

Duration of dual antiplatelet therapy in patients undergoing percutaneous coronary intervention for bifurcation lesions: a systematic review and meta-analysis

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Background The optimal duration of dual antiplatelet therapy (DAPT) in patients undergoing percutaneous coronary intervention for coronary bifurcation lesions remains uncertain. This meta-analysis focused on comparing ischemic and bleeding outcomes between short-term (≤ 6 months) and long-term (> 6 months) DAPT in this high-risk subgroup.

Methods We included six studies comprising 12 066 patients with bifurcation lesions treated with drug-eluting stents and either short- or long-term DAPT. Pooled relative risk (RR) and 95% confidence intervals (CI) were calculated for major adverse cardiovascular events (MACE), all-cause and cardiac mortality, myocardial infarction, stent thrombosis, stroke, bleeding, and target lesion revascularization.

Results Short-term DAPT was associated with significantly higher risks of MACE (RR 1.79; 95% CI 1.05–3.07), all-cause mortality (RR: 2.78; 95% CI: 1.49–5.19), cardiac death (RR 2.29; 95% CI 1.34–3.91), and stent thrombosis (RR: 4.90; 95% CI: 2.78–8.66). Although the risks of myocardial infarction (RR: 1.75; 95% CI: 0.69–4.47), stroke (RR: 1.07; 95% CI: 0.61–1.67), bleeding (RR: 1.49; 95% CI: 0.24–9.48), and target lesion revascularization (RR: 1.35; 95% CI: 0.85–2.12) did not reach statistical significance, the effect estimates consistently favored long-term DAPT.

Introduction

Dual antiplatelet therapy (DAPT), composed of aspirin and a P2Y₁₂ inhibitor, is essential for secondary prevention after percutaneous coronary intervention (PCI) for acute coronary events. In anatomically complex scenarios, such as bifurcation lesions, the thrombotic risk is higher, which historically supported the use of prolonged DAPT to reduce ischemic complications, as suggested by

Conclusion In patients undergoing percutaneous coronary intervention for bifurcation lesions, short-term DAPT was associated with significantly worse ischemic outcomes, including increased rates of MACE, death, and stent thrombosis. These findings support the use of extended DAPT duration as the preferred strategy in this anatomical subgroup, with treatment tailored according to individual bleeding risk. *Coron Artery Dis XXX: XXXX–XXXX* Copyright © 2026 Wolters Kluwer Health, Inc. All rights reserved.

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clinical guidelines [1,2]. However, it is important to note that this risk is not uniform across all bifurcation lesions, as higher anatomical complexity and the use of two-stent techniques are more consistently associated with increased thrombotic risk. Extended treatment does, however, also raise the risk of bleeding, which makes it difficult to determine the ideal ratio of hemorrhagic risk to ischemic protection.

More recently, there has been an increase in interest in customized antiplatelet strategies that consider each patient's unique ischemic and bleeding characteristics. One suggested strategy, especially for patients with

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a higher risk of bleeding, is to reduce the duration of DAPT to one to three months and then administer P2Y12 inhibitor monotherapy [3,4]. Since there are no widely accepted guidelines for this subgroup, extending DAPT past 12 months in complex anatomical settings, such as bifurcation lesions, often depends on clinical judgment and patient-specific factors [5,6].

Longer DAPT courses have historically been justified by the general belief that patients undergoing PCI for bifurcation lesions are at higher risk of ischemic attacks. However, the development of uniform guidance is limited by the lack of a consistent classification for complex PCI and the heterogeneity in study definitions [6,7]. Additionally, many patients in this group also present with high bleeding risk, underscoring the need for refined, risk-adapted therapeutic strategies [8].

In this context, a systematic evaluation of available evidence is needed to compare the efficacy and safety of short- vs. long-term DAPT in patients treated with PCI for bifurcation lesions, considering both bleeding and ischemic outcomes.

Methods

This systematic review and meta-analysis were conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [9] and was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [10] (Supplementary Methods 1 and 2, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>). The protocol was prospectively registered in the International Prospective Register of Systematic Reviews (CRD420251119552).

Search strategy

A comprehensive literature search was performed in PubMed, Scopus, Embase, Web of Science, and the Cochrane Library from database inception to July 2025. Two independent reviewers (J.R. and L.A.) conducted the search using a standardized Boolean strategy designed to capture all relevant studies evaluating short- vs. long-DAPT undergoing coronary interventions for bifurcation lesions. The following search terms were applied across all databases: ('coronary bifurcation' OR 'bifurcated lesions' OR 'bifurcation lesion*' OR 'bifurcation stenting') AND ('dual antiplatelet therapy' OR DAPT OR antiplatelet) AND ('percutaneous coronary intervention' OR PCI OR 'drug-eluting stents'). Only articles in English were included and no restrictions were made regarding publication date.

Study selection

Titles and abstracts were screened independently by two reviewers (J.R. and A.A.), and full texts of potentially eligible studies were retrieved for detailed assessment. Disagreements were resolved by discussion or by

consultation with a third reviewer (R.S.-M.). All stages of study selection were conducted using the Rayyan online platform [11].

Eligibility criteria

We included studies enrolling adult patients undergoing PCI for coronary bifurcation lesions treated with DES undergoing either short duration DAPT (defined as ≤ 6 months of aspirin plus a P2Y12 inhibitor) or long-term DAPT (defined as >6 months for 12 months or more) with the same antiplatelet regimen. Both randomized controlled trials and observational studies were eligible, irrespective of follow up duration. Studies were excluded if they did not include patients without bifurcated lesions, were case reports, conference abstracts, review articles, or other nonoriginal research.

Outcomes

Prespecified outcomes included major adverse cardiovascular events (MACE), as defined by each study [usually a composite of death, myocardial infarction (MI), stroke, target vessel revascularization]. To address the inherent variability in these definitions, each study's endpoint criteria were reviewed to ensure overall clinical comparability for the pooled analysis. Other outcomes included all-cause mortality, cardiac mortality, MI, definite or probable stent thrombosis (per ARC definitions), target lesion revascularization (TLR), and target vessel revascularization.

Data extraction

Data extraction was performed independently by two reviewers (L.M. and L.A.) using a prespecified data extraction form in Excel (Microsoft Corporation, Redmond, Washington, USA). Extracted information included study identifiers (authors, year, and country), study design, sample size, patient demographics, follow up duration and outcomes. Disagreements were resolved through discussion with a third reviewer (R.S.-M.).

Statistical analysis

Statistical analyses were performed using RStudio software (version 4.5.1; Posit Software, PBC, Boston, Massachusetts, USA) and the 'meta' package [12]. Relative risk (RR) with 95% confidence intervals (CIs) were calculated for binary outcomes and mean difference for continuous outcomes. Forest plots were generated to visualize the results. Heterogeneity was assessed using the I^2 statistic, with a threshold of more than 50% used to define significant clinical and methodological heterogeneity. A random-effects model was applied to account for potential variations across the included studies, with statistical significance defined as $P < 0.05$.

Risk of bias assessment and certainty of evidence

Risk of bias was assessed independently by two reviewers (J.R. and L.M.) using Cochrane RoB 2.0 tool for randomized trials and the ROBINS-1 tool for nonrandomized studies [13]. All assessments were conducted manually, with discrepancies resolved by a consensus or adjudication by a third reviewer (R.S-M.). The certainty of evidence for each outcome was evaluated using the Grading of Recommendations Assessment, Development and Evaluation framework. We assessed five specific domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of the evidence was categorized into four levels: high, moderate, low, or very low. The detailed evidence profile is provided in Table S1, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>.

Results

Study selection

A total of 999 records were retrieved through systematic database searches, including PubMed ($n = 91$), Web of Science ($n = 188$), Scopus ($n = 240$), Embase ($n = 425$), and Cochrane ($n = 55$). After removing 327 duplicates, 672 titles and abstracts were screened, of which $\times$ were excluded based on predefined eligibility criteria. Sixteen full-text articles were assessed in detail and 10 were excluded for not fitting the established outcomes. Ultimately, six studies [14–19] met the inclusion criteria and were included in the meta-analysis. The study selection process is illustrated in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow-chart (Fig. 1).

Baseline characteristics of the included studies and patients

The baseline characteristics of the included studies are presented in Table 1. Overall, 74.5% of participants were male, with a mean follow up duration of 28.4 months. The studies varied in design (randomized and observational), geographic location, sample size, follow up duration, and patient profiles. Across studies, participants had established bifurcated coronary lesions and were undergoing intervention either with long or short DAPT. For instance, in the ULTRA-BIFURCAT [14] study, patients in the short DAPT group presented with a higher baseline risk profile compared to those in the long DAPT group. In addition to the ULTRA-BIFURCAT trial, other studies demonstrated significant differences in patient complexity and treatment protocols. For example, the REDUCE trial included only patients treated with a specific bioabsorbable polymer-coated stent, whereas others utilized a variety of newer-generation drug-eluting stents. Furthermore, studies like LEADERS FREE focused on patients at high bleeding risk, a population with baseline characteristics, such as older age and more comorbidities, that

differ substantially from the general population included in trials like SMART-CHOICE or STOPDAPT-2. These variations in clinical presentation and risk profiles contribute to the observed clinical heterogeneity and underscore the importance of a tailored approach to DAPT duration.

Outcomes

All-cause death

Five studies ($n = 9791$; short DAPT = 2721; long DAPT = 7070) reported data on all-cause death. The pooled estimate showed a statistically significant increased risk in all-cause death in patients undergoing short-term DAPT treatment (RR: 2.78; 95% CI: 1.49–5.19; $P = 0.00129$) with substantial heterogeneity ($I^2 = 88.7\%$) (Fig. 2).

Bleeding

Three studies encompassing 3562 patients (short DAPT = 1132; long DAPT = 2430) assessed the risk of bleeding. The pooled estimate showed nonsignificant statistically increased risk of bleeding in patients undergoing short DAPT (RR: 1.49; 95% CI: 0.24–9.48; $P = 0.671$) with substantial heterogeneity ($I^2 = 82.3\%$) (Fig. 3).

Cardiac death

Four studies encompassing 6499 patients (short DAPT: 1602; long DAPT: 4897) assessed cardiac death between groups. The pooled estimate showed significant increased risk of cardiac death in patients undergoing short DAPT (RR = 2.29; 95% CI 1.34–3.91; $P = 0.0025$) with low heterogeneity ($I^2 = 6.1\%$) (Fig. 4).

Major adverse cardiovascular events

Six studies reported data on MACE ($n = 12,066$; short DAPT = 3038; long DAPT = 9028). Short DAPT was associated with a significantly increased risk of MACE (RR = 1.79; 95% CI = 1.05–3.07; $P = 0.034$), with significant heterogeneity ($I^2 = 93.4\%$) (Fig. 5).

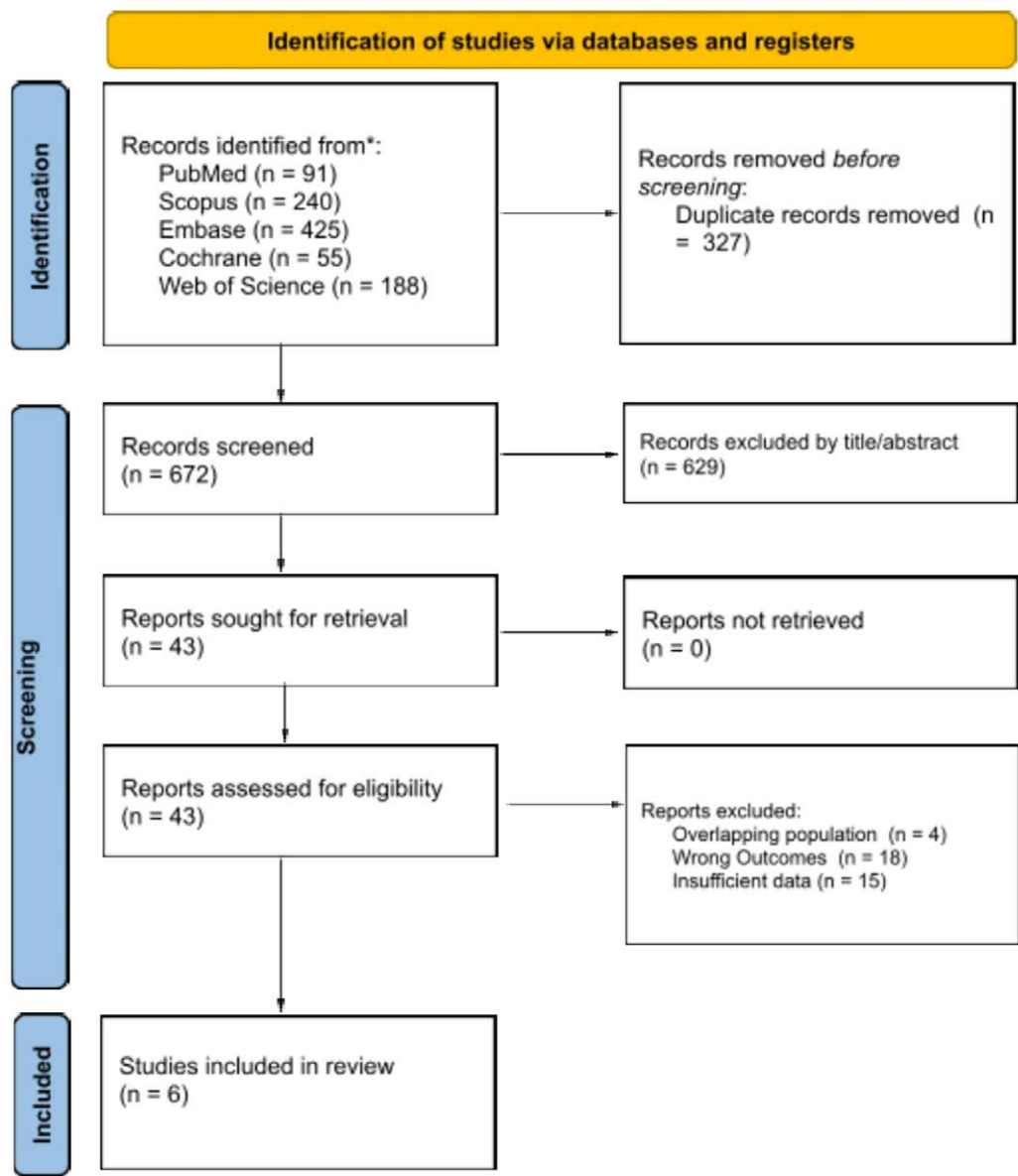
Myocardial infarction

Six studies, encompassing 12,066 patients (short DAPT = 3038; long DAPT = 9028) reported data on MI. The pooled estimate showed short DAPT was associated with increased risk of MI but without statistical significance (RR = 1.75; 95% CI: 0.69–4.47; $P = 0.242$) and significant heterogeneity ($I^2 = 89.5\%$) (Fig. 6).

Stent thrombosis

Four studies ($n = 8791$; short DAPT = 2115; long DAPT = 6676) assessed data on stent thrombosis. The short DAPT usage showed statistically significant increase in risk for stent thrombosis (RR = 4.90; 95% CI: 2.78–8.66; $P < 0.001$), with moderate heterogeneity ($I^2 = 25.6\%$) (Fig. 7).

Fig. 1



PRISMA flow diagram. PRISMA, Systematic Review and Meta-analysis.

Stroke

Four studies encompassing 6,508 patients (short DAPT = 2,296; long DAPT = 4,212) assessed data on stroke. A trend toward increased risk was observed in patients undergoing short DAPT was noticed (RR = 1.07; 95% CI: 0.61–1.67) though the result was not statistically significant ($P = 0.766$) with no heterogeneity ($I^2 = 0$) (Fig. 8).

Target lesion revascularization

Three studies ($n = 7,842$; short DAPT = 1,753; long DAPT = 6,089) assessed data on TLR. The pooled analysis registered a trend of increased risk in patients

undergoing short-term DAPT (RR = 1.35; 95% CI: 0.85–2.12) though results were not statistically significant ($P = 0.2$) with high heterogeneity ($I^2 = 63.7\%$) (Fig. 9).

Sensitivity analysis

A sensitivity analysis using the leave-one-out and funnel plot method was carried out to identify the main sources of heterogeneity (Figures S1 and S2, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>). For the all-cause death outcome, the exclusion of the ULTRA-BIFURCAT[14] reduces the heterogeneity to 56.7% (Figure S2.1, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>). In cardiac death,

Table 1 Baseline characteristics of the studies and patients

Study	Country	Design	Sample size	Gender M/F	Age	Intervention CLO/T/P	Dyslipidemia	Hypertension	Diabetes	DAPT duration	Previous PCI	CKD	Smoking	Follow up (months)
ULTRA-BIFURCAT [14]	Italy	Retrospective	6729	5160/1569	NR	Short: 3828 Long: 2898	Short: 2172 Long: 1158	Short: 3267 Long: 1594	Short: 1215 Long: 892	Short: 3871 Long: 2858	Short: 1114 Long: 395	Short: 703 Long: 99	Short: 76 Long: 13	26
Khelismkii [15]	Russia	Prospective	1000	730/270	62.2	Short: 1212 Long: 788	Short: 243 Long: 165	Short: 563 Long: 369	Short: 155 Long: 96	Short: 606 Long: 349	Short: 242 Long: 196	NR	NR	35
Jang [16]	South Korea	Retrospective	2082	1485/597	61.5	2082 A/CLO	Short: 121 Long: 554	Short: 167 Long: 1000	Short: 71 Long: 487	Short: 306 Long: 1776	Short: 33 Long: 230	Short: 8 Long: 36	Short: 76 Long: 494	12
D'Ascenzo [17]	Italy	Retrospective	2275	1764/511	Short: 68.5 Long: 68.8	Short: 315 Long: 1910	Short: 191 Long: 1092	Short: 230 Long: 1428	Short: 118 Long: 555	Short: 317 Long: 1958	Short: 101 Long: 573	Short: 64 Long: 307	Short: 78 Long: 378	8 - 20
Cirillo [18]	Italy	Retrospective	2284	1576/708	Short: 66 Long: 65	Short: 956 Long: 1206	Short: 679 Long: 895	Short: 740 Long: 1028	Short: 346 Long: 462	Short: 1011 Long: 1273	Short: 322 Long: 497	NR	Short: 470 Long: 675	24
Cho [19]	South Korea	Retrospective	1142	852/290	Short: 63.8 Long: 62.6	1142 A/CLO	Short: 191 Long: 316	Short: 218 Long: 467	Short: 123 Long: 426	Short: 373 Long: 769	Short: 64 Long: 170	Short: 12 Long: 28	Short: 123 Long: 253	60

Data are presented as mean $\pm$ SD, number (no.), or median (interquartile range). A/CLO, aspirin and clopidogrel; CKD, chronic kidney disease; CLO/T/P, clopidogrel, ticagrelor and prasugrel; DAPT, dual antiplatelet therapy; M/F, male/female; NA, not available; NR, not reported; PCI, percutaneous coronary intervention.

removing Khelismkii [15] or Cho [19] reduced the heterogeneity to 0%; however, none of them yielded a different result (Figure S2.3, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>).

Quality assesment

Risk of bias assessment using the ROBINS-I tool [13] revealed that three studies (ULTRA-BIFURCAT [14]; D'Ascenzo [17]; Cirillo [18]) had a serious overall risk, mainly due to uncontrolled confounding and issues in participant selection. In contrast, the studies by Jang [16], Khelismkii [15], and Cho [19] showed a moderate risk of bias, supported by the use of propensity score adjustment or landmark analyses. Overall, the observational nature of these studies and residual confounding highlight the need for randomized trials to better define optimal DAPT duration in bifurcation PCI (Figure S3A and S3B, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>).

Certainty of evidence (Grading of Recommendations Assessment, Development and Evaluation)

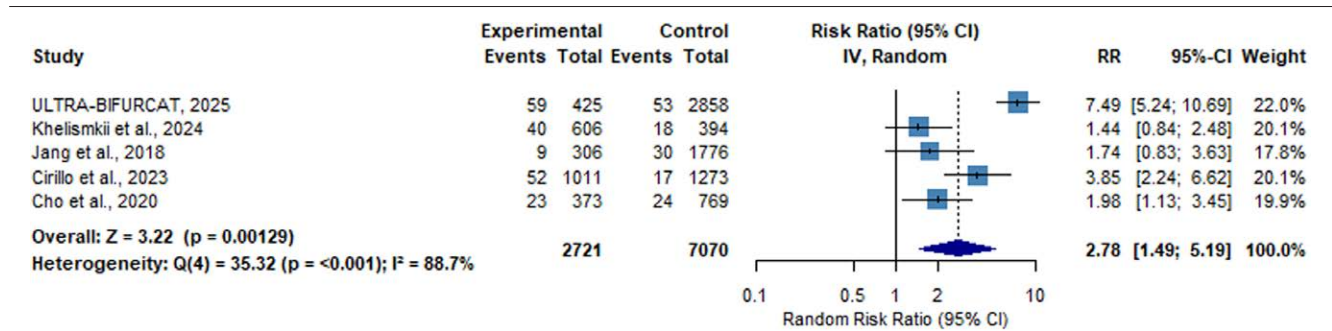
The certainty of evidence for the primary outcome (MACE), all-cause mortality, and stent thrombosis was rated as moderate. This assessment reflects the consistent direction of effect across studies, although it was downgraded by one level due to the inclusion of observational data (risk of bias). For bleeding outcomes, the certainty was rated as low, primarily due to imprecision, as the confidence intervals were wide and crossed the null effect (Table S1, Supplemental Digital Content 1, <https://links.lww.com/MCA/A808>).

Discussion

In this systematic review and meta-analysis, we assessed the effectiveness and safety of short vs. long-duration DAPT in patients undergoing PCI for bifurcation lesions. Our findings show that short-term DAPT carries a significantly higher risk of MACE, all-cause mortality, cardiac death, and stent thrombosis compared to long-term DAPT. Although differences in MI, stroke, bleeding, and TLR did not reach statistical significance, the estimates consistently favored longer therapy durations.

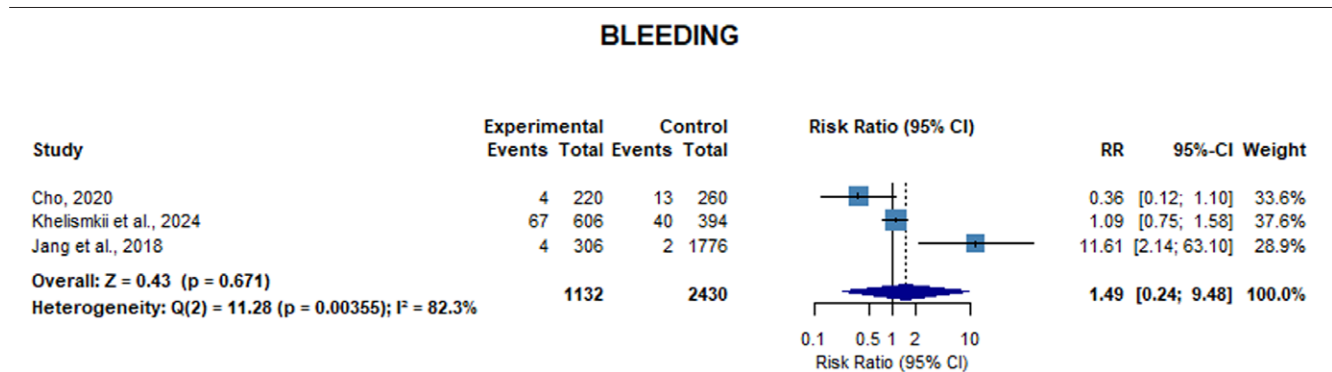
Bifurcation lesions are a notable and challenging category of PCI. They make up about 20% of all PCIs and are linked to greater procedural complexity, lower immediate success rates, and higher restenosis than nonbifurcation lesions [20]. Flow disturbances at bifurcations lead to local atherothrombosis, and performing PCI on these lesions has higher rates of thrombotic complications. Despite this, most DAPT trials and guidelines have not specifically addressed bifurcation anatomy. Focusing on bifurcations is therefore new and clinically important, as the ideal DAPT duration in this high-risk situation remains unclear. A dedicated analysis of bifurcation

Fig. 2



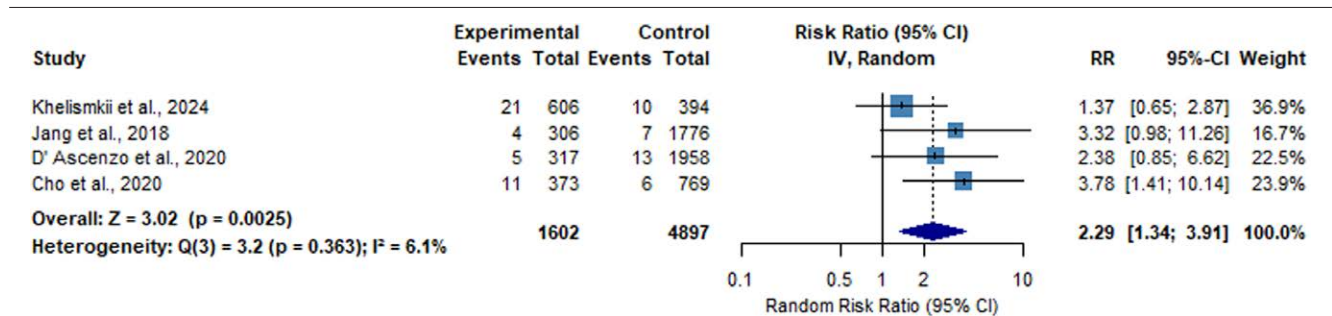
Forest plot of all-cause death comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

Fig. 3



Forest plot of bleeding comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

Fig. 4

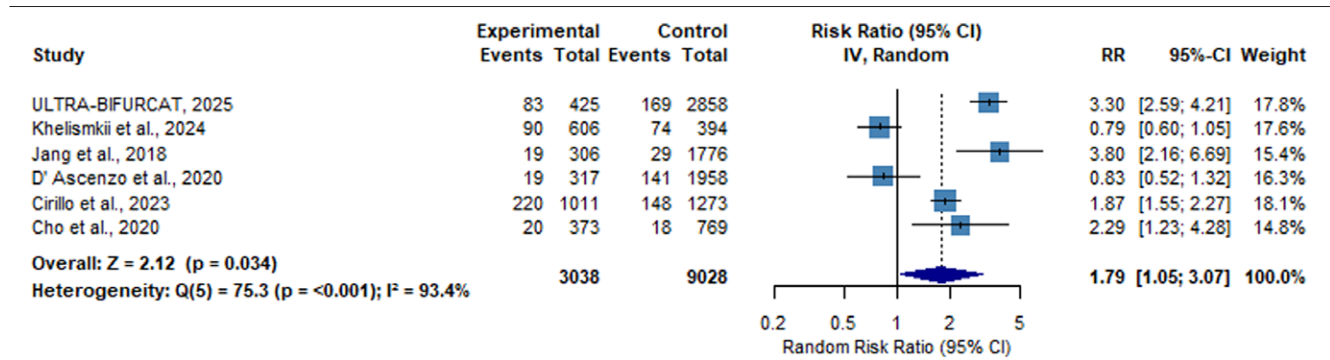


Forest plot of cardiac death comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

PCI fills a significant evidence gap, considering the specific risk of thrombosis associated with these lesions. It is essential to recognize that the thrombotic risk is a spectrum; while simple bifurcations treated with a provisional approach may carry lower risk, complex bifurcations, often involving large side branches or requiring two-stent strategies, represent the highest-risk anatomical scenario [20–22].

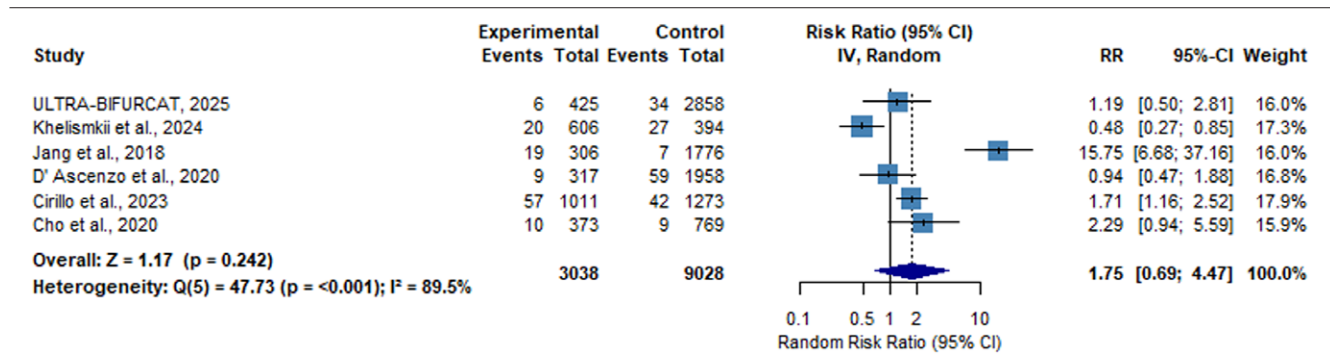
Improved stent designs for bifurcation lesions may change the DAPT duration requirements by tackling key factors that cause thrombosis. These specialized stents could potentially lower the inherent thrombotic risk of bifurcation PCI. This technological advancement might eventually enable shorter DAPT regimens in selected cases, especially when combined with better procedural techniques and improved patient risk assessment [22].

Fig. 5



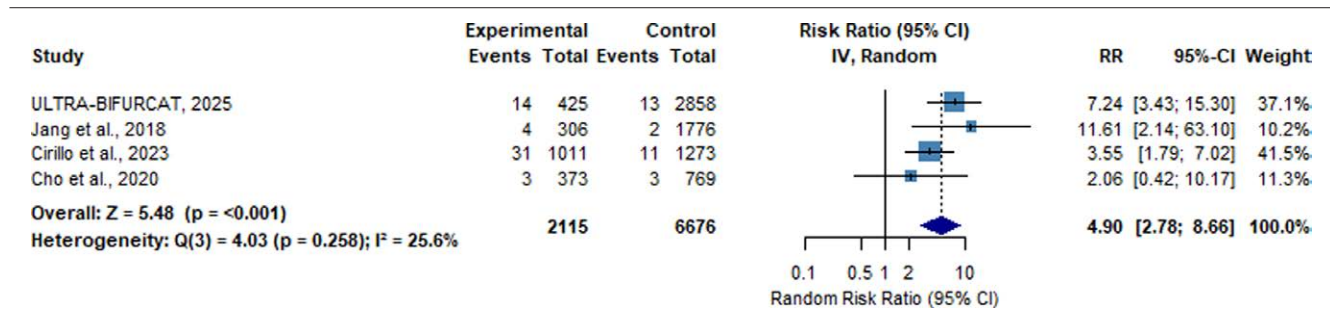
Forest plot of MACE events comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy; MACE, major adverse cardiovascular events.

Fig. 6



Forest plot of myocardial infarction comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

Fig. 7

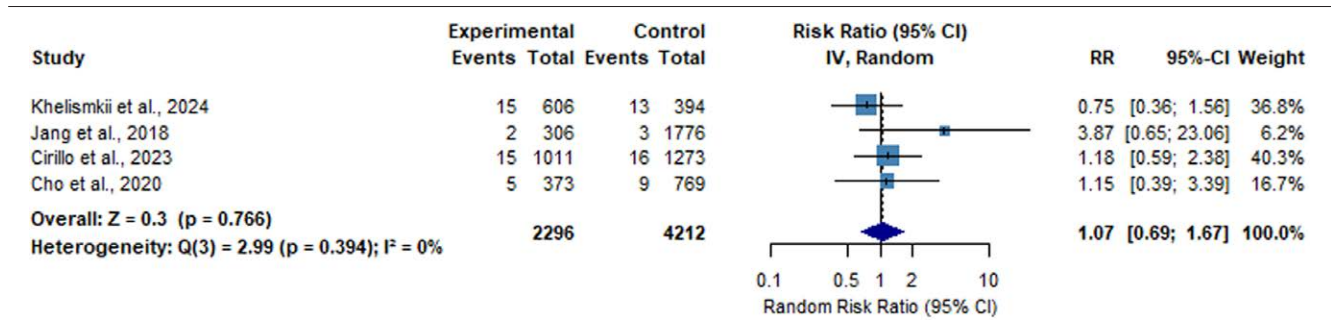


Forest plot of stent thrombosis comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

The higher risk of MACE with shorter DAPT regimens aligns with results from the DK-CRUSH-V trial, which showed that complex bifurcation lesions may benefit from extended antithrombotic therapy. These findings indicate that high-complexity bifurcation PCI may need longer DAPT duration to enhance ischemic outcomes [23].

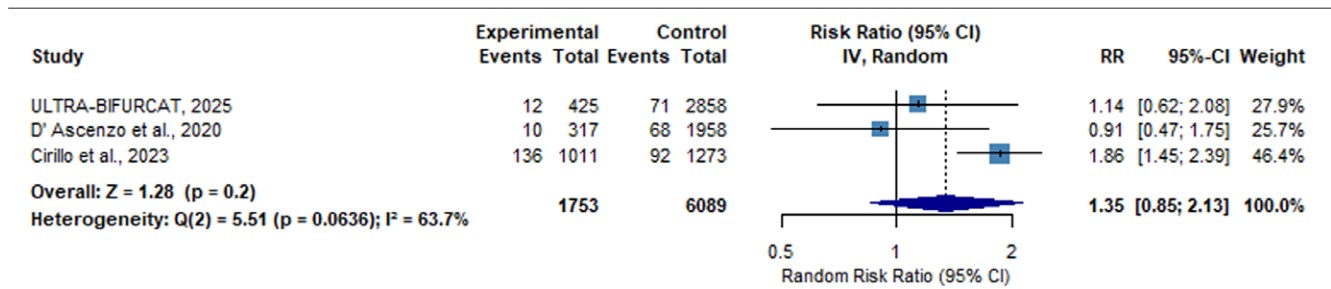
Xiang et al.'s meta-analysis [24], which compared shorter (≤ 6 months) vs. longer (≥ 12 months) DAPT durations including patients with bifurcation, found a significant 49% reduction in major bleeding risk with shorter therapy, without a statistically significant increase in stent thrombosis. In contrast, our meta-analysis did not show a statistically significant difference in bleeding events

Fig. 8



Forest plot of stroke comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

Fig. 9



Forest plot of target lesion revascularization comparing short and long-term DAPT in patients with bifurcation lesions. DAPT, dual antiplatelet therapy.

between the compared DAPT durations. This difference could be due to variations in study selection, patient populations, or bleeding definitions, highlighting the need for further investigation into the optimal DAPT duration that balances bleeding and thrombotic risks.

While provisional stenting is still the favored strategy for most coronary bifurcation lesions due to its procedural simplicity and positive outcomes, ongoing advances in intravascular imaging, specialized bifurcation devices, and new methods like bioresorbable scaffolds and drug-coated balloons offer potential for improving complex bifurcation management. More evidence is needed to determine their definitive clinical roles [25]. The use of intravascular imaging guidance, especially optical coherence tomography, has further improved optimal stent deployment and expansion, possibly reducing the thrombotic burden associated with complex bifurcation anatomy [26].

In conclusion, for patients undergoing PCI of coronary bifurcation lesions, current evidence strongly supports using longer DAPT durations to reduce ischemic risks. While bleeding concerns remain relevant, the specific thrombotic vulnerability of bifurcation lesions suggests that extended therapy should be the standard approach, tailored to individual patient bleeding risk assessments.

Limitations

This meta-analysis has several limitations. First, the high heterogeneity observed across key outcomes likely stems from variability in study designs, patient populations, and definitions of DAPT duration (short DAPT defined as ≤6 months vs. long DAPT as >6 months). Second, this analysis only included observational studies which introduces potential confounding, as unmeasured variables (e.g. procedural complexity, stent type, or adjunctive therapies) may influence outcomes. Also, bleeding outcomes were underpowered (only 3 studies), which demonstrates lack of studies to analyze this outcome. Third, the definition of MACE was not uniform across all included studies. While we reviewed these criteria for clinical consistency, the inherent variability in composite endpoints, such as the inclusion or exclusion of revascularization or specific causes of death, may introduce clinical heterogeneity and should be considered when interpreting the combined results. Fourth, this meta-analysis was limited by the lack of granular patient-level data regarding clinical presentation (ACS vs. CCS) and the specific type of P2Y12 inhibitor prescribed. Additionally, we were unable to perform a subgroup analysis based on the stenting technique (one-stent vs. two-stent), which is known to significantly impact the risk of late thrombotic events. These

factors contribute to the clinical heterogeneity of the included studies and underscore the necessity of a personalized approach to DAPT duration in complex bifurcation lesions.

Conclusion

This systematic review and meta-analysis indicates that for patients undergoing PCI for coronary bifurcation lesions, short-term DAPT is associated with a significantly higher risk of MACE, all-cause mortality, cardiac death, and ST compared to long-term DAPT. While no statistically significant differences were observed for MI, stroke, bleeding, or TLR, the point estimates consistently favored longer DAPT durations. Given the elevated thrombotic risk inherent in bifurcation lesions, these findings suggest that extended DAPT duration should generally be the standard approach to optimize ischemic outcomes, with personalized adjustments considering individual bleeding risk. Further randomized controlled trials are necessary to provide more definitive evidence on the optimal DAPT duration in this high-risk patient subgroup.

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Conflicts of interest

There are no conflicts of interest.

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