Original Article

Ticagrelor versus Clopidogrel in Complex Percutaneous Coronary Intervention in terms of Mortality and Stent Thrombosis

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ABSTRACT

Objective: To compare the effects of ticagrelor and clopidogrel on major adverse cardiovascular events (MACE), 30 day mortality, and stent thrombosis in patients with ST-elevation myocardial infarction (STEMI) undergoing complex percutaneous coronary intervention (PCI).

Methodology: This quasi-experimental study was conducted at the Rawalpindi Institute of Cardiology, Rawalpindi in 3 months from June to August 2025 after ethical approval. After obtaining informed written consent, 376 patients with STEMI treated with complex PCI were included by non-probability convenience sampling technique. The patients were assigned to two groups: Group A received aspirin & clopidogrel, whereas group B received aspirin and ticagrelor. The outcomes assessed were MACE, 30 day mortality, and stent thrombosis. Follow-up was done till 1 month. Data analysis was performed using the Statistical Package for the Social Sciences **(**SPSS) version 25.

Results: Bifurcation stenting was present in 80(42.6%) patients in clopidogrel group, while it was seen in 46(24.5%) patients in ticagrelor group. The left main PCI was also more prevalent in the ticagrelor group [81(43.1%)]. The thrombolysis in myocardial infarction (TIMI) 3 flow was restored in 53.7% versus 30.3% of the patients taking ticagrelor and clopidogrel, respectively. Stent thrombosis and MACE were significantly higher in the clopidogrel group (8.5% versus 2.7%) and (19.1% versus 11.2%), respectively. In contrast, no substantial difference was noted regarding 30 day mortality (9% vs. 8%) between the two groups.

Conclusion: Ticagrelor is associated with improved post-PCI TIMI flow, lower incidence of MACE and stent thrombosis in STEMI patients who underwent complex PCI as compared to clopidogrel. However, 30 day mortality is not significantly different in the two groups.

Keywords: *Ticagrelor. Clopidogrel. Percutaneous coronary intervention.*

INTRODUCTION

Primary percutaneous coronary intervention (P-PCI) with stent insertion is the preferred treatment in patients with ST-elevation myocardial infarction. However, stent thrombosis (ST) continues to be a rare but catastrophic event that can present in the initial 30 days after implantation.[1] Aspirin and clopidogrel are given as conventional antiplatelet drugs. Aspirin inhibits the enzyme cyclooxygenase-1, thereby stops thromboxane A2 production, which facilitates platelet plug formation. Clopidogrel is a P2Y12 receptor inhibitor. These receptors are present on platelets and bind adenosine diphosphate (ADP). So, P2Y12 inhibitors block the ADP-mediated platelet activation and hence clot formation.[2,3]

One of the disadvantages of clopidogrel is its variable efficacy. Even with ongoing oral antiplatelet therapy, atherothrombotic events still occur in some patients. Evidence from several studies suggests that residual platelet activity may be associated with these clinical outcomes, implying that "resistance" to antiplatelet therapy could play a role.[4] Long-term dual antiplatelet therapy decreases the occurrence of ischemic complications, but is also related to high bleeding risk, contributing to greater morbidity, mortality, and increasing healthcare costs.[5] The new P2Y12 receptor antagonist, ticagrelor, has good oral bioavailability. It has a quicker onset of action, more potency, and reversibly inhibits platelet aggregation when compared to conventional P2Y12 inhibitors like clopidogrel and prasugrel.[6]

This study was conducted to compare the effects of ticagrelor and clopidogrel on major adverse cardiovascular events, 30 day mortality, and stent thrombosis in patients with STEMI undergoing complex PCI. Having more efficacy, ticagrelor would be associated with lower frequency of complications and mortality. Over the past few years, there have been controversial results from complex PCI cohorts. In some studies, it has been reported that ticagrelor lowers the incidence of MACE than clopidogrel in complex PCI, whereas others claim that the two drugs are not significantly different. These uncertainties underline the

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requirement for additional assessment of antiplatelet treatment in this high-risk population.

METHODOLOGY

This quasi-experimental study was conducted at the Rawalpindi Institute of Cardiology, Rawalpindi in 3 months from June to August 2025 after approval from the institution ethical review board (Letter No. RIC/RERC/14/25, 17-07-2025). The sample size of 376 was calculated using the incidence of stent thrombosis of 5% with ticagrelor and 13.3% with clopidogrel, 80% power, and 95% confidence interval.[7] After obtaining informed written consent, patients with STEMI treated with complex PCI were included by non-probability convenience sampling technique. Patients of both genders and age >18 years were eligible for inclusion. The diagnosis of STEMI was made from clinical history and ECG findings. Patients complaining of chest pain consistent with myocardial ischemia and a duration of ≥20 minutes along with either ST-segment elevation of ≥1 mm in two contiguous limb leads, or ≥2 mm in two contiguous chest leads, or a new left bundle branch block, were diagnosed with STEMI.[8] Complex PCI was defined by the presence of any of the following: chronic total occlusion, >60 mm stent length, bifurcation stenting, left main PCI, bypass graft, use of multiwires, atherectomy, guiding catheter extensions or multiple stents.[9] The exclusion criteria were patients with known allergy or intolerance of antiplatelet therapy, concomitant anticoagulant use, prior bare-metal stent implantation, and history of coronary artery bypass grafting. The patients were assigned to two groups, with 188 patients in each: group A received 75 mg of aspirin once daily and 75 mg of clopidogrel once daily, whereas group B received 75 mg of aspirin once daily and 90 mg of ticagrelor twice daily. Emergency diagnostic coronary angiography and immediate P-PCI were done if the duration from symptom onset was less than 12 hours. The interventional approach (arterial access, stent type, aspiration thrombectomy) was at the discretion of Interventional Cardiologists. The TIMI flow was evaluated in the infarcted vessel pre- and post-procedure. Afterwards, patients were continuously monitored for at least 1 day, and were hospitalized for a minimum of 72 hours. The outcomes assessed were MACE, 30 day mortality, and stent thrombosis. Follow-up was done after 1 month. Major adverse cardiovascular events included myocardial infarction, stroke, or cardiovascular death.[10]

STATISTICAL ANALYSIS

Data analysis was performed using the Statistical Package for the Social Sciences **(**SPSS) version 25. Categorical variables are reported as frequencies & percentages, and continuous variables as mean±standard deviation (SD)**.** Group comparisons were conducted using Pearson's Chi-square test and a p-value <0.05 was considered statistically significant.

RESULTS

Patients had a mean age of 58.4±10.2 years in the clopidogrel group and 57.9±9.8 years in the ticagrelor group. Patients had a mean body mass index (BMI) of 26.1±3.7 kg/m^2 in the clopidogrel group and 26.4±3.5 kg/m^2 in the ticagrelor group. The mean ejection fraction was 46.2±8.5 and 47.1±8.2 in the clopidogrel and ticagrelor groups, respectively. Regarding gender, the clopidogrel group contained 50.6% of males and 49.4% of females, whereas the ticagrelor group comprised 49.4% of males and 50.6% of females. Diabetes mellitus was more common in the clopidogrel group (50% vs. 39.4%) and so was hypertension (53.3% vs. 46.7%). In the clopidogrel group, 44.4% of the patients had hyperlipidemia versus 47.2% of the patients in the ticagrelor group. The proportion of smokers was 46.1% in the clopidogrel and 47.8% in the ticagrelor group. The history of previous PCI was positive in 50% and 49.4% of the patients in the clopidogrel and ticagrelor groups, respectively.

The procedural characteristics of the two groups are given in Table 1. Significant differences were seen in arterial access, post-PCI TIMI flow 3, bifurcation stenting, and left main PCI.

Major adverse cardiovascular events were significantly higher in the clopidogrel group [36(19.1%)] as compared to the ticagrelor group [21(11.2%)] with a p-value=0.03. In contrast, no substantial difference was noted in 30 day mortality (9% vs. 8%; p-value=0.71) between the two groups. In terms of the stent thrombosis, the clopidogrel group had higher number of cases (8.5%) versus ticagrelor group (2.7%) and this was statistically significant (p=0.01). These data emphasize that despite a similar incidence of mortality between the two groups, ticagrelor was related with a lower incidence of MACE and stent thrombosis, suggesting a possible clinical benefit to clopidogrel (Table 2).

Table 1: Procedural Characteristics of the Study Participants

Variables		Clopidogrel Group (n=188)	Ticagrelor Group (n=188)	Total	p-value
		Frequency and Percentage			
Arterial Access	**Radial**	80(42.6%)	100(53.2%)	180(47.9%)	0.04*
	Femoral	108(57.4%)	88(46.8%)	196(52.1%)	
Severity of Coronary Artery Disease (CAD)	**Single Vessel CAD (SVCAD)**	68(36.2%)	63(33.5%)	131(34.8%)	0.79
	Double Vessel CAD (DVCAD)	53(28.2%)	52(27.7%)	105(28%)	
	Triple Vessel CAD (TVCAD)	67(35.6%)	73(38.8%)	140(37.2%)	
Treated Vessel	**Left Anterior Descending**	55(29.3%)	47(25%)	102(27.1%)	0.69
	Left Main	44(23.4%)	44(23.4%)	88(23.5%)	
	Left Circumflex	47(25%)	56(29.8%)	103(27.4%)	
	Right Coronary	42(22.3%)	41(21.8%)	83(22%)	
Type of Stent	**Drug Eluting Stents (DES)**	95(50.5%)	88(46.8%)	183(48.7%)	0.47
	Bare Metal Stents	93(49.5%)	100(53.2%)	193(51.3%)	
GP2b/3a Inhibitor use	**Yes**	90(47.9%)	91(48.4%)	181(48.1%)	0.92
	No	98(52.1%)	97(51.6%)	195(51.9%)	
Pre-PCI TIMI Flow	**0**	51(27.1%)	41(21.8%)	92(24.5%)	0.23
	1-3	137(72.9%)	147(78.2%)	284(75.5%)	
Post-PCI TIMI Flow 3	**Yes**	57(30.3%)	101(53.7%)	158(42%)	<0.00001*
	No	131(69.7%)	87(46.3%)	218(58%)	
Bifurcation Stenting	**Yes**	46(24.5%)	80(42.6%)	126(33.5%)	<0.0002*
	No	142(75.5%)	108(57.4%)	250(66.5%)	
Left Main PCI	**Yes**	45(23.9%)	81(43.1%)	126(33.5%)	0.00008*
	No	143(76.1%)	107(56.9%)	250(66.5%)	
Bypass Graft as Target	**Yes**	98(52.1%)	83(44.1%)	181(48.1%)	0.12
	No	90(47.9%)	105(55.9%)	195(51.9%)	

**Significant p-value*

Table 2: Clinical Outcomes in Patients Taking Clopidogrel versus Ticagrelor

Outcomes		Clopidogrel Group (n=188)	Ticagrelor Group (n=188)	Total	p-value
		Frequency and Percentage			
MACE	**Yes**	36(19.1%)	21(11.2%)	57(15.2%)	0.03*
	No	152(80.9%)	167(88.8%)	319(84.8%)	
30 day Mortality	**Yes**	17(9%)	15(8%)	32(8.5)	0.71
	No	171(91%)	173(92%)	344(91.5%)	
Stent Thrombosis	**Yes**	16(8.5%)	5(2.7%)	21(5.6%)	0.01*
	No	172(91.5%)	183(97.3%)	355(94.4%)	

**Significant p-value*

DISCUSSION

Patients with acute coronary syndrome receive conventional antiplatelet regimen consisting of aspirin and P2Y12 receptor inhibitor. However, determining the optimal agent among available P2Y12 inhibitors remains a subject of debate.[11] In our study, patients had a mean age of 58.2±10 years and the mean BMI of 26.3±3.6 kg/m^2. The males constituted 50% of the study population. There were 44.7% diabetics, 50% hypertensive, 45.8% dyslipidemic, 46.9% smokers, and 49.7% had previous PCI. In a study, patients had an average age of 59.1±10.1 years with the majority (80.3%) of males. Their mean BMI was 26.1±3.3 kg/m^2. Most of the patients had dyslipidemia (82.8%) followed by hypertension (63.1%), smoking (59.9%), diabetes mellitus (34.3%), and prior PCI (18.8%).[12] In another study, the average age was 54.8±10.1 years with 87.3% males and the mean BMI was 26.9±12.3 kg/m^2. There were 38.4% hypertensive, 30.7% diabetic, 39.5% smokers, 0.4% hyperlipidemic, and 9.6% patients with the history of previous PCI.[13]

In our study, femoral access was predominantly used (52.1%), with the majority of the patients having TVCAD (37.2%), followed by SVCAD (34.8%). In a study by Hakeem et al., radial access was used in 89.9% of the patients. Most of the patients had SVCAD (36.2%) and DVCAD (36.5%).[13] According to our study, 33.5% of the patients had bifurcation lesions and DES were used in 48.7% of the participants. Around 17.7% had bifurcation lesion and DES were used in 94.1% of the study population according to Hakeem et al.[13] In our study, bifurcation stenting and left main PCI were more frequently performed in patients taking ticagrelor. Another study reported that ticagrelor did not reduce periprocedural adverse events compared to clopidogrel. Bifurcation stenting was done in 64.6% and 43.4% of the patients taking ticagrelor and clopidogrel, respectively, whereas left main stenting was done 32.4% and 49.4% of the patients taking ticagrelor and clopidogrel, respectively.[9] Xi et al. also found that ticagrelor was associated with complex procedural outcomes.[12]

Our results revealed that pre-PCI TIMI flow showed no significant variation between the groups, whereas TIMI flow after the procedure was significantly improved in patients taking ticagrelor. A trial reported no variation in TIMI flow before and after procedure in the ticagrelor and clopidogrel groups.[14] In our study, there was a significantly marked reduction in MACE (11.2% versus 19.1%) and stent thrombosis (2.7% versus 8.5%) in the patients taking ticagrelor. In contrast, 30 day mortality was almost the same in the two groups (8% versus 9%). Our results were comparable to other studies. The results of a study showed that ticagrelor was linked to lower incidence of all-cause deaths (1.38% versus 2.85%) and MACE (6.53% versus 9.48%) and the findings were statistically significant.[15] In another study, MACE occurred in 8.6% of patients taking ticagrelor in contrast to 11.2% of the patients taking clopidogrel with a significant difference. Cardiac deaths occurred in 1.2% versus 1.7% in the ticagrelor and clopidogrel groups, respectively with statistically insignificant results.[12] A study by Yan et al. concluded significant reduction in all-cause deaths and stent thrombosis with ticagrelor but there was no difference in cardiovascular deaths between patients taking ticagrelor and clopidogrel.[16] Qiu et al. and Bari et al. showed a marked reduction in MACE with ticagrelor as compared to clopidogrel.[17,18] On contrary, another study revealed no statistical variation in MACE (15% versus 11.8%) and deaths (1% versus) in patients treated with ticagrelor and clopidogrel, respectively.[9] Another study also showed that 30 day all-cause mortality (14.6% versus 13.5%) and MACE (16.1% versus 14.7%) did not differ statistically in patients taking ticagrelor and clopidogrel.[19] Other studies also showed that MACE was not different in the two groups.[14,20] In a study, the frequency of MACE was 2.2% versus 2.9%, all-cause deaths were 1.5% versus 1.8%, and stent thrombosis was 1.6% versus 2.1% in the ticagrelor and clopidogrel groups, respectively but with no significance.[13]

CONCLUSION

Ticagrelor is associated with improved post-PCI TIMI flow, lower incidence of MACE, and stent thrombosis in STEMI patients who underwent complex PCI as compared to clopidogrel. However, 30 day mortality is not significantly different in the two groups.

LIMITATIONS & RECOMMENDATIONS

Our findings suggest that ticagrelor may be preferable to clopidogrel, particularly in patients undergoing complex PCI. However, further multicenter randomized trials with larger sample sizes and longer follow-up periods are required to confirm these results and to more accurately assess mortality, bleeding, and long-term ischemic outcomes. The quasi-experimental design of this study may introduce selection bias. Additionally, bleeding events, which are important when evaluating the safety profile of ticagrelor, were not comprehensively assessed.

Cost-effectiveness analyses are also needed, especially in low- and middle-income countries, where issues of affordability and drug accessibility are significant. Incorporation of individualized risk assessment tools (ischemic vs. bleeding risk stratification) may help guide the selection and duration of antiplatelet therapy in clinical practice.

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Authors' Contributions:
M.M: Conceived and supervised the study.
T.A.R: Reviewed study design and clinical interpretation.
H.A.G: Collected data and performed analysis.
M.U.F: Assisted in data collection and literature review.
E.S: Contributed to data analysis and interpretation.
M.H.Y: Edited and finalized the manuscript.

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