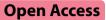
# REVIEW





Ten-year outcomes after percutaneous coronary intervention versus coronary artery bypass grafting for multivessel or left main coronary artery disease: a systematic review and meta-analysis

Shitao Feng<sup>†</sup>, Mingli Li<sup>†</sup>, Jiayue Fei, Anqin Dong, Wenli Zhang, Yanhua Fu and Yang Zhao<sup>\*</sup>

# Abstract

**Background** Short-term and long-term comparative outcomes after percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for multivessel coronary artery (MVCA) or left main coronary artery (LMCA) disease are highly debated.

**Goals** We performed a meta-analysis to evaluate the difference between PCI and CABG for the treatment of patients with MVCA or LMCA in long-term follow-up.

**Methods** Literatures were searched in PubMed, EMBASE and The Cochrane Library from January 1, 2000 to January 1, 2021, including RCTs and observational studies (OSs). The primary outcome was all-cause mortality at 10 years follow-up, and the secondary outcomes included cardiac mortality, repeated revascularization, myocardial infarction, and stroke.

**Results** A total of 5 RCTs reporting data from 3013 participants and 4 OSs of 5608 participants were included for analysis. There was no significant difference between PCI and CABG in all-cause mortality (Odds Ratio (OR) 1.03 [95% confidence interval (CI) 0.89 to 1.19]), whereas PCI was associated with higher cardiac mortality (OR 0.76 [95% CI 0.65 to 0.90]) and repeated revascularization rate comparing to CABG (OR 1.77 [95% CI 1.08 to 2.89];  $I^2 = 94.61\%$ ). The difference between PCI and CABG in repeated revascularization in either RCTs or OSs, in myocardial infarction in either RCTs or OSs were not significant. In OSs, stroke rate in PCI group was lower than those in CABG, but not in RCTs. There was a significant increase of stroke rate in CABG comparing to PCI (OR 0.65 [95% CI 0.53 to 0.80];  $I^2 = 0.00\%$ ). No significant difference between PCI and CABG in myocardial infarction was not observed (OR 0.92 [95% CI 0.64 to 1.31];  $I^2 = 57.84\%$ ).

**Conclusion** Evidence from our study and prior studies suggested the superiority of CABG over PCI in improving 5- but not 10-year survival among patients with MVCA. In the contrast, there was no significant difference between

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CABG and PCI for treating patients with LMCA in either 5- or 10-year survival rate. More long-term trials are needed to better define differences of outcome between 2 techniques.

Keywords Percutaneous coronary intervention, Coronary artery bypass grafting, Meta-analysis

## Introduction

In the past few decades, several randomized clinical trials (RCTs) have compared percutaneous coronary intervention (PCI) with coronary artery bypass grafting (CABG) in patients with multiple vessels coronary artery disease (MVCA) or left main coronary artery disease (LMCA), as CABG was associated with lower incidence of all-cause death than PCI for patients with LMCA or MVCA in 5-year follow-up [1-4]. However, conflicting results between short-term and long-term comparative outcomes were found in this field. Patients with LMCA treated by CABG did not demonstrate significant difference in the incidence of all-cause death than PCI in the 10-year data [5]. On the contrary, a newly revealed RCT failed to demonstrate the non-inferiority of fractional flow reserve-guided PCI comparing to CABG in 1-year follow-up, triggering a heated discussion with regard to the most optimal treatment between PCI and CABG in treating MVCA or LMCA [6].

The 2018 European Society of Cardiology/European Association for Cardio-Thoracic Surgery Guidelines on myocardial revascularization assigned a Class I recommendation ("is recommended") to CABG to improve outcomes among patients with LMCA or MVCA [7]. However, the supporting evidences were studies with no more than 5 years follow-up. To our best knowledge, there has been no meta-analysis of long-term (10 years) follow-up performed to compare the safety and efficacy of PCI and CABG in treating MVCA or LMCA. In this study, we comprehensively collected data and evaluated the difference in both RCTs and observational studies (OSs) that have compared PCI and CABG for the treatment of patients with MVCA or LMCA in 10-year follow-up, providing further insights into the comparative advantages of both revascularization techniques.

## Methods

All supporting data in this article are available. Literatures were comprehensively searched by 2 reviewers in PubMed, EMBASE, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology) from January 1, 2000, to January 1, 2021. Details of searching algorithm were listed in the Additional file 1. This study was directed by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines for RCTs [8], along with the Meta-Analysis of Observational Studies in Epidemiology for OSs [9], and was registered at PROS-PERO, number CRD42021247485.

We included studies comparing outcomes between PCI and CABG in treating coronary artery disease (CAD) of either MVCA or LMCA in 10 years follow-up. RCTs, prospective and retrospective OSs were all taken into consideration. Detailed selection criteria for inclusion/ exclusion were showed in the Additional file 1.

The risk of bias was evaluated by 2 independent reviewers. Cochrane risk of bias assessment was used to evaluate RCT's publication bias of including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias [10]. The quality of OSs was assessed by using the Newcastle-Ottawa Scale [11].

Titles and abstracts of all studies were collected by 2 authors from databases mentioned above. All eligible studies were screened based on the inclusion and exclusion standards in Additional file 1. Divergences were resolved by consensus. Following data were extracted: (1) study features: authors, study design, sample size and quality of studies; (2) baseline information of patients; (3) outcomes: the primary outcomes was all-cause mortality at 10 years follow-up; the secondary outcomes included cardiac mortality, repeated revascularization, myocardial infarction and stroke at 10 years follow-up. Due to the variable definitions of major adverse cardiac and cerebrovascular event (MACCE) in different studies, we did not use MACCE as a measure of outcomes in this study [4, 12].

The Comprehensive Meta-Analysis 3.0 (Biostat, Englewood, NJ) was used to perform the data analysis. Owing to the intrinsic differences between RCTs and OSs, separate analyses of these 2 types of study designs were conducted. Odds ratios (ORs) with 95% confidence interval (CI) were measured and pooled for each outcome. Thanks to the diverse clinical features and methodological differences, a random-effect model was utilized for analyses [13]. We used the Q test and the calculation of  $I^2$  for the assessment of heterogeneity between studies. Substantial heterogeneity would be considered if P < 0.05or  $I^2 \ge 50\%$ . Subgroup and sensitivity tests were performed to investigate the source of heterogeneity. Due to the heterogeneity between studies, subgroup and sensitivity tests were performed in the categorization based on lesion location of patient's baseline (LMCA or MCA) or types of PCI used in the studies(DES or BMS). Difference

between subgroups was assessed by z test, and 2-tailed P < 0.05 was regarded as statistically significant.

## Results

A total of 5 RCTs [5, 14–17] reporting data from 3013 participants and 4 OSs [18–21] of 5608 enrolled participants were included for analysis. A flowchart indicating selection strategy was showed in Fig. 1 and the baseline information of the participants was showed in Table 1. According to the Cochrane collaboration's tool, the risk of bias in RCT was rated low (Additional file 1: Table S1). Owing to low comparability, 2 out of 4 studies were calculated as 6 by the Newcastle-Ottawa scale, while the rest studies were above 6 (Additional file 1: Table S2).

## All-cause mortality

There was no significant difference between PCI and CABG in the incidence of all-cause mortality in RCTs {Odds Ratio (OR) 1.12 [95% confidence interval (CI) 0.95 to 1.33];  $I^2$ =0.00%} or cohort studies (OR 0.85 [95% CI 0.64 to 1.11];  $I^2$ =65.75%) or in total (OR 1.03 [95% CI 0.89–1.19];  $I^2$ =58.5%) (Fig. 2). And a statistical significance of OR was not observed between RCTs and OSs (P for interaction, 0.09). Due to the existence of heterogeneity, subgroup and sensitivity tests were performed in the

categorization based on lesion location of patient's baseline (LMCA or MCA) or types of stents used in the studies (DES or BMS). Significant difference between PCI and CABG in terms of LMCA (OR 0.93 [95% CI 0.72 to 1.19]) and MVCA (OR 0.99 [95% CI 0.83 to 1.19]), DES (OR 1.05 [95% CI 0.85 to 1.30]) and BMS (OR 0.83 [95% CI 0.24 to 2.83]) was not observed (Additional file 1: Tables S3 and S4).

## **Cardiac mortality**

There was a significant increase of cardiac morality rate in PCI comparing to CABG (OR 0.76 [95% CI 0.65 to 0.90];  $I^2$ =0.00%) (Fig. 3). Difference of cardiac morality between PCI and CABG in cardiac mortality in RCTs (OR 0.71 [95% CI 0.50 to 1.02];  $I^2$ =0.00%) was not observed, whereas PCI was associated with higher incidence in OSs (OR 0.78 [95% CI 0.65 to 0.94];  $I^2$ =0.00%). There was no significant difference in OR between RCTs and OSs (P for interaction, 0.66). Although statistic heterogeneity was not observed, subgroup studies were still performed to analyze potential clinical differences within studies. The results showed that there was no significant difference in cardiac mortality between PCI and CABG for LMCA (OR 0.90.95% CI 0.53 to 1.53). However, the difference in cardiac mortality between PCI and CABG

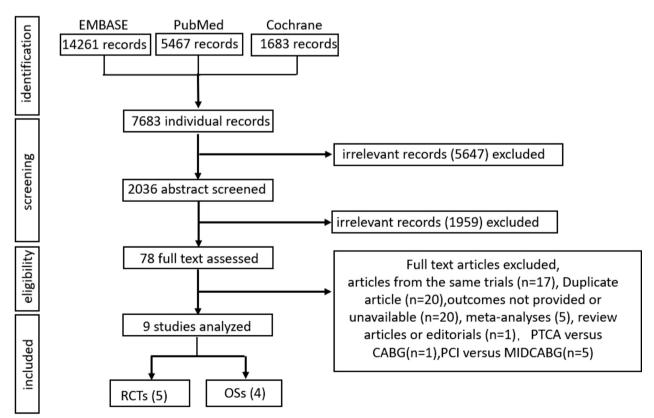


Fig. 1 Flow diagram of the research

Study	SYNTAX PCI/CABG	PRECOMBAT PCI/CABG	SOS PCI/CABG	MASS II PCI/CABG	LE MANS PCI/CABG	MAIN- COMPARE PCI/CABG	ASAN- MAIN PCI/ CABG	Nystrom2017 PCI/CABG	Yu2020 PCI/CABG
Study design	RCT	RCT	RCT	RCT	RCT	Observa- tional study	Observa- tional study	Observational study	Observational study
Type of lesion	LMCA/ MCAD	LMCA	MCAD	MCAD	LMCA	LMCA	LMCA	NR	LMCA
Patients	903/897	300/300	50/50	205/203	52/53	1102/1138	100/250	1863/683	271/201
Age	65.2 (9.7)/65.0 (9.8)	61.8 (10.0)/62.7 (9.5)	54.7 (8.8)/52.7 (9.1)	60 (9)/60 (9)	60.6 (10.5)/61.3 (8.4)	61.3 (11.7)/62.9 (9.4)	55.1 (10.4)/60.7 (9.1)	61.1 (10.5)/57.2 (10.0)	61.7 (10.3)/60.6 (8.8)
Male sex, %	76.0/79.0	76.0/77.0	80.0/78.0	67.0/72.0	60.0/73.0	70.7/72.9	60.0/74.4)	58.9/63.4	74.2 /76.1
BMI, mean	28.1 (4.8)/27.9 (4.5)	24.6 (2.7)/24.5 (3.0)	NR	NR	NR	NR	24.6 (3.1)/24.6 (2.7)	26.0 (3.9)/26.4 (4.3)	NR
Diabetes mel- litus, %	26.0/25.0	34.0/30.0	14.0/18.0	23.0/29.0	19.0/17.0	29.7/34.7	21.0/32.8	100.0/100.0	28.8/28.9
Hyperten- sion, %	69.0/64.0	54.3/51.3	54.0/42.0	61.0/63.0	75.0/70.0	49.5/49.4	23.0/50.0	NR	56.1/50.2
Hyperlipi- demia, %	79.0/77.0	42.3/40.0	46.0/50.0	NR	65.0/60.0	28.6/32.6	34.0/46.0	NR	49.8/38.8
smoker, %	18.0/22.0	29.7 /27.7	44.0/40.0	27.0/32.0	NR	25.6/29.8	36.0/27.2	14.5/15.0	48.3/46.2
previous MI ,%	32.0/34.0	4.3/6.7	38.0/36.0	52.0/41.0	36.0/32.0	8.1/11.6	14.0/16.0	47.6/54.3	17.3/26.9
Previous CVA ,%	4.0/5.0	NR	NR	NR	NR	7.1/7.3	4.0./16.0	9.6/6.6	2.2/14.4
LVEF, %	NR	61.7±8.3 /60.6±8.5	NR	67.0±8.0 /67.0±9.0	53.5±10.7/ 53.7±6.7	60.6±10.8 /57.2±11.9	60.3±9.1 /56.8±11.9	NR	64.0±8.1 /62.0.±11.1
LMCA only, %	42/357 (12%) 49/348 (14%)	9.0/11.3	NR	NR	NR	25.2/6.2	55.0/10.4	NR	19.9/7.0
LMCA + SVD, %	67/357 (19%) 71/348 (20%)	16.7/17.7	NR	NR	13.0/6.0	24.0/10.5	21.0/14.4	NR	27.3/15.9
LMCA + DVD, %	112/357 (31%) 106/348 (30%)	33.7/30.0	NR	NR	27.0/19.0	26.0/26.3	16.0/22.4	NR	30.3/25.9
LMCA + TVD, %	136/357 (38%) 122/348 (35%)	40.7/41	NR	NR	60.0/75.0	24.8/57.0	8.0/52.8	NR	22.5/51.2
2-Vessel disease, %	NR	NR	60.0./58.0	42.0/42.0	NR	NR	NR	NR	NR
3-Vessel disease, %	60.0/61.0	NR	40.0/42.0	58.0/58.0	NR	NR	NR	NR	NR
Type of stent	PES	SES	BMS	BMS	BMS/DES	BMS/DES	BMS	NR	DES

## Table 1 All studies included in the meta-analysis

Data are presented as percentage treated with PCI/percentage treated with CABG, unless otherwise stated

ASAN-MAIN ASAN Medical Center-Left MAIN Revascularization; BMI Body mass index; BMS Bare metal stent; CVA Cerebrovascular disease; CABG Coronary artery bypass graft; DVD Double-vessel disease; DES Drug-eluting stent; LMCA Left main coronary artery; LVEF Left ventricular ejection fraction; LE MANS Left Main Stenting Trail; MASS-II Medicine, Angioplasty, or Surgery Study; MAIN-COMPARE Revascularization for Unprotected Left Main Coronary ArteryStenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization; MI Myocardial infarction; NR No record; PCI Percutaneous coronary intervention; PES Paclitaxel-eluting stent; PRECOMBAT Premier of Randomized Comparison of Bypass Surgery;. Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; RCT Randomizedcontrolled trial; SVD Single-vessel disease; SES Sirolimus-eluting stent; SOS Stent or Surgery; SYNTAX Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; TVD Triple-vessel disease

Study or subgroup		Statistics for	each study	Odds ratio and 95% Cl		
Events/Total						
1. OSs	PCI	CABG	Odds ratio and 95% CI	1		
Yu 2020	63/271	51/201	0.89 [0.58,1.36]			
Nyström 2017	831/1863	364/683	0.70 [0.59,0.84]	•		
Park 2018	248/1102	251/1138	1.02 [0.84,1.25]	+		
Park 2010	0/100	6/250	0.19 [0.01,3.35]	<		
Subtatol (95% CI)	1142/3336	672/2272	0.85 [0.64,1.11]			
Heterogeneity: Tau2=0.04	; df=3 (p=0.03);l <sup>2</sup> =65.7	5%				
Test for overall effect of OS	Ss: Z=-1.20 (p=0.23)					
2.RCT						
Buszman 2016	11/52	16/53	0.62 [0.26,1.51]			
Hueb 2010	49/205	51/203	0.94 [0.60,1.47]			
Park 2020	42/300	40/300	1.06 [0.66,1.69]	- <b>-</b>		
Thuijs 2019	248/903	212/897	1.22 [0.99,1.51]	<b>•</b>		
Buszman 2009	41/50	40/50	1.14 [0.42,3.10]			
Subtatol (95% CI)	391/1510	359/1503	1.12 [0.95,1.33]	T T		
Heterogeneity: Tau2=0.00;	df=4 (p=0.55): l <sup>2</sup> =0.009	%				
Test for overall effect of RC	CT: Z=1.32 (p=0.19)					
Total(95% CI)	1533/4846	1031/3775	1.03 [0.89,1.19]	•		
Heterogeneity :Tau2=0.04;	df=8 (p=0.01);l <sup>2</sup> =58.50	%	_			
Test for overall effect betw	een RCT and OSs: Z=0	0	.1 0.2 0.5 1 2 5 10			
Test for subgroup different	: df=1 (p=0.09)			Favours PCI Favours CABG		

**Fig. 2** Forest plot of OR of the composite of All-cause Mortality at follow-up for PCI vs. CABG (*ASAN-MAIN* ASAN Medical Center-Left MAIN Revascularization; *CABG* Coronary artery bypass graft; *LE MANS* Left main stenting trail; *MASS-II* Medicine, Angioplasty, or Surgery Study; *MAIN-COMPARE* Revascularization for unprotected left main coronary artery stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization; *OSs* Observational study; *PCI* Percutaneous coronary intervention; *PRECOMBAT* Premier of randomized comparison of bypass surgery; Angioplasty using sirolimus-eluting stent in patients with left main coronary artery disease; *RCT* Randomized controlled trial; *SOS* Stent or surgery; *SYNTAX* Synergy between percutaneous coronary intervention with TAXUS and cardiac surgery)

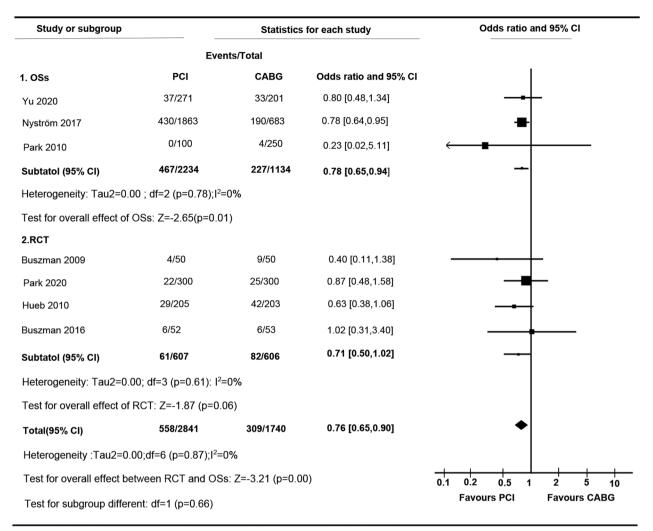
for MVCA was statistically significant (OR 0.59 [95% CI 0.37 to 0.95]) (Additional file 1: Table S3).

## **Repeated revascularization**

PCI was associated with higher rate of repeated revascularization rate comparing to CABG (OR 1.77 [95% CI 1.08 to 2.89];  $I^2 = 94.61\%$ ) (Fig. 4). The rate of repeat revascularization between PCI and CABG was not significantly different in RCTs (OR 1.54 [95% CI 0.89 to 2.67] ;  $I^2 = 67.9\%$ ) and OSs (OR 2.40 [95% CI 0.95 to 6.03] ;  $I^2 = 97.1\%$ ). There was no significant difference in OR between RCTs and OSs (P for interaction, 0.42). Subgroup tests were performed owing to heterogeneity, showing that no substantial difference between LMCA (OR 1.38 [95%, 0.51 to 3.78]) and MVCA (OR 1.77 [95%, 0.62 to 5.07]) was detected (Additional file 1: Tables S3 and S4). In contrast to DES (OR 1.40 [95% CI 0.68 to 2.87]), BMS was associated with higher incidence of repeated revascularization than CABG in OSs (OR 4.16 [95% CI 3.07 to 5.64]).

## Stroke

There was a significant increase of stroke rate in CABG comparing to PCI (OR 0.65 [95% CI 0.53 to 0.80];  $I^2 = 0.00\%$ ) (Fig. 5). In cohort studies, incidence of stroke in PCI group was lower than those in CABG (OR 0.64



**Fig. 3** Forest plot of OR of the composite of Cardiac Mortality at follow-up for PCI vs. CABG (*ASAN-MAIN* ASAN Medical Center-Left MAIN Revascularization; *CABG* Coronary artery bypass graft; *LE MANS* Left main stenting trail; *MASS-II* Medicine, Angioplasty, or Surgery Study; *OSs* Observational study; *PCI* Percutaneous coronary intervention; *PRECOMBAT* Premier of randomized comparison of bypass surgery; Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RCT* Randomized controlled trial; *SOS* Stent or surgery)

[95% CI 0.51 to 0.80];  $I^2 = 0.00\%$ ), whereas no significant difference between PCI and CABG in RCT was observed (OR 0.77 [95% CI 0.44 to 1.37]; I=0.00%). Difference of OR was not observed between RCTs and OSs (P for interaction, 0.54). In subgroup studies, there was not significant difference between LMCA (OR 0.78 [95% CI 0.29 to 2.12]) and MVCA (OR 0.77 [95% CI, 0.38 to 1.55]) (P = 1.00) (Additional file 1: Table S3) (Fig. 5).

## Myocardial infarction

No significant difference between PCI and CABG in myocardial infarction in RCTs (OR 0.84 [95% CI, 0.49 to 1.44];  $I^2 = 58.30\%$ ) or cohort studies (OR, 0.99 [95% CI 0.61 to 1.59];  $I^2 = 68.02\%$ ), or in total (OR 0.92 [95% CI 0.64 to 1.31];  $I^2 = 57.84\%$ ) was not observed. Statistical

difference of OR was not observed between RCTs and cohort studies (P for interaction, 0.67). Due to the existence of heterogeneity, subgroup tests were performed. Comparing to PCI, CABG was associated with higher rate of myocardial infarction in MVCA (OR 0.57 [95% CI 0.25 to 0.92]), while there was no significant difference between PCI and CABG in LMCA (OR 0.78 [95%, 0.29 to 2.12]). Significant difference was observed between LMCA and MVCA (P=0.01) (Additional file 1: Table S4) (Fig. 6).

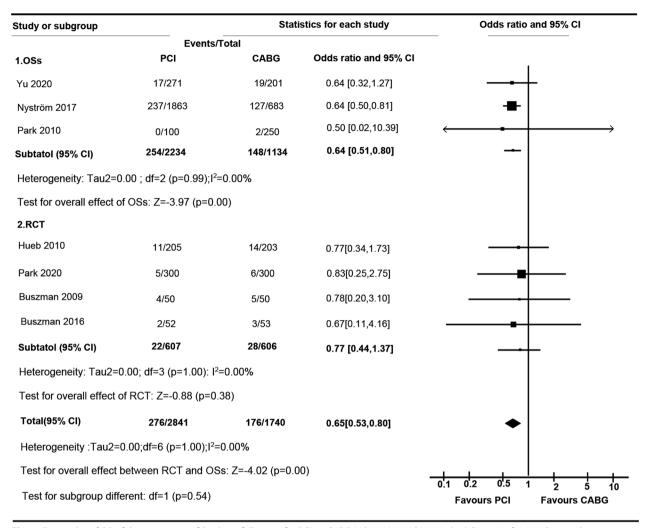
### Discussion

To our best knowledge, our study is the first meta-analysis to present 10-year comparative outcomes between PCI and CABG for treating patients with either LMCA

Study or subgroup		Statistics	s for each study	Odds ratio and 95% Cl		
	Events/Total					
1. OSs	PCI	CABG	Odds ratio and 95% Cl			
Yu 2020	74/271	57/201	0.95 [0.63 1.43]	-+-		
Nyström 2017	1222/1863	166/683	5.94 [4.87,7.25]	+		
Park 2018	435/1102	298/1138	1.84 [1.54,2.20]	+		
Park 2010	2/100	1/250	5.08 [0.46,56.68]	<b>_</b> →		
Subtatol (95% CI)	1733/3336	522/2272	2.40 [0.95,6.03]			
Heterogeneity: Tau2=0.7	72 ; df=3 (p=0.00) ; l²=9	97.09%				
Test for overall effect of	OSs: Z=1.87 (p=0.06)					
2.RCT						
Buszman 2016	14/52	17/53	0.78 [0.34,1.81]			
lueb 2010	86/205	80/203	1.11 [0.75,1.65]			
Park 2020	48/300	24/300	2.19 [1.30,3.68]			
3uszman 2009	21/50	9/50	3.30 [1.32,8.23]	<b></b>		
Subtatol (95% CI)	169/607	130/606	1.54 [0.89,2.67]	<b></b>		
Heterogeneity: Tau2=0.2	20; df=3 (p=0.03): l <sup>2</sup> =6	7.94%				
Test for overall effect of	RCT: Z=1.54 (p=0.12)					
Total (95% CI)	1902/3943	652/2878	1.77 [1.08,2.89]	-		
Heterogeneity :Tau2=0.	61;df=7 (p=0.00);l <sup>2</sup> =94	.61%				
Test for overall effect be	etween RCT and OSs:	Z=2.27 (p=0.02)		0.1 0.2 0.5 1 2 5 10 Favours PCI Favours CABG		
Test for subgroup differ	ent: df=1 (p=0.42)					

**Fig. 4** Forest plot of OR of the composite of Repeated Revascularization at follow-up for PCI vs. CABG (ASAN-MAIN ASAN Medical Center-Left MAIN Revascularization; *CABG* Coronary artery bypass graft; *LE MANS* Left main stenting trail; *MASS-II* Medicine, Angioplasty, or Surgery Study; *MAIN-COMPARE* Revascularization for unprotected left main coronary artery stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization; *OSs* Observational study; *PCI* Percutaneous coronary intervention; *PRECOMBAT* Premier of randomized comparison of bypass surgery; Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RCT* Randomized controlled trial; *SOS* Stent or surgery)

or MVCA. We tried to overcome potential problems that might weaken the credibility of clinical evidence in previous studies. For example, in a meta-analysis of left main coronary artery, data from OSs and RCTs was pooled together without classification, leading to a less credible conclusion due to the internal difference between 2 types of studies [22]. For the same reason, unlike obscure definition of CAD in a meta-analysis involving 23 RCTs, we primarily focused on CAD with LMCA or MVCA, which is more clinical applicable [23]. In our study, after 10-year follow-up, there was no significant difference of all-cause mortality rate between PCI and CABG in treating MVCA or LMCA in both RCTs and OSs group, as well as in subgroups categorized by lesion locations or types of PCI. In our subgroup analysis of mortality, PCI was not associated with better outcome in either LMCA or MVCA subgroups. Previous publications showed that CABG had a mortality benefit over PCI among patients with MVCA, but not among patients with LMCA in both short-term and long-term follow-up studies [5, 24]. Combining the results from our



**Fig. 5** Forest plot of OR of the composite of Stroke at follow-up for PCI vs. CABG (*ASAN-MAIN* ASAN Medical Center-Left MAIN Revascularization; *CABG* Coronary artery bypass graft; *LE MANS* Left main stenting trail; *MASS-II* Medicine, Angioplasty, or Surgery Study; *OSs* Observational study; *PCI* Percutaneous coronary intervention; *PRECOMBAT* Premier of Randomized Comparison of Bypass Surgery; Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RCT* Randomized controlled trial; *SOS* Stent or surgery)

study and prior studies, it showed that CABG improved 5-year survival but not 10-year survival among patients with MVCA. In the contrast, there was no significant difference between CABG and PCI for treating patients with LMCA in either 5-year or 10-year survival rate.

Different results between our studies and previous studies in terms of all-cause death rate could be explained by the discrepancy of patients' lesion complexity in the 2 groups. For example, an included study showed that CABG group has higher rates of myocardial infarction history, left main plus triple-vessel disease and chronic total occlusion than PCI group [20]. The same situation appeared in another 2 included studies, as patients undergoing CABG were with higher clinical and anatomic risk factor profiles than those treated by PCI [18, 19]. Thus,

the therapeutic effect of CABG might be underpowered due to the fact that the lesion of CAD among patients treated by CABG was often associated with higher-risk clinical and angiographic situation than that among those treated by PCI [15, 21]. Except Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trail and Left Main Stenting (LE MANS) trail, other included studies were lack of syntax score evaluation, especially in the observational studies, leading to a unquantifiable and unstandardized process for patients' selection.

In addition, comparing to CABG, our results suggested that PCI was associated with higher incidence in cardiac mortality, but with lower incidence of cardiac death among patients with MVCA. These findings contradicted

Study or subgroup		Statistic	Statistics for each study		
Events/Total					
1.OSs	PCI	CABG	Odds ratio and 95% Cl		
Yu 2020	54/271	29/201	1.48 [0.90,2.42]	┼╼╌	
Nyström 2017	502/1863	224/683	0.76 [0.63,0.91]	-	
Park 2010	8/100	21/250	0.95 [0.41,2.22]		
Subtatol (95% CI)	<b>CI)</b> 564/.2034 274/113		0.99 [0.61,1.59]	_	
Heterogeneity: Tau2=0	0.12 ; df=2 (p=0.04);l <sup>2</sup>	2=68.02%			
Test for overall effect of	of OSs: Z=-0.06 (p=0.	95)			
2.RCT					
Hueb 2010	27/205	42/203	0.58 [0.34,0.99]		
Park 2020	87/300	72/300	1.29 [0.90,1.86]	┼┳╌	
Buszman 2016	6/52	6/53	1.02 [0.31,3.40]	<b> </b>	
Buszman 2009	5/50	9/50	0.51 [0.16,1.64]	<b>e</b>	
Subtatol (95% CI)	125/607	129/606	0.84 [0.49,1.44]	_ <b>-</b> +	
Heterogeneity: Tau2=	1.16; df=3 (p=0.07): l <sup>2</sup>	2=58.29%			
Test for overall effect of	of RCT : Z=-0.63 (p=0	).53)			
Tota(95% CI)	689/2841	403/1740	0.92 [0.64,1.31]	+	
Heterogeneity :Tau2=	0.08;df=6 (p=0.03);l <sup>2</sup>	=57.84%			
Test for overall effect	between RCT and OS	Ss : Z=-0.46 (p=0.65	)		
Test for subgroup diffe	erent:df=1 (p=0.67)				

**Fig. 6** Forest plot of OR of the composite of Myocardial Infarction at follow-up for PCI vs. CABG (*ASAN-MAIN* ASAN Medical Center-Left MAIN Revascularization; *CABG* Coronary artery bypass graft; *LE MANS* Left main stenting trail; *MASS-II* Medicine, Angioplasty, or Surgery Study; *OSs* Observational study; *PCI* Percutaneous coronary intervention; *PRECOMBAT* Premier of randomized comparison of bypass surgery; Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; *RCT* Randomized controlled trial; *SOS* Stent or surgery)

the common perception based on the evidence from 5-year data of SYNTAX trail [25]. Following reasons may play roles in the explanation of this contradiction. Firstly, after investigation for underlying reasons, we identified an included OS which only enrolled diabetic patients might affect the effect size of final result [21]. Except this study, only  $20 \sim 30\%$  candidates in the PCI and CABG group from other 2 included studies had diabetes. We did sensitivity test by excluding the study that primarily focused on diabetic patients [26]. After the exclusion of that study, we found that there was no difference

between PCI and CABG in cardiac mortality, which was in line with previous findings. Secondly, the application of dual antiplatelet therapy after PCI was found to reduce the incidence of death and myocardial infarction in some measure, causing the equivalent cardiac death rate between PCI and CABG [27].

Our results in terms of lower incidence of stroke in PCI group at 10-year follow-up was consistent with previous findings from an individual patient data meta-analysis of 11 RCTs at 3.3-year follow-up, showing that CABG had a significantly higher stroke incidence at 5-year

follow-up [28]. Multifactor were likely to contribute to the increased risk of stroke with CABG. The usage of onpump and off-pump in surgical procedures, intra-operative hypoperfusion, strategies for post-operative bleeding control and post-operative atrial fibrillation might lead to higher stroke risk with surgery. However, in the latest revealed RCT comparing PCI to CABG, there were no obvious differences of stroke rate between 2 groups, as the usage of postoperative double-antiplatelet rates reached up to 45% which was higher or at least consistent with data from previous large RCTS [6]. In our subgroup study, we also found that BMS was associated with higher incidence of repeated revascularization than DES, which is in line with findings from previous publications [29, 30].

## Limitation

Few limitations including the synthesis of heterogeneous trials in terms of variable study design and characteristics were detected. For this reason, we utilized random-effects model and heterogeneity test to reduce statistics bias. What's more, there was one included RCTwith  $9.6 \pm 0.85$  years follow-up on average [14], and another included OS with candidates who were all diabetic and MVCA patients [21]. We performed sensitivity and subgroup analyses showing that all results remained robust when excluding these 2 studies. Besides, thanks to limited numbers of studies and data in this area, we were unable to perform meta-regression to find clinical predictors for better outcomes after treatment. SYNTAX score has been considered as an important predictor for higher survival rate as both 5-year individual data from 11 RCTs and 10-year data from SYNTAX trail confirmed that CAD patients with SYNTAX score  $\geq$  33 treated by CABG had lower mortality rate than PCI [5, 24]. However, only 2 included trails had SYNTAX score so that we were unable to further explore the impact of SYNTAX score on the patients' outcome after treated by PCI or CABG.

## Conclusion

Evidence from our study and prior studies suggested the superiority of CABG over PCI in improving 5- but not 10-year survival among patients with MVCA. In the contrast, there was no significant difference between CABG and PCI for treating patients with LMCA in either 5- or 10- years survival rate.

### Abbreviations

BMS	Bare metal stent
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CI	Confidence interval
DES	Drug-eluting stent

 LMCA
 Left main coronary artery

 MACCE
 Major adverse cardiac and cerebrovascular event

 MVCA
 Multivessel coronary artery

 OSs
 Observational studies

 RCT
 Randomized controlled trial

### Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-023-02101-y.

Additional file 1. Supplemental material.

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None.

#### Author contributions

YZ designed this work. STF searched the articles. STF, LML, and JYF performed the data extraction and statistical analyses. STF and LML wrote this article. AQD, WLZ and FYH participated in the production of Figs. 1, 2, 3, 4, 5 and 6. All authors read and approved the final manuscript.

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#### Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Declarations

#### Ethics approval and consent to participate

This is a meta-analysis and ethics approval and consent to participate are not required.

### **Consent for publication**

This is a meta-analysis and consent for publication is not required.

#### **Competing interests**

The authors declare that they have no competing interests.

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