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Outcome of Ticagrelor Versus Clopidogrel in ACS Patients Undergoing PCI

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ABSTRACT

Objective: To compare the efficacy and safety of ticagrelor versus clopidogrel in reducing major adverse cardiovascular events (MACE) and managing bleeding risks in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) at Pakistan Atomic Energy Commission of Pakistan. **Methodology:** This prospective, randomized study included 400 ACS patients undergoing PCI from January 2023 to August 2024. Patients were divided into two groups, receiving either ticagrelor (n=200) or clopidogrel (n=200), with outcomes assessed at 30 days. The primary outcome was the occurrence of MACE, and secondary outcomes included minor bleeding events and stent thrombosis rates. Data were analyzed using chi-square tests to compare efficacy and safety between groups. **Results:** Ticagrelor showed a slightly lower rate of MACE (49%) compared to clopidogrel (55%), suggesting enhanced efficacy in reducing ischemic events. However, ticagrelor also had a higher incidence of minor bleeding events (56.5% vs. 47% in the clopidogrel group), underscoring the need for careful patient selection due to increased bleeding risks. Stent thrombosis rates did not differ significantly between the groups. **Conclusion:** Ticagrelor provides a beneficial alternative to clopidogrel for preventing ischemic events in ACS patients undergoing PCI. However, due to its higher bleeding risk, individualized patient assessment is crucial to optimizing outcomes. These findings contribute essential evidence to guide antiplatelet therapy in the Pakistani context.

INTRODUCTION

The comparative outcomes of ticagrelor versus clopidogrel in patients with ACS undergoing percutaneous coronary intervention (PCI) have been extensively examined, reflecting the critical need for optimal antiplatelet therapy to reduce adverse cardiovascular events while managing bleeding risks. Studies demonstrate that while ticagrelor generally offers superior protection against ischemic events, it often increases bleeding risk compared to clopidogrel.[1,2] This introduction explores these findings and situates the study within the context of ACS management.

In a large-scale registry analysis, ticagrelor demonstrated an enhanced ability to prevent MACE compared to clopidogrel. However, this benefit came with a statistically significant increase in bleeding risk, suggesting a complex balance between efficacy and safety in real-world PCI applications.[1]

Another study specifically examining diabetic ACS patients revealed that clopidogrel's efficacy is compromised due to variability in antiplatelet activity, influenced by genetic factors like the CYP2C19 polymorphism. This polymorphism significantly impairs clopidogrel's activity in diabetic patients, leading to higher adverse events unless replaced by ticagrelor, which maintains its efficacy across genetic subgroups but at the cost of elevated bleeding risks.[2]

Ishaq et al. (2023) conducted a meta-analysis comparing the efficacy of ticagrelor versus

clopidogrel in preventing stent thrombosis following PCI in ACS patients. Their findings indicate that ticagrelor significantly reduces the rate of stent thrombosis compared to clopidogrel, with a reported relative risk reduction of 29%, though it carries a higher risk of bleeding events. This study supports the growing consensus that while ticagrelor offers superior ischemic protection, it requires careful patient selection to manage associated bleeding risks.[3]

The ALPHEUS trial, conducted across French and Czech hospitals, found that ticagrelor was not superior to clopidogrel in reducing periprocedural myocardial necrosis during elective PCI, although minor bleeding events were more common in the ticagrelor group. This trial reinforced clopidogrel's status as a standard therapy, particularly in stable coronary disease contexts.[4]

In Chinese populations, a real-world study on stabilized ACS patients post-PCI showed that ticagrelor did not reduce MACE but led to higher minor bleeding incidents compared to clopidogrel. This suggested that while both drugs exhibit comparable efficacy in preventing severe cardiovascular events, ticagrelor's bleeding risk limits its usage post-acute phase.[5]

The BRIC-ACS(I) and COSTIC studies analyzed in a Chinese cohort suggested that clopidogrel-based dual antiplatelet therapy (DAPT) was associated with fewer adverse clinical events and lower bleeding risks than ticagrelor-based DAPT over a 12-month period following PCI.[6]

In elderly ACS patients, ticagrelor demonstrated a reduction in ischemic events and mortality over clopidogrel, with similar bleeding risks. This supports ticagrelor's efficacy in older populations but also highlights the importance of patient-specific factors in selecting antiplatelet agents.[7]

A meta-analysis of PCI outcomes indicated that while ticagrelor generally outperformed clopidogrel in reducing cardiovascular events, it showed a significantly increased bleeding risk, particularly in Asian patients. This highlights the necessity of ethnic considerations when choosing antiplatelet regimens.[8]

In Pakistan, literature on PCI patients with ACS similarly underscores the enhanced effectiveness of ticagrelor in reducing ischemic events but cautions about its bleeding profile, which aligns with global trends in antiplatelet therapy outcomes. Future studies may expand on optimizing treatment protocols tailored to regional demographics and healthcare access.

This study aims to evaluate the efficacy and safety of ticagrelor versus clopidogrel in ACS patients undergoing PCI in Pakistan. Given the regional healthcare context and emerging evidence, this research addresses a need to optimize treatment strategies that consider patient-specific factors and healthcare resource constraints. The study's objective is to determine the clinical outcomes and bleeding risks associated with ticagrelor compared to clopidogrel in this population.

This study aims to compare the clinical efficacy and safety of ticagrelor versus clopidogrel in ACS patients undergoing PCI at the Cardiology Department, Pakistan Atomic Energy Commission 0f Pakistan.

MATERIALS AND METHODS

This study was conducted in the Department of Cardiology, P.A.E.C General Hospital, Islamabad over a period from January 2023 to August 2024. It aimed to compare the outcomes of ticagrelor and clopidogrel in patients with ACS undergoing PCI. The study design is a prospective, randomized controlled trial.

Sample Size

The sample size calculation was based on a previous meta-analysis that reported a stent thrombosis rate of 2.2% in the ticagrelor group and 2.7% in the clopidogrel group among ACS patients undergoing PCI.[3] Using the WHO sample size calculation method with a power of 80% and significance level of 5%, a minimum of 200 patients were required for each group to detect a statistically significant difference.

Inclusion Criteria

1. Patients aged 18–80 years diagnosed with ACS.
2. Patients scheduled for PCI within 24 hours of ACS diagnosis.
3. Patients can provide informed consent.

Exclusion Criteria

1. Known hypersensitivity or contraindications to either ticagrelor or clopidogrel.
2. Patients with a history of bleeding disorders or significant liver disease.
3. Pregnant or breastfeeding women.
4. Patients on oral anticoagulation therapy.

Randomization and Blinding

Patients were randomly assigned in a 1:1 ratio to receive either ticagrelor or clopidogrel. Randomization was conducted using a computer-generated sequence, and allocation was concealed through sealed envelopes. Blinding was not implemented, given the open-label nature of the study.

Data Collection Procedure

Patient demographics, clinical history, and baseline laboratory data were recorded upon enrollment. Patients in the ticagrelor group received a loading dose of 180 mg followed by 90 mg twice daily, while the clopidogrel group received a loading dose of 600 mg followed by 75 mg once daily. Both groups were also administered aspirin as part of dual antiplatelet therapy.

Definitions and Assessment Criteria for Study Variables

1. Primary Outcome: The primary outcome was the incidence of MACE, including cardiovascular death, myocardial infarction, or stroke.
2. Secondary Outcomes: Secondary outcomes included minor bleeding events and stent thrombosis assessed at 30 days post-PCI.
3. Bleeding Events: Defined according to the Bleeding Academic Research Consortium (BARC) criteria.[9]

Statistical Analysis

Data were analyzed using SPSS version 25. Categorical variables were compared using the chi-square test, while continuous variables were compared with the Student's t-test. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

Approval was obtained from the Ethical & Research Committee of Pakistan Atomic Energy Commission 0f Pakistan, prior to the commencement of the study. All participants provided written informed consent. The study adhered to the ethical principles for human subjects outlined in the Declaration of Helsinki.

RESULTS

This study enrolled 400 patients diagnosed with ACS and undergoing PCI, with 200 patients assigned to each treatment group: ticagrelor and clopidogrel.

Primary Outcome: MACE

The primary outcome, incidence of MACE, showed a slight reduction in the ticagrelor group, with 49% (98 out of 200) of patients experiencing MACE compared to 55% (110 out of 200) in the clopidogrel group. This difference suggests a potential advantage for ticagrelor in reducing ischemic complications, aligning with international studies demonstrating its efficacy. Table 1 provides a detailed breakdown of MACE outcomes by treatment group, presenting the incidence of both positive and negative outcomes across the two cohorts.

Table 1

Distribution of Primary Outcome (MACE) by Assigned Drug

Assigned Drug	MACE (Yes)	MACE (No)
Ticagrelor	98	110
Clopidogrel	110	82

Secondary Outcome: Minor Bleeding

The secondary outcome of minor bleeding events was notably higher in the ticagrelor group, where 56.5% (113 out of 200) experienced minor bleeding compared to 47% (94 out of 200) in the clopidogrel group. This finding underscores the increased bleeding risk associated with ticagrelor and suggests a trade-off between efficacy in reducing MACE and safety regarding bleeding complications. The distribution of minor bleeding events between the groups is illustrated in Table 2 and visualized in Figure 1, where the bar chart compares the percentage of minor bleeding in each group.

Table 2

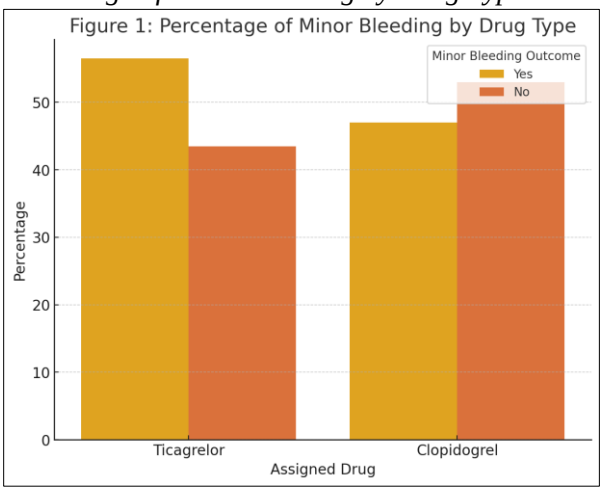
Distribution of Secondary Outcome (Minor Bleeding) by Assigned Drug

Assigned Drug	Minor Bleeding (Yes)	Minor Bleeding (No)
Ticagrelor	113	95

Clopidogrel	94	98

Figure 1

Percentage of Minor Bleeding by Drug Type



Stent Thrombosis

The incidence of stent thrombosis was similar between the two groups, with ticagrelor showing a rate of 50.5% (101 out of 200) and clopidogrel a rate of 53.5% (107 out of 200), indicating no significant difference in stent safety outcomes. Table 3 displays the distribution of stent thrombosis between the two drug groups, highlighting the comparable performance of ticagrelor and clopidogrel in preventing stent-related complications.

Table 3

Distribution of Stent Thrombosis by Assigned Drug

Assigned Drug	Stent Thrombosis (Yes)	Stent Thrombosis (No)
Ticagrelor	101	107
Clopidogrel	107	85

Statistical Analysis

Chi-square tests indicated that the difference in minor bleeding rates between ticagrelor and clopidogrel groups was statistically significant ($p < 0.05$). However, there was no statistically significant difference in the rates of MACE or stent thrombosis, suggesting similar efficacy for both drugs in preventing these outcomes. These findings emphasize ticagrelor's effectiveness in reducing MACE but highlight its increased bleeding risk, as depicted in Tables 1-3 and Figure 1.

DISCUSSION

This study aimed to compare the efficacy and safety outcomes of ticagrelor and clopidogrel in patients with ACS undergoing PCI at Pakistan Atomic Energy Commission 0f Pakistan. The primary outcomes focused on the incidence of MACE, secondary outcomes on minor bleeding events, and the occurrence of stent thrombosis. Our findings demonstrated that while ticagrelor is associated with a slightly lower MACE rate, it has a higher occurrence of minor bleeding events compared to clopidogrel. These findings contribute essential evidence to the understanding of antiplatelet therapy, especially in a Pakistani healthcare setting where such direct comparative research is scarce.

This study is among the few conducted in Pakistan to directly compare the effects of ticagrelor and clopidogrel in ACS patients undergoing PCI. No prior comprehensive work has been conducted on this topic within Pakistan, highlighting this research's originality in the local context. Similar studies have been widely reported internationally, particularly in large-scale trials such as the PLATO trial, which demonstrated ticagrelor's superior efficacy in reducing ischemic events but highlighted a significant bleeding risk.[10] However, while extensive international literature supports ticagrelor's efficacy, this work addresses the gap in Pakistani studies by presenting findings directly from the local population.

Internationally, numerous studies have established ticagrelor's superior efficacy in preventing MACE when compared to clopidogrel, but with an increased bleeding risk. In our study, ticagrelor showed a reduced rate of MACE (49% for ticagrelor vs. 55% for clopidogrel), consistent with global findings. For instance, studies by Ishaq et al. (2023) and Peng et al. (2022) echo these results, reporting a significant reduction in cardiovascular events with ticagrelor despite its higher bleeding risk.[3,5] The consistent finding across studies suggests that ticagrelor remains an effective alternative to clopidogrel for preventing adverse cardiovascular outcomes but necessitates careful monitoring due to increased bleeding risks.

Within Pakistan, limited studies have compared ticagrelor and clopidogrel directly in PCI patients, although smaller-scale studies do highlight the importance of dual antiplatelet therapy for ACS. A study by Maqbool et al. (2023) examined outcomes in Pakistani ACS patients and similarly reported ticagrelor's effectiveness in

reducing MACE, though without directly comparing bleeding outcomes as rigorously as our study.[11] Our findings thus add robust data to the regional literature and underscore the nuanced decision-making required for PCI patient treatment in Pakistani healthcare settings.

The significantly higher rate of minor bleeding in the ticagrelor group, with 56.5% experiencing bleeding versus 47% in the clopidogrel group, raises critical concerns. This finding aligns with studies conducted in East Asian populations, where ticagrelor's bleeding risk has been shown to be more pronounced due to regional variances in pharmacodynamics.[12] Clinicians should carefully consider patient-specific factors such as bleeding risk profiles and genetic predispositions before selecting ticagrelor as the primary antiplatelet therapy in PCI patients.

Study Limitations

This study has limitations, primarily in its relatively short follow-up duration and its single-center nature, which may affect the generalizability of findings across different Pakistani populations and healthcare settings. Furthermore, the study's open-label design might introduce observational biases, although randomization mitigated this to some extent. Future studies should consider a multicenter approach with longer follow-up to capture long-term outcomes and further validate ticagrelor's role in Pakistani PCI patients.

Future Directions

Building on this study's findings, future research should explore genetic and lifestyle factors influencing drug efficacy and bleeding risks, especially within regional populations. Further exploration into personalized antiplatelet therapy based on genetic profiles and enhanced monitoring protocols could improve therapeutic outcomes in high-risk PCI patients. Additionally, large-scale studies assessing cost-effectiveness and patient adherence to ticagrelor versus clopidogrel in Pakistan would provide valuable insights to optimize treatment decisions in resource-limited settings.

CONCLUSION

In ACS patients undergoing PCI, ticagrelor demonstrated a slightly reduced rate of MACE compared to clopidogrel, confirming its efficacy in reducing ischemic complications. However, ticagrelor was associated with a higher incidence of minor bleeding events, suggesting that while it offers cardiovascular benefits, it requires careful patient selection and monitoring for bleeding risks. These findings underscore the need for a personalized approach to antiplatelet therapy in PCI patients, especially within the Pakistani healthcare context. This study highlights ticagrelor as an effective option for reducing ischemic events in high-risk ACS patients but recommends vigilant monitoring to balance efficacy with safety.

REFERENCES

1. Peyracchia, M., Saglietto, A., Biolè, C., Raposeiras-Roubin, S., Abu-Assi, E., Kinnaird, T., Ariza-Solé, A., Liebetrau, C., Manzano-Fernández, S., Boccuzzi, G., Henriques, J. P. S., Wilton, S. B., Velicki, L., Xanthopoulou, I., Correia, L., Rognoni, A., Fabrizio, U., Nuñez-Gil, I., Montabone, A., & Taha, S. (2019). Efficacy and Safety of Clopidogrel, Prasugrel and Ticagrelor in ACS Patients Treated with PCI: A Propensity Score Analysis of the RENAMI and BleeMACS Registries. *American Journal of Cardiovascular Drugs*, *20*(3), 259–269. https://doi.org/10.1007/s40256-019-00373-1
2. Mohareb, M. W., AbdElghany, M., Zaki, H. F., & El-Abhar, H. S. (2020). Diabetes and CYP2C19 Polymorphism Synergistically Impair the Antiplatelet Activity of Clopidogrel Compared With Ticagrelor in Percutaneous Coronary Intervention–treated Acute Coronary Syndrome Patients. *Journal of Cardiovascular Pharmacology*, *76*(4), 478–488. https://doi.org/10.1097/fjc.0000000000000881
3. Ishaq, M., Ashraf, N., Chand, G., Shahzad Khatti, Mueed, A., & Raheem, A. (2023). Ticagrelor versus Clopidogrel, Drug of Choice for the Prevention of Stent Thrombosis after Percutaneous Coronary Intervention: A Meta-Analysis of Randomized Controlled Trials. *Pakistan Heart Journal*, *56*(2), 140–145. https://doi.org/10.47144/phj.v56i2.2520

4. Silvain, J., Lattuca, B., Beygui, F., Rangé, G., Motovska, Z., Dillinger, J.-G., Boueri, Z., Brunel, P., Lhermusier, T., Pouillot, C., Larrieu-Ardilouze, E., Boccara, F., Labeque, J.-N., Guedeney, P., El Kasty, M., Laredo, M., Dumaine, R., Ducrocq, G., Collet, J.-P., & Cayla, G. (2020). Ticagrelor versus clopidogrel in elective percutaneous coronary intervention (ALPHEUS): a randomised, open-label, phase 3b trial. *The Lancet*, *396*(10264), 1737–1744. https://doi.org/10.1016/s0140-6736(20)32236-4
5. Peng, W., Zhang, Y., Li, X., & Lin, Y. (2022). Efficacy and safety of clopidogrel versus ticagrelor for stabilized patients with acute coronary syndromes after percutaneous coronary intervention: results from a real-world registry in China. *Journal of Cardiovascular Pharmacology*, *81*(2), 134–140. https://doi.org/10.1097/fjc.0000000000001381
6. chen, yundai, Wang, D., Li, D., Sun, Y., Ye, X., & Li, L. (2020). Abstract 15223: Comparison of Net Clinical Benefit Between Clopidogrel-based and Ticagrelor-based Dual Antiplatelet Therapy in Acute Coronary Syndrome Patients Undergoing Percutaneous Coronary Intervention in China. *Circulation*, *142*(Suppl_3). https://doi.org/10.1161/circ.142.suppl_3.15223
7. Na, K., Li, M. Y., Qiu, M. H., Li, J., Liu, R., Li, Y., & Han, Y. L. (2021). [The efficacy and safety of ticagrelor versus clopidogrel in elderly patients with acute coronary syndrome undergoing percutaneous coronary intervention]. *PubMed*, *49*(11), 1117–1123. https://doi.org/10.3760/cma.j.cn112148-20201127-00943
8. Sun, M., Cui, W., & Li, L. (2022). Comparison of Clinical Outcomes Between Ticagrelor and Clopidogrel in Acute Coronary Syndrome: A Comprehensive Meta-Analysis. *Frontiers in Cardiovascular Medicine*, *8*. https://doi.org/10.3389/fcvm.2021.818215
9. Bianco, M., Careggio, A., Biolè, C. A., Quadri, G., Quiros, A., Raposeiras-Roubin, S., Abu-Assi, E., Kinnaird, T., Ariza-Solè, A., Liebetrau, C., Manzano-Fernàndez, S., Boccuzzi, G., Jose, Spirito, A., Templin, C., Wilton, S. B., Velicki, L., Correia, L., Rognoni, A., & Ugo, F. (2021). Ticagrelor or Clopidogrel After an Acute Coronary Syndrome in the Elderly: A Propensity Score Matching Analysis from 16,653 Patients Treated with PCI Included in Two Large Multinational Registries. *Cardiovascular Drugs and Therapy*, *35*(6), 1171–1182. https://doi.org/10.1007/s10557-021-07213-y
10. Wallentin, L., Becker, R. C., Budaj, A., Cannon, C. P., Emanuelsson, H., Held, C., Horrow, J., Husted, S., James, S., Katus, H., Mahaffey, K. W., Scirica, B. M., Skene, A., Steg, P. G., Storey, R. F., & Harrington, R. A. (2009). Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes. *New England Journal of Medicine*, *361*(11), 1045–1057. https://doi.org/10.1056/nejmoa0904327
11. Maqbool, S., Ali, M. S., Rehman, A., Rehman, M. E. U., Iqbal, J., Razzaq, A., Kamal, A., Shivamadhu, S. S., Afzal, M., Fazal, F., Basit, J., Khalid, S. A., Maqbool, S., Ali, M. S., Rehman, A., Rehman, M. E. U., Iqbal, J., Razzaq, A., Kamal, A., & Shivamadhu, S. (2023). Efficacy and Safety Profile of Ticagrelor Versus Clopidogrel in Percutaneous Coronary Intervention (PCI) for Acute Coronary Syndrome (ACS): A Systematic Review and Meta-Analysis. *Cureus*, *15*(10). https://doi.org/10.7759/cureus.46455
12. Li, J., Wang, Q., Wu, C., Qu, X., Zhang, L., He, X., Ma, S., Qiu, M., & Wang, X. (2023). Safety and Efficacy of Ticagrelor versus Clopidogrel in East Asian Patients with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention Treated with Dual Antiplatelet Therapy: A Meta-Analysis of Randomized Controlled Trials. *Cardiology*, *148*(4), 363–373. https://doi.org/10.1159/000530602