Intravascular ultrasound-guided percutaneous coronary intervention for patients with coronary bifurcation lesions

A systematic review and meta-analysis

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Abstract

Background and Objective: Intravascular ultrasound (IVUS) could take on a vital position when angiographic images are not clear enough to be precisely visualized or measured by computer-aided technology. This meta-analysis was designed to compare the benefits of IVUS-guided and angiography-guided percutaneous coronary intervention(PCI) strategies for improving clinical outcomes.

Methods: PubMed, Embase, Web of Science, and Cochrane Library were searched for articles published from inception to 13th October, 2019. A comparative study of IVUS-guided and angiography-guided PCI strategies for patients with coronary bifurcation lesions was retrieved. The early endpoint events ($\leq$1 year) and the late endpoint events (>1 years) were determined according to the follow-up time. The former included cardiac death, target lesion or vessel revascularization, stent thrombus, and major adverse cardiac events, while the latter included cardiac death. Statistical software Review Manager Version 5.3 was performed for meta-analysis.

Results: Five studies involving7,830 patients with coronary bifurcation lesions were included in this meta-analysis, the incidence of major adverse cardiac events for IVUS-guided strategy in patients with coronary bifurcation lesions were lower than those of patients with angiography-guided strategy at the early follow-up(OR=0.55, 95% CI 0.42 - 0.70, P < .0001).Meanwhile, cardiac death, target vessel or target lesion revascularization, stent thrombosis were not statistically significant(OR=0.68, 95% CI 0.34 - 1.35, P = .27; OR = 0.78, 95% CI 0.59 - 1.05, P = .10; OR=0.36, 95% CI 0.12–1.04, P = .06).However, significant differences in cardiac death between IVUS-guided and angiographic-guided strategies were observed in the late follow - up (OR=0.36, 95% CI 0.23 - 0.57, P < .00001).

Conclusion: The IVUS-guided PCI strategy was associated with more clinical benefits compared with angiography-guided PCI strategy in patients with coronary bifurcation lesions. These findings suggest that the IVUS-guided PCI strategy can be recommended as an optimization in this kind of patients.

Abbreviations: IVUS = intravascular ultrasound, MACE = major adverse cardiac events, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, TVR = target vessel revascularization.

Keywords: angiography, coronary bifurcation lesion, Intravascular ultrasound, percutaneous coronary intervention

1. Introduction

Coronary bifurcation lesions are defined by the European Bifurcation Club as coronary artery stenosis occurring adjacent to and/or involving the origin of large distal side branches,[1] that is, the opening of the proximal main branch, distal main branch and peripheral branch (the opening and its 3–5 mm segment), and there are more than 50% vascular stenosis, accounting for 15% to 20% of coronary artery lesions in the percutaneous coronary intervention (PCI).[2] It is a severe challenge in the PCI practice due to the overlapping of main and side branch vessels and the stenosis of side branch orifices can be aggravated by the

implantation of main stents, which may lead to complete occlusion of side branch orifices.

Coronary angiography is the current golden standard for the diagnosis of coronary artery disease as a visual method but it has many limitations in its years of application. Computer-assisted quantitative coronary angiography overcomes the drawbacks of the visual method to a certain extent by providing a more accurate evaluation basis however quantitative coronary angiography indirectly determines the structure of the vascular wall by inferring the lumen which results in its major limitations compared to standard angiography techniques. Actually, atherosclerosis often occurs at the bifurcation of a coronary artery due to turbulence and low shear stress. Therefore, traditional coronary angiography with 2-dimensional imaging features can only judge the degree of atherosclerosis, not the accurate identification of its special morphological changes such as the real diameter of the lumen, plaque load, calcification, bifurcation angle, and plaque distribution. In this case, the apparence of intravascular ultrasound (IVUS) changes the position of patients.[3]

In comparison, apart from the accurate evaluation on the distribution of plaques at the bifurcation and the nature of lesions, and the reasonable selection on interventional therapy strategies, IVUS could also realize the evaluation on the effect of stent implantation, the optimization on the interventional treatment of bifurcation lesions, the timely orientation on complications, and the improvements onthe clinical prognosis of patients. It has been reported that guided by IVUS can improve the clinical outcomes of patients with multiple overlapping drug-eluting stents.[4] From 138 original citations, including 3 randomized trials and 12 observational studies with 24,849 patients, which reported that IVUS-guided drug-eluting stent implantation can optimize clinical outcomes.[5] However, the use of IVUS during PCI in the treatment of coronary bifurcation lesions did not show significant clinical benefits in a large retrospective study,[6] from which it could suggest that whether the IVUS can improve the clinical prognosis of patients still remains controversial.

By taking the outcome of patients as the observation point, this study infers the value of IVUS in complex bifurcation lesions through the specific clinical manifestations of patients, aiming to reduce the related clinical complications, the revascularization and hospitalization rate of patients while improving the success rate of interventional surgery.

2. Methods

2.1. Data source and search strategy

This accomplished meta-analysis of data resources was demonstrated and analyzed under the guidance of the conducting and reporting meta-analyses of observational studies (MOOSE)[7] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[8] Guided by search strategies such as Medical Subject Heading terms (MeSH) and keywords, PubMed, Embase, Web of Science, the Cochrane Library, as well as relevant major international conference, were searched for articles published from inception to 13th October, 2019, without restriction to the language. The following keywords such as coronary bifurcation lesions, IVUS, coronary angiography, and PCI were contained. Randomized controlled trials and observational studies comparing the IVUS with coronary angiography-guided PCI strategies were included in patients with coronary bifurcation lesions (true coronary

bifurcation lesions, and other types of complex lesions). Due to the protocol of the review was not registered, no ethical approval or patient consent was required to cite those previous published studies, and the study has got support from ethics committee.

To improve the efficiency in the whole process, some criteria were also clearly confirmed. The appropriate criteria for the systems assessment in this meta-analysis included

(1) the type of lesion as coronary bifurcation,
(2) inclusion of clinical control objectsonly to IVUS versus coronary angiography,
(3) available complete clinical outcomes, such as cardiac death, myocardial infarction, target lesion or vessel revascularization, stent thrombosis, cardiac death, major adverse cardiac events (MACE), and
(4) more than or equal to 1 year follow - up time.

The excluded criteria in this meta-analysis included

(1) studies with incomplete clinical end-point events correlating the above outcomes,
(2) repetitive published studies,
(3) studies without the availability of full-text articles, and
(4) correlative studies that were not retrieved by the initial searching.

2.2. Outcome definition

The outcomes of this analysis were divided into early and late clinical endpoints according to follow-up duration. The early endpoint events limited to trials with in a follow-up duration of 1 year. The late endpoint events consisted of the early endpoint events limited to trials with a follow-up duration of more than 1 year. Coronary bifurcation lesions were classified according to the Medina classification, and true bifurcation was defined as both main vessel and side branch with more than 50% diameter stenosis [Medina classification (1,1,1,), (1,0,1) or (0,1,1)].[9] The death was considered as cardiac death unless non-cardiac reasons were indicated. The myocardial infarction was defined as elevation of cardiac enzymes (data for cardiac enzymes > 1 time of the upper normal limit (UNL) in the Chen et al [10] and ≥ 3 times the UNL in the remaining studies [11]), with or without new pathological Q waves. The cardiac enzymes, assessed for this aim, varied among the studies, including creatine kinase-myocardial band isoenzyme or troponin T or I. Clinically driven the target vessel/lesion revascularization (target vessel revascularization [TVR] or target lesion revascularization) was defined as any revascularization produce stenting or coronary artery bypass grafting performed.[12] The MACE was defined as the composite endpoint of death, myocardial infarction, and TVR or stroke, and the 1 year end points included MACE and its components (including cardiac death, TVR/target lesion revascularization, stent thrombosis). The stent thrombosis was defined according to the academic research consortium definition.[13]

2.3. Data collection and quality assessment

Four evaluators (Yang R.R., Lv Y.H., Guo C., and Li M.) searched for useful documents and removed the non-conforming documents after a clear reading and analysis on the title and abstract, respectively. The first author, year of publication, follow-up duration, page number, baseline characteristics, as well as clinical outcomes of the patients were involved. Moreover, the

literature was also carefully re - screened according to inclusion and exclusion criteria. Any disagreement or uncertainty was resolved by a group consensus or by a third party (Wang Z.L.) if necessary. The quality evaluation of eligible studies and the observational studies were assessed by the Cochrane Collaboration's tool for randomized control trials [14] and the Newcastle - Ottawa scale checklist,[15] respectively.

2.4. Statistical analysis

Data were analyzed by the statistical software Review Manager Version 5.3. (The Nordic Cochrane Centre, The Cochrane Collaboration Network, Copenhagen, 2014). Mantel–Haenszel odds ratio (OR) was used as effect analysis statistics, and the corresponding 95% of confident intervals (CI) were generated to represent the data. As to the heterogeneity among the results, the Higgins I^2-test (the test level was set $I^2 > 50\%$ was significant) was estimated. In this case, a random-effects model was used for meta-analysis. Therefore, to ensure the accuracy, the clinical heterogeneity was treated by subgroup analysis, sensitivity analysis, or only descriptive analysis, among which the sensitivity analysis was carried out by excluding 1 by 1. If the results showed that the combined OR value and 95% CI had no directional changes,it indicated that the mean was basically stable. Meanwhile, publication bias was assessed using funnel plots, and the statistical significance was accepted for a 2-sided $P < .05$.

3. Results

3.1. Search results

A total of 379 relevant literature covering IVUS-guided PCI versus angiography-guided PCI strategies were retrieved in the initial examination. After eliminated ineligible documents by reading the title and abstract of each article, 5 studies met the predefined inclusion criteria in qualitative analysis and meta-analysis (Fig. 1).[10,11,16–18] The quality of the 5 studies is evaluated by Newcastl Ottawa Scale (Fig. 1).

3.2. Clinical characteristics

The clinical characteristics of the included studies are listed in Table 1. A total of 7830 patients were enrolled into this meta-analysis from 5 observational studies. Among them, there were 1631 and 6394 patients with coronary bifurcation lesions in the IVUS-guided PCI strategy and the coronary angiography-guided PCI strategy, respectively, with anaverage age range from 51 to 77 years. Among those patients, male patients accounted for 77.1% of all subjects. The majority of patients had high-risk factors for cardiovascular disease such as diabetes (27.6%), hypertension (67.0%), and hyperlipidemia (44.9%), respectively.

3.3. lesions and procedural characteristics

The lesions and procedural characteristics are summarized in Table 2. Among 8025 coronary bifurcation lesions, 20.0% of patients had a history of PCI and 6.5% of patients had a history of coronary artery bypass grafting. In addition, for patients with coronary bifurcation lesions, the proportion of anterior descending artery, left circumflex artery, and right coronary artery was 64.5%, 19.0%, and 6.8%, respectively. Among them, 82.8%, 4.8%, and 17.4% of patients with coronary bifurcation lesions

after the Medina classification belonged to 1,1,1, 1,0,1, and 0,1,1, respectively. Meanwhile, the IVUS-guided PCI strategy was associated with a longer length (29.90±11.20 vs 27.80± 10.70 mm), larger diameter (3.82±0.33 vs 3.15±0.31 mm) compared with the angiography-guided PCI.

3.4. Comparison of the early clinical endpoints between the IVUS-guided and angiography-guided PCI strategies

The MACE (OR=0.55, 95% CI 0.42 - 0.70, $P < .0001$) are statistically significant compared with the IVUS - guided and angiography-guided PCI strategies, except for cardiac death (OR=0.68, 95% CI0.34 - 1.35, $P = .27$), target lesion or vessel revascularization (OR=0.78, 95% CI 0.59 - 1.05, $P = .10$), stent thrombosis (OR=0.36, 95% CI 0.12 - 1.04, $P = .06$) (Fig. 2).

3.5. Comparison of the late clinical endpoints between the IVUS-guided and angiography-guided PCI strategies

The cardiac death in IVUS-guided PCI strategy are superior to those with angiography-guided PCI strategy (OR=0.36, 95% CI 0.23 - 0.57, $P < .00001$) (Fig. 3)

3.6. Statistical heterogeneity and sensitivity analysis

The extreme heterogeneity in the MACE endpoint at the early MACE follow - up sensitivity analysis results showed that a single study was removed 1 by 1, which is basically in line with the research of Chen et al (2013)[10] (Fig. 4). The publication bias test was not evaluated on account of the number of studies was less than 10 in this meta-analysis.

4. Discussion

This meta-analysis aimed to determine the role of IVUS-guided PCI strategy in patients with coronary bifurcation lesions. The results show that the IVUS-guided revascularization could reduce the incidence of MACE in early follow-up and cardiac death in late follow-up, comparing with angiography-guided revascularization strategy.

The 2018 ESC/EACTS Guidelines on myocardial revascularization recommend the IVUS-guided revascularization (class II; level of evidence B) for patients with coronary bifurcation lesions based on previous clinical data.[19,20] It also suggested better clinical outcomes with IVUS-guided vs. angiography-guided PCI.[21,3] However, a study showed that the possibility of IVUS-guided revascularization was controversial after the emergence of some new Invasive imaging tools.[22] Although the IVUS-guided revascularization was similar to Optical Coherence Tomography (OCT)-guided revascularization, the study showed that OCT-guided stent implantation is relatively more secure compared with IVUS-guided revascularization.[23] Because IVUS-guided and OCT - guided have respective advantages, it could not decide which kind of intracavitary techniqueis more efficient. With the emergence of the IVUS-guided revascularization strategy, the improvement of clinical outcomes compared with those in whom the angiography-guided group was identified in this study. It could be used asa guideline recommendation for patients with coronary bifurcation lesions in clinical practice.

Previously studies showed that there was a significant difference in MACE between the IVUS - guided and angiography-guided revascularization strategies.[16] In addition, there

	studies	Kim et al 2011	B-Z et al 2011	Patel et al 2011	Chen et al 2013	Chen et al 2018
Selection	1.Representativeness of the exposed cohort	A	A	A	A	A
	2. Selection of the non-exposed cohort	A	A	A	A	A
	3. Ascertainment of exposure	A	A	A	A	A
	4. Demonstration that outcome of interest was not present at start of study	A	A	A	A	A
Comparability	5. Comparability of cohorts on the basis of the design or analysis	A	A	A	A	A
Outcomes	6. Assessment of outcome	B	B	B	B	B
	7. Was follow-up long enough for outcomes to occur	A	A	A	A	A
	8. Adequacy of follow-up of cohorts	A	A	A	A	A

Selection: (1) Representativeness of the exposed cohort: A, truly representative of the average patient with coronary bifurcation lesions; B, somewhat representative of the average patient with coronary bifurcation lesions; C, selected special group; and D, no description of the derivation of the cohort.

(2) Selection of the non-exposed cohort: A, drawn from the same community as the exposed cohort; B, drawn from a different source; and C, no description of the derivation of the non-exposed cohort. (3) Ascertainment of exposure: A, secure record (e.g., surgical records); B, structured interview; C, written self-report; and D, no description. (4) Demonstration that outcome of interest was not present at start of study: A, yes; B, no.

Comparability: (5) Comparability of cohorts on the basis of the design or analysis: A, study controls for comorbidities; B, study controls for additional risk factors (such as age and severity of illness); and C, not done.

Outcomes: (6) Assessment of outcome: A, independent blind assessment; B, record linkage; C, self-report; and D, no. description. (7) Was follow-up long enough for outcomes to occur: A, yes; B, no. (8) Adequacy of follow-up of cohorts: A, complete follow-up - all subjects accounted for; B, subjects lost to follow-up unlikely to introduce bias (small number lost), follow-up rate higher than 90%, or description provided of those lost; C, follow-up rate 90% or lower (select an adequate percentage) and no description of those lost; and D, no statement.

Figure 1. Quality assessment for observation studies by Newcastle Ottawa Scale.

were consistent with the impact of complex bifurcation lesions on clinical outcomes after PCI drug-eluting stents[24]. This meta-analysis also found that the lower risk of myocardial infarction (2.7% vs 15.5%) and target lesion revascularization or TVR event (1.9% vs 3.7%) benefited from the IVUS - guided strategy. It further proved that the lower MACE originated from lower risk of myocardial infarction and target lesion or vessel revascularization in the IVUS-guided strategy. However, the clinical outcome existed heterogeneous, the main reasons are similar to a study by Chen et al (2013), which showed that 2-stent technology may be the cause of inconsistency.[10]

Additionally, this study also demonstrated that the risk of cardiac death reaching a statistical difference was limited to trials at different follow-up time. However, there was no significant difference in cardiac death between both different strategies when the follow - up duration was less than 1 year. This difference in cardiac death may be related to the discrepancies in baseline characteristics in the study by Chen et al (2013),[10] such as the lesion site in the left anterior descending artery was 68.1% and 80.1% of Medina stratification belonged to 1,1,1. The meta-analysis showed that there was significant clinical benefits in MACE and late cardiac death. These results may be explained by

Table 1

Baseline clinical characteristics.

	Kim et al 2011		B-Z et al 2011		Petal et al 2011		Chen et al 2013		Chen et al 2018	
	IVUS	CAG	IVUS	CAG	IVUS	CAG	IVUS	CAG	IVUS	CAG
Patient, n (total)	974		4314		449		628		1465	
Patient, n	487	487	226	4088	202	247	324	304	310	1155
Age, y ± (SD)	62.0±9.6	61.8±10.2	64.0±11.0	64.0±11.0	62.0±11.9	65.9±12.2	64.3±9.7	64.5±10.0	64.0±11.0	64.0±10.0
Male, n	324	326	188	188	163	132	261	227	234	894
Hypertension, n	292	284	142	142	198	180	216	185	225	870
DM, n	155	162	51	51	76	77	60	54	93	393
Dyslipidemia, n	168	170	141	141	188	166	108	107	207	764
Current smoking, n	106	111	125	125	132	107	NA	NA	99	431
FHCA, n	19	16	103	103	NA	NA	147	154	2	5
CRF or CRD, n	15	15	15	15	30	24	NA	NA	63	255
Prior MI, n	42	39	92	92	NA	NA	50	35	23	97
Prior PCI, n	NA	NA	78	78	57	70	57	51	24	93
Prior CABG, n	NA	NA	22	22	46	36	0	0	3	6
LVEF(%), n	60.1±10.8	58.8±11.0	53.0±9.0	53.0±9.0	NA	NA	60.9±10.1	59.8±10.6	NA	NA
Clinicalpresentation										
SA, n	228	212	152	2077	50	59	35	57	0	0
UA, n	194	192	59	979	56	55	248	194	310	1155
NSTEMI, n	52	66	10	465	78	78	NA	NA	0	0
STEMI, n	13	17	5	997	24	18	NA	NA	0	0
DAPT	YES	YES	YES	YES	NO	NO	NA	NA	NA	NA
IIb/IIIa inhibitor	17	18	NA	NA	121	123	10	21	69	264

CABG = coronary artery bypass graft, CAG = Coronary Angiography, CRD = Chronicrenal disease, CRF = Chronicrenal failure, DAPT = dual antiplatelet therapy, DM = Diabetes mellitus, EHCA = Family history of coronaryartery disease, FHCA = Family history of coronary artery disease, IVUS = Intravascular ultrasound, LVEF = Left ventricular ejectionfraction, MI = Miocardial infarction, NA = Not accessible, NSTEMI = Non–ST-elevation MI, PCI = percutaneous coronary intervention, SA = Stable angina, STEMI = ST-elevation MI, UA = Unstable angina.

Table 2

lesions and procedural characteristics.

	Kim et al 2011		B-Z et al 2011		Petal et al 2011		Chen et al 2013		Chen et al 2018	
	IVUS	CAG	IVUS	CAG	IVUS	CAG	IVUS	CAG	IVUS	CAG
Lesion, n (total)	[0,2-3]974	[0,4-5]4487	[0,6-7]471	[0,8-9]628	[0,10-11]1465					
Lesions sites, n(total)	487	487	252	4235	258	213	324	304	310	1155
LM	17	19	58	331	37	4	137	83	50	52
LAD	404	402	149	2690	129	94	129	186	216	781
LCX	63	63	33	940	56	70	44	26	32	195
RCA	20	20	12	274	36	45	14	9	11	105
Multivessel disease, n	226	231	75	666	NA	NA	204	207	125	663
Chronictotalocclusion,n	40	40		NA	NA	NA	32	20	20	72
Calcification, n	142	147	NA	NA	NA	NA	154	131	12	39
Thrombus, n	20	21	NA	NA	NA	NA	26	13	14	154
[0,1-11]Medinaclassification, n										
1,1,1	220	239	NA	NA	230	190	NA	NA	244	930
1,0,1	33	23	NA	NA	2	2	NA	NA	NA	NA
0,1,1	66	62	162	NA	6	7	NA	NA	66	225
True bifurcation, n	319	324		2465	NA	NA	NA	NA	251	NA
[0,1-11]Stent number at bifurcation, n										
One-stent	357	409	NA	NA	NA	NA	NA	NA	188	402
Two-stent	130	78	NA	NA	NA	NA	NA	NA	122	753
[0,1-11]Stent technique, n										
MV stenting alone/SB	357	409	94	2795	174	118	NA	NA	NA	NA
T-stenting	77	34	25	538	22	17	27	36	NA	NA
V-stenting	NA	NA	14	118	38	57	NA	NA	NA	NA
Y-stenting	NA	NA	NA	NA	20	17	NA	NA	NA	NA
Crush	30	34	101	605	4	4	52	53	NA	NA
Culottes	2	2	16	97	NA	NA	52	20	NA	NA
Kissing stenting, n	21	8	NA	NA	NA	NA	193	193	NA	NA
[0,1-11]Maximalstentdiameter,mm										
MV	3.20±0.30	3.1±0.30	3.20±0.20	3.20±0.20	NA	NA	3.25±0.48	3.16±0.44	NA	NA
SB	2.8±0.30	2.75±0.25	2.75±0.25	2.75±0.25	NA	NA	2.99±0.57	2.56±0.56	NA	NA
[0,1-11]Total stent length, mm										
MV	32.0±14.0	30.9±13.1	25.0±7.0	22.0±6.0	17.1±5.2	15.0±4.6	32.67±12.6	30.53±13.1	NA	NA
SB	21.4±8.0	22.4±10.5	18.5±5.5	17.5±5.5	NA	NA	12.64±2.7	7.25±1.6	NA	NA
Procedural success, n	809	785	NA	NA	NA	NA	642	589	307	1135

CAG = coronary angiography, IVUS = intravascular ultrasound, LAD = left anterior descending, LCX = left circumflex artery, LM = left main disease, MV = main vessel, NA = not accessible, RCA = right coronary artery, SB = site branch.

Cardiac death
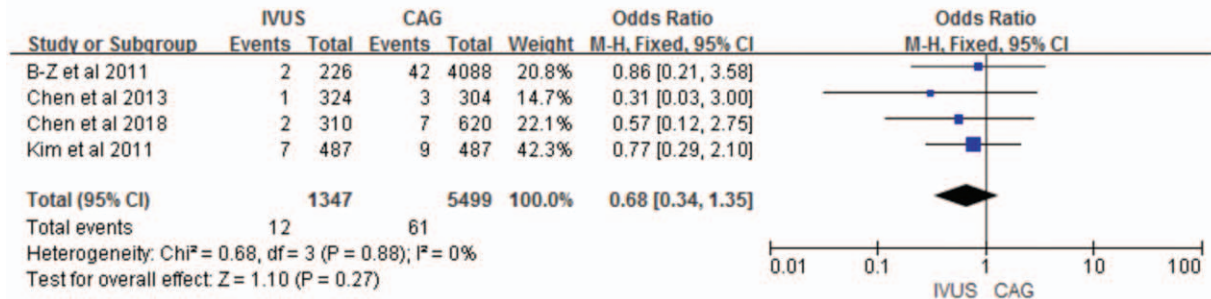
Target lesion revascularization or target vessel revascularization
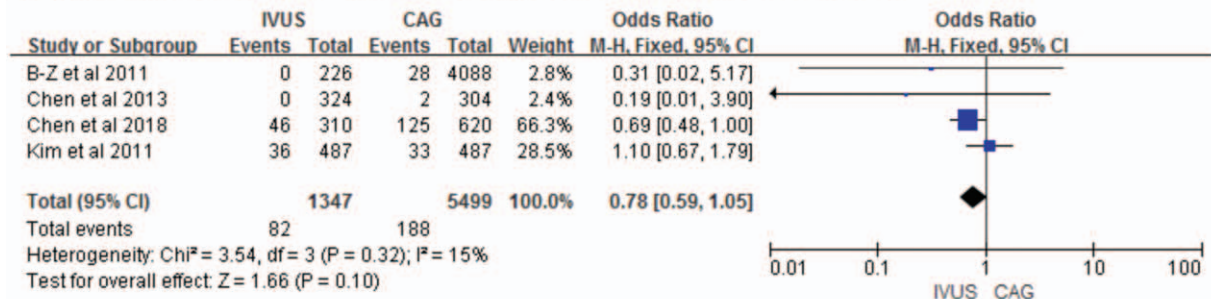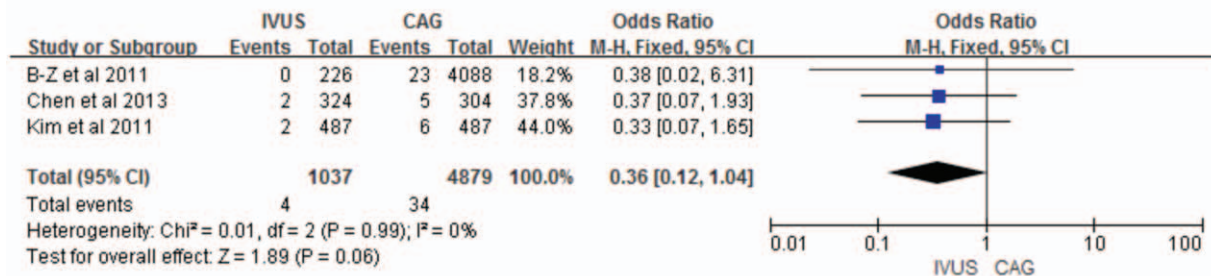
Stent thrombosis

MACE
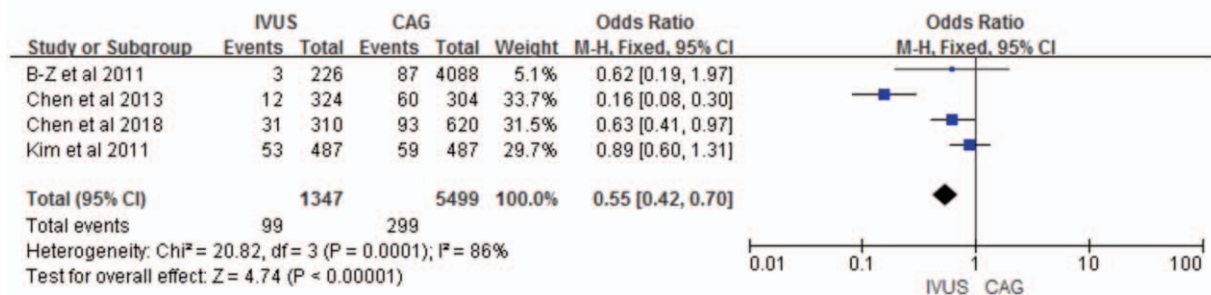
Figure 2. Forest plots comparing early endpoint of cardiac death, target lesion revascularization or target vessel revascularization, stent thrombosis and MACE between the IVUS-guided and angiography-guided PCI strategies. IVUS = Intravascular Ultrasound, PCI = Percutaneous Coronary Intervention, MACE = Major Adverse Cardiac Events.

the higher success rate of final kissing balloon inflation (13.4% vs 12.5%) at the operation process.

Nevertheless, these results should be explained and analyzed from different perspectives. First, an operation strategy mainly depended on dynamic factors such as the experience of the operator and the characteristics of patients. Second, reasons for different underlying pathologic processes might be that rigorous post-dilation after stent implantation guided with IVUS could be beneficial for a larger-size left main disease with stable plaque. However, it could be harmful in acute myocardial infraction with

Cardiac death

Study or Subgroup	IVUS Events	IVUS Total	CAG Events	CAG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Patel et al 2012	14	258	24	213	30.4%	0.45 [0.23, 0.90]
Chen et al 2018	4	310	40	620	32.1%	0.19 [0.07, 0.53]
Chen et al 2013	3	324	10	304	12.5%	0.27 [0.07, 1.01]
B-Z et al 2011	6	226	201	4088	25.0%	0.53 [0.23, 1.20]
Total (95% CI)		**1118**		**5225**	**100.0%**	**0.36 [0.23, 0.57]**
Total events	27		275			

Heterogeneity: Chi² = 2.86, df = 3 (P = 0.41); I² = 0%
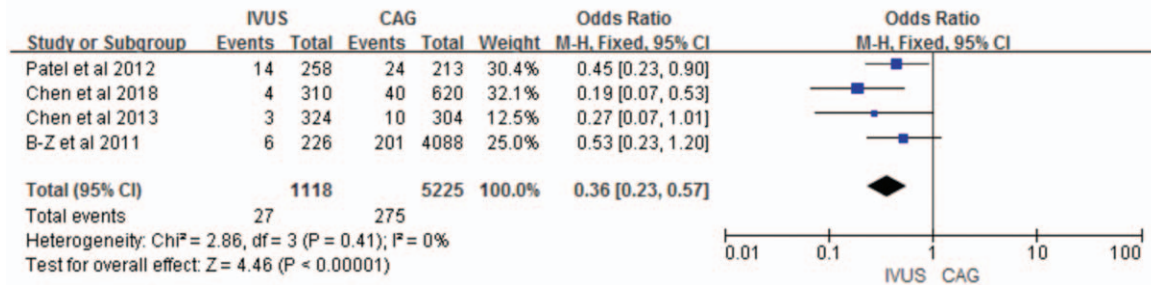Test for overall effect: Z = 4.46 (P < 0.00001)

Figure 3. Forest plots comparing late endpoint of cardiac death between the IVUS-guided and angiography-guided PCI strategy. IVUS = Intravascular ultrasound, PCI = percutaneous coronary intervention.

The early follow-up

MACE

Study or Subgroup	IVUS Events	IVUS Total	CAG Events	CAG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
B-Z et al 2011	3	226	87	4088	0.0%	0.62 [0.19, 1.97]
Chen et al 2013	12	324	60	304	30.1%	0.16 [0.08, 0.30]
Chen et al 2018	31	310	93	620	28.1%	0.63 [0.41, 0.97]
Kim et al 2011	53	487	93	487	41.8%	0.52 [0.36, 0.74]
Total (95% CI)		**1121**		**1411**	**100.0%**	**0.44 [0.34, 0.57]**
Total events	96		246			

Heterogeneity: Chi² = 13.37, df = 2 (P = 0.001); I² = 85%
Test for overall effect: Z = 6.39 (P < 0.00001)

Study or Subgroup	IVUS Events	IVUS Total	CAG Events	CAG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
B-Z et al 2011	3	226	87	4088	6.1%	0.62 [0.19, 1.97]
Chen et al 2013	12	324	60	304	0.0%	0.16 [0.08, 0.30]
Chen et al 2018	31	310	93	620	37.8%	0.63 [0.41, 0.97]
Kim et al 2011	53	487	93	487	56.1%	0.52 [0.36, 0.74]
Total (95% CI)		**1023**		**5195**	**100.0%**	**0.57 [0.43, 0.74]**
Total events	87		273			

Heterogeneity: Chi² = 0.49, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 4.11 (P < 0.0001)

Study or Subgroup	IVUS Events	IVUS Total	CAG Events	CAG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
B-Z et al 2011	3	226	87	4088	5.9%	0.62 [0.19, 1.97]
Chen et al 2013	12	324	60	304	39.4%	0.16 [0.08, 0.30]
Chen et al 2018	31	310	93	620	0.0%	0.63 [0.41, 0.97]
Kim et al 2011	53	487	93	487	54.7%	0.52 [0.36, 0.74]
Total (95% CI)		**1037**		**4879**	**100.0%**	**0.38 [0.28, 0.52]**
Total events	68		240			

Heterogeneity: Chi² = 10.77, df = 2 (P = 0.005); I² = 81%
Test for overall effect: Z = 6.29 (P < 0.00001)

Study or Subgroup	IVUS Events	IVUS Total	CAG Events	CAG Total	Weight	Odds Ratio M-H, Fixed, 95% CI
B-Z et al 2011	3	226	87	4088	7.2%	0.62 [0.19, 1.97]
Chen et al 2013	12	324	60	304	47.9%	0.16 [0.08, 0.30]
Chen et al 2018	31	310	93	620	44.9%	0.63 [0.41, 0.97]
Kim et al 2011	53	487	93	487	0.0%	0.52 [0.36, 0.74]
Total (95% CI)		**860**		**5012**	**100.0%**	**0.40 [0.29, 0.56]**
Total events	46		240			

Heterogeneity: Chi² = 12.99, df = 2 (P = 0.002); I² = 85%
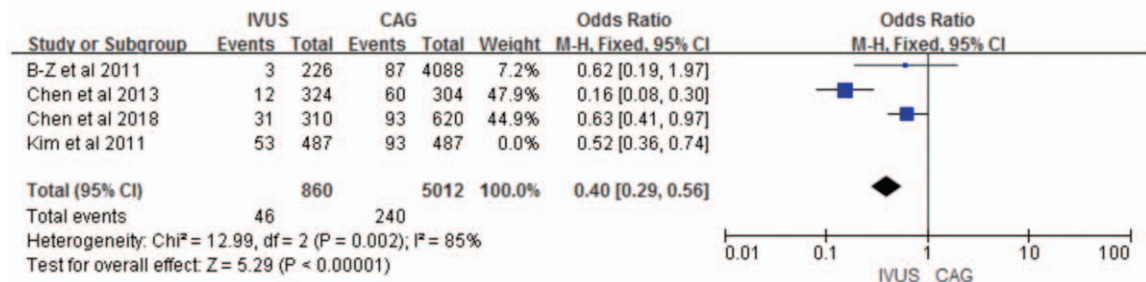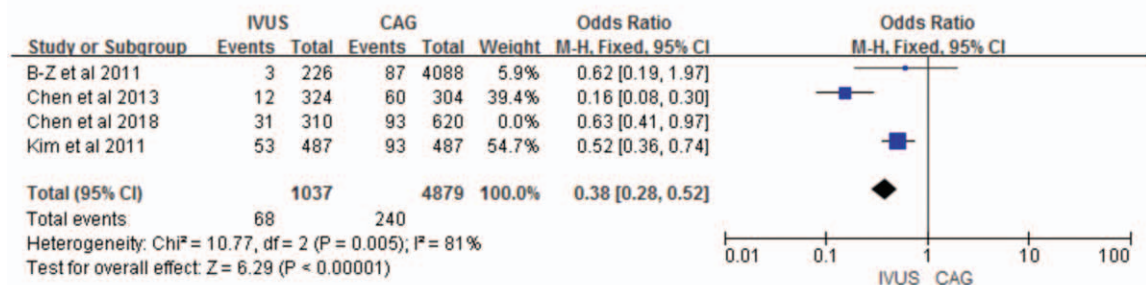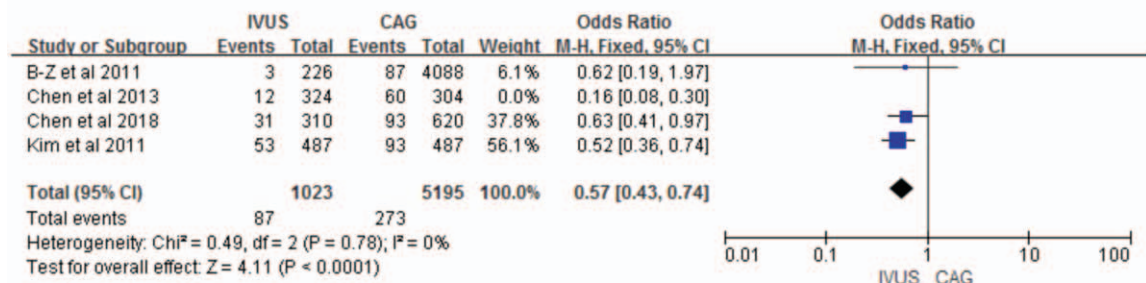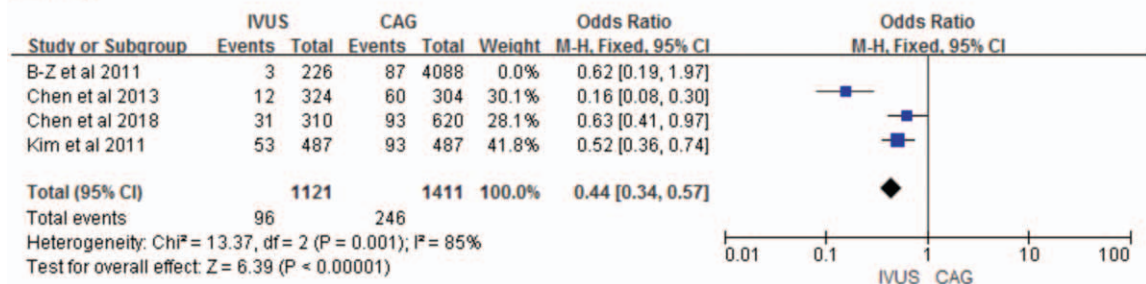Test for overall effect: Z = 5.29 (P < 0.00001)

Figure 4. Heterogeneity analysis in the early endpoint of MACE between the IVUS-guided and angiography-guided PCI strategy. Remove single study one by one show that, Chen et al 2013 is a source of heterogeneity. IVUS = Intravascular ultrasound, PCI = percutaneous coronary intervention, MACE = major adverse cardiac events.
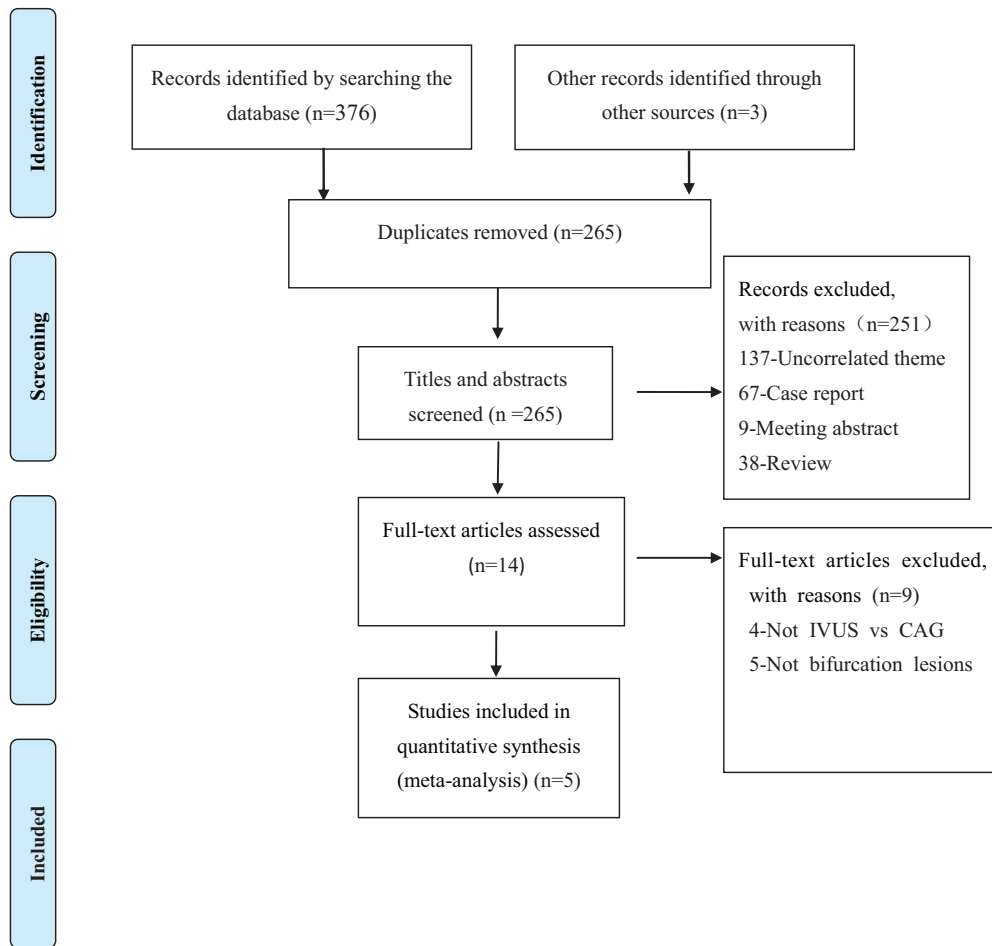
Figure 5. Retrieval Flow Chart.

thrombus. Third, discontinuation of anti-platelet therapy also was a predictor of post-procedural stent thrombosis, although no specific anti-platelet therapy data about each study were obtained in this study. Fourth, different sample sizes and follow-up durations could be another factor. Although the exact mechanism of clinical benefits using IVUS at bifurcation lesions is not clearly explained, the complexity of coronary bifurcation lesions could be an adequate lesion subset for the investigation of the benefits of IVUS during PCI. The morphology and type of bifurcation are crucial factors for selecting optimal treatment strategies to approach bifurcation lesions. The IVUS - guidance may help define its geometry, plaque distribution including characteristics, and degree of side branch - ostium involvement before the procedure. In the true bifurcation, the complex anatomical/morphological features lesions masked with angiogram could be detected by IVUS.

4.1. Limitations

Although this study included a non-randomized, retrospective and observational study, and rigorous statistical adjustments were presented with propensity score matching, confounding factors may still affect the results of the study. Patients at different baseline levels and stent types may have an undetermined effect on the outcome of clinical endpoint events. For example, whether IVUS was used or not by the operator during PCI, the operator was more inclined to patients with more stable hemodynamics and the best surgical strategy. However, the predefined criteria to optimize stent placement procedures were not used in this study. Although astonishingly significant differences between IVUS - guided and angiographic-guided PCI groups were carefully analyzed, other unknown reasons that may result in differences in clinical outcomes between the 2 groups are not comprehensively considered and analyzed. There all - time IVUS analysis is done using online software during PCI, which may be a source of error compared with standard commercial IVUS software. Finally, the sample size is insufficient to assess the low incidence of late stent thrombosis. Most importantly, the main drawback of this meta-analysis is that it only includes 1 recent study, resulting in relatively weak timeliness. In addition, IVUS - guided revascularization had no significant effect on early cardiac death. These limitations above may result in no significant reduction in early cardiac death.

5. Conclusion

The IVUS-guided PCI strategy was associated with more clinical benefits compared with angiography - guided PCI strategy in patients with coronary bifurcation lesions. These findings suggest that the IVUS - guided PCI strategy can be recommended as an optimization in this kind of patients.

Author contributions

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