IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 4 Ser. 4 (April. 2024), PP 29-34
www.iosrjournals.org

Angiographic Evaluation Of Efficacy Of Streptokinase In Patients With Acute Stemi: Smokers Vs. Non-Smokers

Sarker S[1], Chowdhury Aw[2], Ali M[3], Islam N[4], Khan F[5], Poorna Mi[6], Tasnim J[7], Rahman Md M[8], Khan Mh[9], Haque Smz[10]

Dr. Sudhakar Sarker, Assistant Professor, Department Of Cardiology, Green Life Medical College, Dhaka, Bangladesh
Prof. (Dr.) Abdul Wadud Chowdhury, Professor, Department Of Cardiology, Dhaka Medical College, Bangladesh
Dr. Mohammad Ali, Assistant Professor, Department Of Cardiology, Ibn Sina Medical College, Dhaka, Bangladesh.
Dr. Nazmul Islam, Junior Consultant, Bangladesh Specialized Hospital, Dhaka, Bangladesh.
Dr. Fauzia Khan, Specialist, Bangladesh Specialized Hospital, Dhaka, Bangladesh.
Dr. Maliha Islam Poorna, Specialist, Bangladesh Specialized Hospital, Dhaka, Bangladesh.
Dr. Jakia Tasnim, Specialist, Bangladesh Specialized Hospital, Dhaka, Bangladesh.
Dr. Md. Matiur Rahman, Assistant Professor, Department Of Cardiology, Bangladesh Medical College & Hospital, Dhaka, Bangladesh.
Dr. Mahmood Hasan Khan, Consultant, Department Of Cardiology, Delta Hospital Limited, Dhaka, Bangladesh.
Dr. S M Ziaul Haque, Senior Medical Officer, Department Of Cardiology, Salalah Heart Center, Salalah, Sultanate-E-Oman.

Abstract

Background: *Smoking is a common problem with a high public health burden. 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 ST segment elevation myocardial infarction (STEMI). 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. Smoking is associated with many influencing factors for accelerating Myocardial Infarction (MI). In a country like Bangladesh Streptokinase (SK) is used as a leading therapeutic option for the treatment of acute STEMI. SK binds with plasminogen; this SK-plasminogen complex ensures fibrinolysis. The aim of this study was to determine angiographic outcome after SK infusion in patients with STEMI and to compare between smokers and non-smokers.*

Methods: *In this observational, prospective and single-center study conducted between December 2020 and November 2022, a total of 100 patients who were diagnosed with STEMI were included. Patients were divided in two groups, Group I (smokers) and Group II (non-smokers). The patients were treated with thrombolytic (streptokinase) therapy and evaluated for TIMI flow by performing angiography within 72 hours of thrombolysis with SK.*

Results: *The ratio of smokers and non- smokers was 2:1. Total number of male patients were 87 (87.0%) and female were 13 (13%). Smokers were younger than the non-smokers (48.80 ± 10.23 vs 54.57 ± 9.51). After thrombolysis patients were evaluated by symptoms, ECG improvements and ultimately by TIMI flow grades on angiogram. A Total of 55 patients achieved TIMI 3 flow of which 43 (64.2%) were smokers and 12 (36.4%) were non-smokers.*

Conclusions: *Smokers have relatively more hypercoagulable state than non-smokers. Better effect of thrombolysis in smokers group may be because of younger age and lesser comorbidities. Smokers should be motivated and guided properly to quit smoking.*

Keywords: *Thrombolytic therapy, Thrombolysis in Myocardial Infarction (TIMI), Streptokinase.*

Date of Submission: 06-04-2024 Date of Acceptance: 16-04-2024

I. Introduction

Smoking is an important risk factor for ischemic heart disease and is associated with increased rates of myocardial infarction and cardiovascular death[1-3]. However, there are some data showing mortality is lower in smokers than non-smokers in patients with ST-segment elevation myocardial infarction (STEMI), when treated

with thrombolysis or without reperfusion therapy.[4-6]The influence of smoking on outcome in patients with STEMI treated with Streptokinase was the main aim of this study. Coronary Angiographic measurements of Thrombolysis in Myocardial Infarction (TIMI) flow grades can be easily evaluated after treatment with thrombolytic therapy. Ageing is a major risk factor for manifestation of MI followed by smoking. Smoking is injurious to health and its harmful effects also increase with advancing age. However, smoking is one of the major modifiable risk factor and preventable cause of MI.[7] Smoking is associated with many influencing factors for accelerating MI. Despite having hazardous effects of smoking, many studies have reported that smokers get more advantageous effect of thrombolytic therapy than non-smokers for the treatment of MI; this is known as "the smoker's paradox"[8-11]. Thus, the aim of this study was to determine angiographic patency after SK infusion in ST segment elevation myocardial infarction (STEMI) patients and comparison between smokers and non-smokers.

II. Methods

Study design and population:

This was an observational, prospective, single-center study conducted between December 2020 to November 2022 at a tertiary care center in Bangladesh. A total of 100 patients were enrolled during this period. The patients who were admitted to the emergency department and diagnosed with STEMI were included in this study. STEMI was diagnosed in presence of two or three following criteria: Chest pain and/or discomfort for at least 20 minutes or more; ST segment elevation of ≥1 mm in at least two contiguous leads; in leads V2-V3 ST segment elevation of ≥ 2mm in men and ≥1.5mm in women in standard 12-lead electrocardiogram(ECG).[12,13]

The exclusion criteria were: (a) any prior intracranial haemorrhage (b) known structural cerebral vascular lesion (e.g., arterio-venous malformation) (c) known malignant intracranial neoplasm (primary or metastatic) (d) ischemic stroke within 3 months except acute ischemic stroke within 3 hours (e) suspected aortic dissection (f) active bleeding or bleeding diathesis [excluding menses] (g) significant closed head or facial trauma within 3 months (h) history of chronic severe poorly controlled hypertension (i) severe uncontrolled hypertension on presentation (SBP >180mmHg or DBP >110mmHg) (j) history of prior ischemic stroke >3 months, dementia, or known intracranial pathology not covered in contraindications (k) traumatic or prolonged (>10 min) CPR or major surgery (<3 weeks) (l) recent (within 2-4 weeks) internal bleeding (m) non-compressible vascular punctures sites (n) prior streptokinase, exposure (>5 days ago) or prior allergic reaction to these agents (o) pregnancy (p) active peptic ulcer (q) current use of anticoagulants: with high INR.

Study protocol:

Basic characteristics like age, gender, blood pressure, heart rate, presence of diabetes or hypertension, smoking status and chest pain duration were determined at the time of admission for all the patients. According to their smoking status, the patients were divided into two groups, group I- "smokers" and group II- "non-smokers". The ratio was 2:1 between the smokers and non- smokers respectively. Blood samples for biochemistry analysis including lipid panel and ECG were also recorded.

Treatment approach:

Intravenous infusion of 1.5 million IU streptokinase over 1 hour was administered to all the STEMI patients if there was no contraindications. Loading dose with aspirin 300 mg and clopidogrel 300 mg were given orally to all patients; other medications were prescribed accordingly like beta-blockers, angiotensin-converting enzyme inhibitors, low-molecular-weight heparin, nitrates and statin.

Angiographic study:

Within 72 hours of thrombolytic therapy, patients underwent coronary angiographic procedure using standard Judkins technique. Siemens angiography machine was used to perform angiographic procedure. Coronary angiograms were interpreted by two experienced interventional cardiologists who worked independently and were unaware of clinical ailment and laboratory data of patients.

Study endpoints:

After completion of thrombolytic therapy, angiographic TIMI flow grade were determined in the culprit vessel. Previously established grading system was used for the determination of TIMI flow rates.

TIMI 0: No perfusion distal to stenosis
TIMI 1: penetration distal of stenosis but no perfusion
TIMI 2: partial perfusion
TIMI 3: complete perfusion.

Statistical analysis:

The SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA) was used for statistical analysis of the data.

Categorical variables were expressed as numbers (n) and percentages (%), whereas continuous variables were reported as mean and standard deviation or as median and interquartile range wherever appropriate. Chi-square test was used to compare categorical variables between the treatment groups. The Student's t-test or Mann-Whitney U test was used for comparisons between groups. The analysis of variance (ANOVA) or Kruskal-Wallis test was used for comparisons wherever applicable. The statistical level of significance for all tests was considered to be<0.05, confidence interval was 95%.

III. Results

Baseline demographics:

A total of 100 patients were included in this study during the mentioned study period. There were 67 patients in group I (smokers) and 33 patients in group II (non-smokers). Of the total population 87 (87.0 %) were male and 67 of them were smokers. Thirty three patients were diabetic and 16 of them were smokers. There were 22 patients aged <40 years and 19 of them were smokers. Smokers presented with the symptoms of STEMI at younger age than non-smokers and had significantly lower co-morbid condition (p=<0.05). Other demographic details of patients including family history, window period of thrombolysis, left ventricle ejection fraction, coronary angiographic timing, and post streptokinase ECG and TIMI flow details are presented in Table 1. Detailed information on lesions among different segments of vessels is presented in Table 2, and severity of lesion in vessels is depicted in Table 3.

Table 1: Baseline demographics and clinical characteristics of patients. Characteristics (N=100)

	Smoker (N = 67)	**Non-smoker (N = 33)**	**P value**
Demography	**N (%)**	**N (%)**	
Men	66 (98.5%)	21 (63.6%)	<0.001
Age (mean ± SD, years)	48.80 ± 10.23	54.57 ± 9.51	<0.001
Diabetes	16(23.9%)	17(51.5%)	0.006
Hypertension	18 (26.9%)	15 (45.5%)	0.012
Family history	6 (8.9%)	10 (30.3%)	<0.05
TC (mg/dL)	180(157-192)	184 (166-215)	<0.01
HDL (mg/dL)	38 (36-40)	38 (36-42)	0.682
TG (mg/dL)	166 (126-185)	175 (126-193)	0.028
LDL (mg/dL)	112 (95-118)	113 (97-129)	0.572
Young age			
0-40 years	19(28.4%)	3(9.1%)	0.028
>40 years	48 (71.6%)	30 (90.9%)	
Timing of thrombolysis			
0-6 h	46 (68.7%)	19 (57.6%)	0.622
7-12 h	16 (23.9%)	12 (36.4%)	
13-18 h	2 (3.0%)	1 (3.0%)	
19-24 h	3 (4.5%)	1 (3.0%)	
Ejection fraction (EF)			
≤ 30 %	2 (3.0%)	1 (3.0%)	0.879
31-45%	37 (55.2%)	16 (48.5%)	
46-60%	25 (37.3%)	15 (45.5%)	
>60 %	3 (4.5%)	1 (3.0%)	
Coronary angiography timing			
< 24 h	5 (7.5%)	3 (9.1%)	0.733
≥24 h	19 (28.4%)	9 (27.3%)	
≥48 h	29 (43.3%)	12 (36.4%)	
≥72 h	14 (20.9%)	9 (27.3%)	
Post SK ECG			
Not settled	11 (16.4%)	3 (9.1%)	0.321
Settled	56 (83.6%)	30 (90.9%)	
Thrombolysis in myocardial infarction (TIMI)			
TIMI 0	3 (4.5%)	2 (6.1%)	0.029
TIMI 1 & 2	21 (31.3%)	19 (57.6%)	
TIMI 3	43 (64.2%)	12 (36.4%)	

p value obtained by Unpaired t-test, Mann Whitney test and Chi-square test, p<0.05 considered as a level of significant

Table 2: Distribution of lesions among different segments of vessels.

	Smoker (N = 67)	**Non-smoker (N = 33)**	**P value**
Segments of LM, n (%)			
None	66(98.5%)	31 (93.9%)	0.207
Proximal	0 (0.0%)	0 (0.0%)	
Distal	1 (1.5%)	2 (6.0%)	
Diffuse	0 (0.0%)	0 (0.0%)	
Ostial	0 (0.0%)	0 (0.0%)	
Segments of LAD, n (%)			
None	21 (31.3%)	7 (20.2%)	0.289
Ostio Proximal	7 (10.4%)	5 (16.3%)	
Proximal	21 (31.3%)	11 (32.6%)	
Mid	17 (25.4%)	9 (28.7%)	
Distal	1 (1.5%)	1 (2.3%)	
Segments of LCX, n (%)			
None	52 (77.6%)	22 (67.7%)	0.240
Ostio Proximal	3 (4.5%)	4 (12.1%)	
Proximal	6 (9.0%)	4 (12.1%)	
Mid	4 (6.0%)	2 (6.1%)	
Distal	2 (3.0%)	1 (3.0%)	
Segments of RCA, n (%)			
None	40 (59.7%)	17 (51.5%)	0.436
Ostio Proximal	5 (7.5%)	3 (9.1%)	
Proximal	10 (14.9%)	4 (12.1%)	
Mid	10 (14.9%)	7 (21.2%)	
Distal	2 (3.0%)	2 (6.1%)	
Other Vessels 1, n (%)			
None	57 (85.1%)	29 (87.9%)	0.703
Ramus	4 (6.0%)	2 (6.1%)	
OM	0 (0.0%)	0 (0.0%)	
Diagonals	6 (9.0%)	2 (6.1%)	
Other Vessels 2, n (%)			
None	61 (91.0%)	29 (87.9%)	0.0.619
Ramus	0 (0.0%)	0 (0.0%)	
OM	5 (7.5%)	3 (9.1%)	
Diagonals	1 (1.5%)	1 (3.0%)	

p value obtained Chi-square test, $p<0.05$ considered as a level of significant

Table 3: Severity of lesions in different vessels. Characteristics

	Smoker (N = 67)	**Non-smoker (N = 33)**	**P value**
Severity of LM, n (%)			
Normal	66 (98.5%)	31 (93.9%)	0.207
<50%	1 (1.5%)	2 (6.1%)	
50-70%	0 (0.0%)	0 (0.0%)	
>70%	0 (0.0%)	0 (0.0%)	
Severity of LAD, n (%)			
Normal	21 (31.3%)	7 (21.2%)	0.660
<50%	14 (20.9%)	6 (18.2%)	
50-70%	5 (7.5%)	3 (9.1%)	
>70%	27 (40.3%)	17 (51.5%)	
Severity of LCX, n (%)			
Normal	51 (76.1%)	22 (67.7%)	0.761
<50%	5 (7.5%)	4 (12.1%)	
50-70%	4 (6.0%)	3 (9.1%)	
>70%	7 (10.4%)	4 (12.1%)	
Severity of RCA, n (%)			
Normal	40 (59.7%)	18 (54.5%)	0.845
<50%	8 (11.9%)	3 (9.1%)	
50-70%	4 (6.0%)	2 (6.1%)	
>70%	15 (22.4%)	10 (30.3%)	

LM: left main; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery
p value obtained by Chi-square test, $p<0.05$ considered as a level of significant

Study outcomes:

TIMI flow was assessed by coronary angiogram after completion of the thrombolytic therapy. Of the total population, a total of 55 (55%) patients were able to achieve TIMI 3 flow. Forty three (64.2%) patients

from group I (smokers) and 12 (36.4%) patients of the group II (non-smokers) achieved TIMI 3 flow. After angiogram a few patients developed complications like contrast induced nephropathy, local site haematoma, post angiography pulmonary oedema but all the complications were resolved later. Those patients who could not achieve TIMI 3 flow with thrombolytic therapy alone were managed medically and if condition got worse, aggressive medical management or PCI was considered, as indicated by concerned physician.

IV. Discussion:

Mortality is reduced up-to 25% by thrombolysis, as denoted by a review from fibrinolytic therapy trialist's group.[14] One of the landmark study for thrombolytic therapy; GUSTO-1 reported that, TIMI 3 flow after SK therapy was achieved only in 30% of patients, while in our study TIMI 3 was achieved in more than half (55%) of the patients.[15] TIMI 3 flow was significantly higher in smoker group than non- smoker group ($p<0.05$). This could be because of the younger age of patients in smokers group (48.80 ± 10.23 vs. 54.57 ± 9.51, $p<0.001$) than the non-smokers. Along with age as an advantage, smokers were also less affected by other co-morbidities like diabetes and hypertension. Studies showing "the smoker's paradox" also showed similar data, where smokers were significantly younger than the non-smokers.[16-21] There was also significant difference in family history between smokers and non-smokers group (8.9% vs. 30.3%, $p<0.05$). However one interesting finding in the study is that family history of premature IHD is present in only 8.9% of smokers versus 30.3% of non- smokers. This only emphasizes that younger patients, who despite having less co-morbidities or risk factors but continue smoke still suffer an acute MI.

Smoking accelerates atherosclerosis through various mechanisms and also has acute unfavorable effects on blood pressure and sympathetic tone. Along with atherosclerotic progression, long-term smoking may also accelerate oxidation of low-density lipoprotein and weaken endothelium-dependent coronary artery vasodilation. Smoking also trigger spontaneous platelet aggregation, increase monocyte adhesion to endothelial cells, and adverse alteration in endothelial derived fibrinolytic and antithrombotic factors. Thus, the smokers are more susceptible to undergo such procedure earlier than the non-smokers and also smokers have less co-morbidity at such young age than non-smokers. In a meta-analysis of 17 studies, only 6 demonstrated "the smoker's paradox" and concluded that; more focus should be on smoking cessation rather than relying on the "positive effects" of so called "the smoker's paradox".[22]

Smoking cessation is one of the most important interventions regarding cardiac morbidity and mortality. In a review, it was found that smoking cessation reduced coronary heart disease mortality by 36% when compared with mortality in patients who continued smoking.[23] The most important factors of any smoking cessation strategy include community education and physician-based primary prevention approach, also novel smoking cessation programme included direct financial assistance have already been evaluated and found effective.[24]

This study was limited to the measurement of the angiographic patency after thrombolytic therapy with SK. Follow-up of patients was not done. Patients who died during treatment or hospitalization were not included in this study. The ''smoker's paradox'' term should no longer be used because it may be misunderstood by patients and negatively influence smoking cessation both as primary and secondary prevention. This is very important since smoking is one of the strongest risk factors of coronary artery disease, myocardial infarction, and cardiovascular death. Both American College of Cardiology/American Heart Association and European Society of Cardiology STEMI Guidelines strongly encourage patients and their families to stop smoking and to avoid second hand smoke.[25, 26]

Limitations of the study:

Present study has several limitations. The main limitation of the study is its non-randomized nature and the potential of selection bias. Precise data on smoking history was not available; so, we have decided to analyze current smokers vs. non-smokers without former smokers as additional subgroup. However, it is unlikely that these limitations could influence the study outcome because both groups were exposed to these limitations.

V. Conclusion:

Centers where provision for PCI is not available, thrombolytic therapy with SK is a useful substitute specifically in smokers and young patients. Better outcome in smokers group may be because of younger age and lesser co-morbidities. Smokers should be motivated and guided properly to quit smoking.

References:

[1] Doll R, Peto R (1976) Mortality In Relation To Smoking: 20 Years' Observations On Male British Doctors. Bmj 2:1525–1536
[2] Wilhelmsson C, Vedin Ja, Elmfeldt D Et Al (1975) Smoking And Myocardial Infarction. Lancet 1:415–420
[3] Kannel Wb, Higgins M (1990) Smoking And Hypertension As Predictors Of Cardiovascular Risk In Population Studies. J Hypertens Suppl 8:S3–S8

[4] Barbash Gi, White Hd, Modan M Et Al (1993) Significance Of Smoking In Patients Receiving Thrombolytic Therapy For Acute Myocardial Infarction. Experience Gleaned From The International Tissue Plasminogen Activator/Streptokinase Mortality Trial. Circulation 87:53–58

[5] Barbash Gi, Reiner J, White Hd Et Al (1995) Evaluation Of Paradoxic Beneficial Effects Of Smoking In Patients Receiving Thrombolytic Therapy For Acute Myocardial Infarction: Mechanism Of The ''Smoker's Paradox'' From The Gusto-I Trial, With Angiographic Insights. Global Utilization Of Streptokinase And Tissue-Plasminogen Activator For Occluded Coronary Arteries. J Am Coll Cardiol 26:1222–1229

[6] Gourlay Sg, Rundle Ac, Barron Hv (2002) Smoking And Mortality Following Acute Myocardial Infarction: Results From The National Registry Of Myocardial Infarction 2 (Nrmi 2). Nicotine Tob Res 4:101–107

[7] Grundy Sm, Pasternak R, Greenland P, Smith S, Fuster V. Assessment Of Cardiovascular Risk By Use Of Multiple-Risk-Factor Assessment Equations: A Statement For Healthcare Professionals From The American Heart Association And The American College Of Cardiology. Circ. 1999; 100(13):1481-92.

[8] Jaatun Hj, Sutradhar Sc, Dickstein K. Comparison Of Mortality Rates After Acute Myocardial Infarction In Smokers Versus Non-Smokers. Am J Cardiol. 2004; 94(5):632-6.

[9] Suriñach J, Alvarez L, Coll R, Carmona J, Sanclemente C, Aguilar E, Et Al. Differences In Cardiovascular Mortality In Smokers, Past-Smokers And Non-Smokers: Findings From The Frena Registry. Eur J Intern Med. 2009;20(5):522-6.

[10] Gupta T, Kolte D, Khera S, Harikrishnan P, Mujib M, Aronow Ws, Et Al. Smoker's Paradox In Patients With St-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. J Am Heart Assoc. 2016; 5(4):E003370.

[11] Chen Ky, Rha Sw, Li Yj, Jin Z, Minami Y, Park Jy, Et Al. 'Smoker's Paradox' In Young Patients With Acute Myocardial Infarction. Clin Exp Pharmacol Physiol. 2012; 39(7):630-5.

[12] Thygesen K, Alpert Js, Jaffe As, Simoons Ml, Chaitman Br. Esc/Accf/Aha/Whf Expert Consensus Document. Circ. 2012; 126(16):2020-35.

[13] Nikus K, Birnbaum Y, Eskola M, Sclarovsky S, Zhong-Qun Z, Pahlm O. Updated Electrocardiographic Classification Of Acute Coronary Syndromes. Curr Cardiol Review. 2014; 10(3):229-36.

[14] Trialists Ft. Indications For Fibrinolytic Therapy In Suspected Acute Myocardial Infarction: Collaborative Overview Of Early Mortality And Major Morbidity Results From All Randomized Trials Of More Than 1000 Patients. Lancet. 1994; 343(8893):311-22.

[15] Investigators G. An International Randomized Trial Comparing Four Thrombolytic Strategies For Acute Myocardial Infarction. N Engl J Med. 1993; 329(10):673-82.

[16] Gerber Y, Rosen Lj, Goldbourt U, Benyamini Y, Drory Y, Infarction Isgofam. Smoking Status And Long-Term Survival After First Acute Myocardial Infarction: A Population-Based Cohort Study. J Am Coll Cardiol. 2009; 54(25):2382-7.

[17] Rakowski T, Siudak Z, Dziewierz A, Dubiel Js, Dudek D. Impact Of Smoking Status On Outcome In Patients With St-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. J Throm Thrombolysis. 2012; 34(3):397-403.

[18] Robertson Jo, Ebrahimi R, Lansky Aj, Mehran R, Stone Gw, Lincoff Am. Impact Of Cigarette Smoking On Extent Of Coronary Artery Disease And Prognosis Of Patients With Non–St-Segment Elevation Acute Coronary Syndromes: An Analysis From The Acuity Trial (Acute Catheterization And Urgent Intervention Triage Strategy). Jacc Cardiovasc Inter. 2014;7(4):372-9.

[19] Juliard J-M, Golmard Jl, Himbert D, Feldman Lj, Delorme L, Ducrocq G, Et Al. Comparison Of Hospital Mortality During St-Segment Elevation Myocardial Infarction In The Era Of Reperfusion Therapy In Women Versus Men And In Older Versus Younger Patients. Am J Cardiol. 2013; 111(12):1708-13.

[20] Arbel Y, Matetzky S, Gavrielov-Yusim N, Shlezinger M, Keren G, Roth A, Et Al. Temporal Trends In All-Cause Mortality Of Smokers Versus Non-Smokers Hospitalized With St-Segment Elevation Myocardial Infarction. Int J Cardiol. 2014;176(1):171-6.

[21] Arbel Y, Fitzgerald G, Yan At, Tan Mk, Fox Ka, Gore Jm, Et Al. Temporal Trends In All-Cause Mortality According To Smoking Status: Insights From The Global Registry Of Acute Coronary Events. Int J Cardiol. 2016; 218:291-7.

[22] Aune E, Røislien J, Mathisen M, Thelle Ds, Otterstad Je. The" Smoker's Paradox" In Patients With Acute Coronary Syndrome: A Systematic Review. Bmc Med. 2011; 9(1):97.

[23] Critchley Ja, Capewell S. Mortality Risk Reduction Associated With Smoking Cessation In Patients With Coronary Heart Disease: A Systematic Review. Jama. 2003;290(1):86-97.

[24] Volpp Kg, Troxel Ab, Pauly Mv, Glick Ha, Puig A, Asch Da, Et Al. A Randomized, Controlled Trial Of Financial Incentives For Smoking Cessation. N Engl J Med. 2009; 360(7):699-709.

[25] Antman Em, Hand M, Armstrong Pw Et Al (2008) 2007 Focused Update Of The Acc/Aha 2004 Guidelines For The Management Of Patients With St-Elevation Myocardial Infarction: A Report Of The American College Of Cardiology/American Heart Association Task Force On Practice Guidelines: Developed In Collaboration With The Canadian Cardiovascular Society Endorsed By The American Academy Of Family Physicians: 2007 Writing Group To Review New Evidence And Update The Acc/Aha 2004 Guidelines For The Management Of Patients With St-Elevation Myocardial Infarction, Writing On Behalf Of The 2004 Writing Committee. Circulation 117:296–329

[26] Van De Werf F, Bax J, Betriu A, Esc Committee For Practice Guidelines (Cpg) Et Al (2008) Management Of Acute Myocardial Infarction In Patients Presenting With Persistent St-Segment Elevation: The Task Force On The Management Of St-Segment Elevation Acute Myocardial Infarction Of The European Society Of Cardiology. Eur Heart J 29:2909–2945