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Research Article

Pharmacoinvasive Strategy Versus Lysis and Risk Stratification Strategy in Treatment of STEMI Patients

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Abstract

Background: STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis.

Aim of the Study: Was to detect efficacy and predictors of outcomes of pharmacoinvasive treatment strategy in STEMI patients over reperfusion with thrombolysis only in areas with non-PCI capable centers as in most of hospitals in middle east.

Methods and Results: A time limited prospective interventional study started in November 2016 till November 2018. Patients divided into two groups, first group 300 patients treated with Lysis full dose TNK followed by risk stratification, the other 300 will go through pharmacoinvasive strategy as stream study by doing routine coronary angiography 3 to 24 hours after successful lysis, if lysis failed in both groups' patient will go directly to rescue PCI. Successful lysis is defined as > 50% regression of ST segment elevation with pain relief.

Conclusion: Lysis associated with more myocardial damage, more Troponin release and less preservation of myocardial contractility function measured by Echo by EF. Pharmacoinvasive strategy significantly reduce risk of reinfarction, need for CABG, PCI, arrhythmia, preservation of EF and at least is as effective as 1ry PCI.

Keywords: *Lysis; Thrombolysis; Myocardial Infarction*

Abbreviations

MI: Myocardial Infarction; STEMI: ST Elevation Myocardial Infarction; PCI: Percutaneous Coronary Intervention; TNK: Tenecteplase

Introduction

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis [1].

STEMI comprises approximately 25% to 40% of MI presentations, In-hospital (approximately 5% to 6%) and 1-year (approximately 7% to 18%) mortality rates from STEMI also have decreased significantly in association with a substantial increase in the frequency of care that includes GDMT and interventions ("defect-free" care) [1].

In many parts of the world where access to PCI- capable centers 7 days a week and 24 hours a day is available, the preferred approach is for ambulances to bypass a non-PCI capable hospital and directly transport patients to a PPCI facility, Nonetheless, "one size does not fit all" and the preferred reperfusion strategy will depend to a large extent on geographical and logistical constraints such as distance and weather and regional resources [2].

MI is defined pathologically as myocardial cell death due to prolonged ischemia., necrosis progresses from the sub-endocardium to the sub- epicardium over several hours. But biochemical evidence of myocardial cell death due to apoptosis can be detected within 10 minutes of induced myocardial ischemia [3].

Causes of myocardial injury includes could be related to 1ry myocardial ischemia as plaque rupture or thrombus, supply-demand mismatch or multifactorial [3].

Patients can present with prolonged chest pain more than 2 minutes constricting, crushing, compressing or burning radiate to left shoulder, arm, hand, fingers and sometimes pain is epigastric. Other atypical presentation like syncope, weakness, Dizziness or even silent at all [4].

All Routine blood tests and high sensitive troponin should be carried out [5].

Management include:

1. Initial diagnosis by ECG within 10 minutes.
2. Routine blood sampling for serum cardiac markers and laboratory.
3. Relief of pain, breathlessness and anxiety.
4. prehospital logistic of care: STEMI → Time of PCI → < 120 min 1ry PCI → < 90 min reperfusion (wire crossing).

Time of PCI → > 120 min → Lysis strategy < 10 min followed by coronary angiography within 3 - 24 hours [6].

Access route: The preferred Radial than femoral. Rival trial [7]. Preferred stents are DES. Examination trial [8]. Thrombus aspiration is no more indicated.

Multivessel coronary revascularization could be considered as advised in PRAMI trial and CvLPRIT trial.

Platelet inhibition by DAPT with combination of aspirin and P2Y12 inhibitors, the preferred P2Y12 inhibitors as clopidogrel, ticagrelor, and prasugrel. Enoxaparin is recommended than UFH except with renal impairment. OASIS 6 [9]. Bivalirudin can be used according to HORIZON trial. Fibrinolysis is important reperfusion strategy preserving 30/1000 death and is recommended within 12 hours of symptoms if 1ry PCI can`t be done within 20 min and prehospital Lysis reduce early mortality by 17%. If Lysis failed it is preferred to transfer patient for rescue PCI even if Lysis is successful (ST segment resolution > 50% at 60 - 90 minutes). A strategy of routine early angiography is recommended if there is no contraindication (STREAM).

Risk stratification with noninvasive imaging like Echo, MRI, stress MPI, sub-maximum and symptom limited exercise test [10].

Smoking has strong prothrombotic effect and smoking cessation is potentially the most cost effective of all 2ry prevention measures like Diet, alcohol and weight management keeping BMI < 25 [11].

Exercise based cardiac rehabilitation should be offered [12].

Antithrombotic therapy with DAPT for a year is recommended according to current - OASIS 7 trial the benefit of mid and long-term beta blocker treatment is established [13].

Lipid lowering therapy with high potent statin like atorvastatin 40 - 80 mg or rosuvastatin 20 - 40 mg (IMPROVE-IT) trial also pro-protein convertase subtilisin/kexin type 9 (PCSK9) improve lipid profile if statin failed (FOURIER) trial. ACE inhibitors are recommended with impaired systolic function.

Complications following ST segment elevation vary from mechanical like left ventricular dysfunction, 2ry Mitral regurgitation, right ventricular involvement, heart failure, free wall ventricular septal and papillary muscle rupture, pericarditis, pericardial effusion and electrical complications like arrhythmia and conduction dysfunction.

Patients and Methods

Study was designed as time limited prospective interventional study started in November 2016 till November 2018. Patients divided into two groups, first group 300 patients treated with Lysis full dose TNK followed by risk stratification with exercise ECG if their basal ECG is interpretable or stress imaging with nuclear study if not, the other 300 will go through pharmacoinvasive strategy as stream study by doing routine coronary angiography 3 to 24 hours after successful lysis.

Inclusion criteria: Patients with STEMI eligible for reperfusion with lysis ranging from 18 - 75 years old.

Exclusion criteria:

- STEMI patients not eligible for reperfusion with lysis.
- Age Above 75 years old as they should receive half dose Lysis if going for pharmacoinvasive.
- Patients with cardiogenic shock.
- Patient with prior CABG.

Investigations done: All routine blood tests, Chest Xray, ECG, Echo and Coronary angiography is done through radial and femoral approach with use of 2nd generation of DES.

Follow up of patients over 1, 6 and 12 months.

1ry end point: Death, MI related death.

2ry end point: Cerebrovascular accident.

Study was done to evaluate efficacy of pharmacoinvasive strategy in treatment of STEMI patients.

Statistical analysis of data obtained from database and processed by statistical package for social science version 20 (SPSS 20) program.

Study was carried out in Mubarak AL Kabeer university hospital of Kuwait.

Results

Statistically significant findings most of patients were male average 90% vs 10% were female with p value 0.04, 30% were hypertensive with p value 0.03, 20% were hyperlipidemic with p value 0.003, 10% had history of ischemic heart disease with p value 0.003.

Peak Troponin elevation was higher in Lysis group 126 ± 26 than pharmacoinvasive 96 ± 11 with p value 0.03, EF was better in pharmacoinvasive 49 ± 11 vs 45 ± 12 in Lysis with p value 0.001, mitral regurgitation was less in pharmacoinvasive with p value 0.001.

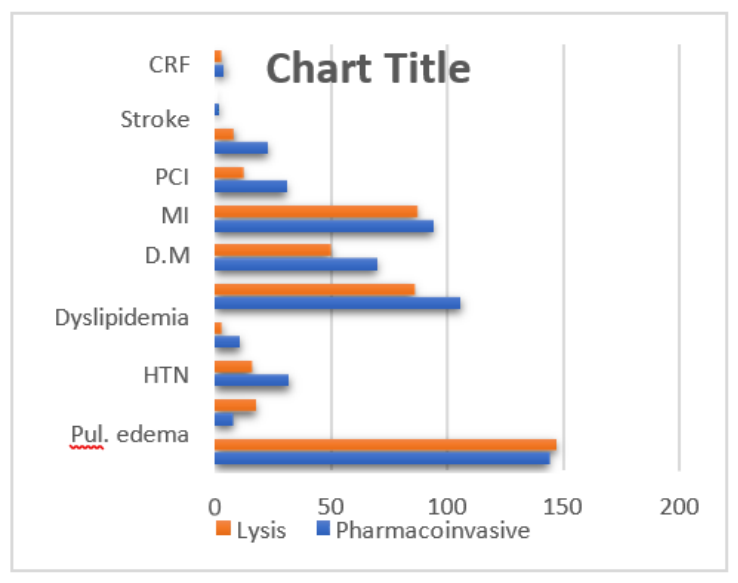

Figure 1: *Reperfusion strategy regarding history, presentation and risk factors.*

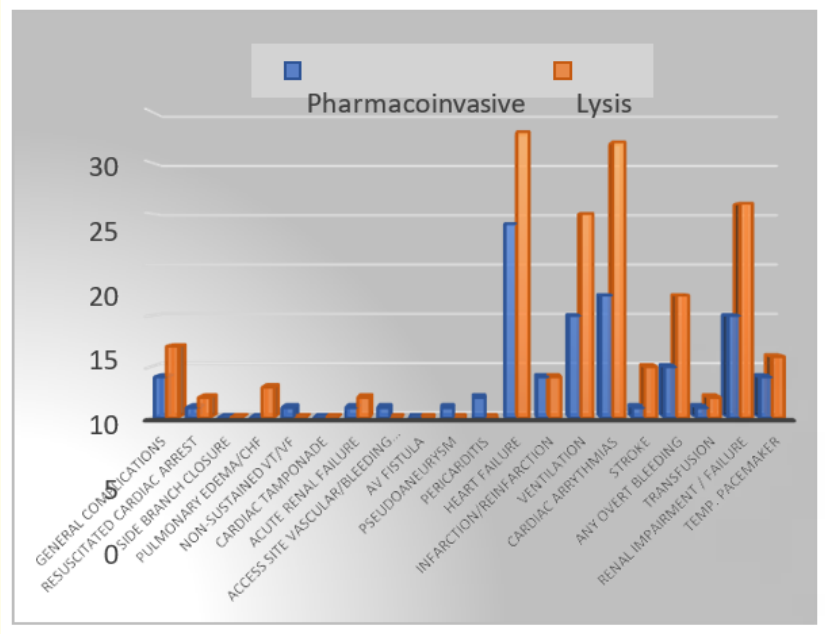

Figure 2: *Reperfusion complication information.*

Reinfarction was less in pharmacoinvasive 1% vs 1.5% in Lysis with p value 0.013, arrhythmias are less in pharmacoinvasive 4% vs 9% in Lysis with p value 0.0001, stroke was more in lysis 5% vs 1% in pharmacoinvasive with p value 0.006, overt bleeding was higher 4% in lysis vs 1.8% in pharmacoinvasive with p value 0.0001.

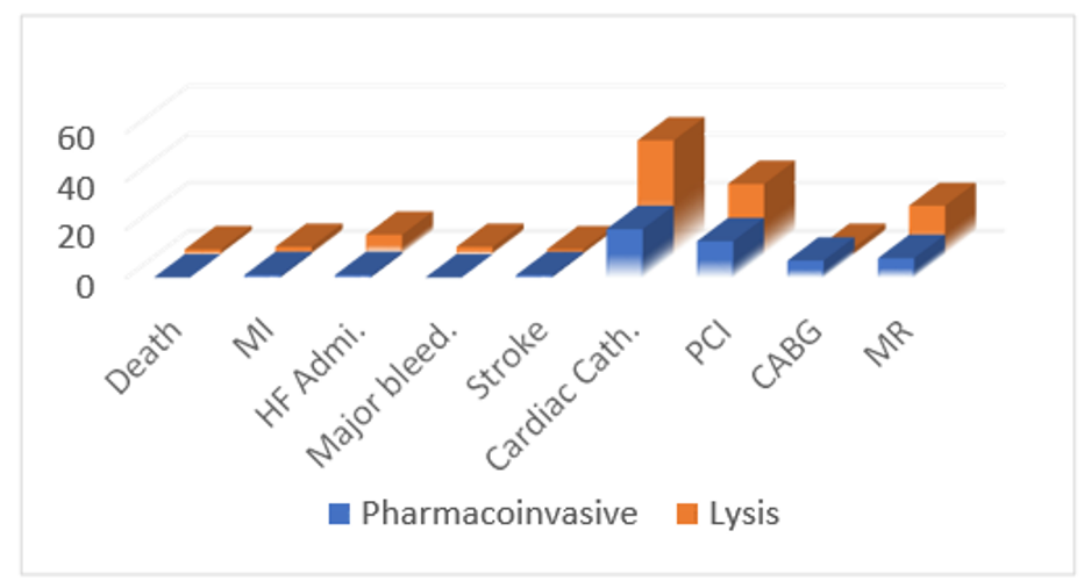

Figure 3: *Complication on follow up after 1 month.*

During follow up HF 0.3% in pharmacoinvasive vs 2.5% in Lysis with P value 0.02, Major Bleeding 0% in pharmacoinvasive vs 1% in Lysis with P value 0.07, Stroke 0.3% in pharmacoinvasive vs 0.5% in Lysis with P value 0.0001, need for coronary angiography 6.5% in pharmacoinvasive vs 15.6% in Lysis with P value 0.0001 and PCI 4.5% in pharmacoinvasive vs 9.5% in Lysis with P value 0.0001. Mitral Regurgitation was significantly higher in Lysis with p value 0.05 and EF was higher in pharmacoinvasive with p value 0.05.

Discussion

Two randomized studies, GRACIA-2 10 and WEST 16, reported comparable efficacy and safety of the pharmacoinvasive strategy versus primary PCI [6] but these findings could not be considered as being conclusive since the total number of patients randomized in both studies was very low (n = 416).

The Strategic Reperfusion Early After Myocardial Infarction (STREAM) study investigated whether prompt thrombolysis at first medical contact, followed by timely angiography or rescue PCI in patients with acute ST-segment elevation myocardial infarction (STEMI) presenting within 3 hours not able to undergo primary PCI within 60 min, is an appropriate and effective reperfusion treatment (pharmacoinvasive strategy) [14].

In our study we found that arrhythmia, bleeding, mitral regurgitation and other complications were significantly higher in Lysis group, but heart failure with presentation was higher in pharmacoinvasive group as patients with heart failure were directed to that strategy but during follow up heart failure was higher in Lysis group, EF was significantly higher in pharmacoinvasive group.

Variable	Number of patients	+ve for ischemia	-ve for ischemia
Submaximum stress ECG on 5th day	200	110	90
	66%	36.66%	30%
Stress MPI	100	90	10
	33.3%	30%	3.3%
Patients had coronary angiography	Total Number	Had PCI Done	
	290	121	
	96.6%	40.3%	

Table: *Risk stratification in lysis group.*

In Lysis group patient risk stratification was carried out and follow up for 12 months significant number of patients had residual ischemia detected as > 5% defect in stress MPI or +ve Exercise ECG and so went for coronary angiography, PCI and CABG. Reinfarction was significant higher Lysis group.

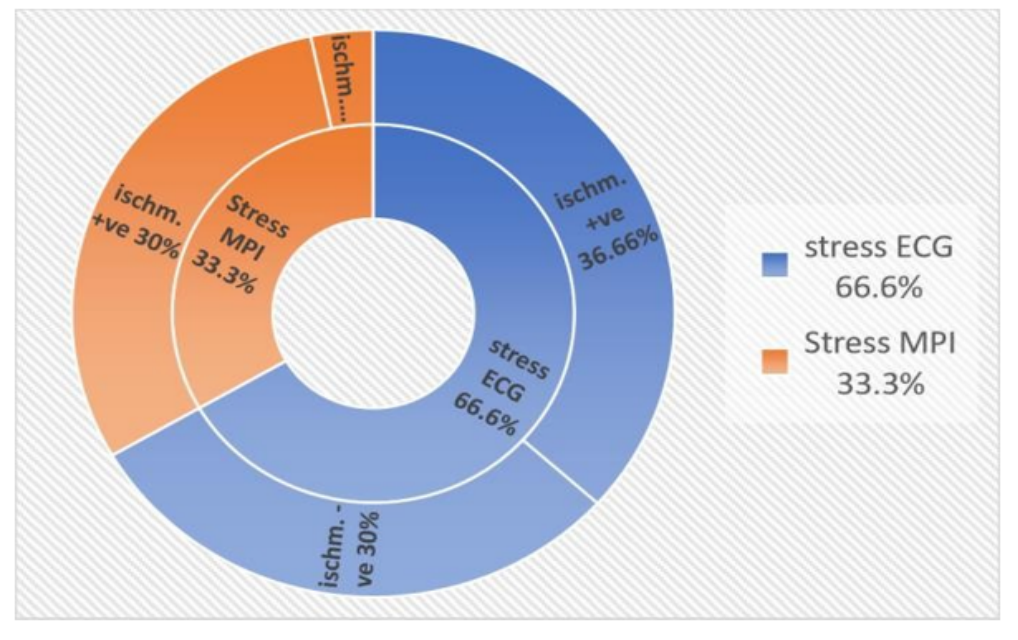

Figure 3: *Complication on follow up after 1 month.*

Conclusion

The highest incidence regarding age group affected was the age between 45 and 65 with increase incidence in the age group below 45 in comparison to before due to bad life style and increase diabetes incidence. Lysis is associated with more myocardial damage in comparison to pharmacoinvasive which was proved by more troponin release and reduced LV EF. The best access site used was the radial

access with least complications and early mobilization although it was more difficult in cases with complicated and complex lesions like bifurcational lesions as smaller sheaths are used. The most common coronary with culprit lesions generally was the LAD, then RCA and LCX then LM. DES were the most common type of stents used to decrease incidence of instant restenosis and reinfarction less than BMS used most commonly in the Lysis group as a rescue PCI or CAG and PCI after risk stratification. Patients with cardiogenic shock or heart failure should be directed for 1ry PCI or at least pharmacoinvasive strategies. Pharmacoinvasive strategies significantly reduce the risk of reinfarction, need for CAG and PCI, arrhythmia, preservation of EF and death than Lysis group, the explanation why the heart failure admissions were in pharmacoinvasive strategy because from the start patients with heart failure or cardiogenic shock were directed for pharmacoinvasive strategy. Pharmacoinvasive strategy is at least is as effective as 1ry PCI and all patients presented with STEMI in non PCI capable centers should be transferred for coronary angiography within 3 - 24 hours and even achieved better culprit coronary artery patency. All patients presented with STEMI and treated with Lysis in centers far away from PCI capable centers and can't be transferred within 24 hours should go through risk stratification with submaximal exercise stress ECG on 5th day or fully symptom limited exercise stress ECG after a month or stress MPI or stress ECHO after the 5th day to assess the need for coronary angiography as more than half of patients treated with Lysis had positive tests of ischemia and had coronary angiography requiring PCI. PCI capable centers should be available for 24/7 days with well-trained experienced teams for 1ry PCI of all STEMI patients and for shifted patients who had lysis and keep thrombolytic therapy on the shelf and in rural areas away from 2ry and 3ry centers capable of PCI.

Recommendations

1. The total number of patients randomized were 600 it was better if more patients can be involved but it was a time limited study.
2. PPCI. In regions with optimal STEMI networks, but with low density of PCI-capable hospitals, our study supports the guidelines-recommended option of a pharmacoinvasive approach for early presenters, with administration of thrombolytics followed by expedite interhospital transfer.
3. Hospital fibrinolysis followed by routine angiography within 6 to 24 hours in stable patients or immediate "rescue PCI "in the remainder is a reasonable alternative to PPCI when delayed by more than 1 hour. Although this study was carefully performed, several issues deserve clarification so that the reader can better put the results in perspective.
4. Our study supports the guidelines-recommended option of a pharmacoinvasive approach for early presenters, with administration of thrombolytics followed by expedite interhospital transfer.
5. On the contrary, avoidance of thrombolysis and rapid transfer to a PCI facility remains advisable for patients presenting later.
6. The best access site used was the radial access with least complications and early mobilization although it was more difficult in cases with complicated and complex lesions like bifurcational lesions as smaller sheaths are used.
7. DES were the most common type of stents used incidence of instant restenosis and reinfarction less than BMS used most commonly in the Lysis group as a rescue PCI or CAG and PCI after risk stratification.
8. Patients with cardiogenic shock or heart failure should be directed for 1ry PCI or at least pharmacoinvasive strategies.
9. Pharmacoinvasive strategy is at least is as effective as 1ry PCI and all patients presented with STEMI in non-PCI capable centers should be transferred for coronary angiography within 3 - 24 hours and even achieved better culprit coronary artery patency.
10. All patients presented with STEMI and treated with Lysis in centers far away from PCI capable centers and can't be shifted within 24 hours should go through risk stratification with submaximal exercise stress ECG or fully symptom limited exercise stress ECG after a month or stress MPI or stress ECHO after the 5th day to assess the need for coronary angiography as nearly quarter of patients treated with Lysis had positive tests of ischemia and had coronary angiography requiring PCI.
11. PCI capable centers should be available for 24/7 days with well trained experienced teams for 1ry PCI of all STEMI patients and for shifted patients who had lysis and keep thrombolytic therapy on the shelf and in rural areas away from 2ry and 3ry centers capable of PCI.

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