Impact of Smoking Status on Hospital Outcome of Patients with ST-Segment Elevation Myocardial Infarction Either Treated by Pharmacy-invasive Strategy or Primary Percutaneous Coronary Intervention.

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Abstract

Background:
Smoking is a common public problem with a high health burden. Many studies have shown that there are many hazardous actions of smoking on body systems especially haemostatic, respiratory and circulatory systems.

Smoking may increase the thrombus burden in patients with acute coronary syndrome. The ‘smoker’s paradox’ has been described for more than 25 years. Its existence and its effect on patients’ outcome post myocardial infarction are debatable. So we conducted our study to assess the impact of smoking status on outcome of STEMI patients and efficacy of pharmaco-invasive strategy in treating STEMI patients compared to PPCI.

Methods:
We conducted our prospective observational study in the Cardiology department from-August 2018 to August 2019 on patients who are presented by STEMI with the duration from onset of symptoms to first medical contact were 12 hours or less we included 199 patients in our study.

Patients are divided into 4 groups  
- **Group 1** (Smokers treated by PPCI)
- **Group 2** (Non-smokers treated by PPCI)
- **Group 3** (Smoker treated by pharmaco-invasive strategy)
- **Group 4** (Non-smoker treated by pharmaco-invasive strategy)

TIMI flow before and after PCI, acute heart failure and death was assessed in each patient.

Results:
Smokers are younger than non-smokers and have fewer co-morbidities. Patients treated by primary PCI and pharmaco-invasive strategy either smokers and non-smokers there was no significant difference between the 4 groups in angiographic data and outcome except that smokers treated by pharmaco-invasive strategy had a lower incidence of TIMI flow III at diagnostic angiography before PCI with P value (0.047)

Conclusion:
There is no actual smokers paradox. Pharmaco-invasive strategy is a good option when a PPCI is not available. Finally, early transfer of smokers treated with a pharmaco-invasive strategy to a PCI
Background
Cigarette smoking is one of the common public problems with a high health burden. Many studies have shown that there are many hazardous actions of smoking on body systems especially haemostatic, respiratory, reticulo-endothelial and circulatory systems. The World Health Organization reported that by 2030 deaths due to tobacco consumption will be about 8.3 million cases. (1)

Smoking was found to produce a state of hypercoagulability, possibly by increasing platelet aggregation and adhesion which is claimed to be due to nicotine. (2)

Cigarette smoking may increase the thrombus burden in patients with acute coronary syndrome (ACS). Thrombosis results largely from platelet aggregation and fibrin formation due to rupture or ulceration of the atheroma. Many studies have shown that smoking affects platelet function. Platelets isolated from smokers exhibit increased aggregation as compared to non-smokers. Also, there is an increased plasma fibrinogen level in smokers. (3)

For patients with STEMI primary percutaneous coronary intervention (PPCI) remains the best and optimal strategy of treatment. On the other hands, many patients cannot have PPCI at its optimal time because of geographical or logistical issues. In such cases, a pharmaco-invasive strategy by the administration of lytic therapy is followed by immediate transfer to (PPCI) capable center for either rescue percutaneous coronary intervention (PCI), in case of failed fibrinolysis, or routine coronary angiography and PCI. (4)

Thrombin activity is increased in patients with acute myocardial infarction was found to increase more after the receiving of fibrinolytic therapy. that may be the cause of failure to achieve initial reperfusion or early reocclusion after initially successful results of lytic therapy. (5)

The ‘smoker’s paradox’ has been described for more than 25 years. The existence of this paradox and its effect on patients’ outcomes post myocardial infarction is debatable.

Methods
We conducted our prospective observational study in the Cardiology department from-August 2018 to
August 2019 on patients who are presented by STEMI with the duration from onset of symptoms to first medical contact were 12 hours or less we included 199 patients in our study.

Patients are either presented to the emergency room of our department directly or received streptokinase in another hospital and referred to our department for (PCI) after clinical and ECG evidence successful thrombolysis.

Patients are divided into 4 groups

**Group 1** (Current Smokers received PPCI directly)

**Group 2** (Non-smokers received PPCI directly)

**Group 3** (Current Smokers received streptokinase with successful results and then PCI was done according to guidelines after 3-24 hours) (pharmaco-invasive strategy)

**Group 4** (Non-smokers received streptokinase with successful results and then PCI was done according to guidelines after 3-24 hours) (pharmaco-invasive strategy)

Patients received thrombolytic therapy at the time of hospital presentation the clinical evidence of successful thrombolytic therapy is a relief of chest pain and resolution of ST-segment elevation by 50% after one and half hours from the start of thrombolysis

Diagnosis of STEMI is made by the presence of ischemic symptoms with the presence of ST-segment elevation in ECG with elevated cardiac troponin according to the fourth universal definition of acute myocardial infarction (6)

Streptokinase was used as the thrombolytic agent as it is the only available lytic therapy in our department.

All patients are subjected to the following

History taking and clinical examination.

Echocardiography to evaluate the presence of mechanical complication and assessment of ejection fraction and segmental wall motion.

Routine lab investigations (urea, creatinine, complete blood count and coagulation profile)

The decision to do PPCI or to give patients streptokinase first was left to the attending physician according to the logistic circumstances and patients presentation.

When doing PCI the decision for doing culprit lesion revascularization versus complete revascularization was left to the operator according to patients' clinical condition and angiographic findings.

Assessment of thrombolysis in myocardial infarction (TIMI) flow grade (7) at diagnostic angiography and after stenting was done by two operators.
“Grade 0: Complete occlusion of the infarct-related artery”

“Grade 1: Some penetration of contrast material beyond the point of obstruction but without perfusion of the distal coronary bed”

“Grade 2: perfusion of the entire infarct vessel into the distal bed but with delayed flow compared with a normal artery”

“Grade 3: Full perfusion of the infarct vessel with normal flow”

Patients are transferred to the coronary care unit after PCI and treatment and management was left the patients' clinical conditions attending physician evaluation.

Our exclusion criteria

STEMI patients who did rescue PCI after clinical evidence failed thrombolysis
Patients with a history of coagulopathy
Patients with renal failure on dialysis
Patients with malignancy
Patients on oral anticoagulants
Patients with prior STEMI
Patients with prior CABG

**Statistical analysis**

The data were evaluated using IBM SPSS software package version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing two means. A one-way analysis of variance (ANOVA) when comparing more than two means. Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters.

**Results**

The study was conducted on 199 consecutive patients presented to our department by STEMI and matching our inclusion criteria during the period from August 2018 to August 2019.

**Demographic data table (1)**

We found in our study as regarding demographic data that smoker patients have younger age with a mean age (54.73) years and non-smokers mean age (58.48) years P-value (0.001).

Smokers also have fewer cardiovascular risk factors they were less hypertensive and diabetics, with the incidence of hypertension and diabetes (27.2% & 24.7%) respectively in smokers and (64.4%& 53.4%) in non-smokers respectively  P-value ( 0.001)
As regard lipid profile there was no significant difference between smokers and non-smokers with P-value (0.770).

Smoking is more common in males than females with only 3 females in smoker groups. (Table 1)

**TIMI flow before PCI** (Tables 2, 3 &4)

*In pharmaco-invasive groups (III and IV)*

Target vessel occlusion at diagnostic angiography with TIMI zero flow, there was no statistically significant difference between smokers and non-smokers (12.5% & 14.0%) P-value (0.867) (table 2) On the other hand, patients with TIMI flow III were slightly significantly higher in non-smokers patients with TIMI flow III occurring in 34.9% of non-smokers and in 12.5 % of smokers P-value (0.047). (table 3)

*In PPCI groups (I and II)*

There was no significant statistically significant difference in arterial total occlusion before PCI with TIMI 0 occurring in 78.9% in smokers and 80% in non-smokers P-value (0.882) (table 2) Also in TIMI flow III before PPCI, there was no statistically significant difference in arterial patency with TIMI III occurring in (3.5% & 1.3%) in smokers and non-smokers respectively (Table 3)

**TIMI flow after PCI** (Tables 2, 3 &4)

The procedural success with achieving TIMI flow III post PCI our data showed that there was no statistically significant difference between smoker and non-smokers in both PPCI and pharmaco-invasive groups with TIMI III (87.7% & 89.3% ) in smokers and non-smokers respectively in PPCI group P-value (0.4). (Table 3)

The same was found in the pharmaco-invasive group with TIMI III (83.3%% & 95.3%) in smokers and non-smokers respectively P-value (0.099). (Table 3)

Also, there is no statistically significant difference in the incidence of no-reflow with TIMI zero flow post PCI (1.8% & 2.7% % ) in smokers and non-smokers respectively in the PPCI group P-value (0.728). (Table 2) the same was found in the pharmaco-invasive group with TIMI zero occurring only in one case of smokers and no cases of no-reflow in non-smokers p-value (0.177). (Table 2)

**Outcome**
There was no statistically significant difference in duration of hospitalization, death or development of acute heart failure between the four groups with P value (0.453, 0.327 & 0.280) respectively. (Tables 5 & 6)

Discussion

Smoking is a modifiable risk factor for ischemic heart diseases. There is no doubt that smoking increases the incidence of premature atherosclerosis. However, there are conflicting data regarding the role of smoking in the prognosis of patients after acute coronary syndromes (ACS). (8)

Some studies, investigating this issue showed that smoking was associated with a better outcome even after considering other influential risk factors. (9)

The fact that smoker patients, when presented with ACS, are at a younger age than non-smokers many researchers have attributed their better outcome to their younger age and lower prevalence of other risk factors. (10) On the contrary, some studies reported a better outcome for smokers after ACS even after adjustment for other risk factors. (11)

In our study, most smoker patients were male with only 4 smokers were female this because of social factors in our region where females rarely smoke. We also found that smokers were younger age with the mean age of smokers were (54.73) & non-smokers(58.48) Which is similar to what Reinstadler Sj et al (12) and many other studies found the same data.

In our study, we showed that smokers less likely to have diabetes and hypertension which were statistically significant compared to non-smokers this was in agreement with Toluey M, et al (13) findings.

Regarding dyslipidemia, our data was matching with what Haig C et al (14) found and we found that there was a statistically significant difference between smokers and non-smokers.

**Angiographic findings in patients who received PPCI**

Our finding regarding arterial patency on angiography before PCI and TIMI flow post PCI was similar to what Liu R, et al (15) found and there was no statistically significant difference between both smokers and non-smokers groups.
Angiographic findings in patients who pharmaco-invasive groups

Hirapur I et al \(^{(16)}\) found that arterial patency in angiography was higher in smoker patients after streptokinase which is to some extent similar to our results as we have a non-statistically significant difference in TIMI zero between non-smoker and smokers but the incidence of TIMI III flow was lower in smokers. This could be explained by less atherosclerosis in smoker patients and arterial occlusion is caused mainly by thrombus rather than heavy atherosclerosis in non-smokers so total arterial occlusion after streptokinase showed no differences but the hypercoagulable state caused by smoking and high thrombus burden may reduce the incidence of TIMI III flow after lytic therapy.

TIMI flow post PCI

We also found that there was no significant difference between the four groups. Rolf Symons, et al \(^{(17)}\). They found that smoking was associated with increased intramyocardial haemorrhage which was used as a marker of myocardial ischemia-reperfusion injury. Rolf Symons, et al concluded that” The intramyocardial haemorrhage abolished the smoking paradox.

The outcome of patients post PCI

Our data suggested that there was no statistically significant difference in death, development of acute heart failure nor duration of hospital stay between the four groups and These findings are not supporting the idea of the smoker paradox.

Conclusion

Our results suggesting that there is no actual smokers paradox and the evidence of better outcomes in some studies in smokers with STEMI may be because they have younger age and fewer risk factors at the time of presentation with STEMI. Also, we can conclude that a pharmaco-invasive strategy is a good option when a PPCI capable center is not available. Finally, early transfer of smokers treated with the pharmaco-invasive strategy to PCI capable hospital for early intervention may be recommended as they have less incidence of TIMI flow III at diagnostic coronary angiography.

List Of Abbreviations

| Abbreviation | Description                           |
|--------------|---------------------------------------|
| ACS          | Acute coronary syndrome               |
| STEMI        | ST-segment elevation myocardial infarction |
| PPCI         | Primary percutaneous coronary intervention |
| PCI          | primary percutaneous coronary         |
| CABG         | Coronary artery bypass graft          |
| TIMI         | thrombolysis in myocardial infarction |
Declarations

Ethics approval and consent to participate

The protocol was approved by the committee of the Cardiology Department of Tanta University in July 2018 (reference 3-7-2018)

The informed written consent was obtained from all the patients.

Consent for publication

Not Applicable.

Availability of data and material

The datasets used and or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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The authors received no specific funding for this work.

Authors’ contributions

AA participated in the following-up of the patients during hospitalization and interpretation of coronary angiographic data. He wrote manuscripts.

TH participated in the following-up of the patients during hospitalization and interpretation of coronary angiographic data and prepared the collected clinical data to be ready for statistical analysis.

MA participated in the following-up of the patients during hospitalization and interpretation of coronary angiographic data. He did the statistical analysis for our study.

All authors have read and approved the manuscript.

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Tables
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