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Systematic Review

Ticagrelor versus clopidogrel after percutaneous coronary intervention for acute coronary syndrome: A meta-analysis and meta-regression of randomized controlled trials

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Abstract

Acute coronary syndrome (ACS) arises from abrupt myocardial ischemia, most commonly due to coronary thrombosis. After percutaneous coronary intervention (PCI), dual antiplatelet therapy (DAPT) with aspirin and P2Y12 inhibitor is standard. Clopidogrel, a widely used P2Y12 inhibitor, shows reduced efficacy in some patients due to genetic variability. Ticagrelor has emerged as a potential alternative in DAPT for ACS post-PCI. The aim of this study was to evaluate the efficacy and safety of ticagrelor compared to clopidogrel as DAPT for ACS patients post-PCI through outcomes of cardiovascular death, myocardial infarction, stent thrombosis, target revascularization, dyspnea, and major bleeding. A systematic search was conducted through databases such as PubMed, Scopus, Cochrane, Epistemonikos, ClinicalTrials.gov, ProQuest, Scilit, and Google Scholar. The quality of the included studies was assessed using the Cochrane RoB 2.0 tool. Meta-analyses were conducted using a random-effects model, and pooled risk ratios (RR) with 95% confidence intervals (CIs) were analyzed using RevMan 5.4 and RStudio. Eight RCTs (n=1,726) showed that ticagrelor significantly reduced the incidence of myocardial infarction (RR=0.44; 95%CI: 0.21–0.91; p=0.03; I^2=0%), stent thrombosis (RR=0.30; 95%CI: 0.14–0.66; p=0.0027; I^2=0%), and target revascularization (RR=0.47; 95%CI: 0.26–0.83; p=0.0098; I^2=0%). No significant difference was observed in cardiovascular death (RR=0.54; 95%CI: 0.27–1.06; p=0.00733; I^2=0%). In terms of safety, dyspnea was more frequently reported in the ticagrelor group (RR=6.20; 95%CI: 1.10–35.04; p=0.039; I^2=0%). In addition, no significant difference was found in the incidence of major bleeding (RR=1.05; 95%CI: 0.43–2.54; p=0.9176; I^2=0%). Ticagrelor appears to be more effective than clopidogrel as part of DAPT in patients with ACS post-PCI, without an increase in serious adverse events. Further studies are needed with longer follow-up periods, more diverse patient populations, and broader adverse events.

Keywords: ACS, aspirin, clopidogrel, post-PCI, ticagrelor

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Introduction

Acute coronary syndrome (ACS) results from a sudden reduction or complete blockage of blood flow to the heart muscle [1]. This disruption is typically caused by plaque rupture within the coronary arteries [2]. World Health Organization (WHO) data reported that ACS is one of the global problems contributing to almost 25% of world deaths. Around 23.3 million cases were found in 2022 [3]. This number is projected to increase by almost twice in 2050. Percutaneous coronary intervention (PCI) is a procedure aimed at mechanically revascularizing occluded coronary arteries using stents or balloons to restore blood flow to the heart muscle [4]. While effective, PCI carries a risk of stent thrombosis, a serious complication where a blood clot forms at the stent site, potentially leading to myocardial infarction (MI) or death. Therefore, antiplatelet therapy is needed to balance ischemic and bleeding risks [5].

While single antiplatelet therapy (e.g., aspirin alone) offers some protection against thrombotic events, it is insufficient for high-risk scenarios like post-PCI management in ACS patients [6]. However, aspirin alone only blocks one pathway of platelet activation, leaving a high risk of thrombus formation at respective sites [7]. Dual antiplatelet therapy (DAPT), which combines aspirin with a P2Y12 receptor inhibitor, has become the gold standard for preventing thrombotic complications following PCI [8]. Scientific evidence supports DAPT's superiority over single antiplatelet therapy in reducing major adverse cardiovascular events (MACE), including myocardial infarction and stent thrombosis [9].

Among the $P2Y_{12}$ inhibitors available for DAPT, clopidogrel and ticagrelor are the most commonly prescribed agents. Clopidogrel has long been considered the gold standard $P2Y_{12}$ inhibitor in clinical practice. However, clopidogrel's reliance on metabolic activation introduces variability in patient response due to genetic polymorphisms affecting cytochrome P450 2C19 (CYP2C19) activity [10]. Individuals carrying loss-of-function alleles exhibit reduced enzyme activity, leading to decreased production of the active metabolite and diminished platelet inhibition [11]. Recent evidence suggests that ticagrelor may offer significant advantages over clopidogrel in certain patient populations [12]. Previous systematic review and meta-analysis have demonstrated the safety comparison of both drugs through bleeding [13]. These highlight the need for a systematic review and meta-analysis to synthesize existing evidence of comparison in both efficacy and safety of both drugs. Therefore, the aim of this study was to evaluate the efficacy and safety of ticagrelor compared to clopidogrel as DAPT for ACS patients post-PCI through the outcomes of cardiovascular death, myocardial infarction, stent thrombosis, target revascularization, dyspnea, and major bleeding.

Methods

Study design

The present study followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist and the Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 (2022) [14]. The protocol of this study was prospectively registered on PROSPERO with registration number CRD420251035087.

Search strategy

A computerized systematic literature search regarding relevant studies was carried out comprehensively through seven different databases, including PubMed, Scopus, Cochrane, Epistemonikos, ClinicalTrials.gov, Proquest, and Scilit. Additionally, literature searches were conducted using the search engine Google Scholar and citation searching. The systematic literature search was conducted using boolean operators 'AND' and 'OR', as described in **Supplementary file 1** (**Underlying data**). All search terms were aligned with the Medical Subject Headings (MeSH) browser.

Study eligibility criteria

The inclusion criteria applied to the population, intervention, control, outcomes, and study design (PICOS) framework and included (1) population: patients with ACS who had undergone

PCI; (2) intervention: aspirin and ticagrelor; (3) control: aspirin and clopidogrel; (4) outcomes: cardiovascular death, myocardial infarction, stent thrombosis, target revascularization, dyspnea, or major bleeding; and (5) study design: randomized controlled trials (RCTs). The exclusion criteria were: (1) publications before 2023 (older than 10 years); (2) full-text articles that were inaccessible; (3) studies published in non-compatible languages; (4) study populations with a history of receiving other medications.

Screening and data extraction

Database screening was conducted across seven databases. Duplicate studies were excluded using Rayyan.ai [15]. After duplicate studies removal, the remaining articles were reviewed based on titles and abstracts. Titles and abstracts were screened independently by two reviewers (AMTS and FPSW). Disagreements were resolved through consultation with a third reviewer (RTHN). Studies that met the criteria were extracted, with the data organized into a Microsoft Excel 2021 spreadsheet. Additional information, including the country of origin, number of participants, sex distribution, and intervention details, was also collected. Data extraction from each included study was presented in a table, consisting of the following components: author name, year of publication, demographic characteristic (country, study design, population, sex, age, body mass index (BMI)), and clinical characteristics (time of follow-up, type of PCI, drug name, type of ACS, type of stent, low-density lipoprotein cholesterol (LDL-C), dose, concomitant therapies, comorbid disease, and side effect). Study characteristics and outcomes were assessed qualitatively by two authors (AMTS and RTHN), while a third author (FPSW) verified the accuracy of the extracted data and conducted the statistical analyses.

Quality assessment and publication bias

The risk of bias in the eight included RCTs was assessed using the Revised Tool for Risk of Bias in Randomized Trials (RoB 2.0), which evaluates five domains: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in measurement of the outcome, and (5) bias in selection of the reported result. Assessments followed the standardized methodology developed by the Cochrane Collaboration and were performed independently by all three authors, with any disagreements resolved through consensus. The results were entered into a bias domain spreadsheet (.xlsx) and uploaded to the ROBVIS website to generate accurate visual representations of the final assessments. The results were visually presented using a traffic light system [16]. This systematic approach ensured a comprehensive and transparent depiction of bias levels in the included studies.

Statistical analysis

Statistical analysis was performed using RStudio (version 4.4.1) with the 'meta' and 'dmetar' packages. All outcomes were assessed using the Mantel-Haenszel model, which was presented in a forest plot using the Risk Ratio (RR) with 95% confidence intervals (CI) and *p*-values; $\alpha=0.05$ defined statistical significance. A random-effects model was applied to interpret the pooled effect size. Heterogeneity was assessed using the I^2 statistic based on Cochrane, with cut-off limits of 0%, 25%, 50%, and 75% indicating no, low, moderate, and high heterogeneity, respectively [17]. Heterogeneity was considered present when Higgins' $I^2>50\%$ or *p*-heterogeneity<0.1. DOI plot for publication bias was performed when fewer than ten studies were included [18]. Additionally, meta-regression analysis was used to evaluate the influence of covariates.

Results

Study selection and identification

A total of 3,199 studies were retrieved from seven databases. After removing 1,425 duplicates, 1,774 records were screened by title and abstract, resulting in the exclusion of 1,729 studies that did not meet the eligibility criteria. Six additional records were excluded due to retrieval failure. Full-text screening was conducted for 39 articles, of which 34 were excluded for reasons including post-PCI treatment setting, non-randomized study design, unavailable extractable data, or absence of relevant outcomes. This process yielded five eligible studies. An additional 4,158

records were identified through manual searches via Google Scholar and citation tracking. After title/abstract screening, 24 articles were selected for full-text review; two records were excluded due to retrieval failure, leaving 22 studies for full-text assessment, of which three additional studies met the eligibility criteria. In total, eight randomized controlled trials were included in the meta-analysis. A summary of the study screening and selection process is presented in **Figure 1**.

Demographic characteristics of the included studies

A quantitative analysis was performed on eight RCTs, comprising a total of 1,726 participants who received ticagrelor as the intervention, while the control groups received clopidogrel. The qualitative analysis included all studies published between 2016 and 2023, conducted across various East Asian countries, including China, Taiwan, and South Korea. All included studies enrolled patients with a minimum age of 59 years, who were randomly assigned to either the intervention or control group. Detailed demographic characteristics of the included studies are presented in **Table 1**.

Table 1. Demographic characteristics of the eight included studies

Author, year	Country	Study design	Intervention	Population	Male/ female	Age (mean±SD)	BMI (mean±SD)
Cao *et al.*, 2019 [19]	China	RCT	Ticagrelor	49	30/19	61.59±11.22	25.09±2.53
			Clopidogrel	48	29/19	62.79±11.37	24.09±2.51
Chen *et al.*, 2018 [20]	Taiwan	RCT, single-blind	Ticagrelor	102	80/22	65.2±13.4	NR
			Clopidogrel	107	74/33	65.4±13.0	NR
Choi *et al.*, 2017 [21]	South Korea	RCT, open-label	Ticagrelor	20	19/1	59±10	24±3
			Clopidogrel	22	15/7	65±7	24±3
Gao *et al.*, 2023 [22]	China	RCT	Ticagrelor	60	54/15	60.45±12.38	23.14±2.27
			Clopidogrel	60	42/18	61.02±10.78	23.25±2.17
Liu *et al.*, 2019 [23]	China	RCT	Ticagrelor	108	58/50	68.27±4.65	NR
			Clopidogrel	100	58/42	69.13±5.13	NR
Tang *et al.*, 2016 [24]	China	RCT	Ticagrelor	200	142/58	64.36±11.41	NR
			Clopidogrel	200	146/54	64.18±11.09	NR
Wang *et al.*, 2019 [25]	China	RCT	Ticagrelor	150	121/27	60.87±12.05	25.82±3.37
			Clopidogrel	148	115/35	59.74±13.04	25.89±3.18
Wu *et al.*, 2020 [26]	China	RCT open-label	Ticagrelor	177	134/43	64.46±9.64	NR
			Clopidogrel	175	124/51	64.14±9.58	NR

BMI: body mass index; RCT: randomized controlled trial

Clinical characteristics of the included studies

The included studies in this meta-analysis encompassed a broad spectrum of patients undergoing various types of ACS, including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), unstable angina, and stable angina. Follow-up durations varied across studies, ranging from 1 month to 2 years. Patients had undergone either emergency or elective PCI. Some studies specified the types of stents used, with most studies using drug-eluting stents or bare metal. Antiplatelet dosages were largely consistent across studies.

Additionally, most studies administered concomitant therapies, including heparin, beta-blockers (BB), angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), nitrate, proton pump inhibitors (PPI), salt, and antidiabetic drugs. Participants commonly had comorbid conditions such as angina pectoris, atrial fibrillation, cerebrovascular disease, chronic renal failure, smoking status, diabetes mellitus (DM), dyslipidemia, hypertension, hyperlipidemia, and peripheral artery disease. The efficacy and safety of ticagrelor were evaluated using a range of clinical outcomes, including cardiovascular death, myocardial infarction, stent thrombosis, target revascularization, dyspnea, and major bleeding. Detailed clinical characteristics of the included studies are presented in **Supplementary file 2**. Several studies also reported side effects such as bradycardia, kidney failure, epistaxis, hematoma, gum bleeding, bruising, epigastric pain, and chest tightness.

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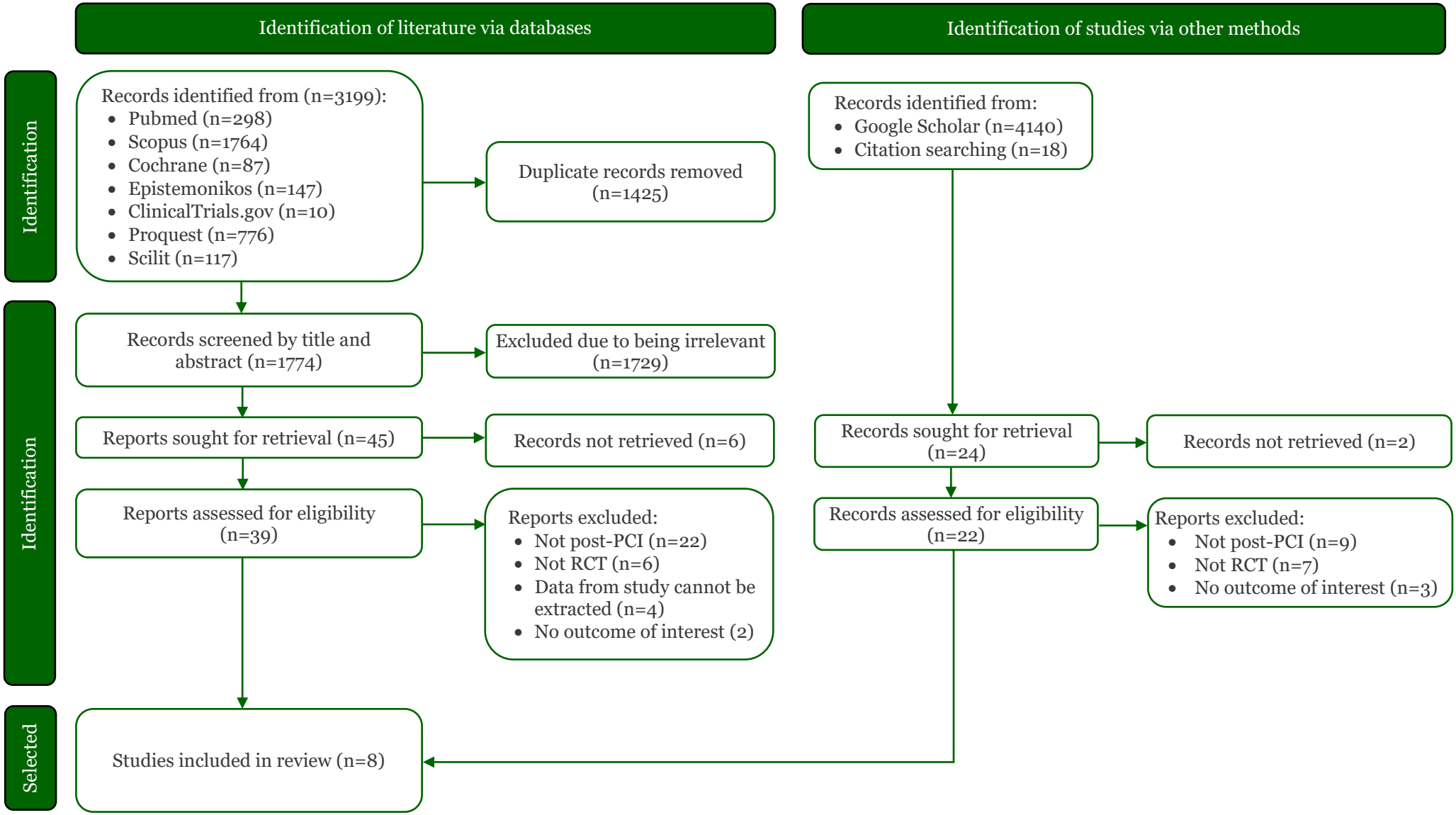

Figure 1. PRISMA diagram flow.

Quality appraisal

The results of the quality appraisal using RoB 2.0 are presented in **Figure 2**. All had a low risk of bias in the randomization process and bias due to missing outcome data. However, four studies were of moderate risk under deviations from intended intervention, primarily because they were either open-label or single-blind trials. Additionally, three studies were of moderate risk under bias due to measurement of the outcome, as studies failed to provide clear judgement on the instruments or methods used to measure dyspnea. One study was of moderate risk of bias in selection of the reported result. The overall result of the assessment shows about 33.5% low risk of bias and about 66.5% on moderate risks.

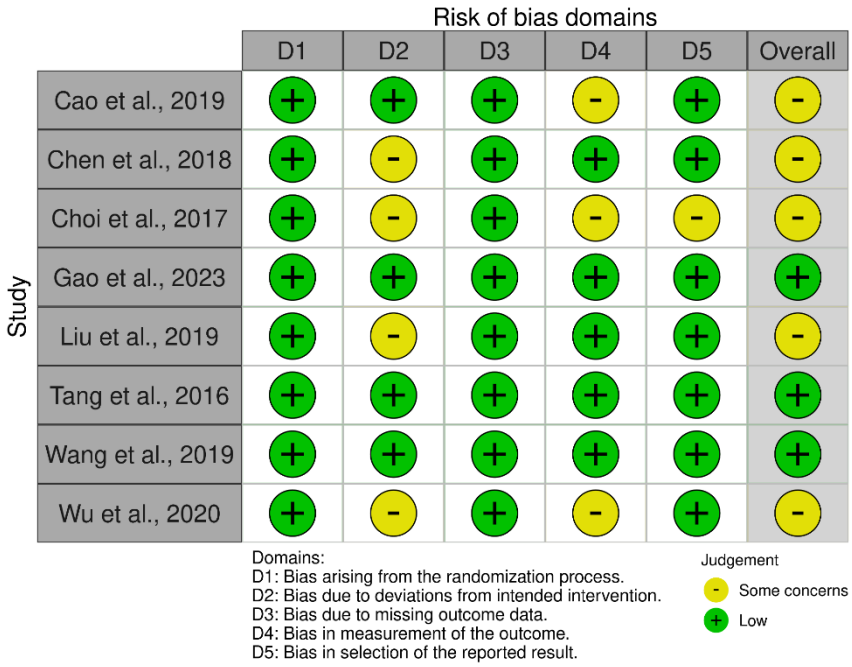

Figure 2. Quality assessment of studies based on Cochrane RoB 2.0.

Efficacy of ticagrelor compared to clopidogrel for ACS patients post-PCI on the primary outcome

The efficacy of ticagrelor compared to clopidogrel in lowering the incidence of cardiovascular death and myocardial infarction was presented in **Figure 3**. The analysis showed that ticagrelor showed no statistically significant difference compared with clopidogrel in lowering the incidence of cardiovascular death with an RR value of 0.54 (95%CI: 0.27; 1.06, p=0.0733). In contrast, ticagrelor significantly associated with a lower incidence of myocardial infarction compared to clopidogrel with an RR value of 0.44 (95%CI: 0.21; 0.91, p=0.0259). No heterogeneity was observed across two outcomes (I^2=0).

Effect of ticagrelor compared to clopidogrel on secondary and safety outcomes in ACS patients post-PCI

The efficacy of ticagrelor compared to clopidogrel on secondary and safety outcomes was presented in **Table 2**. In secondary outcomes, the analysis showed that ticagrelor was associated with a lower incidence of stent thrombosis (RR: 0.30; 95%CI: 0.14; 0.66; p=0.0027) and target revascularization (RR: 0.47; 95%CI: 0.26; 0.83; p=0.0098) compared to clopidogrel. However, regarding safety outcomes, clopidogrel showed a lower incidence than ticagrelor in lowering the incidence of dyspnea with an RR value of 6.20 (95%CI: 1.10; 35.04; p=0.0390). Additionally, there was no significant difference between the groups in lowering the incidence of major bleeding with an RR value of 1.05 (95%CI: 0.43; 2.54; p=0.9176). All four outcomes demonstrated no heterogeneity (I^2=0%). The forest plot for these outcomes was presented in **Supplementary file 3**.

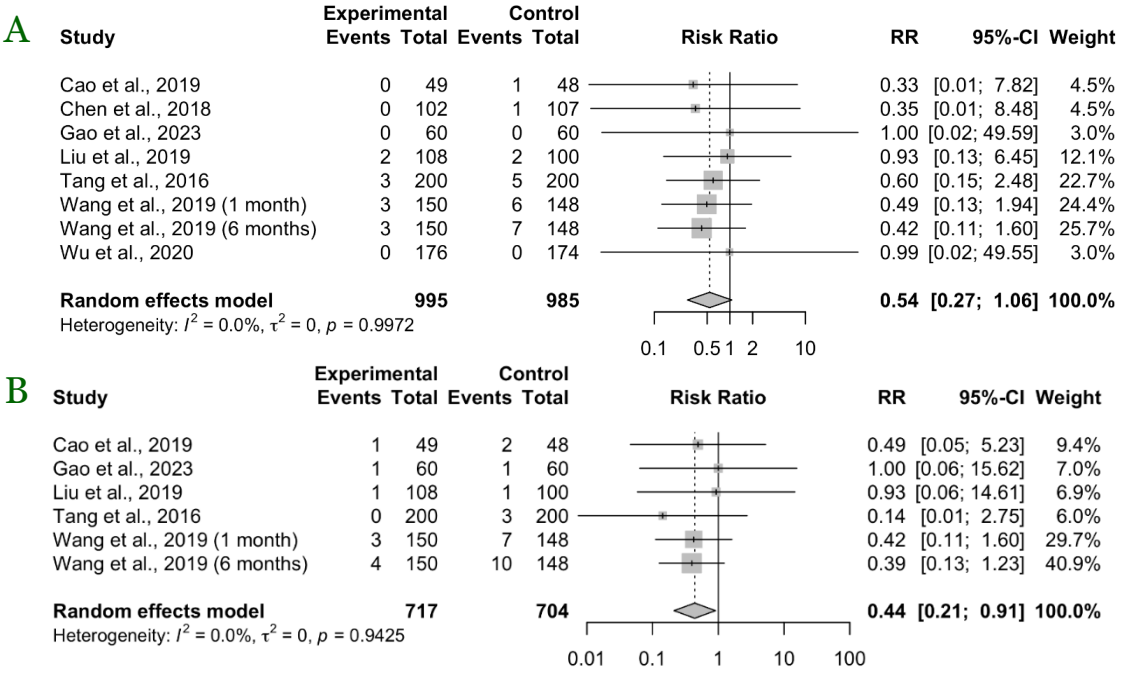

Figure 3. Forest plot of ticagrelor compared to clopidogrel in lowering the incidence of cardiovascular death (A) and myocardial infarction (B).

Table 2. Summary of effect size estimates on secondary and safety outcomes

Outcome	Number of participants	Risk Ratio	95%CI	*p*-value	I^2	Reference
Stent thrombosis	1,117	0.30	0.14; 0.66	0.0027*	0%	[19, 20, 22, 24, 26]
Target revascularization	1,630	0.47	0.26; 0.83	0.0098*	0%	[19, 20, 22-25]
Dyspnea	489	6.20	1.10; 35.04	0.0390*	0%	[19, 21, 26]
Major bleeding	1,376	1.05	0.43; 2.54	0.9176	0%	[22-26]

Meta-regression

Associations between several covariates and six outcomes were identified through meta-regression analysis, as presented in **Supplementary file 4**. The analysis revealed that sex, age, BMI, LDL-C, smoking habit, diabetes, and hypertension, and follow-up time did not significantly influence the estimates for cardiovascular death, myocardial infarction, stent thrombosis, target revascularization, and major bleeding (p>0.05). However, for myocardial infarction and target revascularization, low-risk-of-bias studies significantly reduced the effect size (p=0.0263 and p=0.0061, respectively), indicating that methodological quality may influence observed treatment effects. In contrast, for dyspnea, covariate data were reported only by a limited number of studies, resulting in insufficient data to conduct meta-regressions for the rest of covariates. The bubble plots are presented in **Supplementary file 5**.

Publication bias

Publication bias was assessed using DOI plot, as presented in **Figure 4**. The corresponding Luis Furuya-Kanamori (LFK) indices for both cardiovascular death and myocardial infarction (LFK=1.91 and LFK=1.23) suggested minor asymmetry, indicating the presence of slight publication bias. Moreover, the analysis revealed major asymmetry for stent thrombosis (LFK=−5.14) and major bleeding (LFK=−2.07), indicating a high likelihood of publication bias influencing these outcomes. In contrast, the LFK indices for target revascularization (LFK=0.82) and dyspnea (LFK=0.45) suggested no asymmetry, suggesting a low risk of publication bias. The DOI publication bias of secondary and safety outcomes is presented in **Supplementary file 6**.

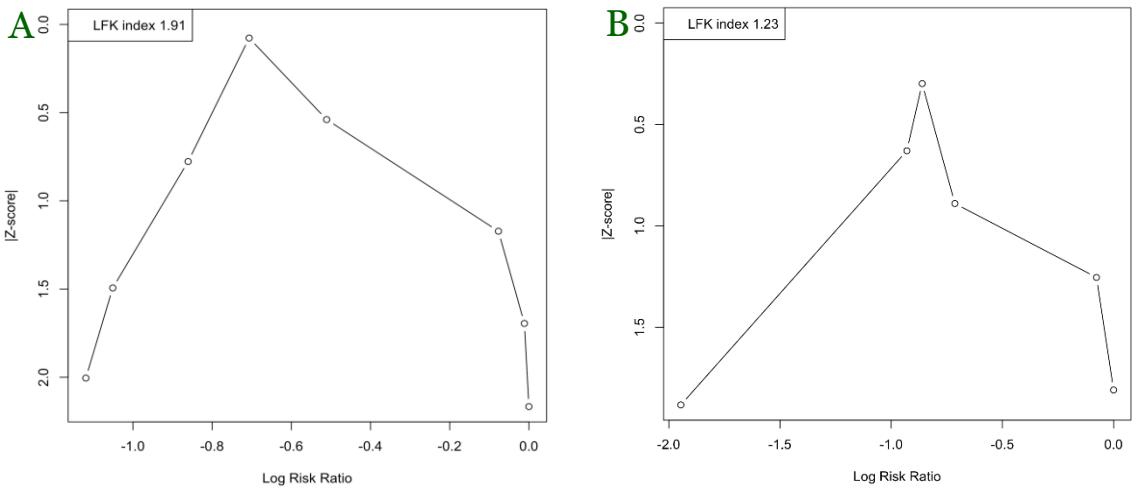

Figure 4. DOI plot for publication bias of cardiovascular death (A) and myocardial infarction (B).

Discussion

The present study revealed that ticagrelor was associated with significantly lower rates of MI, stent thrombosis, and target revascularization compared with clopidogrel in ACS patients post-PCI, with no statistically significant differences in cardiovascular death or major bleeding. Dyspnea was reported more frequently with ticagrelor compared to clopidogrel. These findings align with previous study reporting that ticagrelor reduces ischemic events, including mortality, reinfarction, stroke, and MACE in post-STEMI patients compared to clopidogrel, without a consistent increase in major bleeding risk when assessed by Bleeding Academic Research Consortium (BARC) or thrombolysis in myocardial infarction (TIMI) criteria [27]. In contrast, a previous study using the PLATO criteria has reported a higher bleeding risk with ticagrelor [13]. These discrepancies highlight the influence of bleeding definition choice in reported safety outcomes. In these included studies, only one trial used TIMI criteria, whereas most followed PLATO definitions [25], which may have contributed to the variability in bleeding results.

Differences in cardiovascular death outcomes between studies may also relate to variations in antiplatelet loading dose, follow-up duration, and patient population characteristics. For instance, one trial administered a 300 mg clopidogrel loading dose in both groups, deviating from standard protocols and potentially influencing treatment effects [26]. Furthermore, the duration of follow-up in these included studies did not align with the minimum one-year period recommended by international guidelines for the management of ACS. In the present meta-analysis, the majority of included studies had follow-up durations of less than one year [19, 22-25], while the other two studies conducted follow-ups of two years [20] and under one year [26]. Meta regression analysis revealed that low risk of bias studies tended to report smaller effect sizes for MI and target revascularization, suggesting that study quality may influence effect estimates.

The observed efficacy differences may be explained by pharmacological properties. Ticagrelor is a reversible, direct-acting P2Y12 receptor antagonist with additional pleiotropic effects, notably increased extracellular adenosine levels that promote vasodilation, enhance microvascular perfusion, and support endothelial repair through increased release of endogenous antithrombotic factors and mobilization of endothelial progenitor cells (EPCs) [28,29,30]. In contrast, clopidogrel is a prodrug requiring hepatic activation via cytochrome P450 enzymes [31], particularly CYP2C19. Only a small fraction (~15%) is converted to its active metabolite [32], with the remainder hydrolyzed into inactive forms [33]. Genetic polymorphisms affecting CYP2C19 activity—common in East Asian populations—may reduce clopidogrel's antiplatelet efficacy [34]. Ticagrelor's pharmacokinetics, which bypass metabolic activation, allow for more consistent platelet inhibition across genetic backgrounds [35]. Dyspnea, more frequent with ticagrelor, typically occurs within hours of administration and is often mild, transient, and not linked to objective cardiopulmonary dysfunction [26]. It may resolve with continued therapy, but could affect long-term adherence, particularly in patients with respiratory comorbidities.

Based on current evidence, ticagrelor may be preferred over clopidogrel for reducing ischemic events post-PCI, particularly in populations with high thrombotic risk and no respiratory comorbidities. Meanwhile, clopidogrel is a cost-saving alternative to ticagrelor in patients with ACS, giving it a reasonable alternative to ticagrelor in patients with a higher bleeding risk [36]. To our knowledge, this is the first study that comprehensively assessed the efficacy and safety comparison between ticagrelor and clopidogrel as DAPT in ACS patients post-PCI, incorporating meta-regression and publication bias assessment to enhance robustness. However, several limitations should be acknowledged. First, all included studies were conducted in East Asian populations, where the prevalence of CYP2C19 loss-of-function alleles is relatively high. This genetic predisposition may contribute to diminished response to clopidogrel, potentially influencing the observed outcomes. Second, several side effects were reported qualitatively due to the limited number of studies. Third, the assessment of major bleeding was reported inconsistently due to various bleeding criteria, reducing the reliability of this finding. Furthermore, studies reported in NSTEMI and angina were limited, resulting in an inability to perform subgroup analysis across different ACS subtypes. Future trials should include a broader spectrum of ACS populations to assess direct comparison between ticagrelor and semaglutide in NSTEMI and angina. Studies in more ethnically diverse populations are also necessary to enhance the generalizability of the findings. Moreover, expanding the scope of adverse events with more standardized definitions could also be done to draw more definitive conclusions regarding the safety comparison.

Conclusion

Ticagrelor was associated with a lower incidence of myocardial infarction, stent thrombosis, and target revascularization compared with clopidogrel in ACS patients post-PCI, with no statistically significant difference in cardiovascular death. While ticagrelor increased the risk of dyspnea, it did not significantly raise the incidence of major bleeding. These findings suggest ticagrelor may be preferred for patients at high thrombotic risk without significant respiratory comorbidities, whereas clopidogrel remains a reasonable option for those at higher bleeding risk or with ticagrelor intolerance. Future trials should enroll more diverse populations and apply standardized, comprehensive adverse event reporting to strengthen the evidence base.

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Competing interests

The authors declare no competing interests.

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Underlying data

All supplementary data associated with this study are publicly available via Figshare at https://doi.org/10.6084/m9.figshare.29587280.v2.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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References

1. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and treatment of acute coronary syndromes: A review. JAMA 2022;327(7):662-675.
2. Libby P. The changing landscape of atherosclerosis. Nature 2021;592(7855):524-533.
3. World Health Organization. The top 10 causes of death. Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. Accessed: 5 May 2025.
4. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019, 40(2):87-165. https://doi.org/10.1093/eurheartj/ehy394.
5. Valgimigli M, Frigoli E, Heg D, *et al*. Dual antiplatelet therapy after PCI in patients at high bleeding risk. N Engl J Med 202;wa385(18):1643-1655.
6. Collet JP, Thiele H, Barbato E, *et al*. 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021;42(14):1289-1367.
7. van der Sangen NMR, Claessen B, Kucuk IT, *et al*. Single antiplatelet therapy directly after percutaneous coronary intervention in non-ST-segment elevation acute coronary syndrome patients: the OPTICA study. EuroIntervention 2023;19(1):63-72.
8. Alagna G, Mazzone P, Contarini M, Ando G. Dual antiplatelet therapy with parenteral P2Y(12) Inhibitors: Rationale, evidence, and future directions. J Cardiovasc Dev Dis 2023;10(4).
9. Valgimigli M, Bueno H, Byrne RA, *et al*. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2018;39(3):213-260.
10. Sawayama Y, Yamamoto T, Tomita Y, *et al*. Comparison between clopidogrel and prasugrel associated with CYP2C19 genotypes in patients receiving percutaneous coronary intervention in a Japanese population. Circ J 2020;84(9):1575-1581.
11. Tantry US, Singh S, Raghavakurup LN, *et al*. Can CYP2C19 genotyping improve antiplatelet therapy efficacy in real-life practice? Recent advances. Kardiol Pol 2024;82(9):840-845.
12. Szummer K, Montez-Rath ME, Alfredsson J, *et al*. Comparison between ticagrelor and clopidogrel in elderly patients with an acute coronary syndrome: Insights from the SWEDEHEART registry. Circulation 2020;142(18):1700-1708.
13. Kumar A, Arsal SA, Shafique MA, *et al*. Comparison between ticagrelor and clopidogrel in patients with acute coronary syndrome undergoing percutaneous coronary intervention: A systematic review and meta-analysis. J Med Surg Public Health 2024;2:100064.
14. Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
15. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5(1):210.
16. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods 2021;12(1):55-61.
17. Higgins JPT, Thomas J, Chandler J, *et al*. Cochrane handbook for systematic reviews of Interventions version 6.5 (updated August 2024). UK: The Cochrane Collaboration and John Wiley and Sons Ltd; 2024.
18. Furuya-Kanamori L, Barendregt JJ, Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. Int J Evid Based Healthc 2018;16(4):195-203.
19. Cao B, Qu F, Liu X, *et al*. Short-term efficacy of ticagrelor in acute ST-segment elevation myocardial infarction patients undergoing an emergency percutaneous coronary intervention. Aging 2019;11(20):8925-8936.
20. Chen YC, Lin FY, Lin YW, *et al*. DAPT plus cilostazol is better than traditional DAPT or aspirin plus ticagrelor as elective PCI for intermediate-to-highly complex cases: Prospective, randomized, PRU-based study in Taiwan. Am J Cardiovasc Drugs 2018;19(1):75-86.

21. Choi KN, Jin HY, Shin HC, *et al*. Comparison of the antiplatelet effects of once and twice daily low-dose ticagrelor and clopidogrel after percutaneous coronary intervention. Am J Cardiol 2017;120(2):201-206.
22. Gao ST, Wang Y, Ma L. Effect of ticagrelor and clopidogrel dual antiplatelet therapy on MPVLR, MAADP, and AA inhibition rate in acute coronary syndrome patients after percutaneous coronary intervention. Medicine 2023;102(37):e34974.
23. Liu Y, Ding LY, Li XZ. Therapy with ticagrelor for ST-elevated acute coronary syndrome accompanied by diabetes mellitus. Eur Rev Med Pharmacol Sci 2019;23(Suppl 3):312-318.
24. Tang X, Li R, Jing Q, *et al*. Assessment of ticagrelor versus clopidogrel treatment in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. J Cardiovasc Pharmacol 2016;68(2):115-120.
25. Wang X, Li X, Wu H, *et al*. Beneficial effect of ticagrelor on microvascular perfusion in patients with ST-segment elevation myocardial infarction undergoing a primary percutaneous coronary intervention. Coron Artery Dis 2019;30(5):317-322.
26. Wu X, You W, Wu Z, *et al*. Ticagrelor versus clopidogrel for prevention of subclinical stent thrombosis detected by optical coherence tomography in patients with drug-eluting stent implantation-a multicenter and randomized study. Platelets 2020;32(3):404-412.
27. Geravandi M, Nourabi M, Navabifar S, *et al*. A comparison of the effects of ticagrelor and clopidogrel in patients with acute ST-segment elevation myocardial infarction: A systematic review and meta-analysis of randomized clinical trials. BMC Pharmacol Toxicol 2024;25(1):93.
28. Angiolillo DJ, Galli M, Collet JP, *et al*. Antiplatelet therapy after percutaneous coronary intervention. EuroIntervention 2022;17(17):e1371-e1396.
29. Cattaneo M, Schulz R, Nylander S. Adenosine-mediated effects of ticagrelor: evidence and potential clinical relevance. J Am Coll Cardiol 2014;63(23):2503-2509.
30. Kubisa MJ, Jezewski MP, Gasecka A, *et al*. Ticagrelor - toward more efficient platelet inhibition and beyond. Ther Clin Risk Manag 2018;14:129-140.
31. Sun Y, Venugopal J, Guo C, *et al*. Clopidogrel resistance in a murine model of diet-induced obesity is mediated by the interleukin-1 receptor and overcome with DT-678. Arterioscler Thromb Vasc Biol 2020;40(6):1533-1542.
32. Liu S, Wang Z, Tian X, Cai W. Predicting the effects of CYP2C19 and carboxylesterases on vicagrel, a novel P2Y12 antagonist, by physiologically based pharmacokinetic/pharmacodynamic modeling approach. Front Pharmacol 2020;11:591854.
33. Cattaneo M. The platelet P2Y(1)(2) receptor for adenosine diphosphate: congenital and drug-induced defects. Blood 2011;117(7):2102-2112.
34. Beavers CJ, Patel P, Naqvi IA. Clopidogrel. Treasure Island: StatPearls Publishing; 2025.
35. Krakowiak A, Kuleta J, Plech I, *et al*. Ticagrelor-related severe dyspnoea: Mechanisms, characteristic features, differential diagnosis and treatment. Clin Med Insights Case Rep 2020;13:1179547620956634.
36. van den Broek WWA, van Paassen JG, Gimbel ME, *et al*. Cost-effectiveness of clopidogrel vs. ticagrelor in patients of 70 years or older with non-ST-elevation acute coronary syndrome. Eur Heart J Cardiovasc Pharmacother 2022;9(1):76-84.