CLINICAL STUDY

Sequential Administration of Abbreviated Dual Antiplatelet Therapy and Ticagrelor Monotherapy versus Standard Dual Antiplatelet Therapy after Percutaneous Coronary Intervention: A Meta-Analysis

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ABSTRACT

Background: Dual antiplatelet therapy (DAPT), consisting of aspirin, and a P2Y12 inhibitor, has been crucial for reducing ischemic events following percutaneous coronary intervention (PCI). However, the optimal duration of DAPT remains under investigation. **Objective:** This meta-analysis aims to compare the efficacy and safety of an abbreviated-duration DAPT (Abv-DAPT) regimen (ticagrelor plus aspirin for 1 month or less, followed by ticagrelor monotherapy) with a conventional long-term duration DAPT (L-DAPT) regimen (ticagrelor plus aspirin for 12 months) in patients who have undergone PCI. **Methods:** We systematically searched PubMed-MEDLINE, EMBASE, Scopus, and the Cochrane Central Registry of Controlled Trials for studies with cohorts of patients who had undergone PCI and received DAPT with ticagrelor and aspirin. We analyzed data from the ULTIMATE-DAPT, T-PASS, and GLOBAL-LEADERS trials. Efficacy outcomes for this analysis were all-cause mortality, myocardial infarction, stent thrombosis, and stroke. Safety outcomes were major bleeding. The efficacy and safety events in patients of the Abv-DAPT arm were compared with those of L-DAPT arms. **Results:** The consolidated population from three major trials included in the meta-analysis was 22,218, with a nearly equal distribution between the Abv-DAPT arm (N = 11,106) and L-DAPT arms (N = 11,112). Our analysis found no significant difference in the incidence of stroke (RR = 0.95 [0.70-1.29]; p = 0.76), myocardial infarction (RR = 1.15 [0.94-1.4]; p = 0.18), thrombosis (RR = 1.25 [0.86-1.83]; p = 0.25), and all-cause mortality (RR = 0.85 [0.68-1.07]; p = 0.16) between two arms. However, major bleeding events were less (RR = 0.52 [0.27-1.0]; p = 0.05) in the Abv-DAPT arm than in the L-DAPT arm. **Conclusion:** Ticagrelor-based monotherapy after 1 month of ticagrelor-based DAPT could reduce bleeding complications without compromising ischemic protection. PROSPERO Registration: (CRD42024536139 - https://www.crd.york.ac.uk/PROSPEROFILES/536139_STRATEGY_20240726.pdf)

Keywords: Dual antiplatelet therapy, ticagrelor, risk of bleeding, stroke, thrombosis, myocardial infarction, all-cause mortality

Percutaneous coronary intervention (PCI) is a widely performed procedure for treating coronary artery disease, with its success rate heavily reliant on the use of dual antiplatelet therapy (DAPT) to prevent thrombotic complications such as stent thrombosis[1]. DAPT, typically consisting of aspirin and a P2Y12 inhibitor, has been the cornerstone of post-PCI management, particularly in reducing ischemic events during the critical period following stent implantation. Traditionally, DAPT has been continued for 12 months or longer, especially in patients at higher risk of ischemic events[2-5]. Since prolonged use of DAPT could increase the risk of bleeding, particularly in patients with a high bleeding risk (HBR) the optimal duration of DAPT before transitioning to P2Y12 inhibitor monotherapy remains under active investigation[1,3]. Balancing the benefits of ischemic protection against the risks of bleeding is crucial in tailoring DAPT duration,

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necessitating strategies that mitigate bleeding risk while maintaining therapeutic efficacy[1,3,4].

Several clinical trials have evaluated the safety and efficacy of limiting DAPT to 1-3 months, followed by P2Y12 inhibitor monotherapy in patients who have undergone PCI[1,4-6]. Notably, trials such as the MASTER DAPT have demonstrated that abbreviated DAPT regimens can reduce bleeding complications without increasing ischemic events, suggesting that this strategy may be particularly beneficial for patients with HBR[3].

Furthermore, studies have indicated that ticagrelor-based monotherapy following a short course of DAPT, even a 1-month DAPT duration, followed by monotherapy, offers favorable outcomes, including reduced all-cause and cardiovascular mortality[1,4].

This meta-analysis aims to evaluate the safety and efficacy of ticagrelor and aspirin therapy for 1 month or less, followed by ticagrelor monotherapy for 12 months or more in patients undergoing PCI. By synthesizing data from multiple trials, this study seeks to clarify whether a shorter DAPT regimen can provide comparable protection against ischemic events while reducing bleeding risk, thus potentially offering a safer and more effective treatment strategy for post-PCI patients.

METHODOLOGY

We aimed to evaluate the efficacy and safety of ticagrelor monotherapy after abbreviated exposure (1 month or less) to DAPT composed of ticagrelor and aspirin. We analyzed data from ULTIMATE-DAPT[7], T-PASS[8], and GLOBAL-LEADERS[9] trials (Table 1). We systematically

Table 1. Details of the Studies Included

	ULTIMATE-DAPT (2024)[7]	T-PASS (2024)[8]	GLOBAL-LEADERS (2018)[9]
Study Design	Randomized, placebo-controlled, double-blind clinical trial	Randomized, multicenter, open-label	Randomized, parallel, stratified, concealed
Key Inclusion Criteria	Adults (≥18 years of age) who tested positive for NSTEMI or STEMI or tested negative for unstable angina. The individual should not have any reported events after their PCI with DES within 1 month of DAPT.	Adults (>18 years) implanted with bioresorbable polymer sirolimus-eluting stent for ACS.	Patients with an implant of a biolimus-eluting stent for ACS and undergoing PCI.
Key Exclusion Criteria	Patients with a history of stroke (within last 3 months), CABG, or require a surgery within the 12 months.	Individuals with increased bleeding risk, pregnant women or who are expecting to get pregnant and those with a life expectancy <1 year.	Individuals with a contraindication/poor tolerance to aspirin or ticagrelor, history of use of a CYP3A4 inhibitor, fibrinolytic therapy (within 24 hours of PCI). Patients with hepatic disease, history of stroke, risk of bleeding, CABG, or requiring any other surgery within the next 12 months.
DAPT Strategy	***Ticagrelor plus Aspirin*** ***Duration:*** Experimental arm: 1 month in (IVUS-ACS) and 1 month from the time of enrollment Control arm: 12 months	***Ticagrelor plus Aspirin*** ***Duration:*** Experimental arm: Less than 1 month (Media DAPT duration in the group) Control arm: 12 months	Experimental arm: Aspirin + ticagrelor in the experimental arm (1 month) Control arm: Aspirin + clopidogrel or ticagrelor for stable or unstable coronary disease, respectively (12 months).
Outcome Measures	Types of bleeding based on BARC (2, 3, or 5) Adverse cardiovascular and cerebrovascular events.	Bleeding events based on BARC (3 or 5) at 12 months and major adverse cardiovascular events.	All-cause mortality or nonfatal myocardial infarction and bleeding events based on BARC (3 or 5).
Median Duration of Follow-up	1 Year	1 Year	2 Years
Trial Registration	NCT03971500	NCT03797651	NCT01813435

NSTEMI = Non-ST-elevated myocardial infarction; STEMI = ST-elevated myocardial infarction; PCI = Percutaneous coronary intervention; DES = Drug-eluting stent; DAPT = Dual antiplatelet therapy; ACS = Acute coronary syndrome; CYP3A4 = Cytochrome P450 3A4; CABG = Coronary artery bypass graft; IVUS = Intravascular ultrasound; BARC = Bleeding Academic Research Consortium.

searched PubMed-MEDLINE, EMBASE, Scopus, and the Cochrane Central Registry of Controlled Trials database to ensure we had caught all the important trials (Fig. 1). Predefined keywords were short-term Dual antiplatelet therapy OR ("Dual Antiplatelet Therapy/adverse effects" [MeSH] OR "Dual Antiplatelet Therapy/mortality" [MeSH]) AND Percutaneous coronary intervention OR Coronary intervention OR Coronary Revascularization OR ("Percutaneous Coronary Intervention/adverse effects" [MeSH] OR "Percutaneous Coronary Intervention/mortality" [MeSH] OR "Percutaneous Coronary Intervention/standards" [MeSH]) AND Ticagrelor OR P2Y12 inhibitors OR ("Ticagrelor/administration and dosage" [MeSH] OR "Ticagrelor/adverse effects" [MeSH] OR "Ticagrelor/blood" [MeSH] OR "Ticagrelor/metabolism" [MeSH] OR "Ticagrelor/pharmacology" [MeSH] OR "Ticagrelor/therapeutic use" [MeSH]). The detailed search strategy can be found in the link listed below. No language and publication period restrictions were applied. Further reference lists of eligible studies, key journals, trial registers, and internet resources were also searched. Only randomized control trials were included in the analysis. The current meta-analysis is registered in PROSPERO (CRD42024536139 - https://www.crd.york.ac.uk/PROSPEROFILES/536139_STRATEGY_20240726.pdf)

Inclusion Criteria

The search included studies with cohorts of patients who had undergone PCI and had received DAPT with ticagrelor and aspirin.

Exclusion Criteria

Studies with a nonrandomized trial design, a follow-up duration of less than 12 months, and unclear safety and efficacy points were excluded from the study. Further studies with monotherapy with an antiplatelet agent other than ticagrelor were also excluded from the study.

Comparator Groups in the Included Studies

The experimental group consisted of patients who received DAPT with ticagrelor and aspirin for 1 month or less (Abbreviated DAPT: Abv-DAPT), followed by ticagrelor monotherapy. In contrast, the control group included patients who had received DAPT for 12 months or more (Long-term DAPT: L-DAPT). Both groups had received antiplatelet therapy as part of their standard post-PCI treatment.

The intervention involved administering DAPT with ticagrelor (a loading dose of 180 mg, followed by 90 mg twice daily) plus aspirin (a loading dose of 160-500 mg, followed by 100 mg once daily) for 1 month or less (Abv-DAPT). This was followed by ticagrelor monotherapy (90 mg twice daily) for 12 months or more after the index PCI.

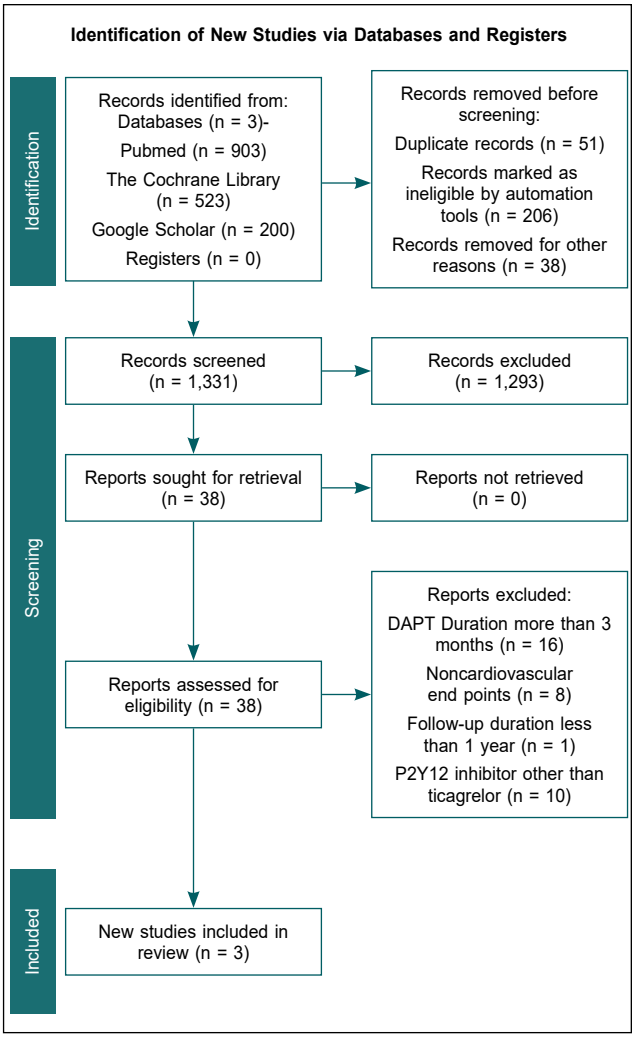


Figure 1. Provides the approach to obtain the studies that fit within the inclusion criteria based on the PICOS strategy.

The comparator was DAPT with any P2Y12 inhibitor (loading dose followed by the standard daily dose) plus aspirin (loading dose of 160-500 mg, followed by 100 mg once daily) for 12 months or more (L-DAPT) after the index PCI.

Similar to the intervention group, antiplatelet therapy in the control group was part of the standard post-PCI treatment. Table 1 provides the characteristics of the included studies.

Outcome Measures

The primary outcome was to assess the efficacy and safety outcomes of interventions. Efficacy outcomes

included all-cause death, cardiovascular death, myocardial infarction, stroke, stent thrombosis, and urgent target vessel revascularization. Safety outcomes focused on major and minor bleeding events.

Measures of Effect

Outcomes for continuous variables were expressed as mean differences (MD) using conventional units. For studies that report results in SI units, conversions to conventional units were performed before analysis. Results were expressed as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous outcomes, such as treatment success. Absolute risk differences were calculated for adverse events following treatment. RevMan Web 5.3 was utilized to compare the MDs of the primary and secondary outcomes between the Abv-DAPT and L-DAPT groups.

Data Extraction (Selection and Coding)

Two authors independently extracted data using standardized forms. If multiple publications from the same study group were identified, the results were consolidated, and relevant data from each report was included in the analysis. As mentioned, data on primary and secondary outcomes was extracted. Patient characteristics, including demographic information and comorbidities, were documented in a tabular format from the included and excluded studies. Any disagreements between the authors were resolved by consensus.

Risk of Bias (Quality) Assessment

Three authors independently assessed the risk of bias using the Review Manager (RevMan) web software. The evaluation considered several factors, including adequate sequence generation to avoid selection bias, proper allocation concealment, and measures to prevent knowledge of allocated interventions during the study. Additionally, the blinding of participants, personnel, and outcome assessors was assessed to minimize performance and detection bias. The assessment ensured that incomplete outcome data had been appropriately addressed and the study reports were free from selective outcome reporting. Finally, the study was evaluated for any other potential sources of bias. A fourth author resolved any disagreements among the authors.

A random effect model was used for data analysis, with outcomes expressed as 95% CI. Results were reported as RR with 95% CI for dichotomous outcomes, such as treatment success. Absolute risk differences were calculated for adverse events post-treatment. Forest plots were generated using RevMan software, with the left side of the graph favoring Abv-DAPT and the right side favouring L-DAPT. A p-value of <0.05 was considered statistically significant.

RESULTS

Our search strategy identified three clinical trials that compared the efficacy of DAPT consisting of ticagrelor plus aspirin or clopidogrel plus aspirin for 1 month or less, followed by ticagrelor monotherapy for 12 months or more in patients undergoing PCI. The total population for the meta-analysis was 22,218, with a nearly equal distribution between the experimental (N = 11,106) and control arms (N = 11,112). Baseline characteristics are as per Table 2. The random-effects model was used to analyze five critical outcomes: incidence of stroke, major bleeding, myocardial infarction, stent thrombosis, and all-cause mortality (Fig. 2).

The incidence of stroke was similar between the control group (n/N = 84/11,112 [0.75%]) and the experimental group (n/N = 80/11,106 [0.7%]). The overall RR was 0.95 (95% CI: 0.70-1.29), with no significant difference between the groups (p = 0.76).

The risk of major bleeding events was also comparable between the control group (n/N = 214/11,112 [1.9%]) and the experimental group (n/N = 145/11,106 [1.3%]). The overall RR for bleeding events was 0.52 (95% CI: 0.27-1.00), which was not statistically significant (p = 0.05). Participant characteristics-based subgroup analysis showed higher bleeding in male patients and those with acute coronary syndrome (ACS). However, the analysis was limited by significant heterogeneity (Fig. 3).

Similarly, the incidence of myocardial infarction was comparable between the control group (n/N = 277/11,112 [2.5%]) and the experimental group (n/N = 203/11,106 [1.8%]). The overall RR for myocardial infarction was 1.15 (95% CI: 0.94-1.40), with no significant difference between the groups (p = 0.18).

The incidence of thrombosis was comparable between the control group (n/N = 48/11,112 [0.4%]) and the experimental group (n/N = 60/11,106 [0.5%]). The RR for thrombosis was 1.25 (95% CI: 0.86-1.83), with no statistically significant differences between the groups (p = 0.25).

The incidence of all-cause mortality was also similar between the control group (n/N = 158/11,112 [1.4%]) and the experimental group (n/N = 134/11,106 [1.2%]). The overall RR for all-cause mortality was 0.85 (95%

Table 2. Baseline Characteristics of Patients

Parameters	ULTIMATE-DAPT[7]		T-PASS[8]		GLOBAL-LEADERS[9]	
	Abv-DAPT (n = 1,700)	L-DAPT (n = 1,700)	Abv-DAPT (n = 1,426)	L-DAPT (n = 1,424)	Abv-DAPT (n = 7,980)	L-DAPT (n = 7,988)
Age, years (mean ± SD)	62 (21.3%)	62.6 (18.9%)	61 (10%)	61 (10%)	64.5 (10.3%)	64.6 (10.3%)
Female (%)	436 (25.7%)	443 (26.1%)	233 (16%)	243 (17%)	1,865 (23.4%)	1,849 (23.1%)
BMI (kg/m^2) mean ± SD	-	-	25.1 (3.6%)	25.0 (3.5%)	28.2 (4-6)	28.2 (4-6)
Initial presentation						
Stable CAD (%)	0	0	0	0	4,230 (53.0%)	4,251 (53.2%)
Unstable angina (%)	668 (39.3%)	708 (41.7%)	347 (24%)	361 (25%)	1,004 (12.6%)	1,018 (12.7%)
NSTEMI (%)	545 (32.1%)	531 (31.2%)	507 (36%)	485 (34%)	1,684 (21.1%)	1,689 (21.1%)
STEMI (%)	487 (28.7%)	461 (27.1%)	572 (40%)	578 (41%)	1,062 (13.3%)	1,030 (12.9%)
Medical history						
Diabetes mellitus (%)	540 (31.8%)	535 (31.5%)	422 (30%)	408 (29%)	2,049 (25.7%)	1,989 (24.9%)
Hypertension (%)	1,058 (62.2%)	1,063 (62.5%)	669 (47%)	679 (48%)	5,882 (74.0%)	5,833 (73.3%)
Dyslipidemia (%)	1,178 (69.3%)	1,157 (68.1%)	1,048 (74%)	1,058 (74%)	5,345 (69.3%)	5,423 (70.0%)
Current smoking (%)	486 (28.6%)	482 (28.4%)	557 (39%)	537 (38%)	2,066 (25.9%)	2,103 (26.3%)
Chronic renal insufficiency (%)	119 (7.0%)	129 (7.6%)	118 (8%)	104 (7%)	1,099 (13.9%)	1,072 (13.5%)
Previous myocardial infarction (%)	143 (8.4%)	156 (9.2%)	27 (2%)	25 (2%)	1,831 (23.0%)	1,879 (23.6%)
Previous PCI (%)	171 (10.1%)	174 (10.2%)	92 (7%)	92 (7%)	2,609 (32.7%)	2,612 (32.7%)
Previous CABG (%)	2 (0.1%)	4 (0.2%)	4 (0.28%)	2 (0.14%)	448 (5.6%)	495 (6.2%)
Stroke history (%)	154 (9.1%)	147 (8.7%)	43 (3%)	49 (3%)	210 (2.6%)	211 (2.6%)

Abv-DAPT = Abbreviated dual antiplatelet therapy; L-DAPT = Long-term dual antiplatelet therapy; SD = Standard deviation; BMI = Body mass index; CAD = Coronary artery disease; NSTEMI = Non-ST-elevated myocardial infarction; STEMI = ST-elevated myocardial infarction; PCI = Percutaneous coronary intervention; CABG = Coronary artery bypass graft.

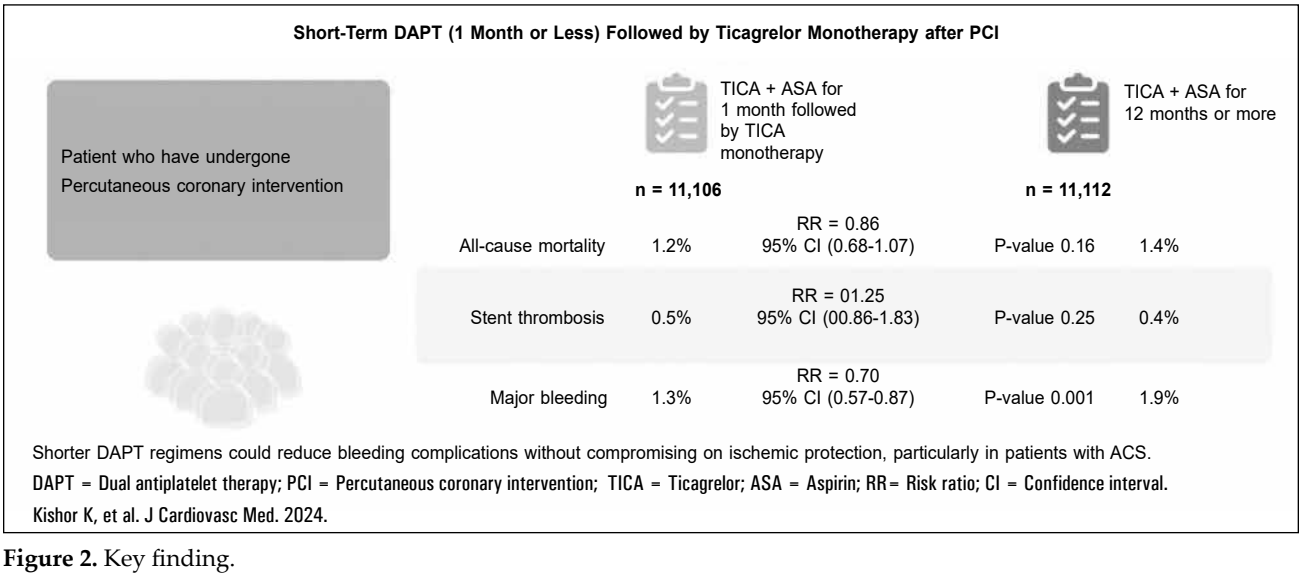


Figure 2. Key finding.

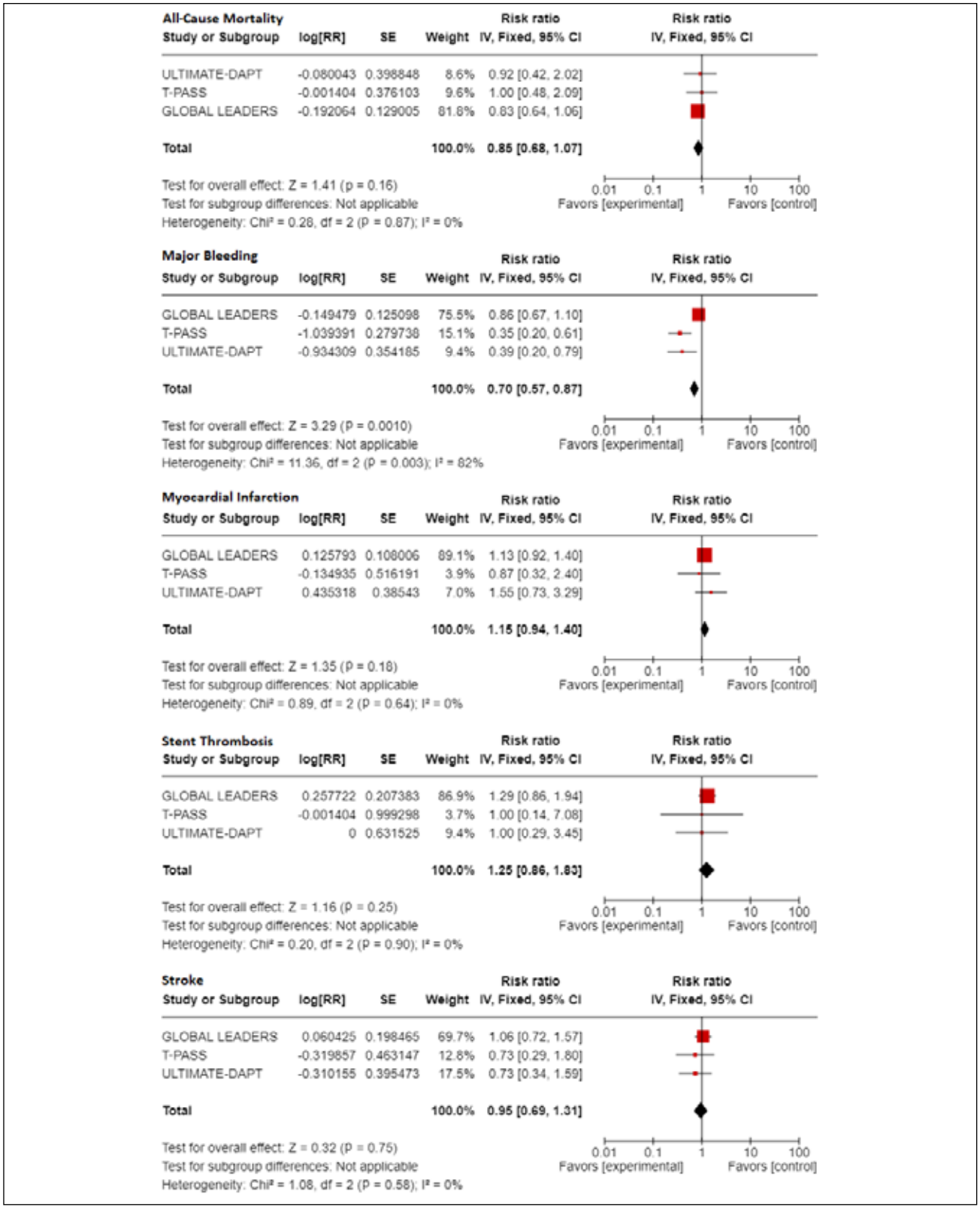
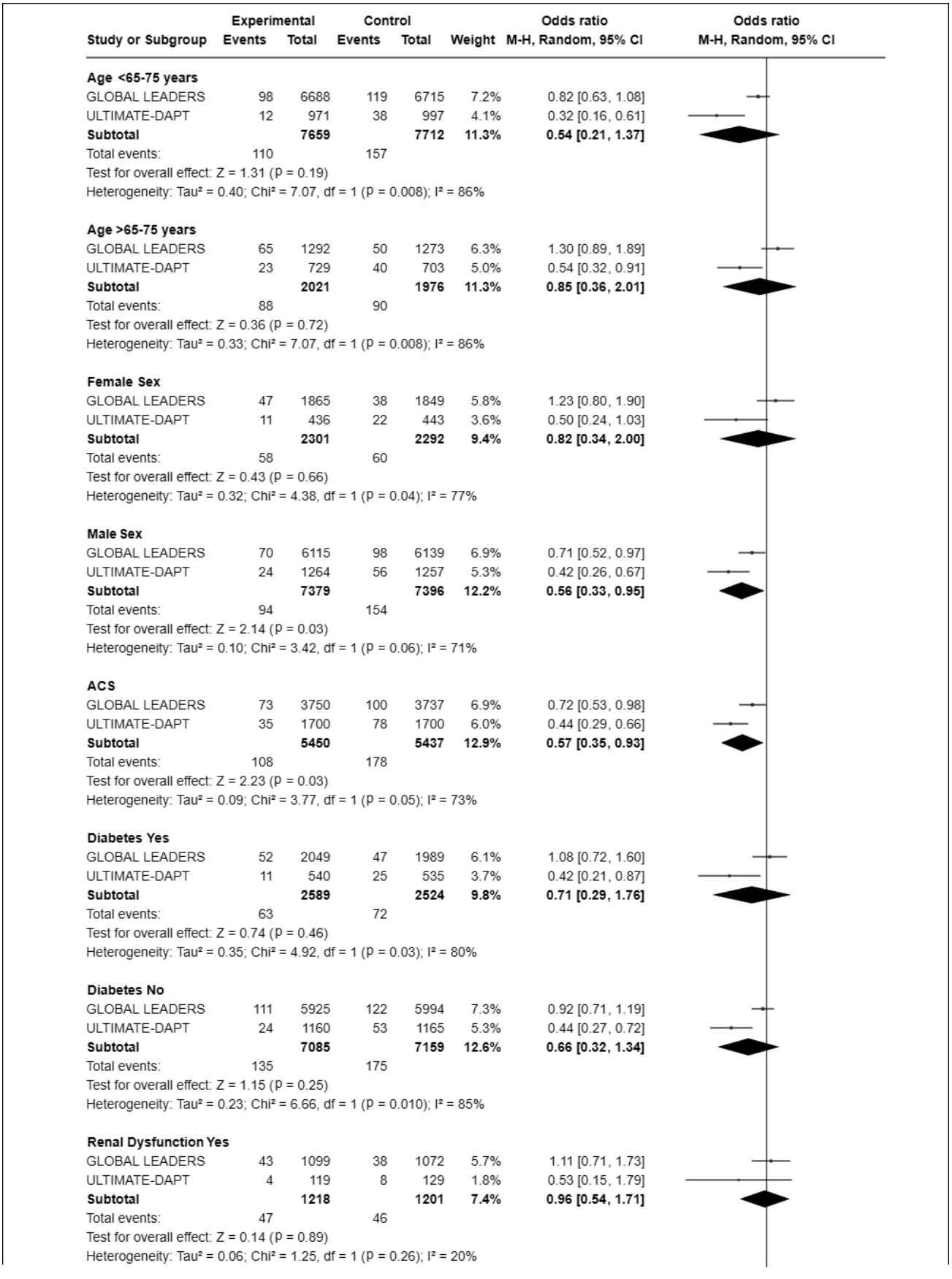


Figure 3. Comparison of the incidence of all-cause mortality, major bleeding, myocardial infarction, stent thrombosis, and stroke between the two groups.

Forrest plots representation of the risk ratio (with 95% CI) of the incidence of all-cause mortality; major bleeding, myocardial infarction, stent thrombosis, and stroke between experimental (Abv-DAPT) vs. control (L-DAPT) groups.


Experimental
Control
Odds ratio
Odds ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
Age <65-75 years
GLOBAL LEADERS 98 6688 119 6715 7.2% 0.82 [0.63, 1.08]
ULTIMATE-DAPT 12 971 38 997 4.1% 0.32 [0.16, 0.61]
Subtotal 7659 7712 11.3% 0.54 [0.21, 1.37]
Total events: 110 157
Test for overall effect: Z = 1.31 (p = 0.19)
Heterogeneity: Tau² = 0.40; Chi² = 7.07, df = 1 (p = 0.008); I² = 86%
Age >65-75 years
GLOBAL LEADERS 65 1292 50 1273 6.3% 1.30 [0.89, 1.89]
ULTIMATE-DAPT 23 729 40 703 5.0% 0.54 [0.32, 0.91]
Subtotal 2021 1976 11.3% 0.85 [0.36, 2.01]
Total events: 88 90
Test for overall effect: Z = 0.36 (p = 0.72)
Heterogeneity: Tau² = 0.33; Chi² = 7.07, df = 1 (p = 0.008); I² = 86%
Female Sex
GLOBAL LEADERS 47 1865 38 1849 5.8% 1.23 [0.80, 1.90]
ULTIMATE-DAPT 11 436 22 443 3.6% 0.50 [0.24, 1.03]
Subtotal 2301 2292 9.4% 0.82 [0.34, 2.00]
Total events: 58 60
Test for overall effect: Z = 0.43 (p = 0.66)
Heterogeneity: Tau² = 0.32; Chi² = 4.38, df = 1 (p = 0.04); I² = 77%
Male Sex
GLOBAL LEADERS 70 6115 98 6139 6.9% 0.71 [0.52, 0.97]
ULTIMATE-DAPT 24 1264 56 1257 5.3% 0.42 [0.26, 0.67]
Subtotal 7379 7396 12.2% 0.56 [0.33, 0.95]
Total events: 94 154
Test for overall effect: Z = 2.14 (p = 0.03)
Heterogeneity: Tau² = 0.10; Chi² = 3.42, df = 1 (p = 0.06); I² = 71%
ACS
GLOBAL LEADERS 73 3750 100 3737 6.9% 0.72 [0.53, 0.98]
ULTIMATE-DAPT 35 1700 78 1700 6.0% 0.44 [0.29, 0.66]
Subtotal 5450 5437 12.9% 0.57 [0.35, 0.93]
Total events: 108 178
Test for overall effect: Z = 2.23 (p = 0.03)
Heterogeneity: Tau² = 0.09; Chi² = 3.77, df = 1 (p = 0.05); I² = 73%
Diabetes Yes
GLOBAL LEADERS 52 2049 47 1989 6.1% 1.08 [0.72, 1.60]
ULTIMATE-DAPT 11 540 25 535 3.7% 0.42 [0.21, 0.87]
Subtotal 2589 2524 9.8% 0.71 [0.29, 1.76]
Total events: 63 72
Test for overall effect: Z = 0.74 (p = 0.46)
Heterogeneity: Tau² = 0.35; Chi² = 4.92, df = 1 (p = 0.03); I² = 80%
Diabetes No
GLOBAL LEADERS 111 5925 122 5994 7.3% 0.92 [0.71, 1.19]
ULTIMATE-DAPT 24 1160 53 1165 5.3% 0.44 [0.27, 0.72]
Subtotal 7085 7159 12.6% 0.66 [0.32, 1.34]
Total events: 135 175
Test for overall effect: Z = 1.15 (p = 0.25)
Heterogeneity: Tau² = 0.23; Chi² = 6.66, df = 1 (p = 0.010); I² = 85%
Renal Dysfunction Yes
GLOBAL LEADERS 43 1099 38 1072 5.7% 1.11 [0.71, 1.73]
ULTIMATE-DAPT 4 119 8 129 1.8% 0.53 [0.15, 1.79]
Subtotal 1218 1201 7.4% 0.96 [0.54, 1.71]
Total events: 47 46
Test for overall effect: Z = 0.14 (p = 0.89)
Heterogeneity: Tau² = 0.06; Chi² = 1.25, df = 1 (p = 0.26); I² = 20%

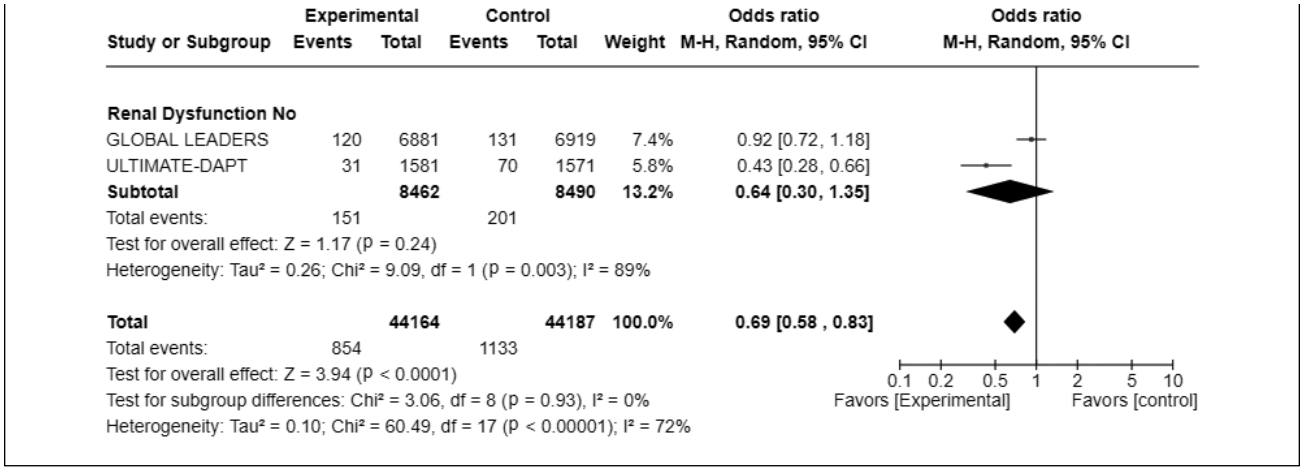


Figure 4. Participant characteristics based subgroup analysis.

Forrest plots representation of the odds ratio (with 95% CI) for the incidence of major bleeding across different participant characteristics between experimental (Abv-DAPT) vs. control (L-DAPT) groups.

CI: 0.68-1.07), with no statistically significant difference between the comparator groups (p = 0.16).

Efficacy outcomes as per age (<65-75 years and >65-75 years), gender, diabetes, and renal dysfunction subgroups is shown in Figure 4.

DISCUSSION

Dual antiplatelet therapy is a crucial component of post-PCI care to minimize ischemic events. Considering the benefit-to-risk ratio, there is a need to optimize the duration of the DAPT regimen to the shortest yet most effective way of reducing ischemic events, especially in HBR cohorts. This meta-analysis identified three trials that administered DAPT for up to 1-month (experimental group) compared to the traditional 12-month period in the control group. Our results from the meta-analysis found no significant difference in the incidence of stroke (RR = 0.95 [0.70-1.29]; p = 0.76), major bleeding events (RR = 0.52 [0.27-1.0]; p = 0.05), incidence of myocardial infarction (RR = 1.15 [0.94-1.4]; p = 0.18), incidence of thrombosis (RR = 1.25 [0.86-1.83]; p = 0.25), and incidence of all-cause mortality (RR = 0.85 [0.68-1.07]; p = 0.16), between the two arms.

The ULTIMATE-DAPT (2024) randomized, double-blind, placebo-controlled trial consisted of diverse patient profiles, including those tested biomarker-positive and biomarker-negative for ACS. The rigorous design of the study and broad inclusion criteria allowed for a comprehensive assessment of DAPT duration across different clinical scenarios, ensuring the findings apply to a wide range of patients[7]. Similarly, the T-PASS (2024) trial, which focused on patients with ACS undergoing bioresorbable polymer sirolimus-eluting stent implantation, provides crucial data on the impact of significantly shortening DAPT duration. This study compared a median DAPT duration of less than 1 month with the standard 12-month regimen, assessing a composite outcome of death, myocardial infarction, thrombosis, stroke, and incidence of any major bleeding events. A key finding from the T-PASS trial was that stopping aspirin within 1 month and transitioning to ticagrelor monotherapy was noninferior and may be superior to the 12-month DAPT regimen for the 1-year composite outcome[8]. This superiority was reflected by a significant reduction in major bleeding events, highlighting the potential benefits of a shorter DAPT duration in this patient population.

Interestingly, the results of the T-PASS trial contrast with those of the GLOBAL-LEADERS (2018) trial, where a 1-month DAPT regimen followed by ticagrelor monotherapy did not demonstrate superiority over the 12-month DAPT regimen in terms of ischemic outcomes[8,9]. The primary factor driving the noninferiority in T-PASS was the significantly lower bleeding rate (1.2% in T-PASS vs. 3.4% in GLOBAL-LEADERS), underscoring the critical role of bleeding risk in determining the optimal duration of DAPT[8]. The findings from ULTIMATE-DAPT and T-PASS are consistent in showing that ticagrelor monotherapy following a shortened DAPT regimen results in a lower rate of clinically relevant bleeding while maintaining similar rates of major adverse cardiovascular and cerebrovascular events compared to more extended DAPT regimens. Both trials focused on populations with ACS, a group at higher risk for both ischemic and bleeding complications, making the balancing of these risks particularly challenging.

Recently, a patient-level meta-analysis concluded that stopping aspirin 1 to 3 months after PCI followed by ticagrelor monotherapy is safer and equally effective as standard DAPT[4]. Unlike clopidogrel, ticagrelor monotherapy significantly reduced major bleeding events (53% reduction in major bleeding), while offering comparable protection against ischemic events[10,11]. Notably, the use of clopidogrel-based monotherapy may pose a considerable challenge in patients with high platelet reactivity[12,13]. While on clopidogrel-based DAPT, the probability of ischemic events in such patients increases as soon as the aspirin is discontinued. The discontinuation of aspirin leaves clopidogrel with suboptimal platelet inhibition and minimal antiplatelet effect due to high platelet reactivity. In contrast, ticagrelor offers more consistent and profound P2Y12 receptor inhibition, thereby substantially reducing ischemic events compared to clopidogrel monotherapy[9]. The analysis has strengths in combining patient-level data from three large trials to quantify the risks and benefits associated with P2Y12 inhibitor monotherapy compared to DAPT continuation after PCI. It also allows for a detailed assessment of the efficacy and safety of ticagrelor and clopidogrel monotherapy across different clinical settings.

Additionally, the analysis captures diverse patient populations and treatment scenarios, enhancing the reliability and applicability of the findings to routine clinical practice. These results and the current meta-analysis suggest that an Abv-DAPT duration, especially with potent P2Y12 inhibitor monotherapy, may effectively balance ischemic risk without significantly increasing bleeding risk. The evidence supports the hypothesis that ticagrelor monotherapy could replace aspirin in DAPT regimens, offering similar protection against ischemic events while reducing the risk of major bleeding.

However, several critical questions remain unanswered, such as determining the best molecule for monotherapy to optimally balance ischemic and bleeding risks, defining the optimal duration of DAPT, and standardizing the factors that should guide DAPT duration in various patient subgroups, such as those who have undergone coronary artery bypass grafting or those at higher risk for bleeding or ischemic events.

The ongoing exploration of these aspects, from complete aspirin elimination to prolonged DAPT regimens, reflects the complexity of managing patients' post-PCI and highlights the need for continued research to refine DAPT strategies further.

CONCLUSION

In conclusion, this systemic literature review and meta-analysis contributes valuable evidence to the growing literature advocating a more personalized approach to DAPT duration. These studies highlight the potential of shorter DAPT regimens in reducing bleeding complications without compromising ischemic protection, particularly in patients with ACS. Future research should address the unresolved issues related to optimizing DAPT strategies and improve patient outcomes following PCI.

LIMITATIONS

This study has several limitations. First, although data from three large trials were combined, the overall sample size may still limit the ability to detect rare safety events and outcomes.

Second, the heterogeneity of the included trials, such as variations in patient populations, procedural techniques, and duration of follow-up, may introduce bias and affect the generalizability of the findings. Additionally, this analysis relies on post-hoc data, which inherently carries the risk of confounding factors that must be fully accounted for. The limitation of long-term follow-up hinders the ability to assess the sustained effects of the intervention strategy.

Acknowledgments: None. No assistance in the preparation of this article is to be declared.

Artificial intelligence generated content: Not applicable.

Declarations

Data availability statement: Not applicable.

Funding statement: None.

Conflict of interest disclosure: The authors declare no conflicts of interest.

Patient consent statement: Not applicable.

Permission to reproduce material from other sources: Not applicable.

Clinical trial registration: Not applicable.

Previous presentations: None.

Author contributions: Dr Kamal Kishor was involved in the conception and design, Dr Kamal Kishor, Dr Lakshmi Nagendra, Dr Devendra Bisht contributed to the analysis and interpretation of the data; Dr Kamal Kishor, Dr Lakshmi Nagendra drafted the paper; Dr Devendra Bisht and Dr Kunal Mahajan revised the manuscript critically for intellectual content; and all authors were involved in approving the final version of the manuscript. All authors agree to be accountable for all aspects of the work.

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