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Application of optical coherence tomography in cardiovascular diseases: bibliometric and meta-analysis

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Significance: Since the advent of Optical Coherence Tomography (OCT) two decades ago, there has been substantial advancement in our understanding of intravascular biology. Identifying culprit lesion pathology through OCT could precipitate a paradigm shift in the treatment of patients with Acute Coronary Syndrome. Given the technical prowess of OCT in the realm of cardiology, bibliometric analysis can reveal trends and research focal points in the application of OCT for cardiovascular diseases. Concurrently, meta-analyses provide a more comprehensive evidentiary base, supporting the clinical efficacy of OCT-guided Percutaneous Coronary Intervention (PCI).

Design: This study employs a dual approach of Bibliometric and Meta-analysis. **Methods:** Relevant literature from 2003 to 2023 was extracted from the Web of Science Core Collection (WoSCC) and analyzed using VOSviewer, CiteSpace, and R for publication patterns, countries, institutions, authors, and research hotspots. The study compares OCT-guided and coronary angiography-guided PCI in treating adult coronary artery disease through randomized controlled trials (RCTs) and observational studies. The study has been reported in the line with PRISMA and AMSTAR Guidelines.

Results: Adhering to inclusion and exclusion criteria, 310 publications were incorporated, demonstrating a continual rise in annual output. Chinese researchers contributed the most studies, while American research wielded greater influence. Analysis of trends indicated that research on OCT and angiography-guided PCI has become a focal topic in recent cohort studies and RCTs. In 11 RCTs (n = 5,277), OCT-guided PCI was not significantly associated with a reduction in the risk of Major Adverse Cardiac Events (MACE) (Odds ratio 0.84, 95% CI 0.65–1.10), cardiac death (0.61, 0.36–1.02), all-cause death (0.7, 0.49–1.02), myocardial infarction (MI) (0.88, 0.69–1.13), target lesion revascularization (TLR) (0.94, 0.7–1.27), target vessel revascularization (TVR) (1.04, 0.76–1.43), or stent thrombosis (0.72, 0.38–1.38). However, in 7 observational studies (n = 4,514), OCT-guided PCI was associated with a reduced risk of MACE (0.66, 0.48–0.91) and TLR (0.39, 0.22–0.68).

Conclusion: Our comprehensive review of OCT in cardiovascular disease literature from 2004 to 2023, encompassing country and institutional origins, authors, and publishing journals, suggests that OCT-guided PCI does not demonstrate significant clinical benefits in RCTs. Nevertheless, pooled results from observational studies indicate a reduction in MACE and TLR.

KEYWORDS

optical coherence tomography, cardiovascular diseases, bibliometric analysis, metaanalysis, percutaneous coronary intervention

1 Introduction

Recent evidence suggests that MACE in chronic ischemic heart disease correlates more with the overall atherosclerotic burden than with specific flow-limiting luminal lesions (1-6). Traditional models simplistically link CAD complications to severe obstructions from narrow atherosclerotic plaques (7-10). However, this perspective is increasingly recognized as overly reductionist. Longitudinal studies on the natural progression of individual coronary plaques have revealed that even those lesions perceived as high-risk and potentially ischemia-inducing maintain stability over several years, seldom progressing to instability or resulting in MACE (11-16). The limitations of angiography in direct PCI, including inaccurate assessments of lesion morphology and the underlying mechanisms of STEMI, as well as suboptimal recognition of post-stent outcomes, underscore the necessity for a more holistic understanding of atherosclerosis within the entire arterial system (17).

OCT provides the highest resolution (1-15 µm) among current intravascular imaging technologies, enabling detailed exploration of microscopic vascular structures (18). In cardiovascular clinical applications, the significance of OCT encompasses: (1) Comprehensive plaque assessment: OCT provides detailed information about plaque size, type, and composition, aiding in understanding the total burden of atherosclerosis, not merely localized stenosis (19); (2) Vulnerable plaque identification: OCT can provide detailed views of potentially hazardous plaques by analyzing tissue characteristics, such as the size of the lipid core and the thickness of the fibrous cap (20); (3) Enhanced risk stratification: The detailed plaque and vascular information provided by OCT can help more accurately assess the risk of cardiovascular events, thus improving the accuracy of risk stratification (21); (4) Complementing traditional imaging techniques: By offering direct observation of vessel walls and plaques, OCT supplements the limitations of traditional imaging methods, providing a more comprehensive cardiovascular health assessment (22). Thus, OCT is not only a potent diagnostic tool but also adds a new dimension to the risk assessment and management of cardiovascular diseases. Its application highlights a deeper and more nuanced understanding of cardiac diseases, contributing to the refinement of existing risk stratification methods for greater precision.

We analyzed trends and applications of OCT in cardiovascular treatment over the past two decades using bibliometric techniques (23, 24). Our meta-analysis indicates OCT as a prominent focus in recent PCI trials. Previous studies comparing OCT-guided with angiography-guided PCI treatment in Meta-analyses have encountered several issues. Firstly, they did not include all significant related studies. Secondly, these meta-analyses did not separate observational studies from RCTs, a methodological rigor essential for enhancing the credibility of results. Therefore, we conducted a stringent Meta-analysis, differentiating RCTs from observational studies, aiming to provide more accurate and reliable evidence to guide clinical practice and future research directions.

2 Methods

2.1 Data sources and search strategy

The Web of Science, esteemed for its extensive interdisciplinary coverage, comprehensive citation indexing, and rich analytical metrics, serves as an exemplary database for bibliometric analysis. This resource enables researchers to identify hotspots and trends within their respective fields. Our study utilized data retrieved from the WoSCC database concerning OCT and cardiovascular diseases for bibliometric analysis. To mitigate data variability due to updates, search activities, data extraction, and downloading were conducted on the same day. The types of literature studied were confined to articles and reviews. The search strategy, specific outcomes, and search terms are detailed in Figure 1 (refer to Supplementary eMethods S1). Overall, 2,758 literature sources were analyzed, with 310 articles ultimately included and downloaded in text format (complete records and referenced citations).

2.2 Data analysis and visualization

In this study, the bibliometrix package in R (version 4.3.2) was utilized to analyze major countries, active authors and institutions, contributing journals, and keyword trends (25). Additionally, CiteSpace (version 6.1), a Java-based freeware developed by Chen (26), was employed for clustering and burst analysis of keywords. Collectively, these two software programs facilitated visual analyses, offering deep insights into the advancements in OCT research within the cardiovascular field and uncovering research frontiers using extensive data.

2.3 Meta-analysis

This work has been reported in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines (27, 28). A systematic review and meta-analysis were conducted on data from 11 RCTs and 7 observational studies. These 18 cohorts were identified through searches of electronic databases including PubMed, Cochrane Library, Embase, and Web of Science, employing a combination of text and MeSH headings in the search strategy (refer to Supplementary eMethods S2 and eTableS1). For this study, primary outcomes of interest were MACE, Cardiac death, and All-cause death, with secondary endpoints including Myocardial Infarction (MI), TVR, TLR, and stent thrombosis. All details regarding the search strategy, data extraction, and study selection are presented in the Supplementary (eMethods S3–S5).

2.4 Statistical analysis

The outcomes of interest were dichotomous variables, and rates of events with the total sample size were extracted for analysis. The



Mantel-Haenszel method's random-effects model was employed to calculate Odds Ratio (OR) and their 95% Confidence Intervals (CI). For inter-study variance, Restricted Maximum Likelihood (REML) was used. An OR estimate and its corresponding 95% CI not including the vertical line at 1 (*p*-value < 0.05) was considered statistically significant. The extent of heterogeneity was approximated using the I^2 test, with 0%–40% indicating negligible, 30%–60% moderate, 50%–90% substantial, and 75%–100% considerable heterogeneity. Given the limited number of studies included, a funnel plot for pre-specified publication bias analysis was deemed inappropriate.

2.5 Cardiovascular clinical research and patients involvement

Following the completion of our initial manuscript, we consulted a patient with cardiovascular disease and a frontline cardiovascular clinical scholar, both of whom suggested acceptance or implementation of PCI for coronary artery disease. The feedback received indicated that the certainty of the evidence

presented in our study was highly useful for evaluating the efficacy of OCT-guided vs. angiography-guided PCI in the treatment of acute coronary syndrome (ACS).

3 Results

3.1 Bibliometric results

3.1.1 Annual growth trends in publications

From 2003 to 2023, a total of 2,758 papers were retrieved from the WoSCC database. After eliminating duplicates and other types of literature, 310 articles were ultimately included for analysis, comprising 246 articles and 64 reviews. Figure 2A displays the annual statistics of publications in this field, revealing a trend in three distinct phases: (1) From 2004 to 2012, the annual publication count did not exceed 10 papers; (2) From 2013 to 2019, the number of annual publications remained relatively stable; (3) A notable increase in publication volume was observed from 2020 to 2023, with a significant spike exceeding 40 papers in 2022. By fitting the data to construct a publication trend,



results indicate a high correlation between the annual number of publications and the years ($y = 0.0541 \text{ x} \wedge 2 + 0.8396 \text{ x} - 1.0807$, R $^2 = 0.8841$) (Figure 2B). The publication trend suggests that by 2024, over 400 articles on this topic are projected to be published, signifying an increasing scholarly focus on this field over time.

In this field, the top 10 countries accounted for over 80% of the total publication output compared to all other countries combined. Statistically, the five countries and regions with the most published

articles were China (77 articles), the United States (68 articles), Germany, Japan, and Italy (Table 1). In terms of the growth rate in the number of publications (Figure 3A), the United States consistently maintained a high output, slightly outperforming China, while Germany, Italy, and Japan showed relatively stable production levels. Moreover, among the top 20 countries for corresponding authors, those with the highest proportions of multiple countries publication (MCP) relative to their total publication output were Canada, the United States, Italy, the United Kingdom, and China. Although the U.S. had the most MCPs (23 articles), it did not rank first in MCP ratio. While China had the highest total number of articles, it had fewer publications in collaboration with other countries (22 articles), thus a lower MCP Ratio (Table 1). Among the limited international collaborations from China, those with the United States were the most frequent (Figure 3B).

These articles were authored by 659 institutions, among which 21 institutions published at least 5 articles each. The top 10 institutions alone authored 176 articles, accounting for 56.8% of the total (Figure 3C). The institutions with the highest number of publications included Harvard University, Harvard Medical School, Harbin Medical University, Icahn School of Medicine, Massachusetts General Hospital, National University of

TABLE 1 Corresponding author's countries.

Rank	Country	Articles	SCP	MCP	MCP Ratio
1	China	77	55	22	0.286
2	Usa	68	45	23	0.338
3	Germany	20	15	5	0.25
4	Japan	20	20	0	0
5	Italy	18	12	6	0.333
6	Canada	12	6	6	0.5
7	United Kingdom	10	7	3	0.3
8	Spain	9	7	2	0.222
9	France	8	6	2	0.25
10	Korea	7	4	3	0.429

MCP, multiple countries publication; SCP, single countries publication.

Singapore, University College London, Case Western Reserve University, and Columbia University, all with over 10 articles each. Chinese institutions such as Harbin Medical University, Tongji University, and Capital Medical University each produced more than 8 articles. As depicted in Figure 3D, institutional collaboration was more extensive than inter-country cooperation, with Harvard University and Harbin Medical University engaging in significant collaborations with numerous universities and research centers in China, as well as institutions in the UK, the US, and other countries.

3.1.2 Author analysis

Figure 4A, created using VOSviewer software, visualizes the author collaboration network in OCT research within the cardiovascular field. The minimum criterion for an author's inclusion was set at 10 publications, encompassing nearly 2000 contributing authors. Among the top 10 most productive authors, Professor Mehran Roxana possessed the highest m-INDEX; Professor Yu Bo boasted the greatest G-index; and Professor Virmani Renu held the highest h-index and total citations (TC) (Figures 4A-B).

Figure 4C presents the network map of co-cited authors, where higher weightage of a co-cited author corresponds to larger labels and circles in the visualization. In the field of OCT research, prominent figures like Professor Yu Bo from China, and Professor Maehara Akiko and Professor Virmani Renu from the United States, hold significant influence and citation weight.



Analysis of countries/regions engaged in OCT research. (A) Top 5 countries with the largest number of publications over time; (B) country cooperation network; (C) top 18 institutions by number of publications; (D) institutional collaboration-network.



Among the authors with the highest publication volumes, Professor Yu Bo is the only one from China, while the others are predominantly from the United States. Many of these authors have collaborated on publications in journals such as the "New England Journal of Medicine" and "JACC Cardiovascular Imaging" (29, 30). This indicates close collaboration among authors within this field.

3.1.3 Analysis of journals

According to our analysis, 179 journals published papers related to OCT and cardiovascular diseases. The top 5 most productive journals — "International Journal of Cardiology", "Frontiers in Cardiovascular Medicine", "Catheterization and Cardiovascular Interventions", "Revista Espanola de Cardiologia", and "Scientific Reports" — showed notable publication numbers and growth trends, as depicted in Figure 5A. Figure 5B illustrates the journal's thematic distribution through a dual-map overlay, with citing journals positioned on the left and cited journals on the right of the map. The labels represent journals covering specific themes, and colored lines trace the reference pathways. Two distinct citation pathways are evident. Two green citation paths indicate that studies from medical/clinical/surgical journals are often cited by those in molecular physiology/medical/clinical journals.

3.1.4 Citation analysis

The results of the citation analysis are presented in Figure 6 and Table 2. Among the top 10 most cited articles, 6 are clinical

trial studies, with one published in "The Lancet" (37), three in "Circulation" (31, 35, 36), and other high-impact journals. Three reviews discussed the application of OCT technology in detecting atherosclerosis in clinical practice. The 2005 randomized controlled trial by Professor Ik-Kyung Jang, "*in vivo* Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography," ranks first with 694 citations.

3.1.5 Co-occurrence analysis

In the study of the structure of scientific knowledge, keyword co-occurrence analysis is an effective bibliometric method to grasp current hotspots. We analyzed the co-occurrence of keywords in the field and the top 50 keywords (Figure 7A), centering around OCT. Figure 7B employs a log-likelihood ratio analysis to generate eight clusters, including: coronary artery disease, deep learning, coronary stenosis, heart transplantation, rupture, OCT, congenital heart disease, plaque and cardiovascular diseases. Burst analysis of keywords was also conducted, revealing overall trends in OCT research in the cardiovascular field, encompassing topics like bare metal stents, acute myocardial infarction, intravascular ultrasound, aortic valve implantation, artery disease, elevation myocardial infarction, coronary disease, and coronary artery disease (Figure 7C).

3.1.6 Changes in trends of research in the recent years

The thematic word analysis method was employed to explore the core issues in OCT research within the cardiovascular field.



Figure 8A indicates that well-developed themes focus on atherosclerotic diseases, blood pressure, stent implantation, and plaque characteristics. The impact of surgery, post-operative care, and survival on disease treatment and prognosis are also noteworthy. Emerging research in areas such as molecular biology and cell biology is also beginning to emerge. Researchers are focusing on the roles and potential molecular mechanisms of "inflammation, oxidative stress, mitochondria, cytokines, and metabolism" in disease development.

Moreover, using multidimensional scaling, we categorized the most frequently occurring keywords and generated a conceptual structure map, resulting in three clusters (Figure 8B). Current research continues to focus on clinical manifestations, diagnosis, interventions, and prognosis of diseases like "coronary stenosis, acute myocardial infarction, atherosclerosis" (red cluster), as well as exploring pathogenic mechanisms and intervention methods related to diseases, such as "interventional methods, post-stent thrombosis formation, and potential impacts of PCI" (blue-green cluster).

Additionally, we visualized the temporal trends of keywords (Figure 8C). In the past five years, new trends in the field include coherence tomographic vascular scanning technology, coronary heart disease, microvascular lesions, vascular pressure, retinal arteriolar abnormalities, atherosclerotic risk, as well as the etiology, pathomechanisms, and clinical outcomes of cardiovascular diseases, all of which are worthy areas for continued exploration. The thematic word analysis method was employed to explore the



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Frontiers in Cardiovascular Medicine

IF (2022)	37.8	24.0	39.3	24.0	37.8	37.8	168.9	3.8	3.5	4.8
Type	RCT	RCT	Review	Review	RCT	RCT	RCT	Review	RCT	RCT
Year	2005	2013	2015	2015	2010	2010	2016	2006	2008	2008
Citations (2023)	694	358	313	301	293	265	259	216	190	179
Journal	Circulation	Journal of the American College of Cardiology	Eur Heart J	J Am Coll Cardiol	Circulation	Circulation	Lancet	Ann Biomed Eng	J Biomed Opt	Am J Physiol- Heart C
Key points	This is the first study to compare detailed <i>in vivo</i> plaque morphology in patients with different clinical presentations.	It defines the histomorphological characteristics of vulnerable plaques, helping to identify such plaques in patients at high risk of acute coronary events.	It explaines the introduction of OCT has facilitated the detection of new atherosclerosis in clinical practice OCT.	It supports the multifaceted hypothesis of the natural course of atherosclerotic plaque rupture is summarized.	It is This first-in-humans trial provides a seminal observation on a small number of patients with a short duration of follow-up. One of the clinical studies looked at the Second Generation of a Bioresorbable Evenolimus Drug-Eluting Vascular Scaffold for Treatment of De with OCT Novo Coronary Artery Stenosis.	It reports OCT findings with corresponding histology in the porcine coronary artery model immediately after and at 28 days and 2, 3, and 4 years after BVS implantation.	It evaluates the safety and performance of a new second-generation drug-eluting absorbable metal stent (DREAMS 2G) in patients with coronary neoplasia.	It evaluates optical coherence tomography can be used to evaluate tissue remodeling for cardiac valve tissue engineering applications.	It addresses the fundamental issues that underlie the tissue characterization of OCT images obtained from coronary arteries. It not only explains the origins of many qualitative OCT features, but also shows that combination of backscattering and attenuation coefficient measurements can be used for contrast enhancing and better tissue characterization.	It demonstrats that plaque instability should not be considered as a result of fiber cap thickness alone, but rather as a combination of plaque thickness, necrotic core thickness, and arterial remodeling index.
Title	<i>in vivo</i> Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography	Histopathologic Characteristics of Atherosclerotic Coronary Disease and Implications of the Findings for the Invasive and Noninvasive Detection of Vulnerable Plaques	Neoatherosclerosis: overview of histopathologic findings and implications for intravascular imaging assessment	The Myth of the "Vulnerable Plaque": Transitioning From a Focus on Individual Lesions to Atherosclerotic Disease Burden for Coronary Artery Disease Risk Assessment	Evaluation of the Second Generation of a Bioresorbable Everolimus Drug-Eluting Vascular Scaffold for Treatment of <i>de novo</i> Coronary Artery Stenosis	Intracoronary Optical Coherence Tomography and Histology at 1 Month and 2, 3, and 4 Years After Implantation of Everolimus- Eluting Bioresorbable Vascular Scaffolds in a Porcine Coronary Artery Model	Safety and performance of the second-generation drug-eluting absorbable metal scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multicentre, non-randomised, first-in-man trial	Heart Valve Tissue Engineering: Concepts, Approaches, Progress, and Challenges	Characterization of atherosclerosis plaques by measuring both backscattering and attenuation coefficients in optical coherence tomography	Necrotic core thickness and positive arterial remodeling index: emergent biomechanical factors for evaluating the risk of plaque rupture
Representative author	Ik-Kyung Jang (31)	Jagat Narula (32)	Fumiyuki Otsuka (33)	Armin Arbab-Zadeh (34)	Patrick W Serruys (35)	Yoshinobu Onuma (36)	Michael Haude (37)	Karen Mendelson (38)	Chenyang Xu (39)	Jacques Ohayon (40)
Rank	1	7	e,	4	ъ	Q	~	×	6	10

A this cg (approximate)	С				
vulnerätte plaque	Keywords	Year	Strength	Begin End	2004 - 2023
atherosolegies plaques plaques intravoscultar ult	assund bare metal stents	2009	4.52	2009 2014	
informer Install	acute myocardial infarction	2009	3.42	2009 2015	
myocard endercon ether coloradis concernity strep deuse coronaly strep deuse	intravascular ultrasound	2008	4.55	2011 2014	
cardiovarder disease en optical coherence tomography	perconanceus coronary intervents aortic valve implantation	2011	3.84	2011 2015	
risk-tensor coronary her tillsasse onary her tillsasse privence axxe myscegial-infarction	news newsion mysercial intercos artery disease	2011	3.48	2011 2018	
autopiereder dezasts ouem	drug of the gateries bare may starts elevation myocardial infarction	2012	3.2	2012 2017	
blog flow	coronary disease	2005	4.2	2014 2017	
n • • • • • • • • • • • • • • • • • • •	coronary artery disease	2009	3.76	2016 2018	
#3 heart transplantation	oct	2017	4.17	2017 2020	
Procession of the second secon	vulnerable plaque	2012	3.75	2019 2021	
	thin cap fibroatheroma	2012	3.53	2020 2021	
#6 optical col	coronary heart disease	2007	6.32	2021 2023	
#5 cöngenital heart disease	optical coherence tomography angi	iography 2021	3.74	2021 2023	
#7 cardiovascular di	eases				

FIGURE 7

Visualized analysis of keywords and literature related to OCT and cardiovascular diseases. (A) Co-occurrence network of terms in 310 publications; nodes represent keywords (top 50), and lines denote co-occurrence relationships; (B) keyword clustering analysis; (C) the burst strength and duration of the top 13 keywords with the strongest citation bursts.



FIGURE 8

Analysis of research directions. (A) Thematic analysis related to cardiovascular diseases and OCT. The horizontal and vertical axes represent centrality and density, respectively. The first quadrant represents mature themes, the second quadrant is less significant to the current field, the third quadrant possibly represents emerging or fading themes, and the fourth quadrant is fundamental but less significant themes; (B) conceptual structure map of Keyword Plus; (C) timeline of research dynamics in the field of OCT and cardiovascular diseases.

3.2 Meta results

3.2.1 Description of included trials

Of 4,350 citations, we reviewed 1,385 after removal of duplicates. We excluded an additional 1,367 studies on the basis of the title and abstract level screening and *a priori* selection criteria (Figure 9). Finally, we included 11 RCTs (n = 5,277) (29, 41–50), and 7 observational studies (n = 4,514) (51–58).

During the quality assessment process, a thorough evaluation of the methodological rigor of each study played a crucial role in enhancing the credibility of the results. Our bias risk assessment revealed that 36% (4 out of 11) of the trials raised some concerns regarding the randomization process, and 43% (3 out of 7) of the observational studies exhibited lower evidence quality regarding outcomes (refer to Supplementary eFigure S1 and eTable S2).

3.2.2 Patient-level baseline characteristics and procedural data

The 11 articles included in this study collectively encompassed 5,277 patients with coronary artery lesions. Table 3 summarizes the baseline characteristics. The median age ranged from 54.5 to 69 years, with 77.2% being male. Cardiovascular risk factor analysis

indicated that 31.5% of the patients had diabetes, 63.1% had dyslipidemia, and 69.0% had hypertension, with 31.7% being current or former smokers. STEMI was the predominant type of ACS, followed by NSTEMI and unstable angina. All patients underwent invasive treatment. A total of 2,653 patients received OCT-guided therapy, and 2,640 patients underwent angiography-guided PCI. Stent implantation was the primary strategy for vascular revascularization. The follow-up period ranged from 3 to 25 months. The characteristics of the observational studies are available in Supplementary eTable S3.

3.2.3 MACE

Six trials (n = 2,109) reported MACE (41, 43, 44, 46–48). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in MACE (OR 0.84, 95% CI 0.65 to 1.10; p = 0.515, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10A). However, the observational studies, comprising 5 studies with 3,674 patients, painted a different picture (51, 52, 54–56). In contrast to coronary angiography, OCT-guided PCI showed a reduction in the risk of MACE (OR 0.66, 95% CI 0.48–0.91; p = 0.243, $I^2 = 26.7\%$, non-relevant heterogeneity, moderate certainty, see Figure 11A).



Study ch	aracteristics					Baseline ch	aracteristi	ics of patie	ents included (OCT group	o/Angiogra	phy group)	Type c managem Angio	of patients nent (OCT graphy gr	and group/ oup)
Author Year	Location	Time Period Under Observation	Study type	Comparator treatment	Follow- up period (median)	Patients (Included in the analysis)	Age, median	Male patients	Hypertension	Diabetes	Smoking [Jyslipidemia	Unstable Angina	NSTEMI	STEMI
Ali 2023 (29)	Multinational	2018-2020	RCT (NCT03507777)	Angiography	12 months	1233/1254	65.5 (10.5)/ 65.7 (10.3)	968 (78.5)/ 956 (76.2)	880 (71.4)/ 928 (74.0)	523 (42.4)/ 521 (41.5)	242 (19.6)/ 247 (19.7)	808 (65.5)/ 860 (68.6)	355 (28.8)/ 331 (26.4)	304 (24.7)/ 299 (23.8)	68 (5.5)/ 73 (5.8)
Holm 2023 (44)	Multinational	2017-2022	RCT (NCT03171311)	Angiography	2 years	600/601	66.4 (10.5)/ 66.2 (9.9)	473 (78.8)/ 475 (79)	422 (70.3)/ 448 (74.5)	103 (17.2)/ 97 (16.1)	305 (50.8)/ 290 (48.3)	456 (76.0)/ 471 (78.4)	53 (8.8)/ 58 (9.7)	79 (13.2)/ 78 (13.0)	138 (23.0)/ 144 (24.0)
Jia 2022 (41)	China	2017-2019	RCT (NCT03571269)	Angiography	369 days	112/114	54.5 (11.2)/ 56.4 (10.4)	89 (79.5)/ 91 (79.8)	47 (42)/45 (39.5)	29 (25.9)/ 19 (16.7)	64 (57.1)/ 73 (64.0)	I	0/0	0/0	112 (100)/ 114 (100)
Ali 2021 (47)	Multinational	I	RCT (NCT02471586)	Angiography	6 months	153/142	66 (59–72) /67 (56–75)	106 (69)/ 104 (73)	120 (78)/104 (73)	51 (33)/ 40 (28)	26 (17)/ 40 (28)	112 (73)/ 110 (77)	I	I	50 (33)/ 51 (36)
Onuma 2020 (45)	Japan 9	2017-2018	RCT (NCT 0297248)	Angiography	6 months	55/50	68.9 (10.2)/ 69 (11.6)	44 (79)/ 40 (74)	43 (76.8)/ 40 (74.1)	29 (51.8)/ 25 (46.3)	13 (23.2)/ 10 (18.5)	48 (85.7)/ 46 (85.2)	4 (7.1)/ 2 (3.7)	1 (1.8)/ 1 (1.9)	I
Ueki 2020 (50)	Multinational	2016-2017	RCT (NCT02683356)	Angiography	6 months	19/19	63.3 (12.7)/ 62.9 (9.1)	15 (78)/ 15 (78)	7 (37)/11 (58)	4 (21)/ 4 (21)	7 (37)/ 6 (32)	13 (68)/ 12 (63)	4 (40)/ 1 (20)	4 (40)/2 (40)	2 (20)/ 2 (40)
Kala 2017 (46)	Czech Republic	2011-2012	RCT (NCT00888758)	Angiography	4.5months	105/96	57/59	87 (83)/ 83 (87)	53 (50)/50 (52)	18 (17)/ 25 (26)	67 (64)/ 57 (59)	1	1	1	105 (100)/ 96 (100)
Ali 2016 (49)	Multinational	2015-2016	RCT (NCT02471586)	Angiography	6 months	158/146	66 (59–72)/ 67 (56–75	109 (68)/ 107 (73)	124 (78)/109 (75)	52 (33)/42 (29)	28 (18)/ 35 (24)	115 (73)/ 112 (77)	25 (16)/ 27 (18)	20 (13)/ 24 (16)	6 (4)/4 (3)
Meneveau 2016 (42)	France	2013-2015	RCT (NCT01743274)	Angiography	6 months	120/120	60.8 (11.5)/ 60.2 (11.3)	95 (79.2)/ 91 (75.8)	67 (55.8)/ 50 (41.7)	26 (21.7)/ 19 (15.8)	47 (39.2)/ 51 (42.5)	59 (49.2)/ 56 (46.7)	10 (8.3)/ 9 (7.5)	110 (91.7)/ 111 (92.5)	I
Kim 2015 (48)	Korea	2011-2012	RCT (NCT01869842)	Angiography	6 months	58/59	58.8 (10.8)/ 61.6 (9.7)	39 (78)/ 37 (72)	27 (54.0)/25 (49.0)	16 (32.0)/ 16 (31.4)	16 (32.0)/ 15 (29.4)	33 (66)/ 37 (72.5)	I	I	I
Antonsen 2015 (43)	Denmark	2011-2013	RCT (NCT02272283)	Angiography	6 months	40/45	61.8 (9.4)/ 62.6 (11.0)	36 (72)/ 34 (68)	28 (56)/28 (56)	8 (16)/5 (10)	23 (46)/ 18 (36)	I	0/0	50 (100)/ 50 (100)	0/0
NSTEMI, non	-ST-elevation r	myocardial Infarc	tion; OCT, optical	coherence tomoç	graphy; RCT, r	randomized cor	ntrolled trial;	STEMI, ST-el	levation myocardia	l infarction.					

TABLE 3 Baseline demographics of trials and populations included in meta-analysis.

MACE Multinational 15/153 11/142 285 Marce Comman 040 2.44 85 Marce Seleco 2.36 0.374 0.34 0.01 7.38 Marce Comman 1011 11.14 2.26 0.34 0.01 7.38 Marce Comman 1011 11.14 2.26 0.97 0.84 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.24 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.23 0.98 0.98 0.23 0.98 0.98 0.24 0.23 0.23 0.21 0.24 0.24 0.23 0.23 0.23 0.21 0.24 0.24 0.23 0.21 0.22	Study	Location	OCT	Angiography	Subjectnumber	Odds Ratio (95% CI)	% Weigh
Mid 2021 Multinational 15/153 11/142 265 Mid 2023 Europe 50/00 83/501 1201 Mid 2023 Europe 50/00 83/501 1201 Mid 2023 Europe 50/00 83/501 1201 Mid 2021 Korea 2/65 3/55 101 Mid 2023 Multinational 6/1233 15/124 2/47 Mid 2023 Multinational 6/1233 15/124 2/47 Mid 2023 Multinational 6/1233 15/511 101 Mid 2023 China 3/112 4/11/4 2/85 Multinational 10/50 1050 105 0.58 (0.28, 1.10) 4/3.22 Multinational 3/123 4/1254 2/47 0.58 (0.28, 1.10) 4/3.22 Multinational 1/150 0.160 105 0.57 (0.48, 1.17) 0.56 (0.48, 1.10) Multinational 1/120 0.160 1020 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1.10) 0.58 (0.28, 1	A. MACE					1	
Artonsen 2015 Denmark 0.40 2.44 85 Monosano 2015 Europe 56000 30201 0.74 (46,41,10) 73.86 Ma 2022 China 31112 11114 220 0.83 (26,21,30) 0.74 (46,41,10) 73.86 Kin 2015 Korea 2.88 3159 101 0.84 (0.85, 1.10) 0.84 (0.85, 1.10) 1000 Scadiac death Ali 2023 Mutinational 61123 101124 2467 0.38 (0.02, 0.13) 3.82 Ali 2023 Mutinational 61123 10114 226 0.54 (0.82, 1.17) 0.58 (0.24, 1.17)	Ali 2021	Multinational	15/153	11/142	295	1.24 (0.59, 2.62)	10.44
Hom 2023 Europe 59:000 23:001 1011 13:2022 China 31112 11114 228 Subtoal (I-squared = 0.0%, p = 0.515) 3:59 101 0.58 (0.28, 1.10) 288 Subtoal (I-squared = 0.0%, p = 0.515) 0.123 101/254 2487 0.58 (0.28, 1.10) 1000 S. Cardiac cleath Al 2023 Multinational 1155 0.50 105 0.58 (0.28, 1.10) 0.28 (0.28, 1.27) 40.72 Ja 2022 China 3112 4114 226 0.58 (0.28, 1.10) 0.28 (0.28, 1.10) 100.00 Ja 2023 Multinational 31123 411264 2487 0.56 (0.28, 1.17) 65.00 C.All-cause death All 2023 Multinational 0.142 2467 0.75 (0.48, 1.17) 0.56 (0.28, 1.13) 34.16 Subtotal (I-squared = 0.0%, p = 0.50) 1120 1120 0.28 (0.21, 1.24, 1.44 2467 0.75 (0.48, 1.17) 0.56 (0.21, 1.27, 3.23) 0.77 (0.48, 1.17) 0.56 (0.22, 1.27) 0.00 D.Matriational 571/233 721/254 2	Antonsen 2015	Denmark	0/40	2/45	85	0.23 (0.01, 4.74)	2.09
jus 2022 Dinin 19112 11/14 228 Kaiz 2017 Europe 3105 109 201 Kin 2015 Korea 2/89 3/59 101 28 0,80 (0.82, 28, 47) 0,86 Kin 2015 Korea 2/89 3/59 101 0 0,80 (0.82, 28, 47) 0,86 Kin 2015 Denmark 0/40 1/45 85 0,80 (0.28, 130) 43.202 Admonsen 2015 Denmark 0/40 1/45 85 0,86 (0.28, 130) 43.202 Onum 2020 Japan 1/55 0.50 105 0.57 (0.48, 117) 65.00 Subtoall (i-squared = 0.0%, p = 0.50) 11/20 240 44/1254 2487 0.81 (0.28, 1.13) 100 Al 2021 Multinatonal 17/123 21/12 205 0.50	Holm 2023	Furone	50/800	83/601	1201	♠ 0.74 (0.54, 1.01)	73.88
Subscr Dime D102 100 200 Subscr Europe 200 3105 101 Subscr Europe 200 3105 101 Subscr Multinational 01123 1011254 2487 Anonsen 2015 Dammark 040 1145 85 Subscr Damark 040 1145 85 Subscr Damark 040 1145 85 Subscr Damark 040 1144 228 Domma 2020 Damark 040 1144 228 Subscr Japan 1120 1144 228 Subscr Trans 1120 1120 246 All 2023 Multinational 01150 01142 2467 All 2023 Multinational 571233 721254 2467 All 2021 Multinational 571233 721254 2467 All 2021 Multinational 571233 721254 2467	lia 2022	China	12/112	11/114	228	1 12 (0.55, 2.54)	0.07
Call 2017 Europe 2109 1100 201 Control (-squared = 0.0%, p = 0.515) Control (-squared = 0.0%, p = 0.517) Control (-squared	Jia 2022	Crimia	2/105	100	220	1.16 (0.00, 25.47)	0.00
Km 2015 Korea 2258 359 101 009 (012, 348) 22.88 Sectoral (I-dyaured = 0.0%, p = 0.510) 040 11/2 2477 Skotoral (I-dyaured = 0.0%, p = 0.501) 040 11/2 2477 Skotoral (I-dyaured = 0.0%, p = 0.500) 1560 1201 0.56 (026, 1.30) 43.22 C. All-cause death 3112 4114 226 0.56 (028, 1.30) 0.56 (028, 1.30) C. All-cause death 3112 41124 2467 0.56 (028, 1.30) 0.56 (028, 1.30) C. All-cause death 3112 411264 2467 0.56 (028, 1.30) 0.56 (028, 1.30) C. All-cause death 1120 0.150 105 0.75 (0.48, 1.17) 0.50 (0.30, 1.02) C. All-cause death 1120 0.142 2467 0.67 (0.48, 1.17) 0.50 (0.28, 1.30) Subtotal (I-dyaured = 0.0%, p = 0.550) 0.1142 245 2467 0.81 (0.58, 1.14) 0.61 (0.28, 1.83) 0.010 (0.00, 1.83) Subtotal (I-dyaured = 0.0%, p = 0.550) 0.1120 1.20 (2.3, 5.41) 0.41 (2.20 (2.3, 5.41) 0.41 (2.20 (2.3, 5.41) 0.41 (2.20 (2.3, 5.41) 0.41 (2.20 (2.3, 5.45)) 0.41 (2.20 (2.3, 5.45)) <td>Kala 2017</td> <td>Europe</td> <td>3/105</td> <td>1/90</td> <td>201</td> <td>2.09 (0.28, 25.47)</td> <td>0.96</td>	Kala 2017	Europe	3/105	1/90	201	2.09 (0.28, 25.47)	0.96
Subtoal (I-squared = 0.0%, p = 0.515) 0.84 (0.65, 1.10) 100.01 S. Cardiac death 41 2023 Multinational 6/1233 16/1254 2487 Amonsen 2015 Demmark 0.40 1/45 85 Onuma 2020 China 3/112 4/114 228 Dumma 2020 Japan 1055 105 105 Subtoal (I-squared = 0.0%, p = 0.893) 1050 105 0.58 (0.28, 1.30) 43.23 All 2023 Multinational 2/123 44/1254 2487 0.58 (0.28, 1.13) 44.124 All 2023 Multinational 0/150 105 0.50 0.50 0.58 (0.28, 1.13) 34.16 All 2023 Multinational 0/153 0/142 245 44.7 48.00.17, 22.3 72/1254 2487 41 2021 Multinational 5/1/233 72/1254 2487 43.80(0.17, 12.30) 100.00 0.70 (0.48, 1.17) 65.00 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162) 0.70 (0.48, 1.162)	Kim 2015	Korea	2/58	3/59	101	0.69 (0.12, 3.98)	2.68
B. Cardiac death Multinational 6/1233 16/1254 2467 Minorsin 2013 Europe 8/000 15/501 1201 Mill 2023 China 3112 4/1414 286 Dinuma 2020 Japan 15/50 105 105 Dinuma 2020 Japan 15/50 105 105 Dinuma 2020 Japan 15/50 105 105 C. Ali-cause death 32/1233 4/1254 2467 Mi 2023 Multinational 32/1233 4/1254 2467 On 70 (0.44, 1.17) 05.60 (020, 1.13) 0.58 (020, 1.13) 0.58 (020, 1.13) Mi 2021 Multinational 5/1/233 72/1254 2467 Mi 2023 Multinational 5/1/233 72/1254 2467 Mi 2021 Multinational 5/1/233 72/1254 2467 Mi 2023 Multinational 5/1/233 5/1/233 10/12 2467 Mi 2023 Multinational 1/158 1/140 286 0.88 (0.69, 1.13) 0.79 Mi 2023 Multinational 1/158 1/	Subtotal (I-squared	= 0.0%, p = 0.515)				0.84 (0.65, 1.10)	100.00
34 2023 Multinational 19/233 19/1224 2487 Amonsen 2015 Demmark 040 1145 85 Admonsen 2015 Demmark 040 15901 1201 Jai 2022 Ohina 3112 4114 226 Dnuma 2020 Japan 1155 0150 051 </td <td>3. Cardiac death</td> <td></td> <td></td> <td></td> <td></td> <td>1</td> <td></td>	3. Cardiac death					1	
Anonsen 2015 Demmark 2000 1/45 85 John 2023 Europe 8800 5800 1201 Ja 2022 China 3112 4114 228 Johna 2020 Japan 11/5 0150 105 Johna 2020 Japan 11/5 0150 105 Johna 2020 Japan 11/5 0150 105 Johna 2020 Japan 11/5 0150 050 C. All-cause death Multinational 22133 44/1254 2467 Mi 2021 Multinational 11/150 01142 246 Mi 2021 Multinational 4/153 21/122 246 Mi 2021 Multinational 4/153 21/122 246 Mi 2021 Multinational 4/153 21/122 2467 Mi 2021 Multinational 2/158 01/120 240 Mi 2021 Multinational 2/158 01/120 2467 Mi 2021 Multinational 2/158 01/120 2467 Mi 2021 Multinational 2/158 01/120 2467 Mi 2021 Multinational 2/158<	Ali 2023	Multinational	9/1233	16/1254	2487	0.58 (0.26, 1.30)	43.23
Nome Bits 201 Europe Bits 001 15801 1201 Numa 2020 Allan 3112 41114 228 0.01 0.54 0.23, 127 40.72 Subtoball (I-squared = 0.0%, p = 0.823) 015 015 015 015 016 017 0.54 0.23, 127 40.72 0.84 0.76 0.44, 31 1.44 0.44 0.81 0.84 0.81 0.84 0.81 0.84 0.81 0.85 0.28 0.17 0.06 0.76 0.44 0.44 0.81 0.85 0.28 0.17 0.65 0.76 0.44 0.41 0.85 0.76 0.44 0.41 0.44 0.81 0.85 0.14 0.28 0.28 0.00 0.70 0.44 0.42 0.45 0.42 0.42 0.41 0.42 0.42 0.42 0.42 0.42 0.42 0.41 0.42 0.42 0.44 0.42 0.42 0.44 0.42 0.44 0.42 0.44 0.42	Antonsen 2015	Denmark	0/40	1/45	85	0.38 (0.02 9.13)	3.82
Diminizous Europe Biolog Iotori Izai Jagan 115 0150 105 007 018, 308 017 018, 308 007 018, 308 007 018, 308 007 018, 308 007 018, 308 007 018, 308 007 018, 308 007 018, 308 007 018, 308 007 008, 308 007 008, 308 007 008, 308 008	Halm 2022	Europa	2/800	151801	1201	0.54 (0.22, 1.27)	40.72
Jag 2022 Johna 3112 4114 220 0.5 0.5 0.5 Johna 2020 Jagan 165 0.50 105 0.5 0.2 0.6 0.5<	Hoim 2023	China	2/112	101001	000	0.34 (0.23, 1.27)	40.72
Druma 2020 Japan 11/5 0/50 105 288 (0.11, 94.43) 1.44 2. All-cause death 0.81 (0.38, 1.02) 1000 2. All-cause death 0.75 (0.48, 1.17) 65.00 41 2023 Multinational 32/1233 44/1264 2467 41 2023 Multinational 0153 0.142 295 2. Multinational 0.153 0.1120 240 1.32 (0.22.1 A) Multinational 0.153 0.1120 1.41 2021 Multinational 0.1120 1.240 2. Multinational 0.1120 1.240 0.88 (0.69, 1.13) 2. Multinational 0.1120 1.240 0.88 (0.69	Jia 2022	Unina	3/112	4/114	220	0.77 (0.18, 3.30)	10.79
Subtoal (I-squared = 0.0%, p = 0.893) 0.81 (0.38, 1.02) 100.00 2.All-cause death 412023 Mutimational 812021 32/1233 44/1254 2487 10010 238 Crope 13800 238011 1201 12023 Europe 13800 238011 1201 0.58 (0.28, 1.13) 34.16 12021 Mutimational 01153 0142 295 0.81 (0.58, 1.14) 66.17 12021 Mutimational 1173 3142 295 0.81 (0.58, 1.14) 0.41 0.81 (0.58, 1.14) 0.41 0.91 0.91 (0.58, 1.14) 0.00 0.070 (0.48, 1.02) 100.00 1.0201 Mutimational 1173 3142 295 0.81 (0.58, 1.14) 0.41 0.91 (0.58, 1.14) 0.41 0.91 (0.58, 1.14) 0.41 0.91 (0.58, 1.14) 0.91 (0.58, 1.12) 0.91 (0.58, 1.13) 0.010 132022 China 0.1120 1.120 240 0.81 (0.58, 1.13) 100.00 0.88 (0.69, 1.13) 100.00 13a 2022 China 51112 1114 286 0.83 (0.35, 4.58) 4.60 1.80 (0.16, 4.65) 1.20 (0.56, 98) <td< td=""><td>Onuma 2020</td><td>Japan</td><td>1/55</td><td>0/50</td><td>105</td><td>2.68 (0.11, 64.43)</td><td>1.44</td></td<>	Onuma 2020	Japan	1/55	0/50	105	2.68 (0.11, 64.43)	1.44
2. All-cause death Ni 2023 Multinational 52/1233 44/1254 2467 Ni 2023 Europe 13/800 23/801 1201 Macreau 2016 France 11/120 01/120 240 Millonational 01/53 01/142 295 0.75 (0.48, 1.17) 0.56 (0.28, 1.13) Subtotal (I-squared = 0.0%, p = 0.550) 01/142 295 0.71 (0.49, 1.02) 100.00 2. Mycoardial infarction 4/153 21/123 72/1237 72/1234 2487 Ni 2023 Multinational 57/1233 72/1234 2487 1.23 (0.28, 541) 2.417 Ni 2023 Multinational 4/153 2/142 295 0.81 (0.052, 1.34) 0.044) 0.42 Subtotal (I-squared = 0.0%, p = 0.823) 0.112 0/114 226 0.03 (0.02, 1.34) 0.01 0.00 0.88 (0.69, 1.13) 100.00 Ni 2023 Multinational 2/143 2/142 295 0.33 (0.02, 41.165) 1.26 (0.35, 458) 4.00 Ni 2023 Multinational 1/153 2/142 295 0.03 (0.34, 1.169) 2.40 0.88 (0.69, 1.13) 1.00 <td>Subtotal (I-squared</td> <td>= 0.0%, p = 0.893)</td> <td></td> <td></td> <td>•</td> <td>0.61 (0.36, 1.02)</td> <td>100.00</td>	Subtotal (I-squared	= 0.0%, p = 0.893)			•	0.61 (0.36, 1.02)	100.00
All 2023 Multinational 32/1233 44/1254 2487 Noimerveau 2016 France 13/800 23/801 1201 Multinational 0/153 0/142 295 D.Mpocardial infarction 0/153 0/142 295 D.Mpocardial infarction 60/1233 72/1234 2487 All 2021 Multinational 57/1233 72/1254 2487 All 2021 Multinational 4/153 31/42 295 D.Mpocardial infarction All 2021 Multinational 4/153 31/42 296 All 2021 Multinational 4/153 31/42 296 40/0 0.81 (0.58, 1.14) 65.17 All 2022 China 0/112 0/114 226 0.90 (0.00, 1.53) 0.79 (0.48, 1.92) 0.00 (0.00, 0.58, 1.91) 0.00 (0.00, 0.58, 1.91) 0.00 (0.00, 0.58, 1.91) 0.00 (0.00, 0.58, 1.91) 0.01 (0.00, 0.58, 1.91) 0.01 (0.00, 0.58, 0.91) 0.01 (0.00, 0.58, 0.91) 0.01 (0.00, 0.58, 0.91) 0.01 (0.00, 0.58, 0.91) 0.01 (0.00, 0.58, 0.91) 0.02 (0.00, 0.58, 0.91) 0.02 (0.00, 0.58, 0.91) 0.00 (0.00, 0.58, 0.91) 0.02 (0.00, 0.58, 0.91) 0.02 (0.00, 0.58, 0.9	C. All-cause death				25		
Holm 2023 Europe 13:000 23:001 1201 Meneveau 2016 France 1/120 0/120 240 All 2021 Multinational 0/133 0/142 295 Subtotal (I-squared = 0.0%, p = 0.550) 0/142 295 0.81 (0.58, 1.14) 56.17 D. Myocardial infarction All 2021 Multinational 4/153 3/142 295 All 2021 Multinational 4/153 3/142 295 0.81 (0.58, 1.14) 56.17 All 2021 Multinational 4/153 3/142 295 0.81 (0.06, 15.81) 0.41 Moleneveau 2016 France 1/120 1/120 240 0.81 (0.06, 15.81) 0.79 Jia 2022 China 0/112 0/114 226 0.88 (0.06, 1.13) 1000 E. Target lesion revascularization 41/2023 Multinational 1/158 2/142 295 0.83 (0.34, 1.16) 2.29 Milo 2023 Europe 10/800 2/168 2/159 101 1.02 (0.15, 6.99) 2.29	Ali 2023	Multinational	32/1233	44/1254	2487	• 0.75 (0.48, 1.17)	65.09
All Date	Holm 2023	Europe	13/600	23/601	1201	0.58 (0.29, 1.13)	34 18
Interventation Interventation Interventation Interventation Interventation Subtotal (I-squared = 0.0%, p = 0.550) 0.13 0.142 295 0.00 0.70 (0.49, 1.02) 100.00 D. Myocardial infarction 4112021 Multinational 41153 31142 295 0.81 (0.58, 1.14) 56.17 Ali 2021 Multinational 41153 31142 295 0.81 (0.28, 1.14) 56.17 Ali 2021 Multinational 21158 01140 298 0.81 (0.08, 15.81) 0.41 Maiz 2022 China 01120 11120 201 0.88 (0.09, 1.13) 1000 Subtotal (I-squared = 0.0%, p = 0.823) 511254 2487 487 1.05 (0.72, 1.54) 58.51 Ali 2023 Multinational 1158 21142 295 0.88 (0.89, 1.13) 100.00 Subtotal (I-squared = 0.0%, p = 0.8250) 1.19 1.19 2.19 1.19 2.12 0.88 (0.28, 1.16) 1.23 0.83 (0.34, 1.16) 2.12 1.12 1.12 1.12 1.12 1.12	fanaurau 2018	Earope	1/120	01120	240	2.08 (0.12, 72.22)	0.75
Naturational Virios 0142 265 265 0.00	AL 2021	France	0/150	01120	240	(5.00 (0.12, 12.32)	0.15
Subtal (I-squared = 0.0%, p = 0.50) D. Myocardia infarction Ali 2023 Multinational 4/153 3/142 205 Ali 2016 Multinational 2/158 0/140 208 Ali 2023 Europe 40/600 5/1601 1201 B. Target lesion revascularization Ali 2023 China 0/112 0/112 0/112 226 E. Target lesion revascularization Ali 2023 Multinational 1/158 1/140 208 Holm 2023 Europe 16/600 28/601 1201 Ja 2022 China 0/112 0/114 226 Usbtotal (I-squared = 0.0%, p = 0.820) E. Target vessel revascularization Ali 2023 Multinational 1/158 1/140 208 Holm 2023 Europe 16/600 28/601 1201 Ja 2022 China 5/112 4/114 226 Usbtotal (I-squared = 0.0%, p = 0.856) E. Target vessel revascularization Ali 2023 Multinational 1/158 1/140 208 Holm 2023 Europe 16/600 28/601 1201 Ja 2022 China 5/112 4/114 226 Usbtotal (I-squared = 0.0%, p = 0.856) E. Target vessel revascularization Ali 2023 Multinational 1/158 2/142 295 Ali 2020 Europe 1/10 119 38 Subtotal (I-squared = 0.0%, p = 0.857) G. Stent thrombosis Ali 2016 Multinational 1/158 0/140 298 Ali 2021 Multinational 1/158 0/140 298 Ali 2021 Multinational 1/158 0/142 2467 Ali 2021 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/142 2467 Ali 2017 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2017 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2017 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2017 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2017 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 248 Ali 2016 Multinational 1/158 0/140 24	All 2021	Multinational	0/153	0/142	295	(Excluded)	0.00
D. Myocardial infarction Ni 2023 Multinational 5/11233 72/1254 2487 Ni 2021 Multinational 2/158 0/140 298 Holm 2023 Europe 48000 511801 1201 Meneveau 2016 France 1/120 1/120 240 Dia 2022 China 0/112 0/114 228 Subtotal (I-squared = 0.0%, p = 0.823) E. Target lesion revascularization 411201 41140 298 Ali 2016 Multinational 51/1233 51/1254 2487 0.88 (0.69, 1.13) 1000 (0.06, 15.81) 0.00 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.88 (0.69, 1.13) 1000 (0.18, 8.14) 248 Mi 2021 Multinational 5112 4/114 228 1.08 (0.18, 6.16) 2.29 1.08 (0.18, 6.16) 2.48 1.00 (0.71, 6.49) 2.28 1.00 (0.71, 6.49) 2.28 1.00 (0.71, 6.49) 2.28 1.00 (0.71, 6.49) 2.29 1.48 (0.18, 6.16) 2.46 (0.11, 6.38) 2.49 1.00 (0.71, 6.49) 2.48 1.48 (0.18, 2.159)	Subtotal (I-squared	= 0.0%, p = 0.550)				0.70 (0.49, 1.02)	100.00
Ali 2023 Multinational 57/1233 72/1284 2487 Ali 2021 Multinational 4/153 3/142 295 Ali 2016 Multinational 1/156 0/140 296 Ali 2022 Europe 46/800 51/801 1201 Meneveau 2016 France 1/120 1/120 240 Jia 2022 China 0/112 0/114 226 Subtotal (I-squared = 0.0%, p = 0.823) 0/112 0/114 226 E. Target lesion revascularization 4/153 2/142 295 Ali 2023 Multinational 53/1235 51/1254 2487 Ali 2021 Multinational 1/158 1/140 296 Ali 2021 Multinational 1/158 1/140 296 Ali 2020 Europe 1/18 2/19 101 0.83 (0.34, 1.16) 29.78 Ja 2022 China 5/112 4/114 226 0.83 (0.34, 1.16) 29.78 Ja 2021 Multinational 4/153 6/1/1254 2487 1.00 (0.72, 1.40) 94.20 Ali 2021 <td>D. Myocardial infarct</td> <td>ion</td> <td></td> <td></td> <td></td> <td></td> <td></td>	D. Myocardial infarct	ion					
Ali 2021 Multinational 4/153 3/142 295 Ali 2016 Multinational 2/158 0/140 298 Ali 2016 Multinational 2/158 0/140 298 Marce 10m 2023 Europe 4/1630 1/120 1/120 2/10 Marce 2016 France 1/120 1/120 2/47 4.38 (0.21, 90.44) 0.42 Marce 2016 France 1/120 1/120 2/40 0.111 0.010, 0.08, 15.31) 0.09 E. Target lesion revascularization Ali 2023 Multinational 5/17254 2/487 0.88 (0.89, 11.3) 100.00 Ali 2021 Multinational 1/158 1/140 298 0.88 (0.34, 11.6) 2.49 Jia 2022 China 5/112 4/114 226 0.83 (0.34, 11.6) 2.49 Liki 2020 Europe 1/16 1/19 38 1.00 (0.17, 1.40) 1.83 (0.34, 9.86) 2.98 Veki 2020 Europe 1/19 1/19 38 1.00 (0.07, 14.60) 1.42 Subtati (I-squared = 0.0%, p = 0.857) I.120 1.1120 240<	Ali 2023	Multinational	57/1233	72/1254	2487	0.81 (0.58, 1.14)	58.17
Ali 2016 Multinational 21158 01140 298 Holm 2023 Europe 438 (0.21, 90, 44) 0, 42 Menevau 2016 France 11/120 11/120 240 Jia 2022 China 0/112 0/114 228 Subtotal (I-squared = 0.0%, p = 0.823) (Excluded) 0.00 E. Target lesion revascularization 1.05 (0.72, 1.54) 58.51 Ali 2023 Multinational 53/1233 51/1254 2487 Ali 2023 Multinational 1/158 1/140 298 Jaia 2022 China 51/1224 2495 0.98 (0.06, 14.05) 1.28 Jaia 2022 China 51/12 4/114 228 0.93 (0.34, 1.16) 29.78 Jaia 2022 China 51/12 4/114 228 0.83 (0.34, 1.16) 29.78 Jaia 2022 China 6/112 4/114 228 0.83 (0.34, 1.16) 29.78 Jaia 2021 Multinational 68/1233 67/1254 2487 1.00 (0.72, 1.40) 94.20 Ali 2021 Multinational 4/153 2/142 2	Ali 2021	Multinational	4/153	3/142	295	1 23 (0 28 5 41)	2 47
All 2013 Hutinational 21:00 01:00 20:0 00:00	41 2018	Multinational	2/158	0/140	208	4 38 (0 21 00 44)	0.42
Noim 2023 Europe 40:000 01:001 1201 0.01 (0.02, 1.34) 40.13 Meneveau 2016 France 1/120 1/120 240 (Excluded) 0.00 Subtotal (I-squared = 0.0%, p = 0.823)	Halm 2000	Europe	48/800	511801	1001	0.01 (0.22, 00.14)	40.45
Weneveau 2016 France 11/20 11/20 240 Na 2022 China 01112 0114 226 Subtotal (I-squared = 0.0%, p = 0.823) E. Target lesion revascularization 0.08 (0.69, 1.13) 100.00 Ali 2023 Multinational 53/1233 51/1254 2487 0.83 (0.89, 1.13) 100.00 Ali 2021 Multinational 1158 11/140 296 0.83 (0.38, 1.16) 2.40 Ali 2023 Multinational 1158 11/140 296 0.83 (0.34, 1.16) 29.78 Jia 2022 China 61112 4114 226 0.83 (0.80, 14.05) 1.22 Liki 2020 Europe 10/600 26/801 1201 0.83 (0.34, 1.16) 29.78 Subtotal (I-squared = 0.0%, p = 0.856) 101 1.02 (0.15, 6.99) 2.29 1.80 (0.18, 9.86) 2.96 Mali 2023 Multinational 68/1233 67/1254 2487 1.00 (0.72, 1.40) 94.20 Leki 2020 Europe 1/19 1/19 38 1.90 (0.07, 14.90) <	Holm 2023	Europe	40/000	01/001	1201	0.91 (0.02, 1.34)	40.15
Jia 2022 China 0/112 0/114 228 (Excluded) 0.00 Subtotal (I-squared = 0.0%, p = 0.823) - 0.88 (0.69, 1.13) 100.00 E. Target lesion revascularization Ali 2023 Multinational 53/1233 51/1254 2487 Ali 2021 Multinational 1/158 1/140 298 0.88 (0.69, 1.43) 50.31 (2.3, 5.51) 2.40 Ali 2016 Multinational 1/158 1/140 298 0.89 (0.00, 14.05) 1.23 (0.35, 4.58) 4.60 Ja 2022 China 5/112 4/114 226 0.89 (0.00, 14.05) 1.23 (0.35, 4.58) 4.60 Ja 2022 China 5/112 4/114 226 0.89 (0.00, 14.05) 1.28 (0.35, 4.58) 4.60 Ja 2022 China 5/112 1/19 38 1.09 (0.19, 19.40) 1.18 Subtotal (I-squared = 0.0%, p = 0.856) - 1.09 (0.72, 1.40) 94.20 1.83 (0.34, 9.86) 2.98 Mali 2021 Multinational 4/153 2/142 295 1.83 (0.34, 9.86) 2.98 Mali 2021 Multinational 6/153 6/1/254	Meneveau 2010	France	1/120	1/120	240	1.00 (0.06, 15.81)	0.79
Subtotal (I-squared = 0.0%, p = 0.823) 0.88 (0.68, 1.13) 100.00 E. Target lesion revascularization Ali 2023 Multinational 53/1233 51/1254 2487 Ali 2021 Multinational 1/153 2/142 298 0.89 (0.09, 14.05) 1.240 Ali 2021 Multinational 1/153 1/142 298 0.89 (0.09, 14.05) 1.23 Holm 2023 Europe 16/600 26/601 1201 0.63 (0.04, 1.16) 29.78 Jia 2022 China 5/112 4/114 226 1.26 (0.35, 4.58) 4.60 Kim 2015 Korea 2/58 2/59 101 1.02 (0.16, 6.99) 2.29 Leki 2020 Europe 2/19 1/19 38 0.94 (0.70, 1.27) 100.00 F. Target vessel revascularization Ali 2021 Multinational 4/153 2/142 295 1.83 (0.34, 9.86) 2.96 Meneveau 2016 France 2/120 1/120 240 1.00 (0.07, 14.490) 1.42 Ueki 2020 Europe 1/19 1/19 38 0.38 (0.29, 0.13) 6.54 G. Stent	Jia 2022	China	0/112	0/114	226	(Excluded)	0.00
E. Target lesion revascularization Ali 2023 Multinational 53/1233 51/1254 2487 Ali 2021 Multinational 2153 2142 295 Ali 2016 Multinational 1158 11440 298 Holm 2023 Europe 12/60 26/601 1201 Jia 2022 China 51112 41114 226 Kim 2015 Korea 2/58 2/59 101 Ueki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) F. Target vessel revascularization Ali 2021 Multinational 68/1233 67/1254 2487 Ali 2021 Multinational 41/53 2142 295 Meneveau 2016 France 2/120 1/120 240 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) G. Stent thrombosis Ali 2015 Denmark 0/40 1/45 85 Ali 2017 Europe 1/105 1/96 201 G. Stent thrombosis Ali 2017 Europe 1/105 1/96 201 Kim 2015 Korea 0/58 1/59 101	Subtotal (I-squared	= 0.0%, p = 0.823)				0.88 (0.69, 1.13)	100.00
Ali 2023 Multinational 53/1233 51/1254 2487 Ali 2021 Multinational 2/153 2/142 295 Ali 2018 Multinational 1/158 1/140 298 Holm 2023 Europe 16/600 28/601 1201 Jia 2022 China 5/112 4/114 226 Kim 2015 Korea 2/68 2/59 101 Ueki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) 1.00 (0.72, 1.40) 94.20 Kin 2015 Korea 2/120 1/120 2487 1.00 (0.72, 1.40) 94.20 Kin 2023 Multinational 66/1233 67/1254 2487 1.00 (0.72, 1.40) 94.20 Kia 2021 Multinational 4/153 2/142 295 1.98 (0.18, 21.59) 1.42 Ueki 2020 Europe 1/19 1/19 38 1.00 (0.07, 1.40) 94.20 Subtotal (I-squared = 0.0%, p = 0.857)	E. Target lesion reva	scularization					
Ali 2021 Multinational 2/153 2/142 295 Ali 2016 Multinational 1/158 1/140 298 Holm 2023 Europe 16/800 26/801 1201 Jia 2022 China 5/112 4/114 226 Jia 2023 Europe 16/800 26/801 1201 Jia 2022 China 5/112 4/114 226 Kim 2015 Korea 2/59 101 1.02 (0.15, 6.99) 2.29 Ueki 2020 Europe 2/19 1/19 38 1.90 (0.19, 19.40) 1.18 Subtotal (I-squared = 0.0%, p = 0.856) France 2/120 1/120 240 1.83 (0.34, 9.86) 2.96 Mereveau 2016 France 2/120 1/120 240 1.00 (0.07, 14.90) 1.42 Ueki 2020 Europe 1/19 1/19 38 1.00 (0.07, 14.90) 1.42 Subtotal (I-squared = 0.0%, p = 0.857)	Ali 2023	Multinational	53/1233	51/1254	2487	1.05 (0.72, 1.54)	58 51
Ali 2016 Multinational 1/158 1/140 298 Holm 2023 Europe 18/600 26/601 1201 Jia 2022 China 6/112 4/114 226 Jia 2020 Europe 18/600 26/601 1201 Jia 2022 China 6/112 4/114 226 Veki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) 1.00 (0.07, 1.27) 100.00 F. Target vessel revascularization Ali 2023 Multinational 66/1233 67/1254 2487 Ali 2020 Europe 1/19 1/19 240 1.00 (0.07, 1.40) 94.20 Ali 2020 Europe 1/19 1/19 38 1.00 (0.07, 14.90) 1.42 Subtotal (I-squared = 0.0%, p = 0.857) 1.04 (0.76, 1.43) 100.00 G. Stent thrombosis Ali 2016 Multinational 1/158 0/140 298 Subtotal (I-squared = 0.0%, p = 0.857)	41 2021	Multinational	2/153	2/142	205	0.03 (0.13, 8.51)	2 40
All 2010 Multinational 1/158 1/140 248 Holm 2023 Europe 16/600 26/601 1201 Jia 2022 China 5/112 4/114 226 Kim 2015 Korea 2/58 2/59 101 Jeki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) 1.00 (0.72, 1.40) 94.20 Ali 2023 Multinational 66/1233 67/1254 2487 Ali 2021 Multinational 66/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 Obstotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 G. Stent thrombosis Ali 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/96 201 0.38 (0.02, 9.13) 6.54 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29)	AI: 0048	Multinational	2/100	414.40	200	0.00 (0.09 44.05)	1.00
Holm 2023 Europe 16/800 28/801 1201 Jia 2022 China 5/112 4/114 226 Kim 2015 Korea 2/58 2/59 101 Jeki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856)	Ali 2016	Multinational	1/158	1/140	298	0.89 (0.05, 14.05)	1.23
Jia 2022 China 5/112 4/114 226 1.26 (0.35, 4.58) 4.60 Kim 2015 Korea 2/58 2/59 101 1.02 (0.15, 6.99) 2.29 Ueki 2020 Europe 2/19 1/19 38 1.90 (0.19, 19.40) 1.18 Subtotal (I-squared = 0.0%, p = 0.856) Multinational 68/1233 67/1254 2487 0.94 (0.70, 1.27) 100.00 F. Target vessel revascularization Ali 2023 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 1.83 (0.34, 9.86) 1.42 Ueki 2020 Europe 1/19 1/19 38 1.04 (0.76, 1.43) 100.00 G. Stent thrombosis Ali 2016 Multinational 1/158 0/140 298 2.64 (0.11, 64.38) 2.49 Ali 2017 Europe 1/105 1/96 201 0.38 (0.02, 9.13) 6.54 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 1/105 1/96 201 0.34 (0.01, 8.29)	Holm 2023	Europe	16/600	26/601	1201 -	0.63 (0.34, 1.16)	29.78
Kim 2015 Korea 2/58 2/59 101 Ueki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) 1.00 (0.19, 19.40) 1.18 F. Target vessel revascularization 0.94 (0.70, 1.27) 100.00 Ali 2023 Multinational 68/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 Jeki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 Jeki 2015 Denmark 0/40 1/45 85 Ali 2016 Multinational 1/158 0/140 298 Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/08 201 Kia 2017 Europe 1/105 1/08 201 Subtotal (I-squared = 0.0%, p = 0.906) 0/58 1/59 101	Jia 2022	China	5/112	4/114	226	1.26 (0.35, 4.58)	4.60
Ueki 2020 Europe 2/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.856) 1.90 (0.19, 19.40) 1.18 F. Target vessel revascularization 0.94 (0.70, 1.27) 100.00 Ali 2023 Multinational 66/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 G. Stent thrombosis 38 1.00 (0.07, 14.90) 1.42 Ali 2016 Multinational 1/158 0/140 298 Ali 2017 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/96 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0/58 1/59 101	Kim 2015	Korea	2/58	2/59	101	1.02 (0.15, 6.99)	2.29
Subtotal (I-squared = 0.0%, p = 0.856) 0.94 (0.70, 1.27) 100.00 F. Target vessel revascularization Ali 2023 Multinational 66/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 1.00 (0.72, 1.40) 94.20 Meneveau 2016 France 2/120 1/120 240 1.88 (0.34, 9.86) 2.96 Subtotal (I-squared = 0.0%, p = 0.857) 1.99 (0.76, 1.43) 1.00 (0.07, 14.90) 1.42 G. Stent thrombosis Ali 2015 Demmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/96 201 0.38 (0.02, 9.13) 6.54 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00 0.71 (0.34, 1.43) 4.89	Ueki 2020	Europe	2/19	1/19	38 -	1.90 (0.19, 19.40)	1.18
F. Target vessel revascularization Ali 2023 Multinational 68/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) G. Stent thrombosis 1.04 (0.76, 1.43) 100.00 G. Stent thrombosis Ali 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/96 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	Subtotal (I-squared	= 0.0%, p = 0.858)				0.94 (0.70, 1.27)	100.00
Ali 2023 Multinational 66/1233 67/1254 2487 Ali 2021 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857)	Tamatura al ann	and a fact in a					
All 2023 Multinational 00/1233 0//1294 2487 All 2021 Multinational 4/153 2/142 295 Meneveau 2016 France 2/120 1/120 240 Jeki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 0/140 298 G. Stent thrombosis 0/40 1/45 85 Holm 2023 Europe 1/105 1/164 80 Kala 2017 Europe 1/105 1/08 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0/58 1/59 101	All oppo	Sudanzation	00//000	07/1051			
All 2021 Multinational 4/153 2/142 295 Meneveau 2018 France 2/120 1/120 240 Ueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 G. Stent thrombosis 1.04 (0.76, 1.43) 100.00 All 2016 Multinational 1/158 0/140 298 Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/98 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	All 2023	Multinational	00/1233	6//1254	2487	1.00 (0.72, 1.40)	94.20
Meneveau 2016 France 2/120 1/120 240 Jueki 2020 Europe 1/19 1/19 38 Subtotal (I-squared = 0.0%, p = 0.857) 1.00 (0.07, 14.90) 1.42 G. Stent thrombosis 1.04 (0.76, 1.43) 100.00 Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 1/105 1/06 201 Kala 2017 Europe 1/105 1/08 201 Subtotal (I-squared = 0.0%, p = 0.906) 0/58 1/59 101	Ali 2021	Multinational	4/153	2/142	295	1.83 (0.34, 9.86)	2.96
Ueki 2020 Europe 1/19 1/19 38 1.00 (0.07, 14.90) 1.42 Subtotal (I-squared = 0.0%, p = 0.857) 6. Stent thrombosis 1.04 (0.76, 1.43) 100.00 G. Stent thrombosis Ail 2016 Multinational 1/158 0/140 298 Antonsen 2015 Denmark 0/40 1/45 85 0.38 (0.02, 9.13) 6.54 Holm 2023 Europe 1/105 1/96 201 0.71 (0.34, 1.48) 79.18 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00 0.72 (0.38, 1.38) 100.00	Meneveau 2016	France	2/120	1/120	240	1.98 (0.18, 21.59)	1.42
Subtotal (I-squared = 0.0%, p = 0.857) 1.04 (0.76, 1.43) 100.00 G. Stent thrombosis Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 12/800 17/801 1201 0.38 (0.02, 9.13) 6.54 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	Ueki 2020	Europe	1/19	1/19	38	1.00 (0.07, 14.90)	1.42
Ali 2016 Multinational 1/158 0/140 298 Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 12/800 17/801 1201 Kala 2017 Europe 1/105 1/96 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0.900 0.72 (0.38, 1.38) 100.01	Subtotal (I-squared	= 0.0%, p = 0.857)				1.04 (0.76, 1.43)	100.00
Ali 2016 Multinational 1/158 0/140 298 Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 12/800 17/801 1201 Kala 2017 Europe 1/105 1/95 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906)	G Stant thromhosis						
Antonsen 2015 Denmark 0/40 1/45 85 Holm 2023 Europe 12/600 17/601 1201 Kala 2017 Europe 1/105 1/96 201 Kim 2015 Korea 0/58 1/59 101 Subtotal (I-squared = 0.0%, p = 0.906) 0/58 1/59 101	Ali 2018	Multinational	1/158	0/140	298	2 84 (0 11 84 29)	2 40
Holm 2013 Europe 12/600 17/501 1201 0.38 (0.02, 9.13) 0.39 Holm 2023 Europe 12/600 17/601 1201 0.71 (0.34, 1.48) 79.18 Kala 2017 Europe 1/105 1/95 201 0.92 (0.06, 14.43) 4.89 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.906) 0.72 (0.38, 1.38) 100.00	Antoncon 2015	Deemark	0/40	1/45	25	2.07 (0.11, 04.36)	8.54
Holm 2023 Europe 12/500 17/501 1201 0.71 (0.34, 1.48) 79.18 Kala 2017 Europe 1/105 1/05 201 0.92 (0.06, 14.43) 4.89 Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	Anonsen 2015	Denmark	0000	171004		0.38 (0.02, 9.13)	0.04
Cala 2017 Europe 1/105 1/05 201 0.92 (0.06, 14.43) 4.89 Cim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	10im 2023	Europe	12/600	17/601	1201	0.71 (0.34, 1.48)	/9.18
Kim 2015 Korea 0/58 1/59 101 0.34 (0.01, 8.29) 6.90 Subtotal (I-squared = 0.0%, p = 0.906) 0.72 (0.38, 1.38) 100.00	Kala 2017	Europe	1/105	1/95	201	0.92 (0.06, 14.43)	4.89
Subtotal (I-squared = 0.0%, p = 0.908)	Kim 2015	Korea	0/58	1/59	101	0.34 (0.01, 8.29)	6.90
	Subtotal (I-squared	= 0.0%, p = 0.906)				0.72 (0.38, 1.38)	100.00

FIGURE 10

Forest plot comparing OCT guided with coronary angiography guided PCI in RCT studies. Data obtained from RCTs using fixed effect meta-analysis and expressed as OR. (A) MACE; (B) cardiac death; (C) all-cause death; (D) myocardial infarction; (E) target lesion revascularization (F) target vessel revascularization; (G) stent thrombosis. CI, confidence interval; OCT, optical coherence tomography; PCI, Percutaneous coronary intervention.

	Location	OCT	Angiography	Subjectnumber		Ratio (95% CI)	Weight
MACE							
D'Ascenzo 2017	Italy	28/197	28/197	394	-	1 00 (0 61 1 63)	27 75
Di 2012	Italy	5/40	9/40	90		0.67 (0.24, 1.90)	9.62
Ji 2013	Linited Kingdom	0/1124	22/1124	2269		0.07 (0.24, 1.05)	14.52
Vhalifa 2021	United Kingdom	12/260	25/1154	2200		0.40 (0.18, 0.85)	14.02
chalita 2021	Japan	13/200	15/130	390		0.46 (0.23, 0.94)	10.21
annaccone 2016	Italy	31/270	47/270	540		0.69 (0.45, 1.06)	32.88
Subtotal (I-squared	d = 26.7%, p = 0.24	13)			9	0.66 (0.48, 0.91)	100.00
Cardiac death							
Cortese 2022	Europe	1/100	4/100	200		0.26 (0.03, 2.26)	13.78
D'Ascenzo 2017	Italy	7/197	2/197	394		3.41 (0.72, 16.24)	21.56
Chalifa 2021	lanan	7/260	8/130	300		0.45 (0.17 1.22)	33 44
Choth 2016	Canada	1/214	16/420	642		0.51 (0.17, 1.22)	21 21
Siletit 2010		4/214	10/420	042		0.51 (0.17, 1.50)	31.21
Subtotal (I-squared	d = 48.1%, p = 0.12	(3)			9	0.07 (0.20, 1.71)	100.00
All-cause death	0.000000						
Cortese 2022	Europe	2/100	6/100	200		0.35 (0.07, 1.68)	23.30
D'Ascenzo 2017	Italy	7/197	2/197	394		3.41 (0.72, 16.24)	23.66
Di 2013	Italy	1/40	2/40	80		0.51 (0.05, 5.43)	12.58
Lannaccone 2016	Italy	7/270	9/270	540		0.78 (0.30, 2.07)	40.46
Subtotal (I-squared	d = 33.5%, p = 0.21	1)			\diamond	0.87 (0.35, 2.18)	100.00
Avocardial infarction	n						
Cortase 2022	Europe	2/100	4/100	200		0.51 (0.10.2.72)	0.55
01 2012	Itoly	1/40	2/40	200		0.35 (0.04, 2.22)	5.55
JI 2013	Italy	0/440	5/40	2200		0.35 (0.04, 3.23)	3.04
Jones 2018	United Kingdom	2/1134	9/1134	2208		0.22 (0.05, 1.03)	11.24
Khalita 2021	Japan	2/260	4/130	390		0.26 (0.05, 1.38)	9.45
annaccone 2016	Italy	18/270	17/270	540		1.06 (0.56, 2.01)	42.61
Sheth 2016	Canada	5/214	11/428	642		0.91 (0.32, 2.59)	21.50
Subtotal (I-squared	d = 14.9%, p = 0.31	19)			9	0.66 (0.38, 1.13)	100.00
Farget lesion revas	cularization						
Cortese 2022	Furone	6/100	9/100	200		0.69 (0.25 1.86)	31 35
D'Acconzo 2017	Itoly	0/107	29/107	204		0.21 (0.15, 0.67)	52 70
JASCENZO ZUTI	lange	0/19/	20/19/	394		0.51 (0.15, 0.07)	0.07
	Japan	2/200	2/130	590		0.50 (0.07, 3.54)	0.3/
annaccone 2016	italy	1/2/0	9/2/0	540		0.11 (0.01, 0.90)	1.50
Subtotal (I-squared	d = 1.6%, p = 0.384	•)			\diamond	0.39 (0.22, 0.68)	100.00
Target vessel revas	cularization						
annaccone 2016	Italy	1/270	10/270	540		0.10 (0.01, 0.80)	40.64
Sheth 2016	Canada	11/214	24/428	642	-	0.92 (0.46, 1.85)	59.36
Subtotal (I-squared	d = 76.4%, p = 0.04	10)			$\langle \rangle$	0.38 (0.04, 3.37)	100.00
Stent thrombosis							
Cortese 2022	Furone	1/100	1/100	200		1 00 (0 06 15 77)	27 21
000000000000000000000000000000000000000	Itolu	0/270	7/270	540		0.07 (0.00, 13.77)	26.40
Lannaccone 2016	Canada	0/2/0	11210	540		0.07 (0.00, 1.19)	20.18
Sheth 2016 Subtotal (I-square)	d = 56,4%, p = 0.10	4/214	5/428	042		1.59 (0.43, 5.86) 0.61 (0.09, 4.39)	40.60
NOTE: Weights are	from random effe	ts analys	is				
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FIGURE 11

Forest plot comparing OCT guided with coronary angiography guided PCI for all-cause death. Data obtained from RCTs using fixed effect metaanalysis and expressed as OR. CI, confidence interval; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

3.2.4 Cardiac death

Five trials (n = 4,104) reported cardiac death (29, 41, 43–45). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in cardiac death (OR 0.61, 95% CI 0.36–1.02; p = 0.893, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10B). Observational studies (51–53, 57), which included 4 studies with 1,626 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of cardiac death when compared to coronary angiography (OR 0.67, 95% CI 0.27–1.71; p = 0. 123, $I^2 = 48.1\%$, indicating moderate heterogeneity and moderate certainty, as shown in Figure 11B).

3.2.5 All-cause death

Four trials (n = 4,223) reported all-cause death (29, 42, 44, 47). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in all-cause death (OR 0.7, 95% CI 0.49–1.02; p = 0.550, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10C). Observational studies (52, 54, 55, 57), which included 4 studies with 1,214 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of all-cause death when compared to coronary angiography (OR 0.87, 95% CI 0.35–2.18; p = 0. 211, $I^2 = 33.5\%$, indicating moderate heterogeneity and moderate certainty, as shown in Figure 11C).

3.2.6 MI

Six trials (n = 4,747) reported MI (29, 41, 42, 44, 47, 49). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in MI (OR 0.88, 95% CI 0.69 to 1.13; p = 0.823, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10D). Observational studies (51, 53–57), which included 6 studies with 4,120 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of MI when compared to coronary angiography (OR 0.66, 95% CI 0.38–1.13; p = 0.319, $I^2 = 14.9\%$, indicating low heterogeneity and moderate certainty, as shown in Figure 11D).

3.2.7 TLR

Seven trials (n = 4,646) reported TLR (29, 41, 44, 47–50). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in TLR (OR 0.94, 95% CI 0.7–1.27; p = 0.856, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10E). However, the results from the observational studies, which included 4 studies with 1,524 patients, showed differing outcomes (51, 52, 54, 57). In contrast to coronary angiography, OCT-guided PCI showed a reduction in the risk of TLR (OR 0.39, 95% CI 0.22–0.68; p = 0.384, $I^2 = 1.6\%$, non-relevant heterogeneity, high certainty, see Figure 11E).

3.2.8 TVR

Four trials (n = 3,060) reported TVR (29, 42, 47, 50). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in TVR (OR 1.04, 95% CI 0.76–1.43; p = 0.857, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10F). Observational studies (53, 54), which included 2 studies with 1,182 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of TVR when compared to coronary angiography (OR 0.38, 95% CI 0.04–3.37; p = 0.04, $I^2 = 76.4\%$, indicating high heterogeneity and low certainty, as shown in Figure 11F).

3.2.9 Stent thrombosis

Five trials (n = 1,886) reported stent thrombosis (43, 44, 46, 48, 49). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in stent thrombosis (OR 0.72, 95% CI 0.38–1.38; p = 0.906, $I^2 = 0\%$, non-relevant heterogeneity, high certainty, see Figure 10G). Observational studies (53, 54, 57), which included 3 studies with 1,382 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of stent thrombosis when compared to coronary angiography (OR 0.61, 95% CI 0.09–4.39; p = 0.101, $I^2 = 56.4\%$, indicating moderate heterogeneity and moderate certainty, as shown in Figure 11G).

4 Discussion

OCT, with its high-resolution imaging (10-20 µm), accurately identifies vascular features like thrombi, lipids, and calcium deposits (59-63). In this study, we analyzed 2,758 articles related to OCT and cardiovascular diseases from the WoSCC. In-depth analyses were conducted on these articles by country, institution, journal, author, and keywords using Bibliometrix R software and CiteSpace. This comprehensive exploration revealed the knowledge structure, research hotspots, and emerging trends in the field, laying the groundwork for future strategies in disease prevention and treatment. Our study found that OCT, as a guiding tool for PCI, has become a focal point in recent cohorts and randomized trials, which was further confirmed in our subsequent meta-analysis. After including 11 RCTs and 7 observational studies, we concluded that OCT-guided PCI did not demonstrate significant association with better clinical outcomes. Although the point estimate and the upper bound of the confidence interval hinted at a possible reduction in MACE, cardiac death, all-cause death, MI, TLR, or stent thrombosis with OCT guided PCI, this did not reach statistical significance. However, the meta-analysis of observational studies showed a significant reduction in MACE and TLR.

4.1 Advantages and limitations of bibliometric analysis

The United States led in the publication output related to OCT and cardiovascular diseases, also exhibiting the highest proportion of international collaboration. Moreover, China's publication numbers are rapidly growing, likely influenced by recent expert consensus from Chinese cardiology societies emphasizing the importance of OCT in PCI (64). Among the top 10 institutions with the highest publication output, 7 were from the USA, while the remaining were from other countries (China, Singapore, and the UK). Professor Yu Bo from China was the most prolific among the top 10 corresponding authors, followed by authors from the USA. Professor Mehran Roxana held the highest m-INDEX, Professor Yu Bo the largest G-index, and Professor Virmani Renu the highest h-index and total citations. Additionally, among the top 10 most cited papers, one was published in "The Lancet" (37), and three in "Circulation" and other high-impact journals (31, 35, 36). Professor Ik-Kyung Jang's 2005 paper "in vivo Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography" ranked highest in citations (31).

Thematic word trend analysis over the past 20 years in the cardiovascular field has centered on eight key terms: coronary artery disease, deep learning, coronary stenosis, heart transplantation, plaque rupture, OCT, congenital heart disease, and cardiovascular diseases. Burst analysis of keywords indicated that studies on OCT and angiography-guided PCI have become hot topics in recent cohorts and randomized trials. Welldeveloped themes focus on atherosclerotic diseases, blood pressure, stent implantation, and plaque characteristics. The field's attention to the treatment and prognosis of diseases such as "coronary stenosis, acute myocardial infarction, atherosclerosis" post-operation and for survival is also noteworthy.

However, this study has limitations. The primary data for the bibliometric analysis was sourced from the WoSCC. Although the WoSCC includes over 11,000 authoritative and high-impact international academic journals with extensive coverage and powerful analysis features, its singular source may lead to potential article omissions from other databases. Additionally, researchers manually removed papers deemed irrelevant to the study objectives, which might introduce selection bias. Despite these limitations, our study comprehensively analyzes the current state and progress of OCT in cardiovascular research, aiding in identifying future research directions.

4.2 Advantages and limitations of meta-analysis

OCT has shown significant technical advantages in the application of cardiovascular diseases (30, 65). Compared to traditional coronary angiography, OCT provides higherresolution spatial three-dimensional images, critical in accurately assessing plaque composition and morphology. Importantly, OCT optimizes angioplasty of bifurcation lesions, avoiding the common issues of perspective shortening and image overlap in traditional angiography (66). These technical strengths theoretically endow OCT with significant clinical application potential. However, in actual clinical practice, these theoretical advantages of OCT have not entirely translated into clinical benefits. Our meta-analysis of RCTs revealed that OCTguided PCI did not exhibit significant clinical benefits in MACE, Cardiac death, All-cause death, MI, TLR, TVR, and Stent thrombosis, compared to angiography-guided PCI. Although studies suggest that OCT-guided PCI can achieve a larger minimum lumen diameter (MLD) (53), its use also leads to longer procedural times and higher contrast agent dosages (67), increasing perioperative risks such as early mortality, emergency coronary artery bypass grafting, cancer, and contrast-induced nephropathy (68, 69). These risks might overshadow the clinical benefits of OCT. However, the metaanalysis of observational studies indicated a significant reduction in MACE and TLR with OCT-guided PCI, aligning with previous research (67, 70).

4.2.1 Limitations

When interpreting the results of our meta-analysis, its inherent limitations must be considered. Firstly, the included trials varied in participant populations, outcome definitions, and follow-up periods, potentially affecting comparability and generalizability. Secondly, pre-planned overall and subgroup analyses were conducted at the study level, not at the individual patient level, precluding precise assessment of the specific impact of stent size pre and post PCI guided by OCT on cardiovascular outcomes. Lastly, variations in intravascular imaging guidance standards among different trials could also influence the results.

4.3 Comparisons with other studies

Although many meta-analyses have studied intravascular imaging-guided PCI, a systematic review of 24 meta-analyses showed that only 9 focused specifically on RCTs (71). Given the potential introduction of confounding factors in observational studies (71), we conducted separate metaanalyses of evidence from RCTs and observational studies for OCT-guided PCI. This approach differs from previous metaanalyses, showing OCT's significant advantages are more pronounced in observational studies (67, 70), consistent with previous high-quality RCTs (29, 49, 53).

Our results, compared with the study led by Niels R. Holm, showed differences in MACE outcomes (44). The fundamental reason is that calculating OR values directly using incidence rates might differ from results reported in that study, as Cox regression analysis incorporates specific time points of events, often overlooked in simple calculations (44, 72). Additionally, the Cox model typically considers multiple covariates potentially influencing outcomes, such as patient age, gender, and medical history (73). This might be one reason our study did not show a significant clinical advantage of OCT. Furthermore, with a median follow-up time of only 1–2 years in the studies included, detecting statistically significant differences between the two interventions would require longer follow-up and higher event rates.

5 Conclusion

In summary, this study primarily employed bibliometric analysis to examine literature published over the past twenty years on OCT and cardiovascular diseases. It identified specific countries, institutions, authors, and journals that have made significant contributions to this field during this period. It was found that OCT as a guiding tool for PCI has become a hot topic in recent cohorts and randomized trials, prompting subsequent meta-analyses. However, OCT-guided PCI did not demonstrate significant clinical benefits, with only the metaanalysis of observational studies suggesting a reduction in MACE and TLR.

Author contributions

WL: Conceptualization, Writing – original draft, Writing – review & editing. CC: Data curation, Formal Analysis, Writing – original draft. JW: Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. JL: Formal Analysis, Methodology, Writing – review & editing. CL: Conceptualization, Methodology, Writing – review & editing. XZ: Conceptualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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