Chen SL, Ye F, Zhang JJ, Tian NL, Liu ZZ, Santoso T, et al. Intravascular ultrasound-guided systematic two-stent techniques for coronary bifurcation lesions and reduced late stent thrombosis. Catheter Cardiovasc Interv 2013; 81: 456-63.
- Kim SH, Kim YH, Kang SJ, Park DW, Lee SW, Lee CW, et al. Longterm outcomes of intravascular ultrasound-guided stenting in coronary bifurcation lesions. Am J Cardiol 2010; 106: 612-8.
- Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, et al, Investigators M-C. Impact of intravascular ultrasound guidance on longterm mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv 2009; 2: 167-77.
- D'Ascenzo F, Barbero U, Cerrato E, Lipinski MJ, Omede P, Montefusco A, et al. Accuracy of intravascular ultrasound and optical coherence tomography in identifying functionally significant coronary stenosis according to vessel diameter: A meta-analysis of 2,581 patients and 2,807 lesions. Am Heart J 2015; 169: 663-73.
- 33. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv 2012; 79: 453-95.
- 34. Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, et al. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions) trial. J Am Coll Cardiol 2011; 57: 914-20.
- 35. Garcia-Garcia HM, Gomez-Lara J, Gonzalo N, Garg S, Shin ES, Goedhart D, et al. A comparison of the distribution of necrotic core in bifurcation and non-bifurcation coronary lesions: an in vivo assessment using intravascular ultrasound radiofrequency data analysis. EuroIntervention 2010; 6: 321-7.
- Medina A, Martin P, Suarez de Lezo J, Novoa J, Melian F, Hernandez E, et al. Ultrasound study of the prevalence of plaque at the carina in lesions that affect the coronary bifurcation. Implications for treatment with provisional stent. Rev Esp Cardiol 2011; 64: 43-50.