

ORIGINAL RESEARCH PAPER

Cardiology

EFFICACY OF THROMBOLYSIS (STREPTOKINASE) IN DIABETIC AND NON-DIABETIC PATIENTS PRESENTING WITH ACUTE ST ELEVATION MI & COMPARISON OF THEIR ANGIOGRAPHIC PROFILE.

KEY WORDS: STEMI, SVD,

DVD, TVD.

Dr. Ashish Chauhan

DM Cardiology, SMS Medical college, Jaipur.

Dr. Rajeev Kumar Gupta* DM Cardiology Resident, Christian Medical College and Hospital, Ludhiana. *Corresponding Author

Dr. V. V. Agarwal

Professor, department of Cardiology, SMS Medical college, Jaipur.

BACKGROUND: To determine the efficacy of streptokinase in diabetic versus non-diabetic patients presenting with acute ST Elevation Myocardial Infarction (STEMI). METHOD AND RESULTS: This is a hospital based observational study conducted in the department of Cardiology, S.M.S. MEDICAL COLLEGE and associated hospital, Jaipur, Rajasthan between March 2016 to August 2017. Two hundred one consecutive patients of acute STEMI admitted to the Cardiology department were enrolled in the study to maintain 95% CI and 80% power of study. Patients with acute STEMI within 12 hours of chest pain without contraindications to fibrinolytic therapy (streptokinase) were included. ECG was done before and at 90 minutes after the start of streptokinase. ST-segment resolution equal to or more than 70% at 90 minutes on ECG was taken as successful reperfusion. The data was analysed by using software SPSS version 10. The quantitative variables were presented as mean and standard deviation while qualitative variables as frequency and percentage. Chi square test was used to estimate significance and p-value of <0.05 was considered significant. Out of 201 patients, 127(63.2%) were non-diabetics and 74(36.8%) were diabetics. The age of presentation of these patients was 32-75yr (mean age=55.59yr). Of these patients, 80% (N=160) were male and 20% (N=40) were female. Among the 74 diabetic patients, streptokinase was not effective in any patients. So streptokinase is non-efficacious in diabetic patients. Among the 127 non diabetic patients, streptokinase was effective in 79 (62.2%). Among the risk factors, smoking and hypertension were found in 84.6% and 62.7% of the patients respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. So, we found smoking as the most common risk and the respectively. The respectively are respectively and the respectively are respectively. The respectively are respectively and the respectively are respectively and the respectively are respectively and the respectively are respectively. The respectively are respectively and the respective and the respective are respectively are respectively and the respective are respectively are respectively and the respective are respectively and the respective are respectively are rfactor followed by HTN and DM in our patients. HTN was found significantly more in diabetic patients (94.59%) vs (44.09% in non-diabetic patients). On angiography, 58.7% patients had SVD, 34.8% had DVD and 6.5% had TVD. Five (2.5%) of these were found to have LM disease. Coronary angiography showed SVD, DVD, TVD in 44(59.46%), 17(22.97%) and 13(17.57%) of diabetic vs 74(58.27%), 53(41.73%) and 0(0%) of non-diabetic patients. So, triple vessel disease is significantly higher in diabetic patients. CONCLUSION: This study shows that streptokinase is significantly more efficacious in non-diabetics as compare to diabetic patients presenting with acute STEMI. It is more efficacious in male than female (M=47.82%; F=5%). We found that the window period of presentation was significantly higher in diabetic patient because of atypical symptoms that may lead to a delay in seeking medical advice and streptokinase was significantly more efficacious in non-diabetics as compare to diabetic patients.

INTRODUCTION

CORONARY ARTERY DISEASE (CAD) is a major public health problem in both the developed & developing world (1). Coronary artery disease (CAD) particularly myocardial infarction secondary to atherosclerosis of coronary arteries remains the leading cause of morbidity and mortality worldwide. Acute myocardial infarction is the most important form of coronary artery disease and is the major cause of death in industrialized countries. Worldwide about 4% of the patients with myocardial infarction (MI) are younger than 40 years of age(2). CAD in Indians occur at a younger age, is more severe and extensive, and follows a malignant course (3). This has been documented in studies in Indian immigrants (4). Cross sectional studies in India have also documented a several fold higher prevalence of CAD than in industrialised nations (5). By the year 2020, the burden of athero-thrombotic cardiovascular disease in India will surpass that in the other region of the world (6). India is experiencing an alarming increase in heart diseases. Cardiovascular disease accounted for 32% of all deaths in 2000 (7). As compared to the developed countries, India has a very large young population with only 3% above the age of 65yrs (8). Diabetes mellitus affects a large population in world. The prevalence of diabetes for all age groups worldwide was 2.8% in 2000 and it is estimated that this will become 4.4% in 2030. So the total number of people with diabetes will increase from 171 million in 2000 to 366 million in 2030 (9). The prevalence of CAD in adult population without diabetes mellitus is 2% to 4%, but this is increased to 55% in adult diabetic cohort. In diabetic adult men, the cardiovascular mortality rate is more than double and more than quadrupled in women compared with

non-diabetes counter parts. The countries with the greatest number of individuals with diabetes in 2013 were China (98.4million), India (65.1 million), United States (24.4 million), Brazil (11.9million, and the Russian Federation (10.9 million). Up to 80% of individuals with diabetes live in low-income or medium-income countries. Diabetes mellitus is a metabolic disorder which increases the rate of atherosclerosis progression of vascular occlusion. The risk of myocardial infarction is 2-4 times higher in diabetics (10).

Although successful thrombolysis of the epicardial vessel is necessary for good prognosis, but the micro-vascular flow more strongly correlates with the outcome. ST segment is therefore a better indicator of prognosis, and provides information, which cannot be assessed on basis of coronary angiogram alone. Cardiovascular diseases are the major cause of death among patients with diabetes mellitus. Myocardial Infarction causes higher morbidity and mortality among diabetics.

Large epidemiological studies such as the Framingham study (11) have identified diabetes mellitus is one of the most important independent risk factors for CAD patients and now diabetes mellitus is considered as CAD risk equivalent. So, a diabetic person without clinical events of CAD has the same future risk for angina pectoris, MI as a person with known CAD. Mortality due to CAD has declined by about 60% during the past 20 years. Unfortunately, this positive tendency in CAD mortality in the non-diabetic population does not apply to the diabetic cohort.

In the USA during the past 30 years, non-diabetic men

experienced a 44% decline in age- adjusted mortality disease due to CAD compared to only 17% in diabetic men. Mortality in non-diabetic women fell 20%, but increased 11% in diabetic women. Ibrahim Shah et al(12), compared the efficacy and safety of streptokinase as thrombolytic agent for ST-elevation myocardial infarction (STEMI) in patients with and without diabetes mellitus. The outcome of thrombolytic therapy is adversely affected by Diabetes mellitus in patients with ST-elevation myocardial infarction. Secondly, the risk of hazards associated with thrombolytic therapy is same in both diabetic and non-diabetic patients.

Chaudhry et al(13), compared the efficacy of streptokinase between diabetic and nondiabetic patients presenting with acute ST Elevation Myocardial infarction. This study confirmed more complete ST-resolution in non-diabetic patients as compared to diabetic patients (non-diabetic group 48.4% vs. diabetic group 19.7%; p<0.001). In 1999, Lindvall et al(14) compared diabetic and non-diabetic patients by coronary angiography regarding previous history, indication for and findings at coronary angiography, use of medication, exercise test result and mortality. They showed that there was no difference in age or sex in the two groups. Diabetic patients more often had depressed myocardial function (EF<35%) than non-diabetic (12% vs.8% respectively; p<0.01) and more extensive CAD (left main vs. TVD; 48% vs. 37%; p<0.001). In 2000, Cariou et al(15) observed that the number of significant coronary stenosis per patient was higher in diabetics than in non-diabetics $(5.06\pm2.16 \text{ vs.} 2.40\pm1.97; p<0.05)$. Diabetics also had more left main CAD (7/50 vs, 1/50; p<0.05) and there were more diffuse distal lesions of diabetic coronary artery trees. In 2005; Javidi et al(16) have done a study on the contribution of DM per se to the severity of CAD, to determine the effect of DM to the characteristics and severity of CAD among young patients. 30 diabetics (group1) were selected from a group of young patients with IHD which was documented angiographicaly. For this retrospective case-controlled study, 60 non-diabetics with CAD (group2) were matched for gender, age, LDL level, hypertension, smoking, family history and obesity. These DM and non-DM groups were compared for different outcomes of CAD; with results that group1 had a higher incidence of 3vessel coronary involvement (56.7% vs. 20%; p<0.005) and more hospitalisations for ischemic episodes (4±4.5 vs. 2.1±1.8; p<0.05) than group2. They also had more previous MI, longer intervals between their first admission and the current hospitalisation and more left main coronary artery

Till now there are limited data from our country, keeping this in mind a study was planned to assess the efficacy of thrombolysis in acute STEMI patient (the diabetic & non-diabetic group) and to know the angiographic profile of these patients (in diabetic/non-diabetic group).

AIMS AND OBJECTIVES:

1. To evaluate the efficacy of thrombolysis in acute STEMI patient (the diabetic/non-diabetic group).

2. To know the angiographic profile in diabetic/non-diabetic group.

MATERIAL AND METHODS:

This is a hospital based observational study conducted in department of cardiology, S.M.S. MEDICAL COLLEGE and associated hospital between march 2016 to august 2017. Two hundred one consecutive patients of acute STEMI admitted to cardiology department were enrolled in study to maintain 95% CI and 80% power of study. All patients who were present with acute STEMI to our department with duration of symptom <12 hours or 12-24 hours with ongoing chest pain, who are eligible for thrombolysis were included in the study. Diabetes is defined on the basis of ADA criteria. Patients who present >12 hours after the onset of chest pain/ >24hours with

ongoing chest pain, patients with previous MI, BBB on ECG, comorbidities like CKD/malignancy or contraindication to thrombolysis, patients not giving consent for thrombolytic treatment were excluded from the study.

METHODS:

All the consecutive patients who meet the inclusion criteria were enrolled. Routine general physical and biochemical examination was done. ECG was done at the time of presentation and then after 90 minutes of thrombolysis. ST segment resolution was assessed by percent of sum of ST-segment elevation at presentation-final ST-segment elevation at 90 minutes/ sum of ST-segment elevation at the presentation. Criteria for efficacy of streptokinase (in the terms of successful reperfusion) was ST segment resolution equal or more than 70% at 90 minutes ECG. Echocardiography was done in all patients for assessment of cardiac function.

CAG was done as per the ACC/AHA guidelines in these patients to assess the effect of thrombolysis, extent and severity of the coronary artery disease. Coronary arteries were visualized in different views (AP/RAO/LAO views) with cranial/caudal angulation to assess the coronary anatomy. At least two views of right and left coronaries are recommended. Syntax score was used to assess the extent and severity of coronary artery disease. SYNTAX score was calculated with the help of online calculator available freely for medical use. Result of angiography and syntax score has been evaluated by two independent observers.

STATISTICAL ANALYSIS:

Quantitative parameters were calculated by taking mean and SD. Qualitative variables were calculated by taking frequency and percentage. Frequency for the outcome variable i.e. the efficacy of streptokinase (in terms of successful reperfusion) was calculated.

Stratification of age, diabetics and non-diabetics, gender and time interval from onset of chest pain to streptokinase and other variables was done to control the effect of modifiers. Chi square test was done for comparison of categorical variables while independent samples t-test was used for comparison of means of continuous variables.

SPSS v. 18.0 by IBM Inc. was used for statistical analysis. In all statistical analysis only p- value <0.05 was considered significant.

RESULTS:

The age of presentation of these patients was 32-75yr (mean age=55.59yr). Of these patients, 80% (N=160) were male and 20% (N=40) were female. Angina was the most common presenting symptom that was present in 72.6% of the patients followed by SOB (22.4%)

(Table 1&Table 2, Figure 1, 2, 3, 4&5).

TABLE1. BASELINE QUANTITATIVE PARAMETERS OF THE PATIENTS.

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
AGE(in years)	201	32	75	55.59	9.642
LIPID PROFILE:	201	140	280	85.57	30.338
Total					
Cholesterol					
TRIGLYCERIDE	201	110	180	143.58	19.852
VLDL	201	22	36	28.72	3.970
HDL	201	30	44	35.72	3.539
LDL	201	76	212	121.46	28.890
Echo%	201	30	45	37.91	6.194
WP(HR)	201	1.0	10.0	4.828	2.7530
STS resolution%	201	20.0	90.0	58.231	18.0998
SYNTAX SCORE	201	2.0	18.5	8.846	4.2888

FIGURE 1. GENDER DISTRIBUTION.

Total Patients=201



TABLE 2. BASELINE QUANTITATIVE CHARACTERISTICS OF THE PATIENTS

	NT-001(0/)		
	N=201(%)		
SEX(M/F)	161/40(80%vs.20%)		
PRESENTING SYMPTOM	146 (72.6%)		
ANGINA	45 (22.4%)		
SHORTNESS OF	10 (5%)		
BREATH			
BOTH			
SMOKING	170(84.6%)		
DM	74(36.8%)		
HTN	126(62.7%)		
CHEST PAIN RESOLUTION	57(28.4%)		
AFTER THROMBOLYSIS			
ST SEGMENT RESOLUTION	79(39.3%)		
AFTER THROMBOLYSIS	28(13.9%)		
>70%	94(46.8%)		
30-70%			
<30%			
NUMBER OF VESSEL	118(58.7%)		
INVOLVEMENT	70(34.8%)		
	13(6.5%)		
SVD	5(2.5%)		
DVD			
TVD			
LM			

FIGURE 2. GRAPHICAL REPRESENTATION OF PRESENTING SYMPTOM AT PRESENTATION.



FIGURE 3. QUANTITATIVE CHARACTERISTICS OF THE PATIENTS.

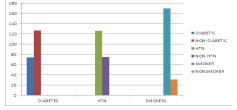
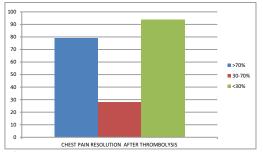


FIGURE 4. GRAPHICAL REPRESENTATION OF CHEST PAIN RESOLUTION AFTERTHROMBOLYSIS.



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FIGURE 5. NUMBER OF VESSEL INVOLVEMENT IN THE PATIENTS.

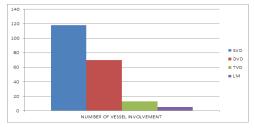


TABLE 3. CLINICAL, ECG AND ANGIOGRAPHIC CHARACTERS OF DM AND NON-DM PATIENTS.

CHARACTERSO	I D	IAT UTA	DIACL	I-DIMI PATI	EMIS.	
				Standard	Mean	P-
				Deviation		Value
AGE (in years)	A	127	53.93	10.428	.925	0.001
	P	74	58.43	7.352	.855	
LIPIDPROFILE:	A	127	178.69	26.110	2.317	< 0.001
TotalCholesterol	P	74	197.38	33.483	3.892	
TRIGYCERIDE	A	127	136.69	17.092	1.517	<0.001
	P	74	155.41	18.740	2.179	
VLDL	A	127	27.34	3.418	.303	<0.001
	P	74	31.08	3.748	.436	
HDL	A	127	36.68	3.548	.315	< 0.001
	P	74	34.08	2.875	.334	
LDL	A	127	114.80	24.527	2.176	< 0.001
	P	74	132.89	32.227	3.746	
Echo %	A	127	38.46	6.092	.541	0.097
	P	74	36.96	6.293	.732	
WP(HR)	A	127	4.500	2.7588	.2448	0.026
	P	74	5.392	2.6680	.3102	
STS resolution%	A	127	66.646	16.2663	1.4434	< 0.001
	P	74	43.789	10.3061	1.1981	
SYNTAX SCORE	A	127	8.669	4.4983	.3992	0.446
	P	74	9.149	3.9141	.4550	

Among these patients, 36.8% (N=74) were diabetics. Only three patients were found to have family history of premature CAD. Among other risk factors, smoking and hypertension was found in 84.6% and 62.7% of the patients respectively. So we found smoking as the most common risk factor followed by HTN and DM in our patients. HTN was found significantly more in diabetic patients (94.59% vs. 44.09% in non-diabetic patients). On angiography 58.7% patients had SVD, 34.8% had DVD and 6.5% had TVD. Five (2.5%) of these were found to have LM disease. Angina was the common presenting symptom in non-diabetics (87%) than in the diabetics (48.6%). Hence, around 50% of diabetic patients present with atypical symptoms. It was also found that successful ST Segment resolution is significantly common in non-diabetic patients (62%) than diabetic patients (0%). In diabetic patients 17.57% had TVD, However no non-diabetic patient was found to have TVD.

(Table-4, Figure 6).

TABLE.4 QUALITATIVE VARIABLES, ECG FINDINGS AND ANGIOGRAPHIC PROFILE OF DM AND NON-DM PATIENTS:

	DM (N=74)	NON-DM(N=127)	P-VALUE
SEX(M/F)	58/16	103/24	0.641
SMOKING	64	106	<0.567
HTN	70	56	<0.001
FAMILY HISTORY	0	3	<0.183
PRESENTING SYMPTOM			
 ANGINA 	36	110	< 0.001
• SOB	28	17	< 0.001
• BOTH	10	0	<0.001

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STSe			
RESOLUTION	0	79	<0.001
• >70%	10	18	
• 30-70%	64	30	
• <30%			
NO. OF VESSELS			
INVOLVED			
• SVD	44/59.46%	74/58.27%	< 0.001
• DVD	17/22.97%	53/41.73%	
• TVD	13/17.57%	0/0%	

FIGURE 6. QUANTITATIVE VARIABLES AND ANGIO-GRAPHIC PROFILES OF DIABETES AND NON-DIABETES PATIENTS.

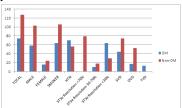


TABLE.5 PROFILE OF THE PATIENTS WITH OR WITHOUT SUCCESSFUL ST SEGMENT RESOLUTION:

		N	Mean	Standard	Standa	p-
				Deviation	rd	value
					Error	
Age (in	Unsuccess	122	57.29	9.562	.866	0.002
years)	ful					
	Successful	79	52.96	9.223	1.038	
LIPID PROFILE :	Unsuccess ful	122	180.2	31.979	2.895	0.045
TC	Successful	79	180.24	26.949	3.032	1
TRIGYCERI DE	Unsuccess ful	122	148.11	20.744	1.878	<0.0 01
	Successful	79	136.58	16.163	1.818	
VLDL	Unsuccess ful	122	29.62	4.149	.376	<0.0 01
	Successful	79	27.32	3.233	.364	
HDL	Unsuccess ful	122	35.61	3.513	.318	0.569
	Successful	79	35.90	3.593	.404	
LDL	Unsuccess ful	122	124.20	30.962	2.803	0.095
	Successful	79	117.23	24.963	2.809	
ЕСНО%	Unsuccess ful	122	37.25	6.559	.594	0.062
	Successful	79	38.92	5.470	.615	
WP(HR)	Unsuccess ful	122	6.119	2.7492	.2489	<0.0 01
	Successful	79	2.835	1.0400	.1170	
STS resolution	Unsuccess ful	122	45.48	10.5385	.9541	<0.0 01
%	Successful	79	77.924	4.5398	.5108	
SYNTAX SCORE	Unsuccess ful	122	8.303	3.9257	.3554	0.025
	Successful	79	9.684	4.6994	.5287	

Among patients with successful thrombolysis statistically significant difference was found in age of presentation, window period of presentation, presentation as typical angina. Among these patients coronary angiography shows significant correlation with number of vessel involvement and syntax score. Patients with higher syntax score were found to have lower rates of successful thrombolysis. (Table - 5&6).

It was found in our study that patients who presented with typical angina has significantly higher rate of ST-Segment resolution than patients with atypical presentation. ST-Segment resolution was significantly greater in male than female patients, in non-diabetic than diabetic patients. In lipid profile mean TG level and VLDL level were significantly higher in patients showing successful resolution on ECG. We also found that WP of presentation was significantly less in patients showing successful thrombolysis (mean=2.84 hr vs. partial/failed lysis; mean=6.12 hrs). Syntax score was also significantly lower in patients showing unsuccessful thrombolysis. On evaluation of angiographic profile diabetic patients were found have more severe coronary involvement (around 40% had DVD & TVD vs. non-diabetic patients; 0% had TVD).

TABLE 6. CLINICAL AND ANGIOGRAPHIC PARAMETERS AND THEIR RELATION WITH ST-SEGMENT RESOLUTION

	Successful ST-segment RESOLUTIO N(N=79)	Incomplete/faile d ST-segment RESOLUTION (N=122)	P- value
SEX: • M- • F-	77	84 38	<0.001
PERSENTING SYMPTOM ANGINA SOB BOTH	70 8 0	75 37 10	<0.001
SMOKING(N=170)	68	102	0.636
HTN	33	93	< 0.001
CHEST PAIN RESOLUTION	79	65	<0.001
NO. OF VESSELS SVD- DVD- TVD-	44 35 0	74 35 13	<0.001
DM(N=74)	0	74	< 0.001

TABLE-7. CLINICAL AND ANGIOGRAPHIC VARIABLES AND THEIR RELATION WITH PERCENTAGE OF STSe RESOLUTION

	>70% RESOLUTI	30-50% RESOLUTI	<30% RESOLUTIO	P- VALUE
	ON	ON	N	
	(N=79)	(N=28)	(N=94)	
SEX				
• M-	77	9	75	<0.001
• F-	2	19	19	
SMOKING (N=170)	68	13	84	0.005
HTN(N=126)	33	13	80	<0.001
CHEST PAIN RESOLUTION	79	21	44	<0.001
NO. OF VESSELS INVOLVED				
• SVD	31	5	82	<0.001
 DVD 	35	23	12	
• TVD	0	0	14	
DM(N=74)	0	10	64	<0.001

DISCUSSION:

Among risk factors for coronary artery disease, diabetes is a major contributor, not only to the development of coronary artery disease but also to outcome following various manifestations of the disease. Several studies have shown that diabetes mellitus significantly affects the efficacy of streptokinase in patients presenting with acute ST elevation myocardial infarction.

Chowdhury et al(10), compare the efficacy of streptokinase between diabetic and nondiabetic patients presenting with acute ST Elevation Myocardial Infarction, confirmed more

complete ST-resolution in non-diabetic patients as compared to diabetic patients, showing that diabetes mellitus might affect the thrombolytic outcome of acute myocardial infarction patients with diabetes mellitus. Samir et al(17), reported efficacy of streptokinase in diabetics vs nondiabetics as 18.8% vs. 62.5% by ECG criteria. Zairis et al(18), showed significant difference between diabetic and nondiabetic patient in relation to complete (34.1% vs. 68.2%; p<0.001) ST segment resolution. Our study showed that streptokinase was significantly more efficacious in nondiabetic as compare to diabetic patients (non-diabetic 62.2% vs. diabetic 0%; p<0.001). It is uncertain whether this difference in efficacy of streptokinase is due to endothelial dysfunction, dysglycemia and coagulation and fibrinolytic disturbances in diabetic patients. But decrease efficacy is associated with increased mortality due to a lower rate of successful thrombolysis, increased re-occlusion after successful thrombolysis, greater ventricular injury or more adverse clinical profile in diabetic patients. These results emphasize that, despite the established benefit of fibrinolytic therapy in acute myocardial infarction, a significant proportion of diabetic patients do not achieve complete reperfusion within 90 min of starting thrombolytic therapy. So, due attention is required for the better management of diabetic myocardial infarction patients. This should, however, be supplemented with further therapies and strategies directed towards the many abnormalities that are associated with diabetes, such as endothelial dysfunction, dysglycemia and coagulation and fibrinolytic disturbances.

CONCLUSION:

This study shows that streptokinase was not efficacious (on ST-segment resolution) in diabetic patients presenting with acute ST elevation myocardial infarction. It is more efficacious in male than female (m=47.82%; f=5%). We found that the window period of presentation was significantly higher in diabetic patient because of atypical symptoms that may lead to a delay in seeking medical advice and streptokinase was significantly more efficacious in non-diabetics as compare to diabetic patients. The diabetic patients had high percentage of multi-vessel involvement than non-diabetics. This suggests that other modalities of reperfusion such as primary PCI should be used in diabetic patients presenting with acute ST elevation myocardial infarction.

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