

ORIGINAL ARTICLE

Comparison of Ticagrelor Versus Clopidogrel in Preventing Early Stent Thrombosis after Primary PCI

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ABSTRACT

Background: Primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) is a potentially life-threatening complication that occurs early after the procedure. Ticagrelor is an agent that is more effective and faster-acting at inhibiting platelets than clopidogrel, and may be more protective against thrombosis.

Objective: To compare ticagrelor and clopidogrel in preventing early stent thrombosis after primary PCI in patients with STEMI.

Methods: This was a comparative observational study conducted at Punjab Institute of Cardiology, Lahore, from February 2023 to August 2023. Patients who underwent primary PCI with stent implantation were consecutively sampled to enroll 93 patients. Dual antiplatelet therapy consisted of ticagrelor (n=47) or clopidogrel (n=46). Participants were observed for 30 days for events of early stent thrombosis and for other clinical outcomes. The data were analysed using SPSS 26.

Results: The incidence of early stent thrombosis was 2 (4.3%) in the ticagrelor group and 7 (15.2%) in the clopidogrel group (p=0.091). Numerically fewer patients had recurrent myocardial infarction, target-vessel revascularization, rehospitalization, or death with ticagrelor. Neither group had high rates of major bleeding. On multivariable analysis, early stent thrombosis was independently predicted by Killip class III–IV (p=0.049).

Conclusion: Ticagrelor was not statistically significantly associated with reduced early stent thrombosis compared to clopidogrel after primary PCI, but the number of such occurrences was lower. The findings are supported by the need for larger randomized studies.

Keywords: Ticagrelor, Clopidogrel, Stent Thrombosis, Primary PCI, STEMI.

INTRODUCTION

Acute coronary syndrome (ACS), especially ST-segment elevation myocardial infarction (STEMI), is still a leading cause of cardiovascular morbidity and mortality around the globe.^[1] In patients with STEMI, when done in a timely manner, primary percutaneous coronary intervention (PPCI) is the preferred reperfusion approach because it significantly improves coronary flow and improves clinical outcomes.^[2] However, stent thrombosis is still one of the most harmful events following PCI, as it can lead to acute myocardial infarction, recurrent revascularisation, cardiogenic shock, and death.^[3] The risk is especially critical in the first days and weeks following PPCI when platelets are activated and the coronary endothelial cells have been damaged, leading to the presence of residual intracoronary thrombus and thus a highly thrombogenic environment.^[4]

The use of dual antiplatelet therapy (DAPT) with aspirin and a P2Y₁₂ receptor inhibitor is thus an integral part of PCI treatment.^[5] The use of clopidogrel has been broad since the drug is effective, widely available, and has a relatively good bleeding profile.^[6] It is metabolized to an active metabolite by hepatic cytochrome P450 enzymes; however, which metabolizes it to an active form varies from patient to patient, causing platelet inhibition to be variable.^[7] However, these drugs may be less effective in the acute phase of STEMI due to genetic variation, drug interactions, delayed response to the drug, and high on-treatment platelet reactivity.^[8] Unlike other direct-acting P2Y₁₂ inhibitors, ticagrelor is a reversible P2Y₁₂ inhibitor that provides more rapid and predictable platelet inhibition, especially in the high-risk setting immediately prior to and following primary PCI.^[9]

The data collected from previous literature indicated that ticagrelor might offer more protection against thrombotic complications than clopidogrel, but this benefit varied in different trials. In a real-world study of STEMI patients undergoing primary PCI, fewer early clinical events were observed in patients receiving ticagrelor or prasugrel than in those receiving clopidogrel, and at 1 year, there were no significant differences between the groups in terms of rates of stent thrombosis (1.3% vs. 2.0%).^[10] A STEMI-

centric analysis also found ticagrelor to be significantly associated with a reduction in definite stent thrombosis versus clopidogrel, which suggests that ticagrelor may offer more effective platelet inhibition in the PPCI setting.^[11]

There were some inconsistencies in the evidence, however. A network meta-analysis of 145,019 patients with ACS in 2020 showed that ticagrelor performed better than clopidogrel with respect to myocardial infarction and all-cause mortality; some short-term outcomes differed across the different P2Y₁₂ inhibitors and endpoints assessed.^[12] In a similar 2021 network meta-analysis, which focused on stent thrombosis following PCI, it was found that ticagrelor and prasugrel were more effective at preventing stent thrombosis, while there was no significant difference between the two.^[13] In contrast, a large meta-analysis published in 2022 showed that ticagrelor most likely reduced stent thrombosis versus clopidogrel, but noted that the overall clinical benefit needs to be weighed against bleeding and other adverse effects.^[14]

The clinical significance of this comparison is of grave importance in patients with STEMI who are being treated with PPCI, as even a relatively uncommon occurrence of early stent thrombosis can have devastating effects. There is no consistent benefit of ticagrelor over clopidogrel for early stent thrombosis, as the drug offers greater and more consistent platelet inhibition. Variations in thrombotic risk, adherence to treatment, comorbidities, procedural factors, and health care environments may affect outcomes. Hence, a head-to-head comparison of ticagrelor and clopidogrel in primary PCI patients may prove to be clinically relevant information about the ideal P2Y₁₂ inhibitor in the early post-stenting period. The present study aimed to compare the effectiveness of ticagrelor versus clopidogrel in preventing early stent thrombosis within 30 days after primary PCI among patients presenting with STEMI.

MATERIAL & METHODS

It was a comparative observational study in the Department of Cardiology at Punjab Institute of Cardiology (PIC), Lahore. The study was carried out for seven months, from February 2023 to August 2023.

The sample size was determined in OpenEpi version 3.01 based on previously reported results of Steg et al., who compared ticagrelor and clopidogrel in the PLATO trial, with reported definite

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stent thrombosis rates of 1.37% for ticagrelor and 1.93% for clopidogrel.^[15] The minimum sample size, as calculated at a 95% confidence level and 80% statistical power, with the expected difference in the frequency of stent thrombosis between the two treatment groups, was 93 patients. A final sample of 93 participants who met the preselected inclusion criteria was created.

A non-probability consecutive sampling technique was used. All consecutive patients presenting over the study period who met the inclusion criteria and underwent primary PCI were evaluated for inclusion in the study. Patients were recruited to a sample size of 93 patients. Participants were divided into 2 groups, i.e., the ticagrelor group and the clopidogrel group, based on the P2Y12 inhibitor administered following primary PCI.

All patients presenting with STEMI aged 18 years or older and undergoing successful primary PCI with intracoronary stent implantation were included. All patients had to have received ticagrelor or clopidogrel as part of dual antiplatelet therapy after PCI and sufficient clinical information for outcome evaluation within the first 30 days after PCI. Patients were excluded from the study in the event of previous stent thrombosis, PCI for indications other than acute STEMI, treatment with ticagrelor and clopidogrel during the index event, known hypersensitivity or contraindication to either study drug, active major bleeding, significant bleeding disorder, concomitant oral anticoagulant therapy, previous intracranial hemorrhage, or incomplete follow-up data. Any patients who were found to have died for any other apparent reason other than cardiac cause before the evaluation of stent thrombosis were also not included in the analysis.

Eligible patients after informed consent were enrolled after approval by the institutional ethics committee. A structured data collection proforma was used to collect baseline demographic and clinical data. Relevant laboratory parameters, age, sex, BMI, diabetes mellitus, blood pressure, heart rate, Killip class, smoking status, previous ischemic heart disease, previous PCI, and family history of IHD were recorded. ECGs and echocardiographic LVEF were recorded. Additional information recorded was for the index PCI, which included the infarct-related artery, number and type of stents, stent diameter and length, presence of multivessel disease, thrombus burden, procedural success, and adjunctive pharmacological therapy.

All patients were treated according to guidelines for STEMI and primary PCI as per the treating cardiologist's evaluation. Details were recorded on the type of P2Y12 inhibitor used and on the loading and maintenance dose of ticagrelor or clopidogrel. Clinical assessment and review of hospital records were performed to follow patients for 30 days following primary PCI. The main outcome was early stent thrombosis, defined as definite or probable stent thrombosis within 30 days of stent implantation, according to the recommended Academic Research Consortium definitions. The early events were additionally classified as acute stent thrombosis, which is defined as occurring within 24 hours of PCI, and subacute stent thrombosis (more than 24 hours to 30 days after PCI). The following outcomes were also recorded during the follow-up: recurrent myocardial infarction, target-vessel revascularization, major bleeding, rehospitalization, and all-cause mortality. Early stent thrombosis occurrence and its significant mortality have been previously shown in the Pakistani PPCI population, with one tertiary-care study reporting 5.8% early stent thrombosis with a significant difference in mortality rates between early thrombosis and non-thrombosis patients.

Data collected were entered and analyzed in IBM SPSS Statistics version 26. The Shapiro-Wilk test was used to check the normality of continuous variables. The quantitative data were presented as mean $\pm$ SD for normally distributed data and as median and interquartile range for the non-normally distributed data. Categorical variables were presented as frequencies and percentages. The independent-samples t-test and Mann-Whitney U test were used for continuous variables and the chi-square test and Fisher's exact test for categorical variables to compare baseline characteristics between the ticagrelor and clopidogrel groups.

The early stent thrombosis rates were compared between the two treatment groups with the chi-square and Fisher's exact test. Odds ratio (OR) with 95% confidence interval (CI) was used to show the association between AT and early stent thrombosis. Univariate analysis was performed for the following potential predictors of early stent thrombosis: age, sex, Killip class, LVEF, symptom-to-door time, infarct-related artery, characteristics of the stents, and antiplatelet therapy. Clinical variables or those with p-values <0.10 in univariate analysis were included in the multivariable logistic regression to determine independent predictors of early stent thrombosis. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

In total, 93 patients with STEMI receiving primary PCI were enrolled, with 47 (50.5%) patients receiving ticagrelor and 46 (49.5%) patients receiving clopidogrel. The groups were similar with regard to demographic parameters, cardiovascular risk factors, cardiac hemodynamic parameters, and previous history of ischemic heart disease or PCI, respectively, and laboratory parameters at baseline, and no statistically significant differences were seen between the groups (Table 1).

There were also similar electrocardiographic, echocardiographic, and procedural parameters between treatment groups. The most common location of the infarcts was anterior, and the most common culprit vessel was the LAD. The mean LVEF was $47.1 \pm 8.6\%$ in the ticagrelor group and $45.9 \pm 9.1\%$ in the clopidogrel group. The majority of patients had drug-eluting stents, and there was a procedural success rate of more than 97% in both groups (Table 2).

Early stent thrombosis was seen in 2 (4.3%) patients receiving ticagrelor and 7 (15.2%) taking clopidogrel; the event rate was lower with ticagrelor, but not statistically significant, during 30-day follow-up ($p=0.091$). There was also a numerical advantage for ticagrelor in recurrent myocardial infarction, target-vessel revascularization, rehospitalization, and mortality, but no significant differences in major bleeding (Table 3).

Early stent thrombosis was significantly associated with Killip class III–IV, LVEF $<40\%$, and high thrombus burden in patients who developed it. Numerous factors were associated with arrhythmia, though none were statistically significant. (Table 4)

In univariate logistic regression, the odds for early stent thrombosis were greater in patients with Killip class III–IV, reduced LVEF, and a high thrombus burden. Multivariable analysis revealed that Killip class III–IV remained an independent predictor ($p=0.049$). The odds of thrombosis were higher with clopidogrel therapy than with ticagrelor, but the relationship was not statistically significant ($p=0.115$) (Table 5).

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n=93)

Variable	Ticagrelor (n=47) n(%) / Mean $\pm$ SD	Clopidogrel (n=46) n(%) / Mean $\pm$ SD	p-value
Age, years	56.8 $\pm$ 10.7	58.4 $\pm$ 11.2	0.477
Male sex	39 (83.0)	37 (80.4)	0.739
BMI, kg/m ²	26.4 $\pm$ 3.2	26.9 $\pm$ 3.5	0.471
Diabetes mellitus	18 (38.3)	20 (43.5)	0.615
Hypertension	22 (46.8)	24 (52.2)	0.609
Current smoking	25 (53.2)	23 (50.0)	0.759
Previous ischemic heart disease	8 (17.0)	10 (21.7)	0.603
Previous PCI	5 (10.6)	7 (15.2)	0.531
Family history of CAD	14 (29.8)	15 (32.6)	0.766
Systolic BP, mmHg	139.2 $\pm$ 21.4	141.6 $\pm$ 23.1	0.604
Diastolic BP, mmHg	82.4 $\pm$ 12.7	83.7 $\pm$ 13.1	0.625
Heart rate, bpm	82.6 $\pm$ 15.8	85.1 $\pm$ 16.4	0.456
Killip class III–IV	6 (12.8)	8 (17.4)	0.545
Symptom-to-door time, hours, median (IQR)	4.2 (2.8–6.7)	4.6 (3.0–7.1)	0.572
Hemoglobin, g/dL	13.7 $\pm$ 1.6	13.5 $\pm$ 1.7	0.553
Platelet count, $\times 10^9/L$	254.6 $\pm$ 58.2	249.8 $\pm$ 61.4	0.706
Serum creatinine, mg/dL, median (IQR)	1.0 (0.8–1.2)	1.0 (0.8–1.3)	0.812
Troponin-I, ng/mL, median (IQR)	5.8 (2.9–11.7)	6.2 (3.1–12.4)	0.741

Table 2. Electrocardiographic, Echocardiographic, and Procedural Characteristics

Variable	Ticagrelor (n=47) n(%) / Mean $\pm$ SD	Clopidogrel (n=46) n(%) / Mean $\pm$ SD	p-value
Anterior STEMI	25 (53.2)	23 (50.0)	0.760
Inferior STEMI	18 (38.3)	19 (41.3)	0.768
Other STEMI location	4 (8.5)	4 (8.7)	0.999
LVEF, %	47.1 $\pm$ 8.6	45.9 $\pm$ 9.1	0.511
LAD culprit artery	25 (53.2)	23 (50.0)	0.760
RCA culprit artery	16 (34.0)	17 (37.0)	0.765
LCX culprit artery	6 (12.8)	6 (13.0)	0.999
Multivessel coronary disease	19 (40.4)	21 (45.7)	0.607
High thrombus burden	12 (25.5)	14 (30.4)	0.601
Drug-eluting stent	44 (93.6)	43 (93.5)	0.999
Bare-metal stent	3 (6.4)	3 (6.5)	0.999
Number of stents, median (IQR)	1 (1–2)	1 (1–2)	0.687
Stent diameter, mm	3.05 $\pm$ 0.38	3.02 $\pm$ 0.41	0.711
Total stent length, mm, median (IQR)	28 (18–38)	30 (18–40)	0.593
Successful PCI	46 (97.9)	45 (97.8)	0.999

Table 3. Antiplatelet Therapy and 30-Day Clinical Outcomes

Outcome	Ticagrelor (n=47) n (%)	Clopidogrel (n=46) n (%)	p-value
Early stent thrombosis	2 (4.3)	7 (15.2)	0.091
Acute stent thrombosis (<24 h)	0 (0.0)	2 (4.3)	0.238
Subacute stent thrombosis (1–30 days)	2 (4.3)	5 (10.9)	0.267
Recurrent MI	2 (4.3)	6 (13.0)	0.143
Target-vessel revascularization	2 (4.3)	5 (10.9)	0.267
Major bleeding	2 (4.3)	1 (2.2)	0.615
Rehospitalization	4 (8.5)	8 (17.4)	0.218
All-cause mortality	1 (2.1)	3 (6.5)	0.359

Table 4. Association of Clinical and Procedural Variables with Early Stent Thrombosis

Variable	Stent thrombosis n (%)	No thrombosis n (%)	p-value
Age >60 years	6 (66.7)	32 (38.1)	0.099
Male sex	8 (88.9)	68 (81.0)	0.717
Diabetes mellitus	6 (66.7)	32 (38.1)	0.099
Hypertension	6 (66.7)	40 (47.6)	0.291
Current smoking	6 (66.7)	42 (50.0)	0.346
Previous IHD	3 (33.3)	15 (17.9)	0.373
Previous PCI	2 (22.2)	10 (11.9)	0.338
Killip III–IV	4 (44.4)	10 (11.9)	0.021
LVEF <40%	4 (44.4)	13 (15.5)	0.047
Symptom-to-door time >6 h	5 (55.6)	24 (28.6)	0.093
High thrombus burden	5 (55.6)	21 (25.0)	0.048
Multivessel disease	5 (55.6)	35 (41.7)	0.427
Ticagrelor therapy	2 (22.2)	45 (53.6)	0.072
Clopidogrel therapy	7 (77.8)	39 (46.4)	0.072

Table 5. Univariate and Multivariable Logistic Regression for Predictors of Early Stent Thrombosis

Predictor	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age >60 years	3.21 (0.76–13.54)	0.111	2.54 (0.53–12.21)	0.243
Diabetes mellitus	3.25 (0.78–13.55)	0.105	2.71 (0.56–13.16)	0.216
Killip III–IV	5.91 (1.39–25.14)	0.016	4.82 (1.01–22.97)	0.049
LVEF <40%	4.37 (1.05–18.18)	0.043	3.71 (0.80–17.25)	0.093
High thrombus burden	3.75 (1.01–13.91)	0.048	3.42 (0.85–13.77)	0.084
Symptom-to-door time >6 h	3.13 (0.79–12.43)	0.104	2.47 (0.56–10.87)	0.232
Clopidogrel vs. ticagrelor	3.99 (0.80–19.86)	0.091	3.76 (0.72–19.63)	0.115

DISCUSSION

The current study assessed the efficiency of ticagrelor versus clopidogrel in preventing early stent thrombosis in primary PCI patients with STEMI. The incidence of early stent thrombosis was lower with ticagrelor compared with clopidogrel (4.3% vs. 15.2%), representing a nearly 400% increase in the unadjusted odds of early stent thrombosis with clopidogrel. However, this difference failed to reach statistical significance ($p=0.091$), and the observed effect in this small sample may have been clinically significant. This lack of statistical significance may have been due to the small number of patients and to the overall small number of thrombotic events.

Our results support the findings of Hee et al. in their 2019 study comparing real-world STEMI patients undergoing primary PCI to which DAPT with either ticagrelor or clopidogrel, which demonstrated that ticagrelor-based DAPT was associated with better clinical outcomes than clopidogrel-based DAPT. Their study

showed decreased mortality with the use of ticagrelor, though the difference in stent thrombosis did not reach statistical significance.^[16] The association between ticagrelor and a numerically lower rate of early stent thrombosis was similar to our results, which did not reach statistical significance. The similarity could be due to the challenging nature of demonstrating statistical differences in observational cohorts for the uncommon endpoint.

However, Brener et al., in a 2019 real-world registry of ACS patients undergoing PCI, found that definite stent thrombosis was significantly less common with ticagrelor than with clopidogrel. But the difference was not statistically significant when only looking at the STEMI group. This subgroup finding was more similar to our experience, with both groups showing a numerical decrease, but not significant. The discrepancies between overall ACS populations and STEMI-specific cohorts can be attributed to several factors, including the sample size, the baseline risk, compliance with therapy, selection of therapy, and differences in endpoint definitions.^[17]

In 2020, Turgeon et al. published a large, population-based cohort of 11,185 patients with ACS who underwent PCI, in which ticagrelor did not significantly lower MACE compared to clopidogrel. Their analysis also did not show any statistically significant decrease in stent thrombosis, but ticagrelor was linked to more major bleeding and dyspnea. The conclusions drawn from these results are consistent with our main outcome, which was not statistically significant, and highlight the fact that the pharmacological benefits of ticagrelor do not necessarily reflect in a statistically significant improvement of all clinical outcomes in real-world populations.^[18]

The results of the TICA-KOREA 2019 randomized trial also offered a valuable contrasting point of view. In those with ACS who were treated invasively, ticagrelor failed to show a statistically significant improvement in the primary outcome of composite ischemic events and was linked to greater bleeding. This study did not limit analysis to “early stent thrombosis” following PPCI, but the findings emphasized the diversity of the ticagrelor benefit in different populations. These differences might be especially important in Asian populations, where body size, genetic factors that influence anti-platelet drug action, bleeding liability, and prescribing patterns are different from Western populations.^[19]

In 2020, the ALPHEUS trial was published, again showing that ticagrelor did not prove to be superior to clopidogrel for the prevention of periprocedural ischemic events in patients undergoing elective PCI. It was found that more intensive platelet inhibition does not always lead to fewer procedural ischemic events, while its population had a significant difference from our STEMI population. This is significant as the thrombotic environment is significantly greater with STEMI compared with elective PCI, which may explain why a numeric benefit of ticagrelor was noted in our study but failed to reach statistical significance.^[20]

The Ebeid et al. (2021) randomized study in 2021 supported our direction of effect, with participants achieving a higher score on the EDI-R questionnaire. Definite stent thrombosis occurred in 0% of those treated with ticagrelor during hospitalization and in 0% overall, versus 8% and 9% for those treated with clopidogrel in 200 patients who had STEMI and were undergoing primary PCI. It could be concluded that the difference was statistically significant. This could be because they experienced significantly more events than our cohort, making them more likely to find a difference in treatment. However, the direction of associations found in both studies suggests that ticagrelor could offer more protection from thrombotic events during the early post-primary PCI period.^[21]

In 2021, another network meta-analysis of 14 studies and 46,983 patients added to the evidence, supporting the potential anti-thrombotic effect of ticagrelor. The stent thrombosis rates were significantly lower with ticagrelor than clopidogrel. The pooled evidence was drawn from a heterogeneous population of patients with PCI and was not restricted to early post-STEMI thrombosis, however overall the results were directionally consistent with our lower event rate with ticagrelor. The larger aggregated sample size and the higher number of outcome events in the study likely

accounted for the higher pooled association compared to our study.^[13]

In 2021, a second extensive meta-analysis, indexed in 2022, was published that encompassed 270,937 patients across 10 clinical trials and 18 observational studies. Ticagrelor had significantly lower odds of stent thrombosis compared with clopidogrel in clinical trials. The observational data, however, did not show a significant decrease in stent thrombosis. This distinction was of special importance to our study as our observations also revealed a similar, albeit not statistically significant, numerical decrease. It was proposed that treatment selection, compliance, patient characteristics, and potential residual confounding can impact the observed efficacy of ticagrelor in the real-world setting.^[22]

In 2021, another de-escalation meta-analysis confirmed a biological benefit of more potent P2Y₁₂ inhibition in the high-risk time following ACS. Ticagrelor was associated with less stent thrombosis than clopidogrel. These results should be interpreted in the context of the bleeding risks associated with high-dose antiplatelet therapy, however. Major bleeding was low and not different between treatment groups, indicating that the observed numerical superiority of ticagrelor in reducing thrombotic events did not seem to be offset by an excess of major bleeding in our relatively short 30-day follow-up.^[23]

The 2021 published TALOS-AMI trial offered a valuable complementary result on the safety of stable patients receiving a switch from ticagrelor to clopidogrel one month after PCI. It was designed to accommodate the notion that the ischemic risk is highest early in the post-PCI period and then may shift to a balance between ischemic risk and bleeding risk. This notion is relevant to our work as our primary endpoint targeted the first 30 days, where potent P2Y₁₂ inhibition may be of particular significance as platelet activation, thrombus burden, endothelial injury, and procedural factors may all be relevant.^[24]

In addition, several clinical parameters were identified in our analysis that were associated with early stent thrombosis. After multivariable adjustment, Killip class III–IV was an independent predictor, but LVEF < 50% and high thrombus burden were associated with increased risk in univariate analysis. These findings were clinically plausible, as hemodynamic instability and large myocardial injury would represent severe infarction and a large intracoronary thrombus burden would be a component of the substrate for acute and subacute stent thrombosis. The failure of the Killip class III–IV to resolve after adjustment implied that the severity of the STEMI might be an independent risk factor for early thrombosis with the use of any particular P2Y₁₂ inhibitor.

In our study, the apparent beneficial effect of ticagrelor could be attributed to the fact that it directly and reversibly inhibits the P2Y₁₂ receptor and thus induces quicker and more sustained platelet inhibition compared with clopidogrel. This distinction is of special significance when primary PCI is considered, when fast platelet inhibition is desired. The confidence intervals for the treatment effect were wide, however, because of the relatively small number of thrombotic events observed in our study, the estimate is less precise. Therefore, the results from this study suggest a higher likelihood of the effect than a superiority result, and the approximately four-fold increase with clopidogrel should be viewed accordingly.

Overall, the results of the present study were generally consistent with the existing body of evidence that ticagrelor may offer superior protection against stent thrombosis compared with clopidogrel, albeit the magnitude and significance of this protection were highly variable across studies. There were conflicting findings from several real-world studies, while evidence from randomized trials and meta-analyses tended to support ticagrelor. This difference highlighted the need for such stratification for patient selection, adherence to treatment, thrombotic risk, bleeding risk, and treatment environment to choose a P2Y₁₂ inhibitor. Based on these findings, current PCI guidelines have recommended that ticagrelor or prasugrel may be considered reasonable alternatives to clopidogrel in ACS patients who are undergoing PCI, especially

for those for whom reducing ischemic events such as stent thrombosis is a priority.

The main advantage of the current study was the inclusion of a clinically relevant and potentially life-threatening outcome in the first 30 days after primary PCI. However, these results need to be considered in the context of the relatively small sample size, single-center, observational design, treatment-selection bias, and limited number of stent-thrombosis events. Larger prospective, preferably randomized studies in Pakistani STEMI patients are needed to establish if the observed numeric decrease with ticagrelor is statistically and clinically significant, with an acceptable bleeding risk.

Limitations: There were some limitations to the study. The study was also single-center and small (93 patients); this restricted the statistical power of the results and generalizability. The observational design may have resulted in selection and treatment-allocation bias because ticagrelor and clopidogrel were not randomly assigned. The low number of early stent-thrombosis events resulted in wide confidence intervals and limited the precision of the effect estimates. Objective assessment of adherence with antiplatelet therapy following discharge was not possible in all patients. Furthermore, the 30-day follow-up was merely a snapshot of early events, and provided no data on long-term ischemic or bleeding outcomes.

CONCLUSION

Ticagrelor was numerically less associated with early stent thrombosis than was clopidogrel in the primary PCI arm of STEMI. The difference observed was of clinical significance but not statistically significant. Killip class III–IV was determined as an independent predictor of early stent thrombosis. Multicentre randomised studies of larger size are needed to validate the relative effectiveness of ticagrelor and clopidogrel in this high-risk group.

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