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SYSTEMATIC REVIEW

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Comparing cross-over stenting and focal ostial stenting for ostial left anterior descending coronary artery lesions: a systematic review and meta-analysis

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Abstract

Background The ideal revascularization approach for ostial left anterior descending coronary artery (L.A.D.) lesions continues to be a matter of debate. Two primary stenting strategies are often contemplated for managing these lesions: focal ostial stenting (F.O.S.) and the provisional strategy, alternatively termed cross-over stenting (C.O.S.) from the LM to the L.A.D. artery.

Aim Our objective is to assess the efficacy of C.O.S. vs. F.O.S. techniques in patients with ostial L.A.D. lesions who underwent percutaneous coronary intervention (P.C.I.).

Methods We systematically searched five electronic databases to identify relevant studies. The data was pooled as odds ratio (O.R.) with its 95% confidence interval (C.I.) using the DerSimonian-Laird random effect model in STATA 17 MP. Significance was determined by a p-value > 0.05 between intervention subgroups.

Results Nine articles with a total of 1492 patients were included in the meta-analysis. The pooled O.R. for Major Adverse Cardiovascular Events (MACE) was 0.88 (95% C.I. [0.39, 1.99], $P=0.76$), indicating comparable rates between F.O.S. and C.O.S. For all-cause death, the O.R. was 1.46 (95% C.I. [0.53, 4.02], $P=0.46$), with no significant differences between the compared techniques. Cardiovascular death showed no preference between treatments (O.R.=0.99, 95% C.I. [0.30, 3.31], $P=0.99$), and similarly for myocardial infarction (O.R.=0.74, 95% C.I. [0.38, 1.44], $P=0.37$).

Conclusion Our meta-analysis comparing C.O.S. and F.O.S. for L.A.D. lesions revealed similar efficacy in clinical and angiographic outcomes.

Keywords Ostial L.A.D., C.O.S, F.O.S, Complex lesions, Crossover, P.C.I

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Introduction

The presence of atherosclerotic plaque distribution in the coronary tree poses significant challenges, particularly in cases involving disease of the left anterior descending coronary artery (L.A.D.) [1]. Although ostial L.A.D. disease may initially appear as straightforward Medina 0.1.0 lesions on angiography, accurately assessing the extent of distal left main (LM) involvement in these cases is often difficult. Research using intravascular ultrasound (IVUS) has shown that isolated ostial L.A.D. disease is considerably less prevalent than suggested by conventional angiography findings [2]. Recent optical coherence tomography (OCT) studies have further supported these findings [3].

According to the latest consensus document released by the European Bifurcation Club, the ideal revascularization approach for ostial L.A.D. lesions continues to be a matter of debate [4]. Two primary stenting strategies are often contemplated for managing bifurcation lesions like this: focal ostial stenting (F.O.S.) and the provisional strategy, alternatively termed cross-over stenting (C.O.S.) from the LM to the L.A.D. artery. Precisely identifying the optimal landing zone for stent placement in the ostial lesion of the L.A.D. artery poses a challenge, primarily due to the unpredictable involvement of the LM artery. Consequently, although the C.O.S. is generally presumed to provide benefits over the F.O.S., the current body of literature on both techniques remains relatively limited.

Despite several small-scale studies, there is a lack of comprehensive evaluation regarding major cardiovascular and cerebral events, as well as non-ischemic events, such as fatal ventricular arrhythmias, in this particular group of patients [5–11]. Moreover, the current literature on isolated ostial L.A.D. disease presents conflicting results. While some researchers support the F.O.S. strategy, others contend that the clinical outcomes of the C.O.S. are more favorable [7–11]. Hence, this study marks the inaugural meta-analysis conducted to compare the efficacy of C.O.S. and F.O.S. techniques in patients with ostial L.A.D. lesions who underwent percutaneous coronary intervention (P.C.I.).

Methods

We carried out this study in strict accordance with the Cochrane Handbook of Systematic Reviews and Meta-Analysis rules [12]. PRISMA statement guidelines were followed while reporting this study [13].

Inclusion criteria

Randomized controlled trials (RCTs) or observational studies that satisfied our PICO criteria were included. (P) population: patients with ostial L.A.D. stenosis. (I) intervention: C.O.S from LM artery to L.A.D. artery. (C) comparator: F.O.S. (O) outcomes: Our primary outcome was major adverse cardiac events (MACE). Our secondary ones were all-cause death, cardiovascular death, myocardial infarction (MI), stroke, target lesion revascularization (TLR), target vessel revascularization (TVR), stent thrombosis, restenosis, and coronary artery bypass grafting (CABG).

We excluded reviews, conference abstracts, and foreign language studies.

Literature search and screening

PubMed, Scopus, Web of Science, Embase, and Cochrane Library were systematically searched from inception till February 2024 utilizing a group of keywords related to cross-over stenting focal ostial stenting, and left anterior descending artery. Our detailed search strategy was (Ostial O.R. Ostium) AND (Cross-over stent) O.R (Left main Cross)) AND ((left anterior descending) O.R. L.A.D.).

Two independent reviewers screened retrieved articles in two phases, first, by title and abstract screening using Rayyan web [14]. Second, the full text of eligible studies was retrieved for full-text screening using Google Sheets. A discussion with a third author addressed any apparent disagreements.

Data collection

Data were collected independently by two matched authors utilizing pre-designed Google Sheets. The following data were collected: Summary characteristics of the included studies such as study design, country, recruitment time, total number of patients, and baseline characteristics of the population of the included studies. Any apparent conflicts were resolved through a discussion with a third author.

Quality assessment

Newcastle-Ottawa-Scale (NOS) was utilized in evaluating the risk of bias for observational studies [15]. NOS assesses the risk of bias through three main domains: selection of the cohorts, comparability between the two cohorts, and outcome assessment and adequacy. Two blinded reviewers assessed the risk of bias, and a discussion with a third author addressed any apparent conflicts.

Statistical analysis

Dichotomous outcomes were pooled as Odds ratio (O.R.) with their 95% confidence interval (C.I.). The DerSimonian-Laird random effect model was utilized in pooling the outcomes. Heterogeneity was assessed using the Chi-square test and I-square test. Significant heterogeneity was considered if the Chi-square p-value was less than 0.1 or I-square more than 50%. The Galbraith plot was constructed to explore the specific source of heterogeneity if present among the included studies in the primary outcome. All the analysis was performed using Stata BE version 18 for Windows.

Certainty assessment

To assess the evidence robustness, we conducted a leave-one-out test in multiple scenarios, excluding one study in each scenario to ensure that the pooled effect size for the primary outcome was not dependent on any individual study.

Publication bias

To evaluate the publication bias among included studies for the primary outcome, the DOI plot model was executed to assess the correlation between effect size and standard error [16].

Results

Search results

Our primary search retrieved 1245 articles. 494 were removed as duplicates using Endnote (Clarivate Analytics, PA, USA). 751 studies were evaluated in the title and abstract screening phase. We also manually screened the references of included studies for any potential included studies. Finally, 9 articles were included in our study. Figure 1 shows the PRISMA flow diagram for the study selection process.

Characteristics of included studies

Nine articles with a total of 1492 patients, of them 604 patients in the C.O.S group and 888 patients in the F.O.S group, were included in the meta-analysis [6–8, 10,

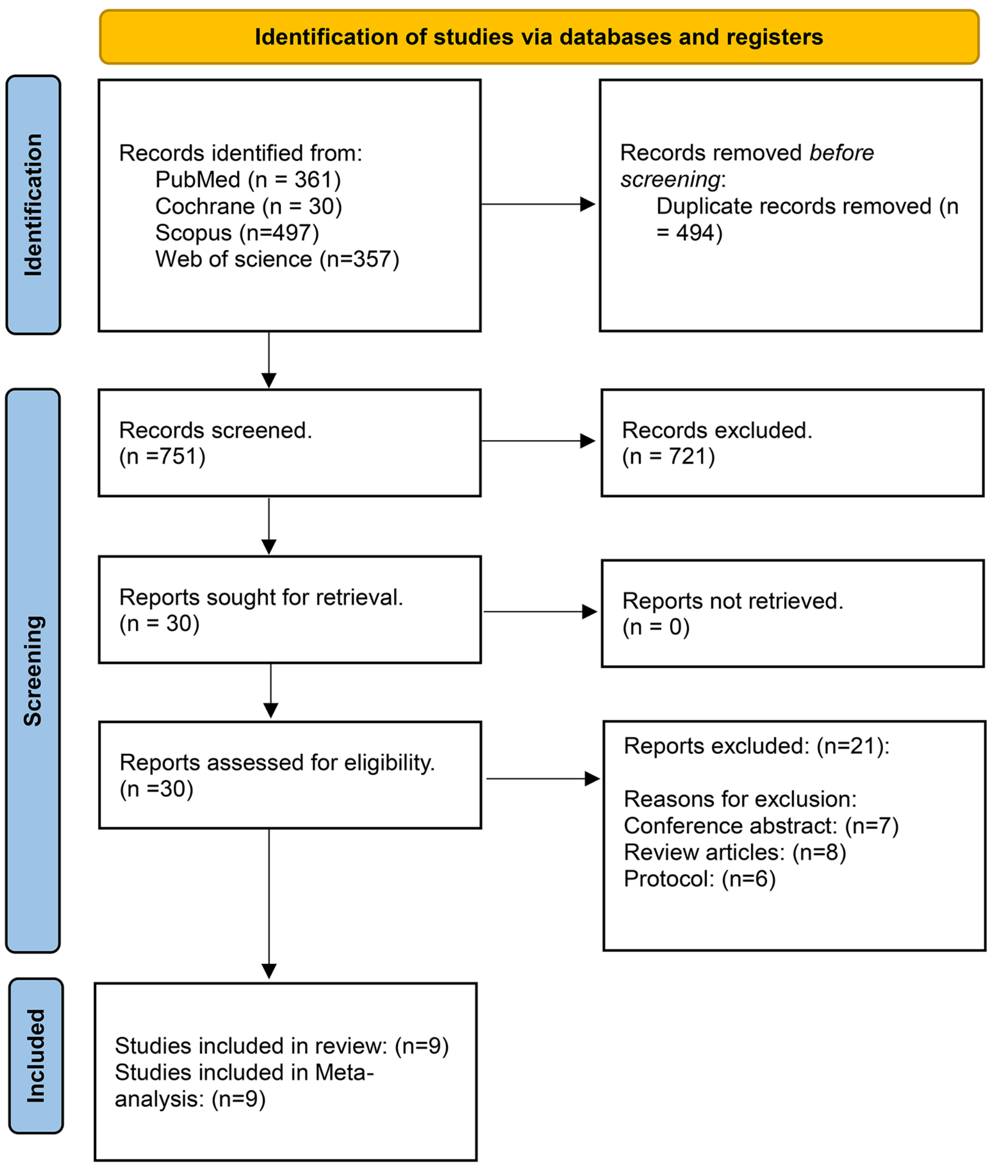

Fig. 1 Prisma flow diagram of the study selection process

11, 17–20]. All the included were observational studies. They were conducted in different countries such as Japan, Italy, Turkey, Taiwan, China, and Canada. All the included studies reported the outcomes of interest at long-term follow-up period. Detailed summarization of the included studies is illustrated in Table 1. The mean age of participants ranged from 53 to 73 years. Detailed characteristics of the population of the included studies are presented in Table 2.

Risk of bias

The quality of included studies ranged from good to fair quality, according to NOS. All studies showed a good representation of the community and outcome assessment. Only two studies demonstrated fair quality due to unexplained issues related to the comparability of the cohorts. (Kishi 2011, Sung 2009). Table 3 shows the detailed risk of bias for included studies.

Study outcomes

MACE

MACE was reported in five studies with an incidence rate of 14.7% (31/210) in the COS group and 18.2% (78/428). The pooled O.R. showed comparable MACE rates between C.O.S. and F.O.S. (O.R.=0.88, 95%C.I. [0.39, 1.98], $P=0.75$). Pooled studies showed significant heterogeneity ($P=0.04$, $I^2=61.10\%$), as illustrated in Fig. 2.

The leave-one-test was conducted, and it demonstrated that no single study has a disproportional effect on the pooled effect estimate, as illustrated in Fig. 3.

We also tested the heterogeneity by conducting a Galbraith test, and it showed that Soylu et al. [8] study located outside 95% of the regression, indicating its heterogeneity from the other studies, as illustrated in Fig. 4.

Further sensitivity analysis was conducted and its showed that upon excluding Soylu et al. [8] study the pooled studies were homogenous ($P=0.31$, $I^2=15.97\%$) and the pooled effect estimate did not differ significantly (O.R. = 0.65, 95% C.I. [0.36 to 1.17], $P=0.15$), as illustrated in Supplementary Fig. 1.

The DOI plot was carried out, and by inspection, no asymmetry was identified with an LFK index of 0.06, which indicated the absence of any potential publication bias, as illustrated in Supplementary Fig. 2.

All-cause mortality

Five studies reported the all-cause mortality in our study. The pooled O.R. did not prefer either C.O.S. or F.O.S. regarding the all-cause mortality rates (O.R.=1.46, 95%C.I. [0.54, 3.93], $P=0.45$). Pooled studies were heterogeneous ($P=0.04$, $I^2=59.69\%$) as illustrated in Fig. 5.

Cardiovascular mortality

The pooled O.R. did not show any preference for either C.O.S. or F.O.S. (O.R.=1.05, 95% C.I.=0.37, 3.03), $P=0.93$). Pooled studies showed significant homogeneity ($P=0.29$, $I^2=19.97\%$), as illustrated in Fig. 6.

Myocardial infarction

The pooled O.R. did not prefer either C.O.S. or F.O.S. (O.R.=0.74, 95% C.I.=0.38, 1.44), $P=0.37$). Pooled studies showed significant homogeneity ($P=0.52$, $I^2=0\%$), as illustrated in Fig. 7.

Stroke

The overall O.R. favored neither (O.R.=0.70, 95% C.I.=0.31, 1.57), $P=0.38$). Pooled studies showed significant homogeneity ($P=0.75$, $I^2=0\%$), as illustrated in Fig. 8.

Stent thrombosis

The overall O.R. didn't prefer either C.O.S. or F.O.S. (O.R.=0.98, 95% C.I.=0.29, 3.28), $P=0.98$). Pooled studies showed significant homogeneity ($P=0.90$, $I^2=0\%$), as illustrated in Fig. 9.

TVR

The overall O.R. did not prefer either C.O.S. or F.O.S. (O.R.=0.64, 95% C.I.=0.26, 1.54), $P=0.32$). Pooled studies showed significant homogeneity ($P=0.19$, $I^2=30.65\%$), as illustrated in Supplementary Fig. 3.

TLR

Eight studies reported the TLR. The pooled O.R. didn't significantly prefer either C.O.S. or F.O.S. (O.R.=0.67, 95% C.I. [0.39, 1.15], $P=0.14$). Pooled results were homogenous ($P=0.26$, $I^2=20.82\%$), as illustrated in Supplementary Fig. 4.

Restenosis

The overall O.R. did not prefer either C.O.S. or F.O.S. (O.R.=0.25, 95% C.I.=0.06, 1.11), $P=0.07$). Pooled studies showed significant homogeneity ($P=0.52$, $I^2=0\%$), as illustrated in Supplementary Fig. 5.

CABG

The overall O.R. did not prefer either C.O.S. or F.O.S. (O.R.=0.25, 95% C.I.=0.06, 1.11), $P=0.52$). Pooled studies showed significant homogeneity ($P=0.52$, $I^2=0\%$), as illustrated in Supplementary Fig. 6.

Discussion

Our study compared clinical outcomes between C.O.S. and F.O.S. in several studies. MACE rates were similar between C.O.S. and F.O.S. All-cause death rates also did not significantly differ between C.O.S. and F.O.S.

Table 1 Summary characteristics of the included studies. Abbreviations: COS: cross-over stenting, FOS: focal ostial stenting, LAD: left anterior descending artery

Study ID	Study design	Country	Recruitment time	Total participants (Number)	Follow-up duration (years)	Inclusion criteria	Definition of ostial LAD stenosis	Definition of FOS	Definition of COS	Performed IVUS [Number (%)]	Conclusion
Guner 2023	Retrospective observational	Turkey	Between January 2011 to December 2021	229	3	Patients who underwent PCI for Medina 0.1.0 LM bifurcation with available medical records, critical LAD stenosis, and performing PCI.	Stenosis presents within 3 mm of LAD ostium in the least foreshortened angiographic projection.	Stenting of LAD only starts from the ostium of LAD.	Stenting from LM to LAD.	FOS: 13(8.6) COS: 14(17.9)	This study showed that the crossover technique has a better long-term outcome for major adverse cardiovascular cerebral events and lower mortality than Ostial LAD stenting
Elkhateeb 2022	Retrospective observational	Canada	Between January 2008 and December 2018	175	5	Patients were eligible if they were < 18 years old and had received a coronary intervention of an ostial LAD lesion.	Ostial LAD was defined by > 50% stenosis within 5 mm of the ostium of the LAD	stenting of the LAD to the ostium (OS) with no crossover back to the LM.	Crossover stenting (CO) from the LM into the LAD, using standard provisional bifurcation techniques and proximal stent optimization (POT), where post-dilatation was typically performed	FOS: 19(12.7) COS: 14(56)	This study demonstrated that percutaneous intervention provides reasonable long-term outcomes and low rates of repeat revascularization for isolated ostial LAD lesions, with no noticeable difference in outcomes with crossover stenting into the LM vs. precise ostial stenting alone
Soylu 2022	Retrospective observational	Turkey	NA	97	2	Patients with ostial LAD stenosis who had undergone stent Implantation	Ostial LAD stenosis is defined as a stenosis within 3 mm of the LAD ostium in the least-foreshortened angiographic projection.	Patients who underwent only LAD stenting starting from the ostial LAD	Stenting from the LM to the LAD	Not Reported	This study showed that the ostial stenting group was associated with better clinical outcomes in treating ostial left anterior descending stenosis.
Yang 2021	Retrospective observational	China	Between January 2017 to December 2018	216	1	Patients with LAD ostial lesions at coronary angiography	Ostial LAD lesion was defined by Visual estimation of luminal diameter narrowing by 70% or greater located within 3 mm of vessel origin in the least foreshortened angiographic projection	Stenting of the ostium of LAD only	Stenting occurs from distal LM to LAD with complete coverage of LCX ostium	FOS: 28(20) COS: 51(65)	This retrospective study showed that the single-stent crossover technique is associated with a better 1-year clinical outcome than accurate ostial stenting in patients with isolated LAD ostial stenosis.

Table 1 (continued)

Study ID	Study design	Country	Recruitment time	Total participants (Number)	Follow-up duration (years)	Inclusion criteria	Definition of ostial LAD stenosis	Definition of FOS	Definition of COS	Performed IVUS [Number (%)]	Conclusion
Rigatelli 2019	Retrospective observational	Italy	Between January 2012 to January 2017	74	4	Consecutive patients with isolated ostial LAD disease. Enrolled to receive Ostial LAD stenting (OS) or LM to LAD cross-over (CO) stenting.	Ostial LAD stenosis is described as a narrowing or constriction located at least 10millimetress proximal to the beginning (ostium) of the left anterior descending coronary artery (LAD).	Second and third-generation drug-eluting stents (DES) are placed in the standard ostial position at the beginning of the left anterior descending artery (LAD).	In LM to LAD cross-over stenting, advanced drug-coated stents of the second and third generation (DES) are positioned in a cross-over fashion, extending from the left main coronary artery (LM) to the left anterior descending artery (LAD).	FOS: 1(2.6) COS: 20(55.5)	On long-term follow-up, crossover stenting seems superior to precise ostial stenting technique for isolated ostial LAD disease, especially in the presence of heavy calcification.
Yamamoto 2018	Retrospective observational	Japan	Between January 2009 and March 2016,	76	1.5	Inclusion focused on patients with AMI where the culprit lesion was specifically located at the ostial Left Anterior Descending artery (LAD). The study included patients who underwent Percutaneous Coronary Intervention (PCI) with stent implantation.	Ostial LAD lesion was defined as narrowing located within 3 mm of the vessel origin in the least foreshortened angiographic projection.	"JP Stenting Group," comprising patients with ostial Left Anterior Descending artery (LAD) Acute Myocardial Infarction (AMI) who underwent stenting at the LAD junctional point (JP).	In the "Cross-over Group," which involved patients with ostial Left Anterior Descending artery Acute Myocardial Infarction (LAD-AMI) treated with Left Main Trunk (LMT) crossover stenting.	FOS: 46(100) COS: 30(100)	The clinical outcomes of the crossover stenting were comparable to the jp stenting in the stenting.

Table 1 (continued)

Study ID	Study design	Country	Recruitment time	Total participants (Number)	Follow-up duration (years)	Inclusion criteria	Definition of ostial LAD stenosis	Definition of FOS	Definition of COS	Performed IVUS [Number (%)]	Conclusion
Kishi 2011	Prospective observational	Japan	Between August 2004 to Novebmer2006	419	3	Patients with ostial LAD lesions underwent sirolimus-eluting stent	Ostial lesion was defined as a narrowing located within 3 mm of the vessel origin in the least foreshortened angiographic projection	stenting of LAD only starting from the ostium of LAD without the introduction of the stent into LMCA	Stenting occurs from distal LM to LAD across LCX	Not Reported	This study showed that the cross-over technique provides easier stent positioning and complete lesion coverage than Ostial LAD stenting, so it might be a good and reasonable option for patients with ostial LAD stenosis lesions.
Capranzano 2010	Retrospective observational	Italy	Between January 2004 and December 2008	162	2	All patients with a de novo isolated unprotected ostial LAD significant stenoses managed with sirolimus-eluting, paclitaxel-eluting, zotarolimus-eluting, or everolimus-eluting stents	Isolated narrowing (< 50%) located within 3 mm from the LAD takeoff based on the view of the least foreshortened angiographic projection.	Stenting right at the ostium of the diseased branch (focal ostial LAD stenting).	From the LM across the LAD ostium into the diseased branch (distal LM-LAD stenting).	FOS: 26(27.4) COS: 13(19.4)	This study suggested that the crossover LM stenting may provide more favorable outcomes compared to the precise ostial stenting.
Sung 2009	Retrospective observational	Taiwan	Between July 2004 and October 2007	44	1	Consecutive patients with ostial LAD lesions who decided to receive coronary intervention with paclitaxel-eluting stents.	Ostial LAD lesion was defined with a diameter stenosis (DS) > 50% within 3 mm of the LAD orifice and a vessel diameter > 2.5 mm.	Stenting of LAD only starts from the ostium of LAD.	Stenting from LM to LAD.	Five patients (11.4), not reported individually for each group	Paclitaxel-eluting stent implantation in ostial LAD lesions with complete lesion coverage achieves a high procedural success rate and acceptable clinical outcomes during hospitalization and at one-year follow-up period

Table 2 Baseline characteristics of the population of the included studies. *Abbreviations* COS = cross-over stenting, FOS = focal ostial stenting, NA = not available, N = number, SD = standard deviation, CABG = coronary artery by bass grafting, PCI = percutaneous coronary intervention, LVEF = left ventricular ejection fraction, MI = myocardial infarction, STEMI = ST-elevation myocardial infarction, NSTEMI = non ST-elevation myocardial infarction, DM: diabetes mellitus, HTN: hypertension

Study ID	Groups	Age years, mean (SD)	Male sex, N (%)	Risk factors, N (%)				CABG, N (%)	PCI, N (%)	MI, N (%)	LVEF, % Mean (SD)	Clinical presentation, N (%)				Medications, N (%)			
				Dyslipidemia	Smoker	HTN	DM					STEMI	NSTEMI	Stable angina	Unstable angina	Beta-blockers	Nitrate	Statin	Diuretics
Guner 2023	**COS**	53.2 (15.5)	57(73.1)	48(61.5)	33(42.3)	56(71.8)	33(42.3)	NA	21(26.9)	NA	47.1(10.5)	NA	25(32.1)	43(55.1)	9(11.5)	70(89.7)	6(7.7)	73 (93.6)	25(32.1)
	FOS	57.2 (13.0)	125(82.8)	100(66.2)	65(43)	93(61.6)	72(47.7)	NA	45(29.8)	NA	44.6(11.3)	NA	46(30.5)	99(65.6)	8(5.3)	133(88.1)	15(9.9)	133 (88.1)	47(31.1)
Elkhateeb 2022	**COS**	67.7 (13.7)	18 (72)	24 (96)	21 (84)	14 (56)	8 (32)	NA	5 (20)	9 (37)	NA	6 (24)	2 (8)	5 (20)	9 (36)	NA	NA	NA	NA
	FOS	64.5 (11.7)	118 (78.7)	101 (70.1)	87 (58)	97 (66.0)	46 (31.3)	NA	23 (15.3)	40 (26.7)	NA	37 (24.7)	35 (23.3)	30 (20)	39 (26.0)	NA	NA	NA	NA
Soylu 2022	**COS**	61.6 (14.7)	30 (73.2)	NA	NA	NA	20 (48.8)	NA	20 (48.8)	NA	53.5 (8.8)	6 (14.6)	13 (31.7)	22 (53.7)	NA	NA	NA	NA	NA
	FOS	59.5 (13.7)	42 (75.0)	NA	NA	NA	24 (42.9)	NA	13 (24.1)	NA	51.7 (9.2)	10 (17.9)	21 (37.5)	25 (44.6)	NA	NA	NA	NA	NA
Yang 2021	**COS**	66(9.67)	67(86)	6(8)	22(28)	50(64)	27(35)	NA	NA	NA	56(6.3)	NA	8(10)	25(32)	45(58)	NA	NA	NA	NA
	FOS	64(10.55)	100(72)	17(12)	40(29)	94(68)	47(34)	NA	NA	NA	54(7.9)	NA	19(14)	62(45)	57(41)	NA	NA	NA	NA
Rigatelli 2019	**COS**	58.9 (9.2)	26(72.2)	16 (44.4)	10 (27.8)	12 (33.3)	18 (50.0)	NA	NA	10 (27.8)	47.5(8.36)	NA	12 (33.3)	NA	24 (66.0)	NA	NA	NA	NA
	FOS	63.1 (13.8)	28(76.4)	12 (31.6)	6 (15.8)	10 (26.3)	12 (31.6)	NA	NA	8 (21.1)	46.2(6.1)	NA	13 (34.2)	NA	25 (65.7)	NA	NA	NA	NA
Yamamoto 2018	**COS**	73 (8)	22 (73.3)	19 (63.3)	11 (36.7)	21 (70.0)	11 (36.7)	1 (3.3)	6 (20.0)	2 (6.7)	NA	16 (53.3)	14 (46.7)	NA	NA	5 (17.9)	3(10.7)	7 (25.0)	6 (21.4)
	FOS	67 (12)	36 (78.3)	21 (45.7)	12 (26.1)	35 (76.1)	24 (52.2)	1 (2.2)	7 (15.2)	7 (15.2)	NA	37 (80.4)	9 (19.6)	NA	NA	7 (15.2)	0(0)	7 (15.2)	5 (10.9)
Kishi 2011	**COS**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	FOS	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Capranzano 2010	**COS**	61.3 (11)	52 (77.6)	38 (56.7)	21 (31.3)	44 (65.7)	11 (16.4)	2 (3.0)	NA	28 (41.8)	52.3 (10)	4 (6)	25 (37.3)	38 (56.7)	NA	NA	NA	NA	NA
	FOS	64.1(11)	75 (78.9)	56 (58.9)	26 (27.4)	60 (63.8)	25 (26.3)	2 (2.1)	NA	27 (28.4)	51.2 (9.1)	6 (6.3)	39 (41.1)	50 (52.6)	NA	NA	NA	NA	NA
Sung 2009	**COS**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	FOS	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Table 3 Risk of bias on the included studies

New Castle Ottawa scale assessment (NOS)									
Study ID	**Cohort studies**								
	Selection				**Comparability**	**Outcome**			**Quality Score**
	Representativeness of the exposed cohort	**Selection of the non-exposed cohort**	**Ascertainment of exposure**	**Demonstration that outcome of interest was not present at the start of the study**	**Comparability of cohorts based on the design or analysis**	**Assessment of outcome**	**Was follow-up long enough for outcomes to occur**	**Adequacy of follow-up of cohorts**	
Guner 2023	*	*	*		**	*	*	*	**Good (8)**
Elkhateeb 2022	*	*	*		**	*	*	*	**Good (8)**
Soylu 2022	*	*	*		**	*	*	*	**Good (8)**
Yang 2021	*	*	*		*	*	*	*	**Good (7)**
Rigatelli 2019	*	*	*		**	*	*	*	**Good (8)**
Yamamoto 2018	*	*	*		*	*	*	*	**Good (7)**
Kishi 2011	*	*	*			*	*	*	**Fair (6)**
Caprazano 2010	*	*	*		**	*	*	*	**Good (8)**
Sung 2009	*	*	*			*	*	*	**Fair (6)**

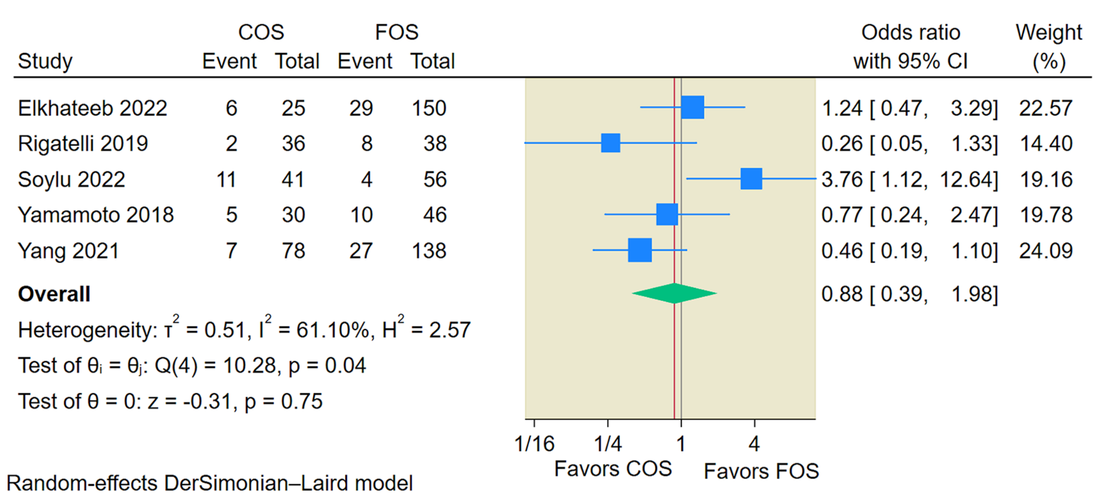

Fig. 2 Forest plot of MACE indicating that COS and FOS are comparable regarding MACE rates. Abbreviations: COS: Cross-over stenting, FOS: Focal ostial stenting, MACE: Major adverse cardiovascular events

Cardiovascular death, myocardial infarction, stroke, stent thrombosis, TVR, restenosis, and CABG rates did not significantly differ between the two stenting methods. Additionally, for TLR, the pooled O.R. did not significantly favor either technique.

The term "high event risk" in patients with established coronary artery disease includes the presence of three-vessel disease with proximal stenosis, LM disease, or severe proximal L.A.D. artery disease [21]. Likewise, the latest guidelines from the European Society of Cardiology (ESC) recommend physiological assessment of coronary stenosis within the range of 70–90% and propose revascularization without physiological evaluation in cases of critical stenosis (≥ 90%) [21]. In their 2021 study, Shin et al. revealed a correlation between the severity of coronary atherosclerosis and target vessel failure subsequent

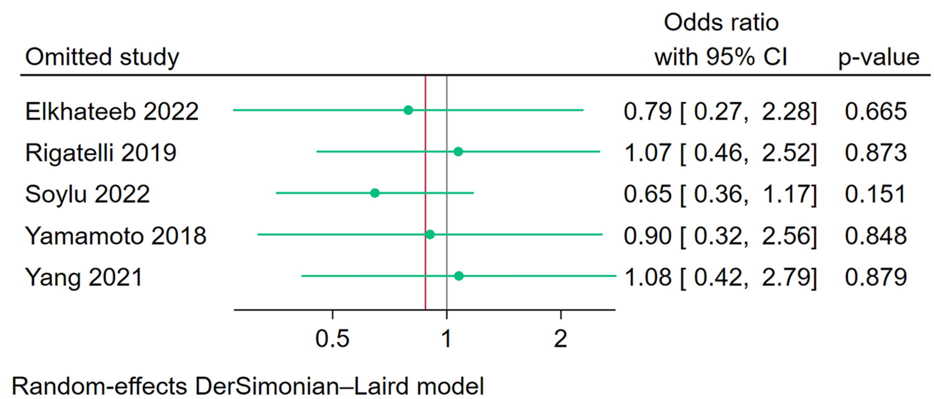

Fig. 3 Leave-one-out test plot showing that no single study has a significant effect on the pooled effect esmate

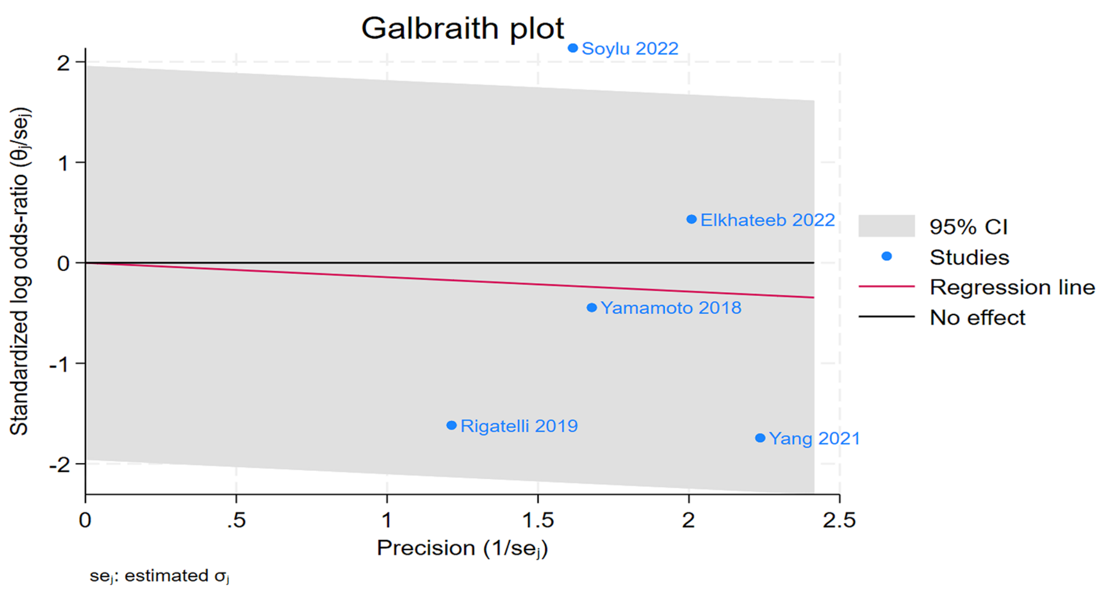

Fig. 4 Galbraith plot showing that one study (Soylu 2022) present outside the 95% CI precision area of the regression line indicating its possible heterogeneity from the other studies

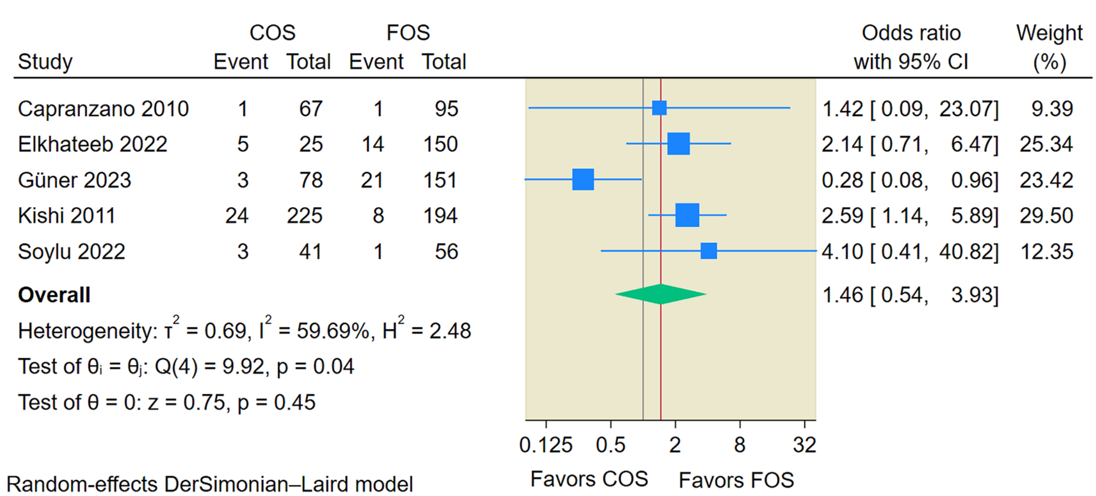

Fig. 5 Forest plot of all-cause mortality showing a comparable all-cause mortality rates between the two approaches. Abbreviations: COS: cross-over stenting, FOS: Focal ostial stenting

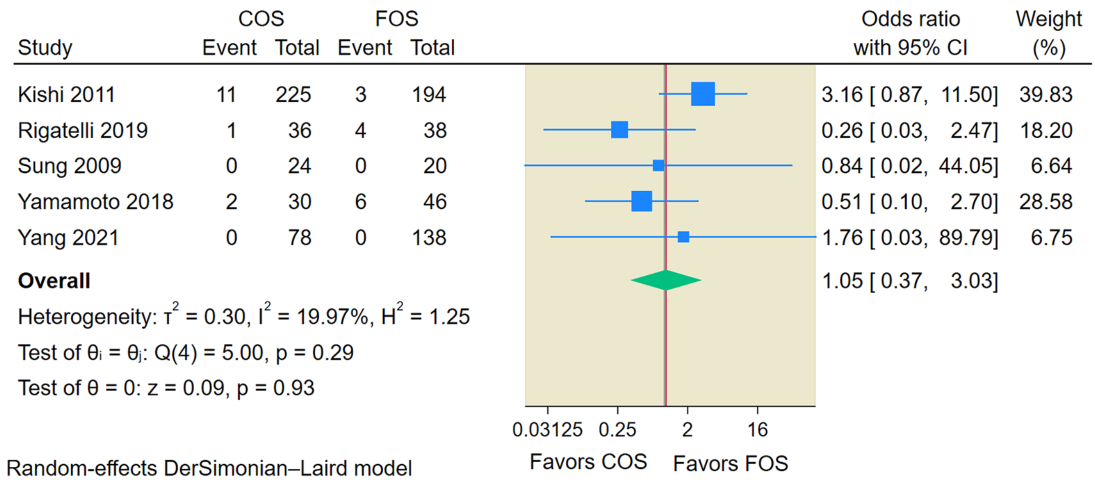

Fig. 6 Forest plot of cardiovascular mortality showing a comparable cardiovascular mortality rates between the two approaches. Abbreviations: COS: cross-over stenting, FOS: Focal ostial stenting

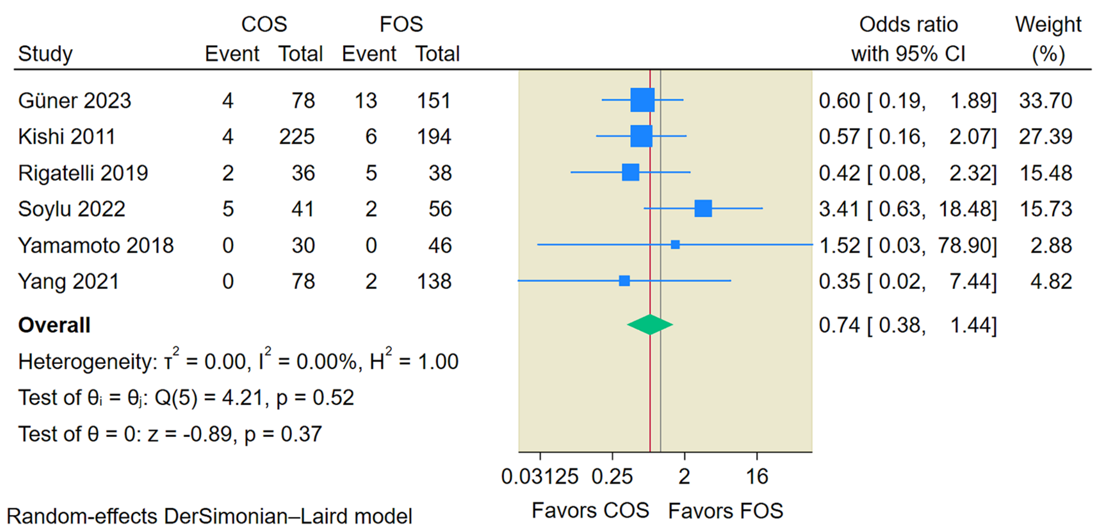

Fig. 7 Forest plot of myocardial infarction showing a comparable myocardial infarction rates between the two approaches. Abbreviations: COS: cross-over stenting, FOS: Focal ostial stenting

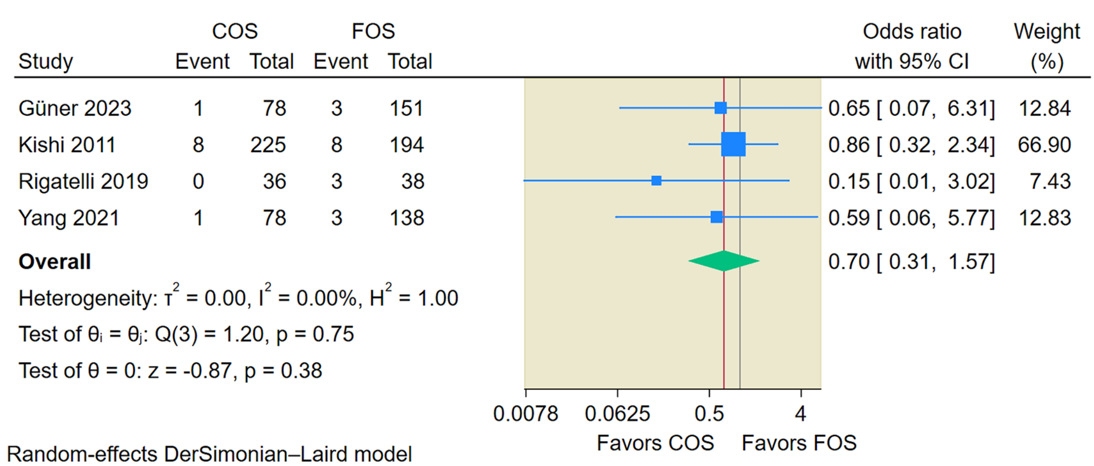

Fig. 8 Forest plot of stroke showing a comparable stroke rates between the two approaches. Abbreviations: COS: cross-over stenting, FOS: Focal ostial stenting

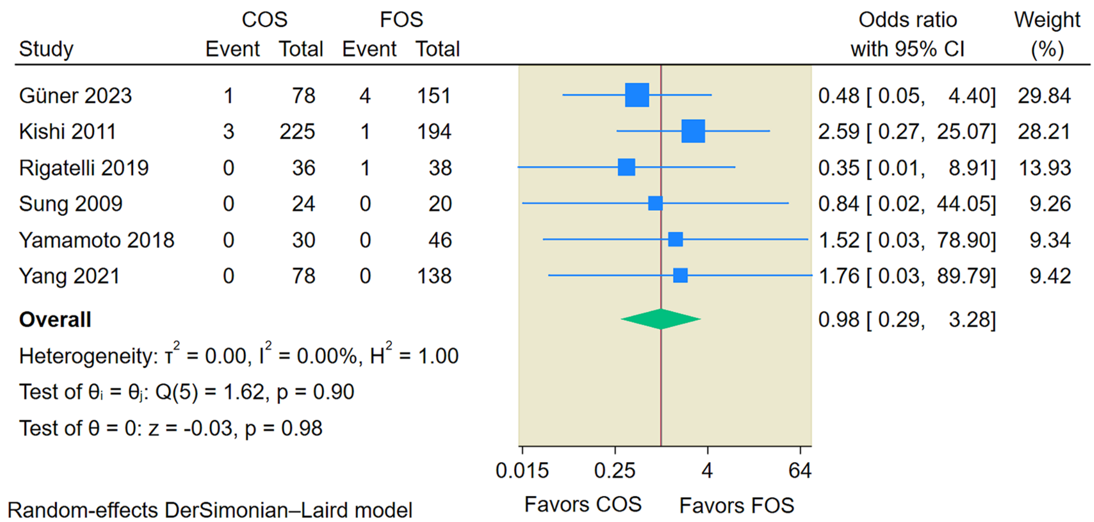

Fig. 9 Forest plot of stent thrombosis showing a comparable stent thrombosis rates between the two approaches. Abbreviations: COS: cross-over stenting, FOS: Focal ostial stenting

to P.C.I. Their findings indicated that successful P.C.I. resulted in a diminished risk of target vessel failure, particularly in cases of less severe and focal lesions [22].

The optimal management of ostial LAD lesions remains a contentious issue within the medical field, necessitating further research and expert consensus [1, 4]. A critical clinical decision arises in cases where the disease extends from the LM to the LAD, involving the choice between F.O.S. and C.O.S. Current guidelines generally recommend a single-stent strategy as the standard approach for managing LM bifurcation lesions, including those localized to the ostial LAD [1]. This recommendation is supported by findings from the EBC MAIN trial, which advocated for a provisional stenting strategy over systematic dual stenting techniques [23]. However, achieving optimal stent positioning at the ostium poses significant challenges, particularly the risk of longitudinal geographic miss. Misplacement of the stent—either too distal, resulting in failure to cover the diseased ostium, or too proximal, leading to free-floating struts in front of the LCx ostium—can increase the risks of stent thrombosis and in-stent restenosis. Even with precise stenting, complications at the LAD ostium can arise, including unintended damage to the LCx ostium due to carina displacement or distortion. Additional procedural challenges, such as plaque shifting (snow-plow phenomenon), vascular spasm, and dissection, may further exacerbate the complexity of managing these lesions [1].

Yamamoto et al. demonstrated that among acute coronary syndrome patients with ostial L.A.D. lesions as the culprit, clinical outcomes were comparable between the strategies of F.O.S. and the C.O.S. Their study found no significant differences in MACE, TLR, MI, or cardiac death between the two techniques [7]. Their conclusion also emphasized the feasibility and safety of the C.O.S. from the LM to the L.A.D. artery in the management of acute MI associated with ostial L.A.D. lesions [7]. In a retrospective study with a mean follow-up duration of 13 ± 4.1 months, it was observed that patients with ostial L.A.D. stenosis treated with the F.O.S. technique had a higher composite outcome rate (19.6% vs. 8.9%; $P = 0.040$) compared to those treated with the C.O.S. technique. This difference was primarily attributed to a more frequent occurrence of target vessel revascularization (17.4% vs. 7.7%; $P = 0.048$) in the F.O.S. group [6]. The authors concluded that the use of the F.O.S. strategy independently predicted poorer clinical outcomes, with a HR of 2.561 with 95% C.I., 1.041–6.299; $P = 0.021$ [6].

There is a lack of data regarding the long-term clinical outcomes associated with C.O.S. or ostial stenting as a P.C.I. strategy for ostial L.A.D. lesions. Rigatelli et al. reported that major cardiovascular events, encompassing death, MI, and stroke, as well as target vessel revascularization (in-stent restenosis and stent thrombosis), transpired at rates of 21.0% and 21% in the F.O.S. groups compared to 10.1% and 5.6% in the C.O.S. group, respectively ($P = 0.20$ and $P = 0.04$, respectively). These findings were observed over a mean follow-up period of 49.7 months, indicating a favorable outcome for the C.O.S. group. However, no significant differences were noted in the incidence of acute MI, stroke, 4-year mortality, stent thrombosis, and in-stent restenosis between the two groups [19]. In a study evaluating the long-term outcomes of ostial L.A.D. lesions, it was found that the rate of MACE, including non-fatal MI, TLR, and all-cause mortality, was higher in the C.O.S. group compared to the F.O.S group (28.2% vs. 8.2%, $P = 0.013$) [8]. However, they did not observe statistical significance regarding non-fatal MI, TLR, and all-cause mortality. Furthermore, the j-Cypher Registry Investigators reported that the

3-year clinical outcomes following the C.O.S. across the LCx artery ($n = 225$) did not significantly differ from those after F.O.S. ($n = 194$) concerning target lesion revascularization (HR: 0.77; 95% C.I., 0.33 to 1.82; $P = 0.55$) and death/myocardial infarction (HR: 1.54; 95% C.I., 0.78 to 3.2; $P = 0.22$). They concluded that utilizing the C.O.S. with a one-stent approach could potentially serve as a reasonable option for the treatment of ostial L.A.D. lesions [18].

In 2016, Sheiban et al. published a study elucidating the 10-year outcomes of 284 patients who underwent P.C.I. for LM bifurcation lesions. The study by Sheiban et al. unveiled that provisional stenting was the predominant strategy employed, and over 10 years, 21% of patients underwent repeat P.C.I. In the Cox multivariate analysis, P.C.I. to coronary vessels other than the LM emerged as the sole independent predictor of MACE (HR: 2, 95% C.I.: 1.4 to 2.7), while the provisional strategy did not exhibit independent predictive significance (HR: 0.8) [24]. Furthermore, a study involving 175 ostial left anterior descending (L.A.D.) lesions indicated that the C.O.S. exhibited a numerically lower 5-year MACE rate compared to F.O.S. (19.3% vs. 25.9%). However, this difference did not reach statistical significance [10]. However, none of the aforementioned studies demonstrated that the provisional strategy is superior to F.O.S. in terms of mortality outcomes.

Contrary to our findings and previously mentioned studies, In Soylu et al., clinical outcomes differed between the two techniques, with a significantly lower rate of MACE in the F.O.S group [8]. Their univariate and multiple regression analyses indicated a significant association between the C.O.S technique and MACE [8]. This emphasizes the importance of considering factors beyond plaque stabilization, such as LM stenting and appropriate post-dilation balloon selection. The study highlights the potential limitations of stent diameter selection in C.O.S., as stents with 3.0 mm and 3.5 mm diameters may not adequately expand in patients with large LM diameters, increasing the risk of restenosis and thrombosis [8]. Insufficient post-dilation balloon selection may contribute to higher MACE rates in C.O.S. due to inadequate stent apposition within the LM [8]. Thus, they considered F.O.S. in scenarios where the distal LM segment exhibits no lesions, the LM diameter is substantial, and the anticipated maximal expansion capability of the chosen stent may be inadequate for C.O.S [8].

However, it is important to note that Solyu et al. used approximately five times more kissing balloon (KB) inflation in C.O.S compared to F.O.S [8]. This increased KB inflation may be attributed to factors such as larger stents and post-dilation balloons used in C.O.S., which could lead to plaque and carina shifting toward the LCx ostium [8]. The findings should be noted that although C.O.S. theoretically intends to enhance plaque stabilization, it might result in complications such as stent strut flotation at the ostium of the LCx [8]. Despite concerns, routine KB inflation post-stenting has not consistently demonstrated clinical benefits, and it may increase the risk of main-branch restenosis [8].

IVUS is one of the suggested approaches for identifying crucial factors that either promote or hinder each technique's efficacy in the ostial L.A.D. lesions. Conventional coronary angiography often underestimates the severity of left main bifurcation atherosclerosis due to its two-dimensional limitations [25]. Introducing intravascular imaging tools before procedures, particularly for ostial L.A.D. lesions, offers crucial insights, reducing procedural risks and long-term complications [26]. IVUS is recommended (Class II A) for assessing LM disease severity plaque extent, providing detailed information on vessel size and distribution within the LM and its branches [21]. IVUS enhances stent implantation optimization, detecting issues like under expansion or dissection not easily seen on angiography. Imaging factors like plaque distribution and morphology guide strategy selection for LM bifurcation lesions, and IVUS confirms stent placement and expansion [27]. Thus, incorporating IVUS alongside conventional angiography improves the evaluation and management of LM disease, enhancing clinical outcomes in complex coronary interventions.

IVUS guidance in ostial lesions has an important role to guide plaque debulking techniques. However, previous literature when compared debulking vs. stenting directly, it showed mixed findings [28–31]. In Kim et al., debulking prior to stenting achieved greater acute lumen gain and increased the postprocedural minimal lumen diameter [28]. However, the enhanced lumen gain with debulking did not translate into a lower restenosis rate due to a tendency for greater late lumen loss. A similar pattern was observed in the Stenting after Optimal Lesion Debulking (SOLD) registry, where the acute lumen gain achieved with debulking and stenting was associated with proportional late lumen loss [31].

Another reason to involve intravascular imaging techniques is to prevent free-floating stent struts in the distal LM. Optical coherence tomography (OCT) guidance enables precise evaluation of ostial stent positioning and facilitates management in cases of excessive protrusion [32, 33]. Given the limitations of angiography in detecting free-floating stent struts, OCT imaging should be used instead for two key purposes: first, to accurately evaluate the LAD stent position; and second, to verify guidewire placement to avoid unintentional abluminal wiring [32, 33].

Added to intravascular imaging, transcoronay pacing one of the most techniques used to optimize difficult stenting. It was initially introduced as a straightforward alternative for managing bradyarrhythmias encountered during coronary balloon angioplasty. This approach was subsequently complemented by left ventricular pacing [34–36]. Over time, numerous additional applications for transcoronary and left ventricular pacing have been developed. These include the management of bradyarrhythmias associated with thrombectomy and rotational atherectomy, the termination of ventricular tachycardia during coronary angioplasty via transcoronary overdrive pacing, the use of left ventricular guidewire pacing as an alternative to transvenous temporary right ventricular pacing during aortic balloon valvuloplasty, and its application in transcatheter aortic valve implantation [34–36]. In the previous literature, the application of transcoronary pacing to enhance and optimize stent positioning during bifurcational and ostial left main stenting. Rapid pacing minimized the pulsatile cardiac motion and coronary blood flow thrust, enabling precise placement of the stent. This technique proved beneficial again when it became evident that a short stent was also required for the side branch due to carinal shift [34–36].

To illustrate, our findings showed comparable outcomes between F.O.S. and C.O.S. techniques. However, F.O.S. may be contemplated to circumvent stenting of the LM when anatomical conditions are favorable, such as a rectangular angle between the L.A.D. and L.C.X. arteries, clear visualization of side branch (SB) take-off, and absence of LM disease. In alternative scenarios, employing C.O.S., which entails covering the affected ostial L.A.D. or ostial L.C.X. along with the diseased portion of LM, followed by proximal optimization technique (POT) and eventual kissing, based on either provisional or "inverted" provisional strategies, emerges as a preferable course of action [4, 19].

To our knowledge, we are the first meta-analysis comparing C.O.S. vs. F.O.S. in ostial L.A.D. lesions, pooling data from nine studies encompassing 1492 patients. However, it is imperative to acknowledge the limitations inherent in our study. The retrospective observational design of the included studies inherently limits the strength of the evidence and introduces potential biases that must be carefully considered. Such biases can stem from factors like incomplete or inconsistent data collection, reliance on pre-existing records, and the inability to establish causal relationships due to the absence of randomization. Additionally, confounding variables that were not adequately controlled for in the original studies may have influenced the results, further limiting the reliability of the findings. These limitations emphasize the need for caution when interpreting our results and highlight that broad generalizations should be avoided.

Furthermore, the reliance on conventional angiography for the identification of ostial L.A.D. lesions may have influenced the accuracy of lesion classification and subsequent outcomes assessment. The underutilization of IVUS, particularly in studies with low IVUS usage despite its recognized benefits in guiding LM stenting, represents a notable gap in our data (Table 1). Additionally, the lack of comprehensive evaluation of stent brands and procedural data such as physiological assessments and three-dimensional quantitative coronary angiography (3D-QCA) restricts the depth of insights gleaned from our analysis.

Conclusion

In our meta-analysis comparing C.O.S. and F.O.S. for lesions in the LAD artery, we observed similar efficacy in both clinical and angiographic outcomes, particularly in MACE, all-cause mortality, MI, and cardiovascular mortality. These findings suggest that both C.O.S. and F.O.S. may provide comparable benefits in the management of LAD lesions. However, we recommend future research endeavors to adopt prospective study designs with standardized protocols, encompassing a larger cohort of patients to enhance the robustness and generalizability of findings. Incorporating advanced imaging modalities such as IVUS and OCT into clinical practice can facilitate more precise lesion assessment and optimize stent selection and deployment strategies.

Supplementary Information

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Supplementary Material 1

Author contributions

Conceptualization: A.K and A.H; screening: A.K, A.E, H.A, M.F; data extraction: A.K, A.E, A.E; quality assessment: A.K, A.H, A.E; data analysis: A.E and A.A; writing—original draft: A.H and A.E; review and editing: all authors; supervision: I.Y and A.A; All authors have read and agreed to the published version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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