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NO-REFLOW PHENOMENON;
INCIDENCES AFTER PCI

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ABSTRACT… Background: Profound reduction in antegrade epicardial coronary flow with concomitant ischemia is seen occasionally during percutaneous coronary intervention despite the absence of evident vessel dissection, obstruction, or distal vessel embolic cutoff. **Study Design:** Descriptive study. **Setting:** Khatum-un-Nabyeen Heart Center for percutaneous coronary intervention. **Period:** January 2016 and December 2016. **Methods and Results:** Both males and females with age 30 years or more, presented. Patients with coronary angiograms suggestive of percutaneous coronary intervention were included in the study by using non-probability, purposive sampling technique. Following ethical and research approval from the hospital administration, clinical profile of the patients was documented. Patients presented with acute coronary syndrome as well as patients with stable coronary artery disease requiring coronary intervention based on clinical, ECG, non-invasive test or coronary angiogram were enrolled in the study. Patients with previous history of PCI or CABG were also included in the study. Pregnant patients were excluded from the study. The objective of this study is to find out the incidence of no reflow phenomenon during PCI in our population. The TIMI flow grade was determined for each treated vessel. The criteria for no-reflow was development of substantial flow reduction (less than TIMI 3 flow) in the absence of apparent dissection, thrombosis, or distal vessel cutoff suggestive of macroembolization. SPSS version 16.0 was used for analyzing the data. Frequency and percentages were used for categorical variables. Mean±SD was used for numerical variables. Data were presented in the form of tables. **Conclusions:** The no-reflow phenomenon, reduction in distal flow without apparent dissection or distal embolization - occurs in 2.25% of coronary interventions.

Key words: PCI: Percutaneous Coronary Angioplasty.

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INTRODUCTION

The "No Reflow" phenomenon refers to microvascular obstruction leading to myocardial ischemia with patent epicardial coronary artery during percutaneous coronary intervention. Various mechanisms are responsible for this complication during PCI (Figure-1). The term "Reperfusion no reflow" is used when this complication occurs in infarct related artery among the patients presented with acute coronary syndrome and is associated with adverse clinical outcome.[1] "Interventional no reflow" describes this complication during PCI of non-infarct related artery in patients of stable coronary artery disease and predictor of higher rates of myocardial infarction and mortality.[2] The "No Reflow" is unpredictable and sometimes not recognized in clinical practice.

Various pathophysiological mechanisms contribute to no reflow after PCI. Preexisting microvascular dysfunction exacerbates this complication after PCI, which explains the higher incidence of this complication in patients with diabetes mellitus and hyperlipidemia. The microvascular spasm, intravascular thrombus, endothelial swelling, capillary compression by edema within the adjacent myocardial tissue and distal coronary embolization of plaque or thrombus are the pathophysiological factors that may lead to microvascular obstruction and "No-reflow" during PCI.

The complication of "No Reflow" during PCI

may be symptomatic or asymptomatic but mostly associated with ECG changes. TIMI (Thrombolysis In Myocardial Infarction) flow grades epicardial coronary flow during coronary angiography. Normal coronary flow is labeled as TIMI 3 flow. During PCI sudden reduction of coronary flow (TIMI flow 0 to 2) in presence of patent coronary arteries is labeled as "No-Reflow" and is associated with adverse clinical outcome.[1] Clinically myocardial tissue hypoperfusion is an important end point after coronary intervention and is associated with adverse clinical outcome. However TIMI flow is a poor surrogate for myocardial tissue hypoperfusion, therefore more prognostic markers have now been developed. Cardiac biochemical markers, myocardial contrast echocardiography and tissue hypoenhancement on contrast-enhanced MRI and CT more sensitive markers of impaired myocardial tissue perfusion and microvascular ischaemia even among patients of coronary intervention complicated by no reflow and predicts worse outcome.[34]

No systematic study of the incidence of this "no-reflow" phenomenon during coronary intervention have yet been reported in Pakistan. The objective of this study is to find out the incidence of this complication during PCI in our population.

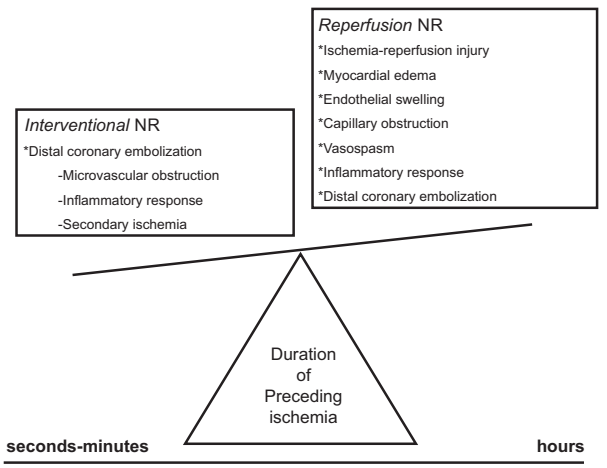

Figure-1. Schematic illustrating the effect of duration of preceding myocardial ischemia on mechanism of no reflow (NR).

MATERIAL AND METHODS

This was a descriptive study. Both males and females with age 30 years or more, presented in Khatum-un-Nabyeen Heart Center for percutaneous coronary intervention between January 2016 and December 2016 were enrolled in the study. Patients with coronary angiograms suggestive of percutaneous coronary intervention were included in the study by using non-probability, purposive sampling technique. Following ethical and research approval from the hospital administration, clinical profile of the patients were retrieved from hospital record. Patient's age, gender, Body Mass Index, smoking status, hypertension, diabetes mellitus, family history of ischaemic heart disease and history of PCI or CABG was documented. In cases of female patients postmenopausal status and use of oral contraceptive pills was also noted. Patients presented with acute coronary syndrome as well as patients with stable coronary artery disease requiring coronary intervention based on clinical, ECG, non-invasive test or coronary angiogram were enrolled in the study. Patients with previous history of PCI or CABG were also included in the study. Pregnant patients were excluded from the study. The objective of this study is to find out the incidence of no reflow phenomenon during PCI in our population. All patients undergoing coronary intervention were treated with double antiplatelet drugs and intravenous heparin during PCI. The cine angiograms then were evaluated by two cardiologist. The TIMI flow grade was determined for each treated vessel. The criteria for no-reflow was development of substantial flow reduction (less than TIMI 3 flow) in the absence of apparent dissection, thrombosis, or distal vessel cutoff suggestive of macroembolization. SPSS version 16.0 was used for analyzing the data. Frequency and percentages were used for categorical variables. Mean±SD was used for numerical variables. Data were presented in the form of tables.

RESULTS

Table-II presents the baseline characteristics of patients admitted for percutaneous coronary intervention. Figure-2 presents the incidence of no-reflow in the study group. The no-reflow phenomenon was noted in 2.25% of coronary interventions.

Parameter	N (%)
Age	43 ± 10 years
Male	241 (60.25%)
Female	159 (39.75%)
BMI	25.4±4
Smoker	101 (25.25%)
Family history of CAD	157 (39.25%)
Hyperlipidemia	211 (52.75%)
Hypertension	216 (54%)
Diabetes Mellitus	279 (69.75%)
Female Using Oral Contraceptive Pills	37 (23.27%)
Post Menopausal Women	51 (32.07%)
History of PCI	127 (31.75%)
History of CABG	0
Presentation with ACS	197 (49.25%)
Presentation with Stable Coronary Heart Disease	203 (50.75%)

Table-I. Clinical characteristics of patients

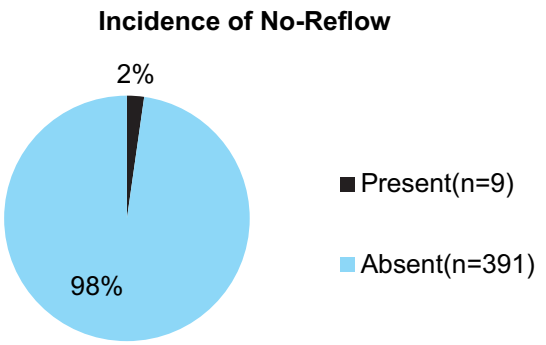

Figure-2. Incidence of No-Reflow after PCI

DISCUSSION

Percutaneous coronary intervention (PCI) is the preferred reperfusion technique of restoring blood flow of the stenotic coronary artery.[5] However it is an invasive procedure and associated with complications. No-reflow is one of serious complication during PCI associated with adverse outcome. The term no reflow describes impaired coronary flow (Thrombolysis in Myocardial Infarction grade 3) despite restoration of epicardial coronary artery patency in the absence of any spasm or dissection is known as no-reflow [2] after PCI.[6,7] This finding implicated ongoing structural or functional problems in the distal microcirculation. This phenomenon was subsequently observed clinically after revascularization of an infarctrelated artery with either thrombolysis or balloon angioplasty.[8-10] More recently, no reflow complicates the intervention of saphenous vein grafts as well as the PCI of native coronary arteries.[11-13] Like patients with the classic no-reflow phenomenon, this newest class of patients exhibits substantial reduction in post-procedure coronary flow despite the absence of proximal coronary obstruction caused by clot, dissection, or spasm and distal vessel cutoff suggestive of macro-embolization. It is thought to be caused by a combination of ischemic endothelial injury that obstructs the capillary lumen and distal embolization of atherothrombotic debris.[14] The fact that the platelet fibrin thrombus suggests that vasoconstrictive substances may be released when such lesions are disturbed, which could trigger distal microvascular spasm sufficiently intense to overcome local autoregulatory control.[15-17] The hypothesis of distal microvascular spasm as an underlying etiology is supported by the poor responsiveness of no reflow to nitroglycerin. In contrast, calcium channel antagonists directly acting on vascular smooth muscle, may avoid this problem and resulting limited infarct size, abort myocardial stunning, and improves endothelium-dependent vasorelaxation.[18-20]

The current study shows that the no-reflow phenomenon is uncommon after coronary intervention, documented in 2.25% cases of interventions. The reported incidence of no-reflow varies depending upon the population being studied. When including all patients undergoing PCI for any indication, the incidence has been reported to be around 2.3–4.8%.[21-28] The reported incidence is higher in patients with STEMI and ranges from 11 to 41%.[21] The higher incidences of no reflow are documented in cases of primary PCI or intervention of the saphenous veingraft.

No-reflow is a strong prognostic marker short as well as long term mortality.[29,30] The poor prognosis with no-reflow is due to larger infarct sizes and reduced systolic function left ventricule.[30] The clinical trials tested a number of treatment strategies for no-reflow have been conflicting and there is no definitive treatment of no-reflow once it has occurred.[31-35] In the absence of an effective treatment strategy, it is crucial to prevent no-

reflow by knowing the predictors or risk factors of no-reflow. Previous studies have identified various predictors of no-reflow, which are different between studies, likely due to the differences in the populations being studied.[36,37]

There are certain limitations to this study. This is a single centered study. No reflow was documented based on TIMI flow grades evaluated by two cardiologists to reduce assessment bias. The relationship of different risk factors with no reflow was not evaluated. Similarly different treatment options of no reflow were not included in the study. The incidences as well as predicting factors requires further confirmation in clinical trials.

CONCLUSIONS

Marked impairment of coronary flow without evident epicardial obstruction or distal embolization -the noreflow phenomenon -occurs in roughly 2.25% of coronary interventions in our population.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Shakeel Ahmad	Drafting	
3	Faiq Ilyas	Statistical analysis	