



Original Article

Clinical and angiographic profiles and six months outcomes of smokers with acute ST segment elevation myocardial infarction undergoing primary percutaneous coronary angioplasty



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ABSTRACT

Background: Outcomes of primary percutaneous coronary intervention (PCI) for acute STEMI (ST-segment elevation myocardial infarction) in smokers are expected to be better than non-smokers as for patients of acute STEMI with or without fibrinolytic therapy.

Objectives: This comparative study was designed to evaluate the outcomes of primary PCI in patients with acute STEMI in smokers and non-smokers. Clinical and angiographic profile of the two groups was also compared.

Methods: Over duration of two year, a total of 150 consecutive patients of acute STEMI eligible for primary PCI were enrolled and constituted the two groups [Smokers (n = 90), Non-smokers (n = 60)] of the study population. There was no difference in procedure in two groups.

Results: In the present study of acute STEMI, current smokers were about a decade younger than non-smokers (p value = 0.0002), majority were male (98.9% vs 56.6%) were male with a higher prevalence of hypertension and diabetes mellitus (61.67% vs 32.28% and 46.67% vs 14.44%, p = 0.001) respectively. Smokers tended to have higher thrombus burden (p = 0.06) but less multi vessel disease (p = 0.028). Thirty day and six month mortality was non-significantly higher in smokers 4.66% vs 1.33% (p = 0.261) and 5.33% vs 2.66% (p = NS) respectively. Rate of quitting smoking among smokers was 80.90% at 6 months.

Conclusion: The study documents that smokers with acute STEMI have similar outcomes as compared to non smokers with higher thrombus burden and lesser non culprit artery involvement. Smokers present at much younger age emphasizing the role of smoking cessation for prevention of myocardial infarction.

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1. Introduction

Smoking is a well-known risk factor for coronary artery disease (CAD) and is associated with increased rates of acute coronary syndrome (ACS) and cardiovascular death.^{1,2,3} Studies have demonstrated that risk of myocardial infarction (MI) is two to three times and sudden cardiac death is about ten times higher in smokers than in non-smokers respectively.⁴ The risk of acute MI is three times higher in patients who continue to smoke after an acute coronary event compared to patients who quit smoking.⁵

The risk of re-infarction in patients who stop smoking is similar to the risk of non-smokers before the first infarction.⁵

The “Smoker's paradox”, typically described in studies where patients who were smoker and had acute ST-segment elevation MI (STEMI) treated with or without thrombolytic therapy^{6–8} has been carried forward today with the primary percutaneous coronary intervention (PCI) also.^{9,10} Young age and associated lesser comorbidities in smokers were the proposed explanations for it. With the advent of primary PCI for acute STEMI, higher thrombus burden with less severe underlying coronary artery stenosis along with minimal or diseased free non-infarct related coronary arteries have also been added in the list to explain this “paradox”.

According to World Health Organization (WHO), tobacco use has caused 100 million deaths in the 20th century worldwide, and if the current trend continues this figure will be 1 billion deaths for the 21st century.¹¹

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In the view of absence of a study that has directly evaluated this “paradox” solely, we planned this study to analyse the difference in clinical and angiographic profiles and outcomes of primary PCI in smokers in comparison to non-smokers. We also evaluated the effects of efforts of smoking cessation in smokers who underwent primary PCI.

2. Methods

2.1. Study design

The present study was a prospective, observational study conducted in department of cardiology, All India Institute of Medical Sciences (AIIMS), New Delhi, India from December 2013 to December 2015. All patients presenting with STEMI during the study period were enrolled in the study and later on grouped according to status of smoking.

2.2. Study population

All patients presenting with STEMI, eligible for primary PCI were included in the study. Patients were excluded from the study if any of the followings was present: age <18 years, patients presenting out of window period (12 h) without any compelling indication to perform primary PCI, pregnancy, inability to comply with dual anti-platelet medications, allergy to stainless steel or contrast material, STEMI secondary to stent thrombosis and inability to give consent for participation in study.

Current smokers were those who were active smokers within the 30-day time frame of the STEMI. Former smokers were defined as those who had stopped smoking more than 30 days prior to the STEMI. Non-smokers were patients who had never smoked in their life.

A loading dose of 325 mg of aspirin along with 600 mg of clopidogrel was used prior to PCI as soon as the diagnosis of STEMI was confirmed and contraindications to carry out primary PCI were excluded. Access site (femoral artery/radial artery), need for GP IIb/IIIa and use of thrombus aspiration catheter for manual thrombus aspiration were at the discretion of operators. Unfractionated heparin (UFH) was used as anticoagulant in all procedures with target ACT of 250–300 s. Only bare metal stents (BMS) were used during the first year of the study due to logistic concerns, however subsequently both BMS and drug eluting stents (DES) were used and their usages were operator dependent. The DES used in our study was Zotarolimus eluting “Endeavour Sprint”(Medtronic, Minneapolis, USA) coronary stents.

2.3. Study outcomes

The primary objectives of the study were (1) to compare the clinical and angiographic (pre-PCI & post PCI) profile of the smokers with non-smokers presenting with STEMI and undergoing primary PCI, (2) Thirty days and six months clinical outcomes in terms of all cause and cardiovascular mortality, fatal and non-fatal MI, stroke, stent thrombosis and major bleeding (eg. intracranial haemorrhage, bleeding requiring blood transfusion), (3) rate of quitting smoking at 6 months after STEMI.

2.4. Statistical analysis

Data was analyzed according to the established standards of descriptive statistics. Results were presented as number (percentages) of patients or mean (\pm SD) where applicable. Difference between groups stratified by smoking status was tested by chi square test and the Fisher’s exact test for dichotomous variables. Then, differences in clinical outcomes between smokers and non-

smokers were assessed. A p value of ≤ 0.05 was considered statistically significant.

2.5. Ethical approval and consent for study

Ethical approval was obtained from the institute ethics committee and written informed consents were obtained from the patients at the time of their enrolment.

3. Results

A total of 150 patients were included in the study. Patients were divided according to smoking status as current smokers (90 patients, 60%) and non-smokers (60 patients, 40%). Baseline characteristics are presented in Table 1. When distribution of patients was analyzed according to age, imbalance in proportion was found with larger proportion of younger patients in smoker’s cohort and older patients in non-smokers group. Current smokers were younger (mean age 51.60 yrs. ± 13.83) as compared to non-smokers (mean age 59.48 yrs. ± 11.56) (p value 0.0002). Males were predominant in the smokers group (98.8%).

Prevalence of diabetes mellitus (DM) and hypertension was significantly higher in the non-smokers than in the smokers. 61.67% among the non-smokers had hypertension while 32.58% had hypertension in the smokers group (p value 0.001). 14.44% had DM in the smokers group while 46.67% of the non-smokers had DM (p value 0.001).

There was no significant difference between the two groups with respect to Killip’s class. Most patients in both groups were in Killip’s class 1, (71% in smokers and 68.3% in non-smokers, p value 0.716). Killip’s class 4 presentation was found in 6.67% in non-smokers group as compared to 13.33% in the smokers group (p value 0.195).

There was similar rate of TIMI (Thrombolysis In Myocardial Infarction) flow in infarct-related artery (IRA) before PCI in both groups (Fig. 1). Also, the two groups did not differ significantly with respect to the thrombus burden in IRA. Grade 5 thrombus burden was found in 75.56% of the patients in the smokers group while it was 80.0% in the non-smokers group. Grade 4 thrombus burden

Table 1
Baseline characteristics of study population.

	Smokers	Non smokers	P value
Age	51.60 \pm 13.83	59.48 \pm 11.56	0.0002
Sex			
Male	89	34	
Female	1	26	
Risk factors			
Diabetes Mellitus	13 (14.4%)	28 (46.6%)	0.0001
Hypertension	29 (32.6%)	37 (61.7%)	0.0001
Killip class I	64 (71.10%)	41(68.3%)	0.716
Killip class IV	12 (13.33%)	4 (6.67%)	0.195
IRA			
LAD	50 (55.6%)	35 (58.3%)	
RCA	27 (30.0%)	21 (35.0%)	
LCX	10 (11.1%)	3 (5.0%)	
LM	3 (3.33%)	1 (1.67%)	0.521
Non IRA disease	33 (36.67%)	32 (53.33%)	0.028
Pre TIMI 3 flow	17 (18.89%)	7 (11.67%)	0.237
Post TIMI 3 flow	70 (78.6%)	45 (75.0%)	0.602
No reflow	4 (4.49%)	1 (1.67%)	0.648
Thrombus			
Grade 3	3 (3.33%)	6 (10.0%)	
Grade 4	19 (21.1%)	6 (10.0%)	
Grade 5	68 (75.56%)	48 (80%)	0.06
Thrombosuction used	41 (45.56%)	12 (20.0%)	0.001

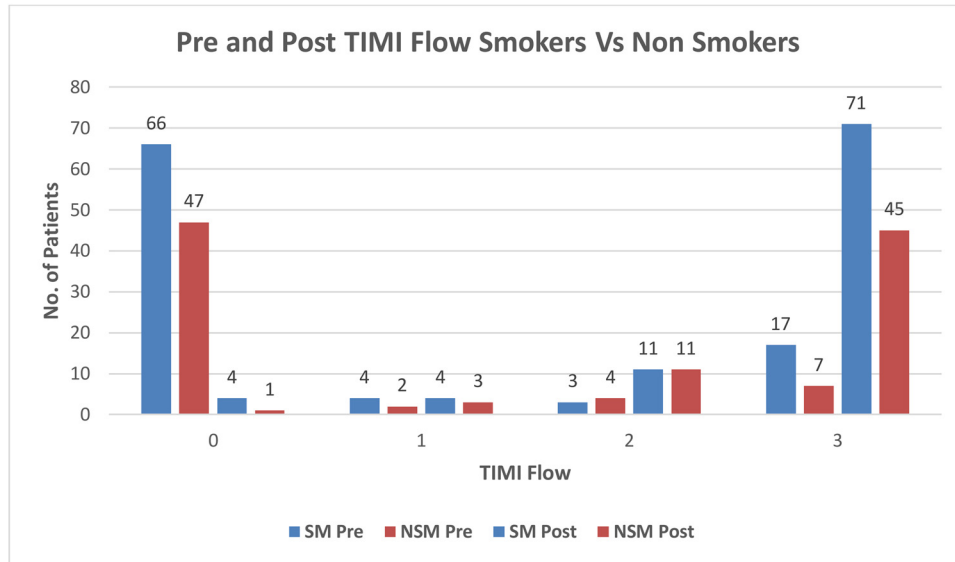


Fig. 1. TIMI flow in Smokers and Non smokers.

was found in 21.10% patients in the smokers group while it was 10.0% patients in the non-smokers group. Although, there was a trend towards higher thrombus burden in smokers but it was not statistically significant (Fig. 2). Also, the two groups did not differ significantly between the final angiographic PCI results. The post PCI TIMI flow grade 3 rate was not significantly different among smokers and non-smokers. The post TIMI flow grade 3 was found in 78.65% of the patients among smokers and 75% of the patients among non-smokers (p value 0.602) (Fig. 1). No reflow was present in 4.49% in smokers group and in 1 patient 1.67% in non-smokers group (p value 0.648). In both the groups, there was no significant difference in terms of involvement of infarct related artery (p value 0.521). Associated significant disease in non-infarct related artery (>70% luminal diameter stenosis in other major epicardial coronary artery that is non culprit vessel for this STEMI) was present in 36.67% patients among smokers which was significantly lower than in non-smokers (53.33%) (p value 0.028). Thrombo-suction was done in 45.56% patients among smokers as compared to 20% patients among non-smokers (p value 0.001) (Table 1).

Severe left ventricular (LV) systolic dysfunction (EF 35% or less) was present in 47.78% of patients among smokers and in 40% of patients among non-smokers. Moderate LV systolic dysfunction

(EF 36–49%) was present in 42.22% of patients among smokers and in 48.33% of patients among non-smokers. Mild LV systolic dysfunction (EF 50–59%) was present in 7.78% of patients among smokers and in 6.67% of patients among non-smokers. Normal LV systolic function was present in 2.22% of patients who were smokers and in 5% of patients who were non-smokers.

Total 9 (6%) patients died at 30 days. Out of them 7 (4.66%) were smokers and 2 (1.33%) were non-smokers (p = 0.261). At 180 days, total 12 (8%) patients died, out of them 8 (5.33%) were smokers and 4 (2.66%) were non-smokers (p = NS) (Table 2). In the smokers group, 72 (80.90%) smokers quit smoking after the PCI procedure as a result of counseling.

4. Discussion

In our study it was seen that the smokers developed STEMI a decade earlier than the non-smokers. This finding is consistent with most of the studies that have assessed the impact of smoking on age at the time of first documented STEMI.^{9,10,12,13} Even though the numbers of women smokers in India has gone up from 5.3 million in 1980 to 12.7 million in 2012,¹⁴ in our study in smokers group, 99.8% of the patients were male.

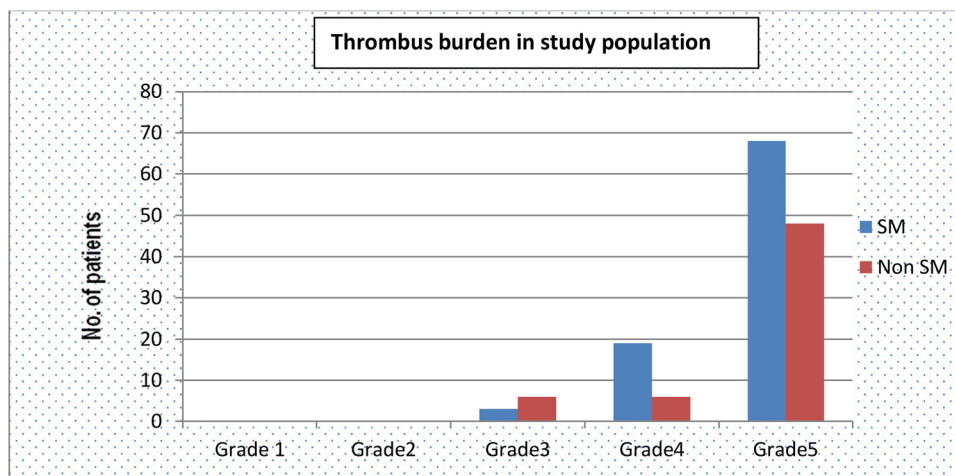


Fig. 2. Thrombus burden in smokers and non smokers.

Table 2

Clinical outcome at thirty days and 6 months.

	Smokers(n= 90)	Non smokers(n= 60)	P value
Ischemic complications at 30days			
Death	7 (4.66%)	2 (1.33%)	NS
Re-infarction	0	0	
Bleeding complications at 30days			
Stroke	0	0	
Major bleeding requiring transfusion	0	0	
Ischemic complications at 6 months			
Death	8 (5.33%)	4 (2.66%)	NS
Re-infarction	0	0	

There was no significant difference in clinical presentation (Killip's class) in both the groups with most of the patients in Killip's class 1 at presentation.

Significantly less prevalence of hypertension and DM in our study among smokers was in accordance with most of the studies and this can be because of younger mean age of the smokers.

Anterior wall MI with Left anterior descending (LAD) coronary artery as culprit vessel was the most frequent presentation in both the groups. However, in few studies inferior wall MI was the more frequent presentation in smokers.^{9,15} LAD coronary artery was also the most common culprit vessel in the previous data from EUROTRANSFER Registry.¹⁰

Another important aspect regarding the finding of a higher incidence of thrombosis rather than atherosclerosis in smokers, was also evaluated in our study. Both the groups were profiled with coronary angiography at the time of STEMI. It was seen that the smokers group had higher thrombotic burden which, however, was not statistically significant. Besides this, thrombosuction, which is an indirect marker of higher thrombus burden was used more frequently in our study in smokers group. Higher use of thrombosuction in smokers in our study is in contrast to previous data from EUROTRANSFER Registry¹⁰ in which no significant difference was seen in both the groups. The use of thrombosuction during primary PCI also depends upon operator's preference so it could not be taken as evidence to generate a hypothesis that smokers have higher thrombotic burden in STEMI. However, data from the CADILLAC trial⁹ has demonstrated a similar amount of thrombus burden in infarct related artery in both smokers and non-smokers.

A lower prevalence of multi-vessel disease in smokers in our study suggests that smokers at the time of their first acute STEMI have less extensive atherosclerotic disease. This data rather contradicts the well-known assumption that smoking promotes atherosclerosis. The lack of extensive CAD may also be explained by the younger age of this population (smokers), as well as a lower prevalence of DM and hypertension at the time of first STEMI in smokers. The pathophysiological explanation for this may be an increased plasma fibrinogen level and increased numbers of activated platelets in circulation in smokers.^{16,17} Hydrocarbons in cigarette smoke can injure arterial endothelium, initiate the atherosclerotic process, decrease levels of high-density lipoproteins, and have a dose-dependent effect on plaque deposition.^{18,19} Hemoglobin bound to carbon monoxide in smokers has been linked to development of atherosclerotic CAD in humans by Wald et al.²⁰

In our study, pre-PCI TIMI flow was comparable in both smokers and non-smokers. Similarly, post PCI TIMI flow was found comparable in both the groups. The results are similar to those described by Weisz et al.⁹ However, Rakowski et al.¹⁰ had demonstrated significantly higher post PCI TIMI 3 flow in smokers. Albertal M et al.²¹ had also described better post PCI TIMI flow grade and TIMI frame in smokers undergoing primary angioplasty for STEMI. Whereas in their study myocardial blush grades were similar between the smokers and non-smokers.

With a total 6% mortality at 30 days and 12% mortality at 6 months in overall study population, no difference in the mortality at 30 days and 6 months was found. Also, there was no stroke or major bleeding requiring transfusion in any patient. However, data by Weisz et al.⁹ from CADILLAC and Rakowski et al.¹⁰ from EUROTRANSFER Registry has shown lower mortality among smokers. At the same time, data from GRACE registry²² has shown no survival advantage in current or prior cigarette smokers and the existence of "Smoker's paradox" has been denied. In data from HORIZONS-AMI trial,²³ smoking has been found as an independent predictor of definite/probable stent thrombosis at one year mainly because of late stent thrombosis related to paclitaxel eluting stent.

We also addressed the rate of quitting smoking in smokers who presented with STEMI and received pre-hospital discharge counseling for smoking cessation. 80.90% of smokers quit smoking at six month's follow-up. This is an important observation as regards the awareness about health hazards related to smoking. Smoking is widely prevalent in the younger age groups and probably only preventable risk factor. Smoking related STEMI is particularly hazardous as it strikes a decade earlier and may cause left ventricular dysfunction which lasts throughout the rest of the persons' life.

The limitations of the current study include a small sample size which is insufficient to generate any hypothesis regarding incidence of mortality in both groups.

5. Conclusion

Our study showed that there was no significant difference between smokers and non-smokers presenting with STEMI in terms of coronary arteries involved, primary PCI procedural outcome and mortality. It was however noted that the smokers were about a decade younger at the time of their first documented STEMI and tended to have higher thrombotic burden in infarct related coronary artery with significantly less multi-vessel disease, DM and hypertension. We have not observed any "Smoker's paradox" in our study but we would like to propose that smoking related STEMI is an important health hazard and is the worst form of heart disease because of smoking. Pre-hospital discharge counseling for smoking cessation is effective and should be encouraged in patients with STEMI.

Conflict of interest

The authors report no relationship that could be constructed as conflict of interest.

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