Original Article

Comparison of the Efficacy in No-Reflow Prevention Between Ticagrelor and Clopidogrel in Diabetic Patients With STEMI

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ABSTRACT

Background: Even when epicardial blood flow is restored, achieving adequate perfusion to the microvascular level is the goal. The generous utilization of antithrombotics may facilitate bleeding. We aimed to compare the efficacy in preventing no-reflow between ticagrelor and traditional loading with clopidogrel in diabetic patients presenting with ST-segment-elevation myocardial infarction (STEMI) and to assess the safety of ticagrelor administration regarding the short-term bleeding risk.

Methods: The present single-center prospective randomized trial consecutively randomized 300 diabetic patients admitted to the emergency department with STEMI into 2 groups: ticagrelor and clopidogrel. All the patients underwent primary percutaneous coronary intervention (PCI), during which the thrombolysis in myocardial infarction (TIMI) flow grade and the myocardial blush grade (MBG) were recorded. We followed up on the patients for 3 months to detect short-term major adverse cardiovascular events (MACE) and bleeding events.

Results: The mean age of the studied population was 56 years, with a male predominance (70%). The median pain-to-door time was 8 hours. The no-reflow phenomenon was encountered more frequently in the clopidogrel group than in the ticagrelor group (37.3% vs 14%). Higher TIMI flow grades and MBGs were achieved in the ticagrelor group, and the difference was statistically significant. No significant differences, however, existed between the groups concerning MACE, stent thrombosis, and mortality. More bleeding episodes were recorded in the ticagrelor group but with no statistical significance.

Conclusions: Ticagrelor should be the first choice among P2Y12 inhibitors in the setting of primary PCI, especially in diabetic patients, due to its high efficacy and safety profile, even in elderly patients. ***(Iranian Heart Journal 2023; 24(4): 14-25)***

KEYWORDS: Ticagrelor, Clopidogrel, No-reflow, Bleeding

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Globally, acute myocardial infarction (MI) is the most common cause of mortality and a leading cause of morbidity. The provision of appropriate and abrupt therapy in terms of emergency revascularization can alter the patient's life span and quality of life. [1]

Primary percutaneous coronary intervention (PCI) as an emergency tool to restore myocardial perfusion is associated with improved quality of life and increased survival, with success rates exceeding 90%. Despite the successful restoration of epicardial blood flow in the culprit territory, some patients suffer inadequate tissue perfusion due to the no-reflow phenomenon, attributable to microvascular occlusion. [2-4]

The nature of the no-reflow phenomenon is not deeply understood and is believed to be multifactorial. Contributing factors in the evolution of the no-reflow phenomenon include vascular spasm, endothelial damage, and leukocyte sequestration. [5, 6]

Routine platelet inhibition using dual-antiplatelet therapy (Aspirin and P2Y12 inhibitors) is the standard level of care during primary PCI. Ticagrelor is an oral P2Y12 inhibitor administered once ST-segment-elevation myocardial infarction (STEMI) is diagnosed. Ticagrelor has more profound action, faster onset, shorter half-life, and faster recovery of platelet function than clopidogrel. [7]

The beneficial effects of antithrombotics in the setting of STEMI are beyond doubt. Nonetheless, many concerns have been raised regarding the increased bleeding risk. Some risk scores, including the CRUSADE risk score, have been validated to predict bleeding events. Major bleeding is the most common cause of the premature discontinuation of antithrombotics, which in turn causes a dramatic increase in major adverse cardiovascular events (MACE) and ischemic thrombotic events. [8, 9]

We performed the current investigation to judge the efficacy of ticagrelor in preventing the no-reflow phenomenon compared with traditional loading with clopidogrel in diabetic patients presenting with STEMI and to assess the safety of ticagrelor regarding the short-term bleeding risk.

METHODS

The inclusion criteria consisted of STEMI presentation, being a candidate for primary PCI, minimum age of 18 years, pre-existing or newly diagnosed diabetes mellitus (elevated HbA1c [≥6.5%], elevated fasting plasma glucose [≥126 mg/dL], and elevated 2-hour postprandial plasma glucose [≥200 mg/dL]), [10] and symptoms consistent with myocardial ischemia in the form of persistent chest pain and electrocardiographic (ECG) findings consistent with STEMI (ie, ST-segment elevation measured from the J point in the following settings: ≥2 contiguous leads with ST-segment elevation ≥2.5 mm in men <40 years old, >2 mm in men >40 years old, and >1.5 mm in women in leads V_2-V_3, and/or >1 mm in all the other leads. [11]

The exclusion criteria were composed of unwillingness to provide written informed consent, contraindications or intolerance to clopidogrel and ticagrelor, hematological disorders or bleeding diathesis, receiving thrombolytic reperfusion therapy, receiving oral anticoagulation therapy, and end-stage renal disease or being on hemodialysis.

Diabetic patients diagnosed with STEMI in the emergency department fulfilling the inclusion criteria were consecutively randomized into 2 parallel groups in a 1:1 ratio according to the type of P2Y12 inhibitor loading that they received: 150 patients loaded with clopidogrel (600 mg) and 150 patients loaded with ticagrelor (180 mg).

The primary endpoint was a comparison between clopidogrel and ticagrelor vis-à-vis the incidence of the no-reflow phenomenon, the thrombolysis in myocardial infarction (TIMI) flow grade, and the myocardial blush grade (MBG). The secondary endpoints were short-term (3 mon) MACE, composed of stent thrombosis, cerebrovascular stroke, and death, and bleeding events.

Three hundred patients with previously diagnosed or newly diagnosed diabetes mellitus who were determined to have STEMI in the emergency department of our tertiary center were consecutively recruited in our study. ECG was done within 10 minutes from admission to achieve a diagnosis of STEMI. Full history was taken from the patients regarding demographic characteristics and current or past medical or surgical diseases. The study population underwent general and local examinations. Venous access was achieved, and blood samples were withdrawn for blood sugar, complete blood count, cardiac biomarkers, and liver and kidney functions.

All the studied patients were given 300 mg of acetylsalicylic acid and randomized into 2 groups: clopidogrel (600 mg) and ticagrelor (180 mg).

The patients were admitted for primary PCI, performed by an expert interventional cardiologist who performs more than 75 primary PCI procedures per year. Before the primary PCI procedure, standard left and right coronary angiograms with at least 2 best projections were obtained for each patient. Tissue perfusion as an immediate outcome and one of the endpoints in this study was reassessed in at least 2 projections using the TIMI flow grade and MBG at a frame rate of 25 per second by 2 independent interventional cardiology experts.

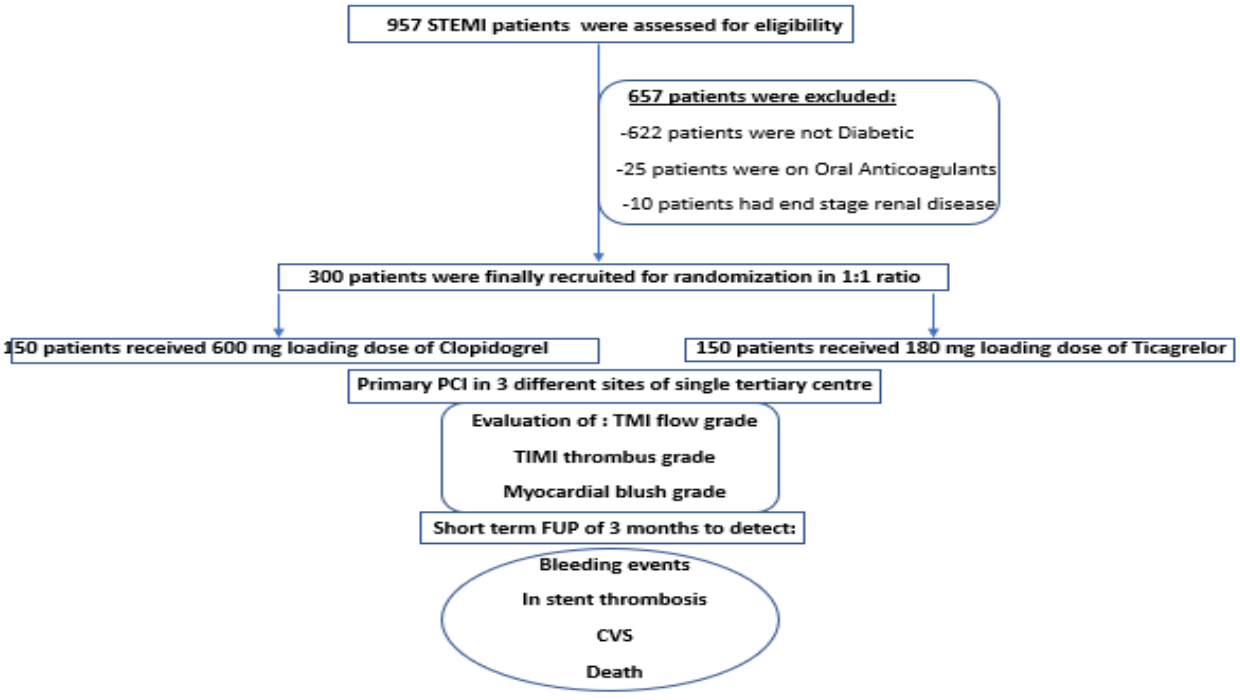

Figure 1: The image presents the diagrammatic flow of the studied patients.

TIMI flow grading was done as follows:
Grade 0 (no perfusion): no antegrade flow beyond the occlusion site
Grade I (penetration without perfusion): the passage of the contrast beyond the occlusion site but its failure to opacify the whole coronary bed for the duration of the cine angiographic sequence
Grade II (partial perfusion): the full opacification of the coronary bed (However, the rate of the entry of the contrast into the vessel distal to the occlusion site or its rate of clearance (or both) is slow compared with another perfused coronary bed.)
Grade III (complete perfusion): the excellent antegrade filling and clearance of the contrast from the coronary bed compared with the proximal non-obstructed segments or compared with another coronary bed [12]

MBG stratifies coronary flow as follows:
grade 0: no myocardial blush (or contrast density) or persisting blush (staining)
Grade I: minimal blush
Grade II: moderate myocardial blush but not as that obtained in the non–infarct-related artery
Grade III: normal blush [13]

Angiographic thrombus burden was graded as follows:
Grade 0: no thrombus
Grade I: possible thrombus
Grade II: the greatest diameter of the thrombus <1/2 the vessel diameter
Grade III: the greatest diameter >1/2 to <2 the vessel diameter
Grade IV: the greatest diameter >2 the vessel diameters
Grade V: total vessel thrombotic obstruction.

The no-reflow phenomenon was defined as a TIMI score of below III and an MBG of 0, I, or II in the absence of a flow-limiting dissection or a distal vessel embolic occlusion. [14]
Major bleeding was defined as any form of intracranial hemorrhage, bleeding with a drop-in hemoglobin level of ≥5 g/dL or a ≥15% reduction in hematocrit or fatal bleeding.
The CRUSADE risk score was utilized to estimate the bleeding risk for the recruited patients as follows:
CRUSADE score ≤20: very low
CRUSADE score =21–30: low
CRUSADE score =31–40: moderate
CRUSADE score =41–50: high
CRUSADE score >50: very high [8,15]

All the patients were admitted to the coronary care unit for at least 48 hours and underwent pre-discharge echocardiography for the evaluation of left ventricular (LV) systolic function via the modified Simpson method, resting wall motion abnormalities, and valvular involvement. Upon discharge, all the studied patients were followed up on for 3 months in the outpatient department for the incidence of MACE (stent thrombosis, cerebrovascular stroke, and death) or bleeding events. [16]

Statistical Analysis: Data were collected, coded, revised, and entered into the Statistical Package for Social Science (IBM SPSS), version 20. The data were presented as numbers and percentages for qualitative data and as means, standard deviations, and ranges for quantitative data with parametric distributions. The χ^2 test was used to compare the 2 groups with qualitative data, and the comparison between the groups with quantitative data and parametric distributions was done using the independent *t* test. A multivariate logistic regression analysis was applied to assess the predictors of the no-reflow phenomenon among the studied patients. The confidence interval was set to 95%, and the margin of

error accepted was set to 5%. Accordingly, a *P* value was considered significant as follows:

P > 0.05: non-significant (NS)
P < 0.05: significant (S)
P < 0.01: highly significant (HS)

RESULTS

The current study recruited 300 STEMI patients with a mean age of 56 years, with a male predominance (70%). All the studied patients had diabetes mellitus, 60% were active smokers, 52% were hypertensive, and 44% were dyslipidemic. The median pain-to-door time was 8 hours, ranging from 1 hour to 48 hours (Table 1).

Table 1: The demographic data among the studied population

Demographic Characteristic		No. = 300
Sex	female	88 (29.3%)
	male	212 (70.7%)
Age, y	mean ± SD	56.17 ± 9.17
	range	30 – 80
Smoking		181 (60.3%)
HTN		156 (52.0%)
PTD (h)	median (IQR)	8 (5 – 18)
	range	1 – 48
IHD		32 (10.7%)
Family history of CVD		42 (14.0%)
Dyslipidemia		133 (44.3%)

HTN: hypertension; PTD: pain-to-door time; IHD: ischemic heart disease; CVD: cardiovascular disease

The patients were stratified into 2 groups according to the type of oral P2Y12 inhibitor administered. No significant difference was witnessed between the 2 groups regarding demographic characteristics and risk factors. Blood sugar control was comparable between both groups, as the mean HbA1c level was 9.33 in the clopidogrel group and 9.24 in the ticagrelor group. Additionally, the mean pain-to-door time was very close between the 2 groups: 7 hours in the clopidogrel group and 8 hours in the ticagrelor group (Table 2).

Comparisons between the groups regarding angiographic findings showed that the left anterior descending coronary artery was the most commonly culprit vessel encountered (78% of the clopidogrel group vs 70% of the ticagrelor group), followed by the right coronary artery and the left circumflex coronary artery. Moreover, 78% of the patients in the clopidogrel group had totally thrombotic culprit vessels compared with 83% of the ticagrelor group, with no statistically significant difference (Table 3).

The post-PCI TIMI flow grade and MBG were recorded for every patient, and a highly statistically significant difference was noted between the 2 groups regarding the TIMI flow grade since TIMI III was achieved in 86% of the clopidogrel group as opposed to 64% of the ticagrelor group. A similarly significant difference was noted regarding MBG since 86% of the ticagrelor group achieved MBG III compared with 62% of the clopidogrel group. The no-reflow phenomenon was encountered more frequently in the clopidogrel group than in the ticagrelor group (37.3% vs 14%), and the difference was statistically significant. Intracoronary drugs were administered more frequently in the clopidogrel group than in the ticagrelor group (37.3% vs 23.3%). The most commonly administered medication was tirofiban, followed by nitroglycerin, adrenaline, adenosine, and verapamil (Table 4).

Postprocedural bedside echocardiography was done for the entire study population to demonstrate LV systolic function. The mean left ventricular ejection fraction (LVEF) was 40.5% in the clopidogrel group and 42.55% in the ticagrelor group; the difference was statistically meaningful. The CRUSADE risk score was calculated for every patient. In the clopidogrel group, 22.7% had low, 47.3% had moderate, 26% had high, and 4%

had very high bleeding risks. In the ticagrelor group, 27.3% had low, 54% had moderate, 11.3% had high, and 7.3% had very high bleeding risks (Table 4).

We followed up on the patients for 3 months to record MACE and bleeding events. With respect to bleeding, 7 patients in the clopidogrel group had bleeding events (3 cases were categorized as major bleeding), and 14 patients in the ticagrelor group had bleeding events (6 cases were categorized as major bleeding). Bleeding events occurred more frequently in the ticagrelor group but with no statistical significance. Two patients in the clopidogrel group had in-stent thrombosis in the first 3 months after PCI, whereas no patients in the ticagrelor group experienced this complication. During the follow-up, 10 patients were switched from ticagrelor to clopidogrel due to annoying dyspnea, while 12 patients were switched from clopidogrel to ticagrelor. Two patients in the clopidogrel group had cerebrovascular stroke in the first 3 months following PCI, as opposed to only 1 patient in the ticagrelor group. Six patients died during the study time-span: 2 patients from acute coronary syndrome, 1 patient from massive cerebrovascular stroke, and 2 patients from bleeding and anemia (Table 5).

A sub-analysis was conducted for the elderly cohort of patients (≥70 y), which revealed that the ticagrelor group had more bleeding events but fewer no-reflow events. Nevertheless, the difference was not statistically relevant.

Table 2: The comparison between the clopidogrel and ticagrelor groups regarding demographic data

		The Clopidogrel Group (No. = 150)	The Ticagrelor Group (No. = 150)	Test value	*P* value	Sig.
Sex	Female Male	39 (26.0%) 111 (74.0%)	49 (32.7%) 101 (67.3%)	1.608*	0.205	NS
Age, y	Mean ± SD Range	56.21 ± 8.72 30-74	56.14 ± 9.62 31-80	0.063•	0.950	NS
Smoking		87 (58.0%)	94 (62.7%)	0.682*	0.409	NS
Hypertension		81 (54.0%)	75 (50.0%)	0.481*	0.488	NS
Ischemic heart disease		20 (13.3%)	12 (8.0%)	2.239*	0.135	NS
Family history		20 (13.3%)	22 (14.7%)	0.111*	0.739	NS
Dyslipidemia		63 (42.0%)	70 (46.7%)	0.662*	0.416	NS
HbA1C	Mean ± SD Range	9.33 ± 1.22 7.3-13	9.24 ± 1.56 6.7-14.8	0.586•	0.558	NS
Pain-to-door time	Median (IQR)	7 (4 - 24)	8 (6 - 12)	-0.961‡	0.337	NS
	Range	1 – 48	1 – 48			

P > 0.05: nonsignificant (NS); *P* < 0.05: significant (S); *P* < 0.01: highly significant (HS)

*: the χ2 test; ‡: the Mann-Whitney test

Table 3: The comparison between the clopidogrel and ticagrelor groups regarding coronary angiographic data

		The Clopidogrel Group		The Ticagrelor Group		Test value*	*P* value	Sig.
		No.	%	No.	%			
STEMI	Anterior	78	52.0%	70	46.7%	0.853	0.356	NS
	Inferior	64	42.7%	67	44.7%	0.122	0.727	NS
	Posterior	2	1.3%	7	4.7%	2.864	0.091	NS
	Lateral	6	4.0%	2	1.3%	2.055	0.152	NS
	Inferoposterolateral	0	0.0%	2	1.3%	2.013	0.156	NS
	Posterolateral	0	0.0%	2	1.3%	2.013	0.156	NS
Culprit Vessel	LAD	78	52.0%	72	48.0%	0.480	0.488	NS

	RCA	48	32.0%	54	36.0%	0.535	0.465	NS
	LCX	16	10.7%	15	10.0%	1.091	0.296	NS
	Diagonal	2	1.3%	2	1.3%	0.000	1.000	NS
	OM	4	2.7%	5	3.3%	0.115	0.735	NS
	Ramus	0	0.0%	2	1.3%	2.013	0.156	NS
	LAD + D1	2	1.3%	0	0.0%	2.013	0.156	NS
Other Vessels	No	66	44.0%	73	48.7%	0.657	0.418	NS
	Yes	84	56.0%	77	51.3%			
TIMI thrombus grade	TIMI III	22	14.7%	17	11.3%	0.737	0.391	NS
	TIMI IV	50	33.3%	50	33.3%	0.000	1.000	NS
	TIMI V	78	52.0%	83	55.3%	0.335	0.563	NS

P > 0.05: nonsignificant (NS); *P* < 0.05: significant (S); *P* < 0.01: highly significant (HS)
*: the χ2 test
STEMI: ST-segment-elevation myocardial infarction; TIMI: thrombolysis in myocardial infarction; LAD: Left anterior descending coronary artery; LCX: Left circumflex coronary artery; RCA: Right coronary artery; D1: First diagonal

Table 4: The comparison between the clopidogrel and ticagrelor groups regarding the no-reflow phenomenon (TIMI flow and MBG), echo ejection fraction, and the CRUSADE risk score

		The Clopidogrel Group (No. = 150)	The Ticagrelor Group (No. = 150)	Test value	*P* value	Sig.
No. of Stents	Median (IQR)	1 (1 - 2)	1 (1 - 2)	-0.180‡	0.857	NS
	Range	0 – 3	0 – 3			
The No-Reflow Phenomenon	No	94 (62.7%)	129 (86.0%)	21.402*	0.000	HS
	Yes	56 (37.3%)	21 (14.0%)			
Intracoronary Drugs	No	94 (62.7%)	115 (76.7%)	6.956*	0.008	HS
	Yes	56 (37.3%)	35 (23.3%)			
Tirofiban		48 (32.0%)	35 (23.3%)	2.815*	0.093	NS
Adrenaline		9 (6.0%)	3 (2.0%)	3.125*	0.077	NS
Nitroglycerine		10 (6.7%)	0 (0.0%)	10.345*	0.001	HS
Adenosine		3 (2.0%)	0 (0.0%)	3.030*	0.082	NS
Verapamil		2 (1.3%)	0 (0.0%)	2.013*	0.156	NS
TIMI Flow Grade	TIMI 0	3 (2%)	2 (1.3%)	21.673*	0.000	HS
	TIMI I	17 (11.3%)	5 (3.3%)			
	TIMI II	34 (22.7%)	14 (9.3%)			
	TIMI III	96 (64.0%)	129 (86.0%)			
MBG	Grade 0	6 (4.0%)	2 (1.3%)	24.408*	0.000	HS
	Grade I	24 (16.0%)	5 (3.3%)			
	Grade II	27 (18.0%)	14 (9.3%)			
	Grade III	93 (62.0%)	129 (86.0%)			
Echo Ejection Fraction	Mean ± SD	40.50% ± 7.93 %	42.55% ± 8.88 %	-2.111•	0.036	S
	Range	20 – 55 %	25 – 70 %			
CRUSADE Risk Score	Low	34 (22.7%)	41 (27.3%)	11.425*	0.010	S
	Moderate	71 (47.3%)	81 (54.0%)			
	High	39 (26.0%)	17 (11.3%)			
	Very high	6 (4.0%)	11 (7.3%)			

P > 0.05: nonsignificant (NS); *P* < 0.05: significant (S); *P* < 0.01: highly significant (HS)
*: the χ2 test;•: the independent *t* test; ‡: the Mann-Whitney test
TIMI: thrombolysis in myocardial infarction; MBG: myocardial blush grade

Table 5: The comparison between the clopidogrel and ticagrelor groups regarding bleeding, in-stent thrombosis, stroke, and death

		The Clopidogrel Group		The Ticagrelor Group		Test value*	*P* value	Sig.
		No.	%	No.	%			
Bleeding	No	143	95.3%	136	90.7%	2.509	0.113	NS
	Yes	7	4.7%	14	9.3%			
Stratification of Bleeding	Minor	4	57.1%	8	57.1%	0.000	1.000	NS
	Major	3	42.9%	6	42.9%			
In-Stent Thrombosis	No	148	98.7%	150	100.0%	2.013	0.156	NS
	Yes	2	1.3%	0	0.0%			
Shift to Another Antiplatelet	No	138	92.0%	140	93.3%	0.196	0.658	NS
	Yes	12	8.0%	10	6.7%			
Death	No	146	97.3%	148	98.7%	0.680	0.409	NS
	Yes	4	2.7%	2	1.3%			
Cerebrovascular Stroke	No	148	98.7%	149	99.3%	0.337	0.562	NS
	Yes	2	1.3%	1	.7%			

P > 0.05: nonsignificant (NS); *P* < 0.05: significant (S); *P* < 0.01: highly significant (HS)
*: the χ2 test

Table 6: The comparison between the clopidogrel and ticagrelor groups in patients ≥ 70 years regarding TIMI flow, MBG, and bleeding events

		The Clopidogrel Group		The Ticagrelor Group		Test value*	*P* value	Sig.
		No.	%	No.	%			
TIMI Thrombus Grade	TIMI III	3	27.3%	1	7.7%	3.524	0.172	NS
	TIMI IV	1	9.1%	5	38.5%			
	TIMI V	7	63.6%	7	53.8%			
The No-Reflow Phenomenon	No	5	45.5%	10	76.9%	2.517	0.113	NS
	Yes	6	54.5%	3	23.1%			
TIMI Flow Grade	TIMI 0	0	0.0%	0	0.0%	2.719	0.257	NS
	TIMI 1	3	27.3%	1	7.7%			
	TIMI 2	3	27.3%	2	15.4%			
	TIMI 3	5	45.5%	10	76.9%			
MBG	Grade 0	3	27.3%	0	0.0%	5.203	0.158	NS
	Grade 1	2	18.2%	1	7.7%			
	Grade 2	1	9.1%	2	15.4%			
	Grade 3	5	45.5%	10	76.9%			
Bleeding	No	8	72.7%	7	53.8%	0.906	0.341	NS
	Yes	3	27.3%	6	46.2%			
Stratification of Bleeding	Minor	0	0.0%	3	50.0%	2.250	0.134	NS
	Major	3	100.0%	3	50.0%			

P > 0.05: nonsignificant (NS); *P* < 0.05: significant (S); *P* < 0.01: highly significant (HS)
*: the χ2 test

TIMI: thrombolysis in myocardial infarction; MBG: myocardial blush grade

DISCUSSION

The current study compared the efficacy between the preprocedural loading of ticagrelor and clopidogrel among diabetic STEMI patients treated via primary PCI in preventing the no-reflow phenomenon, stent thrombosis, and bleeding events. We randomized the study population into 2 groups: clopidogrel and ticagrelor.

Previous studies have confirmed the efficacy of ticagrelor over clopidogrel in treating patients with acute coronary syndromes, in

addition to the more consistent therapeutic effects of the former on platelet inhibition. [17] This superiority of ticagrelor is thought to be reflected in angiographic outcomes in STEMI patients. Still, this privilege could come at the expense of more bleeding tendencies. In our study, all the randomized patients were diabetic, either on treatment or newly diagnosed. The idea behind this inclusion criterion was that diabetes mellitus is a major risk factor for thrombotic and bleeding events.

We encountered the no-reflow phenomenon more frequently in the clopidogrel group than in the ticagrelor group (37.3% vs 14%), and this difference was statistically highly significant (P = 0.001). In regard to the TIMI flow grade, 86% of the ticagrelor group achieved TIMI III compared with 64% of the clopidogrel group, with the difference constituting statistical significance (P = 0.001). We detected the same angiographic difference between the 2 groups concerning MBG since MBG III was achieved in 86% of the ticagrelor group compared with 62% of the clopidogrel group, and this difference was highly significant. We can, thus, conclude that a more desirable acute angiographic outcome was achieved more frequently and effectively in the ticagrelor group than in the clopidogrel group. This angiographic finding reflected in postprocedural LV systolic function insofar as the mean LVEF in the clopidogrel group was 40.50% ± 7.93% compared with 42.55% ± 8.88% in the ticagrelor group (P = 0.03).

Our study findings are concordant with the data released by Wang et al [18] in their study on STEMI patients undergoing primary PCI. They reported that ticagrelor administration, by comparison with clopidogrel administration, resulted in a higher magnitude of ST-segment resolution, a better MBG, and a higher TIMI flow grade. The same outcome was confirmed by Kim et al, [19] who found that ticagrelor reduced microvascular obstruction and minimized infarct size as judged by cardiac magnetic resonance imaging. The authors concluded that this protective effect was independent of drug-mediated platelet suppression. Our study findings also chime with an investigation by Tang et al, [20] who reported that ticagrelor reduced the need for glycoprotein IIb/IIIa inhibitors in STEMI patients compared with conventional clopidogrel loading. Our results are also in line with a Chinese meta-analysis of 14 randomized controlled trials and 1 observational study that depicted the superiority of ticagrelor in preventing the no-reflow phenomenon and reducing MACE. [21]

Our results, however, do not agree with those reported by Di Vito et al, [22] who stated that reperfusion angiographic parameters and ST-segment resolution were comparable between their clopidogrel and ticagrelor groups. In addition, Armstrong et al [23] demonstrated no superiority for ticagrelor in terms of ST-segment resolution as a marker of successful reperfusion. This discrepancy could be explained by what previous research has noted, suggesting that effective platelet suppression is not fully achieved until 2 hours after ticagrelor loading in nearly two-thirds of patients, and the co-administration of pain killers (eg, morphine) may delay ticagrelor absorption. [24, 25]

In the current study, we detected no statistically significant differences between the 2 groups vis-à-vis the incidence of stent thrombosis, stroke, and mortality (P = 0.15, P = 0.56, and P = 0.4, respectively). These findings match a meta-analysis published in 2018 regarding the choice among P2Y12 inhibitors following PCI, showing no differences in all-cause mortality, MACE, and stent thrombosis between ticagrelor and clopidogrel. [26]

In our study, bleeding events, whether minor or major, were witnessed more frequently

with ticagrelor than with clopidogrel; however, the difference was not statistically significant. These data are in agreement with an investigation by Wallentin et al, [27] who showed no significant differences between ticagrelor and clopidogrel regarding the rates of major bleeding as defined by TIMI criteria. These results were consistent among the studied subgroups without heterogeneity except for the body mass index. In contrast, a meta-analysis by Guan et al [26] showed higher rates of major and minor bleeding in the ticagrelor group than in the clopidogrel group; nonetheless, there was no statistically significant difference as regards life-threatening bleeding.

Our sub-analysis, limited to elderly patients (≥70 y), yielded no statistically significant differences between ticagrelor and clopidogrel with regard to the no-reflow phenomenon, stent thrombosis, and bleeding events despite the numerical superiority of ticagrelor in improving angiographic outcomes and numerically more frequent bleeding events. Our findings match the recently published SWEDEHEART registry, which compared the effects of clopidogrel and ticagrelor on acute coronary syndromes in elderly patients (≥80 y) and reported no difference regarding the primary ischemic outcome between the 2 groups. [28] Our results also chime with those reported by the PLATO trial, where no significant increase was noted in major bleeding episodes among patients receiving ticagrelor, regardless of their age group. [29]

Limitations

The salient limitation of the present study is its single-center design with a relatively small sample size. Another weakness of note in our investigation is the need for longer follow-ups and the utilization of more accurate parameters of microvascular perfusion (eg, cardiac magnetic resonance imaging and contrast echocardiography).

CONCLUSIONS

Ticagrelor should be the first choice among P2Y12 inhibitors in the setting of primary PCI especially in diabetic patients for its high efficacy and safety profile, even in elderly patients.

Declarations

Ethical approval and consent to participate:
The Research Ethics Committee of the Faculty of Medicine, Ain Shams University, reviewed and approved the study protocol.
The committee adheres to the guidelines of the International Council of Harmonization (ICH), the Islamic Organization of Medical Sciences (IOMS), the United States Office of Human Research Protection, and the United States Code of Federal Regulations and operates under federal-wide assurance (No. FWA 000017585). The committee does not declare the names of its members according to the university's standard operating procedures. The data of the study population were presented after informed written consent had been obtained from every participating patient. The patients received explanations about all the steps of the research and reassurances regarding the protection of their privacy and confidentiality.

Consent for Publication: Not applicable

Availability of Data and Material: All data, including angiograms and stored echocardiographic loops, are available with the authors and in the Ain Shams University Cath Lab and echocardiography records.

Conflict of Interest: All the authors declare that there are no conflicts of interest.

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