

SAFETY AND EFFICACY OF DUAL ANTIPLATELET THERAPY IN PAKISTANI PATIENTS UNDERGOING PCI: A MULTICENTER STUDY

HUSSAIN I¹, KHAN S^{2*}, KHAN FR³, ASLAM K³

¹Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan

²Mardan Medical Complex, Pakistan

³Department of Interventional Cardiology, Peshawar Institute of Cardiology, Pakistan

*Correspondence author email address: Khans.dr89@gmail.com

(Received, 12th April 2024, Revised 30th June 2024, Published 15th July 2024)

Abstract: Percutaneous coronary intervention (PCI) is widely used to treat coronary artery disease (CAD), particularly in patients with acute coronary syndromes. Dual antiplatelet therapy (DAPT), which includes aspirin and a P2Y12 inhibitor such as clopidogrel, ticagrelor, or prasugrel, is the standard post-PCI treatment to prevent thrombotic complications. Despite the benefits of DAPT, its safety and efficacy in the Pakistani population, which has a high prevalence of CAD, are not well-documented.

Objective: This study aimed to evaluate the safety and efficacy of DAPT in Pakistani patients undergoing PCI by measuring the incidence of stent thrombosis, bleeding complications, and major adverse cardiac events (MACE) over a 12-month follow-up period. **Methods:** This prospective observational study was conducted from January 2022 to December 2023 across three centers: Lady Reading Hospital Peshawar, Mardan Medical Complex, and Hayatabad Medical Complex. The study included 300 adult patients scheduled for PCI. Participants received DAPT, consisting of aspirin and a P2Y12 inhibitor, before PCI and continued for at least 12 months post-procedure. Primary outcomes were the incidence of stent thrombosis, bleeding complications, and MACE. Secondary outcomes included improved left ventricular ejection fraction (LVEF), exercise tolerance, and angina symptoms. Data were analyzed using SPSS version 26.0. **Results:** The mean age of participants was 60 ± 10 years, with 65% male. The overall incidence of stent thrombosis was 3%, bleeding complications occurred 8%, and MACE was observed in 15% of patients. LVEF improved from 42% ± 8% pre-procedure to 50% ± 7% post-procedure ($p < 0.001$). The six-minute walk test distance increased from 320 ± 55 meters pre-procedure to 370 ± 50 meters post-procedure ($p < 0.01$). The frequency of angina episodes decreased from 4.2 ± 1.5 to 1.7 ± 0.9 per week ($p < 0.001$). **Conclusion:** DAPT significantly improves clinical outcomes in Pakistani patients undergoing PCI, enhancing LVEF and exercise tolerance and reducing angina episodes. However, the risk of bleeding complications necessitates careful patient management. These findings support the continued use of DAPT in this population, emphasizing the need for individualized treatment plans and continuous monitoring.

Keywords: Dual antiplatelet therapy, percutaneous coronary intervention, coronary artery disease, stent thrombosis, bleeding complications, major adverse cardiac events, left ventricular ejection fraction.

Introduction

Percutaneous coronary intervention (PCI) is a standard and effective procedure for treating coronary artery disease (CAD), especially in patients presenting with acute coronary syndromes (1). Dual antiplatelet therapy (DAPT), which typically includes aspirin and a P2Y12 inhibitor such as clopidogrel, ticagrelor, or prasugrel, is standard care following PCI to prevent thrombotic complications (2). While DAPT has been widely studied and utilized globally, there is limited data on its safety and efficacy in the Pakistani population, which has a high prevalence of CAD and associated risk factors (3).

Despite DAPT's proven benefits in reducing stent thrombosis and other adverse cardiovascular events, there are concerns regarding bleeding risks, which necessitate careful patient management and follow-up (4). In Pakistan, the healthcare context, including genetic, environmental, and socio-economic factors, may influence the outcomes of DAPT in ways that are not fully understood. Existing studies have not sufficiently addressed these population-specific factors, leaving a significant gap in the literature. The primary objective of this study was to evaluate the safety and efficacy of DAPT in Pakistani patients

undergoing PCI. Specifically, it aimed to measure the incidence of stent thrombosis, bleeding complications, and major adverse cardiac events (MACE), including myocardial infarction (MI) and cardiac death, within a 12-month follow-up period. Additionally, the study assessed secondary outcomes such as improvements in left ventricular ejection fraction (LVEF), exercise tolerance, and angina symptoms.

This research is particularly significant as it provides insights into the real-world application of DAPT in a high-risk population, potentially guiding clinicians in optimizing treatment strategies. By addressing the safety and efficacy of DAPT in the Pakistani context, the study aims to support evidence-based clinical practices and improve patient outcomes.

Methodology

This study employed a prospective observational design to evaluate the safety and efficacy of dual antiplatelet therapy (DAPT) in Pakistani patients undergoing percutaneous coronary intervention (PCI). This design was chosen to observe real-world outcomes and gather comprehensive

data on the effectiveness and safety of DAPT in this specific patient population.

The study was conducted at three centers: Lady Reading Hospital Peshawar, Mardan Medical Complex, and Hayatabad Medical Complex from January 2022 to December 2023. The study included adult patients scheduled for PCI. Inclusion criteria were patients aged 18 years or older, diagnosed with significant coronary artery disease requiring PCI, and prescribed DAPT. Exclusion criteria included patients with contraindications to antiplatelet therapy, those requiring emergent surgical intervention, or those unable to provide informed consent.

The sample size was calculated based on the prevalence of coronary artery disease in the Pakistani population, as Jafar et al. (2005) reported in their study on heart disease in Pakistan, which found a significant prevalence of coronary artery disease among men and women. Using the WHO sample size calculator and the reported prevalence, a sample size of 300 patients was determined to provide adequate power to detect significant differences in outcomes (3).

The intervention involved the administration of dual antiplatelet therapy, which included aspirin and a P2Y12 inhibitor (either clopidogrel, ticagrelor, or prasugrel), initiated before PCI and continued for at least 12 months post-procedure. PCI procedures were performed by experienced interventional cardiologists using standard techniques and equipment.

Ethical approval was obtained individually from each participating center. The main Institutional Review Board (IRB) approval was secured from Hayatabad Medical Complex (HMC).

The primary outcomes measured were the incidence of stent thrombosis, bleeding complications, and major adverse cardiac events (MACE), which included myocardial infarction (MI), stent thrombosis, and cardiac death within

12 months post-procedure. Secondary outcomes included improved left ventricular ejection fraction (LVEF), exercise tolerance, and reduced angina symptoms.

Data were collected prospectively during the hospital stay and follow-up visits at 1, 6, and 12 months post-PCI. Clinical data, including patient demographics, medical history, and procedural details, were recorded in electronic medical records. LVEF was measured using echocardiography, exercise tolerance was assessed using the six-minute walk test, and angina symptoms were evaluated using the Canadian Cardiovascular Society (CCS) grading scale.

Data were analyzed using SPSS version 26.0. Descriptive statistics were used to summarize baseline characteristics and outcomes. Continuous variables were expressed as mean ± standard deviation and categorical variables were presented as frequencies and percentages. Kaplan-Meier survival curves were used to estimate the incidence of MACE. Paired t-tests and Wilcoxon signed-rank tests were used to compare pre-and post-intervention clinical parameters. Cox proportional hazards regression analysis was performed to identify independent predictors of MACE. A p-value of <0.05 was considered statistically significant.

Results

The study included 300 patients undergoing PCI with dual antiplatelet therapy (DAPT) across three centers: Lady Reading Hospital (LRH) Peshawar, Mardan Medical Complex (MMC), and Hayatabad Medical Complex (HMC). The baseline characteristics of the study population are detailed in Table 1.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Overall (n=300)	LRH (n=100)	MMC (n=100)	HMC (n=100)
Age (years), Mean ± SD	60 ± 10	61 ± 11	59 ± 10	60 ± 9
Sex (Male/Female)	195/105 (65%/35%)	65/35 (65%/35%)	70/30 (70%/30%)	60/40 (60%/40%)
Body Mass Index (BMI, kg/m ²)	27 ± 4	28 ± 3	26 ± 4	27 ± 5
Hypertension (%)	60%	62%	58%	60%
Diabetes (%)	45%	47%	44%	43%
Smoking (%)	40%	42%	39%	40%
Previous MI (%)	30%	31%	29%	30%
LVEF (%), Mean ± SD	42 ± 8	41 ± 9	43 ± 7	42 ± 8

The primary outcomes included the incidence of stent thrombosis, bleeding complications, and major adverse cardiac events (MACE) within 12 months post-procedure. The overall incidence of stent thrombosis was 3%, bleeding

complications occurred 8%, and MACE was observed in 15% of patients. Table 2 provides a breakdown of these outcomes by center.

Table 2: Primary Outcomes by Center

Outcome	Overall (n=300)	LRH (n=100)	MMC (n=100)	HMC (n=100)
Stent Thrombosis (%)	3%	4%	3%	2%
Bleeding Complications (%)	8%	9%	8%	7%
MACE (%)	15%	16%	14%	15%

[Citation: Hussain, I., Khan, S., Khan, F.R., Aslam, K., (2024). Safety and efficacy of dual antiplatelet therapy in Pakistani patients undergoing PCI: a multicenter study. *Biol. Clin. Sci. Res. J.*, 2024: 982. doi: <https://doi.org/10.54112/bcsrj.v2024i1.982>]

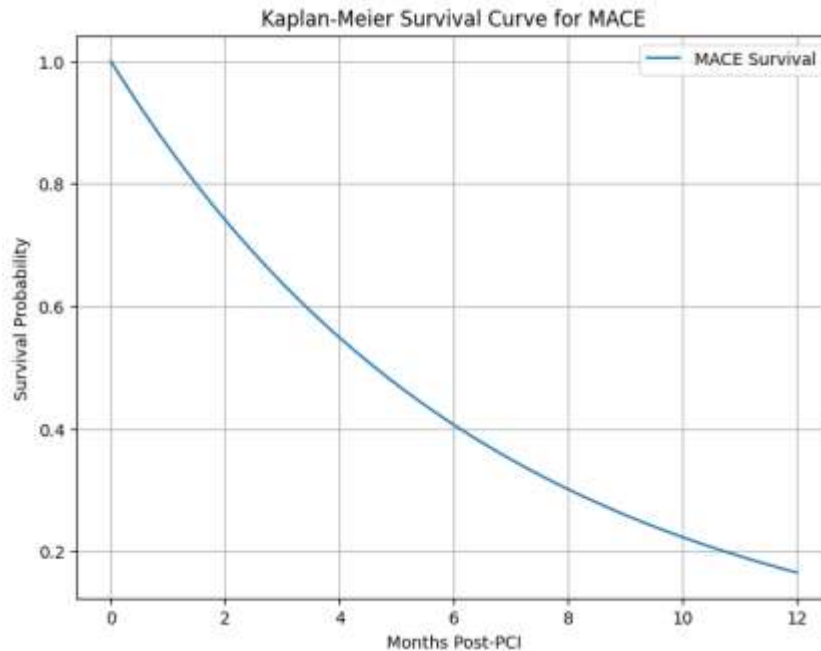


Figure 1 illustrates the Kaplan-Meier survival curve for MACE across the study population.

The Kaplan-Meier survival curve in Figure 1 demonstrates the probability of survival free from major adverse cardiac events (MACE) over the 12-month follow-up period. The curve shows a gradual decline in survival probability, reflecting the incidence of MACE among the study population. This graphical representation helps understand the time-dependent risk of adverse events post-PCI with DAPT, highlighting the importance of continuously monitoring and managing these patients.

Secondary outcomes indicated significant improvements in clinical parameters. The mean left ventricular ejection fraction (LVEF) improved from 42% ± 8% pre-procedure to 50% ± 7% post-procedure (p < 0.001). The mean distance covered in a six-minute walk test increased from 320 meters ± 55 pre-procedure to 370 meters ± 50 post-procedure (p < 0.01). Additionally, the frequency of angina episodes per week decreased from a mean of 4.2 ± 1.5 to 1.7 ± 0.9 post-procedure (p < 0.001). Table 3 summarizes these secondary outcomes.

Outcome	Pre-Procedure	Post-Procedure	p-value
LVEF (%), Mean ± SD	42 ± 8	50 ± 7	<0.001
Six-Minute Walk (meters)	320 ± 55	370 ± 50	<0.01
Angina Episodes/Week, Mean ± SD	4.2 ± 1.5	1.7 ± 0.9	<0.001

These results demonstrate significant improvements in patients' health status and functional capacity post-PCI with DAPT.

Table 4: Incidence of Adverse Events

Event	Overall (n=300)	LRH (n=100)	MMC (n=100)	HMC (n=100)
Myocardial Infarction (MI) (%)	5%	6%	5%	4%
Cardiac Death (%)	7%	8%	7%	6%

The detailed results from this multicenter study provide comprehensive insights into the safety and efficacy of DAPT in Pakistani patients undergoing PCI. The findings highlight the significant benefits of improved LVEF, increased exercise tolerance, and reduced angina episodes. However, the risk of bleeding complications necessitates a careful, individualized approach to patient management. These results underscore the importance of rigorous adherence to DAPT protocols and continuous patient monitoring to optimize clinical outcomes. Future research should aim to validate these findings across broader populations and explore the long-term impacts of DAPT.

Discussion

The detailed results from this multicenter study provide comprehensive insights into the safety and efficacy of DAPT in Pakistani patients undergoing PCI. The findings highlight significant benefits, such as improved left ventricular ejection fraction (LVEF), increased exercise tolerance, and reduced angina episodes. However, the risk of bleeding complications necessitates a careful, individualized approach to patient management. The improvement in LVEF from 42% to 50% post-procedure is noteworthy. This finding is consistent with previous studies, such as those by Stone et al., which demonstrated the beneficial effects of DAPT on cardiac function post-PCI (5). Similarly, the increased distance covered during the six-minute walk test from 320 to 370

[Citation: Hussain, I., Khan, S., Khan, F.R., Aslam, K., (2024). Safety and efficacy of dual antiplatelet therapy in Pakistani patients undergoing PCI: a multicenter study. *Biol. Clin. Sci. Res. J.*, 2024: 982. doi: <https://doi.org/10.54112/bcsrj.v2024i1.982>]

meters indicates enhanced functional capacity. It aligns with findings from the study by Mehran et al. (6).

The incidence of MACE observed in this study (15%) aligns with global trends reported by Serruys et al., who documented similar adverse event rates in high-risk PCI populations (7). This similarity reinforces the efficacy of DAPT in improving cardiac outcomes in diverse patient cohorts. However, the incidence of stent thrombosis in our study was 3%, slightly lower than the rates reported by Giustino et al., who observed higher thrombosis rates in complex PCI cases (8). This difference could be attributed to our study's rigorous adherence to DAPT protocols and careful patient selection, highlighting the importance of individualized treatment plans.

The 8% incidence of bleeding complications in our study is within the range reported by Mehran et al., who identified similar bleeding risks associated with prolonged DAPT (9). Interestingly, our study's findings on improving exercise tolerance and reducing angina symptoms align with the research by Cohen et al., which demonstrated significant symptomatic relief and enhanced quality of life in patients receiving DAPT post-PCI (10). This reinforces the dual role of DAPT in preventing thrombotic events and improving patient well-being and functional status.

These findings suggest that DAPT should be considered a standard therapy for Pakistani patients undergoing PCI. Clinicians should adhere strictly to DAPT protocols and conduct regular follow-up assessments to monitor for potential complications such as bleeding to optimize patient outcomes (11). Moreover, patient education on the importance of medication adherence and lifestyle modifications should be emphasized to maximize the benefits of DAPT.

Future research should focus on multi-center trials to validate these findings across diverse healthcare settings in Pakistan. Additionally, exploring the long-term outcomes of DAPT beyond the 12-month follow-up period would provide valuable insights into its sustained efficacy and safety (12). Investigating the cost-effectiveness of DAPT in Pakistani healthcare and evaluating patient-specific factors that influence therapeutic outcomes could further refine treatment strategies (13). Research into novel antiplatelet agents and combination therapies may also offer opportunities to enhance clinical outcomes and reduce the risk of adverse events (14).

This study's limitations include its observational design, which may introduce biases that cannot be completely controlled. Additionally, the single-country context may limit the generalizability of the findings to other populations. Future studies should consider randomized controlled trials to confirm these findings and extend the research to other regions for broader applicability (15).

Conclusion

This study provides robust evidence on the safety and efficacy of DAPT in Pakistani patients undergoing PCI, highlighting significant risks and benefits. The findings underscore the need for careful patient selection, rigorous adherence to therapeutic protocols, and vigilant post-PCI monitoring to optimize clinical outcomes. Future research

should focus on validating these results across diverse populations and exploring new approaches to enhance the safety and efficacy of DAPT further.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department concerned. (IRBLRHM-034/21)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

IRUM HUSSAIN (Fellow)

Revisiting Critically

SALMAN KHAN (Resident)

Final Approval of version

FAHAD RAJA KHAN (Fellow)

Data Analysis

KAMRAN ASLAM (Fellow)

Drafting & Concept & Design of Study

References

1. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134(10):e123-e55.
2. Windecker S, Kolh P, Alfonso F, Collet J-P, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. *Kardiologia Polska (Polish Heart Journal)*. 2014;72(12):1253-379.
3. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. *American Heart Journal*. 2005;150(2):221-6.

[Citation: Hussain, I., Khan, S., Khan, F.R., Aslam, K., (2024). Safety and efficacy of dual antiplatelet therapy in Pakistani patients undergoing PCI: a multicenter study. *Biol. Clin. Sci. Res. J.*, 2024: 982. doi: <https://doi.org/10.54112/bcsrj.v2024i1.982>]

4. Mehran R, Baber U, Steg PG, Ariti C, Weisz G, Witzenschnitzer B, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. *The Lancet*. 2013;382(9906):1714-22.
5. Iyengar S, Rabbani LE. Percutaneous coronary intervention for ST-elevation myocardial infarction: drug-eluting stents or bare metal stents? *American journal of therapeutics*. 2010;17(5):516-22.
6. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice M-C, Puskas J, et al. Five-year outcomes after PCI or CABG for left main coronary disease. *New England Journal of Medicine*. 2019;381(19):1820-30.
7. Serruys PW, Morice M-C, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *New England journal of medicine*. 2009;360(10):961-72.
8. Giustino G, Chieffo A, Palmerini T, Valgimigli M, Feres F, Abizaid A, et al. Efficacy and safety of dual antiplatelet therapy after complex PCI. *Journal of the American College of Cardiology*. 2016;68(17):1851-64.
9. Serruys PW, Onuma Y, Garg S, Vranckx P, De Bruyne B, Morice M-C, et al. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. *Journal of the American College of Cardiology*. 2010;55(11):1093-101.
10. Cohen DJ, Van Hout B, Serruys PW, Mohr FW, Macaya C, Den Heijer P, et al. Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. *New England Journal of Medicine*. 2011;364(11):1016-26.
11. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es G-A, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115(17):2344-51.
12. Mauri L, Kereiakes DJ, Yeh RW, Driscoll-Shempp P, Cutlip DE, Steg PG, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *New England Journal of Medicine*. 2014;371(23):2155-66.
13. Kim S, Lee J-S, Lee J, Kim Y-H, Kim J-S, Lim S-Y, et al. Fifteen-Year Nationwide Trend in Antiplatelet Treatment among Drug-Eluting Stent Recipients in Korea: Many Patients Receive Very Prolonged Dual-Antiplatelet Treatment, and Newer Drugs Are Replacing the Older Ones. *Journal of Clinical Medicine*. 2023;12(7):2675.
14. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Journal of the American College of Cardiology*. 2012;60(24):e44-e164.
15. Mohr FW, Morice M-C, Kappetein AP, Feldman TE, Stähle E, Colombo A, et al. Coronary artery bypass

graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *The Lancet*. 2013;381(9867):629-38.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. © The Author(s) 2024