

Original Research Article

Survey of effective factors in slow flow and no reflow in primary percutaneous coronary intervention patients

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ABSTRACT

Background: The phenomenon of no reflow is a phenomenon that after angioplasty and the successful insertion of the stent, the blood flow rate is reduced again in the coronary arteries and there is no mechanical obstruction. The slow flow phenomenon is an angiogram that is associated with delayed progression of contrast media during coronary artery during angiography in the absence of coronary stenosis. The aim of this study was to investigate the prevalence and factors affecting these phenomena in Primary percutaneous coronary intervention (PCI) patients.

Methods: This cross-sectional study was performed. The statistical population of the patients is 340 people who were under the Primary PCI. After the patients' data, information was collected through a questionnaire and patients' records.

Results: 48 patients entered the PCI process more than 90 minutes after admission to hospital. The highest frequency is related to anterior MI and LAD was the most frequency based on type of vessel involvement, 12 of them died and 17.1% of patients had no reflow and 12.9% of patients had slow flow. The mean diameter of stents in patients was 2.98 and the mean balloon diameter in patients was 2.01 and there is a significant relation between stent diameter and balloon diameter with slow flow and no reflow ($p < 0.05$).

Conclusions: The results of this study showed that the prevalence of slow flow and no reflow after primary PCI in patients with heart attacks were at a high level with 12.9% for slow flow and 17.1% for no reflow.

Keywords: Initial angioplasty, No reflow, Slow flow

INTRODUCTION

Ischemic heart disease (IHD) is a condition in which there is insufficient blood and oxygen supply to parts of myocardia and it happens specifically when there is an imbalance between supply demands of oxygen in myocardia. This disease causes the most disability and financial difficulties comparing to other disease. In United

States 13 million are suffering from IHD. More than 6 million are suffering from angina pectoris and 7 million are suffering from myocardial infarction. Obesity, Insulin resistance and diabetes type 2 are exceeding and they are considered as important risk factors for IHD. By considering urbanization in developing countries the prevalence of risk factors of this specific disease is rapidly exceed, so the majority of prevalence are in countries with low and medium income.¹ Cardiovascular

diseases are one of 21st century's dominant chronic diseases and it is posed as the main reason of disability and mortality in world. In the meantime coronary artery diseases is the most common cardiovascular diseases.² Which is the top rated heart diseases according to American Heart Association statistics on time diagnosis and treatment of this diseases by using diagnostic methods and test can reduce side effects and mottality.³ The phenomenon of no reflow is a phenomenon that after angioplasty and the successful insertion of the stent, the blood flow rate is reduced again in the coronary arteries and there is no mechanical obstruction and in 2 percent of patients needed coronary artery interrrntions has been reported and this phenomenon is observed in 29% of patients with acute myocardial infraction. In patients with acute coronary syndrome during percutaneous coronary intervention (PCI), no reflow phenomenon can disturb the hemodynamic condition and angina pectin. Micro vascular damages, tissue edema, intravascular plagues and micro emboli have a bowled role in causing this phenomenon.⁴⁻⁶ Coronary slow flow phenomenon is an angiographic finding which is accompanied by delay in progression of contrast agent in coronary arteries during angiography without coronary obstruction.⁷⁻⁹ The mechanism of this phenomenon is getting unknown. Coronary slow flow phenomenon is accompanied with clinical outcomes such as recurrence of pectoris angina, shortness of breath, cardiogenic shock, heart failure myocardial ischemia, total arrhythmias, sudden death and acute coronary syndromes.¹⁰⁻¹² Yilmaz and et al studies indicate that coronary slow flow blood increases total cholesterol and LDL these patients have higher BMI and metabolic syndromes comparing to control group although they have more signs comparing to control group and they are hospitalized longer.¹³

So this study was done with the aim of determination of prevalence and effective factors on slow flow and no reflow in primary DCI patients to prepare a suitable background in reducing the prevalence of this phenomenon.

METHODS

This study has been done descriptive cross-sectional. Statistical society consists of patients who have under gone primary PCI at Imam Khomeini Hospital Cardiac Center in Ardabil city from March 2016 to April 2017. Sample volume for this study was calculated by volume calculation formula for sectional studies.

$$Z=1.96, p=0.29, q=0.71, d=0.05 \quad n=340$$

Inclusion criteria

Patients who have undergone primary PCI were included in the study.

Exclusion criteria

It was incomplete records of patients. Patients who have undergone primary PCI are entered in study after assessment of patients needed information.

In term of demographic information (age, gender, diabetes, blood pressure, cholesterol) has been collected by questionnaire and patients files has been assessed and entered in the check list for collecting angiographic information and intervention (pre-dilatation, stent balloon dilatation pressure, amount of coagulation in coronary artery, stent diameter, vessel diameter). Then the information for statistical assessment collected and entered statistical analysis software. SPSS software has been used for analysis of information and p.values less than 0.05 are considered significant. Patient's information were kept confidential. Existing deficiencies in patients file were one of the limitations of this study.

RESULTS

In this study from 340 patients with acute coronary syndrome 240 patients were men (70.6%) and 100 patients were women (29.4%). In this assessment there were 44 patients with low coronary flow in which 32 of them were men and 12 of them were women and in lack of establishing reflow from 58 patients 28 were men and 30 were women between patient's gender and low coronary flow and lack of establishing reflow were significant connection ($p=0.00$). The average age of patients in study was 60.77 ± 12.10 years. The average age of 44 patients in low flow coronary artery was 64.40 ± 12.70 and 58 patients in lack of establishing reflow was 60.58 ± 9.83 and there was no significant connection between the ages of patients and low coronary artery flow and lack of establishing reflow ($p=0.09$).

High blood pressure was a risk factor which was assessed in patient's results shown that 134 of patients had positive history of high blood pressure. From 44 patients with low coronary flow 18 of them and from 58 patients with lack of establishing reflow 24 of them had high blood pressure. Between patients' blood pressure and low coronary flow and lack of establishing reflow there was no significant relationship ($p=0.9$).

Also diabetes was assessed in patients. Results of this study showed that only 68 patients (20%) had a history of diabetes mellitus. From 44 patients with low coronary flow 10 of them and 58 patients with lack of reflow 10 of them had diabetes. There was no significant relationship between diabetic patients and low coronary flow and lack of reflow ($p=0.7$). Among patients, 110 of them (32.4%) had a history of hyperlipidemia. From 44 patients with low coronary flow 14 of them had a history of hyperlipidemia and from within 58 patients with lack of reflow, 20 of them had a history of hyperlipidemia. There was no significant relationship between hyperlipidemia and low coronary flow and lack of coronary reflow ($p=0.9$).

Patients were assessed from the moment their pain started until they came to hospital. Results showed that average of the time when pain started until the time patients registered in hospital was 286.02 ± 183.69 minutes and there was a significant correlation between the time pain started until the time patient's registered in hospital and low coronary flow and lack of coronary reflow ($p=0.001$). In assessing the time between registering in hospital and starting of PCI process it was observed that 48 of the patients in more than 90 minutes and 292 patients in less than 90 minutes had entered PCI process. The average of the time patients entered hospital until the start of PCI in the entire study group was 52.10 minutes. The averages in group with low coronary flow were 72.50 and in group with lack of reflow were 46.55. There was a significant correlation between the time patient's registered in

hospital and the initial of PCI and low coronary flow and lack of coronary reflow ($p=0.00$).

In patients the types of MI was assessed 172(50.6%) had anterior MI, 98 of them (28.8%) had inferior MI, 14 of them (4.1%) had lateral MI, 38 of them (11.2%) had extensive MI, 4 of them (1.2%) had posterolateral MI, 6 of them (1.8%) had anterolateral MI and 8 of them had inferolateral MI (2.4%). From 44 patients with low coronary flow 20 of them had inferior MI and 24 of them had anterior MI. In 58 patients with no reflow 42 of them had anterior MI, 8 inferior, 2 lateral, 4 extensive and 2 inferolateral. There was a significant relationship between the kind of MI and low coronary flow and no coronary reflow ($p=0.001$) (Table 1).

Table 1: Classification of the type of patient with MI, based on low coronary flow and no coronary reflow.

Type of patient with MI	MI							Total	P value
	Anterior	Inferiore	Lateral	Extensive	Inferiore+posteriore+lateral	Anteriore+lateral	Lateral+inferiore		
Low coronary flow	24	20	0	0	0	0	0	44	0.001
No coronary reflow	42	8	2	4	0	2	0	58	
None of them	106	70	12	34	4	4	8	238	

Table 2: The mean diameter and length of the balloon and the diameter and length of the stent.

		N	M±Sd	p-value
Stent diameter (mm)	Low coronary flow	44	3.15±0.40	0.01
	No coronary reflow	58	2.93±0.52	
	None of them	238	2.96±0.39	
	Total	340	2.98±0.42	
Stent length (mm)	Low coronary flow	44	25.45±6.18	0.052
	No coronary reflow	58	25.65±7.32	
	None of them	238	23.59±6.82	
	Total	340	24.18±6.87	
Balloon length (mm)	Low coronary flow	44	15.22±2.47	0.82
	No coronary reflow	58	15.13±1.53	
	None of them	238	15.05±1.8479	
	Total	340	15.08±1.84	
Balloon length (mm)	Low coronary flow	44	2.18±0.39	0.01
	No coronary reflow	58	2.00±0.32	
	None of them	238	1.98±0.41	
	Total	340	2.01±0.40	
Balloon pressure (atm)	Low coronary flow	44	15.77±1.55	0.00
	No coronary reflow	58	13.79±2.14	
	None of them	238	14.61±2.17	
	Total	340	14.62±2.15	

By the count of involved coronary vessel patients were divided in to 3 groups. 114 patients (33.5%) with one involved vessel, 128 patients (37.6%) with 2 involved vessel and 98 patients (28.8%) with 3 involved vessels. There was a significant relationship between the counts of involved vessel and low coronary flow and no reflow (p=0.001).

218 of the patients had diseased LAD, 40 of them had diseased LCX, 76 of them had diseased RCA, 2 of them had diseased RCA+LAD and 4 of them had diseased RCA+LCX. In slow coronary flow 26 of them had diseased LAD and 18 of them had diseased RCA. In patients with no reflow 46 of them had diseased LAD, 2 of them had diseased LCX and 10 of them had diseased RCA. There was no significant relationship between patient's diseased vessel and low coronary flow and no coronary reflow (p-value=0.001).

The average of stent diameter in patients was 2.98 mm which was 3.15 mm in low coronary flow and 2.93 in no coronary reflow. The average of balloon diameter in patients was 2.01 mm and it was 2.18 in low coronary flow and 2mm in no coronary reflow. There was significant relationship between stent diameter, balloon diameter, low coronary flow and no coronary reflow (p-value=0.01).

The average length of stent in patients was 24.18 mm. It was 25.45 mm in low coronary flow and 25.65 in no coronary reflow. The average length of balloon in patients was 15.08 mm and it was 15.22 in low coronary flow and also it was 15.12 in no coronary reflow. There was no significant relationship between the length of stent, the length of balloon, low coronary flow and no coronary reflow. The average balloon pressure in patients was 14.62 atm and it was 15.77 in low coronary flow and 13.79 in no coronary reflow. There was significant relationship between low coronary flow and no coronary reflow (p=0.00) (Table 2).

Table 4: Leakage fraction in patients under study.

	Leakage fraction							M	P value
	25%	30%	35%	40%	45%	50%	55%		
Low coronary flow	4	6	8	10	12	0	0	36.36	0.00
No coronary reflow	14	14	6	16	6	2	0	34.31	
None of them	6	22	52	58	30	60	10	41.38	

There was a significant correlation between ejection traction with low coronary flow and no coronary reflow (p=0.00) (Table 4).

By assessing patients from the point of low coronary flow and no coronary reflow. It was understood that 44 of the patients had a low coronary flow and 58 of the patients had no coronary reflow.

Table 3: Drug treatment of patients.

Drug intake of patients	N (%)
No drug	238 (70)
Adenosine	14 (4.1)
TNG	2 (0.6)
Adenosine+TNG+Atropine	52 (15.3)
Adenosine+TNG	10 (2.9)
Adenosine+TNG+Verapamil+Atropine	12 (3.5)
Adenosin+TNG+Verapamil	8 (2.4)
Adenosine+Atropine+Adrenaline	2 (0.6)
Atropine+Adrenaline	2 (2.6)
Total	340 (100)

22 of the patient's were supported by CPR and 12 of them were expired. All of these patients were in coronary reflow group and there was a significant correlation between expired and cardial resuscitated patients with low coronary flow and no coronary reflow (p=0.00). 246 of the patients (72.4%) were treated by integrilin and 238 of patients were not having received any medications and the rest of the consumed drugs by patients are mentioned in the table (Table 3).

The assessed ejection tractions in patients by echocardiography were extracted from the patient's case and the results showed that 28 of them had ejection traction of 25%, 42 of them 30%, and 66 of them 35%, and the rest of them patients had an ejection traction over40%. In patients with low coronary flow 12 of them had an ejection fraction of 45%, 10 of them 10%, 8 of them 35%, 6 of them 30%, and 8 of them had ejection traction of 25%. In patients with no coronary reflow 2 of them had an ejection traction of 50%, 6 of them 45%, 16 of them 40%, 8 of them 35%, 14 of them 30% and 14 of them had an ejection traction of 25%. The average ejection traction in patients with no coronary reflow was lower (34.31%).

DISCUSSION

In this study 340 patients with acute coronary syndrome were studied which 70.6% of them were male and their average age were 60.77 years. In the study of Beyranvand and Asadpour on 322 patients, their average age was 59 years old and 61% of them were male.¹⁴ In the study of Sakuma et al which was done on 722 patients with acute coronary syndrome the average age was 53 years old and

58% of patients were male.¹⁵ In the study of Hammoudeh et al which was done on 5000 patients, 66% of patients were male and their average age was 57 years old.¹⁶ In the assessment of these studies it was found that being male is a risk factor for acute coronary syndrome and the prevalence of this disease is higher in males than females. Also it was prevalent in 60s and 70s which is approved by the studies above.

In assessing cardiovascular risk factors it was found that high blood pressure with 39.4%, hyperlipidemia with 32.4% and diabetes mellitus with 20% are the most common risk factors between patients. In the study of Hammoudeh et al in the most of the coronary patients in men (95%) and in women (96%) there is at least one high risk factor (High blood pressure, Diabetes, Smoking and dyslipidemia).¹⁶ Also in people with coronary disease the prevalence of low HDL was 60% in men and 39% in women. In the study of Umesh et al on 122458 patients, results showed that the males had an at least on main risk factor and smoking was the most common risk factor in men and smoking with diabetes was the most common factor in females.¹⁷ In the study of Deepak et al between 67 thousand patients with Athero thrombosis, the most common risk factor at first was high blood pressure (81.8%) and at second was hyperchilestrolemia (72.4%).¹⁸

Low coronary flow syndrome was first propounded by Tambe et al for the new Angio graphic phenomenon. Low coronary flow is a phenomenon which is accompanied by normal or slightly normal Angiography of coronary artery which known with low flow of contrast agent which was injected through coronary vessel.¹⁹⁻²¹ Without obstruction in epicardial coronary vessels this situation which can be happened in one or all of the myocardial coronary vessels the etiology of this disease is unknown.^{19,22,23}

Histological studies, hypertrophy of myofibers, thickening elastic muscular fibers with edema and degeneration of endothelial cells indicate narrowing of vessels lumen in these patients.²⁴ Angiographic articles and reports indicate that 10-30% of patients whom under gone angiography, had abnormal or slightly normal condition which has 1-7% of the low coronary flow angiography.²⁵⁻²⁸ In the current study the prevalence of low coronary flow was 12.1 which is higher than reported amount and it's an indication of high prevalence of this phenomena in patients.

It has been done a lot of researches about the etiology of this phenomenon world-wide which there are some several hypothesis about the pathophysiology logical mechanisms of this disease which contains the early form of myocardial atherosclerosis disease dysfunction of endothelium, obstruction of small vessels, micro vascular increased resistance, micro vascular dysfunction, inflammation, inequivalence between strictor and dilator vessel factors and dysfunction of platletets.^{23,24,29,30}

The no reflow syndrome is a rare complication in primary angioplasty for myocardial infraction.³¹ previous studies has indicated that the patient's prognosis worsens with no reflow phenomenon.³² this phenomenon was firstly done by Kloner et al in a dog by closing coronary vessel for 90 minutes and indicated that by reopening the vessel, normal blood flow is not establish toward myocardial.³³ several pathophysiology mechanisms has been hypothesized which disorder in platelet and leukocyte mediators, endothelial dysfunction, Embolization plague or thrombosis to distal parts of vessels and the local release of vasoconstrictors are part of them.³⁴⁻³⁶ In the current study the incidence of this phenomenon is 17.1%. in some of the studies the incidence of this phenomenon is 12-30% and in some are 0.6-3.2% which the difference between studies are related to the study group and other factors.^{31,32} In general the incidence of this phenomenon in patients is higher. The myocardial risk factors such as blood sugar, hyperlipidemia and hypertension in the current study was similar to the others studies.^{37,38} Which can be contrition of this point that however the myocardial risk factors are affective in myocardial infraction but it has no effect on possible physiopathology of no reflow phenomenon and low coronary flow which merely contains disorder in the evolvment of small vessels, diffused spasm and micro thrombosis. Some of the studies believe that the interval between the beginning of symptoms and myocardial infraction until the reflow is one of the bold reasons in infraction and prognosis.³⁶ some of them also did not mention correlations between these factors.³⁸ In the current study also there was a significant correlation between the mentioned phenomenon's and the interval between the initial of the pain and PCI procedure. In the current study the most involved vessel was LAD which was more likely to have thrombotic disorder and small vessel disorder and diffused spasm due to high incidence of MI in LAD and the high blood perfusion of this vessel. Between the length of balloon and the length of stent with these phenomenon's there was no significant correlation which this result was similar to results of Brosh et al study and it was different with the findings of Hong study. Similar to Brosh et al studies there was a significant correlation between ejection fracture and incidence of no reflow phenomenon's and low coronary flow which was predictable by considering this point that these phenomenons threaten the perfusion of some parts of heart.^{39,40} It is being suggested to choose patients only with low coronary flow or no reflow and also doing case control and assessing each related risk factors separately.

CONCLUSION

The results of this study showed that the incidence of low coronary flow and no reflow followed by PCI in MI patients are highly related with 12.9% incidence of low coronary flow and 17.1% for no reflow and it is also highly related with the interval of the initial of pain until the initial of PCI procedure, ejection fraction, the kind of

involved vessel death, balloon diameter, stent diameter and resuscitation of patient.

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