#### **ORIGINAL PAPER**



# Optical coherence tomography-guided versus angiography-guided percutaneous coronary intervention in acute coronary syndrome: a meta-analysis

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#### Abstract

**Background** Percutaneous coronary intervention (PCI) is standard of care in patients with acute coronary syndrome (ACS) suitable for interventional revascularization. Intracoronary imaging by optical coherence tomography (OCT) expanded treatment approaches adding diagnostic information and contributing to stent optimization.

**Objectives** This meta-analysis aimed to assess the effects of OCT-guided vs. angiography-guided PCI in treatment of ACS. **Methods** A structured literature search was performed. All controlled trials evaluating OCT-guided vs. angiography-guided PCI in patients with ACS were eligible. The primary end point was major adverse cardiac events (MACE).

**Results** Eight studies enrolling 2612 patients with ACS were eligible. 1263 patients underwent OCT-guided and 1,349 patients angiography-guided PCI. OCT guidance was associated with a 30% lower likelihood of MACE (OR 0.70, 95% CI 0.53–0.93, p = 0.01,  $l^2 = 1\%$ ). OCT-guided PCI was also associated with significantly decreased cardiac mortality (OR 0.49, 95% CI 0.25–0.96, p = 0.04,  $l^2 = 0\%$ ). There was no detectable difference in all-cause mortality (OR 1.08, 95% CI 0.51–2.31, p = 0.83,  $l^2 = 0$ ). Patients in OCT-guided group less frequently required target lesion revascularization (OR 0.26, 95% CI 0.07–0.95, p = 0.04,  $l^2 = 0\%$ ). Analysis of myocardial infarction did not result in significant treatment differences. In subgroup or sensitivity analysis the observed advantages of OCT-guided PCI were not replicable.

**Conclusion** The evidence suggests that PCI guidance with OCT in ACS decreases MACE, cardiac death and target lesion revascularization compared to angiography. On individual study level, in subgroup or sensitivity analyses these advantages were not thoroughly replicable.

Keywords Optical coherence tomography  $\cdot$  OCT  $\cdot$  STEMI  $\cdot$  NSTE-ACS  $\cdot$  Percutaneous coronary intervention  $\cdot$  PCI  $\cdot$  Angiography

Abbreviat	tions	
ACS	Acute coronary syndrome	
CI	Confidence interval	
FFR	Fractional flow reserve	
IVUS	Intravascular ultrasonography	
MACE	Major adverse cardiac event	
NRS	Non-randomized controlled studies	

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NSTE-ACS	Non-ST segment elevation acute coronary
	syndrome
NSTEMI	Non-ST segment elevation myocardial
	infarction
OCT	Optical coherence tomography
OFDI	Optical frequency domain imaging
OR	Odds ratio
PCI	Percutaneous coronary intervention
PSM	Propensity score matching
RCT	Randomized controlled trial
STEMI	ST segment elevation myocardial infarction
TLR	Target lesion revascularization
TVR	Target vessel revascularization

# Introduction

Acute coronary syndrome (ACS) is a life-threatening disease with high morbidity and mortality burden. Immediate patient management is required, and invasive coronary angiography remains the diagnostic standard [1, 2]. Coronary angiography allows adequate treatment by percutaneous coronary intervention (PCI) [1, 2]. Balloon angioplasty followed by stent implantation is the predominant revascularization strategy, but in selected cases balloon angioplasty only, thrombus aspiration or conservative management is preferred over stent deployment [1, 3-5]. For decades, stent implantation was based only on fluoroscopic findings [6]. Quantitative standards and measurements were limited until recent technical developments in intracoronary imaging or functional assessment expanded the interventional repertoire [6]. Imaging-guided PCI with stent implantation in an elective setting was advantageous compared to conventional angiography resulting in a significant reduction of cardiac death and major adverse cardiac events previously [7]. Optical coherence tomography (OCT) and intravascular ultrasonography (IVUS) are the most frequently used imaging techniques [6, 8].

OCT is a light-based imaging technique in near-infrared spectrum with excellent near-field imaging, but technically axial range is limited and use depends on blushing the examined artery [9–11]. OCT allows detection of the underlying pathology of ACS, for example, plaque rupture can be distinguished from plaque erosion [10]. Precise measurements and visualization enable defining landing zone or optimal sizing in infarct-related arteries. After stent deployment, OCT may diagnose edge dissection, stent underexpansion, malapposition, or residual disease [10]. The applicability of OCT in PCI was demonstrated in elective circumstances before, but data on efficacy under urgent conditions during ACS are limited [7, 12, 13]. The current meta-analysis aimed to comprehensively assess the effects of OCT-guided compared to angiography-guided PCI in ACS based on efficacy outcomes.

## Methods

This meta-analysis was conducted using a pre-specified protocol and reproducible plan for literature search and synthesis according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines [14].

Controlled trials comparing OCT-guided to angiography-guided PCI in patients with ACS requiring interventional revascularization were included. Randomized controlled trials (RCT) and non-randomized controlled studies (NRS) were eligible. All details regarding search strategy, data extraction, and study selection are in presented in suppl. material 1.

The primary end point was major adverse cardiac events (MACE), a composite of cardiac mortality, myocardial infarction, and target vessel revascularization (TVR). The individual components of MACE, all-cause mortality, and target lesion revascularization (TLR) were secondary efficacy endpoints.

Risk of bias at study level was assessed using the Cochrane Collaborations risk of bias tool (RoB2, version 08/22/2019) for randomized trials [15]. Non-randomized controlled studies were assessed using the Cochrane Collaborations Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I, version 10/20/2016) tool [16]. Risk of bias assessment was performed by two individual investigators (SMM, SH). In case of discrepancy a third independent investigator was consulted (MMM).

Random-effects meta-analyses were performed using the Mantel–Haenszel method for dichotomous data. Pooled odds ratios (ORs) and 95% confidence intervals (CI) are given for each analysis with a two-sided significance level of p < 0.05 (RevMan 5.3, Nordic Cochrane Centre, Cochrane Collaboration). The extent of heterogeneity was approximated by  $I^2$  tests considering 0–40% as non-important, 30–60% as moderate, 50–90% as substantial, and 75–100% as considerable heterogeneity. Pre-specified analysis of publication bias by funnel plot was not appropriately feasible given the low number of studies included.

Follow-up varied between the trials and timing of measurement of outcomes during the study period was heterogeneously performed. Consequently, ORs were calculated from event data of longest follow-up of each study. Post hoc subgroup analyses were performed to test whether timing of OCT (OCT pre- or post-stent implantation) affected the results. This approach allowed differentiation between the use of OCT as diagnostic tool compared to stent optimization and subsequent therapeutically consequences.

Post hoc sensitivity meta-analyses were performed according to risk of bias judgement to assess the impact of study quality on the investigated outcomes. RCTs with "high" risk of overall bias were excluded from sensitivity analysis. NRS with "serious" or "critical" risk of overall bias were eliminated from sensitivity analyses.

We did not obtain ethical approval for this meta-analysis because we did not collect data from individual human subjects.

#### Results

#### **Study selection**

A total of 1706 articles were identified by the described search strategy (see Fig. 1, PRISMA Flow chart). After removing duplicates, titles and abstracts of 1501 remaining articles were screened. 1446 articles were excluded which left 55 references for assessment of the full-text articles. Six additional full texts were assessed for eligibility by hand-searching. Considering exclusion criteria eight studies were finally included in quantitative analyses [17–24].

#### Studies

Eight controlled studies were included in meta-analysis [17–24] (see Table 1). Of these, three were RCTs [18, 23, 24]. Four trials were conducted as case series studies with propensity score matching (PSM), notably D'Ascenzo et al. and Iannaccone et al. each conducted PSM pooling data from the OCT-FORMIDABLE registry [17, 19–21]. The lasting study was designed as case series study without matching [22]. The use of OCT varied in the trials: three studies used OCT preliminary to PCI as diagnostic tool [20–22], one trial

investigated stent optimization and used OCT solely after PCI [17], and four studies used OCT both in the pre- and post-stent implantation period [18, 19, 23, 24].

### Assessment of bias

Assessment of bias was performed in three RCTs using RoB2 tool [18, 23, 24]. Two RCTs were associated with "some concerns" in overall judgement (see Table 2). The OCTACS trial was judged to be at "high" risk of overall bias [24]. This judgement was mainly caused by substantial deviations from defined intervention because two patients underwent imaging using IVUS instead of OCT and one patient with peri-interventional complication likely caused by OCT was excluded from efficacy analysis.

Potential sources of bias were assessed in five NRS by ROBINS-I tool [17, 19–22]. Three trials were judged to have moderate risk of overall bias, whereas two trials were considered to have critical risk of overall bias (see Table 3). The latter were included in the overall analysis, but were precluded from sensitivity analysis. The overall judgement "critical" risk of bias was based on severe differences in patient selection and varying treatment periods and protocols between OCT and comparator group [17, 22].



Fig. 1 PRISMA flow chart diagram. OCT optical coherence tomography, PCI percutaneous coronary intervention, ACS acute coronary syndrome

#### Table 1 Characteristics of included studies and patients

		D'Ascenzo et al. [20]	Di Giorgio et al. [17]	Iannaccone et al. [21]	Khalifa et al. [22]	Meneveau et al. [18] DOCTORS	Jia et al. [23] ERO- SION III	Antonsen et al. [24] OCTACS	Sheth et al. [19] TOTAL
Study characteristics					1		1		1
Study period		01/2014– 10/2015 and 01/2009– 12/2012	10/2009– 02/2010	01/2014– 10/2015 and 06/2009– 10/2015	01/2009– 12/2018	09/2013– 12/2015	12/2017– 11/2019	08/2011– 05/2013	08/2010– 07/2014
Study design		PSM analysis of registry data, mul- ticentric study	PSM analy- sis, case series	PSM analysis of registry data, mul- ticentric study	Case series	RCT	RCT	RCT	PSM analy- sis, case series
Comparator treatment		Angiography FFR guid- ance	Angiogra- phy	Angiography	Angiogra- phy	Angiogra- phy	Angiogra- phy	Angiogra- phy	Angiogra- phy
Follow-up period (median)		25 months	12 months	700 days	1 year	6 months	369 days	6 months	12 months
Baseline characteristics of patie	ents included								
OCT group	Patients	197	40	270	260	120	112	50	214
Angiography group	Patients	197	40	270	130	120	114	50	428
OCT group	Age, median	63 (13)	67.9 (11.3)	60 (13)	70 (13)	60.8 (11.5)	54.5 (11.2)	61.8 (9.4)	60.9 (11.5)
Angiography group	Age, median	64 (10)	62.7 (10.9)	61 (12)	73 (11)	60.2 (11.3)	56.4 (10.4)	62.6 (11.0)	61.2 (12.1)
OCT group	Male patients	153 (77.7)	35 (87.5)	226 (79)	176 (68)	95 (79.2)	89 (79.5)	36 (72)	167 (78)
Angiography group	Male patients	151 (76.6)	31 (77.5)	227 (79)	90 (69)	91 (75.8)	91 (79.8)	34 (68)	354 (82.7)
OCT group	Hyperten- sion	133 (67.5)	30 (75)	160 (56)	219 (84)	67 (55.8)	47 (42)	28 (56)	-
Angiography group	Hyperten- sion	139 (70.6)	32 (80)	168 (59)	109 (84)	50 (41.7)	45 (39.5)	28 (56)	-
OCT group	Diabetes	38 (19.3)	12 (30)	49 (17)	101 (39)	26 (21.7)	29 (25.9)	8 (16)	38 (17.8)
Angiography group	Diabetes	48 (24.4)	13 (32.5)	48 (18)	61 (47)	19 (15.8)	19 (16.7)	5 (10)	79 (18.5)
OCT group	Smoking	113 (57.4)	18 (45)	162 (57)	78 (30)	47 (39.2)	64 (57.1)	23 (46)	93 (43.5)
Angiography group	Smoking	120 (60)	22 (55)	163 (58)	50 (38)	51 (42.5)	73 (64.0)	18 (36)	184 (43.0)
OCT group	Dyslipi- demia	114 (57.9)	29 (72.5)	142 (49)	196 (75)	59 (49.2)	-	-	-
Angiography group	Dyslipi- demia	109 (55.3)	19 (47.5)	135 (47)	97 (75)	56 (46.7)	_	-	-
Type of acute coronary syndrom	me and manager	ment							
OCT group	Unstable Angina	54 (27.4)	0	46 (16)	18 (7)	10 (8.3)	0	0	0
	NSTEMI	89 (45.2)	16 (40)	99 (34)	42 (16)	110 (91.7)	0	50 (100)	0
	STEMI	54 (27.4)	24 (60)	140 (49)	200 (77)	-	112 (100)	0	214 (100)
Stenting (% of patients)		Not separately reported	100	100	100	100	43.8	100	Not separately reported
Angiography group	Unstable Angina	53 (26.9)	0	42 (15)	15 (12)	9 (7.5)	0	0	0
	NSTEMI	80 (40.9)	21 (52.5)	93 (36)	18 (14)	111 (92.5)	0	50 (100)	0
	STEMI	65 (33)	19 (47.5)	150 (53)	97 (75)	-	114 (100)	0	428 (100)
Stenting (% of patients)		Not separately reported	100	100	100	100	58.5	100	Not separately reported

OCT optical coherence tomography, PSM propensity score matching, RCT randomized controlled trial; FFR fractional flow reserve, NSTEMI Non-ST segment elevation myocardial infarction, STEMI ST segment elevation myocardial infarction. (): standard deviation in reported ages, percentages in other rows

Risk of bias	Randomization	Deviations from intended interven- tions	Missing outcome data	Measurement of the outcomes	Selection of the reported results	Overall risk of bias
DOCTORS [18]	Low	Some concerns	Low	Some concerns	Low	Some concerns
EROSION III [23]	Low	Some concerns	Low	Some concerns	Low	Some concerns
OCTACS [24]	Low	High	Some concerns	Some concerns	Some concerns	High

Table 2 Risk of bias assessment of randomized controlled trials

 Table 3
 Risk of bias assessment of non-randomized controlled studies

Risk of bias	Confounding	Patient selec- tion	Classification of intervention	Deviations from the intended inter- ventions	Missing data	Outcome measure- ment	Selection of the reported results	Overall risk of bias
D'Ascenzo et al. [20]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Di Giorgio et al. [17]	Critical	Critical	Low	Low	Moderate	Low	Moderate	Critical
Iannaccone et al. [21]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Khalifa et al. [22]	Serious	Critical	Low	Low	Low	Serious	Moderate	Critical
Sheth et al. [19]	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate

# Patient-level baseline characteristics and procedural data

A total of 2612 patients with ACS were included. Baseline characteristics are summarized in Table 1. The median age ranged from 54.5 to 73 years, and 78.3% were male. Analysis of cardiovascular risk profile revealed that 22.7% had diabetes, 58.2% had dyslipidemia. 63.7% had hypertension, and 49% were ever smokers. STEMI was the predominant type of ACS, followed by NSTEMI and unstable angina. All patients were managed invasively. 1263 patients underwent OCT-guided and 1349 patients angiography-guided PCI. Stent implantation was the predominant revascularization strategy. The follow-up period ranged from 6 to 25 months.

#### **Primary outcome analysis**

Seven trials reporting on 1141 patients treated with OCTguided PCI compared to 1230 patients undergoing angiography-guided PCI were included in quantitative analysis of major adverse cardiac events [17–22, 24]. EROSION III did not explicitly report TVR and was excluded from primary outcome analysis [23]. MACE rate was 8.7% in OCT-guided PCI group compared to 12.3% in angiography-guided group. OCT guidance led to a significant difference with a 30% lower likelihood of MACE (OR 0.70, 95% CI 0.53–0.93, p=0.01,  $l^2=1\%$ , non-relevant heterogeneity, see Fig. 2).

# Secondary outcome analyses

Overall, eight trials were included in secondary outcome analyses [17–24].

# **All-cause mortality**

Five trials reporting on 667 patients treated with OCTguided PCI compared to 672 patients treated with angiography-guided PCI were analyzed [17, 18, 20, 21, 24]. Allcause mortality rate was 2.4% in OCT-guided PCI group compared to 2.1% in angiography-guided group without a statistical difference (OR 1.08, 95% CI 0.51–2.31, p=0.83,  $I^2=0\%$ , non-relevant heterogeneity, see Fig. 3a).



Fig. 2 Primary analysis: Major adverse cardiac events. OCT optical coherence tomography, PCI percutaneous coronary intervention, M-H Mantel-Haenszel method, CI confidence interval

#### **Cardiac mortality**

Four trials reporting on 626 patients treated with OCTguided PCI compared to 717 patients undergoing angiography-guided PCI were included [19, 22–24]. Cardiac mortality rate was 2.2% in OCT-guided PCI group compared to 4.0% in angiography-guided group. OCT-guided PCI led to a significant difference with a 51% lower likelihood of cardiac mortality (OR 0.49, 95% CI 0.25–0.96, p=0.04,  $l^2=0\%$ , non-relevant heterogeneity, see Fig. 3b).

#### **Myocardial infarction**

Seven trials reporting on 1056 patients treated with OCTguided PCI compared to 1147 patients undergoing angiography-guided PCI were analyzed [17–19, 21–24]. Myocardial infarction rate was 2.6% in OCT-guided PCI group compared to 3.2% in angiography-guided group without a statistical difference (OR 0.82, 95% CI 0.49–1.37, p=0.45,  $I^2=0\%$ , nonrelevant heterogeneity, see Fig. 3c).

#### Target vessel revascularization

Seven trials reporting on 1213 patients treated with OCTguided PCI compared to 1304 patients undergoing angiography-guided PCI were included [18–24]. TVR rate was 2.4% in OCT-guided PCI group compared to 5.4% in angiographyguided group without a statistical difference (OR 0.54, 95% CI 0.26–1.13, p=0.10,  $l^2=45\%$ , moderate heterogeneity, see Fig. 3d).

#### **Target lesion revascularization**

Three trials reporting on 570 patients treated with OCT-guided PCI compared to 445 patients undergoing angiography-guided PCI were analyzed [21, 22, 24]. TLR rate was 0.5%

in OCT-guided PCI group compared to 2.7% in angiographyguided group. OCT-guided PCI led to a significant difference with a 74% lower likelihood of TLR (OR 0.26, 95% CI 0.07–0.95, p=0.04,  $I^2=0\%$ , non-relevant heterogeneity, see Fig. 3e).

Subgroup and sensitivity analyses did not demonstrate any statistically significant difference in primary or secondary outcomes (see Suppl. Table 1, Suppl. Table 2, and Suppl. Material 1).

# Discussion

To our knowledge, this is the first meta-analysis comprehensively assessing the effect of OCT-guided compared to angiography-guided PCI in patients with ACS. The main and novel findings of pooled data analyses were as follows:

- OCT-guided PCI resulted in a 30% lower likelihood of MACE and 74% lower odds of target lesion revascularization,
- OCT-guided PCI led to significant decrease of 51% in cardiac mortality, but this did not translate to difference in all-cause mortality.

Pooled data analysis is the uncontested strength of metaanalysis, but interpretation of overall effects requires cautious revision. On individual study level only Khalifa et al. demonstrated a significant MACE reduction and Iannaccone et al. exclusively reported a directed OR favoring OCT in TLR [21, 22]. All other trials did not show a significantly directed treatment effect according to MACE, cardiac death, or TLR on individual study level (see Figs. 2 and 3a–e). Moreover, in subgroup or sensitivity analyses the observed efficacy advantages were not thoroughly replicable. Study

а											
u		OCT guide	d PCI	Angiography-guided PCI		Odds Ratio			Odds Ra	atio	
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random	1, 95% CI	
	Antonsen et al.	0	40	1	45	5.5%	0.37 [0.01, 9.25]				
	D'Ascenzo et al.	7	197	2	197	22.7%	3.59 [0.74, 17.51]		+		
	Di Giorgio et al.	1	40	2	40	9.6%	0.49 [0.04, 5.60]				
	lannaccone et al.	7	270	9	270	56.7%	0.77 [0.28, 2.10]				
	Meneveau et al.	1	120	0	120	5.5%	3.03 [0.12, 75.00]			•	
	Total (95% CI)		667		672	100.0%	1.08 [0.51, 2.31]		-		
	Total events	16		14							
	Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> =	= 3.90,	$df = 4 (P = 0.42); I^2 =$	= 0%			b 01 01		10	100
Test for overall effect: Z = 0.21 (P = 0.83)								0.01 0.1	Guided PCI A	ngiography-guide	d PCI

	-	
	-	

	OCT guided PCI		Angiography-guide	d PCI		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	I M-H, Random, 95% CI	
Antonsen et al.	0	40	1	45	4.2%	0.37 [0.01, 9.25]	]	
Jia et al.	3	112	4	114	19.0%	0.76 [0.17, 3.46]	]	
Khalifa et al.	7	260	8	130	40.9%	0.42 [0.15, 1.19]		
Sheth et al.	4	214	16	428	35.8%	0.49 [0.16, 1.49]	]	
Total (95% CI)		626		717	100.0%	0.49 [0.25, 0.96]		
Total events	14		29					
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> =	0.42,	$df = 3 (P = 0.94); I^2 =$	0%				100
Test for overall effect:	Z = 2.08 (P	= 0.04)					OCT guided PCI Angiography-guid	ed PCI

C								
•	OCT guided PCI		Angiography-gui	ded PCI		Odds Ratio	Odds Ratio	
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
	Antonsen et al.	0	40	1	45	2.6%	0.37 [0.01, 9.25]	
	Di Giorgio et al.	1	40	3	40	5.0%	0.32 [0.03, 3.18]	
	lannaccone et al.	18	270	17	270	56.7%	1.06 [0.54, 2.11]	
	Jia et al.	0	112	0	114		Not estimable	
	Khalifa et al.	2	260	4	130	9.1%	0.24 [0.04, 1.35]	
	Meneveau et al.	1	120	1	120	3.4%	1.00 [0.06, 16.17]	
	Sheth et al.	5	214	11	428	23.2%	0.91 [0.31, 2.64]	
	Total (95% CI)		1056		1147	100.0%	0.82 [0.49, 1.37]	-
	Total events	27		37				
	Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> :	= 3.43,	$df = 5 (P = 0.63); I^2$	= 0%			
	Test for overall effect:	Z = 0.76 (P	= 0.45					OCT guided PCI Angiography-guided PCI

Ь											
G		OCT guide	d PCI	Angiography-guided PCI			Odds Ratio	Odds Ra			
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random	, 95% CI	
	Antonsen et al.	0	40	1	45	4.5%	0.37 [0.01, 9.25]		•		
	D'Ascenzo et al.	8	197	28	197	25.4%	0.26 [0.11, 0.58]				
	lannaccone et al.	1	270	10	270	9.4%	0.10 [0.01, 0.76]				
	Jia et al.	5	112	4	114	16.5%	1.29 [0.34, 4.91]				
	Khalifa et al.	2	260	2	130	10.0%	0.50 [0.07, 3.56]				
	Meneveau et al.	2	120	1	120	7.3%	2.02 [0.18, 22.54]			•	
	Sheth et al.	11	214	24	428	26.9%	0.91 [0.44, 1.90]			_	
	Total (95% CI)		1213		1304	100.0%	0.54 [0.26, 1.13]		-		
	Total events	29		70							
	Heterogeneity: Tau <sup>2</sup> =	0.38; Chi2 :	= 10.87	df = 6 (P = 0.0)	)9); l <sup>2</sup> = 45%			L 01		10	100
	Test for overall effect:	Z = 1.64 (P	= 0.10	i -				0.01	OCT guided PCI Ar	ngiography-guide	d PCI

е										
C	OCT guided PCI		Angiography-guid	ed PCI		Odds Ratio	Odd	Ratio		
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	iom, 95% CI	
- 1	Antonsen et al.	0	40	1	45	16.4%	0.37 [0.01, 9.25]			
	lannaccone et al.	1	270	9	270	39.7%	0.11 [0.01, 0.86]			
	Khalifa et al.	2	260	2	130	43.9%	0.50 [0.07, 3.56]		<u> </u>	
	Total (95% CI)		570		445	100.0%	0.26 [0.07, 0.95]			
	Total events	3		12						
	Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup> =	1.22,	$df = 2 (P = 0.54); I^2$	= 0%				1 10 10	H
	Test for overall effect:	Z = 2.04 (P	= 0.04)	I				OCT guided PC	Angiography-guided PCI	'

Fig. 3 a Secondary analyses: all-cause mortality. b Secondary analyses: cardiac mortality. c Secondary analyses: myocardial infarction. d Secondary analyses: target vessel revascularization. e Secondary anal-

yses: target lesion revascularization. *OCT* optical coherence tomography, *PCI* percutaneous coronary intervention, *M-H* Mantel–Haenszel method, *CI* confidence interval heterogeneity, study quality and low event rates might be possible explanations.

Then, pooled data analysis resulted in a significantly decreased cardiac mortality in OCT group, but all-cause mortality (OR 1.08, 95% CI 0.51–2.31) did not differ in overall analysis. Noteworthy, only OCTACS trial was eligible for both mortality analyses and this study itself lacked statistical power in mortality measurement [24]. Hence, one might speculate that structural interstudy heterogeneity rather than intervention itself might have contributed to the measured effects of all-cause or cardiac mortality. Important structural differences need to be acknowledged.

In included trials OCT was mostly used to examine deployed stents and assess success of revascularization [17–19, 23, 24]. One might hypothesize that the treatment benefit of OCT is mostly caused by its impact on optimizing revascularization strategy rather than its diagnostic role. In DOCTORS trial OCT imaging resulted in decision for stent optimization in 50% of patients and in 27% additional stents were implanted [18]. These data are in line with OCTACS and TOTAL each reporting 46% stent optimization rate following OCT [19, 24]. On the contrary, angiography led to further treatment in 22.5% of patients and additional stents were used in 18% [18]. However, the current study-level data set did not allow adequately powered subgroup calculation according to pre- or post-implantation OCT run (see suppl. Table 1). Consequently, this hypothesis cannot be validated. Potentially, a patient-level approach might add evidence whether the observed treatment effects of OCT are caused by stent optimization or whether competing mechanisms contribute to observed advantages.

Study design, performance, and study quality restrict generalizability to daily routine. Firstly, OCT was mainly performed by experienced operators and teams in designed trials. Secondly, OCT usage significantly increased procedural time (+13 min OCTACS, +14 min EROSION, +20 min TOTAL, +20 min DOCTORS) and resulted in increased amount of contrast medium [18, 19, 23, 24]. Time delay might be harmful in urgent ACS scenario and higher contrast medium volume might decline kidney function [25]. The increased procedural duration and amount of contrast medium performing OCT was observed in elective setting likewise [13]. The EROSION III trial was intentionally designed to reduce stent implantation rate-86% of patients with plaque erosion were managed without stent implantation [23]. However, the majority of trials a priori used stenting as primary strategy to manage revascularization and subsequently used OCT not as diagnostic, but as implicit treatment tool.

The pooled meta-analysis pointed out weaknesses and gaps in the evidence. Upcoming controlled trials will not enroll all entities of ACS patients. They will not add substantial evidence to answer the current research question [26–28]. One might even speculate whether a RCT concomitantly enrolling STEMI and NSTEMI is reasonable given the fact that STEMI almost always requires immediate or rescue PCI [1].

Recently, implementation of the upcoming TACTICS registry was published [29]. This observational uncontrolled study will add further information on feasibility and diagnostic benefit of OCT-guided PCI in ACS patients, but underlies the limitations of a non-randomized study [29].

To definitely answer the research question future controlled studies are required. These trials should acknowledge the following terms to overcome the substantial bias domains:

- Comparable pretreatment
- Directed use of OCT, defined number of runs (if multiple runs are necessary), and limited operator's discretion on treatment
- Precisely defined stenting conditions (Indications for stent deployment? How to treat complex lesions, calcified lesions or stenotic bifurcation? Does plaque erosion require stenting?)

In the absence of adequately powered, high-quality trials the use of OCT in ACS patients undergoing PCI revascularization cannot be generally recommended. Intracoronary imaging is useful, but implementation should not withhold restoration of coronary flow. An increase of procedural time and subsequent prolonged ischemia with loss of myocardium should not outweigh the potential benefits. Timing, the operator's experience in imaging and interpretation, local resources, and patient's characteristics like hemodynamic stability or renal function should be considered in decision making for OCT use in ACS.

#### Limitations

Despite the methodological PRISMA approach, the current meta-analysis underlies inherent limitations. Specific aspects limiting generalizability should be acknowledged: we did not have access to patient-level data. Analysis of patient-level data would potentially produce more reasonable quantitative results, but was not applicable with limited access to only published data.

Patients were predominantly male and cardiovascular risk factors were unequally distributed. Two studies exclusively included STEMI patients, whereas two trials only enrolled NSTE-ACS patients. All studies were unblinded trials, and five were NRS. These facts might have contributed to selection, detection, and performance bias.

The follow-up duration and the timing of OCT runs varied between the trials. Three trials only investigated OCT use prior to stent implantation, whereas all other trials examined stent optimization strategy by OCT. Two trials did not report on stenting strategy and the EROSION III trial was conducted to reduce stent implantation rate by intracoronary imaging. These aspects indicate substantial performance bias.

The judgement of risk of bias on trial level demonstrated variance in study quality. This heterogeneity resulted in the authors' decision to add further post hoc sensitivity analysis. The current meta-analysis only measured efficacy end points, safety outcomes like bleeding, or vascular access complication were not assessed.

# Conclusion

The evidence suggests that PCI guidance with OCT in ACS decreases MACE, cardiac death, and target lesion revascularization compared to angiography in pooled data analysis. On individual study level, in subgroup or sensitivity analyses these advantages were not thoroughly replicable. Study heterogeneity, study quality, and low event rates might be possible explanations.

Future randomized clinical trials with adequate statistical power and enrollment of all ACS entities are required to clarify the role of OCT as stent optimization in ACS revascularization procedures.

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#### Declarations

Conflict of interest SMM, MMM, SH, SB, TT, HW, VM, SB, CA, SL: None.

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# References

1. Ibanez B, James S, Agewall S et al (2018) 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European society of cardiology (ESC). Eur Heart J 39:119–177

- Collet JP, Thiele H, Barbato E et al (2021) 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 42:1289–1367
- Neumann FJ, Chettibi M, Sisakia H et al (2019) 2018 ESC/ EACTS Guidelines on myocardial revascularization. Eur Heart J 40:87
- Jolly SS, Cairns JA, Yusuf S et al (2016) Outcomes after thrombus aspiration for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. Lancet 387:127–135
- Jolly SS, James S, Dzavik V et al (2017) Thrombus aspiration in ST-segment-elevation myocardial infarction: an individual patient meta-analysis: thrombectomy trialists collaboration. Circulation 135:143–152
- Mintz GS, Guagliumi G (2017) Intravascular imaging in coronary artery disease. Lancet 390:793–809
- Buccheri S, Franchina G, Romano S et al (2017) Clinical outcomes following intravascular imaging-guided versus coronary angiography-guided percutaneous coronary intervention with stent implantation: a systematic review and bayesian network meta-analysis of 31 studies and 17,882 patients. JACC Cardiovasc Interv 10:2488–2498
- Wang J, Yuan S, Qi JJ, Zhang QG, Ji Z (2022) Advantages and prospects of optical coherence tomography in interventional therapy of coronary heart disease (review). Exp Ther Med 23:19
- Huang DSE, Lin CP, Schuman JS, Stinson WG, Chang W, Hee MR, Flotte T, Gregory K, Puliafito CA et al (1991) Optical coherence tomography. Science 254:1178–1181
- Araki M, Park SJ, Dauerman HL et al (2022) Optical coherence tomography in coronary atherosclerosis assessment and intervention. Nat Rev Cardiol 19:684–703
- Nagaraja V, Kalra A, Puri R (2020) When to use intravascular ultrasound or optical coherence tomography during percutaneous coronary intervention? Cardiovasc Diagn Ther 10:1429–1444
- Kubo T, Shinke T, Okamura T et al (2017) Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention (OPINION trial): one-year angiographic and clinical results. Eur Heart J 38:3139–3147
- Ali ZA, Maehara A, Genereux P et al (2016) Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation (ILUMIEN III: OPTIMIZE PCI): a randomised controlled trial. Lancet 388:2618–2628
- Page MJ, McKenzie JE, Bossuyt PM et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 10:89
- 15. Sterne JAC, Savovic J, Page MJ et al (2019) RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 366:14898
- Sterne JA, Hernan MA, Reeves BC et al (2016) ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 355:i4919
- Di Giorgio A, Capodanno D, Ramazzotti V et al (2013) Optical coherence tomography guided in-stent thrombus removal in patients with acute coronary syndromes. Int J Cardiovasc Imaging 29:989–996
- Meneveau N, Souteyrand G, Motreff P et al (2016) Optical coherence tomography to optimize results of percutaneous coronary intervention in patients with non-ST-elevation acute coronary syndrome results of the multicenter, randomized DOCTORS study (does optical coherence tomography optimize results of stenting). Circulation 134:906

- 19. Sheth TN, Kajander OA, Lavi S et al (2016) Optical coherence tomography-guided percutaneous coronary intervention in ST-segment-elevation myocardial infarction: a prospective propensity-matched cohort of the thrombectomy versus percutaneous coronary intervention alone trial. Circ Cardiovasc Interv 9:e003414
- D'Ascenzo F, Iannaccone M, De Filippo O et al (2017) Optical coherence tomography compared with fractional flow reserve guided approach in acute coronary syndromes: a propensity matched analysis. Int J Cardiol 244:54–58
- Iannaccone M, D'Ascenzo F, Frangieh AH et al (2017) Impact of an optical coherence tomography guided approach in acute coronary syndromes: a propensity matched analysis from the international FORMIDABLE-CARDIOGROUP IV and USZ registry. Catheter Cardiovasc Interv 90:E46-e52
- 22. Khalifa AKM, Kubo T, Shimamura K et al (2021) Impact of optical coherence tomography imaging on decision-making during percutaneous coronary intervention in patients presented with acute coronary syndromes. Circ J 85:1781–1788
- 23. Jia HB, Dai JN, He LP et al (2022) EROSION III a multicenter RCT of OCT-guided reperfusion in STEMI with early infarct artery patency. JACC Cardiovasc Interv 15:846–856
- 24. Antonsen L, Thayssen P, Maehara A et al (2015) Optical coherence tomography guided percutaneous coronary intervention with nobori stent implantation in patients with non-ST-segment-elevation myocardial infarction (OCTACS) trial: difference in strut coverage and dynamic malapposition patterns at 6 months. Circ Cardiovasc Interv 8:e002446

- 25. Nemoto T, Minami Y, Sato T et al (2019) Contrast volume and decline in kidney function in optical coherence tomography-guided percutaneous coronary intervention. Int Heart J 60:1022–1029
- 26. Kubo T, Shinke T, Okamura T et al (2018) Comparison between Optical COherence tomography guidance and Angiography guidance in percutaneous coronary intervention (COCOA): study protocol for a randomized controlled trial. J Cardiol 72:170–175
- 27. Holm NR, Andreasen LN, Walsh S et al (2018) Rational and design of the European randomized optical coherence tomography optimized bifurcation event reduction trial (OCTOBER). Am Heart J 205:97–109
- Ali Z, Landmesser U, Karimi Galougahi K et al (2021) Optical coherence tomography-guided coronary stent implantation compared to angiography: a multicentre randomised trial in PCI design and rationale of ILUMIEN IV: OPTIMAL PCI. EuroIntervention 16:1092–1099
- 29. Yamamoto MH, Kondo S, Mizukami T et al (2022) Rationale and design of the TACTICS registry: optical coherence tomography guided primary percutaneous coronary intervention for patients with acute coronary syndrome. J Cardiol 80:505–510