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EFFECT OF LOW DOSE INTRACORONARY STREPTOKINASE ADMINSTIRATION IMMEDIATELY AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION ON LEFT VENTRICULAR FUNCTION AS ASSESSED BY SPECKLE TRAKING ECHOCARDIOGRAPHY

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ABSTRACT

Background: Reperfusion injury might be considered as the consequence of insufficient perfusion due to fibrin and fibrinogen deposition in the microvasculature. Therefore, streptokinase, being a fibrinolytic drug, injected in the culprit artery immediately after primary PCI can be a suitable solution for achieving better myocardial perfusion.

Aim of study: To assess the impact of complementary low dose intracoronary streptokinase (ICSK) administration immediately after primary PCI on left ventricular functions.

Patients and methods: This double blinded randomized controlled clinical trial included 64 patients within 12 h of presentation by first STEMI who were candidate for primary percutaneous coronary intervention (PPCI). They were randomized equally to 2 groups. Immediately after primary PCI the first group received 250 kU ICSK vs placebo in the second group. Evaluation of LV functions was done by comparing the baseline echocardiographic parameters including left ventricle (LV) global longitudinal strain (GLS) before and after PPCI. Assessment of ST segment resolution (STR) 90 min after primary PCI, enzymatic infarct size in addition to comparing post-PPCI TIMI flow grade, TIMI frame count (TFC), Myocardial blush grade (MBG) and TIMI myocardial perfusion grade (TMPG) between both groups. Successful reperfusion after PPCI was defined as patients who achieved (TIMI 3 flow, MBG 3, > 70% ST segment resolution)

Results: Post-PPCI LV GLS and LVEF were significantly higher in ICSK group (P = 0.005, 0.02 respectively). Post PPCI E/e' was significantly lower in ICSK group (P = 0.007). Peak CK-MB, CK-MB area under the curve (AUC), Troponin-I (72-hr); representing the enzymatic infarct size, were significantly lower in the ICSK group (P = 0.015, < 0.001, < 0.001 respectively). STR > 70% after PPCI was significantly higher in ICSK group (P = 0.045). Post-PPCI TFC was significantly lower in the ICSK group (P = 0.05). Post-PPCI MBG & TMPG were significantly higher in ICSK group (P = 0.04, 0.03 respectively). Multivariate linear regression analysis showed that each of ICSK administration, pain to stent time interval, post-PPCI MBG were independent predictors for LV GLS improvement after PPCI. Multivariate logistic regression analysis showed that the likelihood of achieving successful reperfusion post-PPCI was also associated with ICSK administration [OR= 0.123, 95% CI (0.02 - 0.75), P = 0.024] and was inversely associated with pain to stent time interval [OR= 0.995, 95% CI (0.990-0.999), P = 0.015].

Conclusion: Low-dose ICSK given immediately after primary PCI significantly led to improvement of LV GLS and LVEF, E/e'. It also reduced the enzymatic infarct size and was an independent predictor of successful reperfusion and LV GLS improvement after PPCI.

Key words: Streptokinase, Primary percutaneous coronary intervention, LV function.

INTRODUCTION

Acute myocardial infarction (AMI) has the lion's share of the causes of congestive heart failure and subsequent mortality worldwide. [1] In ST-segment elevation myocardial infarction (STEMI), urgent revascularization of the culprit coronary artery is the current goal of the initial management strategy.[2] However, ongoing myocardial damage despite the successful elimination of epicardial occlusion limits the efficacy of primary PCI. If the tissue damage and stasis that develop in infarcted myocardial segments are considered together, de novo fibrin formation at the microvascular level will be found to be inevitable.[3] Streptokinase is an effective fibrinolytic agent which has been used since the 1950s to dissolve clots following myocardial infarction.[4] Some of the factors that contribute to impaired microperfusion after primary PCI, such as fibrin deposition, generation of oxygen free radicals, and endothelial dysfunction, can be improved with streptokinase therapy. So intracoronary streptokinase may have a potential beneficial role in the context of PPCI.[5]

AIM OF THE WORK

To assess the impact of complementary low dose intracoronary streptokinase (ICSK) administration immediately after primary PCI on left ventricular functions.

PATIENTS AND METHODS

This double blinded randomized controlled clinical trial included 64 patients within 12 h of presentation by first STEMI who were candidate for primary percutaneous coronary intervention (PPCI) and admitted to cardiology department at Zagazig University, during the period from May 2016 to May 2018.

Exclusion criteria: Patients were excluded from the study if one or more of the following criteria were present:

A. Patients with previous episode of myocardial infarction.

B. Patients having any contraindication for streptokinase.

C. Patients with cardiogenic shock

D. Patients who are candidates for urgent CABG post-Acute St-segment elevation myocardial infarction.

Complete history taking:

Including name, age, gender, special habits, menstrual state, drug history and previous hospital admission with special consideration to history of risk factors to ischemic heart disease and co-morbid conditions.

Thorough clinical examination:

All patients were subjected to thorough clinical general and local cardiac examination.

Electrocardiographic examination:

Twelve lead ECGs were obtained for each patient at rest: with 10 mm/mV amplitude and 25 mm/sec rate with standard lead positions at 0, 1.5, 6, 12 hours after admission, complete ST segment resolution (STR) was defined as ≥ 70% decrease in initial magnitude of STR 90 minutes after treatment.[6]

Trans-thoracic echocardiography:

TTE was done for every patient before and 1 month after PPCI using GE Vivid E9 set (part no GA 091568, Norway 2010) using 5 MHz transducer. Images were taken while the patient is supine or in left lateral position, utilizing two-dimensional (2D), M-mode, Doppler echocardiographic techniques and speckle tracking of evaluation as follows:

1) Left ventricular volumes (end systolic and end diastolic volumes), left ventricular ejection fraction by modified biplane Simpson's method.[7]

2) Assessment of LV diastolic dysfunction: Doppler recordings were obtained with the pulsed sample volume placed at the tip of the mitral leaflets from the apical 4-chamber view. Peak early (E) and late (A) velocities, E-wave deceleration time and were measured. LA volume index, TR jet velocity. In addition, tissue doppler imaging data were acquired to measure the medial and lateral mitral annulus E' diastolic tissue velocities. Average E/e' was calculated.[8]

3) Wall motion score index: based on a 17-segment in which each segment is scored as normal (1 point), hypokinetic (2 points), akinetic (3 points), or dyskinetic (4 points). The

wall motion score index (WMSI) is equal to the sum of these grades divided by the number of segments visualized.[9]

3) Speckle tracking echocardiography: Dynamic 2D ultrasound images of three cardiac cycles from apical two-, three-, and four chamber views will be acquired using conventional ultrasound, with a frame rate of 57 to 72 frames per second. Endocardial boundary of the left ventricle was delineated manually, after which the software automatically drew the epicardial boundary. The widths of the regions of interest was adjusted manually to match the actual endocardial and epicardial boundaries. Automatic frame-by frame tracking of speckle patterns during the cardiac cycle yielded a measure of strain and strain rate at any part of the myocardium. LV myocardium was divided into six segments in each apical view, and each segment was individually analyzed. By averaging all LV segmental values in all views, LV peak global systolic longitudinal strain (GLS) and was calculated.[10]

Primary PCI:

Coronary angiography was performed in Zagazig University Hospitals Catheterization laboratories (Cine angiographic equipment: GE Innova 2100-IQ **:** cine frame: 30 fps). Selective coronary angiography with standard multi-angulated angiographic views was performed through the femoral artery under local anesthesia (2% Lidocaine) using the Judkins catheters and iopromide (Ultravist) as the contrast agent. The angiograms were recorded on a compact disc in DICOM format.

Immediately after Diagnostic Coronary Angiography eligible patients were assigned to either: The Intra-coronary streptokinase (ICSK) group or the control group based on a computer-generated random sequence. All patients received 300 mg Aspirin, 600 mg Clopidogrel, Unfractionated Heparin at a dose of 100 IU/Kg. Primary PCI was done through a femoral approach, In Both groups, Infarct related artery (IRA) was stented. In the ICSK group, immediately after recanalizing the IRA, 250,000 IU of Streptokinase diluted with 20 ml of Saline was infused intracoronary through the guiding catheter within 10 minutes. The control group, immediately after recanalizing the IRA, 20 ml of saline was infused intracoronary through the guiding catheter within 10 minutes.

Final angiographic recordings were performed 30 min after ICSK injection to assess TIMI flow grade [11], TIMI frame count (TFC) [12], myocardial blush grade (MBG) [13] and thrombolysis in myocardial infarction myocardial perfusion grade (TMPG).[14] Baseline & post-PPCI TIMI flow were compared within each group and final TIMI frame count (TFC), myocardial blush grade (MBG) & TIMI myocardial perfusion grade (TMPG) were compared among both groups.

Time intervals was calculated as: Pain to door interval (min): time interval between onset of chest pain and first medical contact (FMC), Door to stent interval (min): time interval between FMC and stent deployment in the infarct related artery, Pain to stent interval (min): time interval between onset of chest pain and stent deployment in the IRA.

STATISTICAL ANALYSIS

Data were then imported into Statistical Package for the Social Sciences (SPSS version 16.0) software for analysis. Quantitative data were expressed as means ± SD and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Differences between means in two parametric groups were compared by Student's t test. Non-parametric data by Mann-Whitney test. Sensitivity & specificity were used to plot Receiving Operative Curve. Multivariate linear regression analysis was used to detect independent predictors of GLS improvement after primary PCI. Multivariate logistic regression analysis was used to detect independent predictors of successful reperfusion. P value was set at <0.05 for significant results & <0.001 for high significant results.[15]

RESULTS

The study included 64 patients, the mean age was 60.8±8.3 years, 39 patients (60.9%) were males and 25 patients (39.1%) were females. Hypertension was reported in 33 patients

(51.6%) of all patients, diabetes in 25 patients (39.1%), positive family history of coronary artery disease in 19 patients (29.7%) and smoking in 18 patients (28.1%) of all patients. There was no significant difference between both groups as regards demographic data and risk factors (p value >0.05) **(Table 1)**.

ECG data showed that 14 patient (43.7%) in group (1) had anterior STEMI, while 18 patient (56.3%) had non anterior STEMI, 31 patients (97%) showed complete ST segment resolution (≥70%) after 90 min from PPCI while in group (2) 13 patients (40.6%) had anterior STEMI, 19 patients (59.4%) had non anterior STEMI, 25 patients (72%) showed complete ST segment resolution, 90 min after PPCI **(Table 2)**.

Regarding cardiac biomarkers in both groups Peak CK-MB was significantly higher in group (2), (P = 0.015), while both CK-MB area under the curve (AUC), Troponin I (72 hr) were highly significant in group (2), (P < 0.001) denoting larger enzymatic infarct size in Group (2) **(Table 3).**

Baseline echocardiographic data showed no significant difference between both study groups regarding baseline LVEDV, LVESV, LVEF, wall motion score index, average GLS (P > 0.05). **(Table 4).**

Post-PPCI echocardiographic data showed significant differece between both study groups regarding LVEF, LV GLS being higher in group (1), E/e' being lower in group (1) **(Table 5)**.

There was no significant difference between both study groups regarding the culprit vessel **(Table 6)** or baseline TIMI flow grade (p > 0.05).

There was significant difference between both study groups regarding Myocardial blush grade (MBG), TIMI myocardial perfusion grade (TMPG); all being higher in Group (1), while mean TIMI frame count (TFC) was significantly higher in Group (2); (p–value < 0.05), **(Table 7)**.

There was no significant difference among both groups as regards pain to door interval or door to stent interval or pain to stent interval (p-value > 0.05)

Univariate linear regression analysis showed that the following variables can predict improvement in the GLS after PPCI: ICSK administration, pain to stent interval, post-PPCI MBG, post-PPCI TMPG, TFC, STR (P < 0.05), however only giving ICSK, Pain to stent & Post-PPCI MBG remained significant in multivariate linear regression analysis, with the most independent predictors were giving ICSK & Pain to stent interval (P < 0.001) followed by Post-PPCI MBG (P = 0.05).

Univariate logistic regression analysis showed that giving ICSK administration [OR = 5, 95% CI (0.97 - 25.77), P = 0.045] & pain to stent interval [OR= 0.996, 95% CI (0.992 - 1.0), P = 0.03] can predict successful reperfusion, in multivariate logistic regression model the independent predictors for successful reperfusion were ICSK [OR= 0.123, 95% CI (0.02 - 0.75), P = 0.024], Pain to stent interval [OR= 0.995, 95% CI (0.990-0.999), P = 0.015].

A ROC curve for pain to stent time which predicts successful reperfusion showed AUC = 0.72, cut-off value = 415 min with sensitivity of 65%, specificity of 80%, **Figure (1)**.

There was no significant difference between both study groups regarding bleeding (1 case of minor bleeding, according to TIMI bleeding criteria, was reported in each group).

DISCUSSION

Despite optimal state-of-the-art pharmaceutical and therapeutic strategies, the prognosis of AMI remains dubious.[1] In spite of prompt reperfusion by primary percutaneous coronary intervention (PPCI), the mortality and morbidity of patients presenting with an acute ST-segment elevation myocardial infarction (STEMI) remain significant with 9% death and 10% heart failure at 1 year.[16]

Approximately half of all STEMI patients have failed microcirculatory reperfusion, as reflected by microvascular obstruction (MVO), and one-third have myocardial haemorrhage,

reflecting severe, 'downstream', potentially irreversible, microvascular injury.[17]

Microvascular malperfusion was attributed in some studies to de novo fibrin depositions which occur at the microcirculation; fibrin mass binds to endothelial junctional adhesion molecules (VEcadherin), constitutes a mesh, and tends to persist in the microvasculature.[18]

Although eliminating epicardial occlusion re-establishes perfusion, it also supplies circulating blood cells downstream that later get entrapped in the microvasculature that contains the fibrin mesh. Blood cells create obstructive plugs and cause significant congestion by enmeshing passively or binding to fibrin actively with their receptors.[19] In this slow-flow condition, fibrinogen also contributes to impeding flow via facilitating blood cell aggregation and mediating the inflammatory process.[20]

Sezer et al., 2009 in concordance with our study showed no statistically significant difference between patients who received 250 kIU after PPCI and the control group who didn't receive ICSK after PPCI regarding baseline variables like age, sex, type 2 diabetes mellitus or hypertension (p value >0.05).[19]

There present study also showed no statistically significant difference between both groups regarding ECG location of STEMI (p value >0.05), which is concordant with Sezer et al., 2007 & 2009 which showed no statistical sgnificant difference between both groups regarding AMI localization whether it was anterior or non-anterior STEMI (p – value > 0.05). [19]

Regarding ST segment resolution ≥ 70 % after 90 min of PPCI in both study groups, the present study was consistent with the pilot study of Sezer et al., 2007 who showed significant difference between both study groups regarding ST-segment resolution with 2 differences from the present study; that they assessed it after 60 min from PPCI and they calculated the absolute percentage of ST resolution from the initial elevation which was higher in the group which received ICSK after PPCI.[20] However, this was discordant with the study conducted by Sezer et al., 2009 where there was no difference between the 2 groups with respect to percent resolution of ST-segment deviation 90 min after primary PCI.[19] This may be explained by different sample size and more frequent anterior STEMI than we had in our study. de Lemos & Braunwald, 2001 emphasized on the role of ST segment resolution as a marker of coronary microvascular and tissue-level reperfusion; stated that several studies support the hypothesis that ST resolution is a surrogate for tissue-level reperfusion and it also has a prognostic significance. When "complete" ST resolution is seen 90 min after fibrinolysis, successful reperfusion has occurred at both the epicardial and microvascular level, and the prognosis is excellent.[21]

The only parameter which was assessed by Sezer et al., 2009 was peak level of troponin T & troponin I which showed no statistically significant difference between both study groups. The present study assessed the enzymatic infarct size by 3 different parameters (CK-MB Peak, CK-MB AUC, Troponin I-72 hr) and is considered up to our knowledge the first study to assess the impact of ICSK following PPCI on these parameters which reflects the enzymatic infarct size.[19]

The present study, in agreement with Sezer et al., 2009, showed no significant difference between baseline LV volumes and EF,[19] however they have not assessed neither WMSI nor GLS.

Post-PPCI Echocardiographic data showed significant difference between both study groups regarding Post- PPCI LVEF and delta change in LVEF, both of which being higher in group (1), (p value < 0.05). This is in concordance with Sezer et al., 2009 where the ejection fraction was significantly higher (57.2% vs. 51.8%; p value= 0.018) in the ICSK group compared with the control group.[19]

Post-PPCI average GLS was significantly higher in group (1), this parameter was not assessed in any earlier studies to predict the efficacy of ICSK immediately after PPCI. Sezer et al., 2009 used SPECT instead to assess the

myocardial infarct size which was significantly lower in the group which received ICSK.[19]

Diao et al., 2017 conducted a systematic review and meta-analysis where eleven trials with a total of 765 patients were included. They concluded that GLS results positively correlated with the infarction size quantified by CMR for patients who had experienced their first MI.[22]

Bergerot et al., 2014 investigated the influence of coronary microvascular obstruction in the acute phase myocardial infarction on GLS. Speckle-tracking echocardiography and contrast-enhanced cardiac magnetic resonance studies were performed in 69 patients 72 hours after first acute MI. A GLS value > -12.5% predicted the presence of MVO with 83% sensitivity and 75% specificity. They concluded that: In the acute phase of MI, segmental and GLS is significantly altered by the presence of MVO, in addition to MI size.[23]

The effect of ICSK on LV diastolic dysfunction was not addressed before in earlier studies. However some studies studied LV diastolic dysfunction after PPCI in general. Shacham, et al., 2016 assessed the relationship of LV filling pressures and remodeling among STEMI patients treated by PPCI and found that Patients with maintained or worsened E/e' ratios to >15 demonstrated worse LV ejection fractions. They concluded that among patients with STEMI undergoing PPCI, early and persistent elevation of the E/e' ratio may be associated with LV remodeling.[24]

CONCLUSION

Low-dose ICSK given immediately after primary PCI significantly led to improvement of LV GLS and LVEF, E/e'. It also reduced the enzymatic infarct size and was an independent predictor of successful reperfusion and LV GLS improvement after PPCI.

Table 1 Demographic data and risk factors among study groups.

		Group (1) (n=32)	Group (2) (n=32)	p-value
Age (years)	**Mean± SD**	60.84±8.8	60.75±7.9	0.96
Sex	**(Male)** %	16 (50%)	23 (71.9%)	0.12
Diabetes Mellitus	**N** (%)	14 (44%)	11 (34%)	0.61
Hypertension	**N** (%)	15 (47%)	18 (56%)	0.62
Smoking	**N** (%)	7 (22%)	11 (34%)	0.41
Dyslipidemia	**N** (%)	14 (44%)	16 (50%)	0.8
Family history	**N** (%)	11 (34%)	14 (44%)	0.61

Table 2 ECG findings among study groups.

		Group (1) (n=32)	Group (2) (n=32)	p-value
Anterior STEMI	**N (%)**	14 (43.7%)	13 (40.6%)	0.69
Lateral STEMI	**N (%)**	7 (21.8%)	5 (15.6%)	
Inferior STEMI	**N** (%)	11 (34.4%)	14 (43.7%)	
ST-segment resolution ≥ 70%	**N** (%)	31 (97%)	25 (78%)	0.045

STEMI: ST-segment elevation myocardial infarction, N: number

Table 3 Laboratory findings among study groups.

		Group (1) (n=32)	Group (2) (n=32)	p-value
CK-MB Peak (ng/ml)	**Mean± SD**	69.75 ±17.7	80.75 ±17.6	0.015
CK-MB AUC (ng/ml)		2422.66 ± 302.6	2896.7 ± 430.2	< 0.001
Troponin-I (72 hr) (ng/ml)		8.44 ± 2.4	14.4 ± 2.49	< 0.001

CK-MB: creatine phosphokinase muscle/brain, AUC: area under the curve, hr: hour

Table 4 Baseline Echocardiographic findings among study groups.

		Group 1 (n=32)	Group 2 (n=32)	p-value
Baseline LVEDV (ml)	Mean± SD	118 ± 13	116.22 ± 8.6	0.5
Baseline LVESV (ml)		65 ± 11.14	65.97 ± 7.6	0.8
Baseline LVEF (%)		44.69 ± 5.67	43.43 ± 3.7	0.29
Baseline WMSI		1.54 ± 0.15	1.48 ± 0.22	0.24
Baseline average GLS		-13.59 ± 1.6	-13.12 ±2.29	0.34

LVEDV= Left ventricular end diastolic volume, LVESV= Left ventricular end systolic volume, LVEF= Left ventricular ejection fraction, WMSI= wall motion score index, GLS= Global longitudinal strain, SD: standard deviation, ml: millilitre

Table 5 Post-Primary PCI Echocardiographic findings among study groups.

		Group 1 (n=32)	Group 2 (n=32)	p-value
Post-PPCI LVEDV (ml)	Mean± SD	113.06 ± 13.44	113.66 ± 7.96	0.88
Post-PPCI LVESV (ml)		57.16 ± 10.17	60.41 ± 6.77	0.14
Post-PPCI LVEF (%)		49.81 ± 5.44	46.44 ± 3.69	0.005
Post-PPCI WMSI		1.29 ± 0.12	1.33 ± 0.15	0.06
Post-PPCI average GLS		-16.7 ± 1.4	-14 ± 5.38	0.02
E/A ratio		1.15 ± 0.71	1.07 ± 0.64	0.63
E/e'		12.24 ± 2.17	13.54 ± 1.44	0.007
LAVI		31.6 ± 4.12	32.88 ± 4.33	0.23

PPCI= primary percutaneous coronary intervention, LVEDV= Left ventricular end diastolic volume, LVESV= Left ventricular end systolic volume, LVEF= Left ventricular ejection fraction, WMSI= wall motion score index, GLS= Global longitudinal strain.

Table (6): Culprit vessel in both study groups:

		Group (1) (n=32)	Group (2) (n=32)	p-value
LAD	**N** (%)	14 (43.7%)	13 (40.6%)	0.69
LCX	**N** (%)	7 (21.8%)	5 (15.6%)	
RCA	**N** (%)	11 (34.4%)	14 (43.7%)	

LAD: left anterior descending artery, LCX: left circumflex artery, RCA: Right coronary artery, N: number

Table (7): Post-PPCI angiographic features of both study groups.

		Group (1) (n=32)	Group (2) (n=32)	p-value
Post PPCI TIMI flow grade				
TIMI 1	**N** (%)	1 (3.125%)	1 (3.125%)	0.06
TIMI 2	**N** (%)	1 (3.125%)	6 (18.75%)	
TIMI 3	**N** (%)	30 (93.75%)	25 (78.125%)	
Post-PPCI MBG				
MBG 0/1	**N** (%)	1 (3.125%)	1 (3.125%)	0.04
MBG 2	**N** (%)	1 (3.125%)	7 (21.875)	
MBG 3	**N** (%)	30 (93.75%)	24 (75%)	
Post-PPCI TMPG				
TMPG 0/1	**N** (%)	1 (3.125%)	3 (9.375%)	0.03
TMPG 2	**N** (%)	2 (6.25%)	7 (21.875)	
TMPG 3	**N** (%)	29 (90.625%)	22 (68.75)	
Post-PPCI TFC				
Mean TFC	**Mean± SD**	26.83±8.2	31.48±7.6	0.05

PPCI: primary percutaneous coronary intervention., TIMI: thrombolysis in myocardial infarction, MBG: Myocardial blush grade, TMPG: TIMI myocardial perfusion grade, TFC: TIMI framae count, c: corrected, LAD: left anterior ascending artery, LCX: left circumflex artery, RCA: right coronary artery.

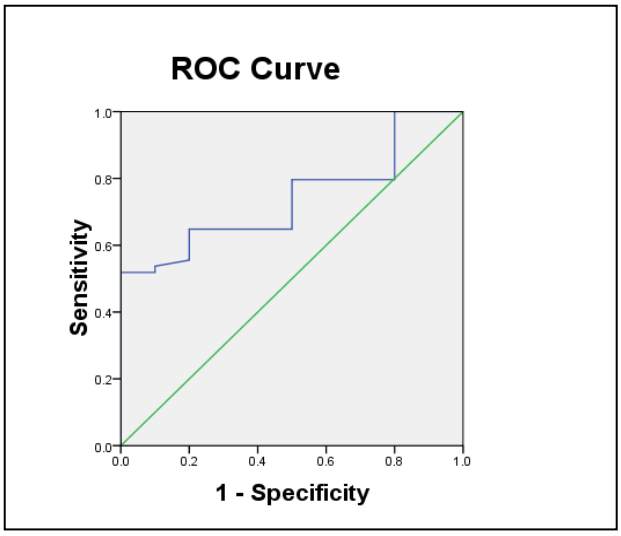

Figure (1): ROC curve for pain to stent interval predicting successful reperfusion.

REFERENCES

1. **Wang C, Han X, Li Y, et al.** Impact of bone marrow mononuclear cells therapy on left ventricular function in patients with ST-elevated myocardial infarction, A meta-analysis. Medicine 2018; 97:16(e0359)
2. **Lu DY, Zhong M, Feldman DN.** Complete Versus Culprit-Only Revascularization in STEMI: a Contemporary Review. Curr Treat Options Cardio Med 2018; 20:41
3. **Petzelbauer P, Zacharowski PA, Miyazaki Y, et al.** The fibrin-derived peptide beta 15-42 protects the myocardium against ischemia-reperfusion injury. Nat Med. 2015; 11:298 –304.
4. **Armstrong, P. w. & Collen, D.** Fibrinolysis for acute myocardial infarction: Current status and new horizons for pharmacological reperfusion, part 1. Circ J. 2001; 103, 2862–2866.
5. **Armstrong P.W.** Intracoronary streptokinase in acute myocardial infarction. Nature reviews Cardiology 2010; 7, 67-68.
6. **de Lemos JA, Braunwald E.** ST Segment Resolution as a Tool for Assessing the Efficacy of Reperfusion Therapy JACC 2001; 38:1283–94
7. **Lang RM, Badano LP, Mor-Avi V, et al.** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28(1):1-39.e14.
8. **Nagueh S, Smiseth O, Appleton C et al.** Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016; 29:277-314.
9. **Solomon SD, Wu J and Gillam L.** Echocardiography, the Standard adult transthoracic examination. Brauwnuald's heart Disease, A textbook of cardiovascular medicine 10th edition. El Seiver, (Ch 14) 2015:191.e1
10. **Voigt J-U, Pedrizzetti G, Lysyansky P, et al.** Definitions for a common standard for 2D speckle tracking echocardiography. Consensus document of the EACVI/ASE/Industry Task Force to Standardize Deformation Imaging. Eur H J, Cardiovascular imaging 2015; 16:1-11.
11. **TIMI Study Group.** The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. N. Engl. J. Med. 1985; 04;312(14):932-6.
12. **Gibson CM, Cannon CP, Daley WL, et al.** TIMI frame count: a quantitative method of assessing coronary artery flow. Circ J.1996; 93: 879–888.
13. **Niccoli G, Cosentino N, Spaziani C, et al.** No-reflow: incidence and detection in the cath-lab. Curr Pharm Des. 2013; 19:4564–4575.
14. **Gibson CM, Cannon CP, Murphy SA, et al.** Relationship of TIMI Myocardial Perfusion Grade to Mortality After Administration of Thrombolytic Drugs. Circ J.2000; 101:125-130.
15. **Dean JA and Coulabier D. (2000):** A word processing database and statistic program for epidemiology on microcomputer CDC, Atlanta, Gorgia, USA**.**

16. **Bulluck H , Yellon D, Hausenloy D.** Reducing myocardial infarct size: challenges and future opportunities. Heart 2016; 102:341–348.
17. **Carrick D, Haig C, Ahmed N, et al.** Temporal evolution of myocardial hemorrhage and Edema in patients after acute ST-Segment elevation myocardial infarction: pathophysiological Insights and Clinical implications. J Am Heart Assoc.2016; 5:e002834.
18. **Bach TL, Barsigian C, Yaen CH, Martinez J.** Endothelial cell VE-cadherin functions as a receptor for the beta 15-42 sequence of fibrin. J Biol Chem; 1998, 273:30719 –28.
19. **Goel MS, Diamond SL.** Adhesion of normal erythrocytes at depressed venous shear rates to activated neutrophils, activated platelets, and fibrin polymerized from plasma. Blood 2002;100:3797– 803.
20. **Lominadze D, Dean WL.** Involvement of fibrinogen specific binding in erythrocyte aggregation. FEBS Lett 2002; 517:41– 4.
19. **Sezer M, Çimen A, Aslanger E, et al.** Effect of Intracoronary Streptokinase Administered Immediately After Primary Percutaneous Coronary Intervention on Long-Term Left Ventricular Infarct Size, Volumes, and Function. JACC 2009; 15:1065–71
20. **Sezer M, Oflaz H, Gören T, et al.** Intracoronary Streptokinase after Primary Percutaneous Coronary Intervention. N Engl J Med 2007; 356:1823-34.
21. **de Lemos JA, Braunwald E.** ST Segment Resolution as a Tool for Assessing the Efficacy of Reperfusion Therapy. JACC 2001; 38:1283–94
22. **Diao K, Yang Z, Ma M, et al.** The Diagnostic Value of Global Longitudinal Strain (GLS) on Myocardial Infarction Size by Echocardiography: A Systematic Review and Meta-analysis. Nature 2017; 7: 10082.
23. **Bergerot C, Mewton N, Lacote-Roiron C.** Influence of Microvascular Obstruction on Regional Myocardial Deformation in the Acute Phase of Myocardial Infarction: A Speckle-Tracking Echocardiography Study. Journal of the American Society of Echocardiography 2014; 27: 93-100.
24. **Shacham Y, Khoury S, Flint N, et al., (2016):** Serial Echocardiographic Assessment of Left Ventricular Filling Pressure and Remodeling among ST-Segment Elevation Myocardial Infarction Patients Treated by Primary Percutaneous Intervention. Journal of the American Society of Echocardiography 2016; 29 (8): 745–749

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