Iranian Heart Journal; 2025; 26 (2)

Original Article

The Efficacy and Safety of Ticagrelor Compared With Clopidogrel in Patients With ST-Segment Elevation Myocardial Infarction Scheduled for a Pharmaco-Invasive Reperfusion Strategy

Ahmed Mahmoud Bendary[1], MD; Osama Sanad Arafa[1], MD;
Zeinab Gomaa Gamal Awad[2*], MBBCH; Yasser Hosny Abd El Rahman[1], MD

ABSTRACT

Background: ST-segment elevation myocardial infarction (STEMI) is a critical component of acute coronary syndrome and is often managed with a pharmaco-invasive strategy when primary percutaneous coronary intervention (pPCI) is not immediately available. Although ticagrelor has demonstrated superior outcomes in pPCI settings, its efficacy and safety compared with clopidogrel in a pharmaco-invasive approach remain less studied. This study aimed to evaluate the safety and efficacy of ticagrelor compared with clopidogrel in STEMI patients undergoing reperfusion with a pharmaco-invasive strategy.

Methods: This randomized controlled trial was conducted among 170 STEMI patients treated with fibrinolytic therapy and scheduled for a pharmaco-invasive strategy. Patients were randomized to receive either ticagrelor (the switch group) or clopidogrel (the no-switch group) in addition to standard therapy. The primary outcomes were major bleeding (safety) and a composite of death, reinfarction, or stroke (efficacy) within 6 months.

Results: The study found no significant differences in in-hospital outcomes, including resuscitated cardiac arrest, shock, and major bleeding between the groups. At 6 months, the composite efficacy endpoint occurred in 1.2% of the ticagrelor group compared with 4.7% in the clopidogrel group (P = 0.368). Kaplan-Meier analysis revealed a divergence in event rates beginning in the fifth month, with the ticagrelor group exhibiting a slightly higher event rate by the sixth month (10% vs 9.8%).

Conclusions: In STEMI patients treated with a pharmaco-invasive strategy, ticagrelor and clopidogrel demonstrated similar safety profiles. Although the ticagrelor group exhibited a lower incidence of the composite efficacy endpoint, this difference was not statistically significant. ***(Iranian Heart Journal 2025; 26(2): 39-48)***

KEYWORDS: STEMI, Pharmaco-invasive strategy, Ticagrelor, Clopidogrel, Randomized controlled trial

[1] Cardiovascular Medicine Department, Faculty of Medicine, Benha University, Benha, Egypt.
[2] New Cairo Specialized Hospital, Cairo, Egypt.

***Corresponding Author:** Zainab Gomaa Gamal Awad, MBBCH; New Cairo Specialized Hospital, Cairo, Egypt.
Email: zainboo2020@gmail.com **Tel:** 01015287137

Received: October 5, 2024 **Accepted:** January 18, 2025

Approximately 32% of acute coronary syndrome (ACS) cases are attributed to patients with ST-segment elevation myocardial infarction (STEMI). The in-hospital death rates for these patients range from 5% to 15%, and these rates vary based on geographic location and baseline variations. [1] For patients with STEMI unable to have primary percutaneous coronary intervention (pPCI) within the designated time frames, a pharmaco-invasive approach is advised in clinical settings. This approach entails administering fibrinolytic treatment as the first step, followed by prompt transfer for PCI within a 24-hour timeframe. [2]

Fibrinolysis, while effective in restoring blood flow, can paradoxically increase platelet reactivity, creating a thrombotic environment in STEMI patients. [3] To mitigate this risk, dual antiplatelet therapy (DAPT) is recommended, typically involving a loading dose of clopidogrel. However, clopidogrel, a pro-drug, requires liver metabolism for activation, and in STEMI patients, this process can be delayed due to circulatory conditions, leading to suboptimal platelet inhibition and variability in drug response due to genetic polymorphisms. [1,4]

Ticagrelor, a novel P2Y12 inhibitor, offers a more rapid onset and offset of action than clopidogrel, providing more consistent platelet inhibition. [5] The PLATO trial demonstrated the superiority of ticagrelor over clopidogrel in patients with ACS, leading to changes in guidelines favoring ticagrelor in STEMI patients undergoing pPCI. [6] Nonetheless, real-world data on ticagrelor's efficacy and safety, particularly in a STEMI population managed with a pharmaco-invasive strategy, remain limited. [7]

This study aimed to assess the effectiveness and safety of ticagrelor compared with clopidogrel in patients with STEMI who were planned to undergo reperfusion using a pharmaco-invasive approach.

METHODS

Study Design and Population

This randomized controlled trial was conducted over 6 months, from September 2022 through February 2023, at New Cairo Hospital. The study enrolled 170 patients hospitalized for acute STEMI who were treated with fibrinolytic therapy and scheduled for a pharmaco-invasive strategy. Patients were randomly assigned to receive either ticagrelor or clopidogrel in addition to standard therapy. The study protocol received approval from the Institutional Review Board. Prior to enrollment, all participants provided informed consent, which ensured their confidentiality and the right to withdraw from the study at any time.

Inclusion Criteria

Eligible participants included male and female patients aged 18 to 74 years with a diagnosis of STEMI within the previous 24 hours. All patients had been treated with fibrinolytic therapy. STEMI was defined by specific ECG criteria, including ST-segment elevation at the J point in 2 contiguous leads and new left bundle-branch block, along with symptoms such as angina-like chest pain or elevated markers of myocardial necrosis (troponin and/or CK-MB). [8]

Exclusion Criteria

Exclusion criteria included contraindications to clopidogrel or ticagrelor, the need for oral anticoagulation therapy, or the concurrent use of medications that strongly interact with CYP3A. Additional exclusion criteria were significant thrombocytopenia or anemia, pregnancy or lactation, and contraindications to fibrinolytic therapy, such as recent intracranial hemorrhage or severe hypertension at presentation.

Randomization and Intervention

Patients were randomized into 2 groups using a simple, concealed randomization

method via an automated web-based system. The ticagrelor group received a loading dose of 180 mg of ticagrelor, followed by 90 mg twice daily, while the clopidogrel group received a loading dose of 300 to 600 mg of clopidogrel, followed by 75 mg once daily. Both groups received acetylsalicylic acid (ASA) throughout the follow-up period, with additional antiplatelet therapy during PCI at the investigator's discretion.

Methods

The data collected for this study included demographic information (age, sex, body mass index, and cardiovascular risk factors), clinical data (heart rate, blood pressure, and medical history), procedural data (time from symptom onset to first medical contact and hospital stay duration), medication data (use of GP2b/3a inhibitors and adherence to therapy), and outcome data (incidence of in-hospital outcomes such as cardiac arrest, shock, heart failure, stroke, recurrent MI, intracranial hemorrhage, and major bleeding).

Outcomes Measure

The primary safety outcome was the rate of major bleeding during the 6-month follow-up, defined according to the thrombolysis in myocardial infarction (TIMI) criteria. The primary efficacy outcomes were composed of a composite endpoint of recurrent MI, stroke, or death from vascular causes within 6 months. The secondary outcomes consisted of the individual components of the composite endpoint, time-to-event analysis using Kaplan-Meier curves, and other in-hospital outcomes such as resuscitated cardiac arrest, shock, and heart failure.

Sample Size Estimations

The sample size was estimated using epi-info software, version 7.2.5.0, based on an expected frequency of a composite endpoint of death, recurrent MI, or stroke of 6.2%. [9] The initial sample size was 140 patients, which was increased to 170 to account for the potential loss of follow-up. The confidence level and margin of error were set at 95% and 4%, respectively.

Statistical Analysis

Data management and statistical analysis were conducted using IBM's SPSS, version 28, in Armonk, New York, United States. The normality of the quantitative data was evaluated using the Shapiro-Wilk test and direct data visualization techniques. Concerning the concept of normalcy, quantitative data were described using either means and standard deviations or medians and ranges. Categorical data were summarized using numerical values and percentages. Quantitative data from the study groups were compared using the independent *t*-test for normally distributed variables and the Mann-Whitney *U* test for non-normally distributed variables. Comparisons between categorical data were conducted using either the χ^2 or Fisher exact test. A Kaplan-Meier analysis was performed to evaluate the time to reach the composite endpoint. The log-rank test was utilized to compare the curves between the groups under study. All statistical tests were 2-sided, with significance defined as *P*-values < 0.05.

RESULTS

In this clinical trial, a total of 226 patients were assessed for eligibility. Out of these, 56 patients were excluded, with 39 not meeting the inclusion criteria and 17 declining to participate. The remaining 170 patients were randomly divided into 2 equal-sized groups of 85 patients each. All enrolled patients were followed up, and no loss of follow-up was reported. Data from all participants were included in the final statistical analysis (Fig. 1).

Demographic and baseline characteristics

The studied groups were comparable regarding age (*P* = 0.126), sex (*P* = 0.239),

body mass index (P = 0.121), heart rate (P = 0.891), systolic blood pressure (P = 0.666), diastolic blood pressure (P = 0.393), dyslipidemia (P = 1.0), hypertension (P = 0.357), smoking (P = 0.269), diabetes mellitus (P = 0.641), family history of coronary artery disease (P = 1.0), past history of coronary artery disease (P = 0.161), past history of MI (P = 1.0), past history of coronary revascularization (P = 0.66), past history of heart failure (P = 0.496), past history of atrial fibrillation (P = 0.246), symptom to first medical contact (P = 0.164), first medical contact-to-fibrinolysis (P = 0.326), hospital stay (P = 0.199), and use of GP2b/3a (P = 0.618) (Table 1).

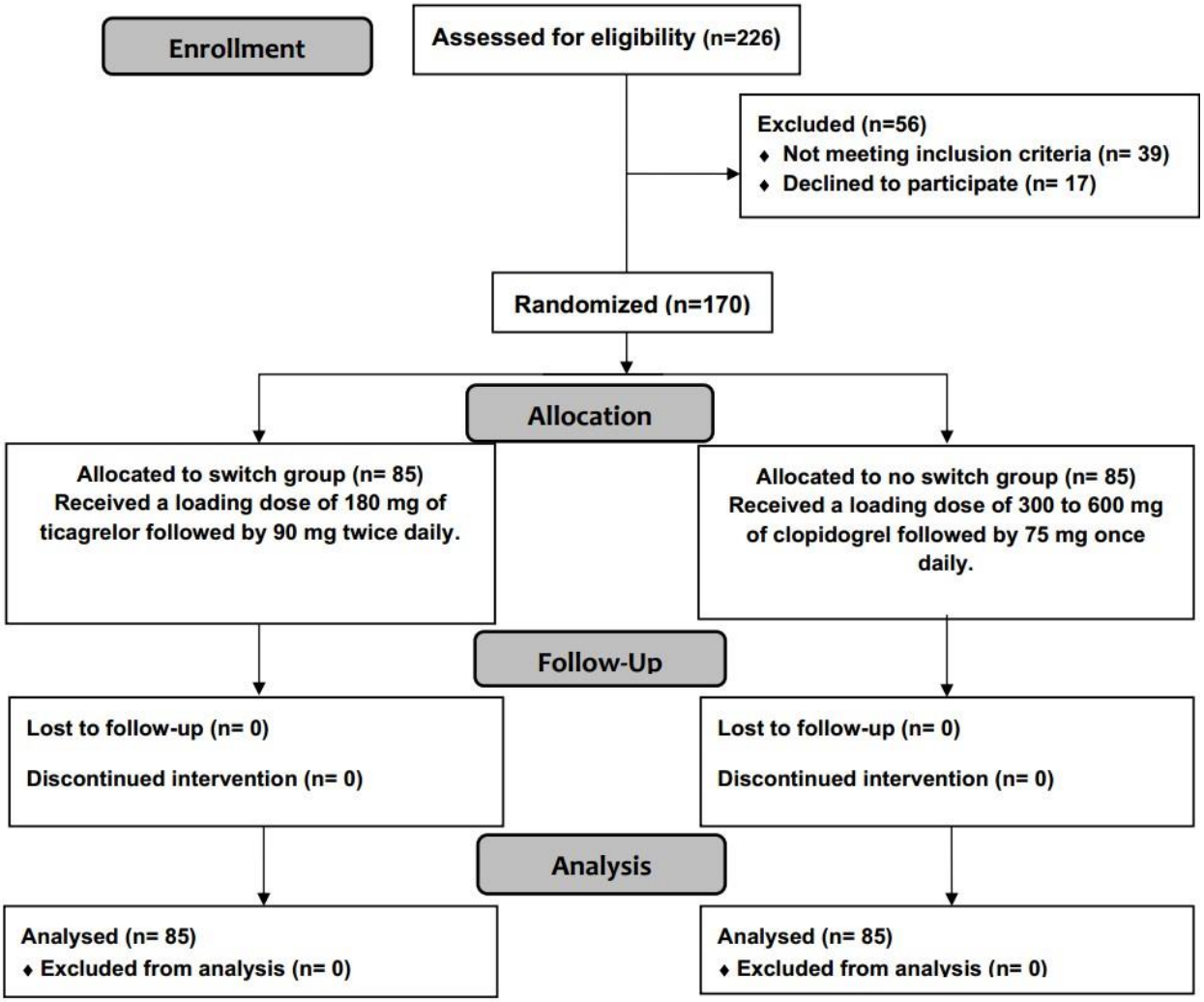

Figure 1. The image presents the CONSORT flow diagram of the studied patients.

Table 1. The demographic and baseline characteristics of the studied patients

		Total (n = 170)	Switch Group (n = 85)	No-Switch Group (n = 85)	*P*
Age, y	Mean ±SD	56 ±9	55 ±10	57 ±7	0.126
Sex					
Males	n (%)	138 (81.2)	72 (84.7)	66 (77.6)	0.239
Females	n (%)	32 (18.8)	13 (15.3)	19 (22.4)	
BMI, kg/m^2	Mean ±SD	26.9 ±2.8	26.6 ±2.4	27.2 ±3.1	0.121
HR, bpm	Mean ±SD	74 ±13	74 ±11	74 ±15	0.891
SBP, mm Hg	Mean ±SD	125 ±19	124 ±21	125 ±18	0.666
DBP, mm Hg	Mean ±SD	76 ±9	75 ±10	77 ±9	0.393
Dyslipidemia	n (%)	64 (37.6)	32 (37.6)	32 (37.6)	1.0
Hypertension	n (%)	86 (50.6)	40 (47.1)	46 (54.1)	0.357
Smoking	n (%)	132 (77.6)	69 (81.2)	63 (74.1)	0.269
DM	n (%)	68 (40)	48 (56.5)	51 (60)	0.641
FH of CAD	n (%)	34 (20)	17 (20)	17 (20)	1.0
PH of CAD	n (%)	44 (25.9)	18 (21.2)	26 (30.6)	0.161
PH of MI	n (%)	9 (5.3)	4 (4.7)	5 (5.9)	1.0
PH of C. revascularization	n (%)	24 (14.1)	11 (12.9)	13 (15.3)	0.66
PH of heart failure	n (%)	9 (5.3)	6 (7.1)	3 (3.5)	0.496
PH of AF	n (%)	3 (1.8)	0 (0)	3 (3.5)	0.246
Symptom to FMC, min	Median (range)	60 (20 - 300)	60 (20 - 300)	90 (30 - 240)	0.164
FMC-to-fibrinolysis, min	Mean ±SD	30 ±5	31 ±7	30 ±2	0.326
Hospital stay, d	Median (range)	3 (2 - 7)	3 (2 - 7)	3 (2 - 5)	0.199
Use of GP2b/3a	n (%)	18 (10.6)	10 (11.8)	8 (9.4)	0.618

SBP: systolic blood pressure, BMI: body mass index, HR: heart rate, DBP: diastolic blood pressure, FH: family history, CAD: coronary artery disease, PH: past history, DM: diabetes mellitus, MI: myocardial infarction, C. revascularization: coronary revascularization, AF: atrial fibrillation, FMC: first medical contact, GP2b/3a: glycoprotein IIb/IIIa

In-hospital outcomes

No significant differences were observed in in-hospital outcomes, including resuscitated cardiac arrest (P = 0.443), shock (P = 0.417), inotrope use (P = 0.417), heart failure (P = 0.130), stroke (P = 1.0), recurrent MI (no events), intracranial hemorrhage (no events), and major bleeding (P = 1.0) (Fig. 2).

Six-month composite endpoint

At the 6-month mark, the efficacy composite endpoint was higher in the no-switch group (4.7%) than in the switch group (1.2%), although the difference was not statistically significant (P = 0.368). Additionally, no safety endpoint events were reported in either group at 6 months (Table 2).

Kaplan-Meier analysis for time to the composite endpoint

In both the switch and no-switch groups, a consistent 0% event rate was maintained from the first to the fourth month. However, a divergence emerged in the fifth month, with the no-switch group experiencing a 2.80% event rate, while the switch group remained at 0%. By the sixth month, the switch group showed a slightly increased event rate of 10% compared with 9.80% in the no-switch group (Table 3 & Fig. 3).

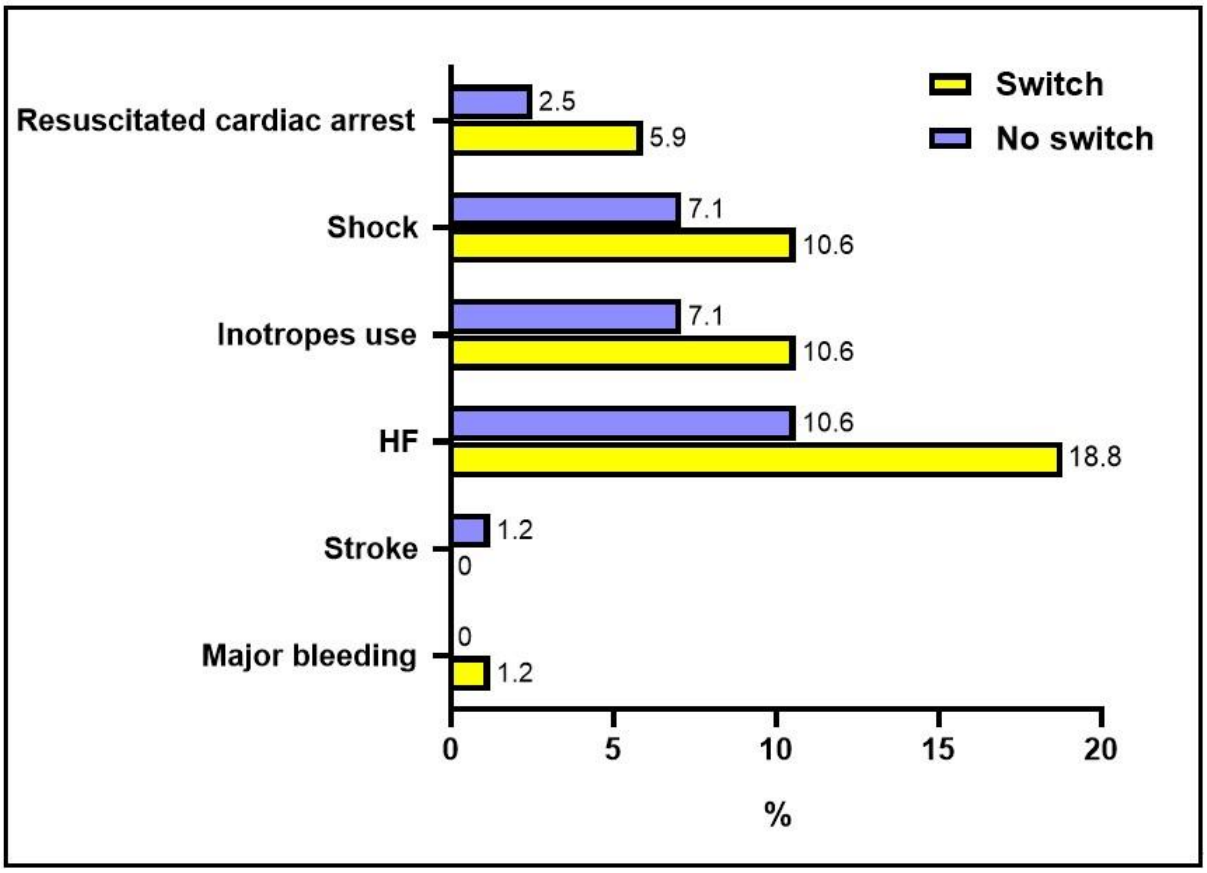

Figure 2. The image presents the in-hospital outcomes in the studied groups.

Table 2. The composite endpoint at 6 months in the studied groups

		Total (n = 170)	Switch Group (n = 85)	No-Switch Group (n = 85)	*P*
Composite efficacy endpoint	n (%)	5 (2.9)	1 (1.2)	4 (4.7)	0.368
Type of the composite endpoint					
Death	n (%)	1 (0.6)	1 (1.2)	0 (0)	0.121
Nonfatal MI	n (%)	4 (2.4)	0 (0)	4 (4.7)	
Nonfatal stroke	n (%)	0 (0)	0 (0)	0 (0)	
No	n (%)	165 (97.1)	84 (98.8)	81 (95.3)	
Safety endpoint (major bleeding)	n (%)	0 (0)	0 (0)	0 (0)	-

MI: myocardial infarction

Table 3. The composite endpoint at different time points in the switch and no-switch groups

	Composite Endpoint Rate					
	At 1 month	At 2 months	At 3 months	At 4 months	At 5 months	At 6 months
Switch	0%	0%	0%	0%	0%	10%
No-switch	0%	0%	0%	0%	2.80%	9.80%

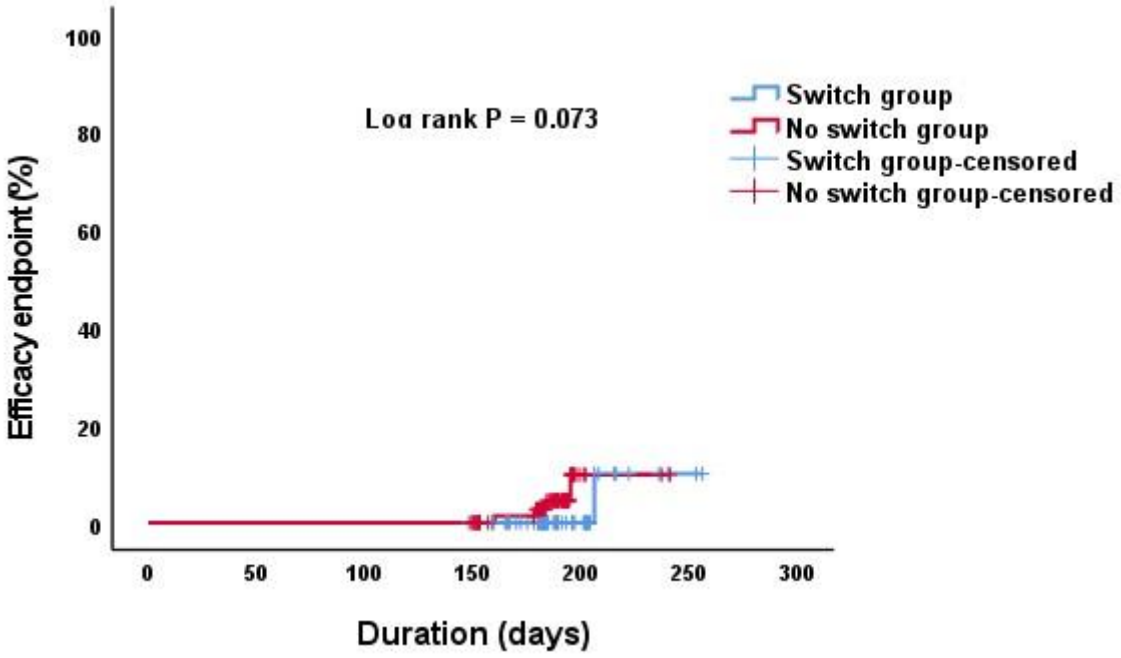

Figure 3. The image showcases the Kaplan-Meier analysis for the efficacy endpoint between the studied groups.

DISCUSSION

STEMI accounts for a significant portion of ACS cases, with in-hospital mortality influenced by geographic and individual factors. [10-12] While DAPT is standard post-ACS, clopidogrel's limitations have led to the adoption of more potent P2Y12 inhibitors like ticagrelor, especially after pPCI. [13,14] For STEMI patients without immediate PCI access, a pharmaco-invasive strategy involving fibrinolysis followed by early PCI is recommended. [15,16] Nevertheless, most clinical trials favoring ticagrelor excluded patients treated with this approach, leaving guidelines to still recommend clopidogrel, with a possible switch to ticagrelor after stabilization. Despite its benefits, early switching to ticagrelor raises safety concerns due to bleeding risks. [17-19] Ticagrelor's rapid antiplatelet effects are crucial in acute STEMI, and studies like TREAT have shown its safe switch from clopidogrel post-fibrinolysis. [20,21]

The present study aimed to assess the effectiveness and safety of ticagrelor compared with clopidogrel in patients with STEMI who were scheduled to undergo reperfusion using a pharmaco-invasive approach.

Our results revealed nonsignificant differences in in-hospital outcomes between the studied groups, indicating that both treatments are similarly safe. Chiming with this finding, Welsh et al, [9] in a study involving 1426 STEMI patients scheduled for a pharmaco-invasive strategy, reported no significant differences in in-hospital events, including major bleeding and intracranial hemorrhage, between patients maintained on clopidogrel and those switched to ticagrelor. Their findings further support the comparable safety profiles of both drugs in the post-fibrinolysis hospital setting.

In the current study, at 6 months, the efficacy composite endpoint was higher in the no-switch group (4.7%) than in the switch group (1.2%), although the difference was not significant, and the safety endpoint was not reported. Similarly, Welsh et al [9] found that switching to ticagrelor resulted in a significantly lower primary composite

occurrence compared with clopidogrel (3.5% vs 7.0%, adjusted HR 0.46), with similar major bleeding rates between the groups. Their findings support the safety profile observed in our research.

The results of the TREAT trial also aligned with our findings in that they showed no significant differences in the primary composite outcome of MI, cardiovascular death, or stroke between patients receiving ticagrelor and those receiving clopidogrel after fibrinolysis in a STEMI population (6.7% vs 7.3%, HR 0.93, 95% CI 0.73 to 1.18; $P = 0.53$). Major bleeding rates were comparable between the groups, although the TREAT trial noted a higher incidence of minor bleeding events in the ticagrelor group, possibly due to differences in patient populations, adherence to protocols, or follow-up duration. [21] A systematic review and meta-analysis conducted by Kheiri et al [22] revealed no significant differences in outcomes between STEMI patients who switched to ticagrelor from clopidogrel and those who continued with clopidogrel while undergoing fibrinolytic therapy. Their study, which included 3 randomized clinical trials with 3999 patients, demonstrated similar short-term outcomes between the 2 drugs regarding major adverse cardiovascular events, mortality, MI, and stroke.

Contrary to our findings, the PLATO trial by Wallentin et al [6] showed that ticagrelor significantly improved cardiovascular outcomes compared with clopidogrel in patients with ACS, including those with ST-segment elevation. Among 18,624 patients, the primary endpoint of death from vascular causes, stroke, or MI was notably lower in the ticagrelor group (9.8%) than in the clopidogrel group (11.7%). The differences between our study and the PLATO trial may be due to variations in study design, patient population, and the longer follow-up and larger sample size in PLATO, likely contributing to the detection of more pronounced benefits with ticagrelor.

In the TOTAL trial by Welsh et al, [23] which included 9932 STEMI patients who underwent pPCI, ticagrelor was associated with a lower rate of the primary composite outcome (cardiovascular death, cardiogenic shock, recurrent MI, or New York Heart Association [NYHA] functional class IV heart failure) than clopidogrel (adjusted hazard ratio [aHR] 0.72, 95% CI 0.57 to 0.91; $P < 0.02$) and prasugrel (aHR 0.65, 95% CI 0.48 to 0.89; $P = 0.02$). Moreover, ticagrelor had significantly lower rates of major bleeding than clopidogrel.

According to our results, the switch and no-switch groups maintained a 0% event rate consistently from the first month up to the fourth month. In the fifth month, a divergence was noted, with the no-switch group experiencing a 2.80% event rate, while the switch group remained at 0%. By the sixth month, the switch group exhibited a slightly higher event rate of 10% compared with 9.80% in the no-switch group. This pattern suggests that the benefits of ticagrelor might become more apparent with longer follow-up periods, as observed in other studies like the PLATO trial, [6] where ticagrelor showed sustained efficacy over time. The absence of a significant difference in the primary safety outcome, particularly concerning major bleeding, is consistent with the findings of the TOTAL trial, where ticagrelor did not increase the major bleeding risk compared with clopidogrel. [23]

The Kaplan-Meier analysis in our study showed a divergence in event rates between the ticagrelor (switch) and clopidogrel (no-switch) groups starting from the fifth month, with the ticagrelor group having a slightly higher event rate by the sixth month. This finding stands in contrast with the TOTAL trial, where ticagrelor consistently outperformed clopidogrel throughout the follow-up period. The difference in our

findings may be due to the specific patient population and the pharmaco-invasive strategy used, which differs from the pPCI strategy in the TOTAL trial. [23]

Limitations

Several limitations should be considered when interpreting the results of this study. First, it was a single-center study with a small sample size, which may restrict the generalizability of the findings to a broader population. Second, the 6-month follow-up period may be insufficient to fully assess the potential late complications associated with ticagrelor and clopidogrel and their impact on long-term outcomes. Lastly, the exclusion of specific patient groups, such as those requiring oral anticoagulation, those with severe liver disease, or those with a history of intracranial hemorrhage, may limit the applicability of the results to the wider STEMI population.

CONCLUSIONS

In STEMI patients undergoing pharmaco-invasive management, ticagrelor did not demonstrate a significant reduction in the composite endpoint of death, stroke, or recurrent MI compared with clopidogrel over a 6-month period. Additionally, both treatment approaches exhibited a similar safety profile.

Future research with larger sample sizes and longer follow-up periods may be necessary to further explore potential differences in efficacy and safety between ticagrelor and clopidogrel in this patient population.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Funding

The authors received no financial support for their research, authorship, or publication of this article.

Acknowledgments

None to declare.

REFERENCES

1. Vercellino M, Sànchez FA, Boasi V, et al. Ticagrelor versus clopidogrel in real-world patients with ST elevation myocardial infarction: 1-year results by propensity score analysis. BMC Cardiovasc Disord. Apr 5 2017; 17(1):97. doi:10.1186/s12872-017-0524-3
2. Li K, Zhang B, Zheng B, Zhang Y, Huo Y. Reperfusion Strategy of ST-Elevation Myocardial Infarction: A Meta-Analysis of Primary Percutaneous Coronary Intervention and Pharmaco-Invasive Therapy. Front Cardiovasc Med. 2022; 9:813325. doi:10.3389/fcvm.2022.813325
3. Sumaya W, Wallentin L, James SK, et al. Impaired Fibrinolysis Predicts Adverse Outcome in Acute Coronary Syndrome Patients with Diabetes: A PLATO Sub-Study. Thromb Haemost. Mar 2020; 120(3):412-422. doi:10.1055/s-0039-1701011
4. Alkhalil M, Kuzemczak M, Bell A, et al. A practical approach to prescribing antiplatelet therapy in patients with acute coronary syndromes. Cmaj. Feb 14 2022; 194(6):E205-e215. doi:10.1503/cmaj.202863
5. Nylander S, Schulz R. Effects of P2Y12 receptor antagonists beyond platelet inhibition--comparison of ticagrelor with thienopyridines. Br J Pharmacol. Apr 2016; 173(7):1163-78. doi:10.1111/bph.13429
6. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. Sep 10 2009; 361(11):1045-57. doi:10.1056/NEJMoa0904327
7. Gao S, Xu H, Huang S, Yuan J, Yu M. Real-World Use of Clopidogrel and Ticagrelor in Patients With Myocardial Infarction With Nonobstructive Coronary Arteries: Patient Characteristics and Long-Term Outcomes. Front Cardiovasc Med. 2021; 8:807494. doi:10.3389/fcvm.2021.807494
8. de Winter RW, Adams R, Amoroso G, et al. Prevalence of junctional ST-depression with tall symmetrical T-waves in a pre-hospital field triage system for STEMI patients. J

Electrocardiol. Jan-Feb 2019; 52:1-5. doi:10.1016/j.jelectrocard.2018.10.092

9. Welsh RC, Shavadia JS, Zheng Y, Tyrrell BD, Leung R, Bainey KR. Ticagrelor or clopidogrel dual antiplatelet therapy following a pharmacoinvasive strategy in ST-segment elevation myocardial infarction. Clin Cardiol. Nov 2021; 44(11):1543-1550. doi:10.1002/clc.23716

10. Qalby N, Arsyad DS, Qanitha A, et al. In-hospital mortality of patients with acute coronary syndrome (ACS) after implementation of national health insurance (NHI) in Indonesia. BMC Health Serv Res. Mar 5 2024; 24(1):284. doi:10.1186/s12913-024-10637-5

11. Ndaba L, Mutyaba A, Mpanya D, Tsabedze N. In-Hospital Mortality Outcomes of ST-Segment Elevation Myocardial Infarction: A Cross-Sectional Study from a Tertiary Academic Hospital in Johannesburg, South Africa. Journal of Cardiovascular Development and Disease. 2023; 10(8):348.

12. Adem F, Abdi S, Amare F, Mohammed MA. In-hospital mortality from acute coronary syndrome in Africa: a systematic review and meta-analysis. SAGE Open Med. 2023; 11:20503121221143646. doi:10.1177/20503121221143646

13. Alagna G, Mazzone P, Contarini M, Andò G. Dual Antiplatelet Therapy with Parenteral P2Y(12) Inhibitors: Rationale, Evidence, and Future Directions. J Cardiovasc Dev Dis. Apr 9 2023; 10(4) doi:10.3390/jcdd10040163

14. Abubakar M, Raza S, Hassan KM, et al. Efficacy, Safety, and Role of Antiplatelet Drugs in the Management of Acute Coronary Syndrome: A Comprehensive Review of Literature. Cureus. Mar 2023; 15(3):e36335. doi:10.7759/cureus.36335

15. Sim DS, Jeong MH, Ahn Y, et al. Pharmacoinvasive Strategy Versus Primary Percutaneous Coronary Intervention in Patients With ST-Segment–Elevation Myocardial Infarction. Circulation: Cardiovascular Interventions. 2016; 9(9):e003508. doi:doi:10.1161/CIRCINTERVENTIONS.115.003508

16. Yildiz M, Wade SR, Henry TD. STEMI care 2021: Addressing the knowledge gaps. Am Heart J Plus. Nov 2021; 11:100044. doi:10.1016/j.ahjo.2021.100044

17. Thrane PG, Olesen KKW, Würtz M, et al. Effectiveness and Safety of Ticagrelor Implementation in Patients with Acute Coronary Syndrome undergoing Percutaneous Coronary Intervention: A Cohort Study in Western Denmark. Lancet Reg Health Eur. Mar 2022; 14:100301. doi:10.1016/j.lanepe.2021.100301

18. Koh L, Kim JH, Tan SYD, et al. Switching from Ticagrelor to Clopidogrel in Asian Patients with ST-Elevated Myocardial Infarction - A Time Dependent Analysis Study. Acta Cardiol Sin. Jan 2020; 36(1):8-15. doi:10.6515/acs.202001_36(1).20190627a

19. Kim C, Shin D-H, Hong S-J, et al. One-year clinical outcomes of ticagrelor compared with clopidogrel after percutaneous coronary intervention in patients with acute myocardial infarction: From Korean Health Insurance Review and Assessment Data. Journal of Cardiology. 2019/03/01/ 2019; 73(3):191-197. doi:https://doi.org/10.1016/j.jjcc.2018.08.005

20. Berwanger O, Nicolau JC, Carvalho AC, et al. Ticagrelor vs Clopidogrel After Fibrinolytic Therapy in Patients With ST-Elevation Myocardial Infarction: A Randomized Clinical Trial. JAMA Cardiol. May 1 2018; 3(5):391-399. doi:10.1001/jamacardio.2018.0612

21. Berwanger O, Lopes RD, Moia DDF, et al. Ticagrelor Versus Clopidogrel in Patients With STEMI Treated With Fibrinolysis: TREAT Trial. J Am Coll Cardiol. Jun 11 2019; 73(22):2819-2828. doi:10.1016/j.jacc.2019.03.011

22. Kheiri B, Osman M, Abdalla A, et al. Ticagrelor versus clopidogrel after fibrinolytic therapy in patients with ST-elevation myocardial infarction: a systematic review and meta-analysis of randomized clinical trials. J Thromb Thrombolysis. Oct 2018; 46(3):299-303. doi:10.1007/s11239-018-1706-2

23. Welsh RC, Sidhu RS, Cairns JA, et al. Outcomes Among Clopidogrel, Prasugrel, and Ticagrelor in ST-Elevation Myocardial Infarction Patients Who Underwent Primary Percutaneous Coronary Intervention From the TOTAL Trial. Can J Cardiol. Oct 2019; 35(10):1377-1385. doi:10.1016/j.cjca.2019.04.026