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A Randomized Study Comparing Patency of Infarction Related Vessel at Time of Primary PCI in Patients Who Received Streptokinase and Who Did Not

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Abstract: Coronary blood flow in an infarct related artery (IRA) in patients that had streptokinase (SK), as the fibrinolytic of choice before percutaneous intervention (PCI), in comparison to the blood flow in patients that underwent primary percutaneous intervention (PPCI) has not been well understood or considered for studies in recent times. All patients presenting with STEMI diagnosis within less than 12 hours from diagnosis either at the centre or referred to the center after SK were screened. 200 patients were randomized into primary PCI (PPCI) or pharmacoinvasive PCI following SK (PhI-SK) administration 3-24 hours after SK. Failed SK patients underwent rescue PCI immediately. The outcome of IRA patency pre- and post PCI in both groups along with short term outcome of bleeding, re-infarction or cardiovascular death in 30 days were looked at. The end points were reached in 81 of 89 (91.0%) in the SK group and 21 of 98 (21.4%) in the PPCI group (p-value <0.001), while TIMI 3 flow was seen in 87 of 89 (98.7%) patients post PCI in the SK group and 69 of 98 (70.4%) patients of PPCI (p-value <0.001). The outcomes of bleeding, MI and death were not different among the groups. We concluded that Fibrinolysis with SK is a viable and safe reperfusion strategy in STEMI especially in low- and middle-income countries (LMICs), where PPCI is not commonly available within the guideline recommended time. It can reduce stress and risk of complications that can occur during PPCI. There is no any difference in the early outcomes of bleeding, MI and death between the two groups.

Keywords: Primary PCI, Streptokinase, Infarction

1. Introduction

Reperfusion is the immediate goal in the management of patients presenting with ST-elevation myocardial infarction (STEMI), this is to reduce morbidity and mortality and improve quality of life. [1]. The reperfusion of choice is the primary percutaneous coronary intervention (PPCI) and where this cannot be achieved within the 120 minutes of presentation, reperfusion using a fibrinolytic agent becomes the target immediately [2, 3].

Delays and limitation of resources for the immediate perfusion using PPCI is worldwide issue and even more in the low and middle income countries (LMICs) [4]. This necessitate the use of fibrinolytic in most cases to provide the lifesaving therapy needed by patients before being transferred or offered invasive therapy, this is termed as the pharmaco invasive strategy and is considered non inferior to the conventional PPCI strategy as reported in many meta-analysis [5].

The preferred fibrinolytic of choice are the fibrin-specific fibrinolytics and the most studied in the studies comparing PPCI and PhI, Alteplase, Tenecteplase and reteplase. [1, 2, 5, 7].

These agents are not readily available or affordable in

LMICs, this makes the easily accessible fibrinolytic Streptokinase (SK) the thrombolytic of choice [8]. and this drug has not been well studied in this era of improved STEMI care. This includes use of life saving medications available and in these LMICs to demonstrate its efficacy and safety in the population or not.

Our aim of this study was to assess the culprit artery patency in the group that received SK and the PPCI group, assess no reflow phenomenon post PCI, bleeding and 30-day major adverse cardiac events (MACE) including; death and Myocardial infarction.

2. Patients and Methods

2.1. Study Area

The study included patients who presented with STEMI at our centers and were randomized for SK prior to PCI vs Primary PCI. It was done from January 2020 to December 2020 after achieving a certain amount patients needed for the study. These patients were classified into the following groups:

Group 1 (SK group): STEMI patients who had streptokinase and subsequently underwent PCI at our centers.

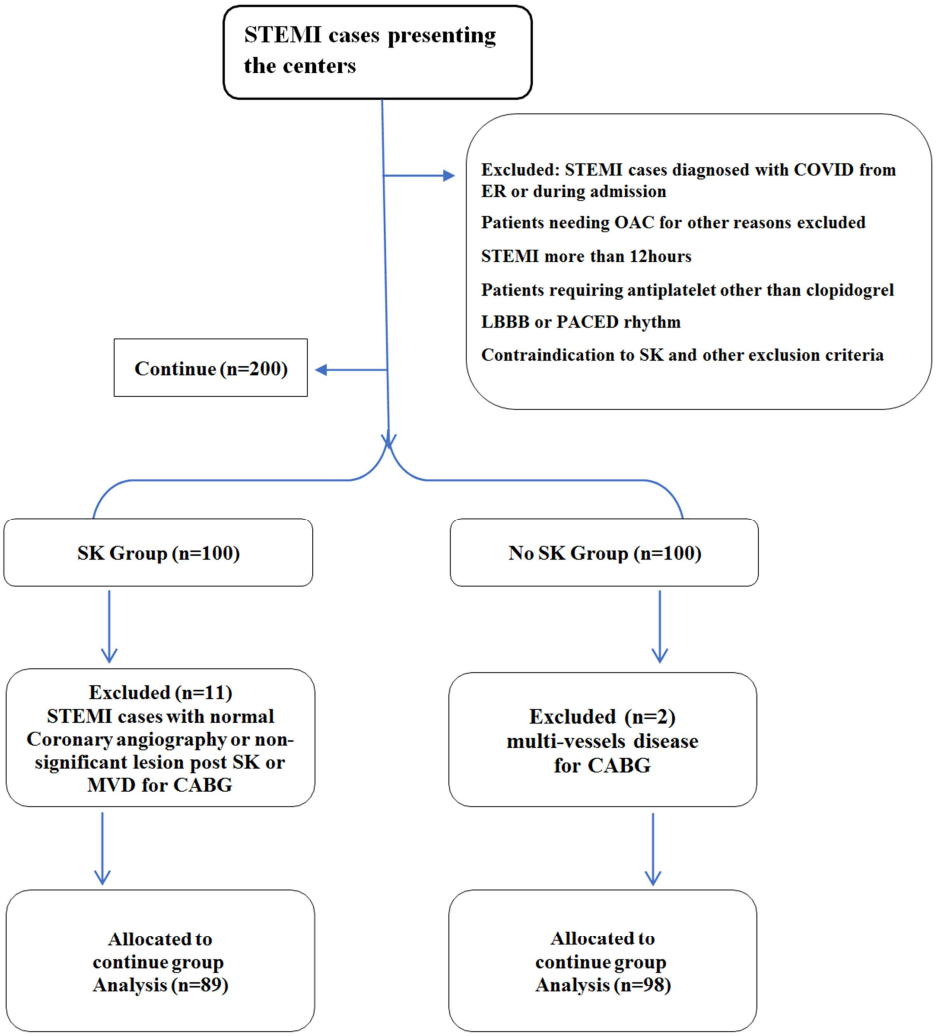

Figure 1. *Flow chart.*

Group 2 (PPCI group): STEMI patients who underwent primary PCI at our centers without prior SK

The inclusion and exclusion criteria are as thus;

2.2. Inclusion criteria

1) Symptoms implicate MI and ECG indicative of STEMI: ST segment elevation ≥2 mm in 2 contagious precordial leads or ≥1 mm in 2 contagious extremity lead
2) Referred STEMI patients following administration of SK who fulfill our patient selection criteria
3) Age ≥18year
4) Informed consent

2.3. Exclusion Criteria

1) Contraindications to SK
2) STEMI more than 12hrs
3) Expected performance PCI < 120 minutes or inability to arrive at the catheterization laboratory within 90 minutes after FMC
4) Known acute pancreatitis or known severe hepatic

dysfunction, including hepatic failure, cirrhosis, portal hypertension (esophageal varices), and active hepatitis
5) Multivessel disease for CABG or prior CABG
6) Normal or non-significant lesion post thrombolytics
7) Age less than 18 year
8) Fibrinolytics other than Streptokinase
9) Associated chronic kidney disease
10) LBBB, and ventricular paced rhythm were excluded
11) Patients with cardiogenic shock—Killip Class 4
12) Patients with a body weight b55 kg (known or estimated)
13) Uncontrolled hypertension, defined as a single BP measurement ≥180/110 mm Hg (systolic BP ≥180 mm Hg and/or diastolic BP ≥110 mm Hg) before randomization
14) Hospitalization for cardiac reason within past 48 h
15) Known acute pericarditis and/or subacute bacterial endocarditis
16) Arterial aneurysm and known arterial/venous malformation
17) Inability to follow the protocol and comply with follow-up requirements or any other reason that the investigator feels would place the patient at increased risk if the investigational therapy is initiated
18) Recent administration of any IV or SC anticoagulation within 12 h, including unfractionated heparin, enoxaparin, and/or bivalirudin or current use of oral anticoagulation (i.e., warfarin or Coumadin)

2.4. Methods

This trial was designed to enroll patients presenting with STEMI within 12 hours of symptom onset and in whom primary PCI is not feasible within 120 minutes of first medical contact and fulfill the patient selection criteria as our inclusion and exclusion criteria. The trial is an open- label, prospective, randomized, parallel and comparative study conducted in Al Azhar University teaching hospitals in Cairo (El Hussein and Sayed Galal teaching hospitals), see figure 1. The patients were loaded with antiplatelets and anticoagulant and then randomized to a strategy of fibrinolysis with streptokinase (SK). They then had cardiac catheterization within 2 to 24 hours, or rescue coronary intervention in the event of failure of fibrinolysis ECG (failure to achieve at least 50% ST resolution in the single lead with maximal elevation) or clinical evidence of failed reperfusion within 90 minutes of commencement of fibrinolytic therapy is present [1, 2]. This strategy was then compared to the strategy of primary PCI done according to the institutional protocols. SK, antiplatelets and anticoagulants were all given according the ESC guideline of STEMI management [2].

The no SK group, had PPCI performed according to institutional protocols and in compliance with international guidelines for STEMI management and myocardial revascularization [1, 3, 9].

This research was approved the Al Azhar university research and ethic s committee and is also in accordance with the WMA ethics of medical research [10].

2.5. Statistical Analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). 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 between two means. Chi- square (x2) test of significance was used in order to compare proportions between qualitative parameters. Fisher's exact test: was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells, while Fisher's exact test is more accurate than the chi-squared test The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: Probability (P-value); P-value <0.05 was considered significant, P-value <0.001 was considered as highly significant and P-value >0.05 was considered insignificant [11].

Table 1. *Demographic representation between the groups.*

Demographic data	SK Group (n=89)		PPCI Group (n=98)		Chi-square test	
	No.	%	No.	%	x2	p-value
Sex						
Female	17	19.1%	29	29.6%	2.768	0.096
Male	72	80.9%	69	70.4%		
Age (years)						
Range	27-64		38-61		t=1.119	0.265
Mean±SD	51.31±6.99		50.32±5.00			

Table 2. *Risk factor distribution among the groups.*

Risk factors	SK Group (n=89)		PPCI Group (n=98)		Chi-square test	
	No.	%	No.	%	x2	p-value
Smoker	58	65.2%	52	53.1%	2.805	0.094
Dyslipidemia	19	21.3%	21	21.4%	0.000	0.989
HTN	35	39.3%	38	38.8%	0.006	0.939
DM	25	28.1%	25	25.5%	0.158	0.691
CVD	15	16.9%	19	19.4%	0.139	0.700

3. Results

All patients that presented with STEMI to the emergency department or referred to the centers for Pharmacoinvasive PCI following SK administration from other Centre were evaluated for this study within the period of January 2020 to December 2020 and 200 patients were randomized into the study. Many cases where excluded due to the COVID-19 pandemic and other exclusion criteria mainly the need for long term OAC and 200 patients were enrolled and randomized. 11 patients were later excluded in the SK group because of either normal CA or non-significant atherosclerotic lesion and MVD for CABG. While 2 patients were excluded from the no SK group, that is the PPCI group because of MVD that need CABG.

Table 3. *STEMI pattern among in the study groups.*

STEMI	SK Group (n=89)		PPCI Group (n=98)		Chi-square test	
	No.	%	No.	%	x2	p-value
Ant.	39	43.8%	35	35.7%		
Ant. and Inf.	1	1.1%	0	0.0%		
Ant. Lat.	0	0.0%	1	1.0%		
Ant. Sept	0	0.0%	1	1.0%		
Ext Ant.	14	15.7%	23	23.5%	19.096	0.086
Inf.	24	27.0%	26	26.5%		
Inf. Lat.	3	3.4%	0	0.0%		
Inf. Post	6	6.7%	2	2.0%		
Lat.	2	2.2%	10	10.2%		

Table 4. *Success of SK group distribution among study group (n=89).*

Success of SK	SK Group (n=89)	
	No.	%
Failed	14	15.7%
Success	75	84.3%
Chi-square test	83.295	
p-value	<0.001**	

Table 5. *Coronary angiographic Comparison between SK Group and PPCI Group according to IRA.*

Culprit vessels	SK Group (n=89)		PPCI Group (n=98)		Chi-square test	
	No.	%	No.	%	x2	p-value
LAD	55	61.8%	59	60.2%	0.050	0.823
- *Subtotal occlusion*	49	55.1%	9	9.2%	45.657	<0.001**
- *Total occlusion*	6	6.7%	50	51.0%	43.424	<0.001**
RCA	24	27.0%	26	26.5%	0.006	0.938
- *Subtotal occlusion*	23	25.8%	7	7.1%	12.071	<0.001**
- *Total occlusion*	1	1.1%	19	19.4%	16.273	<0.001**
LCX	10	11.2%	13	13.3%	0.190	0.663
- *Subtotal occlusion*	9	10.1%	5	5.1%	1.676	0.196
- *Total occlusion*	1	1.1%	8	8.2%	5.097	0.024*
Vascular occlusion						
- *Subtotal occlusion*	81	91.0%	21	21.4%	90.635	<0.001**
- *Total occlusion*	8	9.0%	77	78.6%	90.635	<0.001**

The baseline characteristics and cardiovascular disease risk factors were the same in both groups, see tables 1 and 2. There was no significant difference in the type of STEMI the patients presented between the two groups, see table 3. There was a significant difference in the success rate to SK in the SK group in comparison to failure to SK 84.3% vs 15.7% (P-value <0.001) of which the failed cases had to undergo an emergent rescue PCI, see table 4. There was no significant difference between groups in the culprit vessel involve, see table 5.

There was a significant difference in the degree of vascular occlusion between the groups with more open arteries in the SK group compared to the PPCI 91.0% vs 24.1% (P-value <0.001) and while most case had a total occlusion in the PPCI compared to SK group 78.6% vs 9.0% (P-value <0.001). This finding is also noted in the subgroup analysis of culprit vessels between the groups with the exception of LCX where about 10.1% in SK group and 5.1% in the PPCI group had a subtotal occlusion with no significant difference (P-value =0.196), see table 5.

The TIMI flow outcome post PCI in the SK group was 97.8% and 70.4% in the PPCI group and this is a significant difference (P-value <0.001). There was no any statistical difference between the groups regarding bleeding, myocardial infarction or death within 30 days of MI and intervention, see table 6.

Table 6. *Flow outcome post PCI and 30day outcome between the two groups.*

Outcome	SK Group (n=89)		PPCI Group (n=98)		Chi-square test	
	No.	%	No.	%	x2	p-value
TIMI flow						
0	0	0.0%	2	2.0%	1.789	0.181
1	1	1.1%	6	6.1%	3.238	0.072
2	1	1.1%	21	21.4%	18.452	<0.001**
3	87	97.8%	69	70.4%	25.207	<0.001**
TIMI flow 0-2	2	2.2%	29	29.6%	25.207	<0.001**
TIMI flow 3	87	97.8%	69	70.4%	25.207	<0.001**
Bleeding						
None	65	73.0%	73	74.5%	0.054	0.816
Minimal	24	27.0%	24	24.5%	0.152	0.697
Moderate	0	0.0%	1	1.0%	0.890	0.346
MI						
None	89	100.0%	98	100.0%	0.000	1.000
Mortality						
None	89	100.0%	98	100.0%	0.000	1.000

4. Discussion

In this study, we demonstrated the efficacy and safety of pharmacoinvasive therapy using streptokinase (SK) in comparison to primary PCI as the guideline preferred strategy in the context of our real clinical practice evidence seen on our daily base practice. We also demonstrated that the pharmacoinvasive strategy using SK has similar outcomes compared to the primary PCI strategy with the Pharmacoinvasive strategy having better immediate pre- and post PCI TIMI flow outcome in comparison to the primary PCI strategy. This similar findings has been shown in some meta-analysis, which showed no difference in mortality or re-infarction [12]. Similarly no difference in bleeding, MI and mortality even after long-term follow up, [13]. a similar result was observed by Khraishah et al when they analyzed the data from Kerala and comparing the 30 day outcome of MACE, bleeding, MI and CVD [14].

Low and middle income countries cannot fully implement the guideline [1, 3, 9]. preferred strategy of primary PCI in the immediate care and management of STEMI because of financial and other technicalities involved, [8]. this is a challenge even for big economies like the USA [15]. The pharmacoinvasive strategy using SK in comparison to PPCI strategy has not been studied in a RCT designed to the best of our knowledge in recent times. This study has demonstrated that LMICs can give a safe care to its populace without the fear of patient safety being jeopardized. It has also considered the real-life situation of clinical practice in managing such patients especially in the LMICs because studies like the STREAM that was designed in a strict and unpracticable situations but also demonstrated similar outcomes of bleeding, 30day MI, mortality and even after follow up. TIMI flow before PCI was significantly higher in the PhI-SK compared to PPCI group (P-value<0.001), but there was no significant difference post PCI in both groups [16]. This difference might be due to ethnic and geographic population studied in comparison to our studied population. Although there was a slight increase in bleeding noted in the STREAM trial but this was corrected following amendment in the study protocol by giving half dose of TNK to the elderly ≥ 75 years [7, 17].

Studies all over the continents have demonstrated the efficacy and safety of PhI strategy and occasionally being favored with better outcomes compared to PPCI strategy. Although the study used TNK as the fibrinolytic of choice like in most studies while we used SK, this is because of the limited resources available but this has not limited the level and quality of service we provide.

Similar findings to our study were reported by Iranians, Mexicans and the Canadians [18, 20]., with no difference in bleeding, MACE, MI and CVD. Nima Naghshtabrizi et al., from Iran, reported that PhI PCI ≥ 24 hours after a successful thrombolysis has a significant TIMI flow post PCI in the PhI-SK compared to PPCI with 1.7% vs 9.3% (P-value <0.001) [18]. This finding is similar our results despite the use of different fibrinolytic. Sierra-Fragoso et al., also reported similar findings for patient who had PhI PCI performed 2-24 hours post fibrinolytic irrespective of the fibrinolytic used with similar with no significant difference in bleeding, MACE, MI and CVD on short or long- term [19].. There a thrombus burden in the PPCI group compared to the PhI group on coronary angiographic evaluation pre-stenting, this is similar to our findings which showed high total vascular occlusion in the PPCI group. Pre-PCI coronary flow was established to be significantly higher in the PhI group (p-value<0.001) and trends to toward significance in the post PCI results between the two groups (p-value=0.007) [20]..

The findings of Liviu-Nicolae Ghilencea et al., also corroborate with our results with no difference in short term outcomes of bleeding, MACE, MI or CVDc [21]. Although the study only focused on the in-hospital findings while we had a short term follow up of 30 days. Bendary et al., also showed similar results from their studies which used SK as the fibrinolytic of choice [22].

Several registries like the Mayo Clinic STEMI Network also showed similar outcomes to the results of our findings [23]. So also, the recent report from the Vital Heart Response Registry in Canadian which showed safety and efficacy of

PhI in comparison to PPCI in short term with surprisingly better outcomes on long term follow up after 1 year.

5. Study Limitations

The study is limited by small number of patients and also a single ethnic study. Although randomized but the study was not blinded to reduce bias and also a short follow up time.

6. Conclusion

We demonstrated a significant IRA patency pre-PCI and significant enhanced follow post PCI in the PhI-SK group vs PPCI group. Pharmacoinvasive-SK is an effective, safe and viable strategy in patients presenting STEMI in the setting where PPCI cannot be achieved in <120 minutes from time of first medical contact. The use of SK is a viable option with excellent results especially in LMICs where there is high demand and limited resources. Our result has demonstrated safe and efficacy fibrinolytic with no risk of major bleeding.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

References

[1] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of st-elevation myocardial infarction: A report of the American college of cardiology foundation/american heart association task force on practice guidelines. *J Am Coll Cardiol*. 2013; 61 (4): e78-e140. doi: 10.1016/j.jacc.2012.11.019

[2] Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2018; 39 (2): 119-177. doi: 10.1093/eurheartj/ehx393

[3] Neumann F-J, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2018. doi: 10.1093/eurheartj/ehy394

[4] Pinto DS, Frederick PD, Chakrabarti AK, et al. Benefit of transferring ST-segment- elevation myocardial infarction patients for percutaneous coronary intervention compared with administration of onsite fibrinolytic declines as delays increase. *Circulation*. 2011; 124 (23): 2512-2521. doi: 10.1161/CIRCULATIONAHA.111.018549

[5] Engel Gonzalez P, Omar W, Patel K V., et al. Fibrinolytic Strategy for ST-Segment- Elevation Myocardial Infarction: A Contemporary Review in Context of the COVID-19 Pandemic. *Circ Cardiovasc Interv*. 2020; (September): 1-8. doi: 10.1161/CIRCINTERVENTIONS.120.009622

[6] Welsh RC, Van De Werf F, Westerhout CM, et al. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the strategic reperfusion early after myocardial infarction [STREAM] study). *Am J Cardiol*. 2014; 114 (6): 811-819. doi: 10.1016/j.amjcard.2014.06.011

[7] Armstrong PW, Gershlick AH, Goldstein P, et al. Fibrinolysis or primary PCI in ST- segment elevation myocardial infarction. *N Engl J Med*. 2013; 368 (15): 1379-1387. doi: 10.1056/NEJMoa1301092

[8] Mohan VN, Alexander T, Muraleedharan VR, et al. Economic and societal impact of a systems-of-care approach for stemi management in low and middle-income countries: Insights from the tn stemi program. *Ann Glob Heal*. 2019; 85 (1): 1-5. doi: 10.5334/aogh.2508

[9] World Medical Association. Ethical principles for medical research involving human subjects. *Eur J Emerg Med*. 2001; 8 (3): 221-223. http://www.ncbi.nlm.nih.gov/pubmed/11587468.

[10] Woodward M. *Epidemiology*. Chapman and Hall/CRC; 2013. doi: 10.1201/b16343

[11] Borgia F, Goodman SG, Halvorsen S, et al. Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: A meta-analysis. *Eur Heart J*. 2010; 31 (17): 2156-2169. doi: 10.1093/eurheartj/ehq204

[12] Roule V, Ardouin P, Blanchart K, et al. Prehospital fibrinolysis versus primary percutaneous coronary intervention in ST-elevation myocardial infarction: A systematic review and meta-analysis of randomized controlled trials. *Crit Care*. 2016; 20 (1): 1-7. doi: 10.1186/s13054-016-1530-z

[13] Khraishah H, Alahmad B, Secemsky E, et al. Comparative Effectiveness of Reperfusion Strategies in Patients with ST-Segment Elevation Myocardial Infarction: A Secondary Analysis of the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) Trial. *Glob Heart*. 2020; 15 (1): 68. doi: 10.5334/gh.868

[14] Vora AN, Holmes DN, Rokos I, et al. Fibrinolysis use among patients requiring interhospital transfer for st-segment elevation myocardial infarction care a report from the us national cardiovascular data registry. *JAMA Intern Med*. 2015; 175 (2): 207-215. doi: 10.1001/jamainternmed.2014.6573

[15] Sinnaeve PR, Armstrong PW, Gershlick AH, et al. ST-segment-elevation myocardial infarction patients randomized to a pharmaco-invasive strategy or primary percutaneous coronary intervention strategic reperfusion early after myocardial infarction (STREAM) 1-year mortality follow-up. *Circulation*. 2014; 130 (14): 1139-1145. doi: 10.1161/CIRCULATIONAHA.114.009570

[16] Naghshtabrizi N, Goudarzi F, Naghshtabrizi B, Poorolajal J, Emami F. Comparison of the Incidence of MACCE in Primary Percutaneous Coronary Intervention vs. Delayed Primary Percutaneous Coronary Intervention 24 hours After Taking Fibrinolytic Therapy in Patients with STEMI. *J Clin Diagnostic Res*. 2019: 7-10. doi: 10.7860/jcdr/2019/41582.12991

[17] Sierra-Fragoso ÁA, Galván-García JE, Vargas-Ramírez JF, et al. Pharmacoinvasive strategy versus primary angioplasty in patients with acute ST-segment elevation myocardial infarction. *Rev Mex Cardiol*. 2018; 29 (3): 126-133.

[18] Rashid MK, Guron N, Bernick J, et al. Safety and Efficacy of a Pharmacoinvasive Strategy in ST-Segment Elevation Myocardial Infarction: A Patient Population Study Comparing a Pharmacoinvasive Strategy With a Primary Percutaneous Coronary Intervention Strategy Within a Regional System. *JACC Cardiovasc Interv*. 2016; 9 (19): 2014-2020. doi: 10.1016/j.jcin.2016.07.004

[19] Ghilencea L, Popescu AC, Dimulescu D, et al. An observational, prospective study of the pharmaco- invasive strategy approach to ST-segment myocardial infarction (STEM) in the era of primary percutaneous coronary intervention based on Elias Heart Centre Interventional Registry (EIRE Study). The. 2019; 29 (3): 431-450.

[20] Bendary A, Tawfek W, Mahros M, Salem M. Primary PCI versus pharmaco-invasive strategy in patients with ST-Elevation myocardial infarction; A randomized clinical study. *J Cardiovasc Dis Res*. 2018; 9 (1): 28-31. doi: 10.5530/jcdr.2018.1.7

[21] Siontis KC, Barsness GW, Lennon RJ, et al. Pharmacoinvasive and Primary Percutaneous Coronary Intervention Strategies in ST-Elevation Myocardial Infarction (from the Mayo Clinic STEMI Network). *Am J Cardiol*. 2016; 117 (12): 1904-1910. doi: 10.1016/j.amjcard.2016.03.036

[22] Bainey KR, Armstrong PW, Zheng Y, et al. Pharmacoinvasive Strategy Versus Primary Percutaneous Coronary Intervention in ST-Elevation Myocardial Infarction in Clinical Practice: Insights from the Vital Heart Response Registry. *Circ Cardiovasc Interv*. 2019; 12 (10): 1-12. doi: 10.1161/CIRCINTERVENTIONS.119.008059