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Efficacy and Safety of Intracoronary Administration of Tirofiban through Perforated Balloon Technique in Patients with St-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objective: To assess the safety and efficacy of intracoronary (IC) versus Intralesional (IL) administration of tirofiban during primary (PCI) in patients with acute ST segment elevation myocardial infarction.

Patients and Methods: This research involved 95 patients who were randomly assigned to recieve either IC bolus plus maintenance or IL bolus plus maintenance of tirofiban. Both groups were compared for pre and post intervention for cardiac marker, myocardial perfusion, and Major composite adverse cardiac event incidence at 3 months 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 IL group with p = 0.03*, and 0.022* respectively favoring distal intracoronary strategy. Peak CK-MB values were lower in IL tirofiban group than IC group, 172.79±18.37, 184.58 ± 19.93 respectively with significant (p=0.021). ST segment resolution and 3 months LVEF in IL group were significantly higher in IL group than in IC group (p= 0.016*) respectively.

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Conclusion: local intracoronary tirofiban infusion via perforated balloon technique at the time of PPCI was associated with reduced thrombus burden, improved immediate angiographic outcome, and 3-month EF, compared with intracoronary GPI bolus injection via the guiding catheter.

Keywords: Tirofiban; no-reflow; perforated balloon.

1. INTRODUCTION

"TIMI III flow can be achieved in the IRA in>90% of patients undergoing PPCI. However, epicardial blood flow does not necessarily equate to myocardial perfusion. After the operation, angina pectoris, sudden death, even heart failure, and other serious cardiovascular adverse events are possible. At present, it is believed that this is because effective and sufficient myocardial blood flow perfusion is not achieved, resulting in myocardial stunning, hibernation, and necrosis. So, after successful PCI even with TIMI 3 flow, effective myocardial perfusion may not be achieved"[1-3].

"Excessive platelet activation and aggregation play an important role in the progression of acute coronary syndrome (ACS)" [4].

"Glycoprotein (GP) IIb/IIIa antagonists can effectively prevent the binding of fibrinogen to platelet glycoprotein IIb/IIIa receptor and the adhesion of platelets and damaged endothelial cells.

One such antagonist, tirofiban, was shown to improve myocardial perfusion by inhibiting platelet aggregation" [5].

"Angiographic evidence of a large thrombus, sluggish or absent reflow, or other thrombotic consequences justifies the use of GPIIb/IIIa inhibitors (GPIs) as rescue therapy, according to ESC/ACCF/AHA recommendations" [6,7].

"However, the incidence of hemorrhage is also increased. Tirofiban is administered through both intravenous and intra-coronary artery delivery. It has been suggested that the administration of tirofiban by intra-coronary injection can promote drug absorption in the diseased region and enhance the inhibition of platelet aggregation, thereby decreasing bleeding risk"[8].

Intra-coronary administration of tirofiban can be achieved using either a guiding catheter or perforated balloon as a simple & handy technique, little is known about the comparative efficiency and safety for these two delivery methods.

2. METHODS

2.1 Study design

A prospective cohort randomized comparative study was conducted at Cardiology Department, Tanta University, from 2019 till mid of 2021

2.2 Study Population

95 patients that fulfilled the inclusion criteria were recruited from Cardiology department in Tanta University presented with first recent STEMI, the patients were divided into two groups (grouping was done according to Route of tirofiban administration for bailout indications): Group A: comprised 50 Patients who had primary PCI as a reperfusion strategy then received tirofiban intracoronary through guiding catheter, Group B: comprised 45 Patients who had primary PCI as a reperfusion strategy then received tirofiban in the distal coronary bed through perforated balloon technique .The exclusion criteria was active bleeding, patients with known bleeding diathesis. History of intracerebral mass or aneurysm, cardiogenic shock at admission, renal impairment, history of hepatic disorders or thrombocytopenia.

2.3 Methods

The study sample population was subjected to the following: history taking, Age, sex, history of risk factors for (CAD), Clinical examination, twelve leads ECG & Routine laboratory investigation were done for all patients.

A loading dose of dual anti platelet (Aspirin 300mg chewable) plus P2Y12 inhibitor (Ticagrelor 180 mg) was given. In this study, both femoral and radial arterial approaches were used. The infarcted related artery (IRA) was identified. An interventional cardiologist identified the culprit lesion on the basis of the infarct location on the admission ECG and the angiographic findings (target vessel, lesion characteristics).[113] After securing vascular

access through right femoral or radial arteries, a total of 50-70 IU/kg unfractionated heparin IV bolus was given, then additional weight adjusted unfractionated heparin was given to achieve approximately 250 s of activated clotting time (ACT).

Intra-coronary injection of tirofiban was applied according to the event of angiographic evidence of a thrombus (TIMI) thrombus grade ≥ 2 in the infarct-related artery, slow- or no-reflow, and other thrombotic complications. Patients were randomly divided into 2 groups according to the method used to administer the loading dose of intracoronary tirofiban: the guiding catheter group (group A: n = 50) and the perforated balloon technique group (group B: n = 45) In group A , bolus 25 µg /kg of tirofiban was given through the guiding catheter in infarcted related artery immediately after guidewire crossed the lesion successfully and ante grade flow was restore aiming to secure maximum concentration of the drug at culprit lesion site and distal microvascular bed. In perforated balloon group (Group B) .... coronary balloon catheter used for predilatation of the lesion was prepared. In-vitro inflation of the balloon catheter was performed using the inflation device filled with loading dose of tirofiban. We performed four punctures in different areas of inflated balloon segment using a needle and it is important to not cross the opposite layer of the balloon. Once that was done, we allowed the solution to ooze from the perforated segments to remove all possible micro-bubbles by maintaining 1–2 atmospheric pressure with inflation device. The balloon was inserted over the coronary wire into the guide catheter The balloon was then advanced into distal segment of the culprit coronary artery. IC instillation of drug was performed. Additionally, all patients received intracoronary cocktail (Nitrate 50-200 mic + verapamil (300 mic)75% of the dose after wire passage; 25% after stent deployment), either via the Guiding catheter group (A), or through the perforated balloon (group B). Aspiration thrombectomy catheter was used if needed ((TIMI) thrombus grade ≥ 3 in the infarct-related artery) and finally, a suitable drug eluting stent (FDA approved) was employed in IRA in most of patients [9,10]. Maintenance IV tirofiban 0.15 µg /kg/min for 24 hours was started in both groups after bolus dose.

The following were recorded from the offline angiographic analysis of the whole procedure; post-procedural (TIMI) flow grades and Myocardial blush grade in the culprit vessel (MBG), 12-lead ECGs were acquired immediately after admission and every 30 min after primary PCI. ST resolution was assessed and was categorized as 50% or less. All ECG recordings were analyzed by an experienced physician blinded to treatment groups. Peak CKMP level was recorded 24 H after symptom onset. Maximum CRP level was estimated 48 h after symptom onset [11].

- Echocardiography were performed using (a GE vivid seven Cardiac ultrasound phased array system with tissue Doppler imaging using M4S transducer 4 M. HZ). Assessment of ejection fraction by modified Simpson method done during admission after successful PCI. Clinical follow-up of each patient was obtained from hospital records and interviews. MACE included cardiovascular death, heart failure, recurrent myocardial infarction, stent thrombosis, or target vessel revascularization and bleeding complication. during hospitalization, at 3-month. Safety endpoints in the form of Major, Minor bleeding & thrombocytopenia.

2.4 Statistical Analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 24.0 for windows. 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 [12,13].

3. RESULTS

The two groups showed No statistically significant differences in baseline characteristics. The mean age was 58.5 ± 10.18 years in group A and 55.90 ± 11.66 years in group B. with P-value 0.249.

Patients in group A were divided into 27 male (54%) and 23 female (46%), while in group B there were 23 male (51.1%) and 22 female (48.9%) with no statically significant difference between 2 groups with P value 0.778**.**There was no difference between two groups in

cardiovascular risk profile (Figure 1), door-to-balloon times were not significantly different (p=0.198) (Table 1). Frequency of patients with Killip class 1 was 70% in group A and 77% in group B, (p=0.691). Angiographic characteristics of the groups are presented in Table 2, No significant differences were found between groups in distribution of culprit lesion.

Post procedure TIMI flow III and MBG III were significantly in favor to intralesional (IL) group with p = 0.03*, and 0.022* respectively. Percentage of patients with 50% resolution of ST segment was significantly higher in IL group than in IC group with (p= 0.035*), Peak CK-MB value was significantly lower in IL Glycoprotein IIb/ IIIa group than IC group, 172.79±18.37, 184.58 ± 19.93 respectively (p=0.021). maximum CRP Mean level was significantly lower in group B rather than group A. There was no significant difference in LVEF between both groups 48 hours after PCI (p= 0.116). However, after 3 months of PCI, the average LVEF in IL group was higher than in the IC group (p= 0.016*).

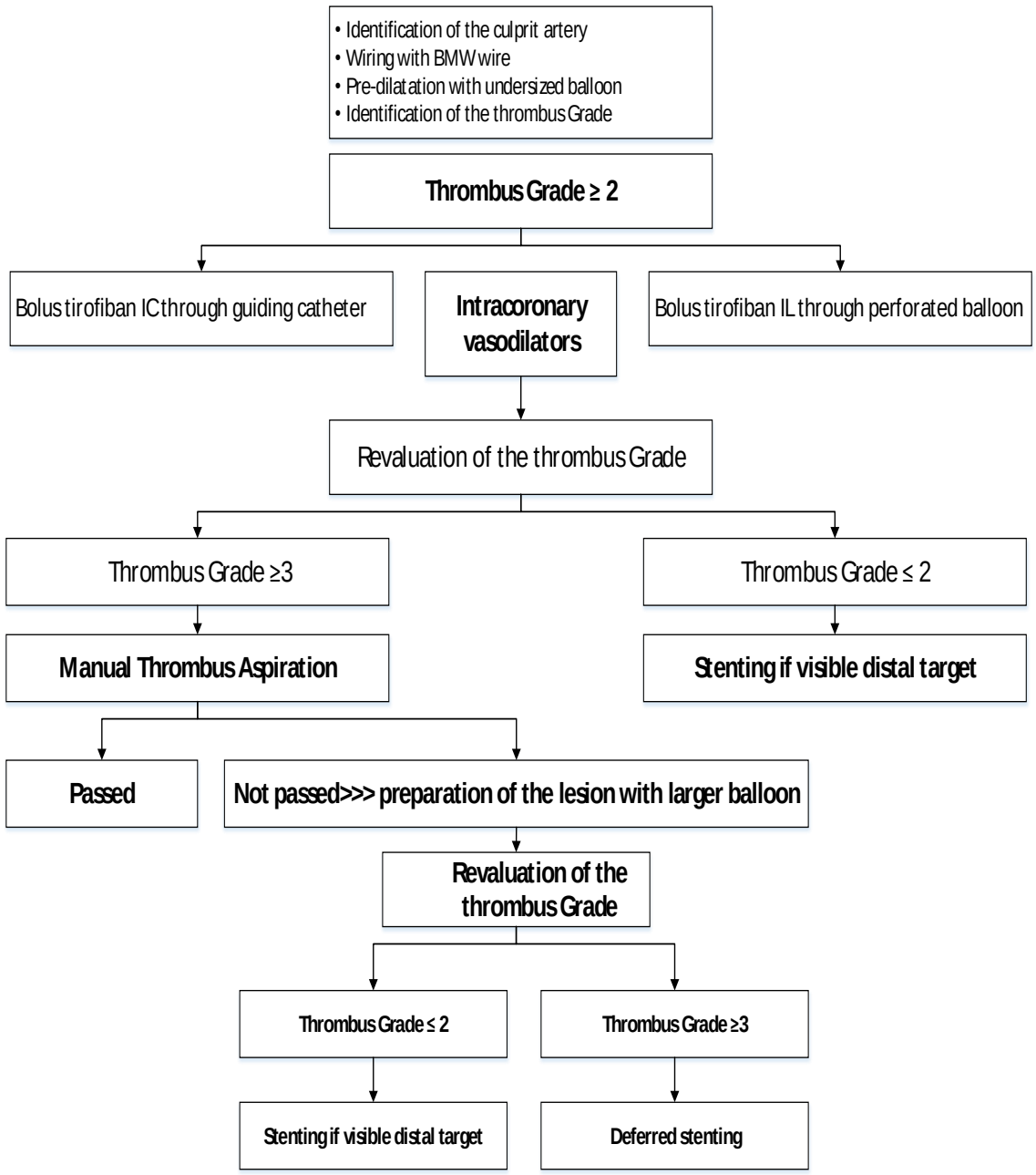

Chart 1. Schematic algorism for the methodology

There were no significant differences between groups with respect to incidence of MACE, major bleeding and minor during hospitalization and at 3-month follow-up as shown in Table 5.

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 5.

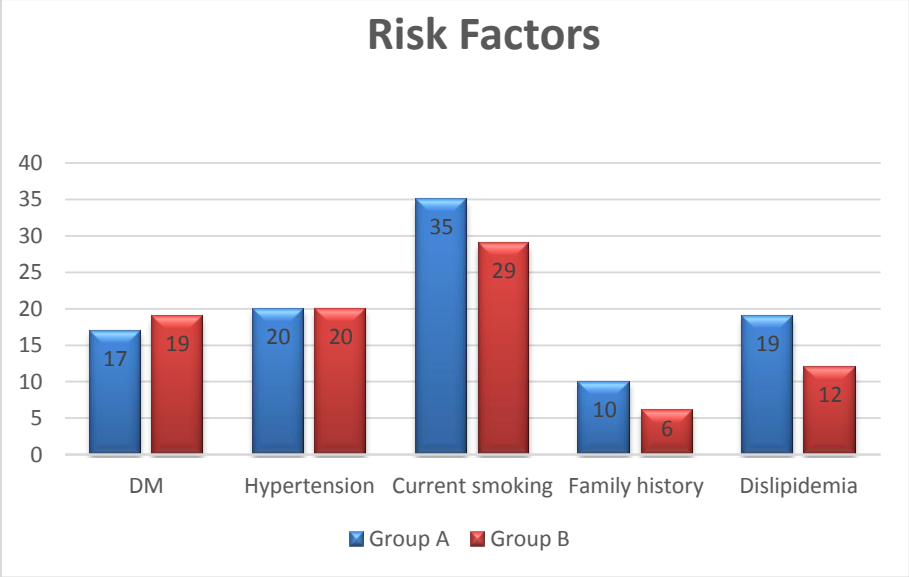

Fig. 1. Comparison between the two studied groups according to risk factors

Table 1. Comparison between the two studied groups according to clinical presentation

	Group A (n = 50)		Group B (n = 45)		P
	No.	%	No.	%	
Time from onset of symptoms to FMC (hours)					
Min. – Max.	0.50 – 12.0		1.0 – 12.0		0.348
Mean ± SD.	5.63 ± 3.61		4.98 ± 3.28		
Pulse (beat/min.)					
Min. – Max.	40.0 – 115.0		50.0 – 125.0		0.108
Mean ± SD.	81.58 ± 18.19		76.55 ± 12.25		
Killip Class					
1	35	70.0	35	77.8	0.691
2	12	24.0	8	17.8	
3	3	6.0	2	4.4	
Systolic blood pressure (mmHg)					
Min. – Max.	100.0 – 170.0		110.0 – 150.0		0.257
Mean ± SD.	135.62 ± 21.47		131.52 ± 13.62		
Diastolic blood pressure (mmHg)					
Min. – Max.	60.0 – 110.0		60.0 – 100.0		0.236
Mean ± SD.	81.56 ± 12.26		78.91 ± 9.84		
Rhythm					
Normal Sinus Rhythm	48	96.0	40	88.9	0.185
Other	2	4.0	5	11.1	
Door to reperfusion method (minutes)					
Min. – Max.	30-90		20-100		0.198
Mean ± SD.	58.63 ± 19.41		64.39 ± 24.72		

Table 2. Comparison between the two studied groups according to angiographic procedure

	Group A (n = 50)		Group B (n = 45)		P
	No.	%	No.	%	
Access site					
Femoral	37	74	35	77.8	0.668
Radial	13	26	10	22.2	
Infarct-related artery					
LAD	34	68.0	27	60.0	0.717
LCX	6	12.0	7	15.6	
RCA	10	20.0	11	24.4	
Stenting					
No	6	12.0	2	4.4	0.185
DES	44	88.0	43	95.6	
Stent length (mm)	26.5± 5.9		24.3± 4.5		0.039*
Thrombus aspiration	20	40	17	38	0.824

Table 3. Comparison of interventional data between group A and group B

Variables		Group A (N = 50)	Group B (N = 45)	p
TIMI Pre	0	9 (18.0%)	8 (17.7%)	0.623
	I	16 (32.0%)	12 (26.7%)	
	II	14 (28.0%)	18 (40.0%)	
	III	11 (22.0%)	7 (15.6%)	
TIMI Post	0	4 (8.0%)	0 (0.0%)	0.03*
	I	4 (8.0%)	1 (2.2%)	
	II	7 (14.0%)	2 (4.4%)	
	III	35 (70.0%)	42 (93.3%)	
Myocardial Blush post	I	7 (14.0%)	2 (4.4%)	0.022*
	II	9 (18.0%)	2 (13.6%)	
	III	34 (68.0%)	41 (82.0%)	
ST segment resolution		33 (66.0%)	20 (44.4%)	0.035*

Table 4. Comparison of ejection fraction between group A and group B

Variable	*Group*	*M ± SD*	*p*
EF (48 hrs.)	Group A	39.65 ± 4.82	0.116
	Group B	41.36 ± 5.91	
EF (3 months)	Group A	42.14 ± 7.17	**0.016***
	Group B	45.93 ± 7.84	

4. DISCUSSION

"The main cause of slow flow and no-reflow is thrombosis and microvascular embolization, these microvascular complications is higher in AMI and primary PCI. Imperfect platelet aggregation inhibition during PCI may increase the MACE. The use of adjuvant medical drugs like GPIs considerably decrease the incidence of distal embolization and thrombotic outcomes in STEMI patients" [14,15], "some experimental studies showed that GPIs exert additional antiplatelet, antithrombotic, and anti-inflammatory effects when local drug concentrations are higher" [16]. These reports eventually gave rise to the logical hypothesis of choosing the intracoronary route for GPIs aiming increased local concentrations with higher levels of platelet GPI receptor occupancy leading to more rapid dissolution of thrombus with improved disaggregation of newly formed platelet aggregates, which might be eventually associated with improved myocardial perfusion.

"This study demonstrates that intracoronary administration of high dose bolus of intralesional tirofiban leads to accelerated myocardial reperfusion, improved coronary flow, and reduced infarction size, improve ejection fraction in STEMI patients undergoing PCI but

Table 5. Comparison of MACE in-hospital and 3-month after procedure and bleeding between group A and group B

Variables		Group A (N = 50)	Group B (N = 45)	p
In-hospital	Death	2 (4.0%)	1 (2.2%)	0.621
MACE	Stroke	0 (0.0%)	0 (0.0%)	-
	Reinfarction	1 (2.0%)	0 (0.0%)	0.340
	Stent thrombosis	1 (2.0%)	0 (0.6%)	0.340
	TVR	1 (2.0%)	0 (0.6%)	0.340
	HF	3 (6.6%)	1 (3.3%)	0.307
3-month	Death	1 (2.0%)	0 (0.0%)	0.340
MACE	Stroke	0 (0.0%)	0 (0.0%)	-
	Reinfarction	1 (2.0%)	1 (2.2%)	1.0
	Stent thrombosis	1 (2.0%)	1 (2.2%)	1.0
	TVR	1 (2.0%)	1 (2.2%)	1.0
Bleeding	Major	1 (2.0%)	1 (2.2%)	1.0
	Minor	5 (10.0%)	4 (8.8%)	0.854
	Thrombocytopenia	2 (4.0%)	2 (4.4%)	1.0

Table 6. Comparison between the two studied groups according to laboratory investigation

Laboratory investigation	Group A (n = 50)	Group B (n = 45)	P
Hb (mg/dl)			
Min. – Max.	7.0 – 15.0	11 – 16	0.525
Mean ± SD.	12.9 ± 2.7	12.7 ± 1.3	
WBCc (number/mm^3)			
Min. – Max.	7500 – 22700	7100-22200	0.132
Mean ± SD.	18470± 3069	19530 ± 3725	
Platelets(number/mm^3)			
Min. – Max.	140000 – 252000	148000- 276000	0.135
Mean ± SD.	196200± 24423	203543 ± 22885	
Serum creatinine (mg/dl)			
Min. – Max.	0.6-1.8	0.6 – 1.9	0.691
Mean ± SD.	1.04 ± 0.38	1.07 ± 0.35	
Blood urea(mg/dl)			
Min. – Max.	23-45	35 – 51	0.133
Mean ± SD.	37.3 ± 8.9	40.1 ± 9.1	
Random blood sugar(mg/dl)			
Min. – Max.	114-412	90 – 600	0.122
Mean ± SD.	186.7 ± 80.4	218.6 ±117.3	
CKMB (Peak) Mean ± SD.	184.58 ± 19.93	172.79±18.37	**0.018***
Maximum CRP level Mean ± SD.	8.2 ± 3.6	6.7 ± 1.9	**0.014***

unfortunately, these findings did not translate into improved MACE at 3 months follow up. Our findings also in concordance with recent studies which proved that IC" [17] and "intra-lesion delivery of tirofiban through aspiration catheter has better myocardial perfusion and less complications even in complex PCI" [18]. These results contradicted with our findings which significantly favored local coronary route as the intralesional group exhibited lower peak levels of post-procedural cardiac enzymes associated with a smaller enzymatic infarct size with statistically significant between both group with mean values of Peak CKMP and improved TIMI flow and Myocardial blush scores in our study as there was statistically significant improvement of TIMI Flow and MBG favor the intralesional route. Furthermore, restoration of microvascular blood flow assessed by ST-segment resolution was significantly accelerated besides that statistically significant resolution of ST segment in ECG 30 minutes after intervention towards intralesional route .We also showed that IL tirofiban has decreased inflammation during myocardial

infarction which is evidenced by significant reduction of peak CRP level with mean values± SD of both groups. Previous studies have reported on the predictive value of CRP in determining the risk of future cardiovascular events [19]. It was not a surprise that the potential beneficial effects of intralesional high dose administration became evident after 3 month in our study and translated into a better recovery of left ventricular function as our result revealed no statistically significant difference of the left ventricular ejection fraction between both groups at the time of discharge, but it is of worth to notice that EF of patients in Perforated balloon strategy was slightly higher than those in Guiding catheter group, while in follow up of the patients, there was statistically significance of measuring EF% between Group A & Group B.

"The fact that improved TIMI flow and MBG blush scores and ST segment resolution did not necessarily translate into better clinical outcomes (MACE) at 3 month follow up might have been due to combination of successful primary PCI and high-dose bolus of tirofiban in both groups, as both of them are powerful-enough confounders to effectively blunt MACE findings at 3 month, and it is very well-known that myocardial blush grade best describes the effectiveness of myocardial reperfusion and is an independent predictor of long-term mortality rate" [20]. This came in agreement with M. Osman et al which concluded that IC administration of tirofiban enhance left ventricular systolic function over IV route, however no distinction between two strategies on MACE or bleeding risk [21]. However, intracoronary administration of GPI via the guiding catheter would eventually lose much of the dose inside branches before reaching the site of thrombus. Local intracoronary infusion of GPI at the site of thrombus formation via a perforated balloon catheter would achieve much higher concentration of the drug, and consequently better thrombus dispersal and improved microvascular perfusion. In the COCTAIL study by Prati et al., bolus abciximab via coronary perfusion catheter reduced thrombus burden as assessed by optical coherence tomography in patients with acute coronary syndrome (38% STEMI) and culprit lesion thrombosis, compared with bolus abciximab delivered via guiding catheter injection. The administration of intracoronary vasodilator may have further contributed to improving the final angiographic outcome in the current study.

Resolution of thrombus before stent implantation in patients with STEMI undergoing PPCI allows for a better angiographic assessment of the infarct-related segment; and therefore, a better selection of the size (length) of the stent to be implanted which was obvious in less mean stent length in IL group with significant difference between both groups. Nevertheless, more often use of thrombectomy device with local intracoronary infusion of tirofiban might have contributed to the better angiographic results.

Platelet count mildly decreased in 4 patients in our study without significant difference between both groups and without any significant impact on the rate of hemorrhagic complications. We suppose that our technique would to be lower in the bleeding risk, unfortunately that was not obvious in the study Mostly as we did give a maintenance IV infusion of tirofiban in both groups after the bolus dose.

5. CONCLUSION

In patients with acute STEMI with slow flow, no-reflow or thrombotic complication, local intracoronary tirofiban infusion via perforated balloon technique at the time of PPCI was associated with reduced thrombus burden, improved immediate angiographic outcome, and 3-month EF, compared with intracoronary GPI bolus injection via the guiding catheter.

ETHICAL APPROVAL AND CONSENT

Ethical committee approval and informed consent were obtained from all the patients who included in the research, and any unexpected risks appearing during the research was cleared to the participants and the ethical committee on time, taking an insight into the privacy of the participants and confidentially of the data. Informed written consent was obtained from all patients after a full explanation of benefits and risks of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kopetz VA, Penno MA, Hoffmann P, et al. Potential mechanisms of the acute coronary syndrome presentation in patients with the coronary slow flow

phenomenon: insight from a plasma proteomic approach. Int J Cardiol. 2012;156:84–91.
2. Ding S, Li Z, Ge H, et al. Impact of early ST-Segment changes on cardiac magnetic resonance-verified intramyocardial haemorrhage and microvascular obstruction in ST-elevation myocardial infarction patients. Medicine (Baltimore). 2015;94: e1438.
3. Pu J, Shan P, Ding S, et al. Gender differences in epicardial and tissue level reperfusion in patients undergoing primary angioplasty for acute myocardial infarction. Atherosclerosis 2011;215:203–8.
4. Pu J, Ding S, Shan P, et al. Comparison of epicardial and myocardial perfusions after primary coronary angioplasty for ST-elevation myocardial infarction in patients under and over 75 years of age. Aging Clin Exp Res. 2010; 22:295–302.
5. Smit JJ, van Werkum JW, ten Berg J, et al. Prehospital triple antiplatelet therapy in patients with acute ST elevation myocardial infarction leads to better platelet aggregation inhibition and clinical outcome than dual antiplatelet therapy. Heart. 2010; 96:1815–20.
6. De Luca G, Navarese E, Marino P. Risk profile and benefits from Gp IIb- IIIa inhibitors among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: ameta-regression analysis of randomized trials. Eur Heart J. 2009; 30:2705–13.
7. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012; 33:2569–619.
8. O'Gara PT, Kushner FG, Ascheim DD, et al. ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127: e362–425.
9. Elfekky EM, Penjameen MN, Nassar AI, et al. Outcome of manual thrombus aspiration for patients undergoing primary PCI for acute STEMI showing large thrombus burden. Egypt Heart J. 2021;73:8.
10. Samy M, Nassar Y, Mohamed AH, Omar W, Elghawaby H. To Whom Thrombus Aspiration May Concern? Open Access Maced J Med Sci; 2019.
11. Pietila KO, Harmoinen AP, Jokiniitty J, Pasternack AI. Serum Creactive protein concentration in acute myocardial infarction and its relationship to mortality during 24 months of follow-up in patients under thrombolytic treatment. Eur Heart J. 1996;17:1345-9
12. Kotz S Balakrishnan N, CB R, B. I. Encyclopedia of statistical sciences. 2nd ed Hoboken, NJ Wiley-Interscience; 2006.
13. LA K, BC F. A simple guide to IBM SPSS statistics for version 20.0. Student ed Belmont, Calif Wadsworth, Cengage Learn; 2013.
14. Thiele H, Schindler K, Friedenberger J, Eitel I, Fu¨rnau G, Grebe E et al. Intracoronary compared with intravenous bolus abciximab application in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention: the randomized Leipzig Immediate Percutaneous Coronary Intervention Abciximab IV versus IC in ST-Elevation Myocardial Infarction trial. Circulation. 2008;118:49–57.
15. Deibele AJ, Kirtane AJ, Pinto DS, Lucca MJ, Neva C, Shui A, et al. Intracoronary bolus administration of eptifibatide during percutaneous coronary stenting for non-ST elevation myocardial infarction and unstable angina. J Thromb Thrombolysis. 2006;22(1):47–50.
16. Romagnoli E, Burzotta F, Trani C, Biondi-Zoccai GG, Giannico F, Crea F. Rationale for intracoronary administration of abciximab. J Thromb Thrombolysis. 2007;23:57–63.
17. Wohrle J, Grebe OC, Nusser T, Al-Khayer E, Schaible S, Kochs M, et al. Reduction of major adverse cardiac events with intracoronary compared with intravenous bolus application of abciximab in patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty. Circulation. 2003;107:1840–1843.
18. Hu S, Wang H, Zhu J, Li M, Li H, Gao D, Zhang H. Effect of intra-coronary administration of tirofiban through aspiration catheter on patients over 60 years with ST segment elevation myocardial infarction undergoing percutaneous coronary intervention. Medicine (Baltimore). 2018;97(21): e10850.

19. (PROVE IT–TIMI 22) Investigators. C-reactive protein levels and outcomes after statin therapy. N Engl J Med. 2005;352:20–28.
20. Matetzky S, Shenkman B, Guetta V, Shechter M, Bienart R, Goldenberg I, et al. Clopidogrel resistance is associated with increased risk of recurrent atherothrombotic events in patients with acute myocardial infarction. Circulation. 2004;109:3171– 3175.
21. Osman M, Yassen I, Elhefny E.H.A.B. Comparison between intracoronary versus intravenous bolus injection of tirofiban on infarct size during primary PCI in patients with acute anterior ST segment elevation myocardial infarction. European Heart Journal. 2020;41(Supplement_2):ehaa 946.1437.

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