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IVUS-Guided versus Angiography-Guided PCI in Unprotected Left Main Coronary Artery Disease: An Updated Systematic Review and Meta-Analysis

Eashan Aneja

theeashananeja@gmail.com

Sir Ganga Ram Hospital

Vinicius de Pontes

Centro Universitário das Faculdades Metropolitanas Unidas

Mauricio Boneli

Centro Universitário das Faculdades Metropolitanas Unidas

Prakhar Gupta

JSS Medical College and Hospital

Shivani Phugat

All India Institute of Medical Sciences

Veda Chanda

Johns Hopkins University

Thierry Trevisan

Centro Universitário das Faculdades Metropolitanas Unidas

Michael Jacoub

Austin Hospital

Vikrant Jagadeesan

West Virginia University

Mohammad Ibrahim

Helios Klinikum Erfurt

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Abstract

Background

The role of intravascular ultrasound (IVUS)-guided percutaneous coronary intervention (PCI) in unprotected left main coronary artery disease (CAD) remains unclear, despite evidence suggesting improved procedural optimization and clinical outcomes compared with angiography-guided PCI.

Methods

We systematically searched the PubMed, Embase, and Cochrane Library databases for randomized controlled trials (RCTs) and non-randomized studies comparing IVUS-guided PCI with angiography-guided PCI in patients with unprotected left main CAD. Risk ratios (RR) with corresponding 95% confidence intervals (CI) were pooled for binary outcomes using a random-effects model. Additional subgroup analyses were performed separately for randomized controlled trials and observational studies.

Results

Twelve studies (five RCTs and seven observational studies) comprising 20,897 patients who underwent PCI for unprotected left main CAD were included, of whom 9,058 (43.4%) underwent intravascular imaging-guided PCI. IVUS-guided PCI was associated with lower all-cause mortality (RR 0.64; 95% CI 0.53–0.78; $p < 0.001$; $I^2 = 45.5\%$), cardiac mortality (RR 0.53; 95% CI 0.34–0.82; $p = 0.005$; $I^2 = 65.2\%$), myocardial infarction (RR 0.80; 95% CI 0.67–0.95; $p = 0.012$; $I^2 = 0\%$), and target vessel revascularization (RR 0.53; 95% CI 0.33–0.85; $p = 0.009$; $I^2 = 73.4\%$) than angiography-guided PCI. However, no statistically significant difference was observed in stent thrombosis. Subgroup analyses demonstrated that observational studies primarily drove the observed benefits, whereas pooled RCT data remained neutral.

Conclusion

In patients undergoing PCI for unprotected left main coronary artery disease, IVUS-guided PCI was associated with improved clinical outcomes compared with angiography-guided PCI, with similar stent thrombosis rates.

INTRODUCTION

Left main (LM) coronary artery disease (CAD) accounts for approximately 5–10% of patients undergoing coronary angiography for myocardial ischemia and is associated with substantial morbidity and mortality.[1] Percutaneous coronary intervention (PCI) has emerged as an effective and safe alternative to coronary artery bypass grafting (CABG), with a lower risk of early stroke than surgery.[2,3] However, the technical complexity of LMCAD requires precise stent sizing, apposition, and expansion. Intravascular imaging, particularly intravascular ultrasound (IVUS), has become an important strategy for LMCAD treatment optimization compared with conventional angiography-guided PCI.

For over a decade, studies have demonstrated that IVUS-guided PCI for unprotected LM disease improves clinical outcomes. A prior meta-analysis reported up to a 40% reduction in all-cause mortality and significant decreases in cardiac death, myocardial infarction (MI), and stent thrombosis compared with angiography-guided PCI, while noting a lack of randomized data on this topic.[6,7] Even so, with the subsequent growth of randomized evidence, recent guidelines have upgraded IVUS guidance during left main or complex PCI to a Class I recommendation.[4,8,9]

Recently, two landmark randomized trials, the OPTIMAL and IVUS-CHIP trials, have provided substantial insights into intravascular imaging-guided PCI for complex lesions, demonstrating no differences between IVUS guidance and

angiography in high-risk patients.[10,11] These neutral findings stand in stark contrast to the prior predominantly observational evidence and have ignited a fundamental debate regarding whether IVUS guidance confers genuine clinical benefits in LM PCI. Therefore, we conducted an updated meta-analysis comparing the clinical outcomes of IVUS-guided and angiography-guided PCI, incorporating all available randomized and observational data, with pre-specified subgroup analyses stratified by study design.

METHODS

Eligibility Criteria

We included studies comparing IVUS-guided versus angiography-guided PCI in adult patients with unprotected LM CAD. Both RCTs and observational studies were included in this review. Studies were required to report at least one of the prespecified clinical outcomes of interest. Case reports, case series, editorials, review articles, and studies without comparator arms were excluded. No restrictions were applied to language or geographic region.

Search Strategy and Data Extraction

A systematic search of the PubMed, Embase, and Cochrane Library databases was conducted from inception to April 2026, using the following search strategy: ("Percutaneous Coronary Intervention"[Mesh] OR "PCI" OR "angioplasty" OR "stent") AND ("left main coronary" OR "unprotected left main coronary artery" OR "unprotected left main disease" OR "left coronary" OR "ULMD" OR "left main" OR "LM disease" OR "LM coronary artery disease" OR "LMCA" OR "ULMCA") AND ("intravascular ultrasonographic guidance" OR "intravascular ultrasound" OR "intravascular imaging" OR "intravascular ultrasound-guided" OR "IVUS" OR "IVUS-guided PCI"). Two reviewers (E.A. and M.F.B.) independently screened the titles and abstracts, followed by a full-text review of the potentially eligible studies. We applied snowballing methods through backward citation searches of the included studies. Disagreements were resolved by consensus or by adjudication by a third reviewer (M.C.I.). Additionally, data were independently extracted by two reviewers (E.A. and T.T.) using a standardized extraction form that captured the study design, patient demographics, sample size, follow-up duration, imaging guidance protocol, and all relevant outcomes.

Outcomes

The clinical outcomes of interest were all-cause mortality, cardiac mortality, MI, target vessel revascularization (TVR), and stent thrombosis. A prespecified subgroup analysis was performed by stratifying the studies by design (RCTs versus observational studies) for all outcomes, given the anticipated heterogeneity in effect estimates between study types.

Quality Assessment

The methodological quality of the included RCTs and observational studies was assessed using the Cochrane Risk of Bias 2.0 (RoB 2.0) and Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tools, respectively. Quality assessment was performed independently by two reviewers (E.A. and V.C.), and disagreements were resolved through discussion.

Statistical Analysis

We pooled risk ratios (RR) with corresponding 95% confidence intervals (CI) for binary outcomes. A random-effects model was applied to account for demographic, clinical, and methodological heterogeneity among the studies, according to the Cochrane recommendations.[12] Statistical heterogeneity was quantified using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Prespecified subgroup analyses were conducted separately for the RCTs and observational studies. Sensitivity analyses were performed by sequentially excluding one study at a time to assess the robustness of the pooled estimates. Statistical significance was set at $p < 0.05$. All analyses were

performed using the meta and metafor packages in R (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Selection and Characteristics

A total of 1,570 records were identified through systematic database searches of PubMed, Embase, and Cochrane Library (Fig. 1). After removing duplicates and screening the titles and abstracts, 30 reports were assessed for full-text eligibility. Twelve studies (five RCTs and seven cohort studies) met our inclusion criteria, enrolling 20,897 patients who underwent PCI.[10,13–23] Among them, 9,058 (43.4%) underwent IVUS-guided PCI, and 11,839 (56.6%) underwent angiography-guided PCI.

Studies were conducted across multiple countries, including South Korea, China, Spain, Sweden, England, Wales, and Egypt, and multinational European centers, with enrollment periods from 2000 to 2023 and follow-up durations from 1 to approximately 10 years. The types of stents used varied among the studies. Three studies included both bare-metal and drug-eluting stents, whereas the remaining studies included only drug-eluting stents. Moreover, two of the most recent trials limited implantation to everolimus-eluting stents.

The mean or median age of the participants ranged from approximately 60 to 76 years, with males comprising 62% to 85% of the study populations. The most common cardiovascular risk factors were hypertension (41%–87%), diabetes mellitus (22%–62%), and dyslipidemia (30%–74%), whereas current smoking rates ranged from 13% to 64%. Previous MI was reported in 7%–39% of patients and prior PCI in 17%–37%, with left ventricular ejection fractions ranging from approximately 49% to 63% across cohorts.

Acute coronary syndrome accounted for up to 75% of patients in some registries, whereas two studies focused exclusively or predominantly on patients with stable coronary syndrome. Angiographic characteristics included SYNTAX scores in 6 of 12 studies, with mean scores ranging from 22 to 34. Distal or bifurcation left main involvement was observed in 43–83% of cases, and three-vessel disease in 21–65% of cases. Drug-eluting stent use was nearly universal, with maximum stent diameters ranging from 3.3 mm to 4.3 mm. A two-stent bifurcation strategy was used in 12%–52% of cases, and the post-dilation rates varied widely. Details of the individual studies are provided in Table 1, and the baseline characteristics of the included populations are summarized in Table 2.

Table 1
Summary of included studies.

Study	Design	Country (centers)	Sample size (IVUS vs Angio)	Enrollment	Follow-up	Stent type	Primary endpoint
Park 2009 [16]	Observational	Korea (multicenter)	756 vs 219	2000–2006	3 yr	BMS & DES	All-cause mortality
de la Torre Hernández 2014 [14]	Observational	Spain (multicenter)	505 vs 505	2002–2010	3 yr	DES only	Cardiac death, MI, TLR
Gao 2014 [15]	Observational	China (single center)	337 vs 679	2006–2011	1 yr	DES only	Cardiac death, MI, TVR (1-yr MACE)
Tan 2015 [22]	RCT (single center)	China	61 vs 62	2009–2012	2 yr	Sirolimus-eluting DES	Death, MI, TLR (2-yr MACE)
Andell 2017 [19]	Observational	Sweden (nationwide)	621 vs 1847	2005–2014	~ 10 yr	BMS & DES	Death, restenosis, stent thrombosis
Tian 2017 [18]	Observational	China (single center)	713 vs 1186	2004–2011	3 yr	BMS & DES	Death, MI (3-yr)
Kinnaird 2020 [17]	Observational	England & Wales	5056 vs 6208	2007–2014	1 yr	DES only (2nd gen)	All-cause mortality
Kwon 2023 [13]	RCT (prespecified LM substudy)	Korea (multicenter)	138 vs 54	2018–2021	2.1 year (median)	EES only	TVF (cardiac death, TV-MI, TVR)
Liu 2018 [20]	RCT (single center, open-label)	China	167 vs 169	2010–2015	1 yr	DES only	Cardiac death, MI, TVR (1-yr MACE)
Bruno 2024 [23]	Observational	Europe (13 centers)	213 vs 414	2002–2015	7.5 year (median)	BMS & DES	CV death, TVR, MI (MACE)
Bendary 2024 [21]	RCT (two-center)	Egypt	90 vs 91	≈ 2020–2023	1 yr	DES only	Cardiac death, MI, TVR (1-yr MACE)
Testa 2026 [10]	RCT (international, multicenter)	Italy/Spain/UK (28 centers)	401 vs 405	2020–2023	2.9 year (median)	EES (platinum–chromium)	Stroke, MI, revascularization, death (POCE)

Sample sizes reflect full study cohorts; pooled analyses used propensity-matched subsets where applicable, so per-arm numbers in the forest plots may differ. BMS, bare-metal stent; CV, cardiovascular; DES, drug-eluting stent; EES, everolimus-eluting stent; IVUS, intravascular ultrasound; LM, left main; MACE, major adverse cardiovascular events; MI, myocardial infarction; POCE, patient-oriented composite endpoint; RCT, randomized controlled trial; TLR, target lesion revascularization; TV-MI, target-vessel MI; TVF, target-vessel failure; TVR, target vessel revascularization.

Table 2
Baseline characteristics of the included studies.

Study	Arm	N	Age (yr)	Male, %	HTN, %	Dyslipid., %	Diabetes, %	Smoker, %	Prior MI, %	Prior PCI, %	LVEF, %
Park 2009 [16]	IVUS	756	59.7 ± 11.5	69.0	47.6	30.3	27.0	25.3	7.4	17.2	62.7 ± 8.5
	Angiography	219	65.4 ± 11.1	72.6	54.8	26.9	32.9	22.4	7.3	23.7	59.4 ± 12.2
de la Torre H. 2014 [14]	IVUS	505	66.1 ± 11.6	80.0	67.7	62.2	36.2	29.3	24.1	21.9	54.9 ± 12.5
	Angiography	505	66.9 ± 11.5	78.7	64.3	56.2	34.6	31.8	25.7	21.2	55.3 ± 13.0
Gao 2014 [15]	IVUS	337	66.0 ± 10.4	81.3	72.4	67.7	32.3	33.1	17.9	17.8	58.7 ± 10.1
	Angiography	679	67.1 ± 10.0	77.5	72.0	71.7	34.2	34.1	18.1	17.5	56.7 ± 11.7
Tan 2015 [22]	IVUS	61	76.5 ± 4.9	62.3	41.0	NR	34.4	44.3	16.4	NR	55.3 ± 5.0
	Angiography	62	75.9 ± 3.5	69.4	46.8	NR	29.0	46.8	21.0	NR	53.3 ± 7.1
Andell 2017 [19]	IVUS	621	70 (62–77)	74.6	69.6	NR	25.8	13.7	32.9	31.4	NR
	Angiography	1847	75 (67–82)	69.5	71.3	NR	23.2	12.8	38.7	26.7	NR
Tian 2017 [18]	IVUS	713	59.6 ± 10.9	80.8	56.1	54.3	24.3	35.9	22.9	23.1	63.2 ± 6.8
	Angiography	1186	60.0 ± 10.2	77.6	55.1	50.3	26.5	26.6	24.7	22.8	62.9 ± 7.4
Kinnaird 2020 [17]	IVUS (imaging)	5056	68.1 ± 11.8	72.3	61.1	NR	22.8	64.0	35.0	29.5	48.9 ± 11.0
	Angiography	6208	71.8 ± 11.7	70.2	65.2	NR	24.8	61.2	39.3	25.0	46.4 ± 12.0
Kwon 2023 [13]	IVUS (imaging)	138	66.7 ± 10.1	84.1	65.2	49.3	36.2	15.2	4.3	18.8	58.4 ± 11.9
	Angiography	54	65.9 ± 10.0	85.2	61.1	42.6	35.2	18.5	9.3	16.7	59.3 ± 11.0
Liu 2018	IVUS	167	65.3 ±	63.5	69.5	37.7	33.5	37.1	17.4	19.8	55.6 ±

Study	Arm	N	Age (yr)	Male, %	HTN, %	Dyslipid., %	Diabetes, %	Smoker, %	Prior MI, %	Prior PCI, %	LVEF, %
[20]			10.6								11.7
	Angiography	169	64.9 ± 11.2	63.9	72.2	37.9	30.8	35.5	14.2	16.6	58.4 ± 10.5
Bruno 2024 [23]	IVUS	213	68 (59–75)	72	87	71	26	48	NR	31	55 (48–60)
	Angiography	414	69 (60–76)	72	83	65	23	34	NR	30	50 (45–56)
Bendary 2024 [21]	IVUS	90	63 ± 9	73.3	75.6	74.4	62.2	57.8	17.8	36.7	55 ± 9
	Angiography	91	61 ± 9	69.2	67.0	63.7	69.2	54.9	14.3	28.6	54 ± 8
Testa 2026 [10]	IVUS	401	71.1 ± 11.0	78.6	79.5	74.0	36.6	13.0	25.0	26.2	53.2 ± 11.1
	Angiography	405	71.7 ± 10.4	78.3	79.3	77.8	32.8	15.1	22.2	24.7	53.4 ± 10.4

Data are % of the respective arm unless otherwise indicated; age and LVEF are mean ± SD or median (IQR). For Kinnaird 2020 and Kwon 2023 the intervention arm used intravascular imaging (predominantly IVUS). Diabetes for Testa 2026 includes insulin- and non–insulin-dependent diabetes. HTN, hypertension; IVUS, intravascular ultrasound; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NR, not reported; PCI, percutaneous coronary intervention.

Pooled Analysis

All-cause mortality. IVUS-guided PCI was associated with a significant reduction in all-cause mortality compared with angiography-guided PCI (RR 0.64; 95% CI 0.53–0.78; p < 0.001; I^2=45.5%). Subgroup analysis showed that this benefit was driven predominantly by observational studies (RR 0.58; 95% CI 0.53–0.64; p < 0.001; I^2=0%), whereas pooled RCT data were neutral (RR 0.83; 95% CI 0.43–1.61; p = 0.584; I^2=51.9%). The test for subgroup differences was not significant (p = 0.299) (Fig. 2A).

Cardiac mortality. IVUS-guided PCI was associated with a significant reduction in cardiac mortality (RR 0.53; 95% CI 0.34–0.82; p = 0.005; I^2=65.2%), although the overall heterogeneity was substantial. Observational studies demonstrated a consistent benefit (RR 0.47; 95% CI 0.34–0.66; p < 0.001; I^2=0%), while the RCT subgroup was neutral and markedly heterogeneous (RR 0.53; 95% CI 0.14–2.03; p = 0.357; I^2=71.8%). The test for subgroup differences was not significant (p = 0.864) (Fig. 2B).

Myocardial infarction. IVUS-guided PCI was associated with a significant reduction in myocardial infarction (RR 0.80; 95% CI 0.67–0.95; p = 0.012; I^2=0%), with no heterogeneity detected across the 10 studies. The observational subgroup favored IVUS (RR 0.75; 95% CI 0.61–0.93; p = 0.007; I^2=0%), while the RCT subgroup was neutral (RR 0.92; 95% CI 0.68–1.26; p = 0.619; I^2=0%). The test for subgroup differences was not significant (p = 0.273) (Fig. 3A).

Stent thrombosis. No statistically significant difference in stent thrombosis was observed between the groups (RR 0.59; 95% CI 0.32–1.08; p = 0.087; I^2=28.2%). Both the observational (RR 0.54; 95% CI 0.28–1.05; p = 0.068; I^2=32.9%) and RCT (RR 0.63;

95% CI 0.19–2.09; p = 0.451; I²=34.4%) subgroups were not significant. The test for subgroup differences was not significant (p = 0.832) (Fig. 3B).

Target vessel revascularization. IVUS-guided PCI was associated with a significant reduction in TVR (RR 0.53; 95% CI 0.33–0.85; p = 0.009; I²=73.4%), although heterogeneity was high. Neither the observational (RR 0.49; 95% CI 0.23–1.08; p = 0.077; I²=86.2%) nor RCT subgroup (RR 0.56; 95% CI 0.28–1.10; p = 0.091; I²=59.9%) reached statistical significance independently. The test for subgroup differences was not significant (p = 0.820) (Fig. 4).

Sensitivity Analyses

Leave-one-out sensitivity analyses confirmed the robustness of the pooled estimates for all-cause mortality, cardiac mortality, and MI, with effect sizes and confidence intervals remaining stable regardless of which study was omitted. For TVR, the statistical significance was preserved across all iterations (Figures S1, S2, S3, and S4).

Testa et al. (2026) were identified as the primary drivers of heterogeneity across outcomes.[10] Its omission substantially reduced the heterogeneity for all-cause and cardiac mortality (RR 0.45; 95% CI 0.33–0.62) and stent thrombosis (Figures S1, S2, and S3). The latter became statistically significant when it was omitted. As the most contemporary trial conducted exclusively in the modern drug-eluting stent era, Testa et al. (2026) likely reflect a context in which optimized stent technology attenuates the incremental procedural benefit of IVUS guidance.

Quality Assessment

In the risk of bias assessment, seven observational studies were rated as having a moderate overall risk of bias by ROBINS-I, with none rated as serious or critical. Confounding was the most common problem, arising from non-random assignment to imaging guidance, which varied by patient. This was addressed using methods such as propensity score matching. Outcome measurement was affected by differences in how results were judged between registry-based and special study designs. The remaining areas were deemed low risk in most studies. Of the five RCTs checked with RoB 2, one trial was rated low risk overall. The other four had some concerns, mainly regarding the randomization process due to limited details on how allocation was concealed, and regarding outcome measurement due to the open-label design. The critical appraisal of individual studies and the summary of risk of bias were provided in the Supplementary Material (Figures S7 and S8, respectively). A funnel plot for myocardial infarction showed a broadly symmetric distribution of studies around the pooled estimate, with no substantial visual asymmetry to suggest publication bias. Egger's regression test was non-significant (t = −1.50, df = 10, p = 0.173), indicating no statistical evidence of small-study effects (Figure S8).

DISCUSSION

In this meta-analysis of 12 studies and 20,897 patients, we compared IVUS-guided and angiography-guided PCI in patients with unprotected LM CAD. In our analysis, we found that IVUS-guided PCI was associated with lower rates of all-cause and cardiac mortality, MI, and TVR than angiography-guided PCI, with no significant differences in stent thrombosis between the two groups. Moreover, when the analysis was restricted to randomized data, none of these benefits were statistically significant.

Unprotected LMCAD is the highest-risk lesion among all obstructive CAD lesions. The LM artery supplies 75–100% of the LV myocardium; hence, without treatment, the disease has a poor prognosis. Revascularization with either CABG or PCI offers a clear survival benefit,[24] and a prior meta-analysis of randomized trials found no significant difference in five-year all-cause mortality between PCI and CABG.[3] Given that PCI is associated with lower acute procedural morbidity, there is increasing interest in optimizing stenting techniques for patients with CAD.[25] Therefore, intravascular imaging, particularly IVUS, has emerged as a key tool in this setting, with previous observational studies consistently showing lower rates of mortality and ischemic events. Nevertheless, because the most recent randomized trials have shown no clear benefit of IVUS in high-risk patients, it remains unclear whether the use of IVUS in unprotected LMCAD leads to better clinical outcomes.

Although previous meta-analyses have shown reduced rates of all-cause mortality, cardiac death, and stent thrombosis with IVUS-guided left main PCI, their analyses were largely based on observational data, which may have introduced significant bias.[6,7] A more recent meta-analysis conducted by Zito et al. (2025) focused solely on randomized trials and found that intravascular imaging guidance reduced TVF.[5] Nevertheless, the authors combined IVUS and OCT and included patients with LM and bifurcation PCI, which may yield more generalizable results. Since then, the two largest RCTs on the topic, the OPTIMAL and IVUS-CHIP trials, have been published.[10,11] Because the current guidelines for IVUS use in LMCAD are largely based on older observational evidence, we aimed to conduct an updated meta-analysis comparing IVUS- and angiography-guided PCI for unprotected LMCAD.

In our analysis, all-cause mortality at follow-up was lower in the IVUS-guided PCI group, indicating a potential mortality benefit compared with angiography-guided PCI alone. This finding is consistent with existing observational studies, which have generally reported lower all-cause mortality rates with IVUS guidance than without. However, the OPTIMAL trial, the largest randomized controlled trial in this population to date, did not demonstrate a statistically significant difference in mortality between the two strategies and largely contributed to the heterogeneity observed in the pooled estimates, as supported by our sensitivity analysis.[10] Of particular note, the observational design is susceptible to selection bias and residual confounding, which may have influenced our results in the overall cohort. To mitigate these limitations, propensity-matched data from observational studies were preferentially extracted when available; nevertheless, residual confounding may persist, and the results should be interpreted accordingly. Furthermore, operators in the OPTIMAL trial were highly experienced with IVUS, having routinely used it for most left main lesions, which may have minimized the performance gap between the two strategies. Thus, when experienced operators perform both strategies, the benefit of IVUS guidance may be less pronounced than in routine clinical practice.

Similarly, cardiovascular mortality was lower in the IVUS-guided group than in the angiography-guided PCI group, consistent with findings from the broader literature. However, the pooled analysis of RCTs did not demonstrate a statistically significant difference in cardiovascular mortality rates. The only RCT to show a significant benefit, conducted by Kwon et al., was a prespecified sub-study of the RENOVATE-COMPLEX-PCI trial.[13] This trial was designed and randomized for complex coronary lesions in general, rather than specifically for left main diseases. Because the presence of left main disease did not stratify randomization, the balance achieved in the overall trial population may not be generalizable to this subgroup, substantially limiting the strength of this finding. The lack of significance in the RCT subgroup likely reflects the similar factors discussed for all-cause mortality, with the OPTIMAL trial serving as the primary source of heterogeneity.

The IVUS-guided group demonstrated a lower MI rate, with pooled analysis indicating a statistically significant reduction compared with angiography-guided PCI. In contrast to mortality outcomes, this result exhibited negligible heterogeneity across the studies. No individual study achieved statistical significance, likely due to insufficient power to detect a modest reduction in the incidence of MI. The pooled analysis provided the statistical power that individual studies lacked. Additionally, the robustness of the leave-one-out analysis, in which the estimate remained stable regardless of which study was omitted, further strengthens the confidence in this finding. As with mortality outcomes, the observed benefit was primarily driven by the observational subgroups.

TVR is a relatively rare endpoint, with an incidence of 6% in patients. Our findings demonstrated that the TVR was significantly lower in the IVUS-guided group. Neither the observational nor RCT subgroup alone reached statistical significance, which may be attributed to insufficient statistical power to detect a clinically meaningful difference in this relatively rare endpoint. The pooled analysis across all study designs provides the statistical power that individual studies lack, and the significant overall result should be interpreted as a strength of the meta-analytic approach. The substantial heterogeneity observed likely reflects genuine methodological differences across studies, including variations in follow-up duration, target lesion definitions, and stenting techniques, rather than inconsistency in the direction of effect, which consistently favored the IVUS guidance. However, the pooled significance was substantially driven by observational data, where IVUS use may serve as a marker of higher-quality procedural care, making it difficult to attribute the TVR reduction solely to IVUS guidance.

The stent thrombosis rates were similar in both groups. This finding should be interpreted with caution, as stent thrombosis is rare, and most studies have wide confidence intervals, making it difficult to detect differences in such uncommon events, even with large groups. Therefore, a non-significant result could indicate insufficient statistical power rather than the absence of a true benefit. In contrast, when the OPTIMAL trial was excluded from the analysis, the pooled result became statistically significant, and the heterogeneity disappeared. This pattern was also observed for other outcomes in the meta-analysis, possibly due to operator-level factors discussed earlier. Still, it is difficult to explain heterogeneity by pointing to a single trial, and it is also possible that the OPTIMAL trial reflects a real reduction in IVUS benefit in current practice.

Several limitations of this meta-analysis should be acknowledged when interpreting the findings. First, seven studies employed an observational design, which is inherently vulnerable to selection bias and residual confounding bias. Although propensity-matched data were extracted from observational studies when available, this approach does not fully address confounding, and the reported benefits should be interpreted with caution. Second, the total number of randomized patients was limited, which may restrict the statistical power of the randomized controlled trial subgroup analyses. Third, substantial heterogeneity was identified across several outcomes, particularly in cardiac mortality and TVR. This heterogeneity likely reflects genuine differences in operator experience, IVUS utilization protocols, stent platforms, lesion complexity, and follow-up duration among the studies included. Fourth, the follow-up duration varied considerably, ranging from 1 to approximately 10 years, which may have influenced event rates differently across studies. Finally, antithrombotic and dual antiplatelet therapy regimens were neither uniformly reported nor standardized, and variations in these regimens may have independently affected ischemic outcomes, particularly stent thrombosis, complicating the isolation of the effect of IVUS guidance.

CONCLUSION

This updated meta-analysis evaluated IVUS-guided versus angiography-guided PCI in unprotected LMCAD. IVUS-guided PCI was associated with significant reductions in all-cause mortality, cardiac mortality, MI, and TVR compared with angiography-guided PCI. These findings suggest that IVUS guidance may be particularly advantageous in routine clinical practice, where operator experience and procedural quality are variable, rather than in the controlled environments of contemporary randomized trials. Further large-scale randomized trials with standardized protocols are required to clearly define the role of IVUS guidance in this high-risk population.

Abbreviations

CABG
coronary artery bypass grafting
CAD
coronary artery disease
CI
confidence interval
HR
hazard ratio
I^2
inconsistency statistic (heterogeneity)
IVUS
intravascular ultrasound
LM
left main
LV
left ventricular
MI

myocardial infarction
OCT
optical coherence tomography
PCI
percutaneous coronary intervention
PRISMA
Preferred Reporting Items for Systematic Reviews and Meta—Analyses
PROSPERO
International Prospective Register of Systematic Reviews
RCT
randomized controlled trial
ROBINS
I—Risk Of Bias In Non—randomized Studies of Interventions
RoB 2.0
Cochrane Risk of Bias 2.0
RR
risk ratio
SYNTAX
SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery
TVR
target vessel revascularization

Declarations

Human Ethics and Consent to Participate: Not applicable. This study is a systematic review and meta-analysis of previously published, aggregate-level data and did not involve any new studies of human participants performed by the authors. Accordingly, approval from an ethics committee or institutional review board (IRB) was not required, and no participant consent to participate was obtained or required.

Ethics approval: Not applicable (no ethics committee/IRB approval was required, as the study analyzed only previously published data).

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Figures

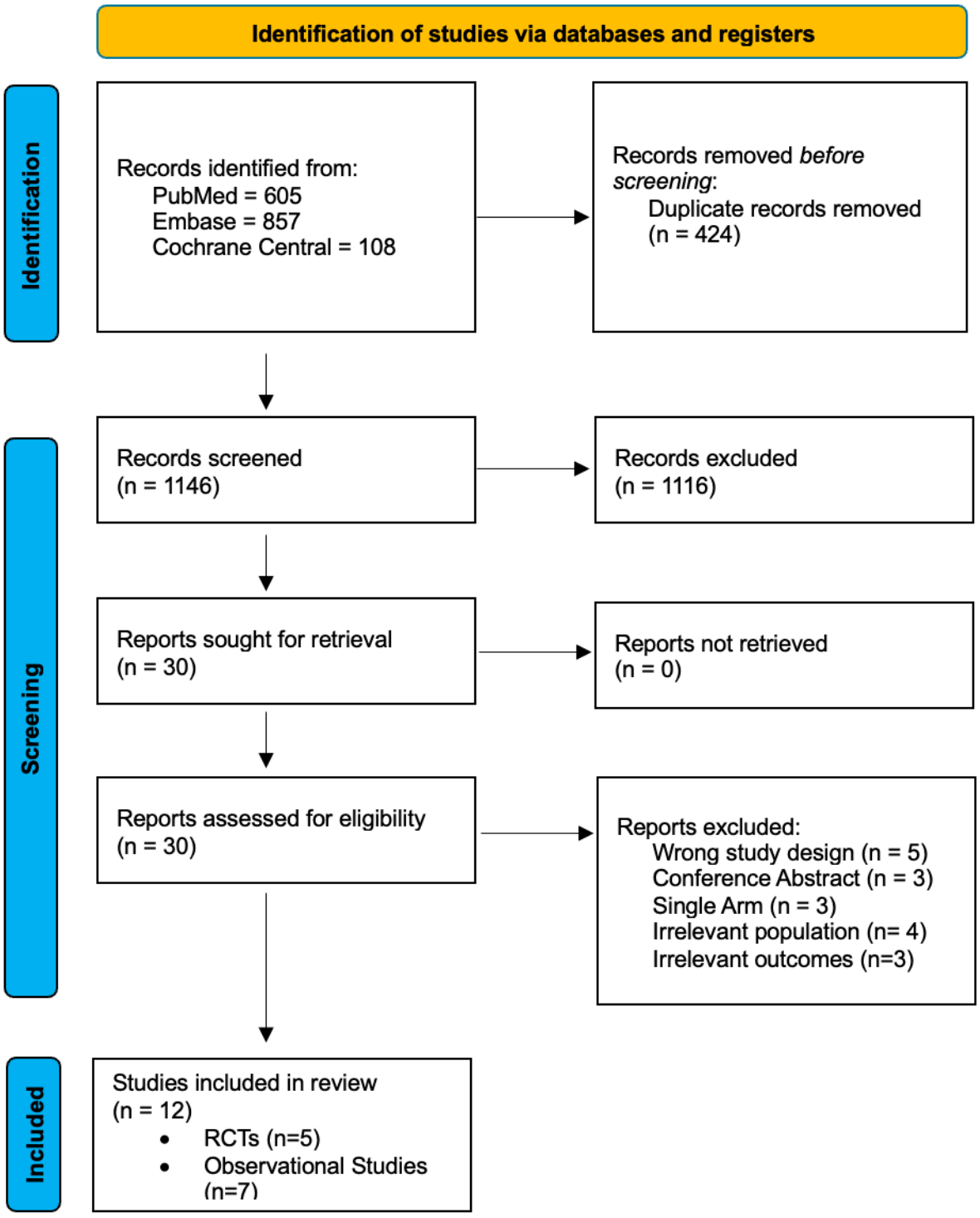


Figure 1

PRISMA flow diagram of study screening and selection.

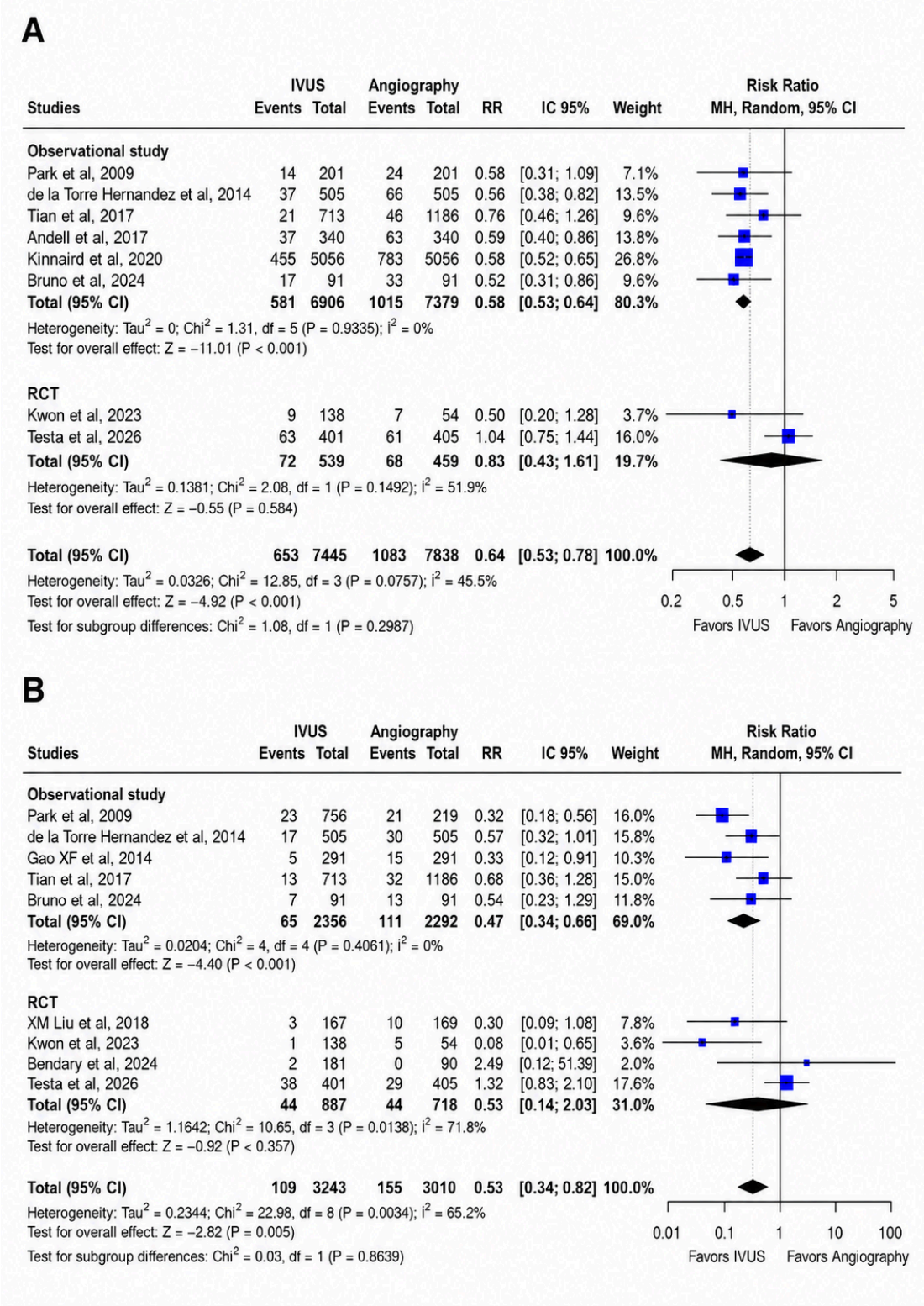


Figure 2

Forest plots of (A) all-cause mortality and (B) cardiac mortality for IVUS-guided versus angiography-guided PCI, stratified by study design. PCI = percutaneous coronary intervention; CI = confidence interval; RR = risk ratio.

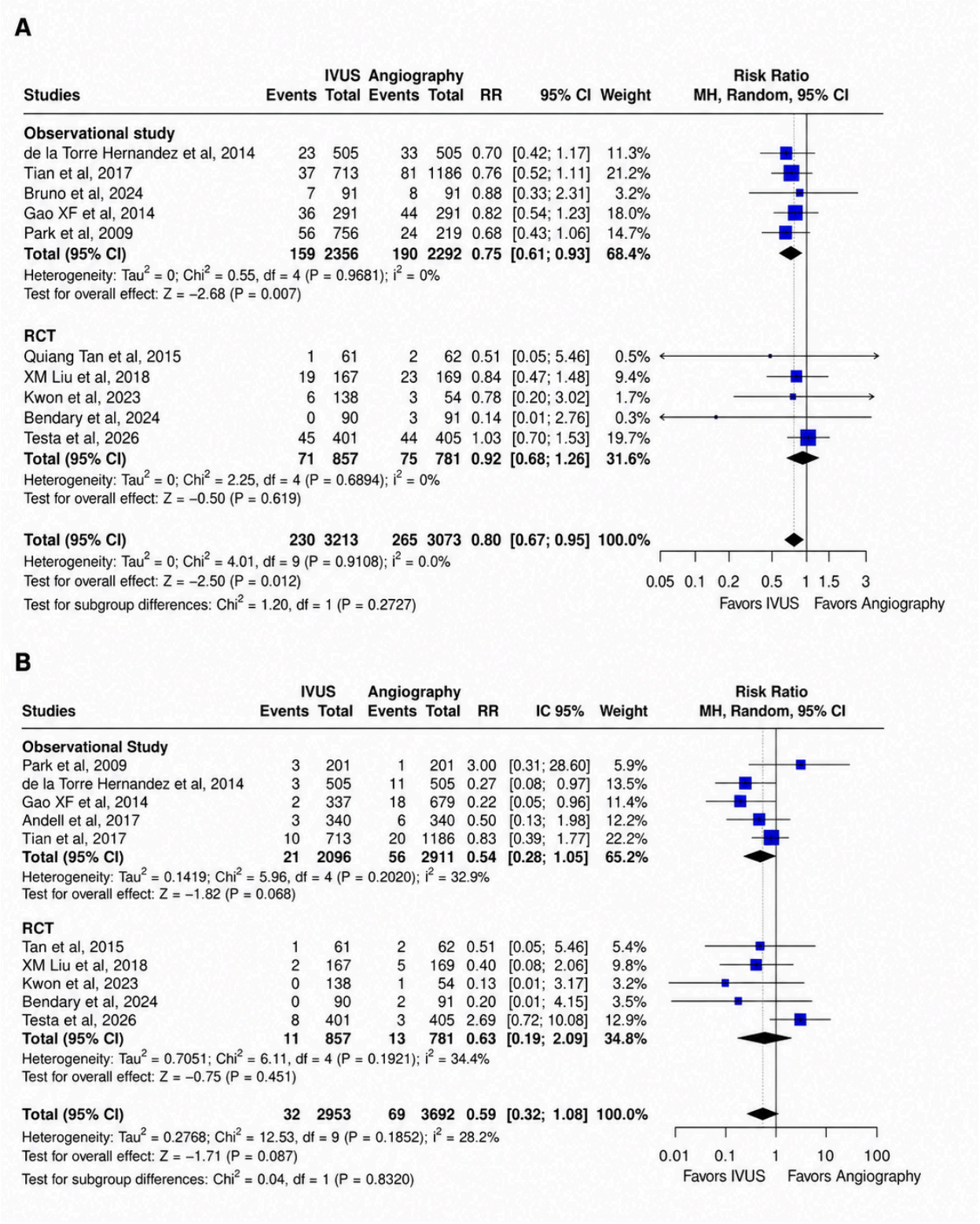


Figure 3

Forest plots of (A) myocardial infarction and (B) stent thrombosis for IVUS-guided versus angiography-guided PCI, stratified by study design. PCI = percutaneous coronary intervention; IVUS = intravascular ultrasound; CI = confidence interval; RR = risk ratio.

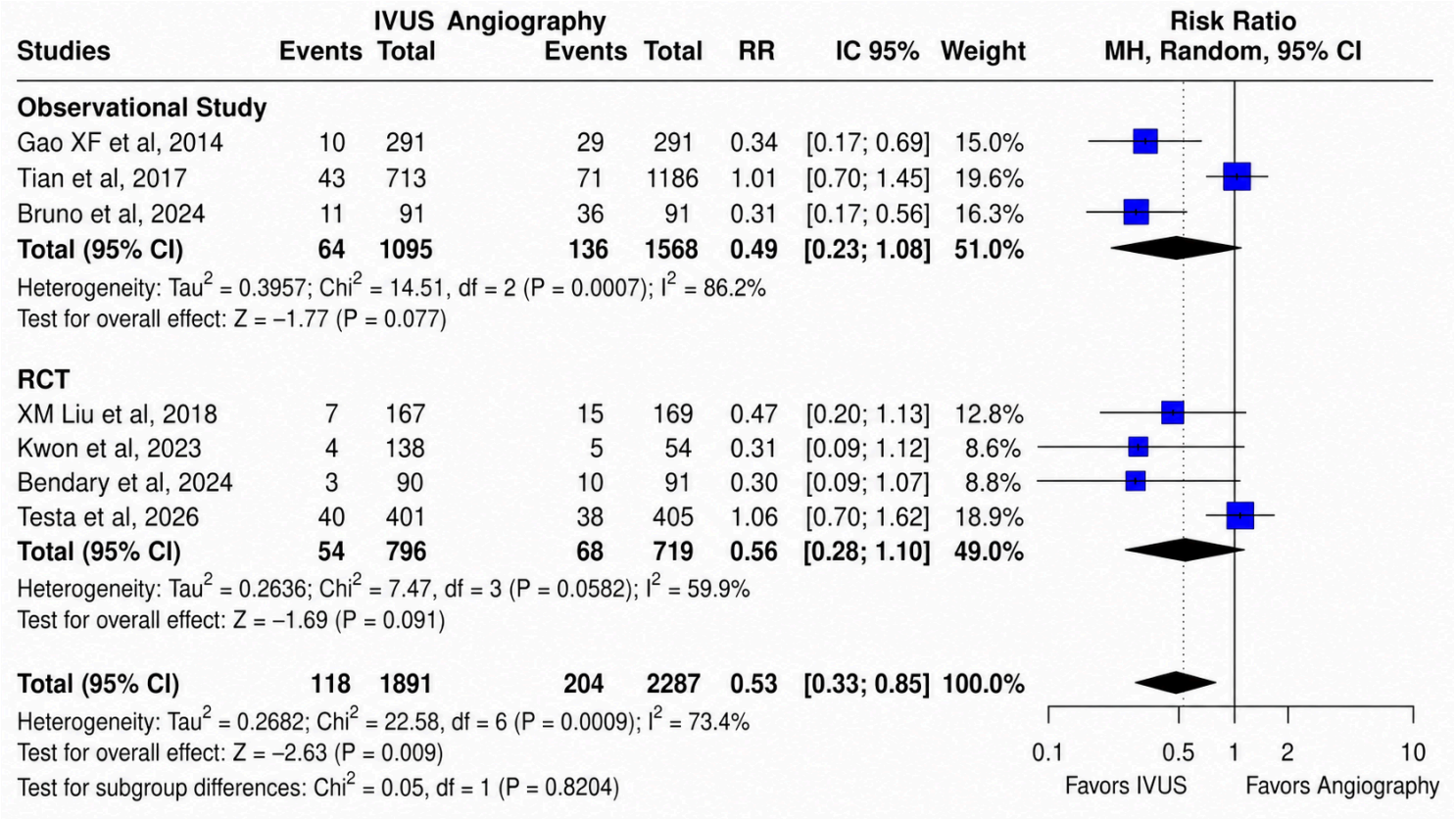


Figure 4

Forest plot of target vessel revascularization for IVUS-guided versus angiography-guided PCI, stratified by study design. PCI = percutaneous coronary intervention; IVUS = intravascular ultrasound; CI = confidence interval; RR = risk ratio.

Supplementary Files

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