

# Effect of Intracoronary Glycoprotein IIb/IIIa Antagonist and Manual Aspiration on Primary Percutaneous Coronary Intervention Outcome in High Thrombus Burden Patients

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## ABSTRACT

**Background:** The opening of a related artery in myocardial infarction as quickly as possible is the key to treating infarct. Percutaneous coronary intervention (PCI) for recanalization of related infarcted arteries is considered the most effective therapy for myocardial infarction. **Aim of the Work:** To estimate the intracoronary delivery of glycoprotein IIb/ IIIa following manual thrombus aspiration on outcomes post PCI for patients with high thrombus burden. **Patients and Methods:** The current study was carried out at the cardiology department of Zagazig University that was conducted on 48 patients presented to zagazig university Hospital's emergence cardiac unit from March 2021 to November 2021. With ST-elevation myocardial infarction for primary percutaneous coronary intervention, the need for reperfusion therapy was assessed according to the ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation with high thrombus burden. **Results:** Combination glycoprotein IIb/IIIa and manual aspiration is the better then single modality for high thrombus burden patients. **Conclusion:** thrombectomy combined with intracoronary GPI treatment could result in improved myocardial reperfusion, smaller infarcts, better cardiac function, and outcomes in high thrombus burden patients compared to each treatment alone.

**Keywords:** Intracoronary Glycoprotein, Manual Aspiration Thrombectomy, Percutaneous Coronary Intervention, ST-segment elevation with high thrombus burden.

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## INTRODUCTION

The opening of a related artery in myocardial infarction as quickly as possible is the key to treating infarct <sup>(1)</sup>.

Percutaneous coronary intervention (PCI) for recanalization of related infarcted arteries is considered the most effective therapy for myocardial infarction <sup>(2)</sup>.

Myocardial recovery after the primary percutaneous coronary intervention (PCI) is often suboptimal despite restoration of thrombolysis in myocardial infarction (TIMI) 3 flow, in part due to thrombus remobilization which results in impaired microvascular perfusion and increased infarct size <sup>(3)</sup>.

Aspiration thrombectomy and intracoronary platelet glycoprotein (GP) IIb/IIIa receptor antagonists are widely used to reduce distal embolization <sup>(4,5)</sup>.

GP IIb/IIIa receptor antagonists can reduce thrombus burden and secondary distal embolization microcirculation <sup>(6)</sup>.

Measuring infarct size after reperfusion therapy offers important prognostic utility. Laboratory measures of infarct size include biomarkers such as creatinine phosphokinase, lactate

dehydrogenase, and troponin levels. While these tests are promptly available and can be obtained in the acute setting, they are unreliable in comparison to infarct size assessed by cardiac imaging<sup>(7)</sup>.

Some studies suggest that the intracoronary application of platelet membrane GP IIb/IIIa receptor antagonists improves myocardial perfusion; however, such studies are currently few, and their results are controversial<sup>(8,9)</sup>. Most of these studies used abciximab as their GP IIb/IIIa receptor antagonist, and tirofiban was rarely used<sup>(10)</sup>. This study aimed to selection of best method for treatment of patients with high thrombus burden.

## PATIENTS AND METHODS

The current study was carried out at the cardiology department of Zagazig University that was conducted on 48 patients presented to Zagazig University Hospital's emergence cardiac unit from March 2021 to November 2021. With ST-elevation myocardial infarction for primary percutaneous coronary intervention, the need for reperfusion therapy was assessed according to the ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation with high thrombus burden<sup>(11)</sup>.

### ***Ethical consideration:***

This study was submitted for approval by the Institution Research Board (IRB) of Zagazig University Institution. Informed consent was obtained from each participant sharing the study. Confidentiality and personal privacy were respected at all levels of the study. Collected data are not used for any other purpose.

***Inclusion criteria:*** Patients age 18 years and older of both genders presented with ST-elevation myocardial infarction with high thrombus burden or new LBBB. ***Exclusion criteria:*** Prior myocardial infarction. Prior systolic dysfunction (ejection fraction < 40%). Prior coronary artery bypass graft. Previously stent implantation. Sever vessel tortuosity. Diffuse disease or severe calcification. Patients with pre- existing valvular HD. Patients with chronic arrhythmias. Advanced hepatic and renal diseases.

Patients fulfilling inclusion criteria were recruited to the study from the attendants of Zagazig University Hospitals and were randomized into three groups; Manual aspiration group. Manual aspiration with intracoronary glycoprotein IIb/IIIa group. Intracoronary glycoprotein IIb/IIIa group.

### **All patients involved in the study were subjected to:**

Patient History and examination included:

- Age and Sex.
- Risk factors for coronary artery disease: (Smoking, HTN, DM, hyperlipidemia).
- Family history of chronic heart disease.
- Obesity.
- History of CKD detected by high serum creatinine.
- Lower extremities arterial disease.
- Prior myocardial infarction or coronary artery bypass graft.
- Patients' vital data including arterial blood pressure, heart rate.
- **12 lead ECG** on admission to detect presence & localization of STEMI<sup>(12)</sup>.

### **Laboratory evaluation:**

- Complete blood count.

- Renal function test. (Urea, creatinine).
- Serum electrolyte (NA, K, and Cl).
- Coagulation profile (PT, PTT, and INR).
- A cardiac enzyme (CKMB & troponin).
- Serology test (HBV, HCV, and HIV).
- Electrocardiography (ECG) included; ST-segment elevation. New left bundle branch block. Right-sided leads electrocardiography. Posterior sided leads electrocardiography.
- Echocardiography (ECHO): evaluation of a systolic function at admission and after discharge.

All Patients were loaded with a dual antiplatelet regimen at the time of presentation (Aspirin 300 mg and clopidogrel 600 mg). Adequate anticoagulation was done using IV unfractionated heparin guided by anti-coagulation time. All patients will be diagnosed by angiography to determine the lesion (thrombus).

### Postoperative follow-up

**Primary endpoint:** Infarct size as reflected by Left ventricular ejection fraction (LVEF%), segmental wall motion score and perfusion blush score assessment.

**Secondary endpoint:** Short term follows up, in hospital outcomes (MACCE) regarding death, heart failure, reinfarction, arrhythmia, stroke. After 6 weeks follow up, Major Adverse Cardiac and Cerebro vascular Events (MACCE) included: death, Heart failure, reinfarction, arrhythmia, and stroke.

## RESULTS

**Table (1):** The demographic characteristic of the study population:

Variables		Frequency	Percent
Gender	Female	19	39.6
	Male	29	60.4
HTN		37	77
DM		27	56.2
SMOKING		28	58.3
Dyslipidemia		27	56.2
Chronic kidney disease:		0	0
Type of Infarction	Ant	22	45.8
	Inferior	19	39.5
	Antero-inferior	7	14.5
Troponin	Negative	0	0
	Positive	48	100
Thrombus grade:	Grade III	22	45.8
	Grade V	26	54.1
Use of (gp IIb/IIIa inhibitors)		13	27.1
Use of (gp IIb/IIIa inhibitors with manual aspiration)		19	39.6
Use of manual aspiration		16	33.3
Myocardial blush grade 2/3	At baseline	38	79.1
	Follow up	42	87.5
TIMI initial	TIMI 0	2	4.1
	TIMI 1	6	12.5

	<b>TIMI 2</b>	<b>10</b>	<b>20.8</b>
	<b>TIMI 3</b>	<b>30</b>	<b>62.5</b>
<b>TIMI follow up</b>	<b>TIMI 0</b>	<b>0</b>	<b>0</b>
	<b>TIMI 1</b>	<b>1</b>	<b>2</b>
	<b>TIMI 2</b>	<b>7</b>	<b>14.6</b>
	<b>TIMI 3</b>	<b>40</b>	<b>83.3</b>

Table 1; showed that one third of the studied patients underwent manual aspiration (33.3%). About 39.6% of them underwent manual aspiration with IC GP I Ib/IIIa inhibitors; however, the remaining 27.1% underwent IC GP I Ib/IIIa inhibitors. The majority of patients 29 (60.4%) were males. The frequency of hypertension was 37 (77.1 %) patients while the frequency of Diabetes mellitus was 27 (56.2%) patients. 22 (45.8%) patients had anterior STEMI while 19 (39.6 %) patient had inferior STEMI, only 7 (14.6 %) patient had anterior- inferior STEMI. Cardiac enzymes showed troponin positivity in 48 patients on presentation. While 26 (54.2%) patients had thrombus grade V and 22 (45.8%) patients had thrombus grade III. Initially 62.5% of patients had TIMI 3 flow, TIMI 2 20.8%, TIMI 1 12.5% and 4.1 % of patients had TIMI 0 flow. Following stent deployment 40 (83.3%) patients had TIMI 3 flow, 7(14.6%) TIMI 2, 1(2%) TIMI 2 and No-reflow (TIMI 0) occurred in 0% of patients.

**Table (2):** The mean variables of the study group.

<b>Variables</b>	<b>Mean ± SD</b>
<b>Age, years</b>	<b>56.3 ± 11.3</b>
<b>EF%</b>	<b>52.2 ± 6.2</b>
<b>WMSI</b>	<b>1.55± 0.22</b>
<b>HB</b>	<b>13.3 ± 1.2</b>
<b>Platelet</b>	<b>277.4 ± 61.6</b>
<b>WBC</b>	<b>10.4± 2.5</b>
<b>INR</b>	<b>1.06 ±0.096</b>
<b>aPTT</b>	<b>34.4 ±16</b>
<b>PT</b>	<b>12.1±1.2</b>
<b>Creatinine</b>	<b>1.0 ± 0.2</b>
<b>Urea</b>	<b>18.6 ± 4.1</b>
<b>NA+</b>	<b>139.8 ± 3.9</b>
<b>K+</b>	<b>4.9 ± 0.4</b>

Table 2; the mean age of 56.3±11.3 years. shows that laboratory finding a routine complete blood picture was withdrawn from the patients showing mean hemoglobin level of 13.3±1.2, mean platelets count of 277.4±61.6, mean white blood cells 10.4±2.5., INR 1.06 ± 0.096, aPTT 34.4 ±16, creatinine 1.0±0.2, and urea 18.6 ± 4.1.

**Table (3):** Myocardial perfusion and infarct size assessment

<b>Variables</b>		<b>Manual aspiration group (n=16)</b>	<b>Manual aspiration + IC GP I Ib/IIIa group (n=19)</b>	<b>IC GP I Ib/IIIa group (n=13)</b>	<b>P-value</b>	<b>SIG</b>
<b>ECG st. segment resolution post PCI</b>		14(87.5%)	19(100%)	10(76.9%)	---	<b>0.01</b>
<b>ECHO (ejection)</b>	<b>Baseline</b>	52.3± 6.1	53.2± 4.9	51.2± 7.6		0.257
						<b>NS</b>

<b>fraction %)</b>	<b>Follow up</b>	49± 8.5	55.5± 4.1	47.3± 9.8		0.008	<b>S</b>
<b>TIMI initial</b>	TIMI 0	1(6.2%)	0(0%)	1(7.6%)	0.423	0.809	NS
	TIMI 1	3(18.7%)	1(5.2%)	2(15.3%)			
	TIMI 2	4(25%)	3(15.7%)	3(23%)			
	TIMI 3	8(50%)	15(78.9%)	7(53.8%)			
<b>TIMI Follow up</b>	TIMI 0	0(0%)	0(0%)	0(0%)	4.244	0.119	NS
	TIMI 1	0(0%)	0(0%)	1(7.6%)			
	TIMI 2	3(18.7%)	1(5.3%)	3(23%)			
	TIMI 3	13(81.2%)	18(94.7%)	9(69.2%)			
<b>Myocardial blush grade 2/3</b>	Baseline	10(62.5%)	17(89.5%)	11(84.6%)		0.112	NS
	Follow up	13(81.2%)	18(94.7%)	11(84.6%)		0.006	<b>S</b>
<b>WMSI</b>		1.75± 0.4	1.3± 0.1	1.6± 0.3		0.01	<b>NS</b>

Table 3; In this table, there is no statistically significant difference between the three study groups in relation to LVEF% at baseline, WMSI, myocardial blush grade 2/3 at baseline or TIMI score. Although the trend for a higher frequency of LVEF% at baseline, WMSI, myocardial blush grade at baseline, and TIMI score in manual aspiration with IC GPIIb/IIIa inhibitors group. However, this trend did not reach statistical significance. On the other hand, ST-segment resolution (STR), follow-up LVEF%, and follow-up myocardial blush grade 2/3 were higher in manual aspiration with IC GP I Ib/IIIa inhibitors group (p value= 0.01, 0.008, 0.006) respectively.

**Table (4): The Clinical outcomes at six weeks**

	<b>Manual aspiration group (n=16)</b>	<b>Manual aspiration with IC GP I Ib/IIIa group (n=19)</b>	<b>IC GP I Ib/IIIa group (n=13)</b>	<b>Test</b>	<b>P-value</b>	<b>Sig</b>
<b>Heart Failure</b>	3 (18.8)	0 (0)	5 (38.5)	8.296	0.01	<b>S</b>
<b>Reinfarction</b>	0(0%)	0(0%)	0(0%)		---	---
<b>Death</b>	4(25%)	0(0%)	2(15.3%)		0.004	<b>S</b>
<b>Bleeding</b>	0(0%)	0(0%)	2 (15.4)	5.61	0.062	NS
<b>Stroke</b>	0(0%)	0(0%)	0(0%)		---	---
<b>Arrhythmias</b>	5(31.2%)	1(5%)	3(23%)		0.001	<b>S</b>
<b>Thrombocytopenia</b>	0(0%)	0(0%)	0(0%)		---	---

Table 4; there is no statistically significant difference between the three study groups about reinfarction, bleeding, stroke, and thrombocytopenia. Results showed a trend for a higher frequency of bleeding among the IC GPIIb/IIIa inhibitors group. However, this trend did not reach statistical significance. On the other hand the frequency of arrhythmias and Death, were high in manual aspiration group (p value=0.001 and 0.004) respectively, and heart failure higher in IC GPIIb/IIIa inhibitors group (p=0.01).

## DISCUSSION

Primary percutaneous coronary intervention (PPCI) has been proved to be the most effective treatment strategy to open the infarct-related artery in ST-segment elevation myocardial infarction (STEMI) patients<sup>(13)</sup>.

Thrombus aspiration (TA) has the potential of reducing distal embolization and improving microvascular perfusion during primary PCI<sup>(14)</sup>.

The effect on the infarct size as reflected by the segmental wall motion score in different management strategies of primary PCI with high thrombus burden is not completely understood.

Regarding WMSI, there was no significant difference between the three groups with a P value of 0.11, which was concordant with.

A trend was also seen towards a reduction in WMSI in manual aspiration with the IC GPIIb/IIIa inhibitor group. However, this trend did not reach statistical significance.

In our study, there was statistically a significant difference in myocardial blush grade 2/3 post PCI (P=0.006) was statistically higher among manual aspiration + IC GPIIb/IIIa inhibitors group. This was concordant with<sup>(15)</sup> a similar conclusion, in which the combination of aspiration thrombectomy and intracoronary abciximab may be conducive to myocardial perfusion in patients with STEMI.

This could be due to Platelets playing a key role in the early formation of microthrombi. Theoretically, a GP IIb/IIIa receptor antagonist can reduce the formation of microthrombi and subsequent effects on the destruction of microcirculation, thereby increasing the level of myocardial reperfusion. Therefore, the routine use of a Gp IIb/IIIa receptor antagonist is recommended<sup>(21)</sup>.

In our study, there was no significant difference in LVEF% at baseline (p=0.257). This was concordant with **T. Geng et al., (2016)** (p=0.087). Although trend numerical higher in manual aspiration with IC GPIIb/IIIa inhibitors group. However, this trend did not reach statistical significance.

In the current study, LVEF% after PCI there was a statistically significant in manual aspiration + IC GPIIb/IIIa inhibitors group (P=0.008). This was concordant with<sup>(20)</sup> regarding combination treatment (P=0.002).

This was discordant with<sup>(15)</sup> there was no statistically significant change in LVEF after PCI (P=0.087) but LVEF improved only at six months (P=0.016).

Regarding short-term follow-up of major adverse cardiac and cerebrovascular events (MACE), there was a nonsignificant statistical difference between study groups about heart failure, death, bleeding, stroke, and arrhythmia, whereas there was trend towards better outcome in studies with follow up MACE.

Results showed a trend for a higher frequency of heart failure, death, and bleeding among the IC GPIIb/IIIa inhibitors group, and arrhythmia higher in the manual aspiration group. However, this trend did not reach statistical significance.

This was concordant with<sup>(25)</sup> the incidence of short-term MACE was significantly reduced with intracoronary GPIs after thrombus aspiration.

Regarding six weeks follow up of major adverse cardiac and cerebrovascular events (MACE), there was a significant difference between study groups, in our study, heart failure was higher in IC GPIIb/IIIa inhibitors group compared to other groups (P=0.01). This was concordant with<sup>(20)</sup> similarly, in a recent individual patient meta-analysis of more than 18000 patients with STEMI, patients treated with both AT and GPI had a lower risk of heart failure within few weeks compared to those receiving AT only.

Also, for death and arrhythmia, there was a significantly higher in manual aspiration group with (p value= 0.004 and 0.01) respectively. A subgroup analysis of INFUSE-AMI<sup>(23)</sup> and a meta-

analysis<sup>(24)</sup> suggest that a combination of thrombus aspiration and GPIs treatment is effective in decreasing infarct size and mortality as compared to each treatment alone or PCI alone. These findings are concordant with those of our study.

This could be due to most thrombotic materials are retrieved by thrombus aspiration catheter, GPIs could further dissolve residual thrombus and microemboli in the microvasculature<sup>(25)</sup>.

We found there was no significant difference between the number of bleeding events between the studied groups ( $P=0.062$ ). Although trend numerical higher IC GPIIb/IIIa inhibitors group. However, this trend did not reach statistical significance.

This was concordant with<sup>(25)</sup>. This might be due to the type of GPIs—tirofiban is a representative of small molecule glycoprotein IIb/IIIa inhibitor with reliable platelet inhibition and reversibility<sup>(26)</sup>.

Several limitations of this study must be mentioned. The sample size was small and the follow-up time was relatively short, which may have influenced the evaluation of long-term prognosis. Although the interventional cardiologists were all experienced, the influence of interventional cardiologist skills should be taken into account. We also need to refine the monitoring of microvascular perfusion. Although TIMI grade flow and STR are used to reflect myocardial reperfusion, defect insensitivity still exists. Despite the limitations of our approach, the study strongly supports the effectiveness of thrombectomy combined with intracoronary administration of GPIIb/IIIa inhibitors in PPCI.

## CONCLUSION

There was significant difference between Manual aspiration group, Manual aspiration with intracoronary glycoprotein IIb/IIIa group and intracoronary glycoprotein IIb/IIIa group as regard the outcomes in high thrombus burden patients. GPIs may have a synergistic effect with thrombus aspiration, while alone has a negative effect.

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