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POST PCI MYOCARDIAL INFARCTION A SILENT KILLER FACT OR FICTION. DOES IT REALLY EXIST? WHERE DO WE STAND

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Contribution
NUK conceived the idea and designed the study. Data collection and manuscript writing was done by TS, MST, MTF, SM and NHR. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To determine the frequency of peri-pocedural myocardial infarction in patients with stable coronary artery disease undergoing elective percutaneous coronary angioplasty.

Methodology: This was a descriptive study conducted in the cardiac cath lab of the National Institute of Cardiovascular Diseases Karachi, Pakistan. Patients with stable obstructive coronary artery disease undergoing elective coronary angioplasty were included in this study. PMI was defined as a rise in troponin I above five times the upper limit of the normal range (the third universal definition of MI). Collected data were entered and analyzed using SPSS 19.

Results: Among the total of 107 patients male predominance, 82.2% (88), was observed and mean ± SD age of the patients was 52.02 ± 9.10 years with a majority, 92(86.0%), of patients between 41 to 80 years of age. Peri-procedural myocardial infarction (PMI) was found in 16(15.0%) of the patients and PMI was observed to be independent of baseline risk profile and angiographic characteristics of the patients. While, based on criteria of troponin I above three times the upper limit of the normal range, PMI was observed in 22(20.6%) of the patients.

Conclusion: High incidence of the post-procedural rise of troponin in our study population is alarming. Further studies are required to identify the cause and hence identifying measures to prevent PMI. Universal single definition is required worldwide in order to get uniform results.

Keywords: Post PCI Myocardial Infarction, Coronary angioplasty, Third universal definition

INTRODUCTION

Percutaneous coronary intervention (PCI) is the mainstay of treatment of coronary artery obstructive disease. More than Two hundred thousand coronary angioplasties are performed worldwide on a yearly basis and the numbers are still rising.[1] Although with the increasing technical experience of operators and technological improvements of equipment in coronary angioplasty, acute procedural complications and long term results have significantly improved, yet peri-procedural myocardial infarction (PMI) remains common.[2]

Third Universal definition of MI, by American College of Cardiology (ACC) defined Coronary Angioplasty related MI (type IVa) elevation of cardiac troponin values more than five times of 99th percentile URL in patients with normal baseline values (that is less than 99th percentile URL) or a rise of cardiac troponin values more than twenty percent if the baseline values are elevated. In addition, either 1) Symptoms of myocardial ischemia or 2) New ECG changes or 3) Angiographic findings indicating a procedural complication or 4) Imaging findings indicating a new loss of viable myocardium or new regional wall motion abnormality (RWMA) are required.[3] This may be surprising as opposed to previous 2007 definition of PMI according to which a rise in cardiac biomarkers alone was enough to define PMI.[4]

In contrary to the unifying mechanism of spontaneous myocardial infarction(typ1) that is acute plaque rupture with superimposed thrombosis, there is not a common process causing Post PCI biomarker elevation.[5] Proposed mechanisms include Side branch occlusions and transient ischemia due to balloon inflation. No flow/slow flow phenomenon which is supposed to be due to distal embolization of plaques disrupted by the balloon or stent, platelet-rich micro-thrombi, and vasospasm is also included among the PMI mechanisms.[3,5]

While the world literature is abundant in research papers highlighting various aspects of PMI, conflicts still exist regarding its true incidence.[6-7] Considering its high incidence and impact on long term outcomes in western society, there was a need to collect the data from our community and compare it with the western counterpart. This will give us a broader vision in the management of our post PCI patients.

METHODOLOGY

This was a descriptive study, conducted in Cath lab of National Institute of Cardiovascular Diseases (NICVD) Karachi during the period of July 2018 to May 2019. Approval of the ethical review committee of the institute was taken for the study and informed consent regarding participation in this study was taken from all the patients. All patients aged between 18 to 80 years with stable coronary artery disease undergoing elective percutaneous coronary angioplasty were included in this study. Elective PCI performed by a single consultant were included in this study. Patients with a history of myocardial infarction (MI) in less than six weeks or acute change in functional class in less than 6 weeks were excluded from the study.

Baseline electrocardiogram (ECG) was done before procedure, post-procedure ECG was done within one hour of the procedure. Pre-procedure troponin I sample was taken before the procedure and patients with high troponin I before the procedure were excluded from the study. Post-procedure troponin I was measured 12 hours after the procedure. Patients were kept in the Coronary Care Unit (CCU) for 24 hours after the procedure for observation of any new chest pain. Post-procedure echocardiography (ECHO) was done in clinically required patients. Peri-procedural myocardial infarction (PMI) was defined in all patients as per the third universal definition of MI proposed by the American College of Cardiology.3

Demographic profile, risk profile, angiographic details, and study outcome of the patients were recorded on predefined structural proforma. Collected data were analyzed using SPSS 19. Descriptive statistics such as mean ± standard deviation were calculated for continuous variables and frequency and percentages were calculated for categorical variables. Effect of demographic profile and risk profile on the study outcome was assessed using the chi-square test. Two-sided p-value $\leq$ 0.05 was taken as criteria for statistical significance.

RESULTS

A total number of 107 patients were enrolled in this study. Male predominance, 82.2% (88), was observed and mean ± SD age of the patients was 52.11 ± 8.93 years with a majority, 86.0% (92), of patients between 41 to 80 years of age. Hypertension was the most common risk factor. More than half of the patients had a previous history of MI. Majority of the patients were stable in functional class II. Most of the patients had single vessel disease (SVD), LAD was the most common culprit lesion, and 65.4% (70) patients had a high C lesion. Risk profile and angiographic details of the patients are presented in **Table 1.**

Significant rise in troponin was found in 22(20.6%) of the patients with criteria of troponin I above three times the upper limit of normal range (Trop I > 3×ULN) and in 16(15.0%) of the patients with the criteria of troponin I above five times the upper limit of normal range (Trop I > 5×ULN). Under the criteria of Trop I > 5×ULN, peri-procedural myocardial infarction (PMI) was observed to be independent of baseline risk profile and angiographic characteristics of the patients except for smoking status. Peri-procedural myocardial infarction (PMI) by risk factors

Table 1: Risk Factors and angiographic details of the patients

Characteristics	Frequency (%)
Risk Profile	
Diabetes Mellitus	25 (23.4%)
Hypertension	60 (56.1%)
Smoking	54 (50.5%)
Hyperlipidaemia	7 (6.5%)
Family History CAD	18 (16.8%)
Previous History of MI	55 (51.4%)
Remote Ischemic Preconditioning (RIPC)	47 (43.9%)
Function Class	
I	15 (14%)
II	77 (72%)
III	13 (12.1%)
IV	2 (1.9%)
Culprit Artery	
Left Anterior Descending (LAD)	71 (66.4%)
Left Circumflex (LCX)	34 (31.8%)
Right Coronary (RCA)	39 (36.4%)
Number of Vessels Involved	
Single vessel disease (SVD)	73 (68.2%)
Two vessel disease (2VD)	27 (25.2%)
Three-vessel disease (3VD)	7 (6.5%)
Type of Lesion	
High C	70 (65.4%)
Non-High	37 (34.6%)

SD = Standard Deviation, CAD = Coronary Artery Diseases, MI = Myocardial Infarction

and angiographic profile of the patients are presented in **Table 2.**

Table 2: Peri-procedural myocardial infarction (PMI) by risk factor and angiographic profile of the patients

Characteristics	Base	Trop I > 5xULN	
		PMI	**P-value
Gender			
Male	88	13 (14.8%)	0.574
Female	19	3 (15.8%)	
Risk Profile			
Diabetes Mellitus	25	3 (12%)	0.456
Hypertension	60	12 (20%)	0.082
Smoking	54	4 (7.4%)	0.025*
Hyperlipidaemia	7	1 (14.3%)	0.719

Family History CAD	18	4 (22.2%)	0.267
Previous History of MI	55	6 (10.9%)	0.175
Function Class			
I	15	3 (20%)	0.878
II	77	11 (14.3%)	
III	13	2 (15.4%)	
IV	2	0 (0%)	
Culprit Artery			
Left anterior descending (LAD)	71	11 (15.5%)	0.536
Left circumflex artery (LCX)	34	6 (17.6%)	0.395
Right coronary artery (RCA)	39	7 (17.9%)	0.348
Number of Vessels Involved			
Single vessel disease (SVD)	73	9 (12.3%)	0.203
Two vessel disease (2VD)	27	4 (14.8%)	0.626
Three vessel disease (3VD)	7	3 (42.9%)	0.067
Type of Lesion			
High C	70	11 (15.7%)	0.501
Non High	37	5 (13.5%)	

SD = Standard Deviation, CAD = Coronary Artery Diseases, MI = Myocardial Infarction, PMI = peri-procedural myocardial infarction
***P-value are based on chi-square test*
**Significant at 5% level of significance*

DISCUSSION

Surprising facts emerged from this study. High incidence of post PCI rise in troponin I is alarming. Although, asymptomatic in most cases but definitely hazardous for the patient in the long term. Studies have proven that post PCI rise in troponin I lead to Left ventricular dysfunction which in long term translates itself into reduced survival.[8] Considering these facts in ACCF/AHA/SCAI PCI guidelines, routine assessment of cardiac biomarker levels after PCI is supported with a class I recommendation in the patient with angiographic complications during PCI or clinical symptoms or ECG changes after PCI, but also a class IIb recommendation after an uncomplicated PCI.[9]

In our study significant (>5 times) rise in troponin, Post PCI myocardial infarction (PMI), occurred in 16 (15.0%) of cases. This is consistent with the prevalence of PMI internationally. Tsabedze N et al.[10], Yang X et al.7 and others have shown similar results. Higher incidence as compared to other studies like Zhang D et al.[11] (3.1%) may be explained by the fact that most of our patients, (65.4% n = 70), had high C lesions. It has been proven in studies that complex PCI patients are more prone to have PMI. Besides Zhang D et al.[11] used Society for Cardiovascular Angiography and Interventions (SCAI) definition of PMI instead of Third Universal definition, which may be the reason of difference in results.

Chen ZW et al.[6] have reported 38% incidence of PMI, which is not surprising as they considered troponin after PCI one value above the 99th percentile of upper reference limit as significant, and hence overestimation of PMI. Besides, the study population in their study was older age group with more extensive coronary artery disease (CAD). Yang X et al.[7] have also advocated that extensive coronary artery interventions with rotablator and more stents are directly related to increased incidence of post PCI myocardial infarction.

Biomarker of choice to detect PMI has been a point of debate in different studies. Many investigators including Lim CC et al.[12] have advocated the superiority of creatine kinase-myocardial band (CK-MB). They consider troponin

more sensitive and responsible for overestimation of PMI. Besides many other studies including large multicenter trials have supported the use of troponin as a reliable biomarker to detect post PCI myocardial injury. Nonetheless, whatever the biomarker used Magnetic Resonance Imaging studies have demonstrated that the rise of biomarker (CK-MB or troponin) both correlate with MRI-detected myocardial damage.[13] In our study we followed the current guideline recommendation that cardiac troponins should represent the marker of choice to detect post-PCI myocardial necrosis, giving more specificity and sensitivity.

Majority of single vessel disease (SVD) in our study population is clearly understandable by the facts that most of the three-vessel disease (3VD) and some two vessel disease (2VD) with left anterior descending (LAD) involvement are referred for CABG and hence explain 70.6% (72) SVD patients in our study. This selection bias may also reflect our lower PMI as compared to many studies. However, in our study, PMI was observed to be independent of baseline characteristics of the patients.

Patient characteristics at the time of presentation (acute coronary syndrome compared to stable coronary artery disease) also play a major role in defining the incidence of PMI. ACS patients have hypercoagulation status, raised inflammatory markers, active platelet rich emboli, etc hence more prone for PMI. Therefore 32% and 47% results reported in two study groups are self-explanatory as the study population was acute coronary syndrome patients.[14] It is evident from the above discussion that magnitude of myocardial damage after PCI is highly variable, depending on the patient's presentation ([CAD]), the angiographic and procedural characteristics and the biomarkers used to detect its presence.

Lack of a universal definition of PMI also one of the factors responsible for gross variation in the incidence of reported PMI[15] this also applies to our study. In our study, significant rise in troponin was found in 20.6% (22) of the patients with criteria of troponin I above three times the upper limit of normal range (Trop I $> 3\times$ULN) and in 15.0% (16) of the patients with criteria of troponin I above five times the upper limit of normal range (Trop I $> 5\times$ULN).

Irrespective of the cause, and whatever the definition of PMI applied the incidence found in our study (20.6% or 15.0%) is very high. This study is an eye opener of the interventional cardiologist. By opening their vessels, are we really giving benefits to our patients? Further large scale studies are required to identify the cause.

LIMITATIONS

Small sample size and single center-based study limits the generalizability of study findings.

CONCLUSION

High incidence of the post-procedural rise of troponin in our study population is alarming. Further studies are required to identify the cause and hence identifying measures to prevent PMI. Universal single definition is required worldwide in order to get uniform results.

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