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CLINICAL AND PROCEDURAL PREDICTORS OF NO-REFLOW IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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ABSTRACT

Objective: To evaluate the clinical and procedural predictors of no reflow in patient with acute myocardial infarction after primary percutaneous coronary intervention in tertiary care cardiac centre.

Study Design: Single centre, prospective observational study.

Place and Duration of study: The study was carried out in Armed Forces institute of Cardiology / National institute of Heart Disease (AFIC / NIHD) over a period of 06 months From Jan 2015 to June 2015.

Patients and Methods: We collected data of 414 patients who underwent Primary PCI for acute myocardial infarction. Acute myocardial infarction registery by R & D Department was used as a data collection tool. According to Thrombolysis in myocardial infarction (TIMI), the patients were divided into a reflow group and a no-reflow group. The clinical data, angiography findings were compared between the two groups.

Results: Sixty seven (16.18%) of the patients developed no flow phenomenon after primary PCI. Analysis showed that age (> 65yrs), time from onset to reperfusion (>6 hrs), systolic blood pressure (SBP) (<100mm of hg) on admission, Killip class III of myocardial infarction, intra-aortic balloon pump (IABP) use during primary PCI, TIMI flow grade before primary PCI (TIMI <1), type of occlusion, thrombus burden on baseline angiography (high), target lesion length (20mm) and reference luminal diameter (2.5mm)

Conclusion: The occurrence of no-re flow after primary PCI for acute myocardial infarction can be predicted by clinical and angiographic features.

Keywords: Acute myocardial infarction, Thrombus; Infarct related artery (IRA), No-reflow phenomenon, Percutaneous coronary intervention.

INTRODUCTION

After acute myocardial infarction (AMI), the immediate therapeutic goal is to establish patency of the infarct-related artery (IRA). Coronary revascularization does not always lead to coronary reperfusion. Percutaneous coronary intervention (PCI) is the standard of care for ST-segment elevation myocardial infarction (STEMI). A proportion of patients develop epicardial coronary artery reperfusion but not myocardial reperfusion after primary PCI. These patients fail to show resolution of the indirect signs of ischemia such as electrocardiographic (ECG) changes and improvements in perfusion abnormalities[1,2]. This condition is referred to as "no-reflow phenomenon"[1,2]. According to Kloner et al,[3] no-reflow is defined as suboptimal myocardial reperfusion through a part of coronary circulation without angiographic evidence of mechanical vessel obstruction. Patients who have developed no-reflow are at an increased risk for left ventricular dysfunction and progressive myocardial damage. The present study was undertaken to identify clinical factors, angiographic findings and procedural features, which predict the no-reflow phenomenon in patients with STEMI after primary PCI.

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PATIENTS AND METHODS

A total of 414 consecutive STEMI patients who had undergone emergency PCI between Jan 2015 and June 2015 at the Cardiology Department Armed Forces Institute of Cardiology / National Institute of Heart Diseases were enrolled in the study. All patients had coronary angiogram. 406 patients who underwent successfully primary PCI within 12 hours after appearance of symptoms

were included in the study .STEMI was defined as typical chest pain for more than 30 minutes and either ST segment elevation of >1 mm in 2 consecutive leads or the onset of left bundle-branch block with 2-fold elevation of creatine kinase (CK) and creatine kinase-MB (CK-MB) fraction. Patients who were treated conservatively for coronary artery disease ≤50% diameter stenosis of the culprit lesion with normal coronary blood flow, those who required emergency revascularization for severe left main coronary artery or mutlivessel diseases, those with saphenous vein grafts or left internal mammary artery lesions and those who did not achieve coronary artery patency were excluded from the study.

All patients received oral aspirin (300 mg) and clopidogrel (300 mg), as well as intravenous 10 000 U un-fractionated heparin along with two bolus of intravenous aggrastat once the culprit vessel is wired. PCI were performed from the radial artery or femoral artery. Morphology of the IRA, angiographic features of the target lesion, TIMI flow grades before and after primary PCI, culprit lesion stenosis degree, target lesion length, previous stent placement and luminal diameter were assessed for every patient. Angiographic data of the lesion responsible for the infarction were recorded: (1) thrombus burden (2) types of total occlusion and (3) length of target lesion; Thrombus burden was scored in five degrees according to Gibson,[4]. The reperfusion therapy (balloon angioplasty or stent placement) was determined by physician's discretion during primary PCI. Both Drug-eluting stents and bare metal stents were used. All patients were divided into two groups based on the post-procedural TIMI flow in the IRA: TIMI flow ≤2 (no-reflow) and TIMI flow 3 (reflow). The patient was considered to exhibit a no-reflow phenomenon if blood flow in the IRA was a TIMI≤2 flow despite successful dilatation and absence of mechanical complications such as dissection, spasm or angiographically evident distal embolization after completion of the procedure.

Data analysis

Data collected was analyzed using SPSS 21 version. Quantitative variables were described with their mean± SD while qualitative variables were described with their frequency and valid percentages.

Table-1: Clinical data in the reflow and no reflow groups.

Variables	Reflow (n=347)		No –reflow (n=67)	
Age(Yrs)	57.3 ± 16.8		65.1 ± 14.9	
Infarct Location				
ANT STEMI	173	49.85%	51	76.11%
NON ANT STEMI	174	50.14%	16	23.88%
SBP	115.7 ± 18.16		97.2 ± 13.42	
DBP	69 ± 13.90		55 ± 19.15	
Perfusion Time	6.2 ± 1.97		7.3±2.13	
kallip Class				
1	251	72.33%	29	43.28%
2	71	20.46%	21	31.34%
3	18	5.18%	5	7.46%
4	7	2.01%	12	17.91%
IABP	0		1	1.49%

Data presented as mean ±SD, Number (%) of patients, SBP: Systolic blood pressure DBP: Diastolic Blood Pressure, IABP: Intra Aortic Balloon Pump, STEMI: ST- segment elevation Myocardial infarction.

RESULT

A total of 414 patients were included in the study. All patients had angiography before percutaneous intervention. 67 patients (16.18%) had no reflow phenomenon while 347 patients (83.81%) had normal flow. The baseline clinical characteristics are shown in table-1. Compared with the reflow group, the no-reflow group had a higher mean age (65.1 ± 15.3 vs.57.3 ±16.8 years for no-reflow and reflow, respectively), a longer mean reperfusion time (7.3 ± 2.13 vs. 6.2 ± 1.97hours, respectively), and a lower level of

SBP on admission (97.2±13.42 vs. 115.7±18.16, respectively). Moreover, there were significant differences between the reflow and no-reflow groups in respect to Killip classes before PCI and IABP use before PCI .The angiographic features (Table 2) revealed that no-reflow was more frequent in patients who had a low (≤1) initial TIMI flow (85.07% vs. 62.53%), a total cut-off occlusion (43.28% vs. 25.07%), a long target lesion (28 ± 9.75 vs. 21 ± 6.11 mm), and a large vessel diameter (3.0 ± 0.5vs. 2.75 ± 0.25 mm, respectively). Moreover, the no-reflow incidence was significantly higher in patients with a delayed reperfusion (>6 hours) and a high thrombus burden. However, IRA, the presence of mutlivessel diseases, types of lesions did not have any effect on the incidence of no reflow.

DISCUSSION

The rate of no-reflow phenomenon after primary PCI in our study (16.18%) was similar to that (5%–25%) reported previously[5].This unique phenomenon is still poorly understood. Originally, it was thought prolonged ischemia and extensive myocardial damage led to micro-vascular (capillary bed) damage, resulting in incomplete reperfusion[3,6] but now other factors have been thought to play a role in the development of no-reflow, specifically distal embolization of the thrombus following balloon inflation. Hyperglycemia in AMI is associated with an increased risk of in-hospital mortality, as well as with the no-reflow phenomenon[7,8]. Patients with no reflow are older, had more previous infarctions, and had higher Killip class, a low TIMI flow before PCI, SBP on presentation <100 mmHg, intra-aortic balloon pump (IABP)during PCI, higher activity of creatine kinase, higher concentrations of serum creatinine and C-reactive protein, and longer time-to-treatment intervals than patients with normal flow after primary PCI. The success rate of primary PCI in elderly patients is lower than in younger patients because of delayed presentation and increased co-morbidities Our study demonstrates that patients with a long duration of reperfusion (>6 hours) had a significantly greater thrombus burden and increase in no-reflow rate than patients with a short duration of reperfusion. Myocardial necrosis occurs in about 6 hours after the appearance of coronary occlusion. The capillary structure becomes disorganized in the no-reflow zone because of endothelial swelling,

Table-2: Angiographic data of reflow and no reflow group (n/%).

	Reflow group		No-reflow group	
Mutlivessel Disease	187	53.89%	37	55.22%
Ira				
Lad	173	49.85%	35	52.23%
Lcx	31	8.93%	8	11.94%
Rca	143	41.21%	24	35.82%
Initial timi flow				
0/1	217	62.53%	57	85.07%
0/2	130	37.46%	10	14.92%
Type of occlusion				
Sub total	139	4.05%	17	25.37%
Tappered	121	34.87%	21	31.34%
Cut off	87	25.07%	29	43.28%
Target lesion length	21 ± 6.11		28 ± 9.75	
Reference diameter	2.75 ± 0.25		3.0 ± .5	
Thrombous burden				
Low	86	24.78%	5	7.46%
Moerate	97	27.95%	15	22.38%
High	164	47.26%	47	70.14%

Data were presented as mean ± SD or the number of patients; IRA: infarct-related artery; LAD: left anterior descending artery; LCA: left circumflex artery; RCA: right coronary artery; TIMI: Thrombolysis in myocardial infarction.

compression by tissue, myocyte edema, and neutrophil infiltration[9]. Micro thromboemboli are thought to be showered downstream after plaque rupture, leading to the obstruction of small arteries and arterioles. Furthermore, delayed reperfusion results in an older well-organized intracoronary thrombus. PCI potentially accelerates this pathologic process and may increase the risk of distal embolization during primary PCI and reduce the likelihood of achieving TIMI 3 flow after the procedure[10]. Yip et al demonstrated that in patients with AMI who had a high thrombus burden, the rate of no-reflow was lower than in those with reperfusion less than 4 hours[11] and vice versa. This indicates the possible correlation of a thrombus burden with the duration of reperfusion.

Thrombolysis in myocardial infarction (TIMI) blood flow grades are used to evaluate the quality of coronary flow during coronary angiography[12]. Patients with low (≤1) TIMI flow in the IRA prior to PCI had a higher rate of no-reflow than those with good (≥2) TIMI flow on baseline angiography. De Luca et al[13] found that pre-PCI good TIMI flow was strongly related to post-procedural TIMI 3 flow, myocardial blush grade 2–3 and lower enzymatic infarct size. Good patency of the IRA prior to PCI suggests a lower thrombus burden, spontaneous endogenous lysis of the thrombus, resolution of vasospasm and smaller infarct size.

Lee et al[14] reported that a systolic BP (SBP) <120 mmHg in patients with AMI was associated with a higher mortality than in those with SBP >120 mmHg. A previous study showed that a low SBP <120 mmHg decreased coronary blood flow (CBF), collateral blood flow, and increased infact size[15]. Their findings showed that low normal BP is associated with decreased CBF. Furthermore, the decreased CBF accelerates leukocyte accumulation, increases trapping of leukocytes in capillaries, adhesion of leukocytes in venules, and no-reflow[15].

Patients with cardiogenic shock and Killip class 3 on admission generally needed IABP supported primary PCI, and these patients had a higher no-reflow rate after the procedure. Killip class ≥3 on admission may be resulted from a larger infarction caused by severe damage to the microvascular bed as well as decreased coronary perfusion pressure. This explains why the patients using IABP had a higher no-reflow rate. A study[16] demonstrated that cardiac cells in the no-reflow area were swollen and that the capillary endothelium was damaged and exhibited regional swelling with large intraluminal protrusions. Thus we consider that cellular edema and cell contracture compressing the capillaries may contribute to microvascular compression. A higher rate of distal embolization was found in patients with advanced Killip class, which may partially explain no-reflow in these patients[17].

This study demonstrated that large the diameter of the vessels, especially those with the IRA diameter above 4 mm, increased the occurrence of no-reflow. Patients with a lesion length larger than 20 mm were more likely to develop no-reflow after primary PCI than those with a lesion larger than <20 mm. Large vessels are able to contain large amounts of plaque lipid or thrombus. The larger the diameter of the vessels, the slower the blood flow velocity. The longer the target lesion, the larger amount of thrombus and plaque burden. This would explain the high risk for slow/no-reflow observed in these patients after primary PCI[18,19].

In summary, the cause of no-reflow can be classified into four main pathogenetic components: distal athero-thrombotic embolization, ischemia-related and/or reperfusion-related injury, as well as the susceptibility of coronary microcirculation to injury[20]. .Elderly patients age, delayed reperfusion, low SBP on admission, IABP use during PCI, low TIMI flow and/or high thrombus burden on baseline angiography and long target lesions are at an increased risk for no-reflow development. Pharmacologic agents i.e., adenosine, verapamil, nitroglycerin, sodium nitroprusside have favorable effects on microvasculature, and they may be of value for no-reflow development. The selective use of glycoprotein 2b-3a inhibitors and thrombectomy devices during intervention may be also appropriate in selected cases,[21]. In recent

years, it has been shown that coronary stent implantation without predilation is feasible and can be performed safely in selected patients with AMI[22]. Because most patients with AMI have a combination of these factors, combined treatment strategies should be preferred

CONCLUSION

The no-reflow phenomenon remains a significant challenge for STEMI patients. It is associated with poor prognosis that is independent of and beyond that provided by other relevant clinical factors including the infarct size. Looking beyond epicardial artery patency and assessing microvascular perfusion is useful for risk stratification in patients with AMI. The identification of mechanisms of microvascular dysfunction is the key to defining specific therapeutic strategies for reperfusion. Although we have a number of drugs and devices to treat the no-reflow phenomenon, there is an increasing need for continuation of research to better understand, prevent and treat this unique phenomenon in patients with STEMI undergoing primary PCI.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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