FACTORS INFLUENCING THE OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

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CERTIFICATE

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DECLARATION

I solemnly declare that the dissertation entitled " ***FACTORS INFLUENCING THE OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION*** *" is done by me at Madras Medical College and Hospital, during 2005-2006 under the guidance and supervision of* ***Prof.K.CHANDRA, M.D.*** *This dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of* ***M.D. DEGREE IN GENERAL MEDICINE (BRANCH I)***.

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CONTENTS

INTRODUCTION

Coronary heart disease has been defined as "impairment of heart function due to inadequate blood flow to the heart compared to its needs, caused by obstructive changes in the coronary circulation to the heart"[1].

It is the cause of 25-30% of death is most of the industrialised countries. In India also it is a major public health problem.

It is aptly called by WHO as the modern epidemic. The increasing incidence of coronary heart disease may be a reflection of increased longevity, adoption of high-fat diet based on meats, decreased exercise, modern life style, made possible by increasing affluence.

It is not surprising to note that Sir William Osler devoted only a few pages in his text book of medicine, published in 1892, to the discussion of Acute Myocardial Infarction.

It was the brilliant work of Herrick in 1912, who performed autopsy on Acute Myocardial Infarction patients that putforward the new concept of thrombotic occlusion of coronary artery as the cause of downstream necrosis of heart muscle.

Definitive proof for the above said concept came from angiographic studies performed during the early hours of the acute coronary event[2].

This prompted scientists to systematically test the thrombolytic strategies to treat Acute Myocardial Infarction, opening that new era of thrombolytic therapy in Acute Myocardial Infarction.

Scientists have developed many effective thrombolytic drugs like, streptokinase, recombinant tissue plasminogen activator (rt PA), Reteplase (rPA), urokinase, APSAC (Anisoylated plasminogen streptokinase activator complex) etc.

Evidence for the use of thrombolytic therapy came from large multi centre studies[3]. GISSI and ISIS-2 confirmed reduction in mortality with the early use of streptokinase[5]. ISAM (intravenous streptokinase in Acute Myocardial Infarction study group) also stands as a proof of efficacy of thrombolytic drugs to reduce mortality.

Success rate of thrombolysis and thus the overall reduction in mortality is different among different agents used[6]. The GUSTO-1 trial showed a 30 day mortality of 6.3% for accelerated t-PA versus 7.4% for streptokinase with intravenous heparin.

But because of the prohibitive cost of tPA, streptokinase became the sheet anchor for thrombolytic therapy in Govt. General Hospital. Thrombolytic therapy has revolutionized the management of Acute Myocardial Infaction[7]. GUSTO angiographic substudy showed a success rate of 54% at 90 minutes using IV streptokinase and Heparin.

Thrombolytic therapy has been consistently proven to reduce the mortality and morbidity. Inspite of this it has been recognised that thrombolytic therapy has failed in a significant population. There is lot of room for improvement. We need to identify the factors that are responsible for failure of thrombolysis.

In this background, we decided to look into our own patients who receive streptokinase for Acute Myocardial Infarction, in the coronary care unit of Govt. General Hospital.

AIM OF STUDY

1. To find out the overall success rate of thrombolysis in the coronary care unit of Govt. General Hospital.

2. To find out whether the following parameters influence the outcome of thrombolysis.

    a. Age

    b. Sex

    c. Time of Streptokinase administration

    d. Pre-infarction angina

    e. Alcohol intake

    f. Smoking status

    g. Pre existing systemic hypertension

    h. Diabetes mellitus

    i. Location of Myocardial infarction

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

Although the anginal syndrome was described in the 1770's, it was not until 1912 that Sir James B.Herrick described Acute Myocardial Infarction.

In the landmark paper by Herrick, he wrote "The clinical manifestation of coronary obstruction will evidently vary greatly... depending on the size, location and number of vessels occluded. The symptoms and end results must also be influenced by blood pressure, by the condition of myocardium not immediately affected by obstruction, and by the ability of the remaining vessels to properly carryout their work, as determined by their health or disease"[8].

Most of his observations hold good even after 90 years.

Levine published a book on coronary thrombosis in 1929.

Only after the classic angiographic study of De Wood and colleagues from Spokane, who demonstrated thrombotic occlusion of coronary arteries in 87% of patients within 4 hours of symptom onset, medical community was convinced that the proximate cause of Acute Myocardial Infarction is coronary thrombosis[2].

PATHOPHYSIOLOGY OF ACUTE MYOCARDIAL INFARCTION

Coronary atherosclerosis is the underlying substrate in nearly all patients with Acute Myocardial Infarction.

The hallmark of atherosclerotic coronary artery disease is the fibrous plaque. It has a fibrous cap, composed of smooth muscle cells and matrix, which covers a variable amount of lipid core, cell debris, macrophages, which may be filled with lipid, often intermixed with variable number of T lymphocytes.

Plaques are not uniform in their constitution. Plaque heterogeneity is important in that which plaque is prone to fissuring or cracking cannot be determined even by angiography.

Those plaques which have a thin fibrous cap, more number of macrophages and T cells, more lipid content and less number of smooth muscle cells are prone to rupture[9]. Smooth muscle cells appear to protect against plaque disruption, whereas macrophages and mononuclear cells, by elaborating proteolytic enzymes like matrix metallo proteinase, stromelysins, elastases tend to weaken the fibrous caps[10]. Mononuclear cells also elaborate monocyte chemotactic protein (MCP-1) which recruits more number of macrophages and mononuclear cells into the fibrous cap.

WHAT PRECIPITATES PLAQUE DISRUPTION?

It is now proved beyond doubt that Acute Myocardial Infarction occurs as a result of disruption of a coronary artery plaque at a site of high density of inflammatory cells namely macrophages and T lymphocytes. Thus Acute Myocardial Infarction can be thought of as resulting from acute exacerbation of a chronic inflammatory response. Precipitating factors work by exacerbating that inflammatory response and/or increasing the physical forces impinging on a coronary artery lesion weakened by inflammation, leading rupture.

1. Infections

An association has been noted between Acute Myocardial Infarction and antecedent mild respiratory syndromes.

Increased antibody titre to *C.pneumoniae* have been associated with increased risk of Acute Myocardial Infarction[11].

Evidence exists for the presence of C.pneumoniae in atherosclerotic lesions.

2. Emotional of Environmental Stress

Distressing or changing life events reportedly occur with increased frequency in the months preceding a Myocardial Infarction[12,13]. It is apparent that any acute stressful event / Intervention can precipitate Acute Myocardial infarction in a patient with active, susceptible coronary atherosclerotic lesions.

3. Circadian and seasonal variation

Peak incidence of Acute Myocardial Infarction is between 6 a.m. and noon. Underlying mechanism is thought to be the diurnal variation in sympathetic nervous system activity and thrombotic tendency.

In the morning hours there is an enhanced platelet aggregability and a trough in intrinsic fibrinolytic activity. Other factors contributing are the increased heart rate and increased coronary artery tone in the morning. PAI-I levels in blood is highest in the morning hours.

THROMBUS FORMATION

Thrombus formation at the site of plaque disruption is the fundamental pathophysiological mechanism of unstable angina and Acute Myocardial Infarction.

ROLE OF PLATELETS

This may be reviewed in 3 headings

1. Platelet adhesion
2. Activation with granular release
3. Platelet aggregation

Platelet Adhesion

Platelets adhere to the subendothelial collagen immediately. Glycoprotein Ib on the platelet membrane links with Von Willebrand Factor (vWF) in the subendothelial collagen. The membrane receptor complex Glyco protein IIb/IIIa bind a number of relevant protein, including vWF, fibrinogen and fibronectin.

Platelet activation and Aggregation

Activated platelets release a number of substances like serotonin, ADP, PDGF (Platelet derived growth factor), Thrombospondin, vWF etc.

PDGF plays a role in the proliferation and migration of smooth muscle cells after vessel damage. Released ADP binds to the specific receptors that change the conformation of GpIIb/IIIa complex so that it binds vWF, fibrinogen, fibronectin, thus linking adjacent platelet into hemostatic plug.

Coagulation cascade

Coagulation cascade plays a critical role in secondary hemostasis. Both intrinsic and extrinsic system take part in this process.

Role of Intrinsic pathway

Exposure of factor XII to subendothelium activates it to factor XII a, which inturn activates factor XI to XIa. XIa converts factor IX to activated factor IXa. Factor IXa along with factor VIII and calcium converts factor X to factor Xa. From here it is a common pathway for both systems.

Extrinsic pathway

This pathway is activated by interaction of tissue factor released from the damaged vessel wall and factor VII. Tissue thrombo plastin and factor VII activates factor X to Xa.

Factor Xa along with factor V and calcium ions converts prothrombin to thrombin. Thrombin has several functions the principal one being conversion of fibrinogen to fibrin. Thrombin also activates factor V, VIII; and XIII and stimulates platelet aggregation and secretion. Finally the fibrin polymer is stabilised by factor XIIIa resulting in an adherent thrombus.

SYSTEMIC FACTORS FAVOURING THROMBOGENESIS

1. Circulating catecholamines increases the platelet aggregability and thrombin generation

Smoking and emotional factors may be operating by increasing the catecholamines level in blood.

2. Elevated levels of homocysteine

Is toxic to endothelium, decrease the capacity of endothelium to make nitric oxide and induces endothelial dysfunction.

3. Diabetes Mellitus

Apart from accelerated atherosclerosis, platelet activity and coagulation are increased in diabetics suggesting that it is a prothombotic state. PAI-I levels are also found to be higher in diabetics.

4. Plasminogen Activator Inhibitor-I (PAI-I)

High levels of PAI-I levels are associated with increased risk of Acute coronary syndromes.

5. Elevated Apolipoprotein (a)

May serve as a competitive inhibitor of plasminogen and cause a prothrombotic stage.

6. Elevated fibrinogen and Factor VII

Is yet another risk factor for thrombosis. Interestingly both are found to be elevated in advanced age, obesity, hyperlipidemia, diabetes, smoking and emotional stress.

FIBRINOLYSIS

Fibrinolysis starts at the same time of thrombogenesis because elements of the fibrinolytic system are incorporated into the fibrin thrombus as it forms.

COMPONENTS OF FIBRINOLYTIC SYSTEM

1. Plasminogen and Plasmin

It is a single chain glycoprotein synthesised primarily by Liver. This is the precursor of the chief proteolytic enzyme plasmin. This conversion is facilitated by the binding of plasminogen to fibrin (thrombus). Plasmin is capable of proteolyzing not only fibrin but also other proteins like fibrinogen, coagulation factors V, VIII and extracellular matrix protein.

2. Plasminogen activators

Intrinsic activators of plasminogen are Kallikrein and factor XIIa, which are direct activators.

Extrinsic activators are tissue type plasminogen activator (t-PA), High molecular weight-two chain urokinase, and low molecular weight-two chain urokinase.

Exogenous activators

Are used therapeutically in Acute Myocardial Infarction. Streptokinase, APSAC, and staphylokinase belong to this category.

TISSUE TYPE PLASMINOGEN ACTIVATOR

t-PA is synthesized predominantly by vascular endothelial cells. It is a serine protease.

In the absence of fibrin tPA has little activity, therefore t-PA mediated activation of plasminogen in plasma is minimal. Both single chain and two chain form of t-PA have proteolytic activity that is enhanced several hundred fold in the presence of fibrin.

Free plasmin in the plasma is rapidly neutralised by α2-plasmin inhibitor where as fibrin-bound plasmin in protected from α2 - plasmin inhibitor.

UROKINASE TYPE PLASMIN ACTIVATORS

Urokinase is a serine protease that is synthesised in the kidney as well as in endothelial cells and initially released as a single chain urokinase or scu-PA.

Limited proteolysis by plasmin converts scu-PA to high molecular weight two chain urokinase (HMW tcUK). Like tPA, HMW tcUK also has relative fibrin selectivity but is enhanced only 10 times by the presence of fibrin.

ENDOGENOUS INHIBITORS OF FIBRINOLYSIS

These inhibitors of plasminogen activators and plasmin belongs to serpin family.

PLASMINOGEN ACTIVATOR INHIBITOR (PAI-I)

Sources

Endothelial cells, hepatocyte, smooth muscle cells and plateletes. It is stored in platelet α-granules from which it can be readily released upon platelet activation. PAI-I is the predominant inhibitor of t-PA and urokinase in human

plasma. It accounts for approximately 60% of the total plasminogen activator inhibitory capacity of plasma.

Thrombin induces PAI-I release from cultured human endothelial cells; so also endotoxin. During inflammatory states PAI-I levels are increased.

There is a diurnal variation in the circulating levels of PAI-I concentration which contribute to the clustering of Acute Myocardial Infarction during morning hours as well as morning resistance of thrombolytic therapy.

PAI-2 is found in placental tissue, where it plays a role in hemostasis.

ALPHA$_2$-PLASMIN INHIBITOR

This single chain glycoprotein directly inhibits plasmin. It is synthesized and secreted from hepatocytes. It is also stored in platelet α-granules. Alpha$_2$-plasmin inhibitor rapidly neutralises free plasmin in plasma. Where as fibrin bound plasmin is protected from its action. Alpha$_2$-Plasmin inhibitor is incorporated into fibrin clots through cross-linking by factor XIIIa thereby preventing uncontrolled or premature fibrinolysis.

PROTEIN C

Actions

It inhibits the release of PAI-I from endothelial cells.

Inactivates PAI-I, factor Va, VIIa.

Regulation of fibrinolysis

Net activation of plasminogen is the result of a delicate balance among zymogens; proteases; inhibitors and protease receptor on the cell surface.

Regulation and control of fibrinolysis occurs at several levels. Secretion of plasminogen activator and also plasminogen activator inhibitor from endothelium, enhancement of plasminogen activation by fibrin and plasmin inhibition by α-2 antiplasmin inhibition. In addition certain cell types such as endothelial cells, monocytes and platelets have receptors for plasminogen and plasminogen activators which when occupied enhance plasminogen activation and localise plasmin activity to the cell surface. By modulating the expression of these cell surface receptors, cellular regulation of fibrinolysis is possible.

ACUTE MYOCARDIAL INFARCTION

Symptoms

Prodromal symptoms are common, most of these symptoms are anginal or anginal like hours or days before the Acute cardiac event.

Retrosternal chestpain, associated with nausea, diaphoresis and dysponea is the cardinal symptom. Pain any radiate to medial aspect of left arm or to both arms. Other sites of radiation are neck or lower jaw, to epigastrium and back.

Duration should be more than 15 minutes. Occasionally presenting symptoms may be syncope, acute confusion, agitation, stroke or palpitations. Approximately 23% of Acute Myocardial Infarction go unnoticed by the patient because of lack of symptoms. Elderly can present as congestive cardiac failure without any history of pain.

Physical findings

Patient may have an anxious look. Sweating may be excessive.

Pulse: Normal or increased rate may be noticed. Persistent sinus tachy cardia beyond the initial 12-24 hours is predictive of high mortality rate.

In patients with inferior Acute Myocardial Infarction upto 60% of patients will be having bradycardia in initial hours.

Blood pressure

Hypotension can occur in inferior wall Acute Myocardial Infarction, with right ventricular involvement, and extensive anterior Acute Myocardial Infarction with cardiogenic shock. Hypertension may be a feature of anterior wall Acute Myocardial infarction.

JVP

Elevated JVP is a feature of major RV infarction. Prominent `a' wave may occur because of the decreased compliance of right-ventricle. Kussmaul sign may also be seen in right ventricular infarction.

PRECORDIAL EXAMINATION

Palpation

Palpation in the left lateral position may reveals a diffuse apical impulse rather than a localised impulse. Apex may be dyskinetic also. Decreased compliance of left ventricle may give rise to presystolic expansion of apex corresponding to the auscultatory S_4.

Auscultation

First and second heart sounds are often very soft because of decreased contractility, prolonged PR interval or both.

A fourth heart sound is often audible. Third heart sound is heard in probably only about 15-20% of Acute Myocardial Infarction patients.

Ischemia of posteromedial papillary muscle can manifest as a crescendo-decrescendo midsystolic murmur of mitral regurgitation. This murmur usually disappear after the first 12-24 hours if it is soft. But a loud or moderate intensity murmur may persist much longer or may be permanent.

DIAGNOSIS

Electrocardiography

Electrocardiographic criteria for diagnosing Acute Myocardial Infarction are the presence in the setting of chestpain of any one of the following.

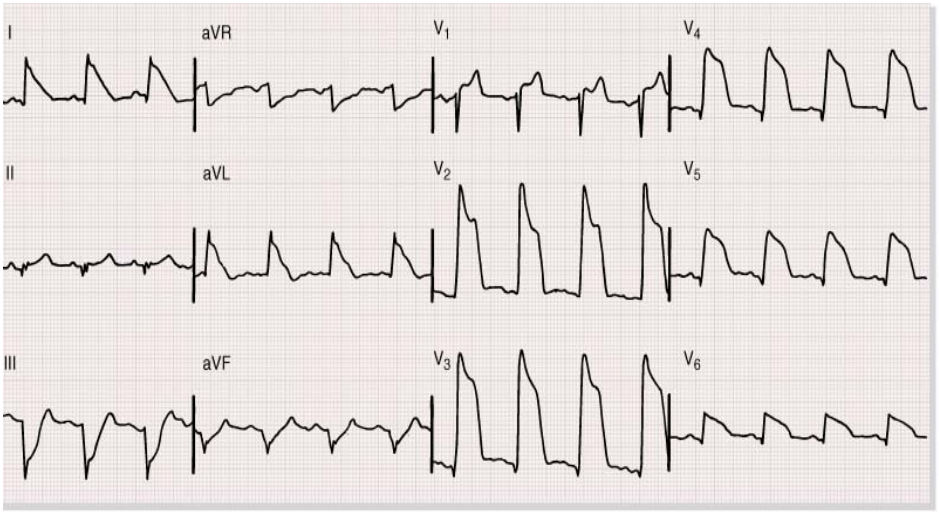
1. New or presumably new Q waves (atleast-30ms wide and 0.20 mv deep) in at least two leads from any of the following. (a) lead II, III, avF (b) Leads, V_1-V_6(c) leads I and aVL.

2. New or presumably new ST-segment elevation or depression ≥ 0.10mv measured 0.02 Sec. after J point in two contiguous leads of the above mentioned lead combination.

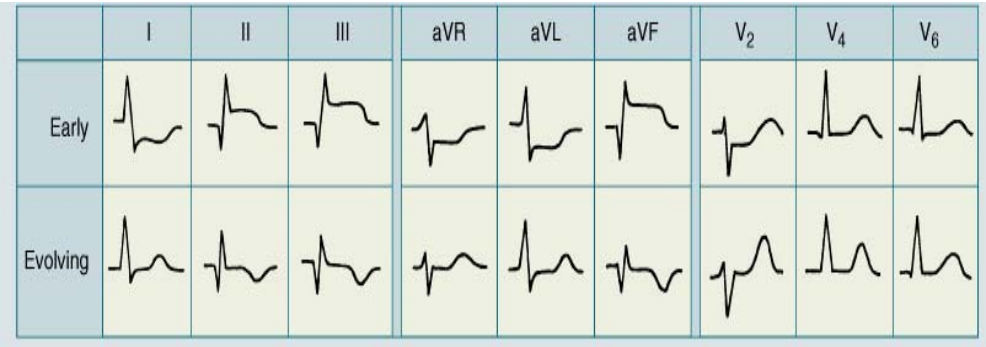
3. Complete LBBB

ELECTROCARDIOGRAPHIC ESTIMATE OF INFARCT SIZE

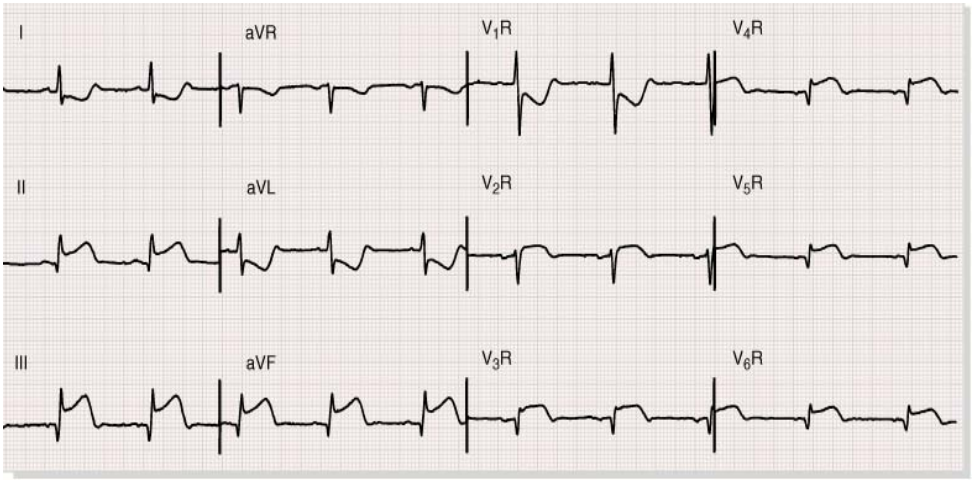
In general there is a direct relationship between the number of leads showing ST elevation and mortality. ST elevation in eight or nine lead is associated with a mortality of three to four times that of patients manifesting ST segment elevating in only two or three leads.



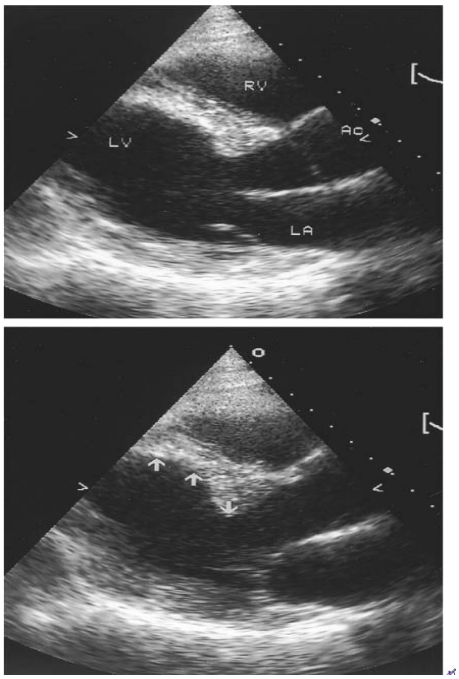
Hyperacute phase of extensive Anterolateral myocardial infarction



Acute inferior wall `q' wave infarctions



Acute Right ventricular myocardial infarction with Acute inferior wall myocardial infarction



Transthoracic Echo cardiography recorded in a patient with Acute anterior anteroseptal myocardial infarction. This tracing was recorded in a parasternal long axis view in diastole (Top) systole (Bottom). In the lower panel note the normal downward motion of the proximal portion of the ventricular septum and the dyskinesis of the more distal portion of the anterior septum (Upward Arrow). AO = Aorta, LA : Left atrium.

DIAGNOSIS OF RIGHT VENTRICULAR MI BY SURFACE ECG

ST-segment elevation in lead V_4R is the single most powerful predictor of right ventricular involvement in Inferior wall Myocardial Infarction.

A new classification of AMI based on electrocardiographic entry criteria with angiographic correlation.

Sl. No.	Categories	Anatomy of occlusion	ECG	30 day mortality	1 year mortality
1.	Proximal LAD	Proximal to first septal perforator	ST↑V_1-V_6, L_1, aVL fascicular or bundle branch block	19.6	25.6
2.	Mid LAD	Distal to first septal perforator, proximal to large diagonal	ST↑V_1-V_6, L_1, aVL	9.2	12.4
3.	Distal LAD or diagonal	Distal to large diagonal or of diagonal itself	ST↑ V_1-V_4, or ST↑ 1, aVL L_5-V_6	6.8	10.2
4.	Moderate to large inferior (posterior; lateral, right ventricular)	Proximal RCA or left circumflex	ST↑ II, III a aVF and any or all of following a. V_1-V_3, R, V_4-R b. V_5, V_6 or c. R>s in V_1, V_2	6.4	8.4
5.	Small inferior	Distal RCA or left circumflex branch occlusion	ST↑ II, III, a VF only	4.5	6.7

Based on GUSTO-I cohort population in each of the 5 categories, all receiving reperfusion therapy.

CLINICAL SIGNIFICANCE OF ABOVE MENTIONED SURGROUPS

Proximal LAD Acute Myocardial infarction is often referred to as the widow-maker Acute Myocardial Infarction. It is often associated with LAHB, RBBB, bifascicular block, LBBB or mobitz type II AV block. Cardiogenic shock is not unexpected.

MID LAD OCCLUSION

- No conduction disturbances
- Cardiogenic shock is less common, when shock is present one should consider prior Acute Myocardial Infarction or non cardiac causes like massive hemorrhage.

DISTAL LAD OCCLUSION

- Cardiogenic shock cannot results from this type of infarction perse.
- But as in the above forms apical hypokinesis and LV thrombus formation can occur.

SIGNIFICANCE OF RVMI

- Here the occlusion is in the proximal RCA prior to the origin of right ventricular branch.
- Mortality jumps from 6% in an isolated inferior wall Acute Myocardial Infarction to 25-30% when RV is involved.

LOCATING THE INFARCT RELATED ARTERY IN INFERIOR WALL ACUTE MYOCARDIAL INFARCTION[14]

- This is possible by looking at the ST depression in V_3 and ST Elevation in L III.

- ST depression in V_3 in maximal in LCX obstruction which produce less ST elevation in L III.

- On the contrary proximal RCA obstruction leads to maximal elevation in L III and lesser ST depression in V_3.

- By dividing ST depression in V_3 by ST elevation in L III a ratio V_3/III is obtained which, if <0.5 identifies proximal RCA occlusion; 0.5-1.2 distal RCA occlusion and >1.2 identifies LCX occlusion.

HEMODYNAMIC CLASS (KILLIP)

Killip classification is the most useful simple method to assign patients into hemodynamic classes.

Class I

No evidence of heart failure. 85% of Acute Myocardial Infarction patients present in this class.

Class II

Early evidence of heart failure manifested by S_3, bibasilar rales (less than 50% of lung fields). 10% of people present in this category.

Class III

Frank pulmonary edema

Class IV

Cardiogenic shock. Only 5% of people with Acute Myocardial Infarction presents in class III or IV category.

ENZYMATIC CRITERIA FOR DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

1. Serial increase then decrease of plasma MB-CK with change of >25% between any two values.
2. MB-CK>10-13 U/L or >5% of total CK activity.
3. Increase in MB-CK activity>50% between any two samples separated by at least 4 hours.
4. If only a single sample available, MB-CK elevation>two fold.
5. Beyond 72 hours, an elevation of troponin T or troponin I or LDH-I>LDH_2.

MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

Immediately begin continuous cardiac monitoring for patients with suspected ischemic type of chest pain and obtain intravenous access.

Administer morphine, oxygen, nitroglycerine, and aspirin (MONA) to patients without contra indication.

OXYGEN: INDICATIONS

Class I

1. Overt pulmonary congestion
2. Arterial O_2 desaturation (SaO_2<90%)

Class IIa

1. Routine administration of O_2 to all patients which uncomplicated Acute Myocardial Infarction during the first 2-3 hours.

Class IIb

Routine administration of supplemental O_2 to patients with uncomplicated Acute Myocardial Infarction beyond 3-6 hours.

ANALGESIA

1. Morphine sulphate 2-4 mg every 15 minutes IV till adequate analgesia is obtained.
2. In those with inferior wall Acute Myocardial Infarction vagolytic drug meperidine may be substituted.

NITROGLYCERIN

Class I :

1. Patients with ongoing ischaemic discomfort should receive sublingual Nitroglycerin (0.4mg).
2. Intravenous Nitroglycerin is indicated for releif of ongoing ischaemic discomfort, control of hypertension or Management of pulmonary congestion.

Class III :

1. Nitrates should not be administered to pations with systolic BP < 90 mmHg / RVMI.
2. Nitrates should not be administered to pts who have received sildenafil with in the last 24 hr.

Treatment should be initiated with a bolus injection of 12.5-25 μg and then followed by infusion by pump of 10-20μg/min with increases of 5-10μg every 5-10 minutes while assessing hemodynamic response. Control of symptoms is a major end point. In the case of high LV filling pressure, a decrease of 10-30% in PCWP is the objective. Or a decrease of 10% mean arterial pressure in normotensive and 30% decrease in hypertensive may be the objective. Systolic B.P. should be above 90mm Hg and heart rate should not exceed 110/mt

ASPIRIN

Aspirin 160-325 mg should be chewed as early as possible by all Acute Myocardial Infarction patients. Those with profound nausea, vomiting may be treated with aspirin suppositories (325 mg).

BETA BLOCKERS

Class I

1. Patients with out a contraindication to β-blocker therapy who can be treated within 12 hours of onset of infarction, irrespective of the administration of concomitant thrombolytic therapy.
2. Patients with continuing or recurrent ischemic pain.

3. Patients with tachyarrhythmia, such as atrial fibrillation with a rapid ventricular response.

Class IIb

1. Non Q wave Acute Myocardial Infarction.

Beta blockers interfere with the positive inotropic and chronotropic effects of catecholamines thus reducing afterload (blood pressure) and therefore myocardial O2 consumption.

It reduces ventricular ectopics, atrial fibrillation and nonfatal cardiac arrest.

Reduces frequency of progression of threatened infarction to completed infarction.

Reduces recurrent ischemia and infarction during first 6 weeks after initial events.

TRIAGE INTO ELECTROCARDIOGRAPHIC SUBGROUPS

Using 12 lead ECG patients are triaged into 3 groups.

1. ST- segment elevation
2. ST-segment depression (≥1 mm)
3. Non diagnostic

It is important to note that development of `q' waves is not taken into consideration as far as thrombolytic therapy is considered.

In one study 53% of patients presenting within one hour of symptoms already had Q waves. This early development of `q' wave appears to predict the infarct size but may not negate beneficial effects of fibrinolytic therapy on mortality or myocardial salvage. Q waves are often found to disappear following successful thrombolytic treatment.

Patients with ischemic type chest pain and ST segment elevation ≥ 1 mm in 2 contiguous leads have 45% sensitivity but 98% specificity for Acute Myocardial Infarction.

Patients with ischemic type of chest pain but normal or non-diagnostic ECGs or ECGs consistent with ischemic (ST-depression only) do not benefit from fibrinolytic therapy.

REPERFUSION STRATEGY

Reperfusion methods now in vogue are intravenous thrombolytic therapy, percutaneous transluminal coronary angioplasty and emergency coronary artery bypass grafting.

Thrombolytic therapy: Indications

Class I

1. ST elevation (greater than 0.1 mv in two or more contiguous limb leads and/or ≥0.2 mv in any two contiguous chest leads at anytime during the observation period). Time to therapy 12 hours or less since the onset of continuous chest pain, discomfort, causing hospital presentation. Age less than 75 years.

2. Left Bundle branch block (obscuring ST segment analysis) and history suggesting Acute Myocardial Infarction.

Class IIa

ST elevation, age 75 years or older.

Class IIb

1. ST elevation as above, time to therapy greater than 12 hours but less than 24 hours. Thrombolysis can be considered in the case of ongoing pain and marked ST-segment elevation although there is only a trend for benefit under these circumstances in clinical trials.

2. Blood pressure on presentation greater than 180mmHg of systolic and/or greater than 110 mm Hg diastolic with a high risk of Acute Myocardial Infarction. Here the risk of intracranial bleeding is high. Lowering the B.P. before administering Thrombolytics have been recommended but is of unproven benefit. If available coronary artery by pass grafting or primary PTCA should be considered.

Class III

1. ST segment elevation; time to therapy greater than 24 hours; ischemic pain resolved.

2. ST depression only

CONTRA INDICATIONS TO THROMBOLYTIC THERAPY

Sl.No.	Absolute	Relative
1.	Active internal bleeding	History of non hemorrhagic CVA in distant past with complete recovery
2.	Intracranial neoplasm or recent head trauma	Recent trauma or surgery >2 wks previously
3.	Prolonged, traumatic CPR	Active peptic ulcer disease
4.	Suspected aortic dissection	Hemorrhagic retinopathy
5.	Pregnancy	History of severe hypertension with diastolic BP>100
6.	History of hemorrhagic CVA or recent non hemorrhagic cerebrovascular accident.	Bleeding diathesis or concurrent use of anticoagulant
7.	Recorded blood pressure >200/120 mmHg	Previous treatment with SK or APSAC if being considered (doesnot apply to rtPA)
8.	Trauma or surgery that is a potential bleeding source within previous 2 weeks	
9.	Allergy to SK or APSAC if being considered	

HISTORY OF THROMBOLYSIS

Human blood has long been known to contain fibrinolytic activity. Well over 110 years ago Denys and Zimmerman observed that the fibrin of human blood obtained from wet cupping dissolved in 12 to 24 hours. Dastre coined the term fibrinolysis.

The property of spontaneous thrombolytic was used by Yudin of Russia who used blood from fresh corpses (who were previously healthy; but died of accidents) for transfusion.

In 1933 Tilet and Garner at the John Hopkin's medical school demonstrated that filtrates of broth cultures of certain strains of hemolytic streptococcus contained a substances capable of inciting rapid fibrinolysis of human plasma clots. They named it streptococcal fibrinolysin.

Christensen renamed it streptokinase in 1945. He demonstrated that SK activates an inactive precursor of a proteolytic enzyme, later found to be plasminogen.

Streptokinase was clinically used first in 1947 by Tillet and Sol Sherry in a young man who developed loculated bloody effusion in the left pleural cavity following pneumonectomy. The response was dramatic in that all the loculation were broken down and a lysed coagulum was drained.

First clinical trial for Acute Myocardial Infarction recruited 24 patients and they found those treated early after the onset of infarction did better than those treated late[16].

But only in 1977 FDA approved streptokinase and urokinase for clinical use in USA-which opened the new era of reperfusion therapy.

THROMBOLYTIC DRUGS

Non Fibrin Selective agents

Streptokinase

It is a single chain polypeptide that lacks the serine residue required for enzymatic activity but it can activate plasminogen to plasmin after forming an equimolar complex with it.

Since it is not fibrin selective, extensive conversion of circulating plasminogen to plasmin occurs with subsequent depletion of fibrinogen, plasminogen and factors V and VIII from blood stream.

The accumulation of fibrin degradation products, depletion of circulating $\alpha 2$ antiplasmin, and hyperplasminemia that occur constitute a systemic lytic state.

Circulating half life of SK is 18-25 minutes. However depletion of fibrinogen to less than 50% of baseline values persists for approximately 24 hours.

Antibodies to SK appears quickly and reaches high value by 5 days and remains above baseline for upto 30 months. So repeated administration is not recommended.

ADVERSE EFFECTS

- Hypotension is the most common which ranges from 10-40% of administrations.
- Allergic reactions reported included fever, chills, urticaria, rash, flushing and muscle pain.
- Minor bleeding can occur especially from vascular puncture and access site. Manual compression for 30 minutes or until bleeding stops is usually effective.
- Intracranial bleeding is the dreaded complication.
- Total stroke incidence in GISSI/international trial was 0.9% In ISIS 3 trial it was 1%.

MODE OF ADMINISTRATION AND DOSAGE

1.5 million units of SK is administrated over 1 hour is the standard regimen. More rapid administration can lead to hypotension and should be avoided.

Urokinase

Is an endogenous trypsin like enzyme. It is a direct plasminogen activator. It is present in urine and occurs in two forms in blood and tissues as a high molecular weight form and a low molecular weight form. It is non fibrin selective, producing a systemic lytic state similar to that produced by SK. It is non immunogenic and can be administrated as an intravenous bolus or by infusion. The recommended dose for Acute Myocardial Infarction, is 1,500,000 unit bolus followed by 1,500,000 units given over 90 minutes.

RELATIVELY FIBRIN SELETIVE AGENTS: TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)

tPA is an endogenous serine protease synthesized and secreted by human vascular endothelium and numerous other types of cells. Cloning and expression of tPA gene in E.coli lead to the large scale production of recombinant tPA since 1984.

Plasma T½ is only 5 minutes but fibrinolytic activity persists on and within clots for 7 hours. rt-PA is metabolised by liver. Plasminogen activator inhibitor-I (PAI-I) rapidly inactivates t-PA. Infused rtPA rapidly saturates PAI-I levels seen in blood. Other slow inhibitors of rtPA in blood are CI esterase inhibitor and α2-antiplasmin.

rtPA is relatively fibrin specific, it has an affinity for fibrin bound plasminogen. But rtPA is also capable of depleting blood fibrinogen levels to as low as an 50% and elevating fibrinogen degradation products. It has no immunogenicity.

ADVERSE EFFECTS

Incidence of intracranial hemorrhage and stroke is slightly higher with rtPA than with SK. In GISSI/international trail it was 1.2%. In ISIS-3 it was 1.4% (total stroke incidence).

DOSAGE

Front loaded regimen is a associated with a 91% patency rate at 90 minutes and it is now approved by FDA. Here 15 mg IV bolus followed by 50 mg IV infusion over 30 minutes followed by 35 mg over next 60 minutes is given.

EFFECTS OF THROMBOLYTIC THERAPY ON MORTALITY

Thrombolytic therapy reduces 35 day mortality by 21% compared with conventional therapy.

When used within the first hour of symptoms it saves 34 lives per 1000 treated patients but it is reduced to 16 lives per 1000 treated cases when used 7-12 hours after the onset of symptoms.

CHOICE OF DRUG

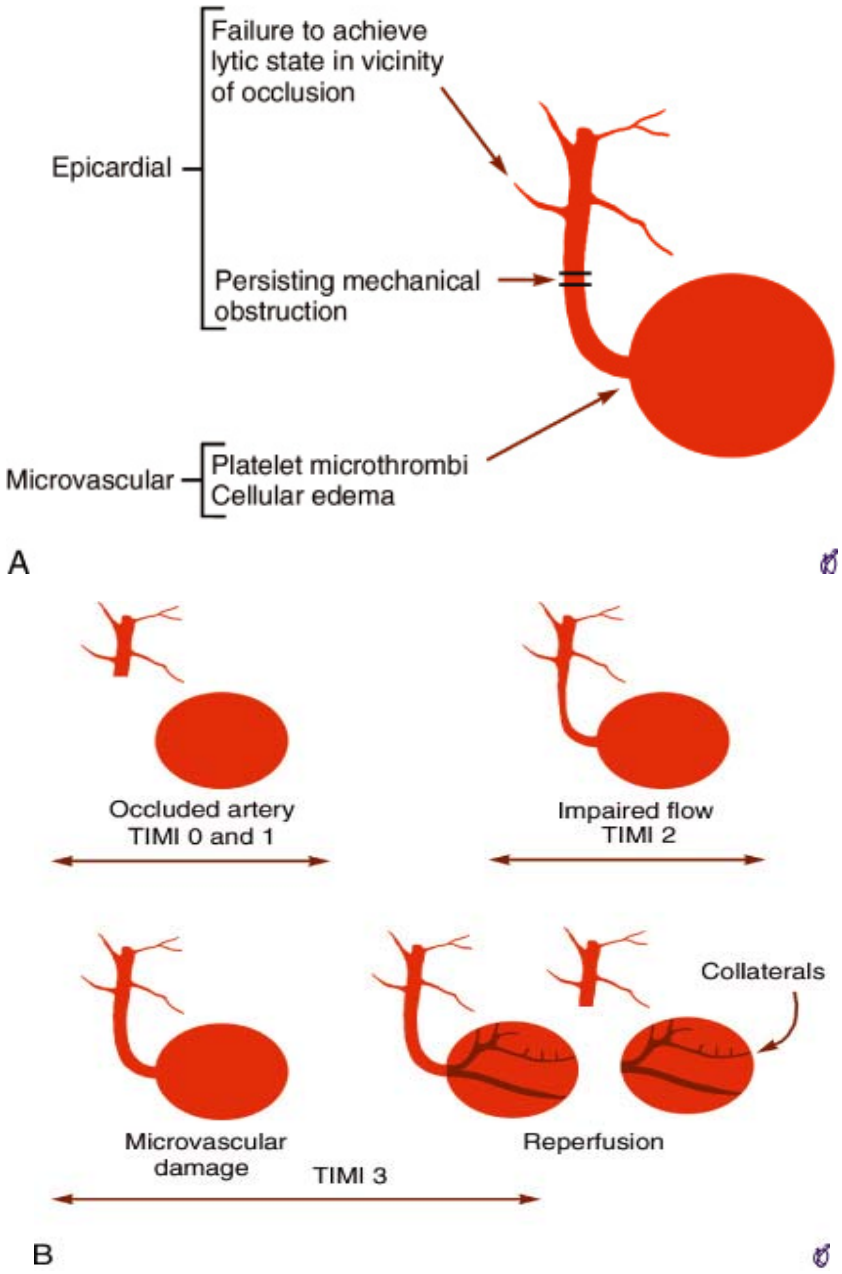
(30 day mortality rate from GUSTO Trial)

Sl.No.	Regimen	Mortality %
1.	SK and subcutaneous heparin	7.2%
2.	SK and intravenous heparin	7.4%
3.	Accelerated rt-PA and intravenous heparin	6.3%
4.	Combination rt-PA and SI without heparin	7.0

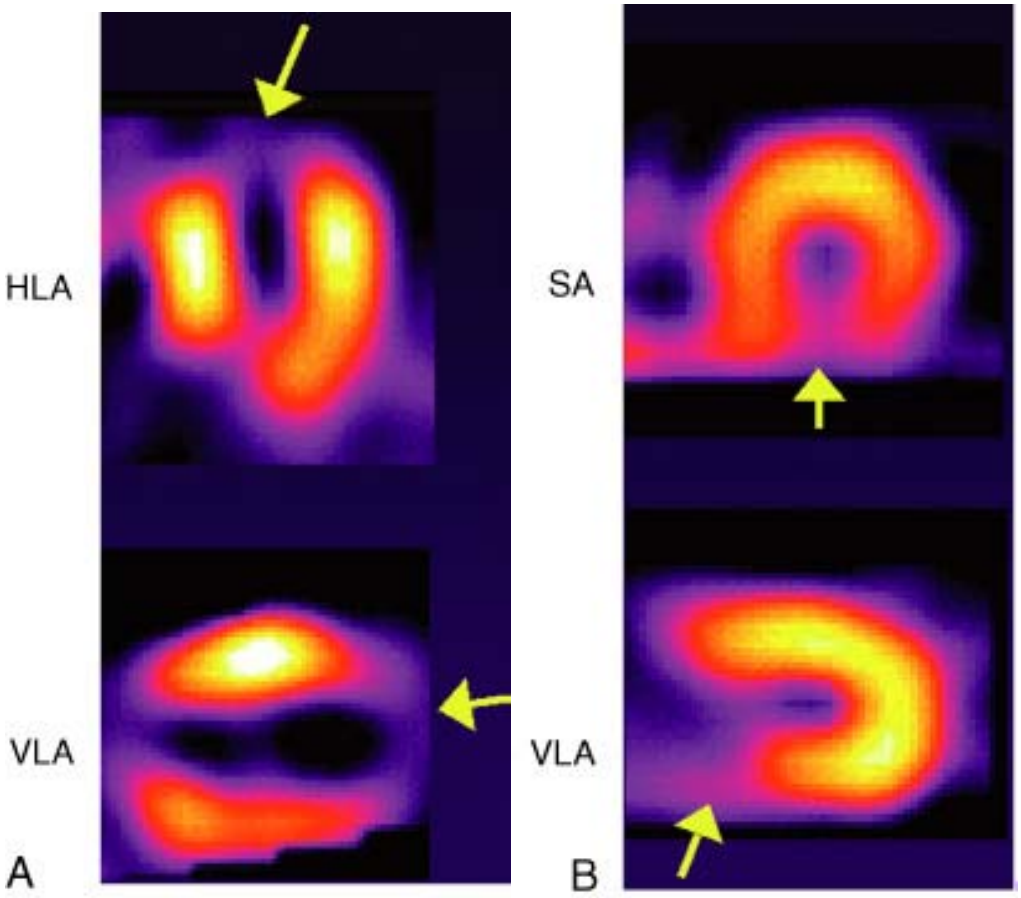
14% reduction in mortality rate was achieved with accelerated rt-PA regimen versus SK strategies (p=0.001).

The 1 year followup of GUSTO-I trail showed that the 1% lower mortality rate compared with SK was maintained, which provided further evidence that rt-PA is more effective than SK.

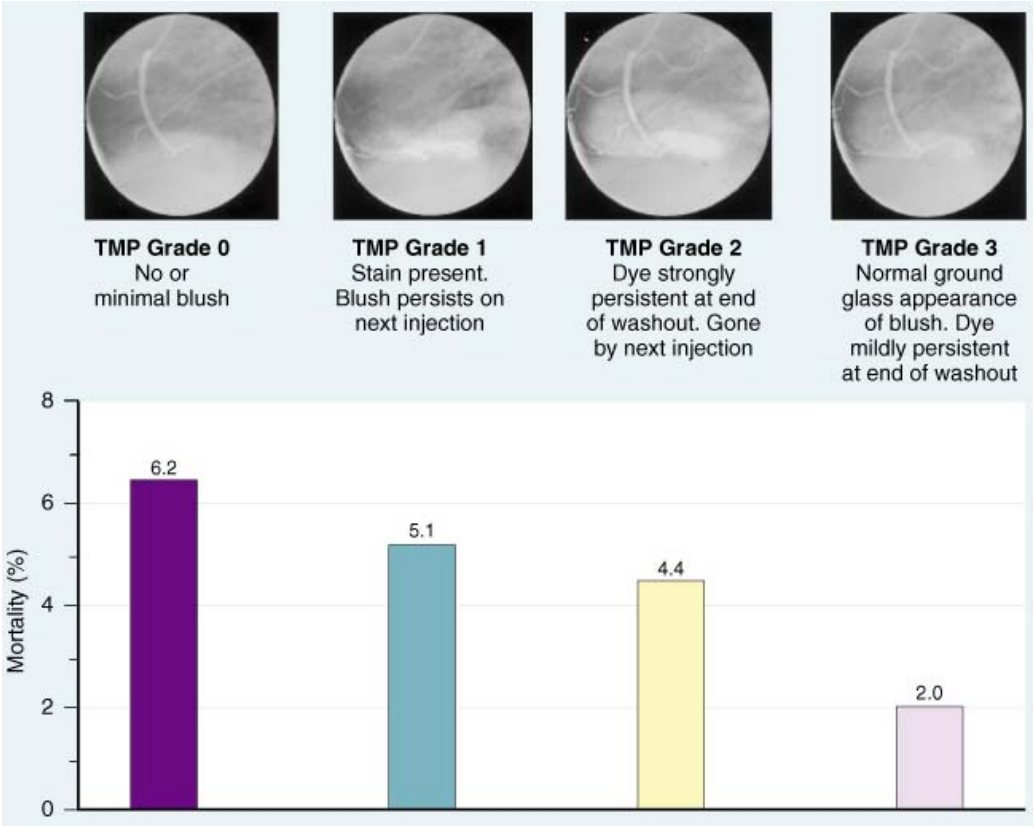
Alteplase (rt-PA) may have the greatest benefit in patients with large infarction and appears to pose a low risk of intracranial haemorrhage in younger patients who present early. SK appears to provide greater benefit in older patients with a smaller amount of myocardium at risk who present later and those with a greater risk to intracranial haemorrhage.



Patterns of response to fibrinolysis : A: failure of epicardial reperfusion can occur due to failure to induce a lytic state or due to mechanical factor at the site of occlusion failure ofmicrovascular reperfusion is due to a combination of platelet microthrombi followed by endothelial swelling and myocardial edema "No reflow" B : Fibrinolysis may fail due to persistent occlusion of the epicardial infarct related artery (TIMI grade 0&1) patency of an epicardial artery in the presence of impaired (TIMI grade 2) flow, or microvascular occlusion in the presence of angiographically normal flow (TIMI grade 3) successful reperfusion requires a patent artery with an intact microvascular network, conversely, reperfusion may occur despite an occluded epicardial artery due to the presence of collateral arteries.



SPECT perfusion images demonstrating myocardial infarction in different locations. A. An apical infarction (arrow) in the horizontal long axis (HLA) and vertical long axis (VLA) views. B. Inferior Myocardial infarction in the short axis (SA) and Vertical long axis (VLA) views. In both studies the severity of the defects suggests minimal myocyte viability with in those territories.



TMP Grade 0 : No or minimal blush. 1. Stain present blush persists on next injection. 2. Dye Strongly persistent at end of wash out Gone by next injection. 3.Normal ground glass appearance of blush. Dye mildly persistent at end of washout. Relation between TIMI, myocardial perfusion grade and mortality. TIMI myocardial perfusion grade 0 or no perfusion of myocardium is associated with highest rate of mortality if the stain of myocardium present (Grade 1). Mortality is also high. A reduction in mortality is seen if the dye enters the micro vasculature but is still persistent at the end of wash out phase (Grade 2). The

lowest mortality rate is observed in those patients, with normal perfusion (Grade 3) where the dye is minimally persistent at the end of wash out phase.

PATENCY OF INFARCT RELATED ARTERY

Angiography assessment

TIMI grading is used to assess the angiographic patency[17].

Grade of flow	Definition
0	Complete occlusion
1	Penetration without perfusion. Coronary bed distal to occlusion fails to opacify completely
2	Partial perfusion. Full but slow opacification of coronary bed distal to occlusion
3	Complete perfusion

The 90 minutes patency rate from Gusto angiographic substudy was as follows; accelerated tPA 81% (54% grade III flow), combination treatment tPA-SK 73% (38% grade 3 flow), SK -iv heparin 60% (32% grade III flow), SK-subcutaneous heparin 54% (29% Grade 3 flow)[6,7].

This clearly shows rt-PA is more effective than SK in bringing out a successful thrombolysis.

CLINICAL DETECTION OF REPERFUSION

Sudden disappearance of chest pain is associated with successful thrombolysis. But this is difficult to assess in the CCU set up when most of the patients receive opioid analgesics.

ECG: A BETTER PREDICTOR OF PERFUSION AT MICROVASCULAR LEVEL

Recent studies have suggested that achievement of TIMI grade 3 flow in infarct related artery is not in and of itself indicative of successful myocardial reperfusion[18].

Myocardial contrast echocardiography was shown that even in the presence of normal epicardial flow after PTCA, impaired myocardial perfusion at tissue level can occur and is associated with poor recovery of LV function.

Resolution of ST-Segment elevation on the surface ECG correlates closely with findings at contrast echocardiography[19]. Less than 50% resolution of ST-Segment elevation in the worst lead and no accelerated idioventricular rhythm has a sensitivity of 81%, specificity of 88%, positive predictive value of 87%, negative predictive value of 83% and overall accuracy of 85% in predicting <TIMI 3 flow in infarct related vessel[20].

PROGNOSTIC SIGNIFICANCE OF ST RESOLUTION

James A. de Lemos *et al.* reported than 30 days mortality was 2.4% among patients who attain >70% ST resolution at 90 minutes where as it was 8.1% in those with <30% ST resolution[21].

Early and stable ST segment recovery is also associated with improved infarct zone wall motion at 48 hours[22].

FACTORS INFLUENCING THE SUCCESS OF THROMBOLYSIS

1. Time interval between Pain onset to initiation of thrombolytic therapy.

This is the most important variable affecting the success of thrombolysis.

As time window increases not only more and more myocardium gets necrosed but also the thrombus gets organised and become more resistant to lysis.

2. Structure of Thrombi

Thrombi rich in platelets are more resistant to lysis than fibrin rich thrombi.

3. Circadian fluctuations

A morning resistance to thrombolytic therapy was observed by Braunwald *et al.*[23] where as better success rate of thrombolysis was found by E Gold hammer *et al*. when SK was administered between 16.00-20.00 hours.

4. Preinfarction Angina

Patients with acute myocardial infarction who have intermittent infarct related pain or unstable angina in the seven days preceding the infarction have faster coronary artery perfusion and smaller infarcts after thrombolytic therapy than patients without preinfarction angina[24].

This may be an additional mechanism for the better prognosis in these patients, the other proposed mechanism being ischemic preconditioning.

5. Sex

Eventhough mortality is high among women who develop Acute Myocardial Infarction; compared to men the rate of induced of coronary patency with thrombolytic drugs are comparable in women.

Menstruation is not a contra indication for thrombolytic therapy because menstrual bleeding is related more to sloughing of tissue than active bleeding.

6. Cognitive heart failure and cardiogenic shock

No significant reduction in mortality occurs when Killip class IV patients an treated with SK. This may partly be due to low rate of adequate recanalization.

7. Elderly patients

Risk of hemorrhagic complications are high in those aged above 75 years. But the relative benefit seen with coronary thrombolysis is greatest for the elderly.

REPERFUSION INJURY

Refers to detrimental metabolic, functional or structural consequence of restoring coronary flow that might be reduced, avoided or reversed by modifying the condition of reperfusion.

LETHAL REPERFUSION INJURY

Refers to the death of myocardium that were still alive at the initiation of reperfusion. The mechanisms underlying the lethal reperfusion injury may be.

1. Ischemia causes an intracellular osmotic load of accumulated catabolites like lactate inside the cardiacmyocytes leading to an increase in the osmolality of cytosol. After reperfusion enough plasma water bathes these cells. Osmotic diffusion of water into the cell causes rupture of cells.

2. Cellular acidosis increases the intracellular excess of calcium, via $Na\text{-}H^{+}$ exchange and $Ca2\text{-}Na^{+}$ exchange. This calcium overload causes myofibrillar hypercontraction and rupture of sarcolemma.

3. Excess free radical formation may damage the myocyte structure including sarcolemma.

NON LETHAL REPERFUSION INJURY

Stunning

It is a form of reversible post ischemic contractile dysfunction.

Reperfusion arrhythmia

Is also considered a form of non lethal reperfusion injury.

EFFECT OF REPERFUSION ON INFARCT REPAIR

Clinical studies has revealed that thrombolytic reperfusion performed more than 6 hours after symptom onset could still improve ventricular function and survival even though myocardial salvage need not be responsible for this effect.

This has been attributed to faster healing, reducing the complication like infarct expansion, aneurysm, as well as cardiac rupture.

Reperfusion gives inflammatory cells access to the infarcted region, with resultant degradation of deed cells which must be removed in order for repair to occur.

REPERFUSION THERAPY: PTCA

Coronary angioplasty provides higher rates of TIMI grade III flow, is successful is >90% of patients and is associated with lower rates of reocclusion and post infarction ischemia than fibrinolytic therapy.

But it is unlikely that many centres will have the required facilities and experience to perform PTCA on a regular basis.

When possible triage of patients at high risk for mortality or severe LV dysfunction with signs of shock, pulmonary congestion, heart rate >100 bpm; SB<100 mmHg to facilities capable of performing cardiac catheterisation and rapid revascularisation should be considered. For patients less than 75 years it is a class I indication. When available without delay, consider primary PTCA for patients who are reperfusion candidates but have a risk of bleeding that contraindicates use of fibrinolytic therapy (Class IIa).

RECURRENT CHEST PAIN

The most common cause of recurrent chest pain after AMI are coronary ischemia and pericarditis.

POST INFARCTION ANGINA

Is defined as chest pain that is frequency similar to the original discomfort occurring at rest or with limited activity during hospitalisation 24 hours or more after onset of Acute Myocardial Infarction. This pain may or may not be associated with ST-Segment, elevation or depression or with pseudonormalisation of inverted T waves on post myocardial ischemia ECG. The incidence of post Acute Myocardial Infarction angina is almost twice as high after non Q Myocardial Infarction than Q wave Myocardial Infarction (25-35%). Thrombolytic therapy also lead to a high incidence of post infarction angina (35-45%), with a 12-15% incidence of reinfarction during the early experience with lytic therapy for reperfusion.

APPROACH TO POST INFARCTION ANGINA

If there is persistent pain (lasting> 30 minutes), a reelevation of CK-MB and ST-T changes consider readministration of thrombolytic therapy. (rt-PA or r-PA). The other option is immediate coronary angiography and PTCA.

COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION

1. Dysrrhythmias

Brady Cardia

Relatively common (30-40%) early in the course of Acute Myocardial Infarction especially in inferior infarction or after reperfusion of right coronary artery because of activation of vagal afferents that ultimately result in enhanced parasympathetic tone.

Atropine in doses of 0.5-1.0 mg is the drug of choice if hypotension and tissue hypoperfusion coexists.

AV block, ventricular asystole

Atropine is useful for treatment of type I second degree AV block especially if complicating inferior wall MI and at times in third degree AV block of AV node in restoring AV conduction or for increasing junctional response rate. For ventricular asystole atropine is used in doses of 1.0 mg every 3-5 minutes during CPR upto a maximum of 2.5 mg if asystole persists.

Heart block

A heart block in the setting of Anterior Myocardial Infarction reflects extensive infarction and concomitant destruction of the conducting system and is associated with relatively high mortality. In contrast heart block with inferior Myocardial Infarction may primarily reflect ischemia of AV node rather than extensive tissue damage and so is associated with a better prognosis.

Ventricular fibrillation

Ventricular Fibrillation can occur in 3-5% Acute Myocardial Infarction patients in the initial 4 hours. It is called primary VF. Mechanism is thought to be micro-reentry in the infarct zone.

Triggering factors include hypokalemia, hypomagnesemia, enhanced adrenergic tone, acidosis, increased intracellular calcium, increased free fatty acids and reperfusion induced production of free radicals.

Incidence of VF is decreased by the use of β-blockers. Prompt defibrillation using unsynchronised shock starting with 200J is the treatment of choice. If unsuccessful give another shock immediately with 200-300 J; if again persists, shock with energy level of 360J.

Ventricular tachycardia

Polymorphic ventricular tachycardia causing hemodynamic collapse is treated with unsynchronised shock starting with 200J. Monomorphic ventricular tachycardia with hypotension (systolic BP<90mm Hg), pulmonary edema or angina should be treated with a synchronised shock with an energy level starting at 100J initially.

Hemodynamically stable ventricular tachycardia is treated with intravenous lidocaine 1-1.5 mg/kg IV bolus with supplemental doses of 0.5-0.75 mg/kg every 5-10 minutes upto a maximum of 3 mg/kg if needed. This is followed by an infusion of 2-4 mg/min (30-50 μg/kg/min) for 24 hours.

Other dysrhythmia that can occur during Acute Myocardial Infarction are ventricular ectopics, atrial flutter and fibrillation, junctional rhythm.

Accelerated idioventricular rhythm

Normally occur frequency during the first hours of Acute Myocardial Infarction and occur after thrombolysis is a reperfusion arrhythmia. Accelerated idioventricular rhythm should not be treated. When the rate exceed 120/mt it should be considered as an automatic rhythm for which suppression with lidocaine should be considered.

MECHANICAL COMPLICATIONS

Mechanical complications are Cardiogenic shock, papillary muscle dysfunction, papillary muscle rupture, ventricular septal rupture, cardiac rupture, ventricular aneurysm formation and pseudoaneurysm.

CARDIOGENIC SHOCK

Cardiogenic shock may occur when 40% or more of left ventricle is infarcted. It is the most common cause of in hospital death in Acute Myocardial Infarction patients. Mortality rate is around 80%. The incidence of cardiogenic shock has decreased from 15% in the early 1970s to approximately 5-7%. This is attributed to use of thrombolytic therapy and better treatment of angina and ischemia.

Characteristics of cardiogenic shock are

1. Evidence of hypoperfusion: Cold, Clammy Skin, impaired mentation, oliguria.
2. Systolic blood pressure < 80-90 mmHg.
3. Left Ventricular End Diastolic pressure or Pulmonary capillary wedge pressure ≥ 18mm Hg.
4. Evidence of primary cardiac abnormality.
5. Cardiac index ≤ 1.8L/mt/m^2

Management of cardiogenic shock

Maintenance of tissue perfusion

When systolic BP is more than 90 mmHg, intravenous dobutamine infusion is tried. When systolic pressure is below 80-90 mmHg dopamine is the preferred agent so as to bring the blood pressure to 90-100 mmHg.

If high doses of dopamine are necessary to maintain adequate perfusion, norepinephrine may be substituted for dopamine because nor epinephrine has more alpha agonist effect and lesser chronotropic and inotropic action of beta-receptor stimulation.

Early mechanical revascularization by PTCA or CABG improves survival. In the waiting period, intra-aortic balloon counter pulsation may be used to buy time. Thrombolytic therapy should be administered if facilities for percutaneous intervention procedures are not available.

PAPILLARY MUSCLE RUPTURE

It occur in 1% of myocardial infarction. Posteromedial papillary muscle is involved 6-12 times than that of anterolateral. Rupture occurs more often distally involving one or several of small heads of muscle. Usually manifests 2-7 days after infarction with the development of pulmonary edema. Mitral valves replacement or repair is the treatment of choice.

PAPILLARY MUSCLE DYSFUNCTION

More common than rupture. Again posteromedial muscle is more often involved. Dysfunction may be transient during ischemia which can disappear with successful treatment.

VENTRICULAR SEPTAL RUPTURE

Incidence is 1-3% of Acute Myocardial Infarction equally divided among anterior and inferior infarction. It occurs more often in first infarction and in the first week. Usually manifest by appearance of new harsh, holosystolic murmur along left sternal border and sudden clinical deterioration with hypotension and pulmonary congestion. Management is essentially surgical closure.

CARDIAC RUPTURE

Free wall of ventricle is the most common site of rupture. Generally occurs within the first 2 weeks and may occur within 24 hours. It occur more often in first infarction, women, elderly, and with systemic hypertension particularly if there is no associated left ventricular hypertrophy. It generally presents as sudden unanticipated death.

Other complication that may occur are pulmonary thromboembolism and systemic embolism.

CONTINUING MANAGEMENT

Uncomplicated Acute Myocardial Infarction patients can be transferred from CCU by 3rd day.

MATERIALS AND METHODS

PLACE OF STUDY

This study was conducted in the coronary care unit of Govt. General Hospital and Madras Medical College and Research Institute.

PERIOD OF STUDY

From Jan 2005 to Feb 2006.

DESIGN

Observational prospective cohort study of patients receiving streptokinase for acute myocardial infarction. A total of 83 patients were included in the study.

METHODOLOGY

A. Subject Selection

1. Inclusion Criteria

a. Presence of typical chest pain suggestive of Acute myocardial infarction along with ECG evidence of Acute myocardial infarction who were thrombolysed. Criteria for thrombolysis being 2 mm or more ST elevation in two contiguous precordial leads or 1 mm or more ST elevation in two contiguous limb leads. ECGs were recorded using Hewlett Packard Page write 100 machine.

b. Time window of 12 hrs from the onset of pain to the initiation of thrombolysis.

2. Exclusion Criteria

1. Late thrombolysis (more than 12 hrs from the onset of pain).
2. Recurrent myocardial infarction.
3. Presence of bundle branch block.
4. Development of pericarditis

DRUG THERAPY

- All patients received streptokinase 1.5 million units in 100ml of Normal saline over 60 minutes.
- Aspirin was given to all patients.
- Use of heparin, β-blockers, ACE Inhibitors was according to CCU protocols, which was in accordance with ACC/AHA recommendations.

DEFINITION OF SUCCESS OF THROMBOLYSIS

- Success was defined by

1. Clinical-complete subsidence of chest pain.
2. Electrocardiographically-more than 50% ST resolution in a lead which showed maximum ST elevation initially. ST elevation is measured manually, 80 ms after J point from isoelectric line. Preceding PR segment is taken as isoelectric line.

Patients were analysed for success of thrombolytic therapy at 90 minutes after initiation of thrombolytic therapy, applying the above mentioned criteria. Those who underwent successful thrombolysis were grouped into group A.

Those with failed thrombolysis -Group B.

The following parameters were analysed among them to know whether they influenced the outcome of thrombolysis.

1. Age
2. Gender
3. Smoking status
4. Drinking status
5. Diabetes mellitus
6. Systemic Hypertension
7. Pre infarction angina
8. Location of Myocardial Infarction
9. Time of Streptokinase administration
10. Time interval between the onset of pain and the initiation of thrombolytic therapy.

DEFINITIONS

Smoking

Patients are considered smokers if they were using tabocco for smoking in any form currently. Ex-smokers were defined as those who quitted smoking for more than 1 year back from the date of admission.

Diabetes mellitus

Patients were considered to be diabetic when

1. Currently on oral hypoglycemic drugs and/or insulin or
2. Plasma glucose> 126 mg% or 2 hr post prandial plasma glucose >200 mg% on more than 2 occasions.

Hypertension

Patients were considered hypertensives when

1. They are already on antihypertension medications.
2. Medically documented history of blood pressure elevation more than 140/90 mm H, on two occasions in the past.

Preinfarction angina

Was defined as history of anginal pain during the preceding 7 days of the acute event causing hospital admission.

Location of myocardial infarction

Inferior wall infarction

Patients with ST elevation, with or without Q wave in leads II; III; aVF. are considered to have inferior wall infarction.

Anterior wall infarction

Those people showing ST elevation with or without Q wave in any two contiguous leads from V_1 - V_6 and or LI and a VL are considered to have anterior wall infarction.

FOLLOW UP

Patients were followed up until they were discharged from the hospital.

ECHO & Angiogram were done whenever possible.

Statistical method

Univariate analysis was done by chi - square test and multivariate analysis by logistic regression.

OBSERVATIONS

A total of 83 patients were studied. Their age ranged from 31 - 76 years (mean 55.01) 68 of them were males (82%) and 15 females (18%); 20 of them were hypertensives (24%); 20 were diabetic (24%). 44 people were smokers (53%) and 29 (35%) used to consume alcohol. 23 patients experienced preinfarction angina (28%). 50 patients had anterior wall infarction (60%) and 33 patients (40%) had inferior infarction.

TABLE - 1

CLINICAL DETAILS OF STUDY POPULATION ACCORDING TO THE OUTCOME OF THROMBOLYSIS

Variables	Sucess (%)	Failed (%)
Number	44 (53%)	39 (47%)
Males	36 (53)	32 (47)
Females	8 (53%)	7 (47%)
Hypertension	11 (55%)	9 (45%)
Diabetes	11 (55)	9 (45%)
Smoking	22 (50%)	22 (50%)
Drinking	20 (69%)	9 (31%)
Preinfarction angina	9 (39%)	14 (61%)
Time window		
0 - 4 hrs	21 (64%)	12 (36%)
4 - 8 hrs	22 (55%)	18 (45%)
8 - 12 hrs	3 (30%)	7 (70%)
Age group		
< 60 yrs	30 (62%)	18 (38%)
> 60 yrs	14 (40%)	21 (60%)
Anterior wall infarct	20 (40%)	30 (60%)
Inferior wall infarct	24 (72%)	9 (28%)

TABLE - 2

UNIVARIATE ANALYSIS FOR INFLUENCING FACTORS

Sl. No.	Variables	Odds Ratio (OR)	(X^2) Chi - Square	P value	Comments
1.	Age < 60 years	2.5	4.11	0.04	Significant
2.	Gender (female sex)		0.00	0.98	
3.	Pre infarction angina	0.46	2.43	0.11	
4.	Diabetes	1.11	0.04	0.83	
5.	Hypertension		0.04	0.4	
6.	Smoking		0.34	0.56	
7.	Drinking	2.78	4.50	0.03	Significant
8.	Infarct location (anterior)	0.25	8.55	0.004	Significant

TABLE - 3

LOGISTIC REGRESSION ANALYSIS

Variables	OR	P - value
Age < 60 yrs	0.4036	0.09
Drinking	3.16	0.06
Location (Inferior)	3.18	0.02
Smoking	0.34	0.08

FIGURE - I

SUCCESS RATE WITH RESPECT TO INDIVIDUAL VARIABLES

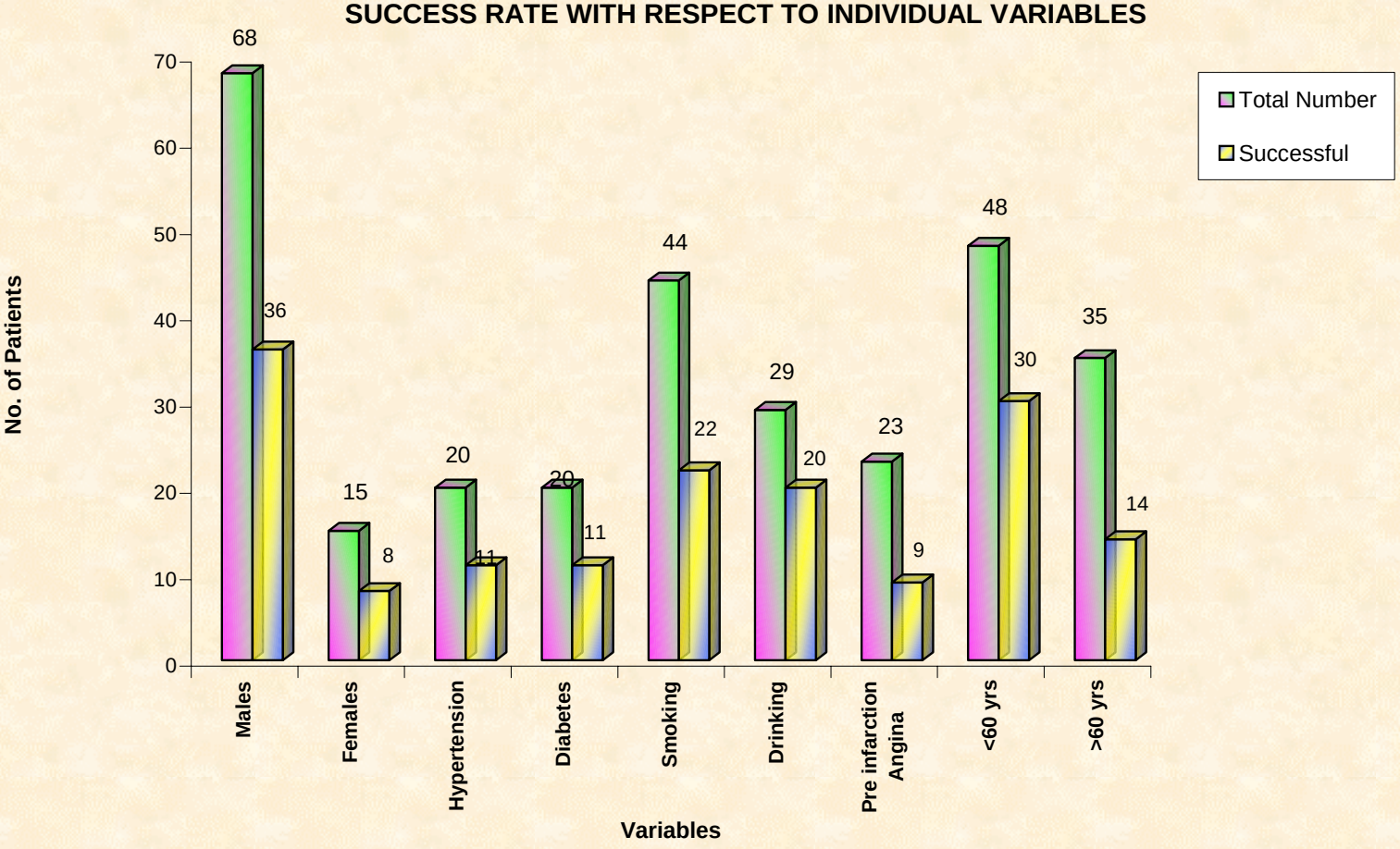


FIGURE 2
EFFECT OF TIME WINDOW ON SUCCESS RATE OF THROMBOLYSIS

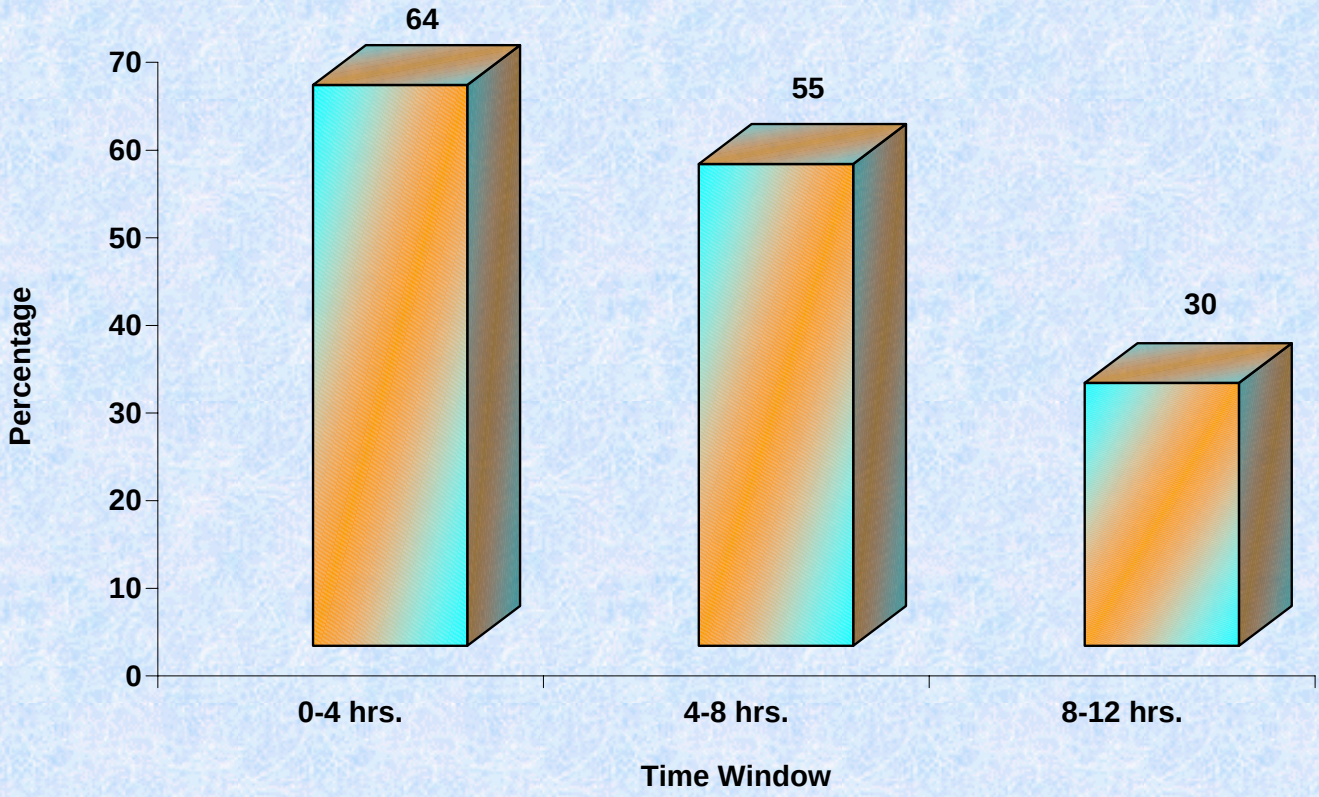


FIGURE - 3 SEX DISTRIBUTION OF STUDY POPULATION

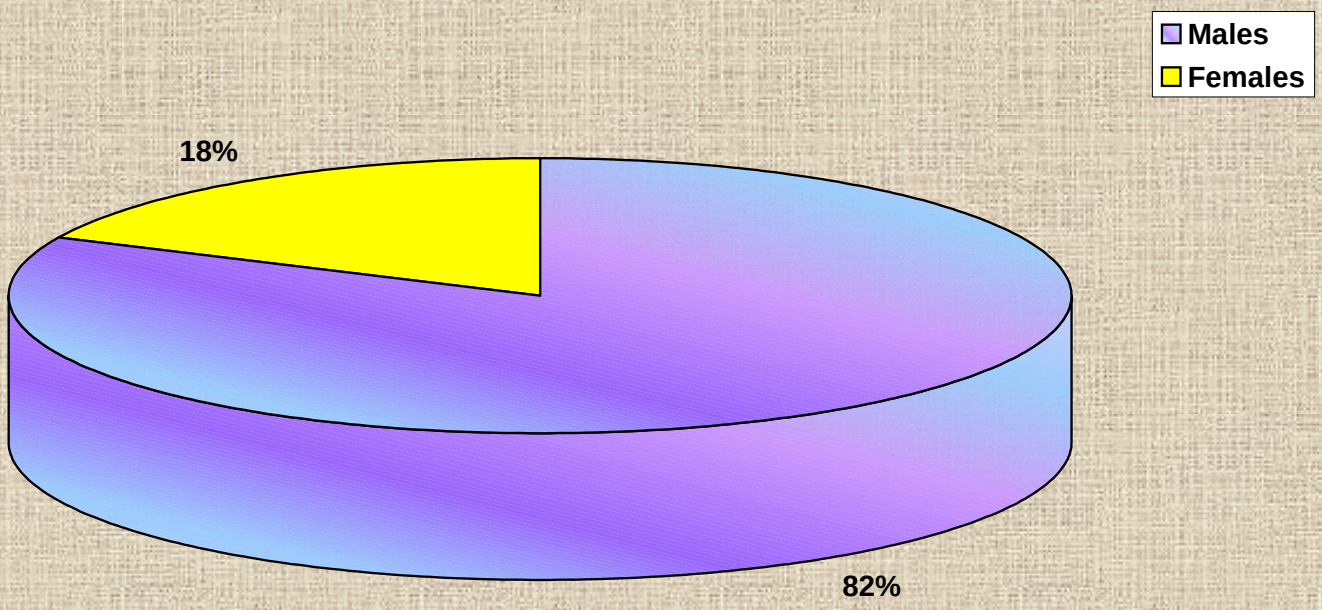


FIGURE - 4
SUCCESS RATE OF THROMBOLYSIS IN ANTERIOR INFARCTIONS

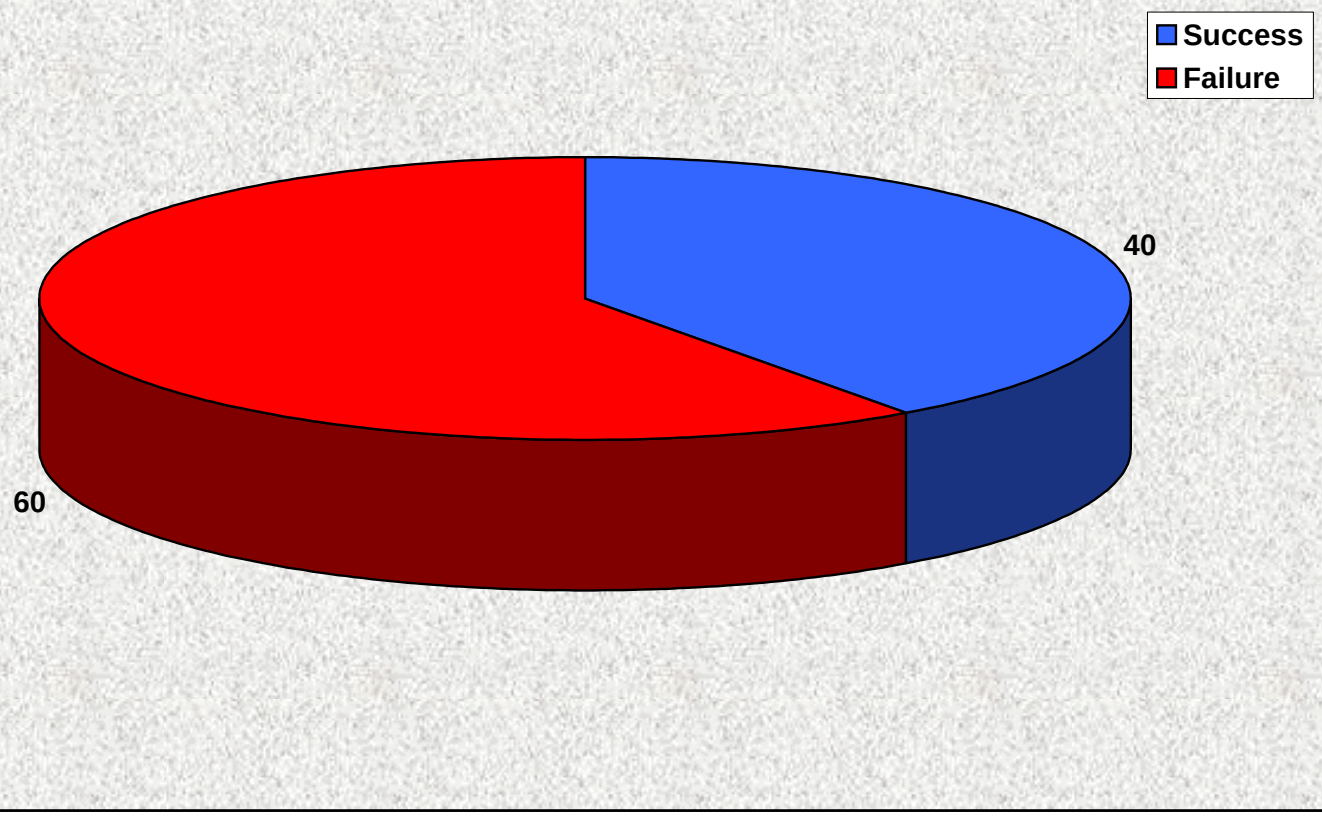
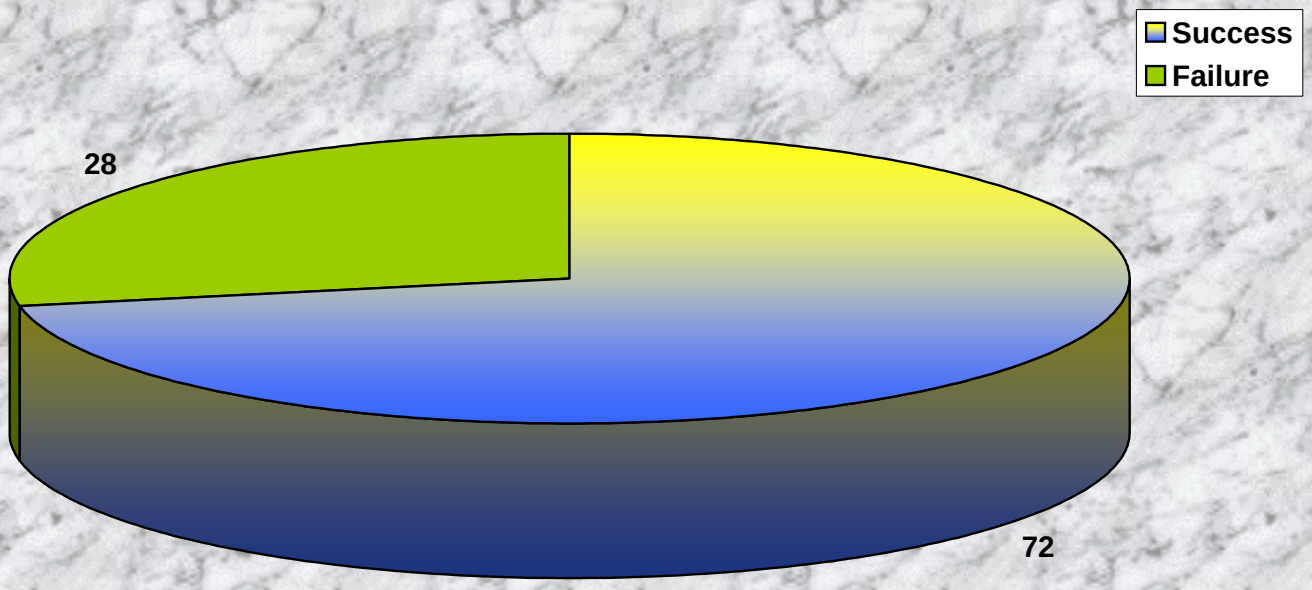


FIGURE - 5
SUCCESS RATE OF THROMBOLYSIS IN INFERIOR INFARCTIONS



DISCUSSION

The major finding of this study is that the location of the infarct significantly affects the outcome of thrombolysis. Those with inferior wall myocardial infarction have a 3.18 times chance of undergoing successful thrombolysis compared to anterior wall myocardial infarction (P=0.02). This is after adjustment for all confounding variable like time window, age, smoking status, gender, diabetes and hypertension.

[25]Similar observations were made by C.Michael Gibson, Sabina Murphy and E. Brawnwald *et al.* (TIMI studygroup). They found that TIMI grade III flow rates were lower for left coronary and circumflex artery compared to right coronary artery after thrombolytic therapy.

The reason for this differential response will be evident when we look into the physiology of coronary circulation in right and left coronary arteries.

Blood flow in right coronary artery is relatively independent of phases of cardiace cycle, being present in both systole and diastole. Where as flow in left coronary artery is almost absent during systole and may even be reversed in conditions of heightened micro vascular tone and left ventricular hypertrophy[26].

The relatively thicker wall, the increased wall thickening during systolic contraction and higher intracavitary pressure of left ventricle may all produce higher intramyocardial pressure than that is observed in the thinner walled right ventricle, which is also subjected to lower filling pressures.

Moreover the extent of necrosis in anterior wall is more resulting in increased myocardial edema compared to inferior infarctions. This may further decrease the reperfusion rates in anterior infarctions. Yet another mechanism, may be, better drug delivery to right coronary artery and prolonged contact of streptokinase with the thrombus, resulting in more efficient fibrinolysis.

ALCOHOL AND THROMBOLYSIS

Alcohol consumption has influenced the outcome of thrombolytic therapy in a favourable way. Univariate analysis revealed a success rate of 69% in drinkers versus 44% among non drinkers. ($p = 0.03$, OR = 2.78). This advantage of drinkers persisted after logistic regression analysis to remove the confounding factors, even though statistically not significant (OR = 3.16; $p=0.06$).

Alcohol is known to reduce coronary artery disease related mortality. In a meta analysis of all experimental studies that assessed the effects of moderate alcohol intake on concentrations of HDL cholesterol, apolipoprotein A_1, fibrinogen, triglycerides, and other biological markers, Eric. B.Rimm, Paige William, Kerry Fosher *et al*[27]. concluded that 30g of alcohol per day would cause an estimated reduction of 24.7% in risk of coronary artery heart disease.

This better success rate observed in patients who consume alcohol may be easily explained by the effect of alcohol on hemostatic factors. In a study conducted on 631 apparently healthy male physicians, the plasmal level of tPA antigen were 10.9, 9.7, 9.1 and 8.1 ng/ml respectively in those who consumed alcohol daily, weekly, once a month and never[28].

Studies have shown an effect on platelets also. Alcohol reduces platelet aggregation in response to most agonists like thrombin, ADP, epinephrine and collagen[29].

By contrast in binge drinkers or in alcoholics after alcohol withdrawal, response to aggregation, especially that induced by thrombin, is markedly increased. This rebound phenomenon may explain ischemic strokes or sudden death known to occur after episodes of drunkenness.

Ethanol intake is also known to decrease blood fibrinogen level. Thus those who consume alcohol on a moderate basis are having better endogenous fibrinolytic response.

INFLUENCE OF AGE OF THE PATIENT OF THROMBOLYSIS

Patients older than 60 years are found to have a lesser success rate in univariate analaysis. (X^2 = 4.11, OR = 2.5, P = 0.04). After adjustment for other parameters in logistic regression, a statistically insignificant reduction in success rate is observed.

This shows that with respect to fibrinolysis elderly people donot behave differently from younger people. This is reflected in reduction in mortality rate among elderly after thrombolysis. In patients aged more than 75 years who were treated with Streptokinase in GISSI-2 trial, there was a reduction of 4.2 fewer deaths per 100 patients than in controls. In ISIS - 2 there was 3.3 fewer deaths per 100 patients in those over 70 years of age who were treated[4].

GENDER

No statistically significant difference was noticed based on gender. Woodfield - SL, Lunderberg - CF, Topol EJ *et al*[30]. performed an angiographic study to find out the patency rate at 90 minutes in men versus women. At 90 minutes TIMI - 3 flow rate was 39% in women and 38% in men, which was not statistically significant. But 30 day mortality was 13.1% in women versus 4.8% in men (P = 0.001).

Thus even though females have a poor outcome after myocardial infarction, they do not behave differently to thrombolytic therapy.

DIABETES MELLITUS

In this study success rate of thrombolysis is not found to be different from non diabetic population.

Gray RP, Yudkin JS *et al*. found a reduction in reperfusion rates in thrombolysed diabetic patients[31].

Diabetes is a prothrombotic state as reflected by the increased blood levels of fibrinogen, factor VII and Willebrand factor. These changes are even more increased if diabetic people happened to be smokers.

Flatelet function is also impaired in diabetics. They aggregate more readily to stimuli like ADP and collagen. Glycation of membrane proteins due to chronic exposure to high blood glucose levels[32], change in fluidity of platelet membrane brought out by high concentration of cholesterol and triglycerides are the proposed mechanisms for these abnormalities.

On the otherhand patients with type II diabetes have profound suppression of fibrinolysis. Plasminogen activator inhibitor - I levels are high in type II diabetic people which is responsible for this effect.

Nevertheless thrombolytic therapy should be administered to diabetics with Acute Myocardial Infarction, because for every 100 diabetic patients treated with thrombolytic drugs four lives are saved.

PREINFARCTION ANGINA

Felicita Andreoti; Vincenzo P et al. had demonstrated by angiographic method that those Acute Myocardial Infarction patients who experienced preinfarction angina within seven days preceding the acute event had a more rapid thrombolysis. Patency rates were higher at 35 minutes but at 90 minutes both were same[33].

In this study success rate was same at 90 minutes in both groups. This is because ECG monitoring was not continuous in this study. Continuous ST segment monitoring may be needed to demonstrate the early achievement of patency in preinfarction angina patients.

SMOKING

Outcome of thrombolysis is not affected by smoking. In this study there is a statistically insignificant trend towards a bad outcome. [34]Cindy L. Gines, E.J. Topol *et al*. reported similar patency rates in smokers and nonsmokers at 90 minutes (73% versus 74%). Smokers tends to have reduced inhospital mortality compared to nonsmokers. But this was due to the favourable baseline

clinical and angiographic variables in smokers. Smokers tended to be younger and thrombosis of less critical atherosclerotic plaque was the culprit lesion in them. Smoking increases blood hematocrit, fibrinogen levels and platelet levels contributing to the hypercoagulable state promoting coronary thrombosis. Smokers are also found to have lesser fibrinolytic activity than nonsmokers.

CIRCADIAN VARIATION

[23]Eugene Braunwald et al. noticed a circadian variation in efficacy of thrombolytic therapy, with better patency rates in the evening hours. This is due to circadian variation in the blood levels of PAI-I, which is highest in the morning hours.

In this study no such circadian variation was observed. Probable reasons for this discrepancy may be the shorter time window observed in patients presenting in morning hours as well as smaller sample size.

PAIN TO STREPTOKINASE INTERVAL (TIME WINDOW)

This is the most powerful predictor of success rate. In this study also it is evident. Success rate was 64% in those patients thrombolysed within 4 hours from the onset of symptoms. The success rate decreased to 55%, when they were thrombolysed after 4 hrs but within 8 hours of onset of symptoms. Success rate came down to 30%, when streptokinase was administered after 8 hours but within 12 hours.

CONCLUSION

- In this study the overall success rate of thrombolysis was 54%.
- Inferior wall myocardial infarctions had a better success rate than anterior wall myocardial infarctions and it was statistically significant.
- Smokers had a lesser success rate than non smokers, but it did not reach statistical significance.
- Alcohol intake was associated with a better success rate eventhough statistically not significant.
- Hypertensives didn't show any difference in the success rate.
- Diabetics donot differ from non diabetics with respect to the success rate of thrombolysis.
- There was a trend towards a worse outcome in those aged more than 60 years. But it was not statistically significant.
- Gender was not found to influence the success rate of thrombolysis.
- Pre infarction angina had no effect on the success rate of thrombolysis.

SUMMARY

The study was conducted to evaluate the success rate of thrombolysis in acute myocardial infarction and the various factors influencing its out come. It was done by observational prospective cohort study of patients receiving streptokinase for acute myocardial infarction in coronary care unit, Government General Hospital, Chennai. The overall success rate of thrombolysis was 54%. Patients with inferior wall myocardial infarction had a better out come than anterior wall myocardial infarction. Alcohol, smoking and age were factors which influenced the out come, but were not statistically significant. Early thrombolysis had a better out come when compared to other predictors. Success rate was 64% in those patients thrombolysed within 4 hrs. from the onset of symptoms. Time window was found to be the most powerful factor influencing the out come of thrombolysis in patients with acute myocardial infarction.

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ABBREVIATIONS IN MASTER CHART

Smo	-	Smoking
Dri	-	Drinking
HT	-	Hypertension
PIA	-	Pre infarction angina
DM	-	Diabetes Mellitus
TOS	-	Time of onset of symptoms
TSA	-	Time of SK administration
TW	-	Time window
REG	-	Reggression
EA	-	Extensive anterior
EF	-	Ejection fraction
$\rightarrow$	-	Pain persisted
-	-	Pain subsided
PoIA	-	Post Infarction Angina

ABBREVIATIONS

LAD	-	Left anterior descending artery
LCA	-	Left Coronary artery
LCX	-	Left circumflex artery
RCA	-	Right Coronary artery
LV	-	Left Ventricle
RV	-	Right Ventricle
AMI	-	Acute myocardial infarction
VF	-	Ventricular fibrillation
VT	-	Ventricular tachycardia
SK	-	Streptokinase
PTCA	-	Percutaneous transluminal coronary angioplasty
rtPA	-	Recombinant tissue plasminogen activator
CABG	-	Coronary Artery by pass grafting
PAI - 1	-	Plasminogen activator inhibitor - 1
PDGF	-	Platelet derived growth factor
vWF	-	Von Willebrand factor
APSAC	-	Anisoylated plasminogen streptokinase activator complex
LBBB	-	Left bundle branch block
RBBB	-	Right bundle branch block

PROFORMA

Serial No.:

Name : Age : Sex : IP :

Occupation : Monthly Income :

PERSONAL DATA

1. Smoking

Current	**Smoking**	**Yes**	**No**
If yes, No.of Cigarettes			

Ex.Smoker > 1 yr

2.

Drinking	**Yes**	**No**	**if yes ml/wk**	

3. Other habits : Specify

4. Life style

Exercise regularly ≥ 3 times / wk		Active		Sedentary

5. Hypertension Yes Bo If yes 1. Duration.....
   2. Treatment Regular Irregular

6. Pre infarction angina Yes No
   If yes 1. Within 24 hrs of infarct
   2. Within 1 week of infarct

7. Hyperlipidemias Yes No

   a. Hypertriglyceridemia Treatment a. Diet alone
      b. Drugs.....
   b. Hypercholesterolemia
   c. Mixed

8. Diabetes

Duration	
Type I	Type II

Insulin	
OHA	

9. Other diseases - specify

10.

Medications	Aspirin	ACE I	. blocker	Others
Dosage				

11. Family History:

SCD	**AMI**	**Stroke**

12. Time of onset of symptoms:

0-6 a.m.	**6-12 noon**	**12-6 p.m.**	**6-12 mn**

13. Physical Examination

Pulse B.P. Crackles

SIII JVP Rub

14. Killip Class.....

15. Time of SK administration

0-6 a.m.	**6-12 noon**	**12-6 p.m.**	**6-12 mn**

16. Pain onset of SK interval in hrs

0-4 hrs	**4-8 hrs**	**8-12 hrs**

17. ECG on admission

1. Location of MI

Extensive Anterior	Antero Septal	Anterolateral	Inferior

2. Peak ST elevation in millimeters: ☐

18. ECG at 90 mts after SK therapy
Maximal ST elevation in millimeter ☐

19. Percentage ST Resolution ☐

20. Clinical condition at 90 mts

a) No Angina
b) Decreased
c) Persistent with same intensity

21. Arrhythmias if any during thrombolysi:

22. Other drugs used

Heparin	
NTG	
Blockers	
Ionotropics	

23. Thrombolysis successful? ☐ Yes ☐ No

24. Post infarction angina ☐ Yes ☐ No

If yes Intervention resorted to

1. NTG 2. Blockers 3.Ca^{++} Channel Blockers
4. Emergency PTCA 5. Others

Other Events and Intervention if any:

25. Laboratory data

1. Hb TC PLE ESR

2. Urea 3. Creat

4. Blood sugar 5. Na^+ $C1^-$
K^+ HCO^3

Admission 6hrs 24 hrs

6.

CPK Total			
CPK - MB			

7. ECHO

8. Angiogram:

9. Others if any

10. Follow up:

MASTER CHART

ge	Sex	Smo	Dri	HT	PIA	DM	TOS	TSA	TW	Kil's Class	Location of MI	ST↑ (Adm)	ST ↑ 90mts	% ST REG	Clini 90mts	Out come	Arrhy	E
39	M	Y	Y	N	Y	N	11 am	3.45 pm	5.45 Hr	I	EA ST ↑ V_1-V_6LI;aVl	4	3	25%	-	F		El
44	M	Y	Y	N	N	N	8 am	12.30 pm	4.30	I	Inf ST ↑ II; III; aVF	4	3	100%	-	S	Hypotension Brady cardia	N f EF
70	F	N	N	N	N	N	11 am	2 pm	3	I	Inf ST ↑ II; III; aVF	11	10	90	-	S		
57	M	N	N	Y	N	N	5.30 pm	6.20 pm	1	I	ANT ST ↑ V_1 - V_4	8	3	62	-	S		El
59	M	Y	N	Y	N	Y	11 am	4.10 pm	5	I	Ant ST ↑ V_1 - V_5	4	3	25	-	F		El m
70	M	N	N	Y	N	N	12 mn	12 noon	12	I	EA ST ↑ V_1 - V_6 aVL LI	6	4	33	-	F		
72	M	Y	N	N	Y	N	12.30 pm	6.30 pm	6	I	Inf ST ↑ II; III; aVF	2.5	2	25	-	F		fu
40	M	Y	Y	N	N	N	8.30 pm	12.40 am	4	I	Ant ST ↑ V_1 - V_4	15	4	73	-	S	VF-defi brillated	El
51	M	Y	Y	N	N	N	10 pm	1.15 am	3.15	I	Ant ST ↑ V_1 - V_6	13	6	58	-	S		El mod
50	M	Y	Y	N	N	N	6.30 am	11.15 am	5	I	EA ST ↑ V_1 - V_6; LI'aVL	6	2	66	-	S		El mod
50	M	N	N	N	N	N	5 pm	8 pm	3	I	Inf with RVMI ST ↑ II'III' aVF' V_4R	6	1	83	-	S		El triv
70	F	N	N	N	N	N	7 am	8.30 am	1.30	I	Inf+Lat Post ST ↑ II; III; aVF; V_5, V_6	4	1	75	-	S		El M
35	M	N	Y	N	N	N	6.30 am	10.30 am	4	III	Ant ST ↑ V_1-V_4	5	2	60	-	S		Nor El
60	M	Y	N	N	N	N	3 pm	6.50 pm	3.15	I	EA.ST ↑ V_1-V_6 L1; aVL	8	5	37	-	F		El m
68	F	N	N	N	N	N	1.30 pm	5.50 pm	3.45	I	Inf. with RVMI	6	1	82	-	S		El M
65	M	N	N	N	Y	N	2 am	4.50 am	2.15	I	Ant ST ↑ V_1-V_6	12	8	33	-	F		
65	M	Y	N	N	Y	N	1 pm	7.40 pm	6.40	I	Ext. Ant	6	4	33	-	F		El
59	M	Y	Y	N	N	N	9 pm	10.50 pm	1.15	I	Inf. with RVMI	6	4	33	-	F		45 LV
71	M	N	N	N	N	N	3 pm	9.30 pm	6.30	I	Ant ST ↑ V_1-V_6	6	4	33	-	F		El mild thr

ge	Sex	Smo	Dri	HT	PIA	DM	TOS	TSA	TW	Kil's Class	Location of MI	ST↑ (Adm)	ST ↑ 90mts	% ST REG	Clini 90mts	Out come	Arrhy	E
60	M	Y	N	N	N	N	7 am	1.40 pm	6.40	I	Ant ST ↑ V_1-V_6	5	5	0	-	F		EI
46	M	Y	Y	N	Y	Y	10 am	2 pm	4	I	Ant ST ↑ V_1-V_6	6	4	33	-	F	VPDST	EI
55	F	N	N	N	Y	N	9 am	2.30 pm	5		EA.ST ↑ V_1-V_6 L1; aVL	3	2	33	-	F		EI
51	M	N	Y	Y	Y	N	8 pm	12.30 am	4.30	I	Inf ST ↑ II; III; aVF	2	1	50	-	S		Nor EI
40	M	Y	Y	N	N	N	3 am	7.45 am	4.45	I	Ant ST ↑ V_1-V_5	6	3	50	-	S	VT	EI
60	F	N	N	N	N	Y	11 pm	1 am	2	I	Inf with RVMI ST ↑ III'III' aVF' V_4R	3	2	33	-	F		EI
70	M	N	N	N	N	Y	4 pm	10 pm	6	I	Ant ST ↑ V_1-V_3	8	4	50	-	S		EI
58	M	N	N	N	N	N	10 am	1.15 pm	4	I	Inf ST ↑ II; III; aVF	7	2	71	-	S		EF
50	M	Y	Y	N	N	N	7.30 am	8.45 am	1.15	I	Inf with RVMI ST ↑ III'III' aVF' V_4R	4	0	100	-	S		EI
45	M	Y	Y	N	N	N	11 am	3.30 pm	4.30	I	Inf with RVMI ST ↑ III'III' aVF' V_4R	3	1	66	-	S		EI
60	M	Y	N	Y	N	N	6 pm	11 pm	5	II	EA.ST ↑ V_1-V_6 L1; aVL			0	-	F		
47	M	N	N	Y	N	Y	3.30 pm	1 am	9.30	I	Ant ST ↑ V_2-V_6	6	4	33	-	F	Hypo Brady Cardia	EI
52	M	N	N	Y	Y	N	10 am	2 pm	4	I	Ant ST ↑ V_5-V_6 L1; aVL	2	1	50	-	S		46 LV
45	M	N	N	N	N	N	9 am	3 pm	6	I	Inf with RVMI ST ↑ III'III' aVF' V_4R	3	1	66	-	S		
50	M	N	Y	Y	N	N	12 noon	2.30 pm	2.30	I	Inf with RVMI ST ↑ III'III' aVF' V_4R	9	2	77	-	S		
62	M	N	N	N	N	N	11.30 am	9.20 pm	11	I	Ant ST ↑ V_1-V_3	4	4	0	-	F		45 LV
50	M	Y	Y	N	N	N	5 pm	9.20 pm	4.20 Hr.	I	Ant ST ↑ V_1-V_6	14	7	50	-	S		
40	M	Y	Y	N	N	Y	12.30 am	3.30 am	3.	I	Inf II; III; aVF' ST ↑	2	0	100	-	S		
57	M	Y	N	N	N	N	11 noon	3.30 am	3.30	I	Ext Ant ST ↑ V_1-V_6 aVL; I	11	2	72	-	S		45
42	F	N	N	N	Y	N	8 am	11.15 am	3.15	I	Inf+RVMI ST ↑ II, III, aVF, V_4R	2.5	2	20	→	F		
49	M	Y	Y	Y	N	N	12 M.Night	2.30 am	2.30	I	Inf II; III; aVF' ST ↑	2.5	0	100	-	S		
65	M	Y	Y	N	Y	N	7 pm	1 am	6	II	EA.ST ↑ V_1-V_6 L1; aVL	5	3	40	-	F	VPDs+ AVR+	
60	F	N	N	N	N	N	5 pm	3.20 am	10.20	I	Ant ST ↑ V_1-V_6	2	1.5	25	→	F		Mild

ge	Sex	Smo	Dri	HT	PIA	DM	TOS	TSA	TW	Kil's Class	Location of MI	ST↑ (Adm)	ST ↑ 90mts	% ST REG	Clini 90mts	Out come	Arrhy	E
72	M	N	N	N	N	N	10 am	10 pm	12	II	EA.ST ↑ V_1-V_6 L1; aVL	7	7	0	-	F		
60	M	N	N	Y	N	Y	11 am	10 pm	11	I	Ant ST ↑ V_1-V_6	6	4	33	-	F		
60	F	N	N	N	N	N	11 am	2.45 pm	4.45	I	Inf ST ↑ II; III; aVF	2	0	100	-	S		40 LV
70	M	Y	N	N	Y	N	4 pm	6.15 pm	2.30	I	Ant ST ↑ V_1-V_4	4	3	25	-	F		50 LV
86	M	Y	T	N	N	N	8 pm	10.50 pm	2.50	I	Inf ST ↑ II; III; aVF	2	2	0	-	F		
44	M	Y	N	Y	Y	N	11 pm	1 am	2	I	Inf ST ↑ II; III; aVF	3	1	66	→	S		EI
60	M	Y	Y	Y	N	N	5 am	3.30 pm	10.30 Hr.	I	Ant ST ↑ V_1-V_6	13	2	84	-	S	-	50
76	M	N	Y	N	Y	Y	3.30 pm	7 pm	3.30	I	Inf ST ↑ II; III; aVF	1	0.5	50	-	S	VT	
51	M	Y	Y	N	N	N	3 am	3.55 am	0.55 mts	I	Inf ST ↑ II; IIII; aVF; aVR	8	10	0	-	F		
53	M	Y	N	N	Y	N	3.30 pm	5.30 pm	2	I	Ant ST ↑ V_1-V_5	3	2	33	-	F		
52	M	Y	Y	N	N	N	7 am	4.30 pm	9.30	I	Inf+RVMI ST ↑ II; III; aVF, V_4 R	7	2	71	-	S		
53	M	Y	Y	N	N	Y	6.30 am	8.30 am	2	I	Ant ST V_1-V_5	8	6	25	-	F		
81	M	Y	Y	N	N	N	10 am	4 pm	6	II	Ant V_1-V_5 ST ↑	11	7	36	-	F	VF	40%
53	M	Y	N	N	N	N	11 am	8.30 pm	9.30	I	Ant V_1-V_5 ST ↑	4	3	25	-	F		
50	M	Y	N	N	Y	N	2 am	6.15 am	4.15	I	Ant V_1-V_3	6	4	33	-	F		
65	F	N	N	N	N	N	8 am	12.25 pm	4.25	I	Ant ST ↑ V_1-V_4	3	2	33	-	F		
52	M	N	N	N	N	N	9.30 am	3.50 pm	6.20	I	Ant ST ↑ V_1-V_4	5	3	40	-	F		
58	M	N	N	Y	N	N	1.30 pm	4.30 pm	3	I	Inf with RVMI ST ↑ II; III aVF; V_4R	7	8	0	-	F		
64	F	N	N	N	N	Y	1 pm	6.40 pm	5.40	I	Inf with RVMI ST ↑ II; III aVF; V_4R	5	2	60	-	S		
58	M	Y	N	N	N	N	1 am	8.50 am	7.50 hrs	I	EA.ST ↑ V_1-V_6 L1; aVL	12	2	83	-	S	VT 24 Hr. & 48 Hrs.	
62	M	Y	N	Y	N	N	7 pm	9.30 pm	2.30	I	Ant ST ↑ V_1-V_3	3	3	0	-	F	-	47% LV
82	M	Y	Y	N	N	N	6.30 am	12.45 pm	6.15	I	EA.ST ↑ V_1-V_6 L1; aVL	5	2.5	50	-	S	-	
60	F	N	N	Y	N	N	2 pm	11.25 pm	9.20	I	Inf with RVMI ST ↑ II; III aVF; V_4R	2	2	0	-	F	-	

ge	Sex	Smo	Dri	HT	PIA	DM	TOS	TSA	TW	Kil's Class	Location of MI	ST↑ (Adm)	ST ↑ 90mts	% ST REG	Clini 90mts	Out come	Arrhy	E
64	M	Y	N	N	N	Y	8.30 pm	12 M.night	3.30	II	Ant ST ↑ V_1-V_6	7	3	57	-	S	VPD+	
47	M	Y	N	Y	Y	Y	11 am	6.30 pm	7.30	II	Ant ST ↑ V_1-V_6	6	7	0	→	F		
67	F	N	N	Y	N	Y	10 am	2.10 pm	4.10	I	Inf ST ↑ II; III aVF	5	2	60	-	S	VPDS; Trans CHB	
75	M	N	N	N	Y	N	3 pm	11.30 pm	8.30	I	Ant V_1-V_6	9	4.5	50	-	S		
62	M	N	N	N	N	Y	1 pm	4 pm	3	I	Inf. Post. Lat, ST↑ II; III aVF; V_5-V_6 ST↓ V_1-V_3	3	0	100	-	S		
75	M	N	N	N	N	Y	1 am	5 am	4	I	Ext. Ant V_1-V_6; aVL, L1	10	6	40	-	F	-	
55	M	Y	N	N	Y	Y	6 am	8.30 am	2.30	II	Ext. Ant V_1-V_6; aVL, L1	15	5	66	-	S	-	
52	M	Y	N	N	N	Y	10.30 am	3.45 pm	5.15	I	Inf. II; III aVF ST↑	5	0	100	-	S		
62	F	N	N	N	Y	Y	6 am	10.30 am	4.30 hrs	I	ST↑ V_1-V_5; Ant	3	2	33	-	F		EI
60	M	Y	Y	N	N	Y	5 pm	10.45 pm	5.45	I	EA, ST ↑ V_1-V_6 L1; AVL Ant.	15	7	53	-	S		
44	M	N	N	N	Y	N	4.30 am	5.30 am	1	I	ST↑ II; III; aVF Inf.	1	0	100	-	S		
59	M	N	N	N	N	N	2 pm	5.15 pm	3.15	II	ST↑ II; III; aVF Inf.	2	0	100	-	S		
38	M	Y	Y	N	Y	N	6.30 pm	10.30 pm	4	I	Ant ST↑ V_1-V_6	7	3	57	-	S	RBBB transient biftasicular block	
60	M	Y	Y	Y	Y	N	1 am	3 am	2	I	Inf. ST↑ II; III; aVF	3	3	0	→	F		
50	M	Y	N	N	N	N	12 noon	3 pm	3	I	EA ST↑ v_1-v_6 L1 aVl	9	9	0	-	F	Brady cardia	
50	M	Y	Y	N	N	N	1 pm	2.30 pm	1.30	I	Inf. ST↑ V_1-V_6 L1 aVF V_4R	4	0.5	87	-	S		
60	F	N	N	Y	Y	N	10 pm	3.30 am	5.30	I	EA ST↑ L1 aVL V_1-V_5	5	1.5	70	-	S		
45	M	N	N	N	Y	N	5 am	10 am	5	I	EA ST↑ aVL V_1-V_6	3	2	33	-	F		58