Comparison of Percutaneous Coronary Intervention and Optimal Medical Therapy on Outcomes in Patients with Chronic Coronary Total Occlusion

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Abstract

Background: Nowadays the optimal strategy for patients with chronic total occlusion (CTO) has not been well established. This meta-analysis aims to evaluate effect of PCI and optimal medical therapy (OMT) on clinical outcomes in these patients.

Methods: Pubmed, Embase and Cochrane Library were searched for studies about patients who had CTO and received PCI or medical therapy as initial strategy, from inception to February 2020. Results of pooled analysis were expressed by risk ratios (RR) and 95% confidence intervals (CI), which were calculated by random effects or fixed effects model according to heterogeneity. Sensitivity analysis was performed by removing one study a time. Funnel plot and Egger's value were used to appraise publication bias. All analysis were calculated by Revmen5.0 and Stata15.0 software.

Results: Total 11 studies were included in our meta-analysis, 4 RCTs and 7 observation studies using PSM. Total 5664 patients with CTO were enrolled. 2904 patients underwent PCI and 2760 patients received OMT. Pooled analysis indicated that compared with OMT, PCI was associated with lower risk of cardiac death (RR 0.59, 95% CI 0.45-0.77, $P < 0.001$). However, there was no significant discrimination in MACE (RR 0.83, 95% CI 0.64-1.06, $P = 0.14$), myocardial infarction (RR 0.98, 95% CI 0.78-1.24, $P = 0.86$), repeat revascularization (RR 0.95, 95% CI 0.71-1.25, $P = 0.71$), and stroke (RR 0.62, 95% CI 0.29-1.34, $P = 0.22$). Sub-analysis by ethnicity showed that PCI was associated with lower incidence of MACE compared with OMT in West European (RR 0.48, 95% CI 0.28-0.84, $P = 0.01$), but not in East Asian (RR 0.94, 95% CI 0.77-1.16, $P = 0.58$).

Conclusions: Compared with OMT, PCI is associated with lower risk of cardiac death. However, there was no significant difference in MACE, MI, repeated revascularization and stroke. Sub-analysis indicates that PCI is favor of West European.

Background:

Chronic coronary total occlusion (CTO) is defined as TIMI flow grade 0 in a coronary artery lasting over 3 months. Prevalence of CTO in patients undergoing PCI is around 18 ~ 30%^[1-3], but this data is increasing with the popularity of angiography. Some studies indicate that patients with CTO are associated with worse outcomes^[4, 5]. Presence of CTO in STEMI patients increase nearly 4 times cardiovascular mortality^[4]. Besides, CTO in stable coronary heart disease is related to greater mortality^[5] and more ventricular arrhythmia occurrence^[6]. Percutaneous coronary intervention (PCI) of CTO is a challenge for interventional cardiologists with low successful revascularization rate more procedural complications, greater radiation exposure^[7], and high cost^[8]. In real word, only a small proportion of patients receive PCI therapy^[9]. NCDR register showed about 4% CTO patients undergoing PCI^[7]. Up to data, the treatment strategies of CTO are debated. According to 2018 ESC guideline^[10], PCI for CTO patients carries a class IIa and level of evidence B recommendation. However, recently some studies indicate that successful PCI of CTO would reduce mortality^[11-14], but majority of these studies just compare successful and failed PCI among CTO patients. While data about comparison of PCI and optimal medical therapy (OMT) are scant, and conclusions remain vague. Some studies suggest that compared with OMT, PCI for CTO patients relieve angina symptoms, improve life quality^[15] and reduce mortality^[16, 17]. To the contrast, other studies are disagreed with these outcomes^[18-21]. Therefore, this systemic review and meta-analysis aims to compare the outcomes of PCI versus OMT as strategy for CTO and further offer more comprehensive understandings for physicians.

Methods:

Search strategy

This meta-analysis was conducted according to the PRISMA statements^[22]. We searched studies about comparison of PCI versus medical therapy in patients with CTO in Pubmed, Embase, Cochrane Library databases separately, from inception to February 2020. Language was restricted to English. Following key terms were used in search, including: coronary chronic total occlusion, percutaneous coronary intervention, cardiac catheterization, revascularization, recanalization, conservational therapy, medical therapy. The search formula is provided in detail in the supplement 1.

Studies fulfilled the following criteria can be included in this meta-analysis: (1) Randomized controlled study or observation study; (2) observation study must use the propensity score matched (PSM) analysis; (3) studies compared different strategies of PCI versus OMT; (4) studies include clinical outcomes. Studies were excluded: (1) patients with no CTO; (2) compare successful and failed PCI; (3) patients with acute myocardial infarction concurrent CTO in non-IRA; (4) observation not use PSM analysis; (5) studies in other language.

Data extraction:

Two reviewers separately extracted detailed data from enrolled studies including: first author; publication year; ethnicity; sample size; follow up duration; age; sex; hypertension; diabetes mellitus; dyslipidemia; smoking; previous MI; previous PCI; previous CABG; CKD; stroke; LVEF (%); location of CTO using pre-specified data extraction form. Disagreement was solved by consensus.

Outcomes pooled in our meta-analysis include MACE; cardiac death; myocardial infarction (MI); repeat revascularization; stroke. MACE was defined by each study.

Quality assessment of studies

Cochrane collaboration’s risk of bias tool was used for assessing RCT included in our study, including: Random sequence generation; Allocation concealment; Blinding of participants and personnel; Blinding of outcome assessment; Incomplete outcome data; Selective reporting; Other bias.

Other observation studies were assessed by The Newcastle-Ottawa Scale^[23], including Representativeness of the exposed cohort; Selection of the non-exposed cohort; Ascertainment of exposure; Outcome of interest not present at start of study; Comparability; Assessment of outcome; Adequacy of duration of follow-up; Adequacy of completeness of follow-up.

Statistic analysis

All analysis was performed by Revmen5.0 and Stata15.0 software. Pooled outcomes were presented by Risk ratio (RR) and 95% confidence interval (CI). Heterogeneity of the summary study was assessed by Cochran’s Q test and I² statistic. If p value of Cochran’s Q test <0.1 and I²>50%, we consider existence of heterogeneity. When heterogeneity exist, pooled RR was calculated by the random effect model, otherwise, RR was calculated by fixed effect model. Sensitivity analysis was carried to explore the source of heterogeneity by sequentially removing one study a time. Visual funnel plots were used to evaluate publication bias. Egger’s test was conducted to assess for publication bias. If p value of Egger’s test <0.1, publication bias was considered to exist. All tests were two-tailed, significance was considered if p value <0.05.

Results:

1. Search results and baseline characteristics of patients

Study selection procedure was detailedly proscribed in Fig1. Total 641 studies were found after excluding the duplicate records. 519 studies were excluded after reading titles and abstracts,. 111 of the remained 122 studies were excluded after reading full text. Eventually 11 studies were identified in our meta-analysis, which involves 4 RCTs and 7 observation studies. 5 of 11 studies were conducted in Europe, 3 were in China and 3were in Korea. Given to the ethnic difference, 5 of all are west European while 6 are east Asian. Baseline characteristics of all studies were available except the IMPACTOR-CTO trial. The baseline characteristics of IRCTO trial were not analysed by PSM method, while clinical outcomes were analysed by PSM method. Our analysis includes total 5664 CTO patients, of whom 2904 patients received PCI therapy and 2760 patients received OMT therapy. The baseline characteristics of included studies were showed in Table1.

Table 1											
Baseline characteristics in PCI vs OMT arms											
Study ID	Years	Ethicity	Number of Population		Follow up (Months)	Age(years)		Male		Hypertension	
			PCI	OMT		PCI	OMT	PCI	OMT	PCI	OMT
Choi SY	2017	Asian	158	158	60M	64±9	64±11	117 (74.1)	113 (71.5)	107 (67.7)	111(70.3)
Lee SW	2018	Asian	417	398	36M	62.2 ±10.2	62.9±9.9	344(83.3)	319(81.6)	262(63.4)	238(60.9)
Yang JH	2016	Asian	533	533	45.8M	63.5±10.3	64.5±11.4	425 (79.7)	419 (78.6)	348 (65.3)	350 (65.7)
Gao L	2018	Asian	80	80	47.2M	64.76 ± 9.58	64.55 ± 11.24	56(70)	58(72.5)	54(67.5)	55(68.8)
Gao L*	2019	Asian	286	286	43.2M	63.3±9.6	63.4±10.5	207 (72.4)	217 (75.9)	199 (69.6)	188 (65.7)
Yan YF	2019	Asian	118	118	45M	62.00 (54.50-67.00)	58.00 (51.00-68.75)	90 (76.3)	93 (78.8)	84 (71.2)	79 (66.9)
Choo EH	2018	Asian	264	264	26.4M	61.5 ± 09.8	61.5 ±10.5	199 (75.4)	201 (76.1)	156 (59.1)	159 (60.2)
Obedinskiy	2018	West-European	39	33	1M	N	N	N	N	N	N
Werner GS	2018	West-European	259	137	12M	65.2±9.7	64.7±9.9	215 (83.0)	118 (86.1)	189 (73.0)	98 (71.5)
Ladwiniec A	2015	West-European	294	294	60M	64.3±10.0	63.9±10.2	220 (74.8)	220 (74.8)	159 (54.1)	157 (53.4)
Mashayekhi K	2018	West-European	101	104	12M	65 (57–72)	68 (61–74)	91 (90.1)	90 (86.5)	81 (80.2)	93 (89.4)

Study ID	Diabetes Mellitus		Dyslipidemia		Smoking		Previous MI		Previous PCI		Previous CABG	
	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT
Choi SY	78 (49.4)	72 (45.6)	51 (32.3)	49 (31.0)	79 (50.0)	94(59.5)	N	N	N	N	N	N
Lee SW	132 (32.0)	134(34.3)	249(60.3)	217(55.5)	125(30.3)	102(26.1)	45 (10.9)	34(8.7)	64(15.5)	75(19.2)	4(1.0)	5(1.3)
Yang JH	252 (47.3)	242 (45.4)	143 (26.8)	139 (26.1)	168 (31.5)	156 (29.3)	146 (27.4)	144 (27.0)	142 (26.6)	142 (26.6)	N	N
Gao L	24(30)	22(27.5)	42(52.5)	41(51.2)	32(40)	35(43.8)	21(26.3)	20(25.0)	5(6.3)	10(12.5)	N	N
Gao L*	107 (37.4)	103 (36.0)	213 (74.5)	210 (73.4)	112 (39.2)	111 (38.8)	111 (38.8)	127 (44.4)	35 (12.2)	40 (14.0)	N	N
Yan YF	118 (100%)	118 (100%)	59 (50.0)	61 (51.7)	68 (57.6)	66 (55.9)	66 (55.9)	67 (56.8)	50 (42.4)	57 (48.3)	N	N
Choo EH	117 (44.3)	121 (45.8)	N	N	71 (26.9)	64 (24.2)	N	N	N	N	N	N
Obedinskiy	N	N	N	N	N	N	N	N	N	N	N	N
Werner GS	85 (32.8)	40(29.2)	210 (81.1)	111 (81.0)	190 (73.4)	92 (67.2)	59 (22.8)	25 (18.3)	145 (56.0)	71 (51.8)	34 (13.1)	10 (7.7)
Ladwiniec A	62 (21.1)	53 (18.0)	146 (49.7)	135 (45.9)	56 (19.1)	62 (21.1)	151 (51.4)	143 (48.6)	18 (6.1)	24 (8.2)	N	N
Mashayekhi K	32 (31.6)	31 (29.8)	N	N	23 (22.8)	21 (20.2)	39 (38.6)	38 (36.5)	28 (27.7)	33 (31.7)	12 (11.9)	14 (13.7)

Study ID	CKD		Stroke		LVEF(%)		LAD		LCX		RCA	
	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT	PCI	OMT
Choi SY	14 (8.9)	13 (8.2)	21 (13.3)	17 (10.8)	50±12	50±12	52 (32.9)	49 (31)	45 (28.5)	43 (27.2)	73 (46.2)	78 (49.4)
Lee SW	6(1.5)	5 (1.3)	29 (7.0)	31 (7.9)	57.3±9.8	57.6±9.1	185(44.8)	163 (41.7)	42(10.2)	42 (10.7)	186(45.0)	186 (47.6)
Yang JH	46 (8.6)	47 (8.8)	47 (8.8)	45 (8.4)	55.6±11.9	55.7±11.7	152 (28.5)	146 (27.4)	170 (31.9)	174 (32.6)	288 (54.0)	293 (55.0)
Gao L	12(15.0)	12(15.0)	7(8.8)	8(10.0)	53.70 ± 8.29	53.63± 7.21	30(36.1)	26(31.3)	19(22.9)	22(26.5)	34(41.0)	35 (42.2)
Gao L*	19 (6.6)	21 (7.3)	N	N	54.6±7.8	53.6±8.2	112 (39.2)	103 (36.0)	65 (22.7)	60 (21.0)	132 (46.2)	146 (51.0)
Yan YF	4 (3.4)	4 (3.4)	7 (5.9)	6 (5.1)	62.00 (57.00-68.00)	61.50 (53.10-67.00)	33 (28.0)	36 (30.5)	31 (26.3)	33 (28.0)	54 (45.8)	49 (41.5)
Choo EH	26 (9.8)	26 (9.8)	25 (9.5)	24 (9.1)	54.8± 11.3	53.6 ± 12.3	84 (31.8)	80 (30.3)	66 (25.0)	72 (27.3)	124 (47.0)	118 (44.7)
Obedinskiy	N	N	N	N	N	N	N	N	N	N	N	N
Werner GS	N	N	N	N	54.5±10.8	55.7±10.8	66 (25.5)	38 (27.0)	28(10.8)	22 (15.6)	165 (63.7)	81 (57.4)
Ladwiniec A	59 (20.1)	64 (21.8)	17 (5.8)	20 (6.8)	213 (72.5)	220 (74.8)	N	N	N	N	N	N
Mashayekhi K	N	N	5 (5.0)	9 (8.6)	N	N	23 (22.8)	17 (16.3)	20 (19.8)	16 (15.4)	58 (57.4)	71 (68.3)

Data are expressed as mean ± SD or absolute numbers (%).

MI: myocardial infarction; PCI:percutaneous coronary intervention; OMT: optimal medical therapy; CABG: coronary artery bypass grafting; CKD: chronic kidney disease; LVEF: left ventricular ejection fraction; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; N: null.

CKD in Ladwiniec A et al study is CKD≥3 stage, LVEF defined in Ladwiniec A et al study is ≥50%

Quality assessment of 4 RCTs were low-to-moderate quality, while, 7 observation studies were moderate quality. Detailed description was showed in supplement 2.

2. Meta-Analysis

2.1 Comparison of PCI vs. OMT in MACE

There were 10 studies reporting the MACE event. Pooled analysis showed that patients with CTO who received PCI had no significant difference in risk of MACE compared with OMT (RR 0.83, 95% CI 0.64-1.06, P=0.14). However, there was a discrepancy in ethnicity. Sub-analysis by ethnicity indicated that PCI is associated with lower incidence of MACE compared with OMT in west European (RR 0.48, 95% CI 0.28-0.84, P=0.01), but not in east Asian (RR 0.94, 95% CI 0.77-1.16, P=0.58). Shown in Fig2.

2.2 Comparison of PCI vs. OMT in cardiac death

There were 9 studies reporting the cardiac death event. Pooled analysis indicated that compared with OMT, PCI had a lower risk of cardiac death in patients with CTO (RR 0.59, 95%CI 0.45-0.77, P<0.001). Result of sub-analysis by ethnicity was in consistence with the main result. However, there was more reduction risk of cardiac death in west European compared with east Asian (east Asian: RR0.67, 95% CI 0.49-0.90, P=0.009; west European: RR0.40, 95% CI 0.22-0.71, P=0.002). Shown in Fig3.

2.3 Comparison of PCI vs. OMT in myocardial infarction

There were 10 studies reporting outcomes of myocardial infarction. When pooled analysis of all studies, we found that there was no significant difference between PCI and OMT in terms of myocardial infarction (RR 0.98, 95%CI 0.78-1.24, P=0.86). Result of sub-analysis according to ethnicity conformed with main results (east Asian: RR 1.13, 95% CI 0.84-1.51, P=0.42; west European: RR 0.75, 95% CI 0.51-1.12, P=0.16). Shown in Fig4.

2.4 Comparison of PCI vs. OMT in repeated revascularization

Outcomes of revascularization were reported in 10 studies. Pooled analysis illustrated that there was no significant difference between PCI and OMT regarding repeated revascularization (RR 0.95, 95%CI 0.71-1.25, P=0.71). Sub-analysis showed that whatever west European or east Asian, risk of revascularization is similar between PCI and OMT (east Asian: RR 1.08, 95% CI 0.81-1.45, P=0.59; west European: RR 0.58, 95% CI 0.30-1.13, P=0.11). Shown in Fig5

2.5 Comparison of PCI vs. OMT in stroke

There were 4 out of 11 studies report outcomes of stroke. Pooled analysis demonstrated that there were no significant difference between PCI and OMT in terms of stroke (RR 0.62, 95%CI 0.29- 1.34, P=0.22). Result of sub-analysis by ethnicity is similar to main results (east Asian: RR 0.64, 95% CI 0.26-1.56, P=0.33; west European: RR 0. 55, 95% CI 0.11-2.69, P=0.46). Shown in Fig6.

3. Heterogeneity, sensitivity analysis and Publication bias

There was significant heterogeneity in MACE and repeat revascularization with I^2 was 64% and 55% correspondingly. We conducted a sensitivity analysis by removing one study a time to locate the origin of heterogeneity. We found that pooled RR of MACE was dramatically changed after removing Gao (2018) study (RR0.78, 95%CI 0.62-0.98, P=0.04). AS for repeat revascularization, there was no significant change in the overall RR. For significant heterogeneity existed in MACE, we performed a subgroup analysis by ethnicity. And we found that significant heterogeneity still existed in Asian (I^2 of MACE and Revascularization was 54% and 55% separately in east Asian), but no significant heterogeneity in west European (I^2 of MACE and Revascularization was 34% and 42% separately in west European).

There no publication bias measured by Egger's value and funnel plots in our analysis. Detailed has been shown in Table2 and Figure7.

Table2. Test of association, Heterogeneity analysis and Publication bias

Outcome	N	Test of association			Heterogeneity analysis			Publication bias	
		RR (95% CI)	P value	Model	Q value	P value	I^2 (%)	Egger's P	
MACE	10	0.83(0.64-1.06)	0.14	R	25.11	0.003	64%	0.952	
Cardiac Death	9	0.59 (0.45-0.77)	0.0001	F	8.05	0.43	1%	0.918	
Myocardial Infarction	10	0.98 (0.78- 1.24)	0.86	F	14.1	0.12	36%	0.761	
Repeat Revascularization	10	0.95 (0.71- 1.25)	0.71	R	19.85	0.02	55%	0.109	
Stroke	4	0.62 (0.29- 1.34)	0.22	F	0.74	0.86	0%	0.73	

R: random effect model; F: fixed effect model

Discussion:

This meta-analysis demonstrated that compared with OMT, PCI was associated with lower cardiac death in patients with CTO. However, there was no significant difference between PCI and OMT therapy regarding MACE, MI, repeat revascularization and stroke. Subgroup analysis according to ethnicity indicated that patients with CTO who received PCI therapy could reduce 52% MACE in West European, but not in East Asian. As for cardiac death, PCI could decrease about 60% cardiac death in west European while just 30% in east Asian when compared with OMT.

As showed by COURAGE trial^[24] that there was no reduction in mortality and MI incidence for CTO patients with stable coronary artery disease who accepted PCI strategy, while PCI could provide a notable improvement in health status. Besides, results from another study indicated that compared with OMT, PCI had no association with lower mortality and cardiac death, but CTO patients were excluded in this study^[25]. That was different with our study population. Recently a meta-analysis demonstrated successful PCI could reduce long-term mortality and the risks of MI, MACE, and CABG, compared with failed PCI for patients with CTO^[26]. As we all known, CTO revascularization procedure is complex with low successful rate. There were more peri-operative complications for failed PCI^[7, 27]. Data from two studies suggested that PCI failure was an independent predictor of worse outcomes^[28, 29]. Apart from that, standard antiplatelet therapy after successful PCI may contribute to better prognosis. These may result in overestimation for the benefit of successful PCI.

A recent meta-analysis^[30], including 5 observation studies, compared PCI and OMT therapy in patients with CTO. Results stated that PCI could improve survival and reduce MACE, which are not consistence with our results. That may be interpreted that more studies were included in our study with a significant greater population. 4 out of 11 studies included in our analysis are RCTs, which is not included in Ma et al study^[30]. EXPLORE trial^[31] suggested that PCI for patients with STEMI concurrent CTO in non-IRA could not significantly reduce MACE compared with OMT. In addition, IMPACTOR-CTO trial^[21] also supported that. These evidences support our results.

Recently DECISION-CTO trial^[19], an open-label multicenter RCT from Korea, recruited 834 patients with CTO who were randomly assigned to PCI and no PCI arms. Results of DECISION-CTO trial showed that there was no difference in the incidence of clinical outcomes. This was contrast with our results. However, Chandrasekhar et al^[32] study claimed that patients in Asians experienced higher rates of cardiac death than whom in European after PCI, which was keeping with our results. Some reasons may account for the association of PCI and lower cardiac death from our results. One reason may be that PCI can improve perfusion of myocardium, relieve ischemic burden and reverse ventricular remodeling^[33, 34], which lead to an improvement of LVEF, and then can avoid deterioration of cardiac function. Previous study indicated that low LVEF is associate with higher risk of cardiac death^[35]. The other reason is that PCI can decrease risk of ventricular arrhythmia^[6, 36], which increase the occurrence of cardiac sudden death.

Interestingly, subgroup analysis of our study reminds us that ethnic discrepancy exist in MACE and cardiac death. Benefits from CTO patients receiving PCI therapy are in favor of Caucasian. Before that, some studies also illustrated the ethnic discrepancy between Asian and Caucasian. Zaman et al^[37] found that PCI can improve angina symptoms, which prefer to Caucasian compared Asian (60.3% vs. 43.6%). Slater et al^[38] also figured out an ethnic difference in clinical outcomes. One year mortality differed in Caucasian and Asian after PCI (7.9% vs. 5.1%). Aforementioned evidence supported our results.

Many reasons may explain out results. Firstly, some studies show that diabetes mellitus, hypercholesterolemia^[39] and smoking^[40] are common in Asian. These factors contribute to the worse outcomes of Asian. Secondly, European compliance and medication after discharge are better than Asian^[40]. Thirdly, the program of cardiac rehabilitation was done better in European than Asian^[41, 42]. Lastly, there was a ethnic discrepancy in response to clopidogrel antiplatelet therapy for patients with CAD. As process of clopidogrel metabolizing to its active substance requires the CYP2C19 enzyme, and gene mutation of CYP2C19, which would lead to the dysfunction of the enzyme, is higher in Asian compared with Western patients^[43]. So Asian patients with CAD are lower response to clopidogrel, which is associated with worse outcomes, especially after PCI. Generally ethnic discrepancies reflect the difference in gene, life habit, hospital medical care and so on.

Limitation

First, the number of studies is relatively small, and the number of studies about west European population is relatively small, which may hamper the statistical power of assessing the association of ethnicity and outcomes. More studies are needed to investigate the association of ethnicity and outcomes. Second, our study dose not explore the relation of CTO in different locations and outcomes. A study indicated that PCI was associates with improved long-term survival in patients with CTO of LAD^[44]. Third, our study dose not assess whether PCI can ameliorate quality of life for CTO patients or not. Last, studies included in our analysis do not report economic data, so that we can not explore the cost-effect relationship. In the future, more studies are required to explore the cost-effect relationship.

Conclusion:

Compared with OMT, PCI is associated with significant reduction of cardiac death, however, without significant difference in MACE, MI, repeated revascularization and stroke. Sub-analysis indicates that PCI is favor of West European because it can reduce risk of MACE and cardiac death.

Abbreviations

PCI: percutaneous coronary intervention; OMT: optimal medical therapy; CTO: chronic total occlusion; RCTs: Randomized controlled trials; MACE: major adverse cardiovascular events; STEMI: ST-segment elevation myocardial infarction; PRISMA: Preferred reporting items for systematic reviews and meta-

analyses; IRA: infarct related artery; PSM: propensity score matched; CABG: Coronary artery bypass graft; MI: myocardial infarction; CKD: chronic kidney disease; LVEF: Left ventricular ejection fraction; CAD: Coronary artery disease; LAD: left anterior descending artery;

Declarations

Ethics approval and consent to participate

This work is a systemic review and meta-analysis, Ethics approval and consent to participate is not applicable.

Consent for publication

All authors approve the consent for publication.

Availability of data and material

The dataset supporting the conclusions of this article is included within the article.

Competing interests

The authors declared that there is no competing interest.

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Authors' contributions

FL Z, N W, and DL J designed the study. MZ L and LF S performed and collected the data. FL Z, QS L, and MZ L analyzed the data. FL Z and DL J wrote the manuscript. All authors approved the contents of the manuscript.

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Figures

Fig1. PRISMA diagram

Figure 1

Study selection procedure was detailedly proscribed in Fig1

Figure 2

Forest plot of MACE

Figure 3

Forest plot of Cardiac death

Figure 4

Forest plot of Myocardial infarction

Figure 5

Forest plot of Repeat Revascularization

Figure 6

Forest plot of Stroke

Figure 7

Funnel plot of Cardiac death

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