

# Efficacy of intravascular imaging-guided stent implantation: A systematic review and meta-analysis of randomized clinical trials

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## Research Article

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# Abstract

**Background:** Traditional angiography only displays two-dimensional images of the coronary arteries during stent implantation. However, intravascular imaging can show the structure of the vascular wall, plaque characteristics. This article aims to evaluate the efficacy of intravascular imaging-guided stent implantation.

**Method:** We conducted a systematic review and meta-analysis of randomized controlled trials of intravascular imaging-guided, including patients with stent implantation guided by intravascular ultrasound (IVUS) or optical coherence tomography (OCT) and traditional angiography. The databases of PubMed, EMBASE, web of science, and Cochrane Library were searched. The primary outcome was target lesion revascularization (TLR). The secondary outcomes included the target vessel revascularization (TVR), myocardial infarction (MI), stent thrombosis (ST), cardiac death, all-cause death, and the major adverse cardiac events (MACE) during the 6-24 months follow-up. The fixed-effects model was used to calculate the relative risk (RR) and 95% confidence interval (CI) of the outcome event. Meanwhile, the trial sequence analysis was employed to evaluate the results.

**Result:** This meta-analysis included eighteen randomized controlled trials with 10413 patients. Compared with angiography-guided stent implantation, intravascular imaging-guided stent implantation can significantly reduce the risk of TLR (RR 0.62, 0.49-0.77,  $P=0.0001$ ), TVR (RR 0.65, 0.52-0.81,  $P=0.0001$ ), cardiac death (RR 0.59; 0.39-0.91;  $P=0.02$ ), ST (RR 0.54, 0.30-0.97;  $P=0.04$ ) and MACE (RR 0.81, 0.71-0.93;  $P=0.003$ ), while there was no significant difference regarding MI (RR 0.78, 0.61-1.00,  $P=0.05$ ) and all-cause death (RR 0.85, 0.58-1.27,  $P=0.44$ ).

**Conclusions:** Compared with angiography, intravascular imaging-guided stent implantation is associated with better clinical outcomes in patients with coronary artery disease (Registered by PROSPERO, CRD 42021289205).

## Introduction

Cardiovascular disease remains the most common cause of death in the world, and its prevalence is constantly increasing<sup>[1]</sup>. Coronary atherosclerosis is one of the main causes of cardiovascular disease. For quite some time, coronary angiography is considered as the “gold standard” for diagnosing coronary artery disease and remains the main imaging modality used worldwide for vascular imaging, and percutaneous coronary intervention guided by angiography is the main revascularization strategy for patients with coronary artery disease<sup>[2-3]</sup>.

However, angiography underestimates the true vessel size, lesion length, and degree of calcification, and cannot further evaluate plaque morphology, plaque vulnerability, presence of thrombus, stent expansion and apposition, residual narrowing post intervention, and the presence of dissections<sup>[2]</sup>. On the contrary, intravascular imaging can provide more detailed information of vascular lumen and wall to guide the intervention therapy. Therefore, intravascular imaging including intravascular ultrasound (IVUS) and optical coherence tomography (OCT) is more and more widely used in percutaneous coronary intervention compared with angiography<sup>[4]</sup>. Meanwhile, the 2011 American College of Cardiology Foundation/American Heart Association/Society of Cardiovascular Angiography and Intervention Guideline for Percutaneous Coronary Intervention recommends that IVUS may be considered for guidance of left main coronary artery stenting (IIb)<sup>[5]</sup>. Although 2018 European Society of Cardiology guidelines on myocardial revascularization recommend IVUS to guide stent implantation for left main coronary artery lesions (IIa), this recommendation is based on a multicenter registry study<sup>[6]</sup>. In addition, many randomized trials and observational studies have shown that the beneficiaries are not limited to patients with left main coronary artery lesions<sup>[7-9]</sup>. Therefore, whether intravascular imaging has clinical benefits remains unclear in all patients undergoing percutaneous coronary intervention, regardless of the lesions type.

We performed a meta-analysis of randomized controlled trials comparing intravascular imaging-guided and angiography-guided stent implantation, to explore the efficacy in patients with coronary artery disease receiving percutaneous coronary intervention. The results indicate that stent implantation guided by intravascular imaging is effective for patients with coronary artery disease, and complex lesions benefit more.

## Method

### Data Source and search strategy

This systematic review and meta-analysis of randomized controlled trials followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline<sup>[10]</sup>. We searched PubMed, Web of Science, EMBASE, and Cochrane Library databases from inception to 31, December 2021, and the following search terms and keywords were used: “angiography”, “angiography-guided”, “intravascular ultrasound”, “intravascular ultrasound-guided”, “IVUS”, “optical coherence tomography”, “optical coherence tomography-guided”, “OCT”, “stent implantation”, “Percutaneous Coronary Intervention”, “PCI”. There were no language restrictions for retrieval. The search strategy of each database is shown (Table S1). The inclusion criteria of this study: (a) randomized controlled trial; (b) comparison between coronary stent implantation-guided by IVUS or OCT and angiography-guided; (c) follow-up for at least 6 months; (d) sample size ≥ 100 patients; (e) availability of complete clinical and outcome data. The exclusion criteria of this study: (a) ongoing trials and non-randomized controlled trials; (b) trials did not have the outcomes needed or the data of incomplete outcomes; (c) duplicate reports; (d) meta-analyzes, reviews, or comments. In this meta-analysis, two investigators (Ying Niu and Nan Bai) independently screened all titles and abstracts, full-text articles of relevant trials, and then evaluated the eligibility of the trials following the inclusion and exclusion criteria. The disagreement was discussed to resolve by a third party (Ying Ma, Peng-Yu Zhong, and Yao-Sheng Shang). The risk of bias for each trial was assessed by the Cochrane tool of collaboration, and the quality of evidence for each outcome was evaluated by the Grades of Recommendations Assessment Development and Evaluation (GRADE)<sup>[11, 12]</sup>. The clinical protocols of all included trials were approved by local ethics and informed consent of patients was obtained. Meanwhile, this study is a secondary research and does not require ethical approval, and the meta-analysis protocol was registered in PROSPERO (CRD 42020289205).

### Data Acquisition and Clinical Outcomes

The two investigators independently extracted the characteristics of each trial included, the baseline characteristics of the patients, and the outcome of each trial. The differences should be settled by a third party through consultation (Zhi-Lu Wang). The primary outcome was target lesion revascularization (TLR). The secondary outcomes included target vessel revascularization (TVR), myocardial infarction (MI), cardiac death, all-cause death, stent thrombosis (ST), and major adverse cardiac events (MACE). MACE was defined as the composite of all-cause death, cardiac death, MI, and repeat coronary revascularization. The latter was assumed as TLR, TVR, or any coronary revascularization. TLR, MI, cardiac death, all-cause death, and ST was defined based on the definition adopted of the clinical trials included. Meanwhile, based on the trials included, complex lesions were defined as one of the following: lesion type B2 and C according to the American Heart Association; chronic total occlusions (CTO); bifurcation lesions; proximal left anterior descending artery; long lesions (≥ 20 mm); small vessels (reference vessel diameter ≤ 2.5mm); left main coronary artery lesions and patients requiring 4 or more stents; insulin dependent diabetes mellitus and acute coronary syndrome.

### Statistical Analysis

All data were analyzed by Review Manager version 5.4 software (The Nordic Cochrane Center, Copenhagen, Denmark) and Stata version 14.0 software. The risk ratio (RR) and 95% confidence interval (CI) of each outcome were expressed and calculated by the fixed-effects model and Mantel-Haenszel method, and the statistical heterogeneity between trials

was assessed with chi-square tests and  $I^2$  statistics. When the  $P$ -value of the chi-square test was  $< 0.10$ , significant heterogeneity was considered, and  $I^2$  was used to judge the degree of heterogeneity. The sources of heterogeneity were found through sensitivity analysis and subgroup analysis. Meanwhile, the sensitivity analysis was employed to test the impact of any individual study results on the overall results. Egger's and Bgger's test as well as visual inspection of funnel plots were used to assess publication bias, and the trim method will be used when the Egger's test  $P < 0.05$ . Finally, calculate the sample size followed by Trial Sequential Analysis version 0.9.5.10 software (Copenhagen Trial Unit, CTU) and evaluate the results.

## Results

### Search Results and Study Characteristics

A total of 1641 articles were retrieved, and 653 citations were screened by checking the title or abstract. Of these, 53 full texts were reviewed, and eighteen randomized controlled trials were included in this meta-analysis finally (Fig. 1).

The baseline characteristics of the included trials were shown (Table 1). A total of 10413 patients were selected, including 4995 patients receiving intravascular imaging-guided stent implantation and 5418 patients receiving angiography-guided stent implantation. The enrolled population of ten trials was patients with complex lesions [13, 14, 16, 17, 20, 22-24, 28, 29], two trials included patients with left main coronary artery lesion [24, 28], and seven trials excluded obvious left main coronary artery lesion [15, 16, 18, 19, 21, 23, 25]. Meanwhile, the outcomes of subgroup for these patients were also reported. Two trials were related to OCT and seventeen trials were related to IVUS. The follow-up time ranged from six months to two years. In addition, sixteen trials reported the outcome of MACE and showed the difference defined of MACE.

Table 1  
Baseline characteristics of the included trials.

Study	Publication year	Type	Country	Lesion type	Study total size	Randomization	MACE	Follow up (month)
<b>AIR-CTO</b> [13]	2015	RCT	China	CTO	115/115	IVUS VS Angiography	all-cause death, MI, TLR, ST	24
<b>AVIO</b> [14]	2013	RCT	European countries	Complex lesions <sup>a</sup>	142/142	IVUS VS Angiography	Cardiac death, MI or TVR	24
<b>CRUISE</b> [15]	2000	RCT	America	NR	270/229	IVUS VS Angiography	NR	9
<b>CTO-IVUS</b> [16]	2015	RCT	Korea, America	CTO	201/201	IVUS VS Angiography	Cardiac death, MI or TVR	12
<b>DIPOL</b> [17]	2007	RCT	Poland	Long lesions	83/80	IVUS VS Angiography	all-cause death, MI, RCR <sup>b</sup>	6
<b>DOCTORS</b> [18]	2016	RCT	France	Non-complex lesions	120/120	OCT VS Angiography	all-cause death, MI, TLR, ST	6
<b>EXCELLENT</b> [19]	2012	RCT	Korea	Non-protected left main	619/802	IVUS VS Angiography	all-cause death, MI, TVR, ST	12

Abbreviations:

RCT, randomized controlled trial; CTO, chronic total occlusion; IVUS, intravascular ultrasound; OCT, optical coherence tomography; Angio, angiography; MI, myocardial infarction; TLR, target lesion revascularization; ST, stent thrombosis; TVR, target vessel revascularization; RCR, repeat coronary revascularization; NR, not reported.

a. Based on the trials included, complex lesions were defined as one of the following: lesion type B2 and C according to the American Heart Association; chronic total occlusions (CTO); bifurcation lesions; proximal left anterior descending artery; long lesions ( $\geq 20$  mm); small vessels (reference vessel diameter  $\leq 2.5$ mm); left main coronary artery lesions and patients requiring 4 or more stents; insulin dependent diabetes mellitus and acute coronary syndrome.

b. Based on the trials included, RCR was defined as target lesion revascularization, target vessel revascularization or any coronary revascularization.

c. ILUMIEN III-IVUS and ILUMIEN III-OCT come from the ILUMIEN III trial.

Study	Publication year	Type	Country	Lesion type	Study total size	Randomization	MACE	Follow up (month)
<b>HOME DES IVUS</b> [20]	2010	RCT	Czech Republic	Complex lesions <sup>a</sup>	105/105	IVUS VS Angiography	all-cause death, MI or TLR	18
<b>ILUMIEN III-IVUS</b> <sup>c</sup> [21]	2021	RCT	America	Non-complex lesions	136/142	IVUS VS Angiography	Cardiac death, MI or TLR	12
<b>ILUMIEN III-OCT</b> <sup>c</sup> [21]	2021	RCT	America	Non-complex lesions	153/142	OCT VS Angiography	Cardiac death, MI or TLR	12
<b>IVUS-XPL</b> [22]	2015	RCT	Korea	Long lesions	700/700	IVUS VS Angiography	Cardiac death, MI or TLR	12
<b>Kim et al</b> [23]	2013	RCT	Korea	Long lesions	269/274	IVUS VS Angiography	Cardiac death, MI, TVR or ST	12
<b>Liu et al</b> [24]	2019	RCT	China	Unprotected left main	167/169	IVUS VS Angiography	Cardiac death, MI or TVR	12
<b>OPTUCIS</b> [25]	2001	RCT	European countries	Non-complex lesions	273/275	IVUS VS Angiography	all-cause death, MI, RCR <sup>b</sup>	12
<b>RESET</b> [26]	2013	RCT	Korea	Non-complex lesions	662/912	IVUS VS Angiography	Cardiac death, MI or TVR	12

**Abbreviations:**

RCT, randomized controlled trial; CTO, chronic total occlusion; IVUS, intravascular ultrasound; OCT, optical coherence tomography; Angio, angiography; MI, myocardial infarction; TLR, target lesion revascularization; ST, stent thrombosis; TVR, target vessel revascularization; RCR, repeat coronary revascularization; NR, not reported.

a. Based on the trials included, complex lesions were defined as one of the following: lesion type B2 and C according to the American Heart Association; chronic total occlusions (CTO); bifurcation lesions; proximal left anterior descending artery; long lesions ( $\geq 20$  mm); small vessels (reference vessel diameter  $\leq 2.5$ mm); left main coronary artery lesions and patients requiring 4 or more stents; insulin dependent diabetes mellitus and acute coronary syndrome.

b. Based on the trials included, RCR was defined as target lesion revascularization, target vessel revascularization or any coronary revascularization.

c. ILUMIEN III-IVUS and ILUMIEN III-OCT come from the ILUMIEN III trial.

Study	Publication year	Type	Country	Lesion type	Study total size	Randomization	MACE	Follow up (month)
SIPS [27]	2000	RCT	Germany	No CTO or emergency procedures	121/148	IVUS VS Angiography	all-cause death, MI, RCR <sup>b</sup>	24
Tan et al [28]	2015	RCT	China	Unprotected left main	61/62	IVUS VS Angiography	all-cause death, MI, TLR	24
TULIP [29]	2003	RCT	Holland, America	Long lesions	74/76	IVUS VS Angiography	NR	6
ULTIMATE [9]	2018	RCT	China	All comer	724/724	IVUS VS Angiography	Cardiac death, MI or TVR	12

Abbreviations:

RCT, randomized controlled trial; CTO, chronic total occlusion; IVUS, intravascular ultrasound; OCT, optical coherence tomography; Angio, angiography; MI, myocardial infarction; TLR, target lesion revascularization; ST, stent thrombosis; TVR, target vessel revascularization; RCR, repeat coronary revascularization; NR, not reported.

a. Based on the trials included, complex lesions were defined as one of the following: lesion type B2 and C according to the American Heart Association; chronic total occlusions (CTO); bifurcation lesions; proximal left anterior descending artery; long lesions ( $\geq 20$  mm); small vessels (reference vessel diameter  $\leq 2.5$ mm); left main coronary artery lesions and patients requiring 4 or more stents; insulin dependent diabetes mellitus and acute coronary syndrome.

b. Based on the trials included, RCR was defined as target lesion revascularization, target vessel revascularization or any coronary revascularization.

c. ILUMIEN III-IVUS and ILUMIEN III-OCT come from the ILUMIEN III trial.

The baseline clinical characteristics of the included patients were shown (Table 2). In all trials included, the average age of patients was approximately 63 years old in the intravascular imaging-guided coronary stenting group and about 73.5% of patients were male. In addition, 29.5% of patients had diabetes, 59.7% of patients suffered from dyslipidemia, 62.7% of patients accompanied hypertension, and 35.1% of patients had a history of current smoking. The period of follow-up ranged from 6 to 24 months. Meanwhile, the average age of patients was approximately 64 years old in the angiography-guided coronary stent implantation, of which 72.4% of patients were male. Furthermore, 28.2% of patients had diabetes, 60.1% of patients merged dyslipidemia, 62.6% of patients amalgamated hypertension, and 36.1% of patients suffered from a history of current smoking approximately. Angiography and procedural characteristics are shown (Table 3).

## Assessment of quality and Publication Bias

The risk of bias assessment showed that there were no obvious bias of selection, detection, attrition, reporting, and others, meanwhile, the performance bias was unclear (Figure S1). The funnel plot showed that the distribution was symmetrical for all outcomes (Figure S2). However, the *P*-value of MI outcome by Egger's test was 0.00 ( $P < 0.05$ ) (Figure S3), which implied publication bias. No signs of publication bias was found by trim method (no new trials added) (Figure S2). In addition, the *P*-value of TLR, TVR, cardiac death, ST, MACE, and all-cause death were more than 0.05 by Egger's and Bgge's test, which meanted that there were no publication bias (Figure S3). The quality of GRADE evidence was

moderate for the TLR, TVR, cardiac death, ST, MACE, and all-cause death, while the quality of evidence was low for MI outcome (Table S2).

## Trial Sequential Analysis

Trial sequential analysis (TSA) were performed for each outcome (Figure S4). The cumulative Z curve of TLR, TVR, and MACE exceeded the traditional boundary and the TSA boundary, which meant the results were reliable. However, the cumulative Z curve of cardiac death, ST, and MI exceeded the traditional boundary and did not reach the TSA boundary and expected sample size, which may be a false positive caused by a small number of studies and small sample size. In addition, the cumulative Z curve of all-cause death did not cross the traditional boundary or the TSA boundary, and the sample size did not reach the expected amount of information, indicating that there was no statistical significance between the two groups, and more trials may be needed to prove this.

## The Primary Outcome

The risk of TLR was reported in fifteen trials (3.3% vs 5.4%, RR 0.62, 0.49–0.77,  $P=0.0001$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.85$ ), which showed that it is favor of intravascular imaging-guided coronary stent implantation (Fig. 2).

## The Secondary Outcomes

Of all trials, eleven trials reported the event of TVR. The results showed that compared with angiography-guided coronary stent implantation, coronary stent implantation guided by intravascular imaging can significantly reduce the risk of TVR (3.4% vs 4.9%, RR 0.65, 0.52–0.81,  $P=0.0001$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.50$ ) (Fig. 3a). Meanwhile, the cardiac death outcome was established in ten trials, the results demonstrated that the risk of cardiac death was significantly lower in the coronary stent implantation guided by intravascular imaging than that in the angiography-guided coronary stent implantation (0.8% vs 1.3%, RR 0.59; 0.39–0.91;  $P=0.02$ ) without significant heterogeneity ( $I^2=0\%$ ;  $P_{heterogeneity}=0.97$ ) (Fig. 3b).

The ST outcome was also reported in eleven trial, and which indicated that intravascular imaging-guided coronary stenting was associated with a reduced risk of ST (0.5% vs 0.9%, RR 0.54, 0.30–0.97;  $P=0.04$ ) without heterogeneity across the trials ( $I^2=0\%$ ;  $P_{heterogeneity}=0.94$ ) (Fig. 3c). In addition, MACE was selected as the outcome for fifteen trials. The results indicated that intravascular imaging-guided coronary stenting significantly reduced the risk of MACE compared with angiography guidance (7.6% vs 9.0%, RR 0.81, 0.71–0.93;  $P=0.003$ ,  $I^2=36\%$ ;  $P_{heterogeneity}=0.07$ ) (Fig. 3d).

However, all included trails analyzed the incidence of MI, and fourteen trials reported the data regarding all-cause death. There was no significant difference in incidence of MI (RR 0.78, 0.61–1.00,  $P=0.05$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.17$ ), and all-cause death (RR 0.85, 0.58–1.27,  $P=0.44$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.69$ ) between the two groups (Fig. 3e-f).

## Subgroup Analysis

The subgroup analysis was performed according to the lesion type with MACE as the outcome, to explore the possible causes of the heterogeneity, which suggested that there was significant heterogeneity ( $P_{heterogeneity}=0.07$ ,  $I^2=36\%$ ) (Fig. 4). Meanwhile, the results showed that intravascular imaging guidance can reduce the risk of MACE in patients with complex lesions (RR 0.61, 0.50–0.75,  $P<0.00001$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.66$ ). However, in patients with non-complex lesions, there was no statistical difference between intravascular imaging-guided and angiography-guided groups (RR 1.08, 0.89–1.31,  $P=0.45$ ,  $I^2=0\%$ ,  $P_{heterogeneity}=0.67$ ). In addition, there was significant difference in the interaction analysis between the two subgroups ( $P_{interaction}<0.0001$ ,  $I^2=93.8\%$ ), while no heterogeneity was found within the two subgroups ( $P_{heterogeneity}=0.66$ ,  $I^2=0\%$  and  $P_{heterogeneity}=0.67$ ,  $I^2=0\%$ ). Therefore, subgroup analyzes of other outcomes

were performed according to the lesion types and intravascular imaging type, and presence or absence of left main coronary artery to explore the impact of these factors on each outcome. The results also showed that intravascular imaging guidance can reduce the risk of TVR in patients with complex lesions (RR 0.53, 0.39–0.72,  $P < 0.0001$ ,  $I^2 = 0\%$ ,  $P_{\text{heterogeneity}} = 0.98$ ). However, there was no significant difference between the two groups in patients with non-complex lesions (RR 0.83, 0.59–1.15,  $P = 0.17$ ,  $I^2 = 40\%$ ,  $P_{\text{heterogeneity}} = 0.17$ ), and the differences of interaction analysis between the two groups was statistically significant ( $I^2 = 72.3\%$ ,  $P_{\text{interaction}} = 0.06$ ). In addition, there were no significant differences in the risk of TLR, MI, cardiac death, ST, and all-cause death in the subgroup analyses of lesion types (Figure S5). Furthermore, compared with angiography guidance, intravascular imaging guidance can reduce the risk of MACE in patients with left main coronary artery lesion (RR 0.56, 0.37–0.85,  $P = 0.006$ ,  $I^2 = 0\%$ ,  $P_{\text{heterogeneity}} = 0.62$ ) and non-left main coronary artery lesion (RR 0.85, 0.74–0.99,  $P = 0.03$ ,  $I^2 = 34\%$ ,  $P_{\text{heterogeneity}} = 0.11$ ), and heterogeneity was observed between the two groups ( $I^2 = 71.8\%$ ,  $P_{\text{interaction}} = 0.06$ ). However, there is no significant difference in the risk of TLR, cardiac death, and ST between the two groups (Figure S6). In addition, there were also no statistical significance in the risk of MI, all-cause death, ST, and MACE between intravascular imaging type subgroups (Figure S7).

## Discussion

This meta-analysis indicates that intravascular imaging-guided stenting has a lower risk of TLR, TVR, cardiac death, ST and MACE than coronary angiography-guided stenting. Meanwhile, the level of GRADE evidence is moderate for TLR, TVR, cardiac death, ST, MACE and all-cause death, while the level of evidence of MI is low according to the certainty of the evidence.

All included studies were randomized controlled trials. The risk of bias was low for selection, detection, attrition and reporting. The performance bias cannot be determined owing to fifteen trials did not report the blinding of participants and personnel only. Although intravascular imaging-guided stenting can significantly reduce the risks of TLR, TVR, cardiac death, ST, and MACE, the subgroup analysis showed that patients with complex lesions seemed to benefit more from the outcome of TVR and MACE. Meanwhile, TSA showed that the TLR, TVR, MACE outcomes intersected with traditional boundary and TSA boundary, which proves that the conclusion is reliable and does not need to be verified by more randomized controlled trials. In addition, we performed a subgroup analysis of patients with left main coronary artery lesions and non-left main coronary artery lesions, and the result showed that patients with left main coronary artery lesions can benefit more in the outcome of MACE. The conclusions of this meta-analysis are also similar to those of the 2018 European Society of Cardiology guidelines on myocardial revascularization [8]. This meta-analysis searched the basic databases without language restrictions, the detailed search strategy can be repeated. Meanwhile, no significant publication bias was found among the funnel plots, the Egger's test, and the trim method.

A meta-analysis of fifteen trials showed that IVUS-guided drug-eluting stents implantation was associated with a significantly reduced risk of MACE (OR 0.63, 0.53–0.73,  $P < 0.001$ ) in patients with complex lesions in 2017 [30], while the meta-analysis included only six randomized controlled trials, which may reduce the quality of evidence. Another meta-analysis evaluated the efficacy of angiography-guided and IVUS-guided left main coronary artery stenting, which confirmed that IVUS guidance can improve the clinical prognosis of these patients [31], especially cardiac death, all-cause death, and ST. This study only included patients with left main coronary artery lesions, and recruited only one randomized controlled trial. However, our meta-analysis recruited 18 randomized controlled trials, including the lesions of left main coronary artery, and the results showed that stent implantation guided by intravascular imaging can benefit from more outcomes. Meanwhile, similar to the results of the above two studies, our subgroup analysis also supported that patients with complex lesions have more benefits from TVR and MACE. In addition, patients with left main coronary artery lesions benefit more from MACE under the guidance of intravascular imaging. However, there was no

heterogeneity between complex lesion and non-complex lesion subgroups in the outcomes of TLR, MI, cardiac death, ST, and all-cause death. Meanwhile, the result of subgroup analysis also showed that there was no heterogeneity in the risk of MI, ST, and all-cause death between IVUS and OCT subgroups.

The results of this meta-analysis need to be applied cautiously. On the one hand, compared with Caucasians and East Asians, South Asians have a higher incidence of ST-elevation myocardial infarction due to plaque rupture. Meanwhile, the incidence of three-vessel disease and long lesions in South Asians is also significantly higher than that in Caucasians and East Asians<sup>[32]</sup>. Therefore, South Asians may benefit more from intravascular imaging guidance. However, white and East Asians accounted for the majority of our study, which means it is feasible to guide stent implantation by intravascular imaging in Caucasians and East Asians. In addition, the clinical benefit of intravascular imaging in South Asians needs to be further explored. On the other hand, gender and age may be important factors affecting the nature of plaques. In our meta-analysis, three-quarters of the patients were male nearly, suggesting that intravascular imaging guidance can significantly reduce the incidence of TLR, TVR, cardiac death, ST, and MACE. Meanwhile, some studies show that the plaque burden of patients with male increase significantly with age, and the risk of plaque rupture in patients with male is significantly higher than that in patients with female and the gender difference decreases with age<sup>[33–35]</sup>. Therefore, it is reasonable to consider the application of intravascular imaging in patients with male and elderly patients to improve the clinical benefit of subsets.

## Limitation

However, our meta-analysis may have some limitations. Firstly, most of the included randomized controlled trials are small-sample trials, with a low incidence of positive events and wide confidence interval, which reduces the quality of evidence. Secondly, TSA showed that MI, ST, and cardiac death led to false positive results due to insufficient sample size. Meanwhile, TSA results of all-cause death showed that there was no statistical significant between the two groups. Therefore, large-scale randomized controlled trials are still needed. In addition, owing to the different definitions of MACE in the included trials, it was not used as the primary outcome in this meta-analysis. Finally, the underlying disease of patients, the location of lesions, the number of disease vessels, the type of stent, and the specific treatment strategies may also affect the clinical outcome, but most trials do not provide these detailed data, further analysis cannot be conducted.

## Conclusions

Compared with traditional angiography, stent implantation guided by intravascular imaging can reduce the risk of TLR, TVR, cardiac death, and ST. Meanwhile, intravascular imaging-guided stent implantation is associated with a lower risk of MACE. In addition, patients with complex lesions will benefit more. However, whether it is necessary to routinely use intravascular imaging to guide stent implantation still needs to be further explored.

## Declarations

### Authors' contributions

Ying Niu: Study design, Data collection, Data analysis, Manuscript. Nan Bai: Data collection, Data analysis, Validation. Ying Ma: Data collection, Validation. Peng-yu Zhong: Data collection, Validation. Yao-sheng Shang: Data collection, Validation. Zhi-Lu Wang: Scientific revision of the manuscript.

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Competing interests

The author declares that there are no competing interests regarding the publication of this article.

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## Tables

Tables 2 and 3 are available in the Supplementary Files section.

## Figures

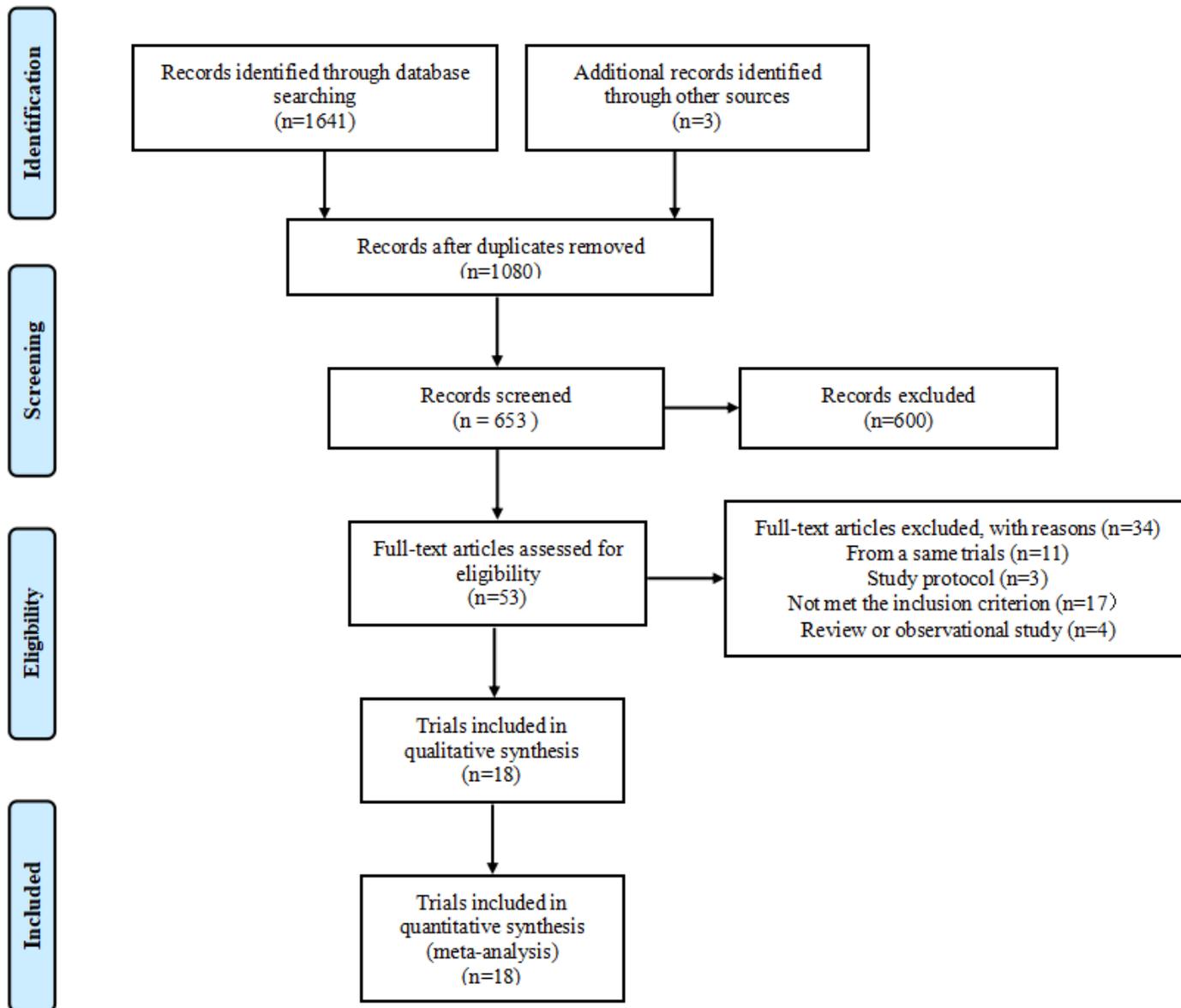
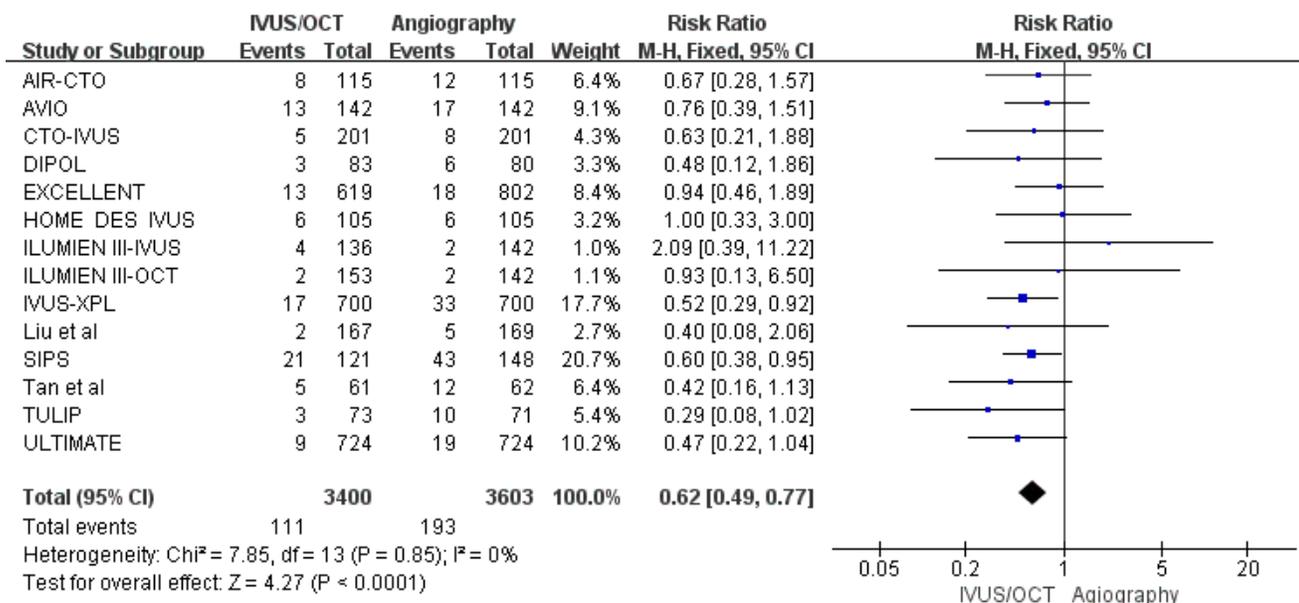


Figure 1

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**Figure 2**

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**Figure 3**

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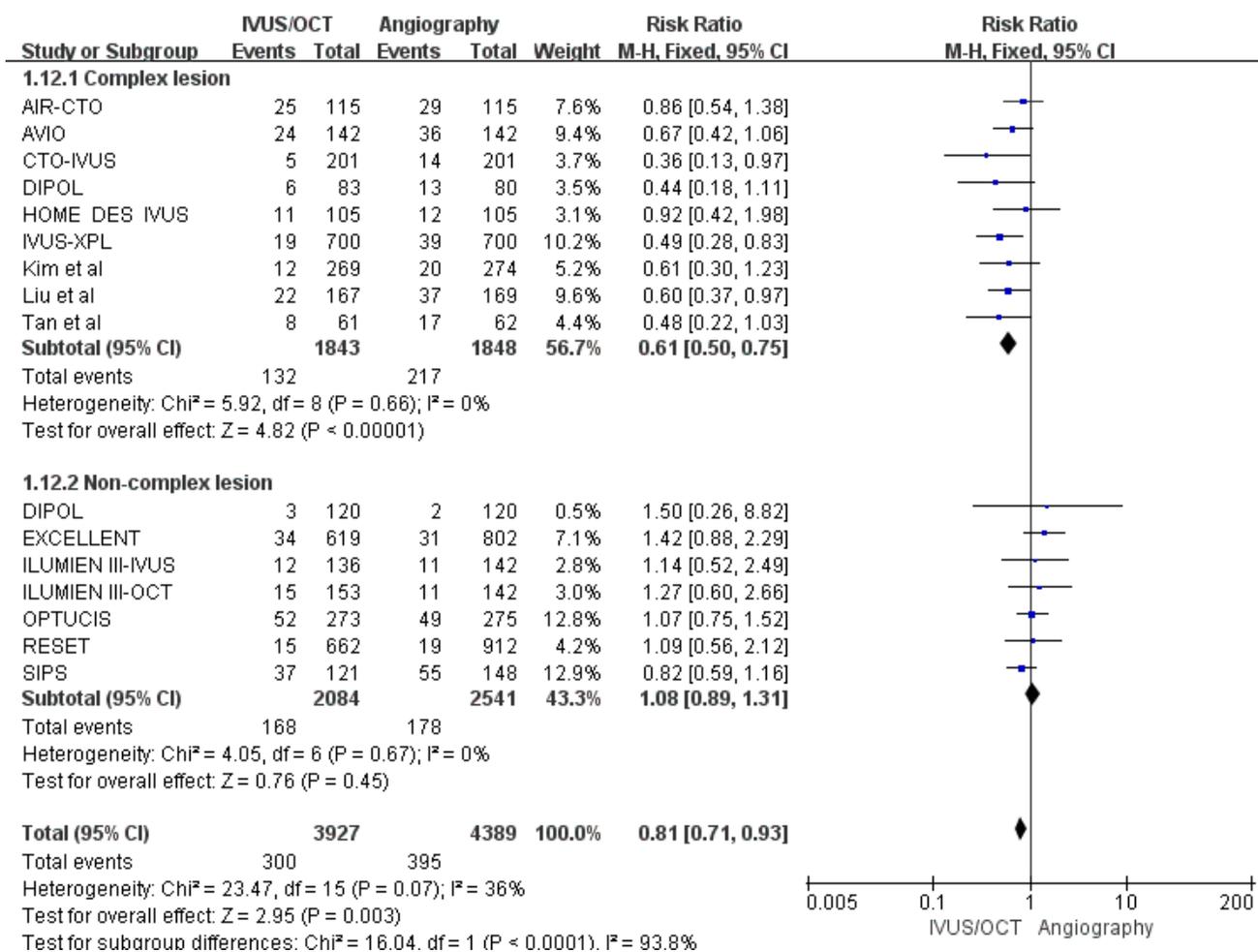


Figure 4

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