

Original Research Article

The Relationship between Visible Thrombus Aspiration Material and No Reflow with Its Impact on In-Hospital Mortality and Early Outcomes in Patients with ST-Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention

Abstract

Background: The no-reflow phenomenon is critical and, if not reversed, causes a high rate of morbidity and mortality. It was demonstrated that the no-reflow phenomenon after Primary percutaneous coronary intervention (pPCI) is a strong predictor of mortality after the acute event in patients with STEMI. The aim of this study was to investigate the impact of visible thrombus aspiration (VTA) material on no reflow and its relation to hospital mortality and early outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI).

Methods: This prospective observational study conducted on 100 patients admitted with acute STEMI and treated with primary PCI within 24 hours of presentation. Patients were divided into two groups: Group VTA (n=58): who had visible thrombus aspiration material (VTA) (defined as collected visible aspiration material, including atherothrombotic debris or thrombus) & Group non VTA (n=42): who had non-VTA (defined as no visible aspiration material and only blood).

Results: There was significant statistical difference between group VTA & Group non VTA as regard No reflow after aspiration (15.5% vs 45.5%, $P = 0.001$), In hospital mortality (0% vs 9.5% , $P = 0.016$), LVEF at hospital (47.90 ± 5.38 vs 42.36 ± 5.95 , $P = 0.001$) and LVEF after 1 month (51.90 ± 4.36 vs 48.83 ± 4.53 , $P = 0.001$). However, there was no significant

statistical difference between both groups as regard baseline TIMI flow, syntax score, in-hospital MACE, length of hospital stays.

Conclusions: Our study resulted in aspiration of macro visible thrombus materials led to lower rates of no reflow after aspiration and better short-term clinical outcomes and prognosis than those patients with non-visible thrombus aspiration materials with ST-elevation myocardial infarction treated with pPCI.

Keywords: Visible Thrombus Aspiration, No Reflow, In-Hospital Mortality, Early Outcome, STEMI

UNDER PEER REVIEW

Introduction:

The preferred therapy for ST-segment elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (pPCI). Early revascularization and the return of normal coronary flow are the critical targets of STEMI therapy. Nevertheless, in certain instances, microvascular blockage still occurs despite the restoration of epicardial infarct-related artery flow ^[1].

Current therapy options are limited for No-reflow, which is considered to be a dynamic process with numerous pathogenic components involving ischemic damage, distal atherothrombotic embolization, reperfusion injury, and sensitivity of coronary microcirculation to injury. ^[2]

According to several research, the method of thrombus aspiration may have a lower risk of distant embolization of atherothrombotic material, improving vascular perfusion and reducing infarct size. ^[3]

The first meta-analysis showed thrombus aspiration (TA) to have a clinical advantage, however subsequent research has been unable to show that TA is superior than the commonly used pPCI. ^[4]

Furthermore, visible aspiration material is not consistently retrieved after thrombus aspiration. This study's hypothesis was that visible atherothrombotic material gathered during TA may prevent no-reflow from occurring again. Therefore, the purpose of this research was to examine the effects of visible thrombus aspiration (VTA) material upon myocardial flow in STEMI patients who had pPCI.

The purpose of the study was to examine the effect of VTA material on no-reflow and its relationship to hospital mortality and initial outcomes in individuals with ST-segment elevation myocardial infarction (STEMI) after pPCI.

Patients and Methods:

The study design was prospective observational study, planned to be achieved on 100 patients underwent primary coronary angioplasty after STEMI at Tanta university hospital cardiology department, according to recent STEMI guidelines indications to primary PCI. from August 2019 to August 2021.

Inclusion criteria were patients who received percutaneous coronary intervention (pPCI) within 12 hours of the start of symptoms, had a STEMI Thrombolysis in Myocardial Infarction (TIMI) flow score of 0 or 1, and had a ST elevation of ≥ 2 mm in 2 consecutive precordial leads were prospectively. correspondences between the ECG data and the pathoanatomical structure of the culprit artery, a visual assessment of at least 70% stenosis there, and the ability to execute thrombus aspiration.

Exclusion criteria included the requirement for emergency coronary artery bypass grafting, previous myocardial infarction, previous CABG, incapacity to give informed consent, cardiovascular shock at admission, renal insufficiency (eGFR < 60 mL/minute/1.73 m²), hepatic disorders, and known malignancy.

History taking, clinical examination, laboratory data (Troponin and CKMB, which are biomarkers of myocardial damage, a CBC with attention to the Haemoglobin levels at hospital admission prior to primary PCI, serum cholesterol and triglyceride, liver enzymes, random blood sugar on admission, serum creatinine (S.Cr) level was determined on hospital admission, HCV antibodies & HBV antigens), twelve leads surface ECG and echocardiography were done.

Primary PCI was performed on all patients within 24 hours of presentation. Grade of blood flow before procedure was determined by TIMI blood flow grade classification system: There are four levels of perfusion: grade (0) no perfusion; no antegrade flow over the point of

occlusion, grade (1) penetration with no perfusion; weak antegrade coronary flow beyond the obstruction, but inadequate filling of the distal coronary bed, grade (2) Delay in flow, slow antegrade flow, and full filling of the distal area, and grade (3) complete perfusion; The distal territory is fully filled by flow.

To evaluate the burden of clots, The following Thrombus grade was used: TIMI thrombus grade 0: no cine-angiographic thrombus characteristics had been detected, grade 1: possible thrombus existed with angiographic features like reduced contrast density, irregular contour of lesion, haziness or a smooth convex "meniscus" at the area of total occlusion suggesting but not diagnosis of thrombus; and grade 2 : a thrombus was definitely present, and its biggest dimensions were $\leq 1/2$ the vessel's diameter, grade 3 : A definite thrombus was seen, although the maximum linear dimension was $>1/2$ and < 2 vessel diameters, grade 4: A definite thrombus was seen, and the biggest dimension ≥ 2 diameters of vessel, grade 5: the ischemic vessel was totally occluded with TIMI 0 flow^[5].

Cardiovascular disease severity was assessed using the SYNTAX score, and its utilized to predict complications, calculated on coronary angiography to demonstrate the coronary artery disease severity and give information about the outcome^[5].

Thrombus Aspiration Technique: The first step was putting a flexible guidewire through the offending lesion, The causative lesion was located before an advanced thrombus aspiration catheter. Before traversing the lesion, aspiration was commenced, and the aspiration catheter was pushed through the lesion many times such that at least 2 aspiration injectors were loaded with aspirated blood and thrombus material (≥ 40 mL in total), If the aspiration catheter didn't reach the target lesion, pre-dilation was performed with a small-diameter balloon catheter to facilitate aspiration, and PCI was conducted according to recent recommendations, Utilization of a manually TA catheter (6f VMAX Astron, crossing profile, 0.068 in; Biotronik AG)^[6].

No-reflow was characterised as flows with TIMI grades 0, 1, and 2, or TIMI grades 3 either with a myocardial blush grade (MBG) of 0 or 1. The main outcomes were the appearance of no-reflow^[7].

According to the VTA, the patients were separated into two groups: group (1) VTA was identified as material aspirated that was visible, such as thrombus or atherothrombotic debris,

and group (2) non-VTA was characterized by the absence of visible aspiration material and the presence of just blood. In-hospital death and early outcomes, follow-up the patients during hospital admission comparing among both groups in hospital mortality, hospital stay duration and PCI complications when hospitalised (bleeding, cardiac tamponade, perforation and stroke), ST segment resolution, Killip classification, systolic, diastolic blood pressure, acute stent thrombosis, cardiac arrest and other variables will be illustrated during the study, follow-up visits during the first three months after hospital discharge involving clinical assessment, 12-lead ECG, and transthoracic echocardiography.

Statistical analysis

The SPSS software application, version 25, was used to calculate the analysis. While the quantitative variables were defined by mean, standard deviation, and range, the qualitative characteristics were represented by number of frequency and percentage. The Kolmogorov-Smirno test was used to determine the normality of qualitative variables. The T independent test was used to compare independent quantitative variables. Monte Carlo, Fisher's exact Fisher, and Chi square tests were used to compare two qualitative variables. The risk estimate was assessed by the odds ratio with a 95% confidence interval.

Results:

Group 1 (58 patients): those who had visible thrombus aspiration material (VTA) was defined as collected visible aspiration material, including atherothrombotic debris or thrombus. Group 2 (42 patients): those who had non-VTA was defined as no visible aspiration material and only blood.

There was no statistically significant difference between the two groups regarding age, gender distribution, body mass index (BMI) and risk factors.

Table 1: Comparison between the two studied groups according to demographic data and risk factors

	VTA	Non – VTA	p. value
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		(n = 58)	(n = 42)	
Age		53.03±9.85	54.95±9.46	0.331
Sex	Male (%)	32 (55.2%)	22 (52.4%)	0.782
	Female (%)	26 (44.8%)	20 (47.6%)	
BMI		27.63±3.16	26.87±2.91	0.223
Risk factors				
Smoking		27 (46.6%)	17 (46.6%)	0.546
Diabetes		45 (77.6%)	30 (71.4%)	0.483
Hypertension		25 (43.1%)	18 (42.9%)	0.980
Dyslipidemia		17 (29.3%)	10 (23.8%)	0.541
Family history		27 (46.6%)	18 (30%)	0.714

Data are presented as mean ± S.D or frequency (%). BMI= body mass index.

There was statistically significant difference between the two groups as there was increase in systolic blood pressure and diastolic blood pressure in group II (P value =0.006 and 0.001 respectively) and in ischemic time (P value =0.024).. There was no statistically significant difference between the groups regarding heart rate, door to balloon time, killip class and STEMI location.

Table 2: Comparison between the two studied groups according to ischemic time and door to balloon time, systolic, diastolic blood pressure, heart rate , Killip classification and STEMI location.

		VTA (n = 58)	Non – VTA (n = 42)	p. value
Vital signs				
SBP		123.45±11.05	131.12±16.09	0.006*
DBP		79.40±7.32	85.83±11.58	0.001*
HR		81.62±10.45	83.43±11.71	0.419
Killip class	I	52 (89.7%)	38 (90.4%)	0.864
	II	2 (3.4%)	2 (4.8%)	
	III – IV	4 (6.9%)	2 (4.8%)	
Location of infarction	Anterior STEMI	35 (60.3%)	25 (59.5%)	0.732
	Inferior STEMI	15 (25.9%)	9 (21.4%)	
	Lateral STEMI	8 (13.8%)	8 (19.1%)	
Ischemic Time	> 6 hours	20 (35.5%)	24 (57.1%)	0.024*
	< 6 hours	38 (65.5%)	18 (42.9%)	
Door-balloon time		60.24±5.80	61.43±6.57	0.342

SBP= systolic blood pressure, DBP= diastolic blood pressure, HR= heart rate.

Laboratory findings showed no statistically significant difference between the two groups.

Table 3: Comparison between the two studied groups according to laboratory findings

		VTA	Non – VTA	p. value
Glucose		184.60±49.19	188.21±53.43	0.728
Total cholesterol		205.36±44.61	208.36±43.50	0.738
HDL		43.50±9.66	42.95±12.90	0.809
LDL		120.76±34.55	118.29±28.53	0.705
TG		160.76±42.66	165.36±51.63	0.627
Hb		14.16±1.61	13.94±1.57	0.486
WBCs		13.59±2.42	12.95±2.02	0.168
PLT		243.43±67.82	236.14±64.38	0.589
CKMB	Normal	2 (3.4%)	1 (2.4%)	0.757
	Elevated	56(96.6%)	41 (97.6%)	
Troponin	Normal	3 (5.2%)	2 (3.4%)	0.936
	Elevated	55 (94.8%)	40 (95.2%)	

HDL= High density lipoprotein, LDL= Low density lipoprotein, TG= Triglycerides, Hb= Hemoglobin, WBCs = white blood cells , PLT= Platelets and CKMB= Creatinine kinase myocardial band.

There was no statistically significant difference between the groups regarding Intervention time, Number of diseased vessels and Infarct related artery, with statistically significant difference in ST segment resolution ≥ 70 .

Table 4: Comparison between the two studied groups according to intervention time

		VTA	Non – VTA	p. value
Intervention time		10.12±2.30	10.67±2.43	0.255
ST segment resolution ≥ 0		39(67.2%)	17 (40.5%)	0.008*
No. of diseased vessels				
Single vessel disease	41 (70.7%)	30 (71.4%)	0.985	
Two-vessel disease	9 (15.5%)	6 (14.3%)		
Three vessel disease	8 (13.8%)	6 (14.3%)		
Infarct –related artery				
LAD	35 (60.3%)	25 (59.5%)	0.732	
RCA	15 (25.9%)	9 (21.4%)		
LCX	8 (13.8%)	8 (19.1%)		

LAD=Lactate dehydrogenase, CA=Root Cause Analysis, LCX= left circumflex artery.

There was no statistical significance difference between both groups regarding Base line TIMI flow, P= 0.765. TIMI flow After Aspiration: In group 1: 9 patients had no reflow (15.5%),6 patients had TIMI flow I (10.3%), 5 patients had TIMI flow 2 (8.6%), and 38 patients (65.5%) had TIMI 3 flow. In group 2: 19 patients had no reflow (45.2%),6 patients had TIMI flow 2 (14.3%), 7 patients had TIMI flow 2 (16.7%), 10 patients (23.8%) had TIMI

3 flow. There was statistical significance difference between both groups as regard no reflow and TIMI 3, P value =0.001 but there was no significant difference between both groups as regard TIMI 1 and TIMI 2 with P value= 0.549 and 0.222 respectively. Figure 1

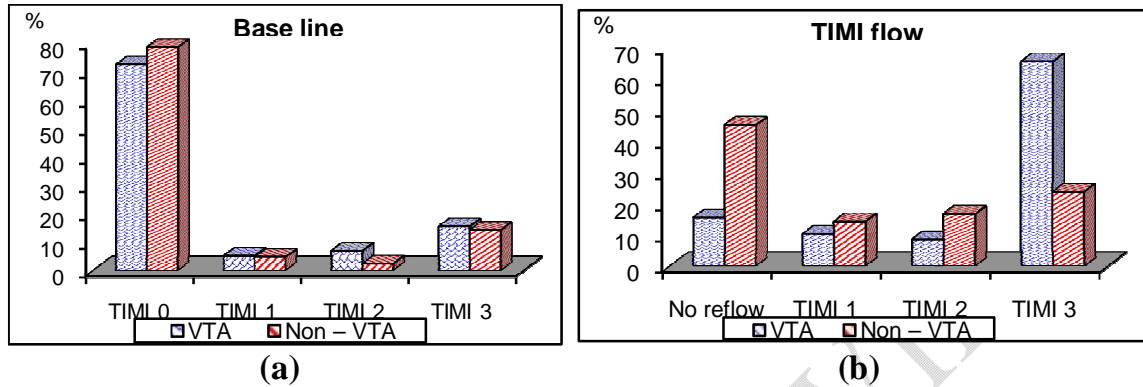


Figure 1: TIMI flow in both groups (a) base line (b) after aspiration.

There was no statistically significant difference in Syntax Score, Stent Diameter, Total Stent Length, left main Coronary Artery (LMCA)lesion, Bifurcation Intervention, Side Branch Loss, Glycoprotein II B III A inhibitors use, Stent count, Predilatation

Table 5: Comparison between the two studied groups according to different angiographic results, syntax score, stent diameter and length

	VTA	Non – VTA	p. value
SYNTAX score	17.52±4.00	17.09±3.69	0.582
Stent diameter	3.29±0.26	3.20±0.24	0.081
Total stent length	23.86±5.95	24.90±5.10	0.361
LMCA lesion	2(3.4%)	1(2.4%)	0.757
Bifurcation intervention	1 (1.7%)	3 (7.1%)	0.172
Side branch loss	2 (3.4%)	3 (7.1%)	0.403
Pre-dilatation	3 (5.2%)	4 (9.5%)	0.400
Glycoprotein II B III A inhibitors	19 (32.8%)	15 (35.7%)	0.758
Stent count	1.33 ± 0.47	1.43 ± 0.50	0.307

In-hospital mortality was significantly higher in Nob-VTA compared to VTA group (P =0.016). There was no statistically significant difference between the two groups in in-hospital MACE, duration of hospital stays, follow up after 30 days, Follow up after 3 months.

Table 6: Comparison between the two groups according to in-Hospital mortality and MACE, duration of hospital stays, LVEF at hospital and after 1 and 3 months.

In hospital Mortality & MACE	VTA	Non – VTA	p
In hospital Mortality	0	4 (9.5%)	0.016*
Coronary Dissection	2 (3.4%)	1 (2.4%)	0.757
Re-infarction	2 (3.4%)	3 (7.1%)	0.403
Cerebrovascular stroke	1 (1.7%)	0	0.392
Contrast induced nephropathy	0	1 (2.4%)	0.238
(Vascular Complication) Limb ischemia	1 (1.7%)	0	0.392
Bleeding complication	4 (6.9%)	3 (7.1%)	0.962
CHF	4 (6.9%)	6 14.3%	0.224
Length of stay (days)	2.55 ± 0.98	2.86 ± 1.07	0.142
LVEF			
LVEF at hospital	47.90±5.38	42.36±5.95	0.001*
LVEF post 1m.	51.90±4.36	48.83±4.53	0.001*
LVEF post 3m.	52.02±2.17	49.95±5.26	0.053
30 days Follow up			
Mortality	1 (1.7%)	2 (4.8%)	0.459
CHF symptoms	3 (5.2%)	5 (11.9%)	0.303
Re-infarction	0	2 (4.8 %)	0.162
3 months Follow up			
Mortality	0	0	0.222
CHF symptoms	1 (1.7%)	3 (7.1%)	0.163
Re-infarction	0	0	0.222

MACE= Major adverse cardiovascular events, CHF= Congestive Heart Failure.

Discussion

Current therapy options are limited for No-reflow, which is considered to be a dynamic process with numerous pathogenic components involving ischemic damage, distal atherothrombotic embolization, reperfusion injury, and sensitivity of coronary microcirculation to injury ^[1]. According to several research, the method of thrombus aspiration may have a lower risk of distant embolization of atherothrombotic material, improving vascular perfusion and reducing infarct size ^[3]. Furthermore, visible aspiration material is not consistently retrieved after thrombus aspiration. This study's hypothesis was that visible atherothrombotic material gathered during TA may prevent no-reflow from occurring again.

In our research, 15.5% of participants developed no-reflow following aspiration in group 1 (VTA), 45.2% developed no reflow in group 2 (non VTA). We seem to have a comparatively greater no-reflow rate. This may be due to our routine usage of clopidogrel which is linked with a greater no-reflow rate [8]. Furthermore, unavailability of thrombus aspiration devices due to financial issues is an important contributor to the relatively high rate of no reflow [9]. Also long time to intervention due to due to logistic reasons may be another cause [10]. Large registries have reported a low prevalence of 1–10% based on TIMI flow degree, ST resolution, and myocardial blush grade. The incidence of no-reflow was 6.2 % Based on research by *Ipek et al.* [11] It was carried out between January 2012 and January 2014 on 2375 consecutive participants with a diagnosis of acute STEMI who received primary PCI at a tertiary cardiovascular unit.

In a study conducted by *Harrison et al.* [12]. between January 2004 and September 2008 and included 305,694 patients across 880 hospitals to describe the prevalence, causes, and consequences of the no reflow phenomenon, No reflow was reported in 2.3% of the participants with acute STEMI (6,553 patients). In *Al Azzoni et al* [13]. evaluated the prevalence and predictors of the no-reflow phenomena in 10732 participants who presented with STEMI and had PCI with or without thrombectomy. The incidence was 2.6%. Additionally, it is well known that larger rates have been seen using various techniques for measuring microvascular flow: 34-39 percent utilizing myocardial contrast echocardiography [14].

In our study, participants in group I were matched to group II regarding baseline demographic and clinical characteristics, angiographic characteristics and treatment options.

In our study, the incidence of VTA in group 1 was slightly more common in males 55.2% Vs 52.4% in group 2 non VTA but this variation lacked statistical significance (P. value=0.782).

The participants in VTA group were younger: In the VTA group, the mean age was 53 years, but in the other group, it was 55 years.

In contrary to our research, *Ipek et al.*^[11] showed that the no-reflow group had substantially more females than males (27.9% versus 18.4%, P. value < 0.01).

In their meta analysis, *Fajar et al.*^[209] that evaluated a number of variables (Angiographic findings, laboratory results, ECG, echocardiogram, and demographic and clinical factors) that could have an effect on the no-reflow phenomenon following PCI in individuals with STEMI. This study, which included 46 articles within August and October 2017, included these variables. No-reflow phenomena was seen in this study's elderly individuals, whose mean age was (61 Vs 59 years for no-reflow and normal flow group, respectively). In that research, it was shown that male patients (71.9%) were more likely to have the no-reflow phenomena.
[15].

Similarly, a study conducted by *Soeda et al.*^[16] and enrolled 145 individuals hospitalized to a tertiary center in Japan with STEMI and had primary PCI guided by both IVUS and OCT within 12 hours after the beginning of symptoms between January 2013 and June 2014 found that no-reflow phenomenon occurs much more in males and elder patient. Also, the large multicentre study conducted by *Harrison et al.*^[12] Age was shown to be an independent predictor of no-reflow in patients with STEMI and non-STEMI.

research by *Ndrepepa et al.*^[17]. To determine predictors and the effect of no-reflow compared to individuals with normal flow restoration, paired angiographic examinations were performed on 1140 STEMI participants receiving primary PCI. Individuals in the no-reflow group were older (mean age, 65.8 y Vs 61.4 y, P. value= 0.001).

However, there is limited age-related variation in no-reflow. It is likely that this mechanism results from pre-existing microvascular malfunction.^[18] Because aging has a substantial role in the development of arterial endothelial damage and the stiffness of big elastic arteries,

advanced age is one of the main risk factors for cardiovascular diseases. Furthermore, endothelial dysfunction has been linked to decreased coronary flow reserve (CFR), which makes the afflicted myocardium more susceptible to PCI-related injury. ^[19].

Our findings demonstrated no difference in clinical heart failure between the 2 groups at the time of admission, but a substantial difference in left ventricular ejection fraction between the 2 groups at the time of hospital discharge. The mean EF% in groups I and II, respectively, was 47.9% and 42.36%, with a P-value of 0.001.

Nevertheless, a study by Gagliard et al. [20], which included 742 individuals suffering from acute MI treated with primary PCI within October 2001 and May 2011, discovered that heart failure was substantially more prevalent in patients with no-reflow (17.6% versus 10.1%; P value = 0.01) at the time of admission.

In our study, according to killip classification II-IV, there were 6 patients (10.3%) in group I compared to 4 patients (9.6%) in group II with no with no significance variation among 2 groups, P value = 0.864.

In *Fajar et al.* ^[15] meta-analysis, Subjects with a killip classification ≥ 2 had a 2.82-fold increased chance of no-reflow.

A research performed by *Azzoni et al.* ^[13] discovered that the no-reflow group had higher prevalence of Killip class II–IV in comparison with the control group, (P.value=0.0058).

In our study, the location of infarction and infarct-related artery were found to have no significance variation among the 2 groups with P value > 0.05.

In contrast to our analysis, *Ipek et al.* ^[11] found that anterior MI patients were more likely to have no-reflow (60.4%) than non-anterior infarction patients (39.6%).

Also, the research carried out by *Hassan et al.* ^[21]. No-reflow was more frequent in anterior MI (52.5%) compared to non-anterior infarction (47.5%), according to 310 consecutive

patients with STEMI who were enrolled. Additionally, it was discovered that the LAD was more often the culprit vessel in cases of no-reflow (51.5%), (P value = 0.002).

Gagliard et al. ^[22] study also revealed that no-reflow was more common with anterior myocardial infarction.

Regarding in-hospital mortality and MACE, In the research by *Sabin et al.* ^[23]. Compared to the reflow group, congestive heart failure was rather more common in the no-reflow group, although this variation was not significant statistically (P = 0.172). The no-reflow group had 6 instances of in-hospital mortality, while the reflow group had 7 cases. This variation lacked statistical significance (P = 0.084).

In the study by *Celik et al* ^[24]., In-hospital main adverse cardiovascular events (MACE), such as cardiovascular mortality, appeared to be more common in the no-reflow group of patients than in the reflow group (p < 0.001). In the study by *Karabağ et al* ^[25]. Additionally, the no reflow group had a greater rate of in-hospital deaths than the standard flow group did.²²³ In the research conducted by *Mazhar et al* ^[26]., Participants with no-reflow group had a higher 12 month mortality (13% versus. 6%, p = 0.004). There was no variation in re-infarctionin during follow up 12 months.

Limitations: The small size of the research population was caused by a number of issues, one among them was that not all participants were open to the concept of follow-up after one and three months. Others rejected PCI at our facility because of logistical or cultural considerations. Also, we excluded patients who did previous CABG and who had prior myocardial infarction. The investigation did not take into consideration intracoronary imaging indicators of the no-reflow phenomena, like diffuse coronary atherosclerosis, attenuated plaque, or significant vascular calcification.

Conclusions:

Our study resulted in aspiration of macro visible thrombus materials led to lower rates of no reflow after aspiration and better short-term clinical outcomes and prognosis than those patients with non visible thrombus aspiration materials with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention.

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

Ethical Approval

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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