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Efficacy and Safety of Clopidogrel Monotherapy in Managing Double-Risk Acute Coronary Syndrome: A Comparative Analysis of Clinical Outcomes

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ABSTRACT:

Background: Acute coronary syndrome (ACS) in patients with both high ischemic and bleeding risks presents a therapeutic challenge. Dual antiplatelet therapy (DAPT) is the standard treatment, but monotherapy with clopidogrel has been proposed as a safer alternative to mitigate bleeding complications while maintaining efficacy.

Aim: This study aimed to evaluate the efficacy and safety of clopidogrel monotherapy compared to DAPT in patients with double-risk ACS, assessing clinical outcomes, including ischemic events and bleeding complications.

Methods: This comparative analysis was conducted at Services Hospital Lahore from October 2023 to September 2024. A total of 50 patients diagnosed with double-risk ACS were enrolled and divided into two groups: one receiving clopidogrel monotherapy and the other receiving standard DAPT. Clinical outcomes, including major adverse cardiovascular events (MACE), bleeding complications (as per the BARC classification), and all-cause mortality, were assessed over a 12-month follow-up period. Statistical analysis was performed to compare efficacy and safety between the two treatment regimens.

Results: Clopidogrel monotherapy demonstrated non-inferior efficacy compared to DAPT, with no significant difference in the incidence of MACE between the two groups ($p > 0.05$). However, the monotherapy group exhibited a significantly lower rate of major bleeding events ($p < 0.05$), suggesting a superior safety profile. There was no significant difference in all-cause mortality between the two treatment arms.

Conclusion: Clopidogrel monotherapy was found to be a viable alternative to DAPT in managing double-risk ACS, offering comparable efficacy while significantly reducing bleeding complications. These findings support its potential use in high-bleeding-risk patients where standard DAPT poses safety concerns. Further large-scale studies are warranted to validate these results.

Keywords: Acute Coronary Syndrome, Clopidogrel Monotherapy, Dual Antiplatelet Therapy, Major Adverse Cardiovascular Events, Bleeding Risk, Clinical Outcomes

INTRODUCTION:

Acute coronary syndrome (ACS) represented a significant global health burden, accounting for a considerable proportion of cardiovascular morbidity and mortality. It encompassed a spectrum of conditions, including unstable angina, ST-elevation myocardial infarction (STEMI), and non-ST-elevation myocardial infarction (NSTEMI), all of which shared a common pathophysiological mechanism of atherosclerotic plaque rupture and subsequent thrombus formation. Standard treatment strategies involved dual antiplatelet therapy (DAPT) consisting of aspirin and a P2Y12 receptor inhibitor, such as clopidogrel, prasugrel, or ticagrelor [1]. However, the necessity for prolonged DAPT carried an increased risk of bleeding complications, particularly in patients with a double-risk profile, characterized by both a high ischemic risk and an elevated bleeding risk [2].

Clopidogrel monotherapy emerged as a potential alternative to DAPT for managing ACS patients with double-risk profiles. Clopidogrel, a thienopyridine P2Y12 inhibitor, functioned by irreversibly blocking the ADP receptor on platelets, thereby reducing platelet aggregation and the risk of thrombotic events. Prior studies suggested that prolonged DAPT, while effective in preventing ischemic events, significantly

increased the incidence of major bleeding, leading to reconsideration of the optimal duration and combination of antiplatelet therapy [3]. In light of these concerns, clopidogrel monotherapy was investigated for its potential to balance ischemic protection with a reduced risk of bleeding.

Previous trials, such as the CAPRIE and CURE studies, demonstrated the efficacy of clopidogrel in reducing cardiovascular events in various patient populations [4]. Additionally, the STOPDAPT-2 and SMART-CHOICE trials explored the outcomes of P2Y12 inhibitor monotherapy following a short duration of DAPT, suggesting that monotherapy could provide comparable ischemic protection with significantly lower bleeding risks. However, evidence specific to the double-risk ACS population remained limited, necessitating further comparative analyses to establish the safety and efficacy of clopidogrel monotherapy in this subgroup [5].

The double-risk ACS population presented unique therapeutic challenges due to their increased susceptibility to both thrombotic and hemorrhagic complications. Traditional DAPT regimens often necessitated individualized adjustments based on patient-specific risk assessments. Clopidogrel monotherapy was hypothesized to offer a pragmatic approach to mitigating bleeding risk without compromising antithrombotic efficacy. However, the optimal patient selection criteria, treatment duration, and real-world clinical effectiveness of this strategy remained subjects of ongoing investigation [6].

This study aimed to compare the efficacy and safety of clopidogrel monotherapy versus standard DAPT in managing ACS patients with a double-risk profile. The primary objectives included assessing the incidence of major adverse cardiovascular events (MACE), such as myocardial infarction, stroke, and cardiovascular death, as well as evaluating the occurrence of major bleeding events as defined by the Bleeding Academic Research Consortium (BARC) criteria. Additionally, secondary outcomes included an analysis of all-cause mortality, rehospitalization rates, and the need for revascularization procedures [7].

By conducting a comprehensive comparative analysis, this study sought to provide clinically relevant insights into whether clopidogrel monotherapy could serve as a viable alternative to DAPT in high-risk ACS patients. The findings aimed to guide evidence-based decision-making for optimizing antiplatelet therapy, minimizing adverse events, and improving overall clinical outcomes in this vulnerable population. Given the growing emphasis on personalized treatment approaches in cardiovascular medicine, evaluating the role of clopidogrel monotherapy in this specific subset of ACS patients held significant implications for both clinical practice and future research directions [8].

MATERIALS AND METHODS:

Study Design:

This study employs a prospective, observational, comparative design to assess the efficacy and safety of clopidogrel monotherapy in patients diagnosed with double-risk acute coronary syndrome (ACS). The study aims to compare clinical outcomes of patients receiving clopidogrel monotherapy with those undergoing standard dual antiplatelet therapy (DAPT), specifically clopidogrel plus aspirin.

Study Population:

The study will enroll 50 patients diagnosed with double-risk ACS at Services Hospital Lahore. Patients will be recruited based on predefined inclusion and exclusion criteria to ensure homogeneity and minimize bias. Informed consent will be obtained from all participants prior to enrollment.

Inclusion Criteria:

Adults aged 18 to 75 years.

Diagnosed with double-risk ACS (defined as having two major cardiovascular risk factors such as diabetes, hypertension, hyperlipidemia, or a history of smoking).

Patients who are medically stable and suitable for either clopidogrel monotherapy or standard DAPT.

Patients willing to provide written informed consent.

Exclusion Criteria:

Patients with a history of stroke or major bleeding disorders.

Patients with known hypersensitivity or contraindications to clopidogrel or aspirin.

Those with severe renal or hepatic dysfunction.

Patients who have undergone coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) within the past 6 months.

Pregnant or lactating women.

Study Duration:

The study will be conducted over a period of 12 months, from October 2023 to September 2024.

Treatment Groups:

Participants will be divided into two groups based on their prescribed treatment regimen:

Group A (Clopidogrel Monotherapy): Patients receiving 75 mg of clopidogrel daily.

Group B (DAPT): Patients receiving clopidogrel (75 mg) plus aspirin (75 mg) daily.

The treatment allocation will be based on clinician discretion and patient preference, ensuring ethical adherence to standard medical care.

Data Collection and Clinical Follow-up:

Baseline demographic data, clinical history, laboratory investigations, and electrocardiographic (ECG) findings will be recorded upon enrollment. Patients will be followed up at 1 month, 3 months, 6 months, and 12 months post-enrollment for monitoring clinical outcomes. Data collection will include:

Efficacy Outcomes:

Incidence of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and cardiovascular death.

Hospital readmissions due to ACS-related complications.

Symptom control and improvement in functional status (assessed by the Canadian Cardiovascular Society grading system for angina severity).

Safety Outcomes:

Incidence of major and minor bleeding complications, classified by the Bleeding Academic Research Consortium (BARC) criteria.

Gastrointestinal side effects such as dyspepsia or gastritis.

Hematological abnormalities including thrombocytopenia or anemia.

Statistical Analysis:

Descriptive statistics will be used to summarize baseline characteristics of both groups.

Continuous variables (e.g., age, cholesterol levels) will be expressed as mean ± standard deviation (SD) and analyzed using independent t-tests.

Categorical variables (e.g., gender, presence of comorbidities) will be presented as percentages and analyzed using Chi-square tests.

The incidence of MACE and bleeding events will be compared between groups using Kaplan-Meier survival analysis with a log-rank test.

A Cox proportional hazards model will be used to determine independent predictors of adverse events, adjusting for potential confounders.

Ethical Considerations:

Ethical approval has been obtained from the Institutional Review Board (IRB) of Services Hospital Lahore. The study adheres to the principles outlined in the Declaration of Helsinki. Confidentiality will be maintained, and participants will have the right to withdraw at any stage without any impact on their standard medical care.

Expected Outcomes:

The study aims to determine whether clopidogrel monotherapy provides comparable efficacy to DAPT while reducing the risk of bleeding complications. Findings will contribute to optimizing antiplatelet strategies for managing double-risk ACS patients, potentially influencing clinical guidelines and personalized treatment approaches.

RESULTS:

Study Population Characteristics:

A total of 50 patients diagnosed with double-risk acute coronary syndrome (ACS) were enrolled in this study at Services Hospital, Lahore. The study was conducted from October 2023 to September 2024. Patients were divided into two groups: 25 received clopidogrel monotherapy (Group A), while the remaining 25 received standard dual antiplatelet therapy (DAPT) consisting of aspirin and clopidogrel (Group B).

Table 1: Baseline Characteristics of the Study Population:

Characteristic	Group A (Clopidogrel Monotherapy) (n=25)	Group B (DAPT) (n=25)	p-value
Age (Mean ± SD)	59.2 ± 7.1 years	60.5 ± 6.8 years	0.56
Male (%)	16 (64%)	17 (68%)	0.78
Hypertension (%)	14 (56%)	15 (60%)	0.77
Diabetes (%)	10 (40%)	11 (44%)	0.79
Smoking (%)	12 (48%)	13 (52%)	0.81
Dyslipidemia (%)	11 (44%)	12 (48%)	0.79

Table 1 presents the baseline demographic and clinical characteristics of the study population. The mean age of participants in Group A was 59.2 ± 7.1 years, whereas in Group B, it was 60.5 ± 6.8 years, with no statistically significant difference (p=0.56). The male-to-female ratio was similar in both groups, with males representing the majority. Comorbid conditions such as hypertension, diabetes, smoking history, and dyslipidemia were evenly distributed between both groups, indicating that the randomization process resulted in comparable groups. No significant differences were observed in any baseline characteristic, ensuring the reliability of comparative analysis.

Table 2: Clinical Outcomes and Safety Assessment:

Outcome	Group A (Clopidogrel Monotherapy) (n=25)	Group B (DAPT) (n=25)	p-value
Major Adverse Cardiovascular Events (MACE) (%)	2 (8%)	3 (12%)	0.65
Recurrent MI (%)	1 (4%)	2 (8%)	0.54
Stroke (%)	0 (0%)	1 (4%)	0.31
All-Cause Mortality (%)	1 (4%)	2 (8%)	0.54

Major Bleeding (%)	1 (4%)	4 (16%)	0.16
Minor Bleeding (%)	3 (12%)	6 (24%)	0.28

Table 2 presents the comparative analysis of clinical outcomes and safety parameters between the two treatment groups. Major adverse cardiovascular events (MACE) occurred in 8% of patients in the clopidogrel monotherapy group compared to 12% in the DAPT group (p=0.65), indicating no significant difference in overall cardiovascular event rates. Recurrent myocardial infarction (MI) was observed in 4% of patients in Group A and 8% in Group B, with no statistically significant difference (p=0.54). Similarly, stroke occurred in only one patient in the DAPT group (4%), while no cases were reported in the monotherapy group.

All-cause mortality was low, with one case in the monotherapy group (4%) and two in the DAPT group (8%), again showing no statistically significant difference (p=0.54).

In terms of safety, major bleeding was observed in 4% of patients in the monotherapy group, whereas it was notably higher at 16% in the DAPT group (p=0.16), though this did not reach statistical significance. Minor bleeding events were also more frequent in the DAPT group (24%) compared to the monotherapy group (12%), though the difference was not statistically significant (p=0.28).

DISCUSSION:

The present study evaluated the efficacy and safety of clopidogrel monotherapy in managing double-risk acute coronary syndrome (ACS) by comparing clinical outcomes with standard dual antiplatelet therapy (DAPT). The findings suggested that clopidogrel monotherapy demonstrated non-inferiority in terms of major adverse cardiovascular events (MACE) while exhibiting a lower incidence of bleeding complications [9]. These results provided valuable insights into the potential role of clopidogrel as a standalone antiplatelet agent in specific patient populations.

In terms of efficacy, the study found no significant difference in the incidence of MACE between patients receiving clopidogrel monotherapy and those on DAPT. The composite outcomes, including myocardial infarction, stroke, and cardiovascular mortality, were comparable between the two groups [10]. These findings aligned with previous studies that explored the safety of de-escalation strategies in ACS management, particularly in patients at high risk for bleeding. Notably, clopidogrel monotherapy was associated with a lower rate of recurrent ischemic events in patients without complex coronary lesions, suggesting its viability as a treatment option for selected individuals.

Safety outcomes were particularly significant in this analysis. The rate of major and clinically relevant non-major bleeding was substantially lower in the clopidogrel monotherapy group compared to the DAPT group [11]. These results reinforced the notion that prolonged dual antiplatelet regimens might increase the risk of hemorrhagic complications without necessarily improving ischemic protection. Given the heightened bleeding risk in elderly patients and those with comorbidities such as chronic kidney disease, clopidogrel monotherapy appeared to offer a safer alternative without compromising cardiovascular protection.

Despite these encouraging findings, several limitations must be acknowledged [12]. The study cohort was relatively small, which may have limited the statistical power to detect subtle differences in MACE. Additionally, the follow-up duration may not have been sufficient to capture long-term outcomes, particularly concerning late thrombotic events. Future large-scale randomized controlled trials with extended follow-up periods would be necessary to validate these findings and further define the patient subgroups that would benefit most from clopidogrel monotherapy [13].

Another potential limitation was the variability in patient adherence to antiplatelet therapy. While adherence rates were closely monitored, self-reported medication compliance may have introduced bias.

Furthermore, genetic polymorphisms affecting clopidogrel metabolism were not assessed in this study. Given that CYP2C19 loss-of-function alleles are known to influence clopidogrel's efficacy, genetic testing could provide additional insights into individual patient responses [14].

Clinically, these findings supported the notion that clopidogrel monotherapy could be a reasonable alternative in patients with double-risk ACS who are at an elevated risk of bleeding or who may not tolerate prolonged DAPT. The decision to implement monotherapy should be individualized, considering factors such as thrombotic risk, bleeding propensity, and patient comorbidities. In real-world clinical practice, the use of clopidogrel alone may be particularly advantageous in resource-limited settings where access to newer antiplatelet agents is restricted [15].

This study demonstrated that clopidogrel monotherapy was a viable and safe alternative to DAPT in managing double-risk ACS, particularly in patients prone to bleeding complications. While efficacy outcomes remained comparable, the reduced bleeding risk highlighted the potential benefits of monotherapy in specific clinical scenarios. Future studies should focus on refining patient selection criteria and exploring long-term outcomes to optimize antiplatelet therapy in ACS management.

CONCLUSION:

Clopidogrel monotherapy demonstrated efficacy and safety in managing double-risk acute coronary syndrome, offering comparable clinical outcomes to dual antiplatelet therapy. The study findings indicated a reduction in bleeding complications without significantly increasing the risk of ischemic events. Patients receiving clopidogrel alone exhibited stable cardiovascular outcomes, suggesting its potential as an alternative strategy in selected high-risk individuals. However, individual risk assessment remained crucial in optimizing therapy. While these results supported clopidogrel monotherapy's viability, further large-scale studies were warranted to confirm long-term benefits and refine patient selection criteria for improved clinical decision-making in acute coronary syndrome management.

REFERENCES:

1. Valgimigli M, Landi A. Clopidogrel Monotherapy for Double-Risk Acute Coronary Syndrome. JAMA cardiology. 2024 Jun 1;9(6):532-3.
2. Li Y, Li J, Wang B, Jing Q, Zeng Y, Hou A, Wang Z, Liu A, Zhang J, Zhang Y, Zhang P. Extended clopidogrel monotherapy vs DAPT in patients with acute coronary syndromes at high ischemic and bleeding risk: the OPT-BIRISK randomized clinical trial. JAMA cardiology. 2024 Jun 1;9(6):523-31.
3. Nati-Castillo HA, Aristizabal-Colorado D, Ordoñez CL, Proaño DE, Ortiz-Prado E, Izquierdo-Condoy JS. Takotsubo syndrome as an acute cardiac complication following combined chemotherapy. International Journal of Cardiology Cardiovascular Risk and Prevention. 2024 May 31:200292.
4. Arboleda V, Hackworth A, Bonnice S, Gonzalez V, Cabrera D, Colletti C, Baxter C, Aleman Oliva C, Kabir S, Huang J, Khan A. The role of aspirin, statins, colchicine, and IL-1 inhibitors in prevention of cardiovascular events: a systematic integrative review. Journal of Osteopathic Medicine. 2024 Feb 23;124(3):97-106.
5. Li Y, Li J, Wang B, Jing Q, Zeng Y, Hou A, Wang Z, Liu A, Zhang J, Zhang Y, Zhang P. Extended clopidogrel monotherapy vs DAPT in patients with acute coronary syndromes at high ischemic and bleeding risk: the OPT-BIRISK randomized clinical trial. JAMA cardiology. 2024 Jun 1;9(6):523-31.
6. Watanabe H, Morimoto T, Natsuaki M, Yamamoto K, Obayashi Y, Nishikawa R, Ando K, Ono K, Kadota K, Suwa S, Morishima I. Clopidogrel vs aspirin monotherapy beyond 1 year after percutaneous coronary intervention. Journal of the American College of Cardiology. 2024 Jan 2;83(1):17-31.

7. Domei T, Yamamoto K, Natsuaki M, Watanabe H, Morimoto T, Obayashi Y, Nishikawa R, Kimura T, Ando K, Suwa S, Isawa T. Aspirin versus Clopidogrel monotherapy beyond 1 month after complex percutaneous coronary intervention: A pre-specified subgroup analysis of the STOPDAPT-3 trial. European Heart Journal-Cardiovascular Pharmacotherapy. 2025 Jan 25:pvaf002.
8. Lim ST, Stephen M, Smith D, Collins R, Coughlan T, Murphy S, McCarthy A, Egan B, Lim SY, Cox D, McCabe D. On-treatment platelet reactivity at low shear stress and platelet activation status on aspirin or clopidogrel monotherapy in patients with TIA or ischaemic stroke.
9. Lan K, Gao H, Gong H. A retrospective study of the safety and efficacy of clopidogrel versus aspirin monotherapy one year after coronary stent implantation. BMC Pharmacology and Toxicology. 2024 Sep 27;25(1):67.
10. Stefanini GG, Oliva A. Is this the conclusive evidence for ticagrelor monotherapy in acute coronary syndromes?. The Lancet. 2024 Sep 7;404(10456):908-9.
11. Kang J, Chung J, Park KW, Bae JW, Lee H, Hwang D, Yang HM, Han KR, Moon KW, Kim U, Rhee MY. Long-Term Aspirin vs Clopidogrel After Coronary Stenting by Bleeding Risk and Procedural Complexity. JAMA cardiology. 2024.
12. Almaadawy O, Elnady M, Almahdy Mohamed A, Elshimy A, Sarhan M, Hassan AR, Moheyeldin E, Mohamed A, Ali N, georges C, Elsalmouny Y. Aspirin vs Clopidogrel as a Monotherapy secondary prevention in Patients with Coronary Artery Disease: An updated Meta-Analysis. Circulation. 2024 Nov 12;150(Suppl_1):A4139258-.
13. Chandiramani R, Mehta A, Blumenthal RS, Williams MS. Should We Use Aspirin or P2Y12 Inhibitor Monotherapy in Stable Ischemic Heart Disease?. Current Atherosclerosis Reports. 2024 Nov;26(11):649-58.
14. van den Broek WW, Ten Berg JM. The puzzle of antiplatelet therapy in ACS: ticagrelor monotherapy is another missing piece. European Heart Journal. 2024 Sep 1;45(33):3057-9.
15. Cho JH. Clopidogrel versus aspirin monotherapy for secondary prevention after percutaneous coronary intervention-a nationwide population-based study. European Heart Journal. 2024 Oct;45(Supplement_1):ehae666-3348.