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REAL-WORLD SAFETY AND EFFICACY OF TICAGRELOR IN PATIENTS WITH ST SEGMENT ELEVATION MYOCARDIAL INFARCTION AT ASSIUT UNIVERSITY HEART HOSPITAL

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Objectives: *The new generation antiplatelets are generally recommended by the current US and European guidelines. This article aimed to address the efficacy and safety of using ticagrelor in patients with ST-elevated acute coronary syndromes.*
Methods: *This was a prospective observational study on 120 patients admitted to the Cardiology Care Unit of Assiut University Hospital with ST-segment elevation acute coronary syndrome, who were admitted for urgent revascularization and received aspirin and the P2Y12 antagonist ticagrelor. The patients were followed for three months between May 2018 and September 2019. The primary efficacy end point was the incidence of major adverse cardiovascular events (MACE).*
Results: *At three months, the primary efficacy end point, a composite of cardiovascular death, myocardial infarction, or stroke - occurred in 11/120 (9.2%) patients. The primary safety end point, the incidence of major bleeding, was observed in two patients (1.7%) with no fatal bleedings. Minor and minimal bleeding occurred in 2.5% and 20.8% of patients, respectively. Other efficacy endpoint was myocardial infarction 4.2% and stent thrombosis (1.7%). Severe dyspnea found in 5.0% patients and led to 1.7% ticagrelor discontinuation. Multivariate regression analysis revealed no association between bleeding and patients' age, sex nor IV administration of glycoprotein IIb/IIIa inhibitor.*
Conclusion: *The MACE with ticagrelor was higher than previously reported in most studies. Dyspnea rate was higher and more pronounced than bleeding rate. The majority of bleeding cases was minimal with no fatal major bleeding and no bleeding led to comorbidity.*

INTRODUCTION

Ischemic heart disease (IHD) is considered the single leading cause of death worldwide which accounted for a combined 15.2 million deaths in 2016[1]. Egypt is ranked third in IHD-related deaths among lower-middle-income countries according to the data of the World Health Organization 2010[2]. Dual antiplatelet therapy (DAPT) has a mandatory role in the management of IHD patients for its proven benefit of prevention of further ischemic cardiac events and reduction in mortality rates[3].

Aspirin and clopidogrel DAPT have being used as the mainstay DAPT in Egypt; yet many fundamental genetic and clinical problems exist[4]. Clopidogrel has a relatively low bioavailability in which less than 10%–15% of the administered dose becomes an active P2Y12 inhibitor and plasma concentration is further decreased in low creatinine clearance[5&6]. In addition to the slow onset of

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platelet inhibition and different genotyping with high rate of CYP2C19 loss-of-function (LOF) alleles in Egyptian individuals[7]. This genotyping manifested as delayed onset/offset of action and incomplete inhibition of platelet aggregation[7&8]. The new generation of P_2Y_{12} inhibitor antiplatelet ticagrelor and prasugrel are generally recommended by the current American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) over clopidogrel for ACS management[3&9].

Ticagrelor is a reversible and direct-acting antiplatelet that provides rapid inset/offset onset of action with more pronounced and consistent P2Y12 inhibition[10]. In a broad population of patients with acute ST-elevated myocardial infarction (STEMI) managed by primary percutaneous coronary intervention (PPCI), ticagrelor reduced death risk resulting from vascular causes, myocardial infarction (MI), or stroke during first year of index event without increasing the overall risk of major bleeding[11]. There were also reductions in cardiovascular and total mortality, MI, and stent thrombosis[12].

The recent introduction of ticagrelor in the Egyptian market along with the current global guidelines drove physicians to substitute clopidogrel with ticagrelor for many patients. However, real-world evidence of efficacy and safety and therapeutic response of ticagrelor in Egyptian patients with STEMI who are managed by PPCI is limited.

This study aimed to explore and monitor the safety and efficacy of ticagrelor in Egyptian patients with STEMI and treated with PPCI at Assiut University Heart Hospital.

Ethical approval

This study was approved by the Research Ethics Committee at the Faculty of Medicine of Assiut University (reference number IRB 17100775). The informed consent obtained from the participants verbally because the study comprised observation of the routine medical care and a review of patients' medication profiles with no intervention imposed by authors.

PATIENTS AND METHODS

This was a prospective observational study that was conducted on patients admitted to the Coronary Critical Care Unit (CCU) of Assiut University Heart Hospital after undergoing PPCI in the Catheterization Unit (CU) in the same hospital. Each patient was followed for three months between May 2018 and September 2019. The CCU comprised three rooms each has a capacity of 4-6 beds.

Patients were eligible for the study if they were adult and admitted to the CCU with new STEMI and treated with PPCI within 12 hrs after symptoms onset. Patients were diagnosed and treated according to the usual clinical practice in the institution. An electrocardiogram was initially recorded for each patient. After the STEMI diagnosis is confirmed, all patients received PPCI. The PPCI (defined as PCI within the first 12 hrs after onset of symptom) was performed by three physicians via femoral access and manual compression was used after sheath removal.

Patients who had any contraindications to the use of ticagrelor (such as hypersensitivity, active pathological bleeding, history of cerebral hemorrhage, intracranial hemorrhage, hemorrhagic stroke and moderate to severe liver disease) as well as those prescribed fibrinolytic therapy within 24 hrs before PCI or oral anticoagulation therapy or strong CYP3A4 inhibitors such as (e.g. ketoconazole, clarithromycin, nefazodone, ritonavir and atazanavir) therapy were excluded from the study[13].

The patients' medication profiles were clinically reviewed during the CCU stay and at the discharge by the researcher (first author) who is a trained clinical pharmacist with five years of work expertise at the Cardiology Department at the time of this study.

Patients were then followed for three months after the index date (in-hospital initiation of ticagrelor) using phone interviews. The minimum follow-up period was one month.

During the index admission, a 300 mg loading dose of aspirin was given to all patients who were treatment naïve. All patients were pre-treated with a loading dose of ticagrelor 180 mg before PCI. At the discretion of the attending physician, patients were discharged

on ticagrelor 90 mg bid or clopidogrel 75 mg daily in addition to aspirin (75-100 mg once daily).

Therefore, patients who were discharged on clopidogrel and/or stopped ticagrelor during hospitalization - because of severe adverse effects of ticagrelor or any other reason described in the results section- were excluded. Patients who discontinued ticagrelor before one month or lost in follow up within the first month were also excluded (Fig. 1).

All patients administered the following parenteral medications before and during PPCI: iopromide dye, lidocaine, heparin, chlor-pheniramine, hydrocortisone and prophylactic antimicrobials (amoxicillin clavulinate and gentamicin). Intracoronary tirofiban antiplatelet was used if needed.

The major prescribed medication classes after PPCI during CCU admission were angiotensin- converting enzyme inhibitors, beta-blockers, statins, nitrates, diuretics, trimetazidine, nicorandil, antacids and antimicrobials. Tirofiban, calcium channel antagonists and ivabradine were prescribed for some patients.

The collected data during hospital stay included demographic details, admission and discharge dates, chief complaint, diagnosis, patient and family history of cardiovascular diseases, comorbid conditions, hemodynamic measurements and other laboratory investigations, encountered ticagrelor-related adverse effects, and causes of death (if any).

Patients without complications are often discharged within 2-3 days after admission if they had fulfilled the discharge criteria.

Study outcomes

The primary efficacy outcome for ticagrelor treatment was evaluated by reporting the incidence of major adverse cardiovascular events (MACE), which is a composite endpoint of death from vascular causes, MI, or ischemic stroke at three months follow-up. The primary safety outcome for ticagrelor was the incidence of major bleeding. Secondary efficacy outcome was the occurrence of stent thrombosis and MI alone. Secondary safety outcome was severe dyspnea, dyspnea led to ticagrelor discontinuation and minor bleeding. Ticagrelor-associated dyspnea was identified using the criteria published by Parodi *et al.* 2015[14]. Medical events recorded in hospital were not included in primary and secondary outcome measures.

Outcome measures

Because of the observational nature of the study, all the outcome measures including cardiovascular death, myocardial infarction, stent thrombosis and ischemic stroke were diagnosed and documented in patient's profiles by the treating physicians and acknowledged in the study. However, bleeding as a safety outcome is defined according to the Bleeding Academic Research Consortium published in 2011[15]. Major fatal bleeding was defined as bleeding that directly causes death with no other explainable cause. Major non-fatal was defined as overt bleeding plus hemoglobin drop ≥3 to <5 g/dL or any transfusion with overt bleeding (type 3a) or overt bleeding plus hemoglobin drop ≥5 g/dL or cardiac tamponade or bleeding requiring surgical intervention for control (excluding dental/nasal/skin/ hemorrhoid) or bleeding requiring intravenous vasoactive drugs (type 3b) or intracranial hemorrhage or intraocular bleed compromising vision (type 3c). Minor bleeding included any bleed requiring medical intervention to stop or treat.

The Thrombolysis in Myocardial Infarction (TIMI) risk score for STEMI was used for mortality risk estimates in the study patients[16].

RESULTS AND DISCUSSION

Results

Of 169 eligible patients for the study, 17 patients were dropped out during the hospital stay. Then further 32 patients left the study before the end of the first month of follow-up. The reasons of taking out those patients are listed in figure 1. A total of 120 patients completed at least one-month study duration, of whom 109 patients completed the three months follow-up. Patients who had prematurely discontinued ticagrelor intake were 11/120 (9.2%). The mean follow-up period was 84 days. The age of patients ranged from 30 to 87 years (mean = 55.4±2.06) and 76.7% were males. Illiterate patients and smokers accounted for 52.5% and 64.2% of the study population, respectively. Patients diagnosed with anterior STEMI were 59.2% (Table 1).

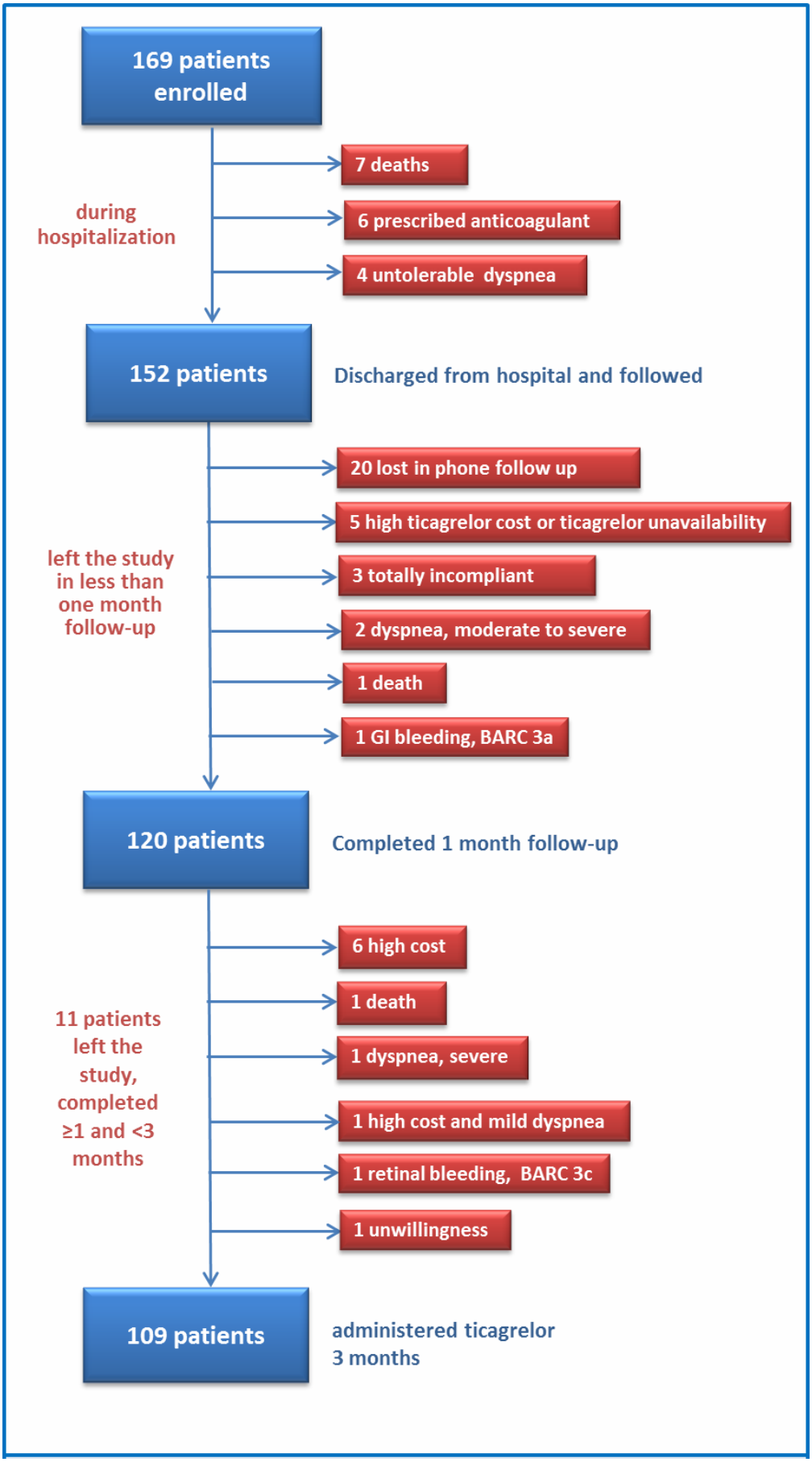

Fig. 1: Flow chart. BARC; Bleeding Academic Research Consortium, GI; Gastrointestinal.

Table 1: Patients' baseline characteristics.

	Frequency (%) *n*= 120	Mean (Standard deviation) *n*= 120
Age		55.4 ± 2.06
Weight (kg)		79.6 ± 3.0
BMI (kg/cm²)		28.4 ± 0.9
Sex		
Male	92 (76.7)	
Female	28 (28.3)	
Education		
Illiterate	63 (52.5)	
Primary	4 (3.3)	
Vocation	14 (11.7)	
University	26 (22.7)	
Past medical history		
Diabetes Mellitus	38 (31.7)	
Hypertension	37 (30.8)	
Cardiovascular	23 (19.2)	
Previous PCI	10 (8.3)	
Unstable angina	8 (6.7)	
Previous MI	5 (4.2)	
CSA	5 (4.2)	
Arrhythmia	1 (0.8)	
Dyspnea	10 (8.3)	
Liver dysfunction	3 (2.5)	
Non-hemorrhagic stroke	3 (2.5)	
Smoking status		
Current smoker	77 (64.2)	
Heavy smokers	66 (55)	
Moderate smokers	10 (8.3)	
Mild smokers	1 (0.8)	
X- smoker	7 (5.8)	
STEMI type		
Anterior	71 (59.2)	
Inferior	30 (25)	
Infero-posterior	19 (15.8)	
Culprit vessel		
LAD	73 (60.8)	
RCA	33 (27.5)	
LCX	13 (10.8)	

BMI: body mass index, CSA: central sleep apnea, MI: myocardial infarction, LCX: left circumflex artery, LAD: left anterior descending artery, PCI: percutaneous coronary intervention, RCA: right coronary artery, STEMI: ST-segment elevation myocardial infarction.

Comorbidities and disease prognosis of the followed sample

The majority of patients suffered from multiple concurrent comorbidities. The most common were diabetes (31.7%), hypertension (30.8%) followed by cardiovascular diseases (19.2%) and other comorbidities as shown in table 1.

The TIMI risk score for the enrolled STEMI patients was >2 points in 31.7% of patients. Only two patients were killip-classed more than 2. Risk scores, laboratory data and medical events/procedures during hospitalization are shown in table 2.

Table 2: Risk scores, laboratory data and medical events/procedure during hospitalization.

	Frequency (%) (*n*= 124)	Mean (Standard deviation) (*n* =124)
Killip score		
Killip I	107 (89.2)	
Killlip II	7 (5.8)	
Killip III	1 (0.8)	
Killip IV	1 (0.8)	
Killip class >2	2 (1.7)	
TIMI risk score		
TIMI 0-1	30	
TIMI 2	48	
TIMI 3	17	
TIMI 4	14	
TIMI 5	4	
TIMI 6-7	3	
TIMI STEMI risk score >2	38 (31.7)	
Serum Creatinine (µmol/L)		99 ± 7.3
White blood cells (X10³/µL)		10.7 ± 0.8
Hemoglobin (mg/dL)		13.4 ± 0.3
Platelet count (10³/L)		242.0 ± 13.4
Prothrombin Time		17.7 ± 3.31
Prothrombin concentration		80.6 ± 3.6
INR		1.1 ± 0.0
Medical events/procedure	26 (21.7)	
Total bleeding	11 (9.2)	
Minimal (BARC type 1)	7 (5.8)	
Minor (BARC type 2)	3 (2.5)	
Major non-fatal (BARC type 3)	1 (0.8)	
Dyspnea	10 (8.3)	
Bradycardia	8 (6.7)	
Heart block	8 (6.7)	
Second look	6 (5)	
Stent thrombosis	4 (3.3)	
Coronary angiography	3 (2.5)	
Pacemaker insertion	1 (0.8)	

BARC: bleeding academic research consortium, INR: Internal Normalized Ratio, STEMI: ST-Elevation Myocardial Infarction, TIMI: Thrombolysis in Myocardial Infarction.

Patients excluded during hospitalization

Seven patients died during the first five days of hospital stay after receiving ticagrelor. One death was during revascularization as a result of ventricular fibrillation and cardiac arrest. Others died after revascularization. The cause of death was as follows: Two (2/7) patients had cardiac arrest as a consequence of bradycardia; 2/7 patients had cardiogenic shock; 1/7 patient had respiratory failure and one patient's death details were unavailable.

Further, six patients were excluded because of prescribing anticoagulation during hospital stay; of whom 3/6 patients developed atrial fibrillation, 2/6 patients had dilated right atrium ≥ 5.5 cm and 1/6 patient's echocardiography revealed LV thrombus.

Four patients complained moderate to severe dyspnea and were diagnosed as ticagrelor-related dyspnea so switched to clopidogrel. All the above mentioned 17 patients were excluded from the study.

Exclusion before one month of the index event

Further 32/152 patients left the study during the first month as follows: 20/152 patients were lost in phone follow-up. Five (5/152) patients had stopped drug administration by physician decision and were switched to clopidogrel due to the high cost of ticagrelor or due to drug unavailability in rural pharmacies. Three (3/152) patients were found incompliant to ticagrelor intake.

Efficacy outcomes at 3 months follow-up

A total of 120 patients included in the study; 109 patients completed three months follow-up. The primary endpoint occurred in 11/120 (9.2%) of patients receiving aspirin/ticagrelor DAPT therapy, which was a composite of death from CVD 4.2% (5/120), MI 4.2% (5/120) and ischemic stroke 0.8% (1/120).

Secondary endpoints, such as stent thrombosis occurred in 1.7% (2/120) of patients. No observed cases of transient ischemic attacks (TIAs) or thrombotic events.

Safety outcomes at three months follow-up

There was nil fatal bleeding and CABG-related bleeding. Two cases (1.7%) suffered from major non-fatal bleeding. One had vaginal bleeding (BARC type 3a) who received one pack RBC transfusion and the other had GI ulcer bleeding (BARC type 3a) which necessitated transfusion of two RBCs packs. Three cases (2.4%) of minor bleeding were observed as follows: procedural site bleeding, subcutaneous bleeding (hematoma) and GI bleeding.

Total bleeding was observed in 25/120 (20.8%) of the followed patients from 12 bleeding sites which were presented as epistaxis, subcutaneous or dermal, hemoptysis, procedural site, oral, post-procedural site, retinal, GI ulcer, hematemesis, hemorrhoidal, urinary tract and vaginal bleeding respectively. The majority of bleedings were minimal (BARC type 1) mostly presented as epistaxis (Table 3).

Multivariate regression analysis of bleeding risk displayed no association with the patients' sex (p= 0.51); patients' age of 65 years or older (p= 0.77), nor with glycoprotein IIb/IIIa inhibitor GPI (tirofiban) administration during hospitalization (p= 0.77).

Dyspnea was the chief complaint in the study and varied in severity. Most reported dyspnea cases were mild. Six cases (6/52) complained of severe dyspnea, of whom 3/6 patients stopped ticagrelor; one stopped medication without replacement and two patients were switched to clopidogrel. The other 3/6 cases suffered ticagrelor-related severe dyspnea but continued medication; one of them caused the patient to rush to the ER twice and despite three hospital clinic visits, physicians didn't switch treatment to another DAPT.

Switching from ticagrelor to other P2Y12 inhibitors

Figure 1 illustrates that since the start of patients' enrollment, 31 out of 169 (18.3%) patients were switched from ticagrelor to the P2Y12 inhibitors clopidogrel. The causes of 18.3% ticagrelor-to-clopidogrel de-escalation were reported as 38.7% (12/31) high ticagrelor cost, 22.6% (7/31) dyspnea, 19.3% (6/31) anticoagulant prescription (exclusion criterion), 12.9% (4/31) drug noncompliance and 6.5% (2/31) major non-fatal bleeding.

Table 3: Clinical efficacy and safety outcomes at three months; reported undesirable effects.

	Frequency (%) (*n*= 120)
Cardiovascular mortality	5 (4.2)
Cardiac death and MI	4 (3.3)
Unknown cause	1 (0.8)
Cardiac events	12 (10)
UA	4 (3.3)
STEMI	3 (2.5)
NSTEMI	2 (1.7)
Post MI angina	2 (1.7)
Stent thrombosis	2 (1.7)
In-stent restenosis	2 (1.7)
Ischemic stroke	1 (0.8)
CABG	1 (0.8)
Bleeding severity	
Minimal	25 (20.8)
Minor	3 (2.5)
Major, non-fatal	2 (1.7)
Dyspnea, all	52 (43.3)
Mild	31 (25.8)
Moderate	15 (12.5)
Severe	6 (5)
Led to discontinuation	2 (1.7)
Undesirable adverse effects	82 (68.3)
Dyspnea	52 (43.3)
Fatigue	32 (26.7)
Total bleedings	29 (24.2)
Headache	20 (16.7)
Dizziness	13 (10.8)
Hypertension	6 (5)
Arthralgia	4 (3.3)
Cough	4 (3.3)
Gastritis	4 (3.3)
Hypotension	4 (3.3)
Dyspepsia	3 (2.5)
Back pain	2 (1.7)
Insomnia	2 (1.7)
Parasthesia	2 (1.7)
Vertigo	2 (1.7)
Vomiting	2 (1.7)
Others	4 (3.3)

Note: Undesirable effects reported maybe contributed to medications other ticagrelor.

Discussion

This observational study explored the efficacy and safety of ticagrelor in a group of patients indicated for urgent revascularization.

The findings recorded a primary endpoint - a composite of death from vascular causes, MI, or ischemic stroke, at 3 months in 9.2% of patients. The calculated net clinical benefit – which was the composite of cardiovascular death, unplanned hospitalization leading to urgent coronary revascularization, stroke, and bleeding episodes (defined by the BARC classification ≥2) occurred in10.7% of patients. Bleeding events in this study excluding minimal bleeding were reported in 4.2% of patients. Ticagrelor was also associated with a low incidence of major bleeding and a high incidence of dyspnea which was the main cause of drug discontinuation.

The primary endpoint was obviously higher than that of ticagrelor arm of the STEMI intended for PPCI subgroup analysis of the PLATO study at 3 months (6.2%)[11]; however, it was close to the cumulative MACE incidence at 12 months (9.4%)[11] and that reported in the PHILO study (9%) which enrolled Asian patients[17]. The incidence was also higher than other reported in some studies; The Efficacy and Safety of Ticagrelor versus clopidogrel in Acute coronary syndrome observational pilot study in Taiwan (ESTATE)[18], in which primary efficacy outcome was 7.1%. The Greek AntiPlatElet registry (GRAPE)[19] reported a primary endpoint of 6.8%. In the CHANGE DAPT study[20], the primary endpoint was one-half lower (4.7%) compared to this study. The higher primary outcome in this study may be related to the high number of patients left the study or switched to clopidogrel before the end of three months, thus it may not reflect the true efficacy of ticagrelor.

The calculated net clinical benefit occurred in 10.7% of patients was much lower than net clinical benefit (26.3%) of the (TOPIC) study[21] and may be explained by the less observed BARC grade ≥2 cases in this study.

Cardiovascular mortality incidence (4.2%) in this study was higher as compared to the STEMI PLATO study (3%)[11], the GRAPE registry (3.1%)[19], the PHILO study (2.2%)[17], the TOPIC (1.2%)[21] and CHANGE DAPT studies (2.9%)[20]; however, it was close to the

vascular mortality rate (4.5%) reported in the ESTATE study[18]. This may be attributed to the small sample size of this study and different statistical power.

The observed myocardial infarction rate (4.2%) in this study was more than that reported in previous studies such as the STEMI patients intended for PPCI subgroup analysis of the PLATO study (3%)[11], the ESTATE (3.1%)[18], the CHANGE DAPT (2.2%)[20] and the GRAPE (1.1%)[19] studies. However, the rate was less than reported in the PHILO study (6%)[17] and the unchanged DAPT arm in the TOPIC study (9.3%)[21].

The incidence of ischemic stroke (0.8%) were comparable to that of the PLATO[11], ESTATE[18], GRAPE registry[19], CHANGE DAPT[20] and TOPIC studies[21] (1%, 0.4%, 0.7%, and 0.9% and 1.1% respectively). However, the stroke incidence was less than that reported in the PHILO study (2.2%)[17].

Stent thrombosis rate was lower than the STEMI PLATO subgroup analysis[11]; 3.3%, while the rate was higher as compared to the CHANGE DAPT (0.8%)[20].

Bleeding events in this study (4.2%) - excluding minimal bleeding, which is bleeding not prompt medical attention, were three times lower than reported in the STEMI arm of PLATO subgroup analysis study (13.1%.)[11]. We observed no major fatal bleeding (BARC type 5) compared to 4.7% of PLATO subgroup analysis and no major CABG-related bleeding (BARC type 4) compared to 5.1%. Major non-fatal bleeding incidence (BARC type 3) was about five times lower compared to 8.2%. Minor bleeding (BARC type 2) was lower to half compared to 4.9% of PLATO study. The majority of bleeding events in this study were minimal (BARC type 1). Minimal bleeding was not reported in the PLATO study[11] and 7.3% required blood transfusion versus two cases (1.7%) in this study.

No fatal bleeding (BARC type 5) was observed compared to 0.4% in ESTATE population and minor bleeding (BARC type 2) was 2.5% compared to 6.3% in ESTATE population[18]. The total bleeding and minimal bleeding rates in our study population were higher in comparison with the Eastern Asians, however, with less bleeding sites (12 versus 44 bleeding sites in ESTATE population)[18].

However, the total bleeding was much lower in this study compared to the GRAPE study[19]; total BARC and BARC type 1 were one-half lower than the GRAPE study (BARC 2 was less by 2.3% and BARC ≥2 was 2.6 times less).

The incidence of major and minor bleeding in this study was four times lower and six times lower than that of the PHILO study's major and minor non-CABG related bleeding, (8.3% and 15.2%, respectively)[17]. This finding may give clinicians some convenience to use ticagrelor without the big concern about major bleeding and its associated morbidity and mortality in Egyptian patients

Quite the contrary, the incidence dyspnea was more than seven-fold higher than that reported in the PHILO study[17]; more than three-fold higher than reported in the STEMI PLATO population[11] and was double that of the findings of the ESTATE study[18].

The incidence of dyspnea of any grade of severity -observed at three months- was consistent with that of the Australian study of the real-world incidence of patient-reported dyspnea with ticagrelor[22]. However, this study reported lower proportions of drug discontinuations; 1.7% versus 7.14%. This seems because of many physicians in this study to continued ticagrelor therapy despite dyspnea symptoms because some patients encountered comorbidities and were at moderate to high risk of re-infarction.

Considering a future study of ticagrelor de-escalation after the early phase of ischemic event may be beneficial in reducing the incidence of dyspnea and reducing prescription cost, thus minimizing drug malcompliance.

Limitations of the study

The findings of this study need to be viewed in light of some limitations. The principal limitation was the nature of study design as an observational study of physician practice without researcher intervention and therefore, the lack of a comparison group – clopidogrel group – and randomization. Assiut hospital revascularization management protocol stipulates the use of ticagrelor for its – faster than clopidogrel- onset of action, which in turn affects the results' strength. Second is the short duration of patient follow-up and small sample size, which may affect the drawn

conclusion and results' significance on ticagrelor efficacy. This was because of many patients' attrition after one month and before the three months follow-up as they were switched to clopidogrel or left the study. Eventually, many results at three months were compared to 12 months-results of previous studies due to their lack of detailed percentages at different follow-up periods.

Statistical analysis

Patients' baseline characteristics were summarized as mean, standard deviations and 95% CI for continuous variables such as age, weight, body mass index and laboratory measurements. Categorical variables such as sex, education, and comorbidities were summarized as proportions. Multivariate regression analysis was performed for the association between safety outcomes (bleeding and dyspnea) and demographic and medicine-related factors.

All the statistical analyses were performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA). The significance level was set at *p* value <0.05.

Conclusions

Ticagrelor induced a composite of death from vascular causes, MI, and ischemic stroke that was higher than those reported in some previous studies. Ticagrelor was also associated with a much lower incidence of major bleeding despite using femoral access approach in PPCI and a higher incidence of dyspnea than previously reported. Many of dyspnea cases necessitated drug discontinuation than bleeding did with no effect on the mortality rate.

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أمان وفعالية عقار التيكاجريلور المستخدم لعلاج مرضى احتشاء عضلة القلب المصاحب بارتفاع القطعة إس تي في مستشفى القلب الجامعي بأسيوط

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الهدف من الدراسة: مراقبة أمان وفعالية عقار التيكاجريلور المستخدم حاليا كعلاج أساسي لمرضى احتشاء عضلة القلب الحاد المصاحب بارتفاع القطعة إس تي في مستشفى القلب الجامعي بأسيوط.

المكان: وحدة العناية المركزة لمرضى القلب بمستشفى القلب الجامعي بأسيوط.

طريقة الدراسة: تضمنت هذه الدراسة رصد وملاحظة ١٢٠ مريضا تم تشخيصهم باحتشاء حاد في عضلة القلب المصاحب بارتفاع القطعة اس تي في رسم القلب ، والذين تم علاجهم باستخدام القسطرة التداخلية العلاجية العاجلة. هؤلاء المرضى خضعوا للعلاج الثنائي المضاد لتجمع الصفائح الدموية المكون من الاسبرين والتيكاجريلور. تم متابعة المرضى ورصد حالتهم الصحية لمدة ثلاثة أشهر ما بين مايو ٢٠١٨ وحتى سبتمبر ٢٠١٩.

قياس النتائج: تم استخدام معدل حدوث الوعكات الصحية القلبية كمقياس لمدى فعالية التيكاجريلور ، ومعدل حدوث النزيف الحاد أو مهدد للحياة كمقياس لمدى أمان التيكاجريلورالمتبع في بروتوكول العلاج بالمستشفى.

النتائج: في نهاية الشهور الثلاث، كان المقياس الأولي لفعالية التيكاجريلور– والذي يتضمن معدل حدوث وفيات قلبية، احتشاء لعضلة القلب أو جلطات دماغية– يمثل ٢.٩% من المرضى (١٢٠/١١). أما المقياس الأولي لأمان التيكاجريلور–والذي يمثل معدل حدوث نزيف شديد– كان يساوي ١.٧% من المرضى بدون رصد أى حالة نزيف واحدة مهددة للحياة. تم تسجيل معدل النزيف المتوسط والضعيف في ٢٠.٨% من المرضى حدثت خلال فترة المتابعة بعد مغادرة المشفى. خلال هذه الفترة أيضا تم تسجيل حدوث احتشاء لعضلة القلب مرة أخرى بنسبة ٤.٢% من المرضى، وكان ١.٧% منها بسبب انسداد الدعامات الشريانية التي تم تركيبها سابقا باستخدام القسطرة التداخلية العلاجية للقلب. وتم أيضا ملاحظة ٥.٠% من المرضى ممن عانوا صعوبة شديدة في التنفس أدت لأن ينهى ١.٧% منهم تعاطي التيكاجريلور ، واستبداله بنظيره الأقدم الكلوبيدوجريل. أثبتت التحاليل الإحصائية لتحديد عوامل الارتباط أنه لا يوجد ارتباط بين النزيف وعمر المرضى أو جنسهم أو تناولهم مضادات الصفائح الدموية الوريدية التي تلقاها البعض خلال فترة علاجهم بالعناية المركزة.

الملخص: كان معدل حدوث المضاعفات القلبية خلال متابعة المرضى الذين تناولوا عقار التيكاجريلورأعلى من المعدلات المسجلة في الدراسات السابقة من نفس النوع. وجد أن معدل حدوث عرض صعوبة التنفس لمن يتناولون التيكاجريلور ، أعلى من معدل حدوث النزيف الحاد. معظم حالات النزيف كانت نزيفا بسيطا ولم تسجل أية حالة نزيف حاد مهدد للحياة أو نزيف أدى إلى مضاعفات وتدهورالحالة الصحية.