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Intracoronary Versus Intravenous Administration of Glycoprotein IIb/IIIa inhibitors in Diabetic Patients Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: *Previous trials remained inconsistent regarding benefits and possible risks associated with intracoronary (IC) administration compared with intravenous (IV) are still questionable. We aimed at evaluation safety and effectiveness of IC versus IV tirofiban administration during primary percutaneous coronary intervention (PCI) for diabetic patients (DM) presented with acute ST segment elevation myocardial infarction.*

Methods: *This trial included 100 patients who were randomized either IV high bolus plus maintenance or IC high bolus plus maintenance of tirofiban. Both groups were compared for pre and post intervention for myocardial perfusion, cardiac marker and Major composite adverse cardiac event incidence at 30 days were recorded.*

Results: *Incidence of major adverse cardiac events was not different between groups, but Post procedure TIMI flow III and MBG III were significant in IC group with p = 0.45, and 0.21 respectively favoring intracoronary strategy. Peak CK-MB values were lower in IC tirofiban group than IV group, 155.68 ± 121, 192.4 ± 86 respectively with significant (p=0.021). Peak hs-TnT value was significantly were lower in IC tirofiban group [4291 ± 334 ng/dL vs 5342 ± 286 ng/dL in IV group; (p=0.035). ST segment resolution and 30 days LVEF in IC group were significantly higher in IC group than in IV group (p= 0.023) respectively.*

Conclusion: *IC GpIIb/IIIa inhibitors is more effective in improving coronary blood flow and myocardial tissue perfusion in DM after STEMI 30 days post PCI despite the bleeding event and MACE rates showed no significant difference,IC tirofiban group, showed better improvement in LVEF.*

Keywords

Diabetes mellitus, STEMI, Intracoronary GpIIb/IIIa inhibitors, Primary coronary intervention.

Introduction

Glycoprotein IIb/IIIa is an intravenously administered nonpeptide GpIIb/IIIa inhibitors, IIb/IIIa receptor antagonist which specifically inhibits fibrinogen-dependent platelet aggregation and prolongs bleeding times in patients with acute coronary syndromes Tirofiban reduces the risk of ischemic complications in patients with unstable angina/non-Q-wave MI and high-risk patients undergoing revascularization when used against a background of heparin and aspirin. Furthermore, the drug has an acceptable tolerability profile. Therefore, intravenous tirofiban is likely to be used as an adjunct to heparin and aspirin in patients with acute coronary syndromes including high-risk patients undergoing revascularization. Adenosine diphosphate (ADP)-induced platelet aggregation returns to near-baseline levels within 4 to 8 hours after cessation of a tirofiban infusion, a finding consistent with the drug's elimination half-life of approximately 2 hours Impaired glucose metabolism is one of the main risk factors of arteriosclerosis, and 80% of patients with diabetes mellitus (DM)

die from cardiovascular diseases [1]. Studies have demonstrated a significant positive correlation between hyper glycaemia and occurrences of heart failure, arrhythmias and other complications; moreover, hyperglycaemia significantly increase the mortality of patients with diabetes complicated by MI [2,3].

Acute (STEMI) usually caused by acute occluding of major epicardial coronary artery. Successful recanalization and patency of the infarct - related vessels by percutaneous coronary intervention (PCI) or fibrinolytic diminishes the size of infarction, save the function of ventricle and decrease morbidity and mortality [4-6].

Several consequences such as no-flow and slow-flow, increased major adverse cardiac events (MACE), complications and high mortality, have been observed in patients with DM complicated by acute MI (AMI) and undergoing primary PCI [7,8]. Platelet aggregates into the distal microvasculature or thrombus embolization after immediately successful intervention impair micro vascular flow. Administration of glycoprotein IIb/IIIa inhibitors (GPI) and many mechanical strategies have been proposed to overcome this phenomenon [9,10].

American guidelines recommend GpIIb/IIIa inhibitors at the time of PCI in patients with STEMI for high burden thrombus or patient who did not receive inadequate loading of P2Y12 inhibitors, and in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) and high-risk criteria [11,12]. European guidelines recommend tirofiban using in PCI for bailout situations if there are angiographic evidence of massive thrombus, slow or no-reflow, or thrombotic complication [13,14].

This trial targeted to assess if intracoronary administration of high dose bolus plus infusion of GpIIb/IIIa inhibitors lead to better efficacy, safety and enhance clinical outcomes more than the standard intravenous high dose bolus plus infusion regimen during primary percutaneous coronary intravenous bolus plus infusion regeimen during PCI for diabetic patients with acute STEMI.

Methods

Subjects

The Study evaluated 100 consecutive diabetic patients with ST-elevation myocardial infarction (STEMI) undergoing primary PCI. Patients were recruited to receive either intravenous (group A: n = 50) or intracoronary (group B: n = 45) high-dose bolus (25 micg/kg) plus maintenance (0.15 micg/kg/min) infusion for 24 hours.

We included Adult patient ≥ 18 years old and less than 75 years with clinical presentation of STEMI and specific ECG criteria in the form of ST-segment elevation ≥ 1 mm in ≥ 2 limb leads and/or ST-segment elevation in adjacent precordial leads except v2 and v3 must be ≥ 1.5 mm in females, ST-segment elevation ≥ 2.5 mm in male less than 40 years or ≥ 2 mm in male more than 40 years or presence of new-onset or presumed new left bundle branch block [15].

The study was approved by the institutional ethics committee and informed consent was provided from all patients. Patient with marked uncontrolled hyper tension (more than 180 /110 mmHg), rescue PCI after thrombolytic therapy, and emergency coronary artery bypass grafting were excluded, other Exclusion criteria were patients presented with cardiogenic shock, severe liver or kidney failure, need for emergency coronary artery bypass grafting, bleeding diathesis, presence of a disease with a life expectancy of less than 1 year, rescue PCI after thrombolytic therapy, inability to provide informed consent and any contraindication for the use of tirofiban, such as Hypersensitivity, history of thrombocytopenia with tirofiban, platelets <150,000/cu.mm, Active/history of internal bleeding (within last 30 days), intracranial hemorrhage or neoplasm, history of stroke within last 30 days or any history of hemorrhagic stroke, AV malformation or aneurysm, aortic dissection, acute pericarditis, Current use of another parenteral glycoprotein IIb/IIIa inhibitor, hemorrhagic retinopathy and chronic hemodialysis.

Study protocol

All patients were pretreated with aspirin (300 mg) and clopidogrel (600 mg). After securing vascular access through right femoral or radial arteries, a total of 70-100 IU/kg unfractionated heparin IV bolus was given, then additional weight adjusted unfractionated heparin was given to achieve approximately 250s of activated clotting time (ACT). In both groups, bolus 25 mic/kg of GpIIb/IIIa inhibitors was given immediately after guide wire crossed the lesion successfully and ante grade flow was restore in order to secure optimal drug concentration at both the culprit lesion site and distal micro vascular bed. The bolus dose of GpIIb/IIIa inhibitors was administrated through the guiding catheter in the infarcted related artery (IRA) at 30 s.in intracoronary group. Maintenance IV GpIIb/IIIa inhibitors 0.15 mic/kg/min for 18 hours was started in both group after bolus dose. Aspiration thrombectomy catheter was used if needed and as the final step, a proper FDA-approved drug eluting stent was placed in IRA in all patients.

Acetylsalicylic acid, clopidogrel 75 mg, beta-blocker, statin and an angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers, were prescribed as per guidelines. When the ACT was less than 160 s and 0r 4 h passed after the anticoagulation vascular sheath was removed by manual compression.

From the onset of chest pain till visualization of at least TIMI 2 flow in IRA during PCI was recorded as the time to reperfusion. Thrombolysis in Myocardial Infarction (TIMI) flow grades [16], myocardial blush grade (MBG) in the culprit vessel [17], before and after coronary intervention was evaluated by 2 blinded interventional cardiologists. The Biplane Modified Simpson's Method was used for evaluation of left ventricular EF 48 hours after PCI then again after 30 days.

Both groups were compared for TIMI flow grades before and after intervention, MBG, maximum CRP level, peak level of both CKMB and troponin, time to peak for CKMB and troponin and time to 50% ST resolution and major composite adverse cardiac event rates at 30 days were recorded. Safety endpoints as significant bleeding, minor bleeding, and thrombocytopenia.

of a contra or ipsilateral non-IRA .[18] MACE [19] was defined as cardiovascular death, recurrent myocardial infarction, stent thrombosis, or target vessel revascularization during hospitalization, at 1-month. Platelet count <100 000/mm3 was defined as thrombocytopenia. [18] Intracranial hemorrhage and decrease in hemoglobin concentration ≥5 g/dL are considered as major bleeding. Minor bleeding was defined as blood loss of 3 to 5 g/dL in hemoglobin concentration or 10% to 15% decrease in hematocrit, or no observed blood loss with ≥4 g/dL decrease in hemoglobin concentration. [20]

Clinical points

MBG was graded according to dye density score into four grades, grade 0 = no myocardial blush, 1 = minimal myocardial blush or contrast density, 2 = moderate myocardial blush or contrast density, but less than that obtained during angiography of a contra or ipsilateral non-IRA, and 3 = normal myocardial blush or contrast density, comparable with that obtained during angiography of a contra or ipsilateral non-IRA [18]. MACE [19] was defined as cardiovascular death, stent thrombosis, recurrent myocardial infarction, or target vessel revascularization during hospitalization, at 1-month. Intracranial hemorrhage, ≥5 g/dL decrease in hemoglobin concentration ≥5 g/dL considered as major bleeding. Minor bleeding was defined as blood loss of 3 to 5 g/dl in hemoglobin concentration or 10 %to 15 %decrease in hematocrit, or no observed blood loss with more than 4 g/dl decrease in hemoglobin concentration.

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 25.0 for windows (IBM Corp., Armonk, NY, USA). Data are presented as the Mean ± standard deviation (SD), frequency, and percentage. Categorical variables were compared using the chi-square ($\chi 2$) and Fisher's exact tests (if required). Continuous variables were compared by the Student t test (two-tailed) and one – way ANOVA test for parametric data with Bonferroni post hoc test to detect differences between subgroups. Mann-Whitney U and Kruskal – Wallis tests for nonparametric data. The level of significance was accepted if the P value < 0.05.

Results

The 2 group showed No statistically significant differences in baseline characteristics or medications (Table 1). The mean age was 58.5 ± 10.18 years in IV tirofiban group (IV group) and 55.90 ± 11.66 years in IC tirofiban group. There was no difference between two groups in cardiovascular risk profile, cardiac history. Baseline level of Glycated hemoglobin (HbA1c) was similar between groups (p=0.08). Pain-to-balloon and door-to-balloon times were not significantly different (p=0.08, 0.3, respectively) (Table 1). Frequency of patients with Killip class >1 was 18% in group A and 24% in group B, (p=0.33).

Peak CK-MB value was significantly lower in IC Glycoprotein IIb/IIIa group than IV group, 155.68 ± 121, 192.4 ± 86 respectively (p=0.021). Peak hs-TnT value was significantly were lower in IC group [4291 ± 334 ng/dL vs 5342 ± 286 ng/dL in IV group; (p=0 GpIIb/IIIa inhibitors 035). Percentage of patients with 50% resolution of ST segment was significantly higher in IC group than in IV group with (p= 0.016), maximum C – Reactive protein level, peak and time to peak Creatine kinase-myocardial MB, and time to peak troponin showed statistically significant differences as shown in table 2. There was no significant difference in LVEF between both groups 48 hours after PCI (p= 0.632). However, after 30 days of PCI, the average LVEF in IC group was higher than in the IV group (p= 0.023).

Parameters		Group (A) N = 50	Group (B) N = 45	P value
Age (Mean ± SD)		58.56 ± 10.18	55.90 ± 11.66	0.41
Sex (male), n (%)	**Male**	27 (54)	23 (51.1)	0.49
	Female	23 (46)	22 (48.9)	
Body mass index (Kg/m2) (mean + SD)		26.1 ± 6.5	25.4 ± 8.2	0.78
Smoking n (%)		34 (68)	31 (68.8)	0.48
Hypertension n (%)		20 (40)	19 (42)	0.78
Family history of coronary artery disease n (%)		9 (18)	7 (15.5)	0.54
Killip class > 1 n (%)		9 (18)	11 (24)	0.33
Aspirin n (%)		49 (98)	43 (95.5)	0.87
Clopidogrel n (%)		50 (100)	44 (97.7)	0.64
Beta blockers n (%)		41 (82)	39 (86.6)	0.85
ACEI or ARBS n (%)		39 (78)	36 (80)	0.79
Statin n (%)		44 (88)	39 (86.6)	0.73
Warfarin n (%)		3 (6)	1 (2.2)	0.068
Pain to balloon time (min) (mean + SD)		167 ± 12.4	151 ± 18.3	0.089
Door to balloon time (min) (mean + SD)		46.8 ± 8.9	44 ± 7.6	0.38
Fasting glucose (mg/dL) (mean + SD)		168 ± 29.8	192 ± 46.6	0.074
Glycated hemoglobin (HbA1c) (mean + SD)		7.8 ± 2.2	9 ± 1.3	0.087
Creatinine (mg/dL) (mean +SD)		1.17 ± 0.41	1.08 ± 0.56	0.251
Low-density lipoprotein cholesterol (mg/dL) (mean +SD)		132.6 ± 46	147.09 ± 51	0.091

Table 1: Baseline characteristics of both groups.

Parameters	Group (A) N = 50	Group (b) N = 45	P value
Peak Creatine kinase-myocardial MB (U/L)	192.4 ± 86	155.68 ± 121	0.021*
Time to peak CKMB	12.9 ± 5.8	8.96 ± 3.2	0.001*
Peak high sensitive troponin T (ng/dL)*	5342 ± 286	4291 ± 334	0.035*
Time to peak troponin	13.5 ± 3.1	9.24 ± 2.8	0.001*
ST segment 50% resolution (%)	56%	77%	0.016*
Left ventricle ejection fraction (%) at 48 hours	38.6 ± 5.3	41.5 ± 3.2	0.632
Left ventricle ejection fraction (%) at 30 days	42.6 ± 4.2	48.2 ± 6.1	0.023*
Maximum C – Reactive protein level	9.2 ± 2.3	5.7 ± 1.4	0.026*

Table 2: Comparison between both groups regarding cardiac biomarkers and Left ventricle ejection fraction.
*Normal High-sensitive Troponin level up to 14 ng/dl

Angiographic characteristics of the groups are presented in Table 3., Post procedure TIMI flow III and MBG III were significant in IC group with p = 0.045, and 0.021 respectively. No significant differences were found between groups in distribution of culprit lesion, frequency of patients with triple-vessel disease. There were no significant differences between groups with respect to incidence of MACE, major bleeding and minor during hospitalization and at 1-month follow-up as shown in table 3. In group A, 1 patient developed major bleeding due to upper gastrointestinal system bleeding and 5 patients developed minor bleeding (3 patients developed access site bleeding, and 2 patients developed hematuria). In group B, 1 patient developed major bleeding due to lower gastrointestinal system, and 4 patients developed hematuria. Bleeding events are summarized in Table 3.

Parameters		Group (A) N = 50	Group (B) N = 45	P value
TIMI III flow after procedure n (%)		39 (78)	42 (93)	0.045*
Myocardial Blush Grade 3 after procedure		34 (68)	41 (82)	0.021*
Infarct-related vessel n (%)	Left anterior descending artery **n (%)**	30 (60)	25 (55)	0.72
	Circumflex artery **n (%)**	7 (14)	5 (11.1)	0.91
	Right coronary artery **n (%)**	10 (20)	13 (28.8)	0.92
	Triple vessels **n (%)**	3 (6)	2 (4.4)	1.00
Balloon **n (%)**		10 (20)	13 (28.8)	0.98
In-hospital MACE n (%)	In-hospital death **n (%)**	2 (4)	1 (2.2)	1.00
	In-hospital Stroke **n (%)**	0	0	1.00
	In-hospital reinfarction **n (%)**	1 (2)	0	0.993
	In-hospital stent thrombosis **n (%)**	1 (2)	0	0.993
	In-hospital TVR **n (%)**	0	0	1.00
1-month MACE n (%)	1-month death **n (%)**	1 (2)	0	1.00
	1-month Stroke **n (%)**	0	0	1.00
	1-month reinfarction **n (%)**	1 (2)	1 (2.2)	1.00
	1-month stent thrombosis **n (%)**	1 (2)	1 (2.2)	1.00
	1-month TVR **n (%)**	1 (2)	1 (2.2)	1.00
TIMI major bleeding n (%)		1 (2)	1 (2.2)	1.00
TIMI minor bleeding n (%)		5 (10)	4 (8.8)	0.95
Thrombocytopenia n (%)		2 (4)	2 (4.4)	1.00

Table 3: Summary of angiographic characteristics, MACE and bleeding event in both groups.

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 23.0 for windows. Data are presented as the Mean ± standard deviation (SD), frequency, and percentage. Categorical variables were compared using the chi-square (χ^2) and Fisher's exact tests (if required). Continuous variables were compared by the Student t test (two-tailed) and one – way ANOVA test for parametric data with Bonferroni post hoc test to detect differences between subgroups. Mann-Whitney U and Kruskal – Wallis tests for nonparametric data. The level of significance was accepted if the P value < 0.05.

Results

Variables	*Frequency (N= **45**)*	*%*
***Age** (M ± SD)*	57.38 ± 10.67	----
Group	25	55.6
A (IV GP IIbIIIa)	20	44.4
B (IC GP IIbIIIa)		
Gender	43	95.6
Male	2	4.4
Female		
HTN	19	42.2
Hypertensive	26	57.8
Non hypertensive		
Smoking	29	64.4
Smoker	16	35.6
Non smoker		

Table 4: Some demographic data of the studied sample.

Table 4 show some demographic data of the studied sample. The table clarifies that the mean age of the studied population was 57.38 ± 10.67 yrs. In addition, the table demonstrate that the male pts. Constitute the main bulk of the studied sample. Also the table showing that non hypertensive pts. More than hypertensive ones. On the other hand, pts. Who are smoking more than non-smokers?.

Variables	Frequency (N= 45)	%
Target vessel	19	42.2
LAD	2	4.4
LCX	24	53.4
RCA		
Death	0	0.0
MI	0	0.0
Bleeding	2	4.4
TVR	0	0.0

Table 5: Some interventional and MACE data of the studied sample, show interventional and MACE data of the studied sample. As shown in the table and figures, pts. Presented with ACS related to RCA lesion more than those presented ACS related to LAD and LCX lesions. Also the table and figures clarified that only 4.4 percent of the studied sample were complicate bleeding after intervention.

Variable	*Group*	*M ± SD*	*p*
Age (yrs.)	Group A	58.56 ± 10.18	0.412
	Group B	55.90 ± 11.66	

Table 6: demonstrate comparison of age between group A and group B. There was no significant difference between the two groups regarding the age.

Variables		*Group A (N = 25)*	*Group B (N = 20)*	*p*
Gender	Male	23 (92.0%)	20 (100.0%)	0.495
	Female	2 (8.0%)	0 (0.0%)	
HTN	Hypertensive	11 (44.0%)	8 (40.0%)	0.787
	Non hypertensive	14 (56.0%)	12 (60.0%)	
Smoking	Smoker	15 (60.0%)	14 (70.0%)	0.486
	Non smoker	10 (40.0%)	6 (30.0%)	

Table 7: Clarifying comparison of some demographic and clinical data between group A and group B. There were no significant differences between 2 groups regarding gender, hypertension, and smoking.

Variables		**Group A (N = 25)**	**Group B (N = 20)**	**p**
Target vessel	LAD	13 (52.0%)	6 (30.0%)	0.130
	LCX	0 (0.0%)	2 (10.0%)	
	RCA	12 (48.0%)	12 (60.0%)	
Bleeding	Positive	2 (8.0%)	0 (0.0%)	0.495
	Negative	23 (92.0%)	20 (100.0%)	
TIMI Pre	0	4 (16.0%)	3 (15.0%)	0.714
	I	8 (32.0%)	5 (25.0%)	
	II	7 (28.0%)	9 (45.0%)	
	III	6 (24.0%)	3 (15.0%)	
TIMI Post	0	1 (4.0%)	0 (0.0%)	**0.004**
	I	10 (40.0%)	1 (5.0%)	
	II	8 (32.0%)	5 (25.0%)	
	III	6 (24.0%)	14 (70.0%)	

Table 8: Demonstrates comparison of some clinical data and major adverse cardiac events between 2 groups. There were no significant differences between 2 groups regarding target vessel, bleeding and pre intervention TIMI flow in the target vessel. On the other hand, post intervention TIMI flow in the target vessel showed statistically significant difference between both groups.

Table 9 Comparison of some laboratory data between group A and group B.

Variable	*Group*	*M ± SD*	*p*
HgbA1c	Group A	9.39 ± 1.89	**0.12**
	Group B	7.98 ± 1.68	
CKMB (Peak)	Group A	192.42 ± 9.46	**< 0.001**
	Group B	155.68 ± 10.77	
CKMB (Time to peak)	Group A	12.90 ± 4.73	**0.037**
	Group B	9.96 ± 4.38	
Troponin	Group A	5342.36 ± 37.75	**< 0.001**
	Group B	4291.00 ± 32.15	
Troponin (Time to peak)	Group A	13.50 ± 4.14	**0.001**
	Group B	9.24 ± 3.76	
LDLC	Group A	95.60 ± 38.80	**< 0.1**
	Group B	35.09 ± 44.33	

Table 9: Demonstrate comparison of some laboratory data between 2 groups. As demonstrated in the table laboratory data showing significant statistical differences between both groups.

Variable	*Group*	*M ± SD*	*p*
EF (Pre)	Group A	38.60 ± 13.07	0.917
	Group B	39.10 ± 11.81	
EF (Post)	Group A	43.80 ± 11.86	0.671
	Group B	41.90 ± 11.88	
ST Resolution	Group A	1.37 ± 0.87	**0.013**
	Group B	0.68 ± 0.10	
DTBT	Group A	46.80 ± 35.52	0.606
	Group B	40.80 ± 10.88	

Table 10: Showing comparison of some Echocardiographic and interventional data between 2 groups. There were no significant statistical differences in all parameters except for ST resolution, which shows significant statistical difference.

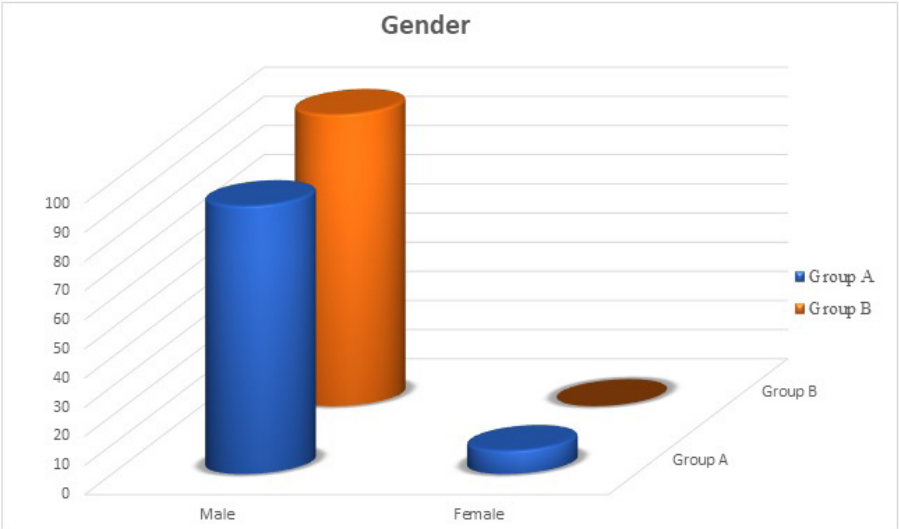

Figure 1: clarifying comparison of some demographic and clinical data between group A and group B. There were no significant differences between 2 groups regarding gender.

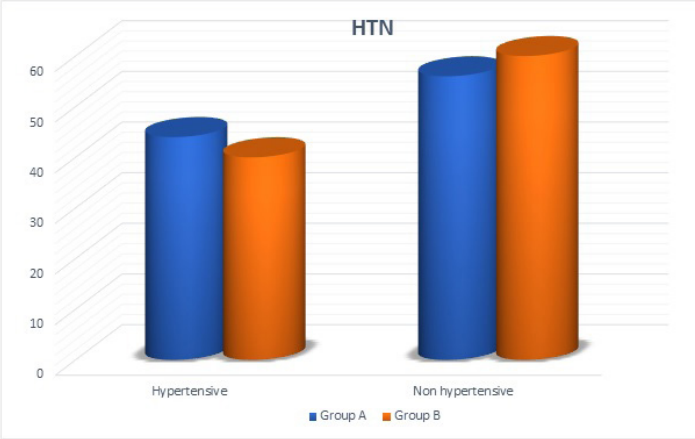

Figure 2: clarifying comparison of some demographic and clinical data between group A and group B. There were no significant differences between 2 groups regarding HTN.

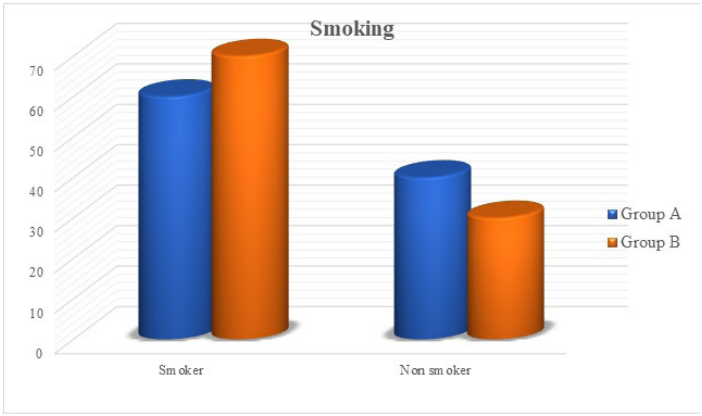

Figure 3: Clarifying comparison of some demographic and clinical data between group A and group B. There were no significant differences between 2 groups regarding smoking.

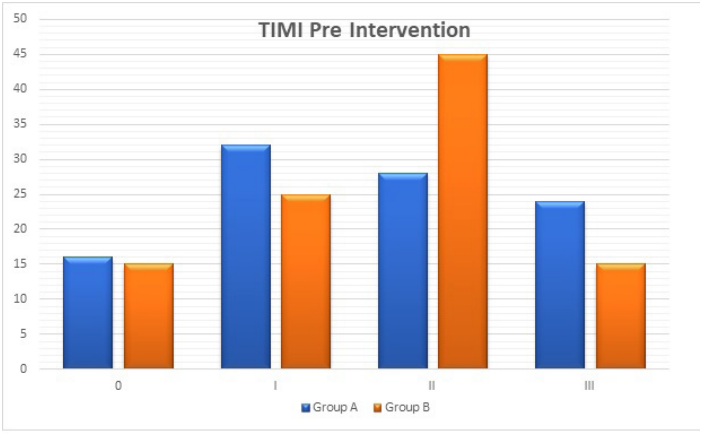

Figure 4: Demonstrate comparison of some clinical data and major adverse cardiac events between 2 groups. There were no significant differences between 2 groups regarding pre intervention TIMI flow in the target vessel.

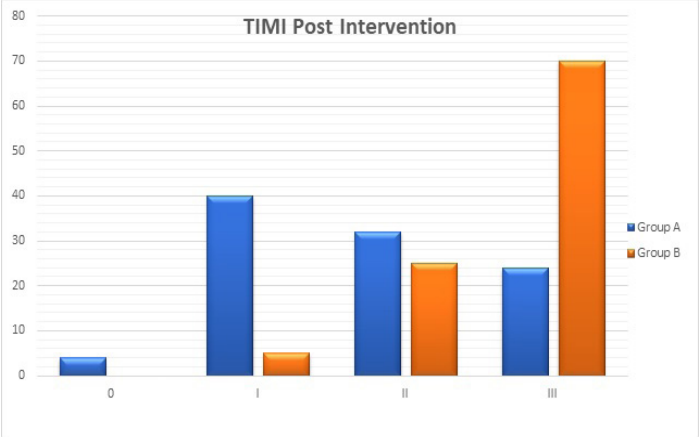

Figure 5: demonstrate comparison of some clinical data and major adverse cardiac events between 2 groups. Post intervention TIMI flow in the target vessel showed statistically significant difference between both groups.

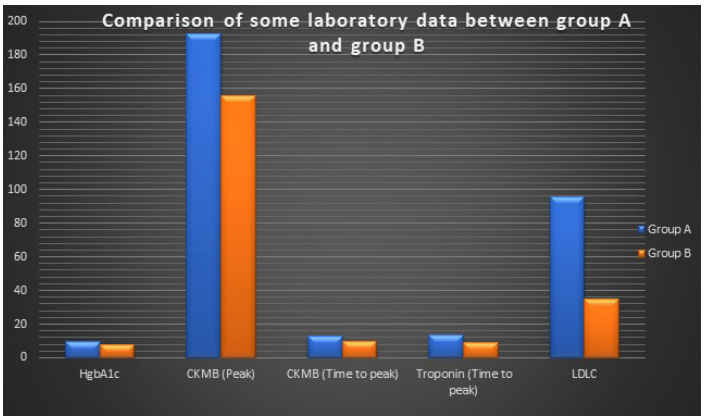

Figure 6: Demonstrate comparison of some laboratory data between 2 groups. As demonstrated in the Figure laboratory data showing significant statistical differences between both groups.

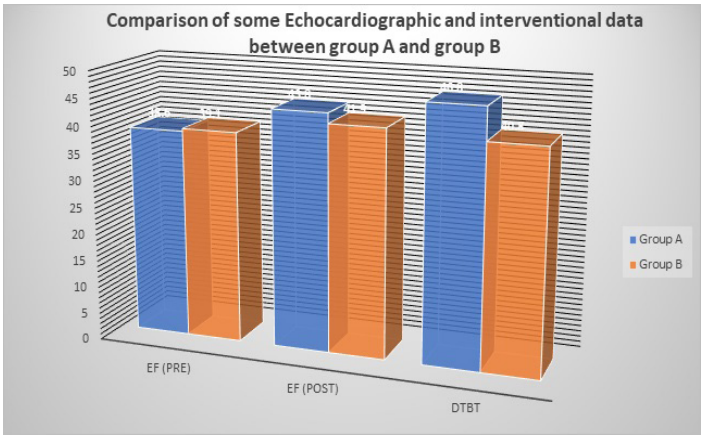

Figure 7: showing comparison of some Echocardiographic and interventional data between 2 groups. There were no significant statistical differences in all parameters except for ST resolution, which shows significant statistical difference.

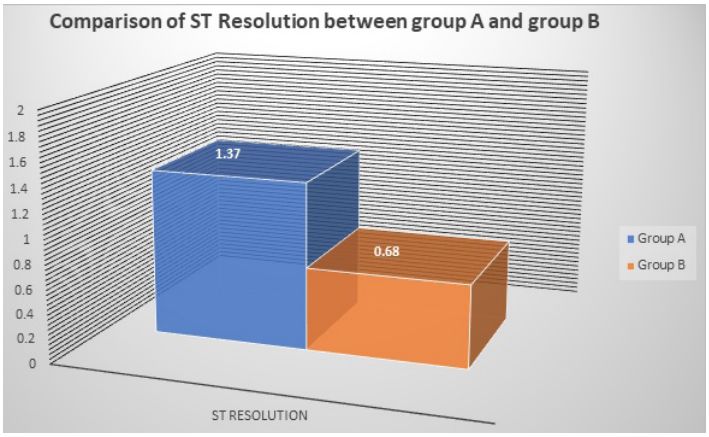

Figure 8: showing comparison of some interventional data between 2 groups. There were significant statistical differences in ST resolution.

Discussion

Epicardial coronary arteries in diabetic patients usually have Microangiopathy and micro vascular dysfunction always. When epicardial blood flow is restored to normal level [21,22]. Still there is 25% to 30% of patients have insufficient myocardial tissue reperfusion (i.e., no-reflow and slow flow) Compared with non-diabetic patients, diabetic patients have a higher incidence of re-infarction, heart failure, stroke, and death regardless of the acute or chronic phase [23].

The main cause of no-reflow and slow flow is thrombosis and microcirculation embolization, these micro vascular complications is higher in acute coronary syndrome and primary PCI. Thrombus suction can remove visible thrombus in coronary angiography can be removed by suction catheter but it was found that only 39% of the thrombus was visible in AMI. The remaining invisible thrombus, is the main cause of no-reflow and slow flow after PCI and is also one of the reasons for increased incidence of complications, such as heart failure, arrhythmia, and cardiogenic shock in diabetic patients with AMI [24,25], imperfect inhibition of platelet aggregation at the time of PCI may increase the MACE [28]. The use of Adjunctive medical therapies such as GPIs has considerably reduced the incidence distal embolization and ameliorate clinical outcome in STEMI patients [26-29].

This study demonstrates that IC administered for thrombotic complications or bailout situations Glycoprotein IIb/IIIa addition to loading oral anti platelets in diabetic patients is associated with greater reduction of peak hs-TnT, CK-MB levels and ST segment resolution compared with IV GpIIb/IIIa inhibitors in patients with ACS who underwent PCI. However, the 2 regimens are similar in terms of angiographic measures, MACE, and major or minor bleeding events during hospitalization and after one month follow up. Intracoronary administration of GpIIb/IIIa inhibitors does not appear to increase the risk of bleeding or platelet reduction. Topol et al. showed that GpIIb/IIIa inhibitors (tirofiban) provided greater platelet inhibition in diabetic patients at various time points as compared to abciximab and help for the prevention of ischemic events with percutaneous coronary revascularization. [30] The theory for IC administration of GpIIb/IIIa inhibitors (tirofiban) during PCI is to achieve a higher drug concentration in the area of the culprit lesion and in small vasculature of the distal bed of the affected vessel. Compared with IV delivery of glycoprotein IIb/IIIa, IC delivery of glycoprotein /IIb/IIIa, leading to a greater procedural success rate (e.g., TIMI grade 3 flow) [31,32].

Our findings revealed that IC injection of GpIIb/IIIa inhibitors (tirofiban) effectively reduced the occurrence of no-reflow and slow flow, improved TIMI flow and MBG. Loss of endothelium – dependent vasodilatation, inflammatory reaction and platelet-dependent micro-thrombosis, is enhanced by hyperglycemia, thereby aggravating the perfusion disturbance of coronary microcirculation [33,34]. The mortality is much higher in patients when MBG decreased to MBG 0 to MBG 1 as well as patients [35-37].

To the best of our knowledge, this study is the first to demonstrate the safety and short-term outcomes of administration of high-dose bolus GpIIb/IIIa inhibitors intracoronary plus IV maintenance compared to IV GpIIb/IIIa inhibitors in diabetic patients with ACS. We also showed that IC tirofiban as GpIIb/IIIa inhibitors has decreased inflammation during myocardial infarction which is evidenced by significant reduction of peak CRP level. Previous studies have reported on the predictive value of CRP in determining the risk of future cardiovascular events. [38,39] Other studies have documented a post-procedure CRP rise in relation to my necrosis [40]. Tirofiban strongly inhibits the platelet aggregation. The decreased platelet aggregation can suppress the inflammatory protein, chemokine, and adhesion molecule expression [41].

Although there was no significant difference in the bleeding events and MACE rates within 30 days of PCI, a higher average LVEF was observed in the intracoronary tirofiban group, suggesting an improvement in left ventricular function. However, larger multicenter randomized trials to evaluate whether IC administration of tirofiban during primary PCI improves clinical outcome in diabetic patients at long-term still needed.

Conclusion

IC GpIIb/IIIa inhibitors is more effective in improving coronary blood flow and myocardial tissue perfusion in DM after anterior STEMI 30 days post PCI DESPITE THE BLEEDING event and MACE rates showed no significant difference, IC GpIIb/IIIa inhibitors group showed better improvement in LVEF.

Limitation

The results of the present study have certain limitations as non-random selection of the patients for IC GpIIb/IIIa inhibitors. The number of patients was relatively small; we evaluated of intracoronary GpIIb/IIIa inhibitors on STEMI and did not compare the effects in non- ST-elevation ACS. In addition, despite we included elderly patients in the present study, but we did not compare the major and minor bleeding incidence and platelet reduction in different age population. Improvement of left

ventricular systolic function and possible improvement of clinical outcome should be observed for longer follow-up periods.

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