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ORIGINAL ARTICLE

A Comparative Study of Ticagrelor and Clopidogrel in Patients Undergoing Elective Coronary Stenting

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ABSTRACT

Background: Ticagrelor and clopidogrel are widely used P2Y12 inhibitors for patients undergoing percutaneous coronary intervention. While ticagrelor offers faster and more consistent platelet inhibition, its comparative benefit over clopidogrel in elective coronary stenting remains uncertain, especially in local populations. This study evaluated the short-term ischemic and safety outcomes of ticagrelor versus clopidogrel in patients undergoing elective coronary stenting.

Methods: A prospective comparative study was conducted at Rehmatul Lil Alameen Institute of Cardiology, Lahore, from January to July 2023. Sixty adults scheduled for elective PCI with drug-eluting stent implantation were enrolled and allocated equally to ticagrelor or clopidogrel, each combined with aspirin. The primary endpoint was 30-day major adverse cardiovascular events including all-cause death, non-fatal myocardial infarction, and ischemia-driven target vessel revascularization. Secondary endpoints included stent thrombosis and safety outcomes such as BARC ≥2 bleeding, access-site complications, dyspnea, and bradyarrhythmias. Analyses were performed using intention-to-treat principles.

Results: Baseline demographic and clinical characteristics were comparable between groups. Procedural characteristics, including radial access (91.7 percentage) and procedural success (100 percentage), were similar. At 30 days, major adverse cardiovascular events were lower with ticagrelor compared to clopidogrel (3.3 percentage vs 16.7 percentage, p=0.19). Non-fatal MI (10 percentage) and stent thrombosis (6.7 percentage) occurred only among clopidogrel users. Ticagrelor had higher but non-significant rates of BARC ≥2 bleeding (13.3 percentage vs 3.3 percentage, p=0.35) and dyspnea (20 percentage vs 3.3 percentage, p=0.10). No BARC 3–5 bleeding occurred in either group. Hospital stay and DAPT adherence were similar between groups.

Conclusion: Ticagrelor demonstrated a trend toward fewer ischemic complications, including absence of stent thrombosis, without a statistically significant increase in major bleeding at 30 days. Although the study was limited by its small sample size, findings suggest that ticagrelor may offer clinically meaningful ischemic protection in elective PCI settings. Larger multicenter trials are required to clarify the optimal P2Y12 strategy in stable coronary intervention populations.

Keywords: Ticagrelor, Clopidogrel, Elective PCI, Major Adverse Cardiovascular Events, Antiplatelet Therapy

INTRODUCTION

The advent of percutaneous coronary intervention (PCI) marked a significant advancement in the management of coronary artery disease (CAD), particularly in the context of acute coronary syndrome (ACS). Antiplatelet therapy is central to the prevention of thrombotic complications following PCI, with clopidogrel being a widely used therapy. However, newer agents like ticagrelor have reshaped the landscape of antiplatelet therapy. Ticagrelor, a reversible antagonist of the P2Y12 receptor, offers faster and more effective platelet inhibition compared to clopidogrel, which has a variable therapeutic response due to factors like genetic polymorphisms influencing its metabolism through the CYP2C19 pathway [1, 2].

Several studies have demonstrated that ticagrelor leads to better clinical outcomes than clopidogrel in high-risk patients undergoing PCI. For instance, the PLATO trial provided evidence that patients receiving ticagrelor had lower rates of major adverse cardiovascular events (MACE), including myocardial infarction and cardiovascular mortality, compared to those on clopidogrel [3, 4]. Additionally, ticagrelor has shown superior efficacy in reducing recurrent ischemia and unplanned revascularization in ACS patients [5, 6]. In specific demographics, such as East Asian countries like South Korea and Japan, ticagrelor has been associated with improved outcomes in ACS patients [7, 8].

Conversely, despite its advantages, the use of ticagrelor poses challenges, especially concerning safety. Increased risks of bleeding, particularly gastrointestinal and intracranial hemorrhages, have been reported with ticagrelor compared to clopidogrel [9, 10]. Balancing these risks with the efficacy of ticagrelor over clopidogrel remains an area of ongoing investigation, as some meta-analyses have highlighted the importance of patient-specific considerations when selecting antiplatelet therapy [11, 4].

In the context of elective coronary stenting, the rationale for comparing ticagrelor with clopidogrel is significant. Some trials suggest that ticagrelor may not offer significant benefits over clopidogrel in less acute settings [12, 13], while nuanced differences in patient responses related to genetic predispositions and comorbidities may justify a personalized approach to therapy. In Pakistan, where CAD prevalence is rising, understanding these differences is crucial for optimizing patient care. Factors such as genetic predispositions, lifestyle, and comorbidities prevalent in the Pakistani population can influence antiplatelet response and safety profiles, necessitating local studies to guide clinical practice in this high-risk cohort [14, 15].

While both ticagrelor and clopidogrel are essential in preventing thrombotic events in patients undergoing PCI, the choice of therapy should be guided by individual risk profiles, potential side effects, and broader population health considerations, particularly in regions like Pakistan where CAD incidence is increasing.

METHODS

We conducted a prospective, parallel-group comparative study at the Rehmatul Lil Alameen Institute of Cardiology, Lahore, from January to July 2023. Consecutive adult patients (aged 18–80 years) scheduled for elective percutaneous coronary intervention (PCI) with drug-eluting stent(s) for stable ischemic heart disease were screened for eligibility. Inclusion criteria comprised: ability to provide informed consent, planned radial or femoral access PCI with contemporary drug-eluting stent implantation, and clinical equipoise for either study antiplatelet strategy. Exclusion criteria included: acute coronary syndrome within the preceding 30 days, ongoing oral anticoagulation, history of hemorrhagic stroke or intracranial pathology predisposing to bleeding, active pathological bleeding, known platelet disorder, severe hepatic impairment,

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estimated glomerular filtration rate <30 mL/min/1.73 m², baseline bradyarrhythmia requiring pacing, or known hypersensitivity to study drugs. Pregnant or lactating women and patients unable to comply with the 30-day follow-up were excluded.

Eligible participants were allocated 1:1 to receive either ticagrelor (180 mg loading dose ≥2 hours pre-PCI; maintenance 90 mg twice daily) or clopidogrel (600 mg loading dose ≥2 hours pre-PCI; maintenance 75 mg once daily), in addition to aspirin (300 mg loading dose, then 75–100 mg daily). Periprocedural anticoagulation with unfractionated heparin was administered according to body weight and institutional protocol, with the use of a glycoprotein IIb/IIIa inhibitor left to the operator's discretion. PCI was performed using standard techniques: stent selection and lesion preparation. Procedural success was defined as residual stenosis <20% with Thrombolysis in Myocardial Infarction (TIMI) grade-3 flow and no in-laboratory complications.

Participants were clinically evaluated before discharge and followed up in person or via structured telephonic follow-up at 30 days. The primary endpoint was 30-day major adverse cardiovascular events (MACE), a hierarchical composite of all-cause death, non-fatal myocardial infarction, or ischemia-driven target-vessel revascularization. Myocardial infarction definitions followed the Fourth Universal Definition, with Type 4a MI adjudicated using post-PCI cardiac troponin criteria and corroborative evidence. Stent thrombosis was classified as definite or probable per the Academic Research Consortium (ARC) criteria. Key safety endpoints included Bleeding Academic Research Consortium (BARC) type ≥ 2 bleeding, access-site complications, bradyarrhythmias, dyspnea leading to documentation or therapy adjustment, and discontinuation of the study drug. Pill count and structured patient report assessed medication adherence; high-intensity statin, ACE inhibitor/ARB, and β-blocker prescriptions were recorded at discharge.

The sample size was fixed at 60 (30 per arm), consistent with an exploratory comparative analysis designed to estimate effect sizes and feasibility in the local context rather than to provide definitive non-inferiority or superiority testing. All analyses followed the intention-to-treat principle. Continuous variables were examined for normality using Shapiro–Wilk tests and presented as mean ± SD or median [IQR]; between-group comparisons used independent-samples t-tests or Mann–Whitney U tests, as appropriate. Categorical variables were summarized as counts (%) and compared using χ^2 or Fisher's exact tests. For binary endpoints, effect sizes were expressed as risk ratios (RR) with 95% confidence intervals; when a cell contained zero events, the Haldane–Anscombe correction was applied. Two-sided p-values <0.05 were considered statistically significant without multiplicity adjustment, given the exploratory nature of the study. Analyses were performed with standard statistical software (e.g., SPSS v27 or Stata v17). The institutional ethics review committee approved the study protocol, and all participants provided written informed consent.

RESULTS

A total of 60 patients undergoing elective coronary stenting were enrolled, equally divided between the Ticagrelor group (n=30) and the Clopidogrel group (n=30). The mean age of the cohort was 58.1 ± 9.6 years, with no significant age difference between groups (p=0.88). The study population consisted predominantly of males (71.7%), with similar proportions in both the Ticagrelor (73.3%) and Clopidogrel (70.0%) groups (p=0.78). The mean BMI was comparable between groups (27.6 ± 3.5 kg/m²; p=0.82). The prevalence of diabetes mellitus was 38.3%, and hypertension was present in 58.3% of participants, with no statistically significant difference between the two groups (p=0.79 for both). Dyslipidemia was recorded in half of the patients (50%), and current smoking in 26.7%, again with no group-wise difference.

A prior history of myocardial infarction was reported in 11.7% of the participants, while multivessel coronary artery disease was found in 31.7% of angiograms. The mean estimated glomerular filtration rate (eGFR) was 79.8 ± 16.3 mL/min/1.73 m², and among diabetic participants, the mean HbA1c was 7.9 ± 1.1%, showing no significant intergroup variation. (Table 1)

As shown in Table 2, the majority of procedures were performed for stable angina (81.7%), with radial access used in 91.7% of cases. All patients received drug-eluting stents, with a mean of 1.4 ± 0.7 stents per patient. The median total stent length was 27 mm [IQR: 18–36], and the mean stent diameter was 3.0 ± 0.4 mm, with no differences between groups. The mean contrast volume was 145 ± 38 mL, and the fluoroscopy time was 11.2 ± 5.0 minutes, both of which were comparable between groups. (Table 2)

At 30-day follow-up (Table 3), the rate of major adverse cardiac events (MACE) was lower in the Ticagrelor group (3.3%) than in the Clopidogrel group (16.7%), though this difference did not reach statistical significance (RR 0.27, 95% CI 0.05–1.55; p=0.19). All-cause mortality occurred in one patient (3.3%) receiving Clopidogrel, whereas non-fatal MI (Type 4a) was seen in three Clopidogrel patients but none in the Ticagrelor group. Ischemia-driven target vessel revascularization (TVR) was required in 3.3% of Ticagrelor and 6.7% of Clopidogrel patients (p=0.56). Stent thrombosis (definite/probable per ARC criteria) occurred in two Clopidogrel patients (6.7%) and none in the Ticagrelor group. (Table 3)

As summarized in Table 4, BARC ≥2 bleeding was observed in 13.3% of Ticagrelor patients versus 3.3% in the Clopidogrel arm (RR 4.00, 95% CI 0.47–34.0; p=0.35), though the difference was not statistically significant. In BARC 3–5, bleeding events occurred in both groups.

Access-site hematoma >5 cm was slightly more frequent with Ticagrelor (6.7%) compared to Clopidogrel (3.3%). Dyspnea was reported in 20% of Ticagrelor users versus 3.3% with Clopidogrel (RR 6.00, 95% CI 0.79–45.6; p=0.10). One case of bradyarrhythmia requiring intervention occurred in the Ticagrelor group. Discontinuation of the study drug was rare, reported in 2 Ticagrelor and 1 Clopidogrel patients. (Table 4)

The median hospital stay was 2 days [IQR: 2–3] in both groups (p=0.84). Dual antiplatelet therapy (DAPT) adherence at 30 days was high and comparable—93.3% in the Ticagrelor group and 96.7% in the Clopidogrel group (p=0.55). All patients were discharged on high-intensity statins, while use of ACE inhibitors/ARBs and β-blockers was similar between groups (p>0.7 for both). (Table 5)

*No more than one missed daily dose per week by pill-count/telephonic check.

Overall, the findings suggest that Ticagrelor showed a trend toward reduced ischemic events without a significant increase in major bleeding within 30 days. However, these differences did not reach statistical significance, likely due to the modest sample size.

Table 1: Baseline Characteristics of the Study Population.

Variable	Overall (n=60)	Ticagrelor (n=30)	Clopidogrel (n=30)	p-value
Age, years	58.1 ± 9.6	57.9 ± 9.8	58.3 ± 9.5	0.88
Male sex	43 (71.7)	22 (73.3)	21 (70.0)	0.78
BMI, kg/m²	27.6 ± 3.5	27.7 ± 3.6	27.5 ± 3.5	0.82
Diabetes mellitus	23 (38.3)	11 (36.7)	12 (40.0)	0.79
Hypertension	35 (58.3)	17 (56.7)	18 (60.0)	0.79
Dyslipidemia	30 (50.0)	15 (50.0)	15 (50.0)	1.00
Current smoker	16 (26.7)	7 (23.3)	9 (30.0)	0.56

Prior MI	7 (11.7)	3 (10.0)	4 (13.3)	0.69
Multivessel CAD on angiography	19 (31.7)	10 (33.3)	9 (30.0)	0.79
eGFR, mL/min/1.73 m²	79.8 ± 16.3	80.6 ± 15.9	79.1 ± 16.9	0.74
HbA1c, % (diabetics only)	7.9 ± 1.1	7.8 ± 1.2	8.0 ± 1.0	0.57

Table 2: Procedural characteristics

Variable	Overall (n=60)	Ticagrelor (n=30)	Clopidogrel (n=30)	p-value
Indication: stable angina	49 (81.7)	25 (83.3)	24 (80.0)	0.74
Radial access	55 (91.7)	28 (93.3)	27 (90.0)	0.64
Drug-eluting stent used	60 (100)	30 (100)	30 (100)	—
No. of stents per patient	1.4 ± 0.7	1.4 ± 0.7	1.4 ± 0.7	0.98
Total stent length, mm	27 [18–36]	26 [18–35]	27 [19–37]	0.77
Max stent diameter, mm	3.0 ± 0.4	3.0 ± 0.4	3.0 ± 0.4	0.90
Procedural success*	60 (100)	30 (100)	30 (100)	—
Contrast volume, mL	145 ± 38	143 ± 36	147 ± 40	0.67
Fluoroscopy time, min	11.2 ± 5.0	11.1 ± 4.8	11.3 ± 5.2	0.88

Table 3: Primary and secondary ischemic outcomes at 30 days (intention-to-treat)

Outcome	Ticagrelor (n=30)	Clopidogrel (n=30)	RR (95% CI)	p-value
Primary: MACE†	1 (3.3)	5 (16.7)	0.27 (0.05–1.55)	0.19
All-cause mortality	0 (0)	1 (3.3)	—	0.31
Non-fatal MI (Type 4a)	0 (0)	3 (10.0)	—	0.24
Ischemia-driven TVR	1 (3.3)	2 (6.7)	0.50 (0.05–5.30)	0.56
Definite/probable stent thrombosis (ARC)	0 (0)	2 (6.7)	—	0.49

Table 4: Bleeding and other safety outcomes at 30 days

Outcome	Ticagrelor (n=30)	Clopidogrel (n=30)	RR (95% CI)	p-value
BARC ≥2 bleeding	4 (13.3)	1 (3.3)	4.00 (0.47–34.0)	0.35
BARC 3–5 bleeding	0 (0)	0 (0)	—	—
Access-site hematoma >5 cm	2 (6.7)	1 (3.3)	2.00 (0.19–21.1)	0.56
Dyspnea (any)	6 (20.0)	1 (3.3)	6.00 (0.79–45.6)	0.10
Bradyarrhythmia needing intervention	1 (3.3)	0 (0)	—	0.31
Discontinuation of study drug	2 (6.7)	1 (3.3)	2.00 (0.19–21.1)	0.56

Table 5: Hospital course and medication adherence

Measure	Ticagrelor (n=30)	Clopidogrel (n=30)	p-value
Hospital stay, days	2 [2–3]	2 [2–3]	0.84
DAPT adherence at 30 days*	28/30 (93.3)	29/30 (96.7)	0.55
High-intensity statin at discharge	30 (100)	30 (100)	—
ACEi/ARB at discharge	22 (73.3)	21 (70.0)	0.78
β-blocker at discharge	24 (80.0)	23 (76.7)	0.76

DISCUSSION

The current study aimed to compare the effectiveness and safety of ticagrelor versus clopidogrel among patients undergoing elective coronary stenting. The baseline characteristics of our cohort, composed predominantly of middle-aged males (mean age 58.1 years), revealed no significant clinical differences between the two treatment arms, confirming the randomized allocation (Table 1). Existing literature corroborates our findings regarding demographic and clinical profiles, with studies like those by Li et al. and Jin et al. noting similar distributions in their cohorts undergoing PCI, indicating consistency of participant characteristics across different studies [16, 17].

In terms of procedural characteristics, the majority of interventions were performed for stable angina, aligning with common practices in elective PCI, as noted in the evaluation of antiplatelet strategies in patients undergoing elective procedures by Giang et al. [18]. The high rate of radial access (91.7%) in our study is reflective of contemporary PCI trends aimed at reducing access-related complications, consistent with findings from broader studies that advocate for this approach due to its safety profile and patient comfort [19, 20]. Notably, all patients received drug-eluting stents (DES), with the average number of stents and total stent lengths being consistent with current standards, suggesting adequate procedural planning and execution in line with recent guidelines [21,22].

Despite anticipated differences between ticagrelor and clopidogrel, our findings at 30-day follow-up showed a lower incidence of major adverse cardiac events (MACE) in the ticagrelor group (3.3% vs. 16.7% in the clopidogrel group). However, the relative risk reduction was not statistically significant (p=0.19). This trend aligns with the findings of You et al., who reported improved clinical outcomes with ticagrelor. However, their results did not consistently reach statistical significance across certain patient subsets [23]. Furthermore, the absence of stent thrombosis in the ticagrelor group, compared with 2 cases in the clopidogrel group, supports the growing body of evidence that ticagrelor may offer a safety advantage regarding thrombotic events after PCI, as shown in a meta-analysis by Li et al. [16, 24].

Regarding bleeding events, our results showed a trend toward increased BARC ≥2 bleeding events in the ticagrelor group (13.3% vs. 3.3% with clopidogrel), but this difference was not statistically significant (p=0.35). This pattern aligns with findings from Abraham et al., which noted a similar trend of higher incidence rates for adverse bleeding events associated with ticagrelor usage, particularly among patients with acute coronary syndrome [21]. The reported rate of dyspnea (20% in ticagrelor patients vs. 3.3% in clopidogrel patients) supports prior studies establishing ticagrelor's association with increased dyspnea reports, potentially limiting its use in certain patient populations, particularly as reflected in insights from Kang et al. [25, 26].

Additionally, the median hospital stay was comparable between groups, highlighting the efficiency of both antiplatelet strategies regarding clinical management post-PCI. Adherence to dual antiplatelet therapy was notably high in both groups (93.3% vs. 96.7%), reflecting well-established protocols for surgical follow-ups and mirroring adherence rates in similar contemporary studies [24].

In summary, while ticagrelor demonstrated a trend toward fewer ischemic events and comparable bleeding risk in our study cohorts, larger-scale studies are needed to definitively establish it as the preferred antiplatelet therapy for patients undergoing

elective coronary stenting. Our findings contribute to a nuanced understanding of antiplatelet therapy's risk-benefit profile, underscoring the importance of tailoring antiplatelet strategies based on individual patient characteristics supported by existing literature.

CONCLUSION

Ticagrelor showed a favorable trend toward reduced ischemic events, including lower rates of MACE and absence of stent thrombosis, compared with clopidogrel in patients undergoing elective coronary stenting. Safety outcomes, including bleeding and dyspnea, were more frequent with ticagrelor but not significantly different. While the results are promising, the modest sample size limits the ability to draw definitive conclusions. Larger, adequately powered studies are needed to determine whether ticagrelor should be preferred over clopidogrel in stable PCI patients.

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