A STUDY ON PROGNOSTIC SIGNIFICACE OF MEAN PLATELET VOLUME IN PATIENTS PRESENTING WITH ST ELEVATION MYOCARDIAL INFARCTION

Dissertation submitted in partial fulfillment of the

requirement for the award of the Degree of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

APRIL 2016

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

CERTIFICATE

This is to certify that the dissertation entitled "**PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION"** is the bonafide work of **Dr. INDHUJA.M.V** in partial fulfillment of the university regulations of The Tamilnadu Dr. M.G.R. University, Chennai, for MD (Branch I) General Medicine examination to be held in April 2016.

Dean,

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CERTIFICATE FROM THE GUIDE

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DECLARATION

I, **Dr. INDHUJA.M.V,** hereby declare that, I carried out this work entitled "**PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION"** at Kanyakumari Government Medical College Hospital, Asaripallam, under the guidance of **Prof. V.Antony David Devadhas, MD,** Professor of Medicine, during the period of February 2014 to September 2015. I also declare that this bonafide work has not been submitted in part or full by me or any others for any award, degree or diploma to any other University or Board either in India or abroad

This is submitted to the Tamilnadu Dr. M.G.R. University, Chennai, in partial fulfillment of the university rules and regulations for MD (Branch I) General Medicine examination to be held in March 2016.

Place: Asaripallam Dr. M.V.INDHUJA

Date:

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Contents

INTRODUCTION

INTRODUCTION:

Ischemic heart disease and cerebrovascular disease are the most common cause of mortality and morbidity worldwide. Over three quarters of death and 85 % of disability from cardiovascular disease occurs in developing countries. The huge burden of cardiovascular disease in Indian sub-continent is due to the huge population and high incidence of prevalence of cardiovascular risk factors. Cardiovascular diseases also manifests 10 years earlier than the rest of the world in the Indian population.

The incidence of myocardial infarction in India is 64.37/1000 people among men aged between 29- 69 years of age. In the recent years India has seen a huge transition in its disease burden pattern. The load of communicable and non communicable disease is expected to be reversed by 2020.India is on the threshold of an epidemic of cardiovascular disease. A recent concern is that the incidence of CVD has one up significantly for people in the age group 25 – 69 years, which means losing more productive people to the disease. Urban India has higher prevalence than rural India.

Platelets are the main agents in the pathogenesis of many acute cardiovascular events. Platelet size and activity can be measured as mean platelet volume by automated hemolysers.MPV shows positive correlation with

markers of platelet activity like expression of glycoprotein Ib and glycoprotein IIb / IIIa receptors. Patients presenting with acute coronary syndromes have been shown to have higher values of MPV than those presenting with stable angina or non cardiac chest pain. It has been recognised as an independent risk factor of both stroke and acute coronary syndromes. An elevated MPV is also poorer outcome in patients with long time follow up.

Diabetes is emerging as a major pandemic worldwide. The prevalence of this disease is increasing in a log phase with around 340 lakh people around worldwide suffering from this metabolic disorder in 2011 according to a WHO report. Diabetic patients are more prone to develop both micro vascular and macro vascular complications .Diabetics have been shown to have increase in the platelet activity .The mean platelet volume measured in these patients are found to be in the higher end. This index has been evaluated in many studies for its role in the disease process of this metabolic disorder. Mean platelet volume has been shown to be positively correlating with HbA1c values among diabetics. Diabetes is now considered a cardiovascular disease equivalent because of its major contributing role in CAD.

Many studies have evaluated the role of Mean Platelet Volume in diabetes and acute coronary syndromes separately. In this study we try to emphasize the key role of platelets in the pathogenesis of diabetes and acute cardiovascular events and its role in predicting long term mortality and morbidity.

AIM OF THE STUDY

PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION

Aims &objectives:

I) To find the association between mean platelet volume in patients presenting with Acute STEMI on admission.

II) To compare this index among diabetics and non-diabetics presenting with acute STEMI.

III) To assess whether this index can be used for long term prognosis in patients presenting with STEMI.

REVIEW OF LITERATURE

According to a 2007 expert consensus committee, ACUTE MYOCARDIAL INFARCTION is redefined as "the detection of rise and / or fall in cardiac Troponin with at leastone of the value above the 99thpercentile of the upper reference limit (URL) with an assay with less than 10% coefficient of variation at the level of detection along with the evidence of ischemia.Ischemia was defined as

- Symptoms of ischemia
- New or presumed new significant ST-segment T wave (ST-T) changes or new LBBB
- Development of pathologic Q waves on the ECG
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
- Identification of an intracoronary thrombus by angiography or autopsy"

The present approach to patients with ischemic painis to consider them to be having either stable angina or acute coronary syndrome (ACS), which incorporates unstable angina,non ST segment elevation Myocardial Infarction (NSTEMI) and ST segment Elevation Myocardial Infarction (STEMI)

For the diagnosis of ST elevation MI “ST segment elevation of greater than 0.1 mV should be present in two or more contiguous leads.In precordial leads V1 to V4, a ST segment elevation of 0.2 mV increases the diagnostic accuracy”.There are two situations in which coronary reperfusion therapy has been shown to be beneficial in the absence of ST elevation in 12 lead eg. This includes

1. Acute myocardial infarction of the posterior wall

2. Presence of new onset of LBBB

Recent classification of Acute Myocardial Infarction:

“Type 1: spontaneous myocardial infarction

Type 2:Myocardial infarction secondary to ischemic imbalance

Type 3: Myocardial infarction resulting in death when cardiac biomarker values are unavailable

Type 4 a: myocardial infarction related to percutaneous coronary intervention (PCI)

Type 4b: myocardial infarction related to stent thrombosis

Type 5: myocardial infarction related to coronary bypass grafting”

Nearly all ACS events result from atherosclerotic plaque lesions of the coronary vessels. In most circumstances the coronary atherosclerotic lesion is associated with superadded thrombosis of the coronary vessels with the rupture or erosion of the plaque. Non atherogenic forms of coronary artery disease are also seen.

CORONARY ARTERY DISEASE OTHER THAN ATHEROSCLEROSIS:

1.Arteritis (Kawasaki, SLE, Takayasu arteritis , PAN, Rheumatoid arthritis)

2.Mechanical injury to coronary vessels

Laceration

Thrombosis

Iatrogenic

Radiation (radiation therapy for neoplasia)

3.Coronary artery mural thickening

Mucopolysaccharidosis(Hurlers disease)

Homocysteinuria

Amyloidosis

Intimal hyperplasia associated with contraceptives or with the postpartum period

4. Luminal narrowing by other mechanisms

Prinzmetal angina

Spasm after nitroglycerin withdrawal

Dissection of the aorta

Dissection of the coronary artery

5. Embolisation to coronary vessels

6. Developmental coronary artery anomalies

7. Oxygen supply demand mismatch

8. Intravascular thrombosis

9. Miscellaneous

Cocaine induced coronary vasospasm

Contusion injury of myocardium

When acute coronary atherothrombosis occurs, the resulting intracoronary thrombus may partially obstruct the lumen , which usually leads to subendocardial ischemia in the absence of ST elevation, or completely occlude the vessel wall and cause transmural myocardial ischemia and STEMI. Previously before the era of thrombolytic therapy it was a general practise to

divide myocardial infarction into Q wave MI and non Q wave MI based on the ecg changes that evolve in days. Q waves denote infarcted tissue or dead tissue. The Q wave infarction are synonymous with transmural infarction and non Q wave infarctions with subendocardial infarction. However recent studies using cardiac MR has shown that the presence of Q waves is dependant on the extent of infarction rather than the depth of mural infarct.

The recent classification of MI into STEMI and NSTEMI is preferable because immediate clinical decision of fibrinolysis or PCI depends on the presence of diagnostic ST elevation on surface ecg. Hence ecg remains the main diagnostic tool in the management of patients presenting with chest pain. The cardiac biomarkers and other investigations come into play only when the electrocardiogram is inconclusive in making the initial diagnosis

PATHOPHYSIOLOGY :

Atherosclerotic plaque erosion followed by overlying thrombosis in the coronaries is postulated to be the main mechanism accounting for most of the acute coronary syndromes

6 different morphological types of atheromatous plaque have been identified. Different types of plaque of different constitution and morphology may be found in the vasculature of the same individual.

Type 1: lesion is characterised by foam cell infiltration, intimal thickening and macrophages infiltration

Type 2: In these lesions lipids accumulate in the cytoplasm of infiltrating macrophages and smooth muscle cells

Type 3: In addition to the above changes, there is extracellular deposition of lipids.Lipids also accumulate in the connective tissue layer

The above three lesions are called early lesions. They are present in normal individuals in their early decades of life and are usually produce no symptoms.They are more common in areas where there is more shear stress in the vessel wall.Certain co morbid conditions like hyperglycemias, elevated lipids, smoking accentuate this process

Type 4 (atheroma) : This lesion is characterised by large lipid core in the intima of the vessel wall. There is also a large inflammatory cell infiltrates.

Type 5:

V a - Atheroma with fibrous cap

V b - Atheroma with superadded calcification

V c - Fibrosed atheroma

Type 6 (complicated lesion): This represents disrupted type 4 or 5 lesions with intramural hemorrhage with or without overlying thrombosis

As the atherosclerotic lesions progress they become more and more softer. This is due to the increase in the lipid content of the plaque as the plaque matures. These softer plaques are more prone to rupture.

Early (type 1-3 lesions) are asymptomatic. Type 4 and 5 may be associated with angina pectoris, but they can also be asymptomatic.

Type 4 is usually associated with acute coronary syndrome or asymptomatic lesion progression. When the lesion causes significant stenosis without sufficient collateralization, it results in acute coronary syndrome.

After the plaque rupture, the lesion organizes itself either into a chronic calcificlesionor fibrotic lesion .These patients may present with chronic stable anginal pain.

Plaque rupture is not unique to advanced stenosis, it can occur in lesion of any size and degree of stenosis based on vascular remodelling.

The gradual process by which the atheroma forms over years is punctuated by rapid burst of growth in the plaque. Such abrupt episodes account for many acute coronary syndromes rather than the chronically developing occlusive plaque.

PHASES OF ATHEROSCLEROTIC PLAQUE GROWTH :

The growth of atherosclerotic plaque is divided into 5 different phases based on the characteristics of the lesion and associated clinical presentation

PHASE 1 (Early lesions)

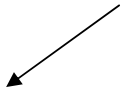
Type 1 to 3

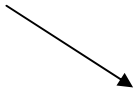
Usually asymptomatic.

PHASE 2 (atheroma)

Type IV to V a

Presents with stable angina or sometimes asymptomatic.





PHASE 3

Complicated nonocclusive lesion

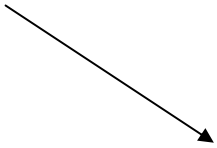
With mural thrombosis (lesion type 4)

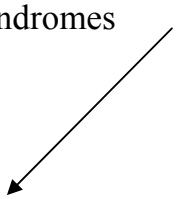
Asymptomatic sudden progression of lesion

PHASE 4

Complicated lesion with flow limiting thrombus (lesion type 6)

Presents with acute coronary syndromes





PHASE 5 (lesion type Va or Vb) Stable angina pectoris, or late silent occlusion

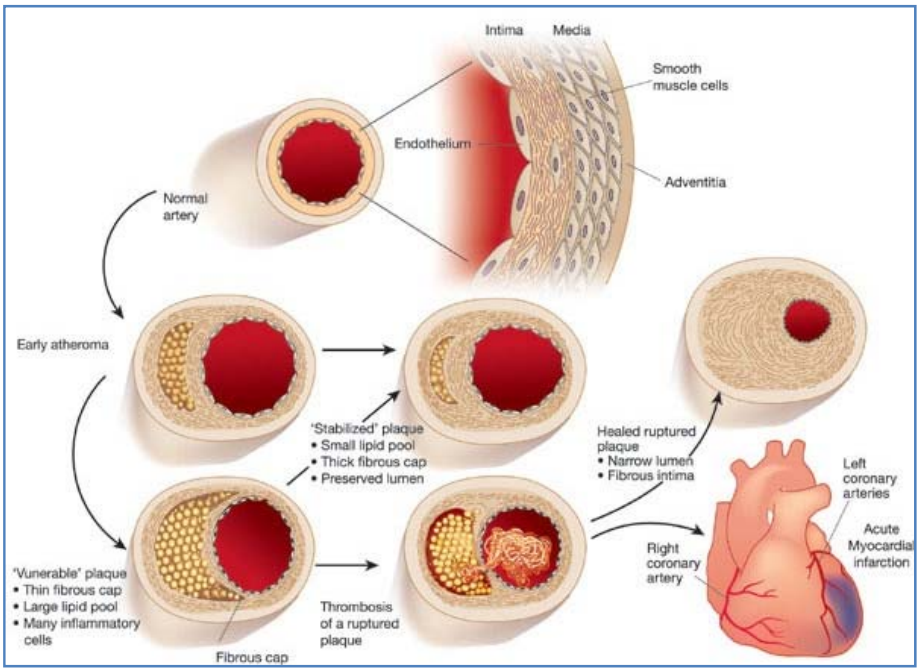


Fig 1. Phases of atherosclerotic plaque growth

FACTORS IMPLICATED IN PLAQUE INSTABILITY AND DISRUPTION:

1. Factors which are intrinsic to the plaque which makes it more prone for rupture includes size, location and lipid content and solidarity of the fibrous cap. The cap is weak at its stalk.
2. Activity of the macrophages, monocytes and T cells in the atherosclerotic plaque also has a role in plaque stability. Macrophages and monocytes derived foam cells secrete metalloproteinases. They degrade the collagen content of the plaque.
3. The activated macrophages, monocytes and lymphocytes may produce inflammatory cytokines which in turn recruit cytokines and produce oxidative stress by producing reactive oxygen species.

4. There is increased programmed cell death of the smooth muscle cells in the mature atherosclerotic lesions. T lymphocytes and macrophages also undergo apoptosis in advanced lesion. These factors may weaken the plaque.

AFTER PLAQUE RUPTURE :

Following rupture of the fibrous cap the more prothrombotic underlying denuded materials are exposed to blood circulation. Circulating platelets first deposit which directly overlies the disrupted plaque leading to the formation of ‘white clot’.Red cells and fibrin deposit over white clot forming red clot.

Fibrinolytic agents lyse the red clot.When used alone they are prothrombotic by the release of thrombin.They should be used in conjunction with anti platelet agents and anti coagulants. Thrombin which is a clotting factor aids in the conversion of fibrinogen to fibrin and also stimulates platelet aggregation.Hence fibrinolysis should be always followed by anti platelet and anticoagulant therapy.

Of the constituents of plaque lipid core has maximum thrombogenicity. This increased thrombogenicity is due to the increased expression of factors like tissue factor in lipid core.The tissue factor produced by the infiltrating cells

in the plaque which via activation of coagulation cascade produce thrombin. This leads to thrombus production and vast spectrum of clinical possibilities.

CORONARY ARTERY DISEASE:

The most common symptom of patients presenting with coronary artery disease is angina or chest pain.Angina may be stable or unstable.The most widely used scoring system for angina is Canadian Cardiovascular Association classification

CANADIAN CARDIOVASCULAR ASSOCIATION CLASSIFICATION OF ANGINA :

"Class 1 : Patients with no pain with ordinary physical activity

Class 2 : Patients who present with slight limitation of physical activity (pain occurs while climbing stairs, walking, stress etc)

Class 3 : Patients who present with severe limitation of daily activity (pain occurs on minimal exertion)

Class 4 : Patients who present with pain at rest or unable to carry out normal activity without pain."

STABLE ANGINA:

Stable angina is defined as chest pain which occurs during exertion,emotion or activity.The pain is usually relieved by rest or nitrates.The pain lasts for short periods of time usually less than 10 minutes.

Males constitute 70% of patients with ischemic cardiac even in greater proportion in patients less than 50 years of age. Angina is typically crescendo and decrescendo in nature lasts for 2 to 5 mins, radiates to either shoulder or arm, to the jaw, root of the neck, epigastrium and teeth. Myocardial chest pain usually donot radiate to trapezius and this differentiates it from pericardial chest pain Patient cannot pinpoint anginal pain and they typically place a clenched fist over the sternum to localise the pain (LEVINE SIGN). Anginal equivalents include dyspnoea, nausea, fatigue, retching, faintness etc.

STRESS TESTING :

ELECTROCARDIOGRAPHIC: This is the most commonly employed test for the diagnosis of ischemic heart disease and for assessing the risk and prognostification of coronary artery disease. The test is carried out by incremental increase in external workload and assessing patients ‘ symptoms, ecg changes and blood pressure.

The test is discontinued when the patient experiences chest pain, breathlessness, severe fatigue, ST segment depression >0.2 mV, development of ventricular tachycardia, fall in sBP greater than 10 mm Hg. A positive stress test

is considered when there is ST segment depression of more than 0.1 mV for more than 0.08 sec. Negative exercise testing in which the target heart rate (85% of the predicted heart rate for age and sex) is considered non diagnostic.

However a positive stress test is highly suggestive of ischemic heart disease in males more than 50 years of age who have typical history of chest pain and who develop chest discomfort during stress test. False negative stress may be seen in Left circumflex artery occlusion because these changes are not recorded in surface ecg.

Contraindication for stress test include rest angina, unstable angina in the last 48 hours, severe aortic stenosis, severe pulmonary hypertension, acute infective endocarditis, acute myocarditis

CARDIAC IMAGING :

This includes stress myocardial perfusion imaging after the intravenous administration of Thallium 201 or 99 m Technetium. Pharmacological stress testing includes administration of dobutamine, dipyramidamole or adenosine.

Cardiac Magnetic Resonance stress testing is also an effective alternative for PET scan, radionuclide or echocardiographic stress testing.

CORONARY ARTERIOGRAPHY :

This test visualises the lumina of the coronary arteries and helps in ruling out serious coronary obstruction. Indications include

1. Patients with chronic angina not relieved with medication.
2. Patients with troublesome symptoms to confirm or rule out diagnosis of IHD
3. Patients with angina who survived cardiac arrest.

UNSTABLE ANGINA :

Unstable angina is defined as

- Pain occurring at rest – duration > 20min, within one week of first visit
- New onset angina – ~ Class 2 severity, onset with last 2 months
- Chest pain which is worsening in quality,duration and frequency.
- Angina refractory to medical therapy

PATHOPHYSIOLOGY :

1.plaque rupture or erosion with superimposed non occlusive thrombus

2.dynamic obstruction (eg.coronary spasm)

3.Progressive mechanical obstruction

4. UA secondary to increased myocardial oxygen demand and or decreased supply.

Patients with ST segment elevation in ECG which is persistent usually have total occlusion of the coronary vessels.They usually benefit from opening up of the coronary vessels by reperfusion therapy either medical or catheter based.

Patients with anginal chest without ST segment elevation in ECG usually have partial occlusion of the coronary vessels. They donot benefit from reperfusion therapy but they require anti ischemic therapy.

Thus the 12-lead ECG remains the main diagnostic tool for the management of patients with ACS.

ROLE OF CARDIAC BIOMARKERS :

Myocardial injury can be detected by the presence of certain proteins released from damaged myocardial cells.Cardiac biomarkers with enhanced sensitivity has enabled clinicians to identify lower levels of myocardial injury. However it must be borne in mind that these biomarkers donot provide any insight into the cause of injury.MI is due to myocardial injury that results from ischemia. Other non ischemic insults like myocarditis, direct myocardial toxins can result in myocardial injury.It is recommended that therapy should be initiated immediately without waiting for cardiac biomarker assay reports and treatment can be initiated based on clinical presentation and electrocardiographic findings in patients presenting with acute chest pain.

Cell death with lysis breaks the integrity of the sarcolemmal membrane. Intracellular molecules diffuses into the cardiac interstitium from where they are absorbed into capillaries and lymphatics and reach the blood stream.The presence of these biomarkers in blood depends on many factors like the location of the biomarker inside the cell,its molecular mass,blood flow in the region of infarct and the speed of elimination from the bloodstream.

An ideal cardiac biomarker should be present in a higher concentration in myocytes, specific to myocardium,released early in injury,released in proportion to injury and cheap for testing.

Cardiac biomarkers include:

- Troponins
- CKMB
- Myoglobin
- Other markers

Cardiac Troponin :

It is the preferred biomarker to detect myocardial injury.It contains 3 subunits: troponin C, troponion T and troponin I.Troponin is present in actin myosin complex and regulates calcium mediated muscle contraction.6 to 8 % of TnT and 2 to 3 % of TnI is found in cytosolic pool. Following myocardial injury, troponin is first released from cytoplasmic pool followed by release from structural pool .Separate genes encode troponins in cardiac and skeletal

muscles. This allows specific antibody production for the cardiac forms (cTnT and cTnI), enabling the quantitative measurement of them. Detection of a rise and fall in cardiac troponins in an appropriate clinical setting has become the centre of the new diagnostic criteria for MI.

Newer high- sensitivity assays are available for precise measurement of very low concentrations of cardiac specific troponin. The term high sensitivity troponin is reserved for assays that can detect cardiac troponin in more than 50% of an apparent healthy population.These assays are more sensitive but lack the specificity for MI.However in multiple studies in patients with non traumatic chest pain, the diagnostic accuracy has been increased by hsTn assays.

In patients with MI, cardiac troponins begin to rise by 3 hours after the onset of chest pain and persist for 7 to 10 days after MI.This prolonged persistence allows for late diagnosis of MI.Patients who undergo successful recanalisation of the thrombosed artery also have a rapid rise in troponin levels.

In the absence of cardiac specific troponin assay, CK MB measured with a mass assay is the best alternative.Cardiac muscle has both MM and MB isoenzymes of CK. Other tissues like small intestine, tongue, diaphragm, uterus, prostate contain small amount of the CK MB isoenzyme. Strenuous exercise can cause increase in both total CK and CK MB. Because of this, the cut off value

for abnormal elevation of CKMB is usually set a few units above the upper reference limit for a given laboratory.

Cardiac troponins and CKMB are said to be increased only if the values exceed the 99% of a reference control group. Assays that have a level of imprecision (i.e., coefficient of variation)of less than 10% at the specific 99th percentile cut off are considered optimal for clinical practice.

Indicators of inflammation or activation of coagulation cascade like myeloperoxidase, soluble CD40 ligand, IL6, hsCRP, d dimer, prothrombin fragment 1 & 2 are elevated before the onset of irreversible injury, however they lack the specificity.

B –type Natriuretic Peptide, Pregnancy Associated Plasma Protein A (PAPP-A) and heart fatty acid binding protein are other biomarkers without much sensitivity or specificity.

2007 ACC/AHA guidelines regarding cardiac biomarkers :

- Cardiac biomarkers should be measured in all patients presenting with acute onset of chest pain (class Ib)
- Troponin is the preferred cardiac biomarker(Class 1 B)
- If troponin values measured within 6 hours of onset of chest pain they should be repeated 8 to 12 hours later.

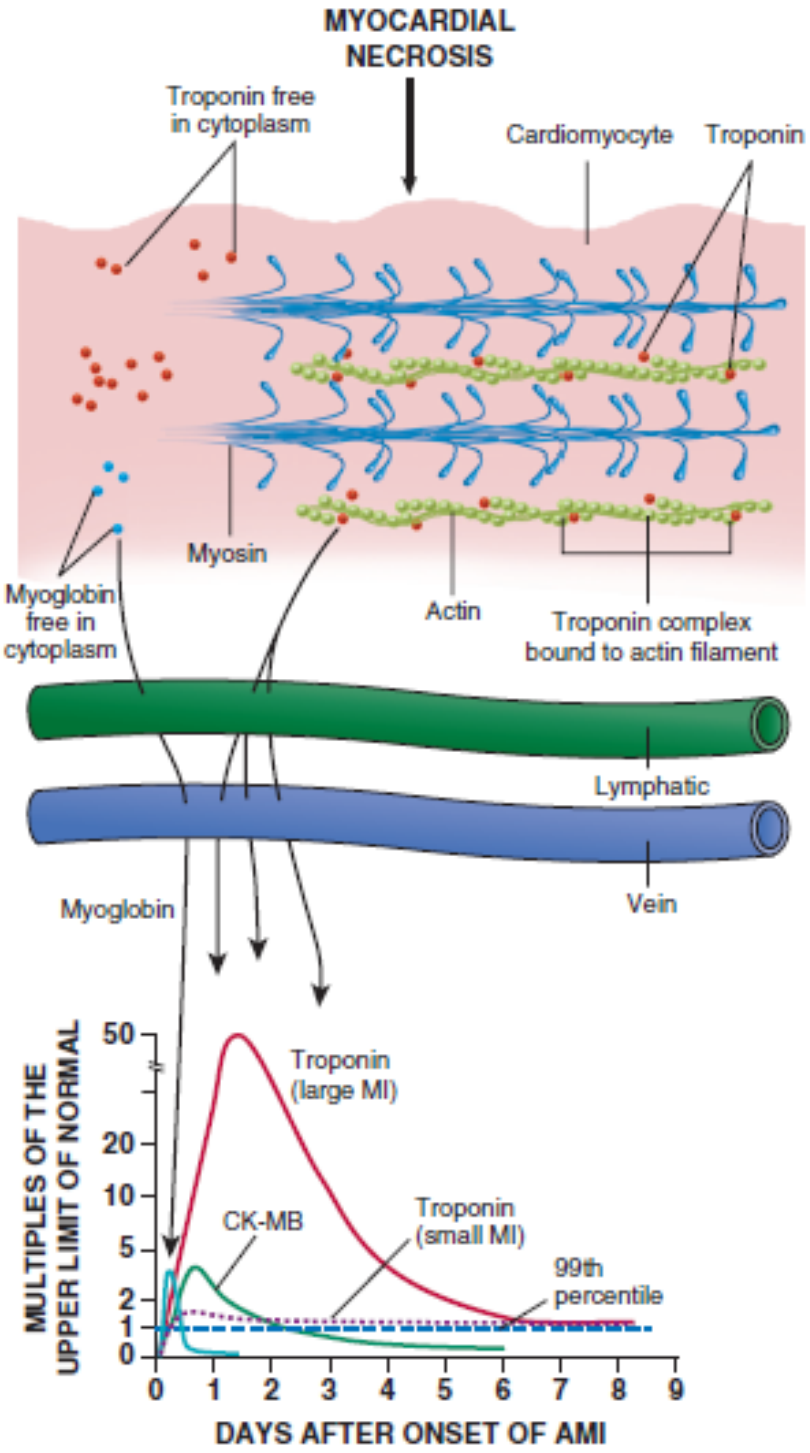


Fig 2 : Release of Cardiac Biomarkers and their serum level

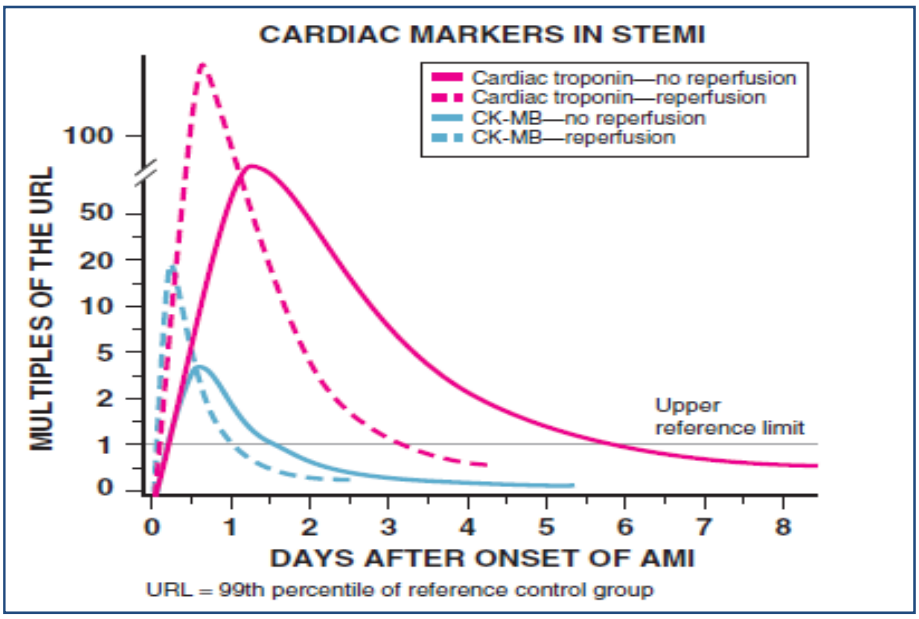


Fig 3 : Cardiac biomarkers in MI

Thrombolysis in Myocardial Infarction (TIMI) Score for ST elevation Acute Myocardial Infarction(increase in mortality with increasing score ~40% all cause mortality at 14 days for patients requiring urgent revascularization)

- “Diabetes, history of hypertension or angina(1 point)
- Systolic BP less than 100 mm hg(3 points)
- HR more than 100 BPM (2 points)
- Killip class II-IV (2 points)
- Body weight less than 67 kg (1 point)

- ST elevation in anterior leads or left bundle branch block morphology (1 point)
- Time at presentation more than 4 hours(1point)
- Age

  >=75 years old (3 points)

  65-74 ears old (2points)

  Less than 65 (0 points)

KILLIP SCORE :

Class 1 : no evicence of CHF 5.1 % mortality rate

Class 2 :Rales,increased JVP or S3 13.6 % mortality rate

Class 3 : Pulmonary edema 32.2 % mortality rate

Class 4: Cardiogenic shock 57.8 % mortality rate

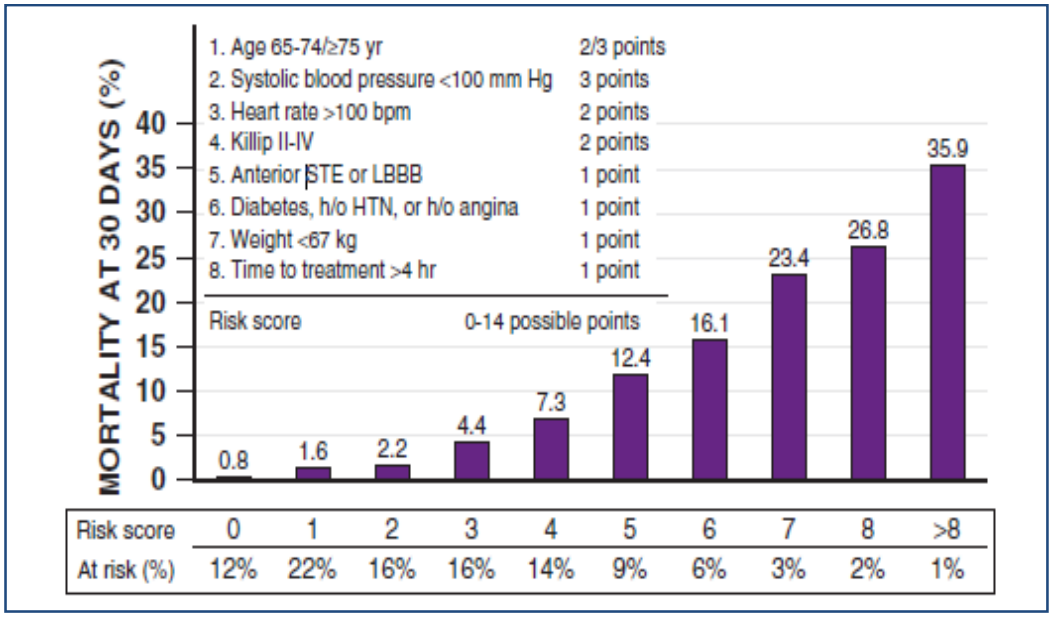


Fig 4 : TIMI score and mortality risk in days

MANAGEMENT :

General considerations

ECG should be obtained within 10 minutes of hospital arrival.

Presence of ST elevation of 0.1 mV in 2 contiguous leads must alert the physician for rapid evaluation of reperfusion therapy

Benchmark standards for medical systems to use when assessing the quality of their healthcare and performance are a door-to-needle time for initialisation of thrombolytic therapy of 30 minutes or less and door-to-balloon time of 90 minutes or less for PCI

General treatment measures include high dose aspirin, analgesics like morphine, nitrates, beta adrenergic blocking agents (in the absence of hypotension sBP< 90), bradycardia (HR <60 bpm), Significant atrioventricular (AV) block and killip class ii or more .

MEDICAL THERAPY FOR THE TREATMENT OF ACUTE CORONARY SYNDROMES

1. Thrombolytics

2. Anti platelet agents:

Aspirin

Adenosine diphosphate antagonists : clopidogrel, ticlopidine

Glycoprotein II b/III a antagonists : Abciximab, Ebtifibatide, Tirofiban

3.Anticoagulants :

Heparin either low molecular weight or unfractionated

4.Antianginals

Oxygen

Nitrates

Beta adrenergic receptor blockers

5. Other agents

Angiotensin converting enzyme inhibitors

Statins

THERAPY PRIOR TO REPERFUSION:

According to 2007 ACC/AHA guidelines, the initial management consists of:

It involves rapid triage of the patients.

If the electrocardiogram is inconclusive or the diagnosis is doubtful, cardiac biomarkers should be ordered

Patients who have inconclusive ECG and negative biomarkers at 12 hours should be subjected to stress test at 72 hours.

OXYGEN :

Supplemental oxygen by means of nasal canula is advised for all patients with MI.When patient presents with acute pulmonary edema or cardiogenic shock oxygen administration of oxygen through aace mask or endotracheal tube is indicated.

ANALGESICS:

MORPHINE: Still has Class 1 recommendation for STEMI, should be given in titrated doses.

NSAIDs should be avoided in patients presenting with acute STEMI

ANTI ANGINALS:

BETA BLOCKERS :

- BETA BLOCKERS
- Modified recommendation
- Oral Beta Blockers should be started as soon as possible, if there are no contra-indications (heart failure, risk of cardiogenic shock)
- Patients who present with early contra indications should be re-evaluated later for possible use
- IV B blockers – are used in hypertensive patients with STEMI and it should not be administered to patients with heart failure or risk of cardiogenic shock.
- Beta blockers are proved to have both mortality and morbidity benefit

NITRATES:

Sublingual nitroglycerin is given to patients with acute MI to determine whether the ST segment elevation represents coronary vasospasm while arrangements for reperfusion is considered.They are particularly useful in the management of MI complicated with CHF,ongoing symptoms or hypertension.Both oral or intravenous dosing can be used.

ANTIPLATELET THERAPY:

It receives Class I recommendation

- Aspirin should be given immediately on admission to all patients who present with acute STEMI.Enteric coated formulation should be avoided. Chewable buccal aspirin is given as 325 mg stat dose followed by a maintenance dose lifelong unless there are any contraindications.
- Higher doses for patients who undergo stenting .
- CLOPIDOGREL – now recommended in all STEMI patients in addition to aspirin, whether undergoing reperfusion or not. Dosage 75mg daily or a duration of 14 days
- In patients < 75yrs – Clopidogrel 300mg loading dose recommended

  long term maintenance therapy should be considered, 75mg daily for 1year
- For patients who have been planned for PCI – aspirin & clopidogrel or IV glycoprotein 2b/3a therapy is recommended
- Abciximab is used if there is no delay in angiography/PCI, eptifibatide/tirofiban if delayed angiography is planned (LOE B)
- Abciximab is not recommended if PCI is not planned.

ANTICOAGULANT THERAPY :

Unless there is any contraindication patients should be started on anticoagulant therapy.Unfractionated heparin given as 60 units /kg bolus followed by 12 u/kg infusion.LMWH is an effective alternative. However dose adjustments is needed for renal failure patients.

LIMITATION OF INFARCT SIZE :

Size of the infarct is an important indicator of prognosis in patients with MI. Infarct size limitation is the primary goal in the treatment of MI. In addition to saving lives saving myocardium is important in patients presenting with STEMI .Spontaneous recanalization of an occluded artery occurs in up to 1/3 rd of patients . This delayed spontaneousreperfusion may be beneficial by enhancing left ventricular function. Yet, maximal salvage of myocardium is done by strategies involvingfibrinolysis and catheter-based reperfusion of the occluded coronary artery.

CONCEPT OF REPERFUSION THERAPY :

Rapid opening of the infarct artery and reperfusion of the damaged myocardium is the most efficient way of restoring normal cardiac function. The time elapsed for reperfusion therapy greatly affects the amount of salvaged myocardium in patients treated with either fibrinolysis or PCI.As the clot matures, it becomes resistant to fibrinolytic therapy. In some patients with cardiac failure the infarction occurs in a slowly progressive way rather in an abrupt fashion. They should be evaluated by careful history to ascertain whether they were having recurrent episodes of chest pain.In such patients rigid time interval should not be advocated while determining the time interval for reperfusion therapy

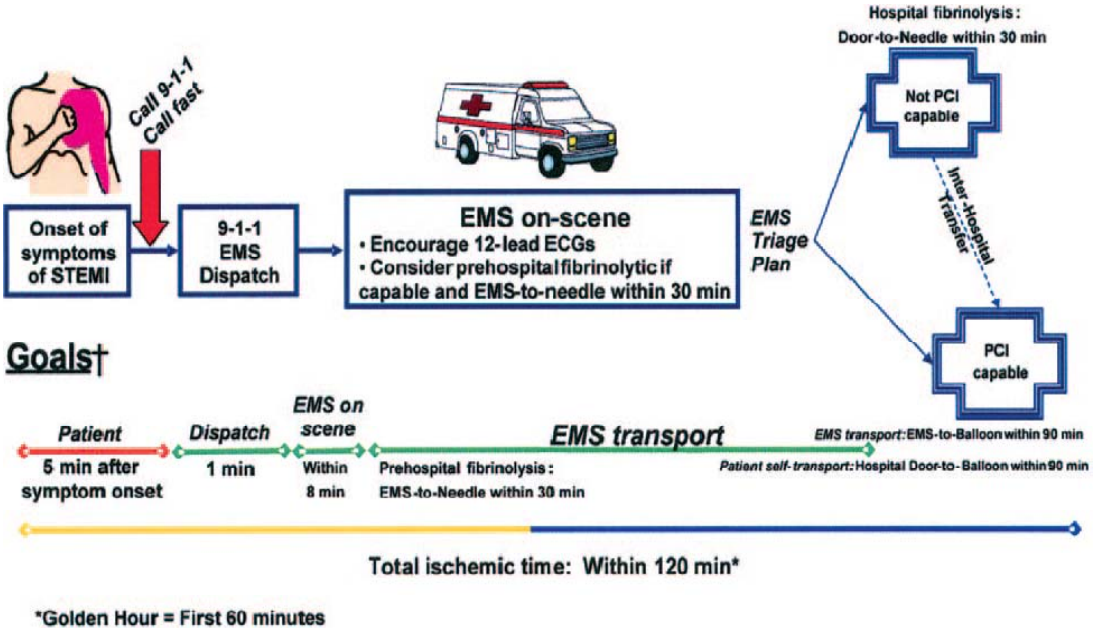


Fig 5: Initial reperfusion therapy in patients with STEMI

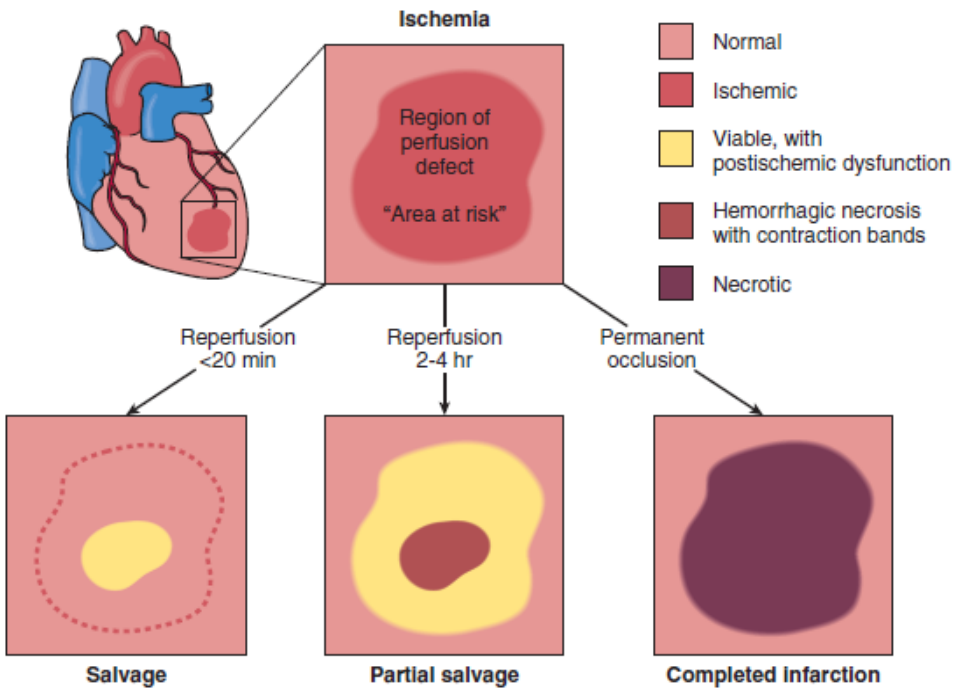


Fig 6 : Consequence of reperfusion at various time after coronary adhesion

Prevention of cell death by revascularisation depends on the severity and duration of pre existing ischemia. With earlier restoration of blood flow, the left ventricular systolic function, diastolic function and mortality are favourably influenced. Presence of Collateral coronary vessels also influence left ventricular functioning following reperfusion. A phenomenon called Myocardial stunning which is the reversible contractile dysfunction seen after successful reperfusion in some patients.

REPERFUSION INJURY :

Although reperfusion is associated with myocardial salvage, it may be accompanied by adverse events termed as Reperfusion Injury. Types of reperfusion injury includes :

1. Lethal reperfusion injury : Here there is death of myocytes following reperfusion
2. Vascular reperfusion injury : Reperfusion induced expansion of zone of no reflow and loss of coronary vasodilatory reserve
3. Stunned myocardium : myocytes exhibit a period of transient defective contraction following reperfusion
4. Reperfusion arrythmias : Bursts of VT or VF that occurs within seconds of reperfusion.

Transient sinus bradycardia and hypotension can occur in some patients with inferior wall infarcts. Premature ventricular contractions, accelerated idioventricular rythm(AIVR) and non sustained VT are common. When present rythm disturbances may actually indicate successful reperfusion, but their specificity is minimal. Although reperfusion arrhythmias cluster around the time of restoration of coronary perfusion, this brief electrical storm is usually innocuous and usually no prophylactic or specific anti arrhythmic therapy is

needed unless there is hemodynamic compromise following reperfusion arrhythmias.

Microvasculature damage in the reperfused myocardium leads to hemorrhagic infarct, which is more seen with fibrinolytic therapy than with catheter based reperfusion.

A variety of therapies have been proposed to mitigate the effects of reperfusion injury including preservation of microvascular integrity by using anti platelets and anti thrombins. These agents minimize embolisation of atheroembolic debris and prevent inflammatory damage. Remote conditioning which is the induction of transient ischemia in other vascular beds has been associated with a reduction in reperfusion injury..Another approach is Post conditioning ,which involves introducing brief repetitive episodes of ischemia alternating with reperfusion. This activates cellular protective mechanisms centering around pro survival kinases.

Late reperfusion of the stenosed infarct related artery may also improve myocardial function. Poorly contracting myocardium in the zone of infarct related artery may contain viable myocytes. The function of this hibernating myocardium can be improved by PCI.

FIBRINOLYTIC THERAPY :

Fibrinolysis recanalizes the thrombotic occlusion in vessel wall associated with STEMI. Patients treated in the initial 1 to 2 hours has the maximum benefit. Time is muscle and hence early treatment is associated with maximum benefits

The absolute contraindication for Fibinolytic therapy :

- "Patients with any history ofprevious intracranial bleed.
- Known vascular lesion in brain (e.g., arteriovenous malformation).
- Known intracranial neoplasm (primary or metastatic).
- Ischemic stroke within 3 months *except* acute ischemic stroke within 4.5 hours
- Suspected aortic dissection..
- Active bleeding or bleeding diathesis (excluding menses).
- Significant closed-head or facial trauma within 3 months.
- Intracranial or intraspinal surgery within 2 months.
- Severe uncontrolled hypertension (unresponsive to emergency therapy).
- For streptokinase, previous treatment within the previous 6 months."

All fibrinolytic agents exert their effect by converting the inactive plasminogen to the active enzyme plasmin. Fibrin specific fibrinolytics are those that are inactive in the absence of fibrin and substantially increases its activity on plasminogen in its presence. The tissue plasminogen activator molecule contains 5 domains. Fibrin provides a scaffold in which t PA and plasminogen are held in such a way that the activity of t PA is increased manyfold. Accelerated dose of tPA is preferred ,where it is administered over a period of 90 minutes. Modification in the native structure of t PA led to the discovery of newer fibrinolytic agents that have increased plasma clearance allowing bolus dosing. These agents include alteplase, tenecteplase and reteplase. Streptokinase ,a protein secreted by streptococci ,is an inexpensive fibrinolytic agent which is used in developing countries. It is fibrin non specific.

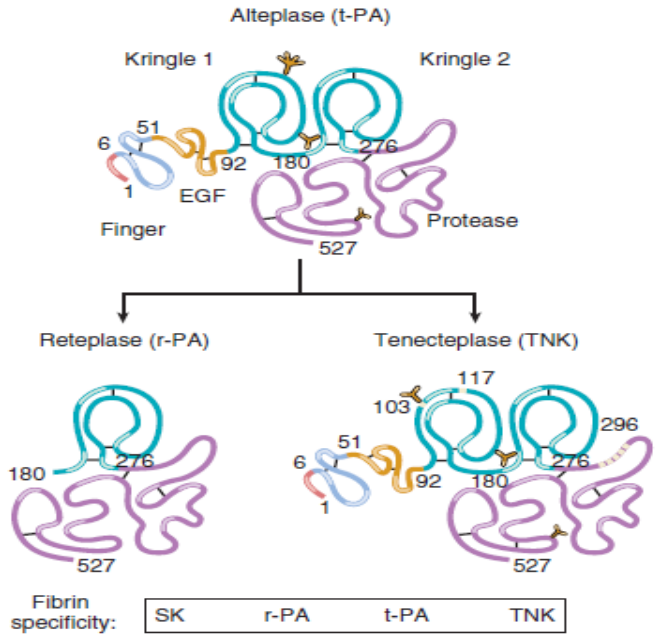


Fig 6 : Molecular Structure of Different Fibrinolytics

Table 1: Comparison of approved fibrinolytic agents

FIBRINOLYTIC AGENT	DOSE	FIBRIN SPECIFICITY	FIBRINOGEN DEPLETION	ANTIGENIC
Tenecteplase	Single iv weight based bolus	++++	minimal	-
Reteplase(r PA)	10 units + 10 units iv boluses 30 min apart	++	moderate	-
Alteplase (t PA)	90 min wt based infusion	++	mild	-
Streptokinase	1.5 million units iv over 60 mins	No	marked	+

TENECTEPLASE:

Bolus of 30 mg for weight less than 60 kg, 35 mg for 60 to 69 kg, 40 mg for 70 to 79 kg, 45 mg for 80 to 89 kg, and 50 mg for 90 kg or greater.

ALTEPLASE:

Bolus of 15 mg, infusion of 0.75 mg/kg for 30 minutes (maximum, 50 mg), then 0.5 mg/kg (maximum, 35 mg) over the next 60 minutes; the total dose not to exceed 100 mg.

Fibrinolytics of differ in their molecular structure and biochemical action but they seem to be more equivalent in their clinical complication and biological activity. All these drugs degrade the thrombus through plasmin, resulting in hypocoaguability. They are usually given in infusions and the duration of infusion is inversely proportional to the half life of the compounds. After therapy is discontinued there is a hypocoaguability due to reduced fibrinogen in the plasma and this continues till the activator is eliminated from the blood .Coagulation and platelet may be transiently increased after administration of the agent. Within the initial hours coronary reperfusion can be achieved with almost all thrombolytics (50 – 60 % of all patients).With greater hour of thrombus the efficacy is better with rt-PA than streptokinase. However reocclusion is commoner with rt-PA than streptokinase. Anti-platelet agents have greater additive role in preventing re-occlusion when used along with

thrombolytics and they have shown mortality benefit too. Intracranial bleeding and cerebrovascular accident are the most common side effect of thrombolytic use. If the patient presents more than 12 hours, the risk of bleeding outweighs the benefit from thrombolysis.Failure rates will also be very high. In cases of failure of the therapy the patient is treated conservatively with anticoagulants to complete the infarct or may be advised to undergo percutaneous coronary intervention.

PERCUTANEOUS CORONARY INTERVENTION:

Primary PCI when performed can open the infarct related artery in around 95 % of cases compared to spontaneous recanalisation of arteries. Primary PCI includes performing coronary angiogram to identify the occluded vessel followed by angioplasty to open up the infracted artery.

ASSESSMENT OF REPERFUSION :

The TIMI flow grade

The TIMI frame count

Myocardial perfusion

Electrocardiography :

The extent of ST-segment resolution provides powerful prognostic information early in the management of patients with STEMI

Non invasiveimaging :

Myocardial contrast enhanced echocardiography

Invasive imaging : Doppler flow wire studies

In ECG successful thrombolysis can be assessed by : ECG should be obtained immediately after 30 minutes of completion of thrombolysis. Resolution of ST segment elevation by more than 70 % of the previous ecg

Relief of chest pain

Return of hemodynamic stability

Presence of reperfusion arrhythmias

In the presence of failed thrombolysis patients should be immediately advised for Rescue PCI.

Even in the presence of successful thrombolysis patient should be advised for Coronary angiogram to identify the culprit vessel and to remove any residual plaque. Patients can be advised for CAG immediately after lysis with tenecteplase but should wait for atleast 1 day following lysis with Streptokinase.

Increased focus is now been laid on secondary prevention of acute coronary syndromes which includes

- Risk factor modification
- Diet modification and ideal body weight maintenance
- Hypertension management
- Hypercholesterolemia management
- Exercise
- Diabetes management

DIABETES MELLITUSAND CORONARY ARTERY DISEASE :

Diabetes mellitus is characterised by recurrent or persistently elevated blood sugar and diagnosed by one of the following

" 1. fasting plasma glucose level greater than or equal to 7 mmol/l or 126 mg/dl

2. Plasma glucose greater than or equal to 11.1 mmol/l or 200 mg/dl 2 hours after a 75g oral glucose load in a glucose tolerance test

3. Symptoms of high blood sugar plus a random plasma glucose greater than or equal to 11.1 mmol/l or 200 mg/dl

4. Glycated haemoglobin (HbA1c) greater than or equal to 6.5%"

Besides diabetes ,diabetics present with other cardiovascular risk factors like hypertension, dyslipidemia, atherosclerosis etc. But beyond this clustering there are numerous other implicated mechanisms in the increased risk among

patients with diabetes. There is a clear association between the severity of hyperglycemia and cardiovascular mortality.

The vascular injuries seen in diabetes include autonomic dysfunction, effects of circulating reactive oxygen species fatty acids, adverse effects of advanced glycation end products , and increase in the systemic mediators of inflammation. Exposure to increased insulin therapy, sympathovagal imbalance also contributes to atherosclerotic risk.The various contributing factors in diabetic patients leading to atherosclerosis include:

ENDOTHELIUM:

↑ NF-κB activation

↓ Nitric oxide production

↓ Prostacyclin bioavailability

↑ Endothelin 1 activity

↑ Angiotensin II activity

↑ Cyclooxygenase type 2 (COX-2) activity

↑ Thromboxane A2 activity

↑ Reactive oxygen species

↑ Lipid peroxidation products

↓ Endothelium-dependent relaxation

↑ RAGE expression

Vascular smooth muscle cells and vascular matrix:

↑ Proliferation and migration of vascular smooth muscles into intima

↑ Incresed degradation of matrix.

Altered matrix components:

Inflammation ↑ IL-1β, IL-6, CD36, MCP-1

↑ ICAMs, VCAMs, and selectins

↑ Activity of protein kinase C

↑ AGEs and AGE-RAGE interactions

The injurious effects of hyperglycemia can be divided into microvascular and macrovascular complications.

MACROVASCULAR COMPLICATIONS:

Diabetes is a major risk factor in the development of atherosclerosis. Atherosclerotic lesion plays a major role in macrovascular complications.

This includes

a) Ichemic cardiovascular disease
b) Peripheral arterial disease
c) Cerebrovascular disease

MICROVASCULAR COMPLICATIONS:

a) Eye – Retionopathy (proliferative and non proliferative)

   Macular edema

b) Neuropathy –mainly small fibre neuropathy both sensory and motor

   Mononeuropathy and polyneuropathy

c) Nephropathy

Microvascular complications should be screened immediately for type 2 diabetics and can wait for 5 years in type 1 diabetics.

Genetic factors appear to contribute to the susceptibility to microvascular disease.

CAD AND DIABETES :

Coronary artery disease accounts for nearly 80% of deaths in patients with diabetes. Once recognised as a disease of adulthood it is now frequently seen in adolescent population. There are more women diabetics than males. Patients with diabetics have a varied presentation of symptoms of myocardial infarction usually without chestpain. Hence the term silent infarction is used. The risk of cardiac failure and other postmyocardial infarction complications is also high in diabetics. They present with massive infarction compared to non- diabetics. This increased mortality and morbidity

may be attributed to the chronic hyperglycemia seen in diabetes per se rather than the associated comorbid conditions.

Atherosclerosis play the central role in the macrovascular complications of diabetes. It involves blood vessels in the periphery as well as coronary blood vessels. In coronary vasculature there is more diffuse and severe stenosis of blood vessels and more severe left main disease. In diabetics there is an increase in the expression of adhesion molecules on the endothelial surface. This causes the endothelium to become more adherent to passing cells in the bloodstream. The leucocytes get attached through selectins on their surface to the vascular endothelium. The monocytes get attached to the endothelium and transform into macrophages. They take up oxidised LDL to become macrophage foam cells.

There is a significant reduction in the activity of nitric oxide in diabetic patients. Nitric oxide is essential for normal functioning of vascular endothelium. When it is reduced there is increased activation of adhesion molecules, leucocyte infiltration, reduced vasodilatation, platelet aggregation and thrombosis. The increased oxidative stress ,high circulating lipids, elevated blood glucose levels adversely affects nitric oxide synthesis and function.

Platelet function is also highly abnormal in diadetics. There is increase in the expression of glycoproteins on the platelet surface, increased activation and adhesion. Many clotting factors are also upregulated in diabetics.

FactorVII, thrombin, tissue factor and plasminogen activator inhibitor I are seen in diabetics increases the tendency towards thrombus formation.

Other independant ardiovascular risk factors also cluster in diabetics. Metabolic syndrome is common in diabetics. Because of this diabetes is now considered as a cardiovascular disease equivalent rather than an individual risk factor

PLATELETS :

Platelets also known as thrombocytes are discoidal blood cells that participate in hemostasis. On a stained blood smear , platelets are dark purple in colour about 1/5 th the diameter of red blood cells. They are anucleated and are found only in mammals. The ratio of platelets to red blood cells in adults is 1 : 10 to 1: 20.The main function of platelets is the formation of primary hemostatic plug: they gather at the site of interrupted endothelium and plug the hole. The process includes

adhesion – the platelet attach to substance outside the injured endothelium

activation–they change their structural configuration, secrete chemical messengers and turn on receptors.

Aggreggation-platelets connect with one among themselves.

Once the primary hemostasis is achieved ,coagulation cascade is activated leading to the formation of the fibrin clot (secondary hemostasis) Structurally platelets have 4 zones from outside to inside

1.Peripheral zone : This zone is abundant in glycoprotein required for platelet function (i.e GP II b/III a ;GP Ib/ IX ;GP VI)

2.Solgel zone : This layer has microfilaments and microtubules, which help the platelets to maintain their shape and structure.

3.Organelle Zone : This zone is rich in platelet granules. Alpha granules contain clotting factors like factor V, VIII, I, fibronectin, PDGF. Delta granules contain platelet activating mediators like ADP, calcium and serotonin.

4.Membranous zone : This zone is responsible for thromboxane A2 synthesis.

Megakaryocyte and platelet production is regulated by thrombopoetin which is synthesised in liver and kidney. A megakaryocyte produces 1000 to 3000 platelets during its lifetime. The average lifespan of platelets is 7 to 9 days.

FUNCTIONS OF PLATELTS:

- Prevention of bleeding through formation of hemostatic plug.
- The contractile proteins in platelets causes clot retraction.
- Activation of clotting cascade through the intrinsic mechanism.
- Secretes various vascular growth factors which helps in the growth of endothelial and vascular smooth muscle cell following injury.

MECHANISM OF FORMATION OF PRIMARY HEMOSTATIC PLUG :

At the site of vascular injury ,platelets get attached to the underlying exposed collagen. After attachment platelets change their morphology. Then the alpha and delta granules are released from the platelet surface.ADP is released from the platelet granules which causes the aggregation of platelets.

The platelets which are aggregated adhere to the von willebrand factor. Following this there is more release of ADP and more aggregation of platelets. Platelet aggregation is more reinforced by the release of Thromboxane A2 which causes even more aggregation and more release of ADP. This leads to the formation of primary hemostatic plug

The aggregated platelet plug not only physically seal the break in the vessel but, also perform three other important roles:

- Actin and myosin present in the platelets by contracting strengthens the primary hemostatic plug.
- Secondly, various chemicals released from the platelet plug include several vasoconstrictors (serotonin, epinephrine and Thromboxane A_2) cause vascular vasospasm
- They aid in blood clotting

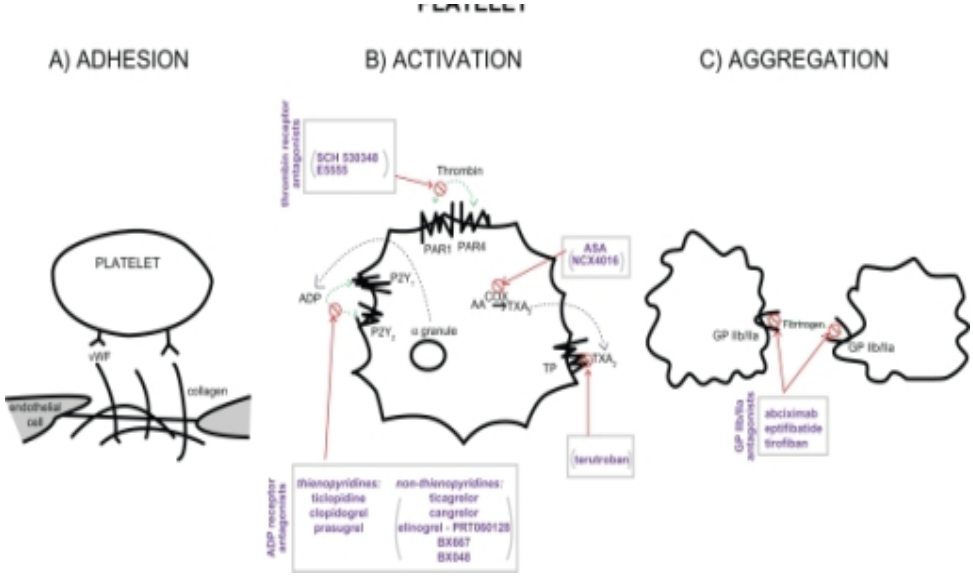


Fig 7:Functions of platelets

Prostacyclin generated in the vascular endothelium prevents platelet aggregation and prevents the spread of spread of platelet plug to the normal vessel wall

PLATELET ACTIVITY AND DIABETES :

The metabolic complications seen in diabetes maybe attributed to the increased platelet activity seen in this metabolic condition. The micro and macrovascular complications seen in diabetics is attributed to altered platelet morphology and function. Platelet hyperactivity and increased baseline activation which is seen in diabetes is multifactorial. There is also an increased surface expression of glycoprotein receptors and increase in the production of growth factors. There is non enzymatic glycation of proteins on the surface of platelets, by the osmotic effect of glucose and by the activation of protein

kinase C. Membrane fluidity is altered by this mechanism and this results in increased platelet activity .Insulin also regulates platelet activity via functional Insulin Receptor found in human platelets. Superoxide released during inflammation increases intraplatelet release of calcium after their activation and increasing their reactivity. Superoxide also inhibits nitric oxide activity and prostacyclin production .Platelets from diabetics have increased expression P selectin and Gp II b/III a receptor and more sensitivity to stimulation from agonist than non diabetics.

Platelet activation causes thrombosis and microcapillary embolisation with release of constrictive, mitogenic substances like PDGF and VEGF.

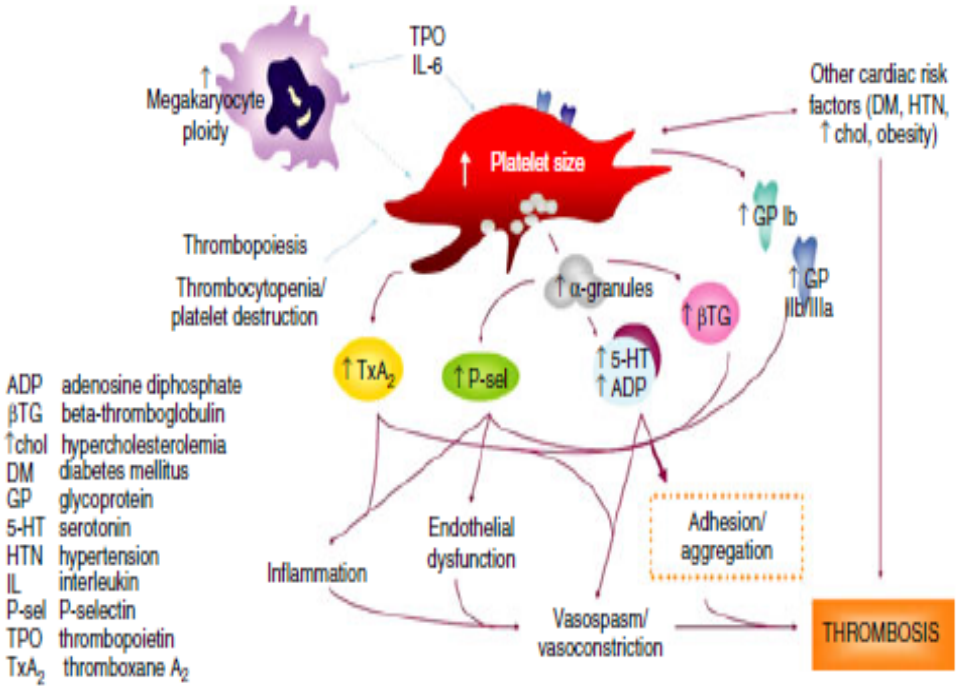


Fig 8:Platelets in CAD patients

MATERIALS AND METHODS:

STUDY POPULATION:

This study is to be conducted among 100 patients diagnosed with STEMI admitted in ICCU within 12 hours of onset of symptoms at Kanyakumari Government Medical College hospital

INCLUSION CRITERIA

- Patients admitted with diagnosis of STEMI within 12 hours from the onset of symptoms.

EXCLUSION CRITERIA:

- Co existing autoimmune diseases
- Acute / chronic infectious /inflammatory diseases
- Known malignant diseases
- Use of steroids
- Admission platelet count below 100 & above 4.5 lakh cell/mm^2

METHODOLOGY:

Patients admitted with ST elevation MI admitted within 12 hours of the onset of symptom were enrolled

Venous blood samples were collected immediately after admission prior to the administration of anti platelet therapy in standardized dipotassium ethylene dinitro acetic acid (EDTA tubes)

Samples were tested within 30 minutes of collection to minimize variations due to sample ageing

Diabetes was defined as

1) Pre existing diabetes diagnosed prior to admission for STEMI (patient on insulin, OHAs or diet)
2) Newly diagnosed diabetes mellitus based on fasting plasma glucose levels. Fasting plasma glucose levels were checked on the third day of admission to avoid stress hyperglycemia

STEMI was defined by :

ST segment elevation consistent with MI of 2 mm in contiguous precordial leads and or ST segment elevation of 1 mm in two or more contiguous limb leads or new onset left bundle branch block

Patients are treated with 300 mg of aspirin & 300 mg of clopidogrel and subjected to thrombolysis with streptokinase

Successful thrombolysis is defined as ST segment resolution > 50% of the original and or symptomatic relief of chest pain.

Admission time Random blood glucose was taken initially to screen diabetics and non diabetics, followed by fasting plasma glucose on day once the patient stabilises.

Since cardiac troponin assay was not available in our setting, CK MB measured with a mass assay was carried out.

Echocardiogram was taken on the third day after thrombolysis to evaluate left ventricular systolic and diastolic functions and other associated complication. Patients were followed up for a period of 1 month for mortality & morbidity. Repeat Echocardiogram is done after 1 month for the evaluation of patient 's cardiac status

Interested patients may be subjected to Angiographic evaluation.

ANTICIPATED OUTCOME:

Diabetic patients are expected to have high MPV than non diabetics.

Both in diabetic and non diabetics MPV proved to have good prognostic value for in-hospital and 1 month mortality

Diabetic patients are expected to have higher mortality at lower MPV values than non diabetic

STATISTICAL ANALYSIS :

Analysis was done using SPSS 16.0 software. Data were expressed in terms of percentages, mean values with standard deviation or median values. Differences between the groups were analyzed using Mann Whitney U test for median and chi square test for proportions. The association of each predictor variable with NAFLD was assessed using Simple Linear Regression models. Results were said to be statistically significant if the p value was less than 0.05.

RESULTS :

In our total study population out of 100 who presented with acute STEMI , 41 were diabetic and 50 were non diabetic. The age pattern of the study population is given in table 1.Most of the patients belonged to the age group 50 to 70 years. There were 64 males and 36 females in the study.

Oldest Patient recorded -33 years

Youngest patient recorded- 90 years

DISCUSSION

PATIENT CHARACTERISTICS :

Table 2: Patient Characteristics

Characteristics	Number of patients
Male	64
Female	36
Smokers	24
Alcoholics	4
Patients with prior cad	15
Hypertensives	36
Infarct wall	Ant wall – 60 Inferior wall – 33 Inf wall ,post wall &right ventricle – 3 Ant wall &inf wall -2

Table 3: Age distribution of the study population

Age	Patients
30 - 40	3%
41 -50	13%
51 - 60	36%
61- 70	28%
>71	20%

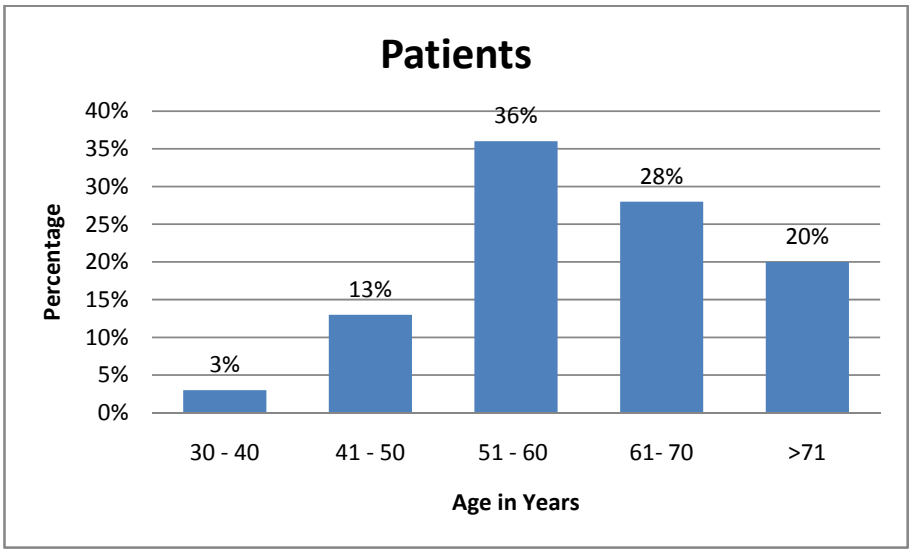


Fig 8: Bar diagram showing age distribution

The patients who presented with STEMI clustered in the age group above 50 years with maximum incidence in the age group 51 to 60 years.

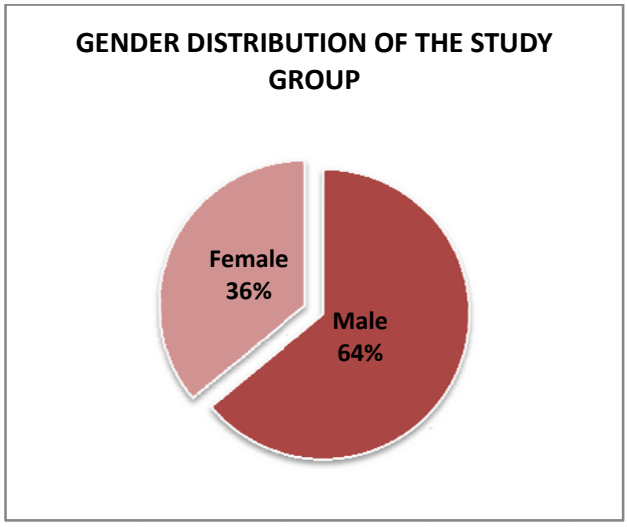


Fig 9: Genderwise distribution of study population

Total no of males with acute STEMI : 64

Total no of females with acute STEMI : 36

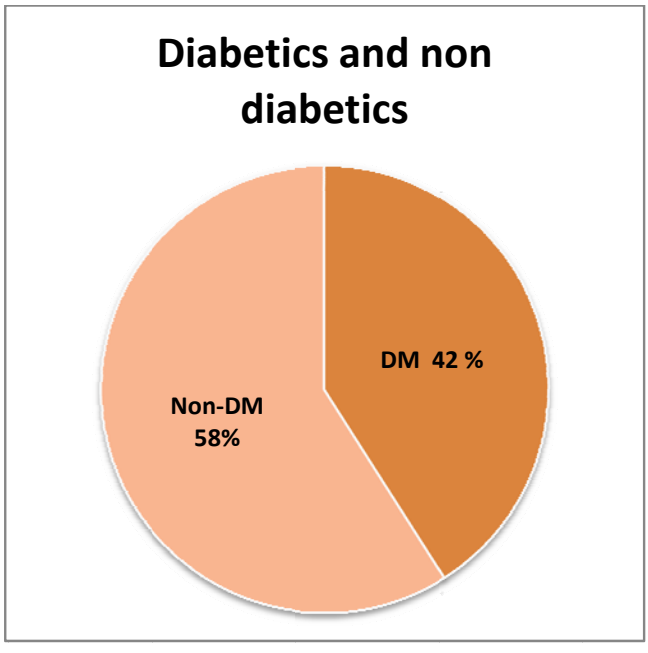


Fig 10: Pie chart showing % of diabetics and non diabetics

Total no of Acute MI patients who were diabetics : 42

Total no of Acute MI patients who were non diabetics : 58

Table 3: SEX DISTRIBUTION AMONG DIABETICS AND NON DIABETICS

	NO OF MALES	% OF MALES	NO OF FEMALES	% OF FEMALES
DIABETICS	25	59.52 %	17	40.47 %
NON DIABETICS	40	68.96 %	18	31.03 %

In our study, among diabetics 59.52 % were males and 40.47 % were females. Among the total males presented 39.06 % were diabetic and among the total female presented 47.22 % were diabetics. This shows that among the patients presented with MI the incidence of diabetes was higher among females in our study

Table 4: HbA1C value among diabetics and non diabetics

	HbA1C	SD
DM	8.08	0.84
Non-DM	5.83	0.42

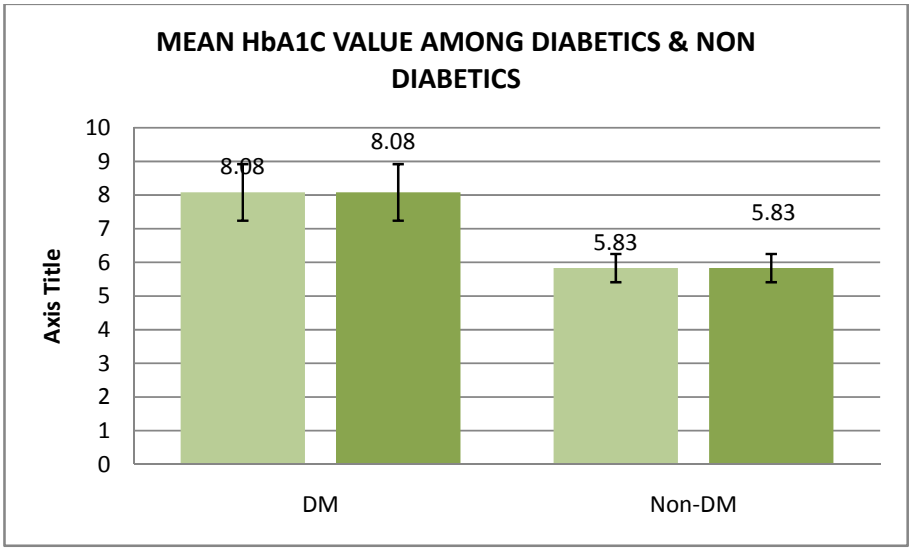


Fig 11: Mean HbA1C value among Diabetics & Non Diabetics

The mean HbA1c values were significantly higher in diabetics compared to non diabetics. The average value was 8.08 for diabetics and 5.83 in non diabetics. The p value of this test is also clinically significant .

Table 5: Mean Platelet volume among Diabetics and Non Diabetics

MPV	N	Mean	S.D	P Value
DM	41	9.94	0.9	<0.0001
Non-DM	59	9.06	0.98	

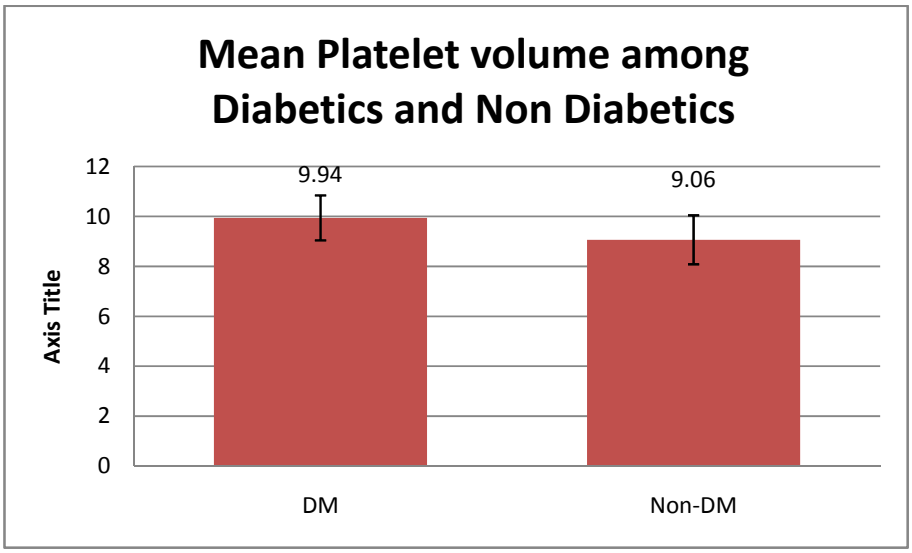


Fig 12: Mean Platelet volume among Diabetics and Non Diabetics

The mean platelet volume was significantly higher among diabetics. The p value of the test was $p< 0.0001$.This study confirms the hypothesis that the platelets in diabetics are large and hyperactive .

Table 6: CKMB volume among Diabetics and Non Diabetics

CKMB	N	Mean	S.D	P Value
DM	41	48.35	38.96	0.847
Non-DM	59	49.61	25.98	

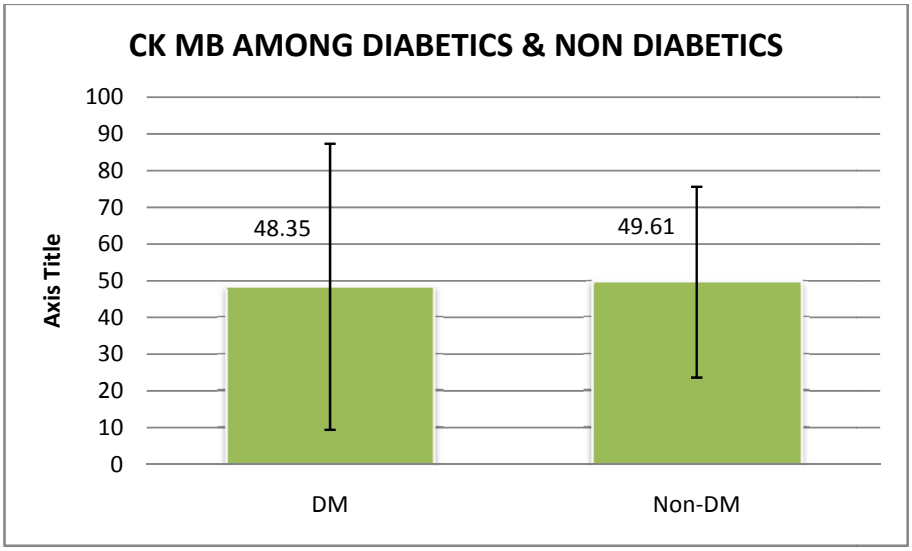


Fig 13: CKMB among Diabetics and Non Diabetics

There was no significant variation in total CKMB value among diabetics and non diabetics presenting with acute STEMI. p value of the test is higher than 0.05 making the correlation insignificant.

Table 7: Mortality among Diabetics and Non Diabetics

	MORTALITY	IP	Follow Up
41	DM	24%	14%
59	NON-DM	8%	0

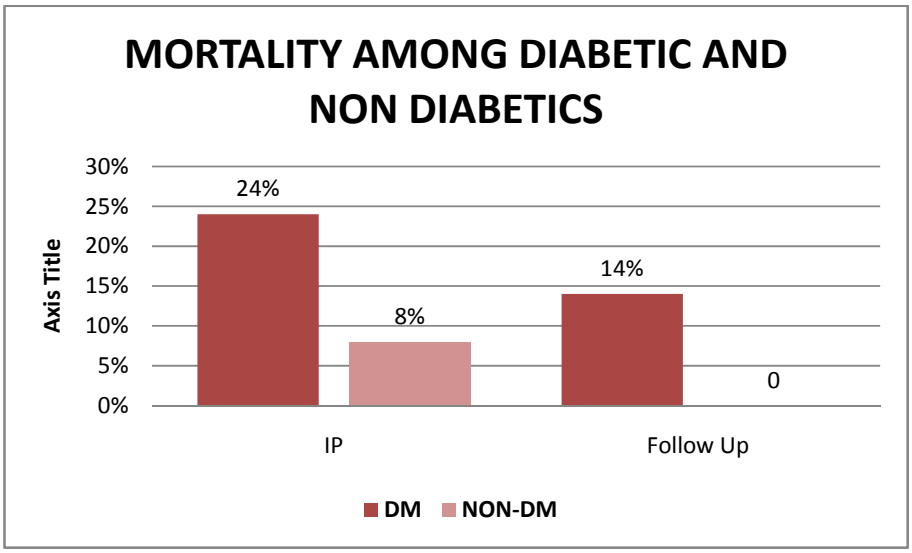


Fig 14: Mortality among Diabetics and Non Diabetics

Diabetics had higher mortality than non diabetics. Both in patient mortality and mortality during 1 month follow up was higher in diabetics.

Table 8: Sex wise Mortality distribution among Diabetics and Non Diabetics

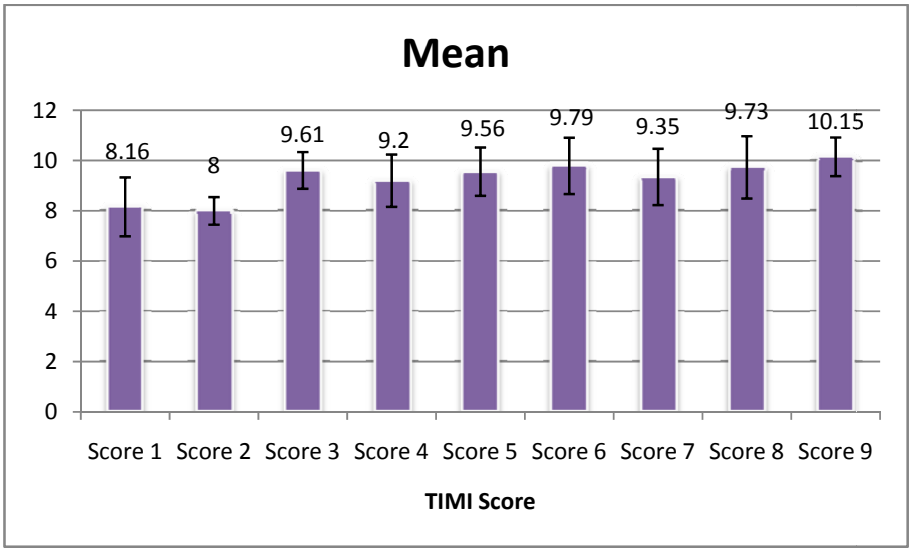
	No of males expired	% of males	No of females expired	% of females
Diabetics	8	50%	8	50%
Non diabetics	4	80%	1	20%

Among the total 21 deaths , 16 were diabetic and the remaining 5 were non diabetics. Among diabetic deaths 8 were males and 8 were females. Among non diabetics 4 were males and 1 was female

Table 9: TIMI score and MPV

	MPV	
TIMI	Mean	SD
Score 1	8.16	1.17
Score 2	8	0.55
Score 3	9.61	0.73
Score 4	9.2	1.04
Score 5	9.56	0.96
Score 6	9.79	1.12
Score 7	9.35	1.12
Score 8	9.73	1.24
Score 9	10.15	0.77

Fig 15: : TIMI score and MPV



Higher TIMI score is associated higher Mean Platelet volume. With progressively increasing TIMI score there is increase in mean MPV with the TIMI score 9 having mean MPV of 10.15 fl

Table 10: KILLIP class and MPV

	MPV	
KILLIP	Mean	SD
Class 1	9.24	1.04
Class 2	9.59	0.93
Class 3	9.68	1.19
Class 4	10.65	0.07

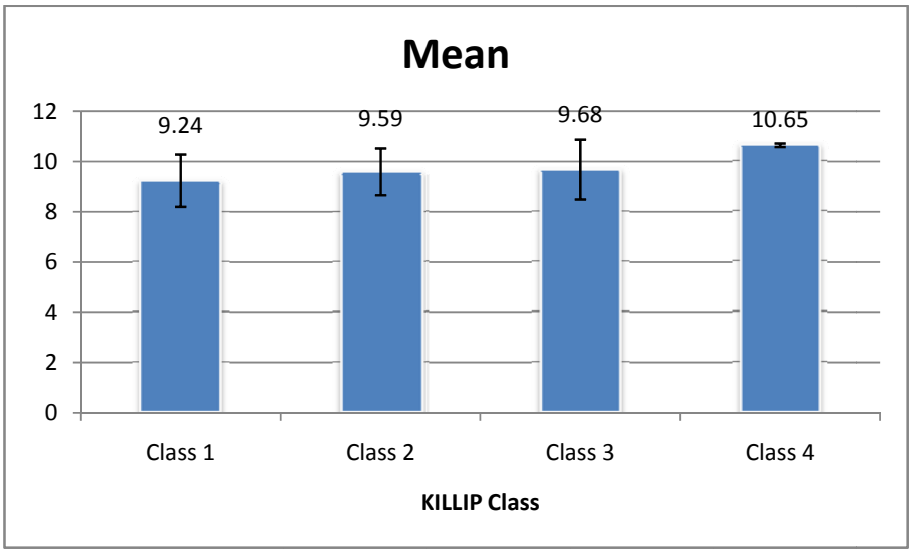


Fig16: KILLIP class and MPV

There is positive correlation between patient ‘s admission KILLIP class and mean MPV,with KILLIP class 4 having highest mean MPV.

Table 11: KILLIP class among Diabetics and Non Diabetics

Killip Score	DM	non-DM
1	13	44
2	18	11
3	8	4
4	2	0

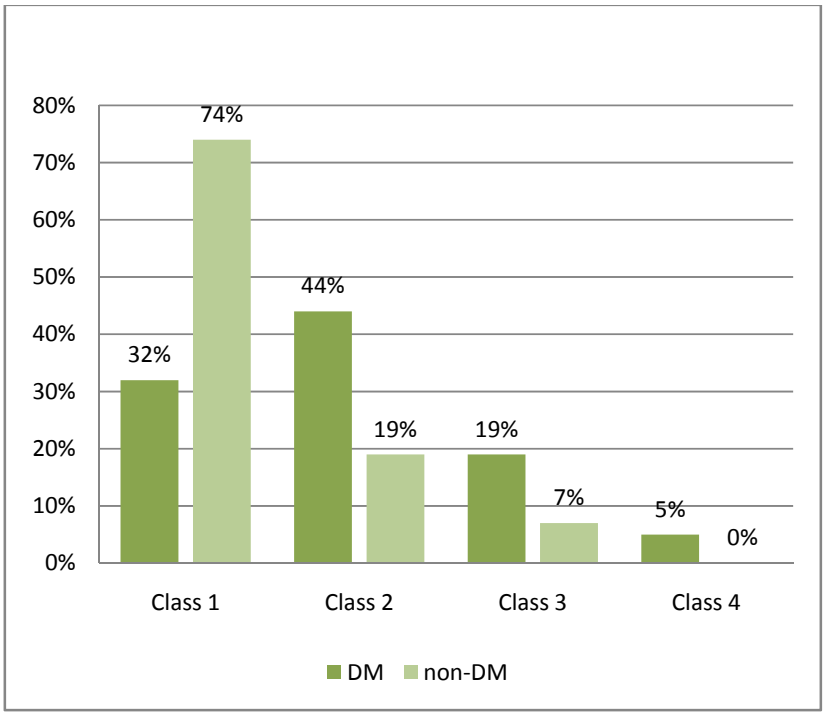


Fig17: KILLIP class among Diabetics and Non Diabetics

The study shows that diabetics presented with higher killip on admission than non diabetics. With Killip class presentation there were more non diabetics

Table 12: KILLIP class and Mortality

KILLIP Score	Correlation Coefficient	p value
Mortality	0.253	0.004

Table 13: TIMI Score and Mortality

TIMI Score	Correlation Coefficient	p value
Mortality	0.242	0.012

Our study shows strong correlation between higher KILLIP class and TIMI score on admission with mortality. The p value of the test is also significant

Table 14: Mortality and Higher Mean platelet volume

Mortality	Correlation Coefficient	p value
MPV	0.065	0.433

There is also correlation between Mean Platelet volume and mortality thus proving our hypothesis

Table 15: Mortality comparison between diabetics and non diabetics with admission MPV

Mortality	Correlation Coefficient	p value
DM	-0.057	0.669
NON-DM	-0.09	0.414

However correlation could not be reached for mortality among diabetics and non diabetics with admission MPV value. This may be due to the small sample size we enrolled in this study

In our study : **PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS PRESENTIN WITH ST ELEVATION MYOCARDIAL INFARCTION** conducted at Kanyakumari Government Medical College Hospital analysing 100 patients presenting to ICCU with acute STEMI has elucidated many findings.

DEMOGRAPHY OF THE POPULATION :

In 100 patients with acute MI, 36 % were females and 64 % were males. The number of diabetics were 42 and non diabetics were 58. Among diabetics 59.52 % were males and 40.47 % were females. Among the total males presented 39.06 % were diabetic and among the total female presented 47.22 % were diabetics which showed that among the females presented the incidence of diabetes is higher in them compared to males. Higher incidence of MI was noted in the age group of 51 to 60 years with overall clustering of cases seen above the age group of 50 years.

According to NCEP (National Cholesterol Education Programme), decades of observational meta analysis of various studies have clearly shown that the incidence of MI is higher in males compared to pre menopausal women. However after menopause the risk remains the same.

This is clearly demonstrated in our study. Among the females presented only 3 were under 50 years of age and with only one female below 45 years of age. The remaining 23 were above 50 years of age.

Among the patients presented diabetics had higher HbA1c values compared to non diabetics. The mean HbA1c was 8.08 for diabetics and 5.83 for non diabetics. Diabetics also presented with higher mean platelet volume. The average MPV for diabetics was 9.94 fl and for non diabetics was 9.06 fl.

According to a study conducted by Dr. Thomas Alex Kodiatte et all, Departments of Pathology and 1Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar, India named Mean Platelet Volume in type 2 Diabetes Mellitus, which showed that in diabetic patients the MPV was significantly higher than that seen in non diabetics (p value < 0.0001).Among the diabetic subjects a positive Pearson correlation was seen between MPV and HbA1c.

This finding is confirmed in our study with high statistical significance. There is a positive correlation between admission MPV and HbA1c value (r – 0.34 ; p value < 0.0001)

A correlation could not be reached between admission CK MB values among diabetics and non diabetics. CKMB mass assay is not a highly specific test for myocardial ischemia and its sensitivity and specificity is less compared to cardiac troponins. The p value was >0.05

Mean platelet volume and mortality and mortality indices :

In our study Mean platelet volume positively correlated with mortality indices like TIMI score and KillipScore. In our study , TIMI score had a positive correlation with MPV in Pearson correlation test(r -0.189 and p value – 0.059),and KILLIP score had a strong correlation with MPV in Pearson correlation test (r – 0.238 and p value – 0.017).

According to a study conducted by Andrzej Lekston et all, Third department of cardiology, Poland , it was shown that the Mean platelet volume positively correlated with admission KILLIP class which was proved in our study also

Individual risk factors like systemic hypertension, prior CAD was not analysed separately as they were statistically evaluated via the TIMI score which predicts 14 day mortality in patients presenting with acute MI.

Comparing the correlation between admission MPV and overall mortality (both in hospital and one month mortality taken together) our study showed a correlation between the two variables. According to Kendall Tau's test, by which the above parameters were analysed it showed a correlation coefficient value of 0.065 and a p value of 0.433. Then comparing mortality among diabetics and non diabetics, the mortality was higher in diabetics than

non diabetics with a p value of < 0.0001.Both in patient and 1 month follow up mortality was significantly higher in diabetics.

Many studies have highlighted this finding emphasizing that diabetics have a higher mortality. In the study conducted by Andrzej Lekston et all, Third department of cardiology, Poland, the findings wee postulated as : diabetic patients have a higher MPV value than non diabetics; MPV value serves as a good prognostic indicator of long term mortality; MPV values correlated positively correlated with admission hemodynamic status; overall mortality higher for higher MPV values

Another study published in JACC, done by Zeron Huczeck et all, Poland it is shown that there is positive correlation between admission MPV value and no reflow phenomenon and slower CTFC values, with patients with higher baseline values of MPV showing no reflow phenomenon.

Our study too supports many of these findings with mortality higher with higher MPV values, diabetics having higher MPV values, MPV values positively correlating with admission hemodynamic status which is assessed by KILLIP score.

KILLIP score and TIMI score independently had strong correlation with mortality : with higher admission scores having higher mortality. This has been proved by many studies.

In our study we could not arrive at a statistically significant correlation between MPV value among diabetics and mortality in comparison with MPV values among non diabetics and mortality. This drawback would have been due to the limited sample size of our present study.

SUMMARY

Cardiovascular diseases account for vast majority of mortality and morbidity in developing countries. Acute Coronary Syndrome which is a major cause of cardiovascular mortality encompasses a spectrum of conditions namely : unstable angina, NSTEMI and STEMI.

Various risk factor assessment tools and mortality predictors have been developed for STEMI. Among these in this study we evaluated the role of Mean Platelet Volume in predicting overall mortality in patients presenting with acute MI.

Diabetics presenting with acute MI had higher MPV values than non diabetics. This has been proven in many studies and our study also confirms that. In addition cardiovascular mortality was also higher in diabetics compared with non diabetics This is due to the fact that the platelets in diabetics are larger and more reactive.

MPV values in our study showed positive correlation for mortality, admission TIMI score and admission KILLP class. This finding emphasizes the fact that Mean Platelet Volume can be used an independent and cheap indicator for predicting overall cardiovascular mortality.

CONCLUSION

- Mean Platelet Volume was higher in diabetics than non diabetics
- Mean platelet Volume has positive correlation with overall mortality ;mortality rate higher with higher MPV values
- Mean Platelet Volume correlated with admission hemodynamic status which is assessed by KILLIP class and TIMI score
- Mean platelet volume had significant correlation with HbA1c values
- Mean Platelet Volume can be used as a predictor of long term cardiovascular mortality.

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BRAUNWALD ‘S HEART DISEASE :A textbook of cardiovascular Medicine 10 th edition

PROFORMA

Performed by: **date**

Name : Age/Sex: Occupation:

Ht : wt : BMI :

Ward IP NO

Diagnosis

Presenting complaints:

Past history:

H/o DM, HIV, PT, HT, CKD, CVD, COPD etc

Diabetes (y/N) duration

Clinical examination:

General examination:

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy,

Vitals: PR, BP,Temp, RR, SpO2,JVP,Heart rate

TIMI SCORE KILLIP CLASS

Systemic examination: CVS: RS: Abd: CNS:

Laboratory investigations:

Mean platelet volume

Platelet count

Complete blood count

RBS,FBS,PPBS

ECG

ECHO: 3 rdday and after 1 month

ABBREVIATIONS

CAD - Coronary Artery Disease

CVD - Cardiovascular disease

MPV – Mean Platelet Volume

STEMI – ST segment Elevation Myocardial Infarction

TIMI – Thrombolysis In Myocardial Infarction

DM – Diabetes Mellitus

IL – interleukin

MASTER CHART

S.NO	NAME	AGE	SEX	DM	HT	PRIOR CAD	SMOKER/ALCOHOLIC	MI	HBA1C	RBS (mg/dl)	MPV (fl)	PLATELET COUNT (lakh/cu. mm)	CPK	CK-MB	ECHO (EF)	TIMI score	killip score class	FOLLOW UP
1	Rasaiya	63	M	P	A	A		AWMI	9.5	225	10.5	2.3	350	85	42%,RWMA +	3	1	expired (F)
2	Iyappan	63	M	A	A	A		AWMI	6.6	135	9.7	0	450	70	50%	4	3	follow up
3	Anthony dhas	60	M	A	A	A		AWMI	6	94	9.2	2.3	200	35	40%	3	1	follow up
4	sornam	55	F	A	P	A		AWMI	5.6	115	9.2	1.3	442	95	33%	4	1	follow up
5	Muthunayaki	69	F	A	A	A		IWMI	6	125	9.6	1.2	542	155	47%	7	1	follow up
6	chellaya nadar	50	M	A	P	A		AWMI	6	115	10.4	1.2	232	56	not done	8	1	expired (H)
7	vallinayagam	33	M	A	A	A		AWMI	5.8	90	9	1.9	151	41	not done	5	3	expired (H)
8	paramasivam	68	M	A	P	A	smoker	AWMI	5.6	99	9.8	1.8	144	65	44%	5	1	follow up
9	solomon	52	M	A	A	A	smoker	IWMI	5	99	9.5	1.6	65	25	43%	1	1	follow up
10	muhamed thayub	63	M	A	A	A	smoker	IWMI	6	130	7.3	1.87	345	100	RHD , RWMA+ ; EF 42 %	1	1	follow up
11	devaraj	54	M	A	P	A	Smoker	AWMI	6.2	120	9	1.4	500	55	50%	3	1	follow up
12	devi	60	F	P	P	A		AWMI	9	345	8	2.3	779	143	44%	4	2	follow up
13	aparna	56	F	P	P	A		IWMI	9.2	346	8.4	2.2	800	240	not done	2	1	expired (H)
14	paramaeswari	80	F	A	A	A		AWMI	5.5	97	8	2	450	80	RWMA + ; 34 %	7	1	follow up
15	sebastiyal	40	F	P	P	A		AWMI	7.2	105	8.9	2.4	204	28	not done	3	1	expired (H)
16	pichandi	45	M	A	A	A		IWMI	6.2	145	7.7	1.9	98	22	42%	1	2	follow up
17	Kishore dhas	45	M	A	P	A		AWMI	5.9	108	7.2	2.5	252	33	38%	4	1	follow up
18	Lakshmi	45	F	P	P	A		AWMI	8.2	120	8.4	1.7	380	45	RWMA + ; 34 %	4	1	follow up
19	sajeev	37	M	A	A	A		IWMI	5.4	135	7.6	2.3	221	32	RWMA + ; 39 %	2	1	follow up
20	murugan	65	M	A	P	A		AWMI	6.1	92	10.3	1.8	320	58	RWMA + ; 28 %	4	1	follow up
21	murugesan	60	M	P	P	P		AWMI	7.6	98	10.9	1.6	200	40	RWMA +; 40 %	3	1	follow up
22	mariageorge	65	M	P	P	A	smoker	IWMI	7.3	235	10.3	1.6	234	38	RWMA + 40 %	5	3	follow up
23	Sarojini	58	F	A	A	A		IWMI	5.6	98	9.2	2.4	140	40	RWMA + 52 %	4	2	follow up
24	swamidhas	57	M	A	A	A		AWMI	5.8	90	10.9	1.8	345	90	38%	5	2	follow up
25	Wilson	65	M	P	A	P	Smoker	IWMI	7.9	322	11	3.5	400	56	RWMA + ; 28 %	7	3	expired (H)
26	Filomina	70	F	P	P	A		AWMI	8	112	10.4	2.4	250	32	RWMA + 32 %	6	2	follow up
27	Babu	60	M	A	P	A		IWMI	6	115	10	0.9	330	44	RWMA + 30 %	3	1	follow up
28	Sornappan	42	M	A	A	A	alcoholic	IWMI	5.2	135	9.9	1.4	100	19	RWMA + 56 %	3	1	follow up
29	Jaffer	72	M	P	A	P		IWMI	8.2	120	10.1	2.4	254	35	RWMA + 22 %	7	2	follow up
30	Rajammal	70	F	A	A	A		ASMI	5.5	98	9	3.2	344	44	RWMA + 46 %	4	2	follow up
31	balasubamanian	50	M	A	A	A		AW, IWMI	6	96	7.7	0.87	574	88	RWMA+ 26%	7	1	follow up
32	Michel raj	52	M	P	P	A		AW, IWMI	7.5	240	10.4	3.2	180	25	RWMA + 39%	6	2	follow up
33	Ranjithakumari	65	F	A	A	a		AWMI	6.1	165	9.2	1.4	560	54	RWMA + 35 %	3	1	follow up
34	Gnanaselvam	58	F	P	A	A		AWMI	9.2	224	10.7	3.2	245	25	RWMA + 41 %	8	3	follow up

35	Bagyamani	63	F	A	A	P		IWMI	5.9	67	10	0.75	229	40	RWMA + 29%	4	1	follow up
36	Muthuraj	56	M	P	P	A		AWMI	7.8	90	10.1	3.2	238	27	RWMA + 26 %	7	2	expired (F)
37	Ayyanpillai	62	M	A	A	A		AWMI	5.8	70	9.8	1.6	340	30	RWMA + 45 %	5	2	follow up
38	oorkavalan	48	M	A	A	A	smoker	LWMI	6.2	120	10.2	3.2	428	42	RWMA + 52 %	4	1	follow up
39	Velmurugan	45	M	P	A	P	smoker	IWMi	7.8	140	9.9	2.4	130	35	RWMA + 29%	7	2	follow up
40	Kumar	52	M	P	P	P	smoker	AWMI	8	230	9.1	1.8	255	60	RWMA + 36%	7	2	follow up
41	gunaseelan	66	M	P	P	A		AWMI	7.2	155	10.7	1.9	265	56	RWMA + 31 %	8	2	follow up
42	Mohan	57	M	A	P	A	Smoker	AWMI	5.3	110	8.2	1.4	224	56	RWMA + 33 %	5	1	follow up
43	john rose	60	M	A	A	P	smoker / alcoholic	IWMI	4.9	102	8.2	2.3	132	26	RWMA + 48%	6	2	follow up
44	danny		F	A	A	A		AWMI	6.2	188	9.8	1.4	240	35	RWMA + 32%	4	1	follow up
45	chirsti bai	67	F	P	A	A		IWMI	7.8	145	10.9	2.2	255	30	not done	5	1	expired (H)
46	theresammal	72	F	P	P	A		AWMI	8.2	108	9.9	1.9	450	70%	RWMA +;28%	7	3	expired (F)
47	valarmathi	53	F	P	A	A		AWMI	9	302	10.8	3.1	300	54	RWMA +; 40 %	6	2	follow up
48	sundharadhas	50	M	A	A	A	Smoker	inf,RV ,PW	5.6	212	9.2	1.2	155	29	RWMA + ; 56%	3	3	follow up
49	chellathai	67	F	P	P	A		inf wall	7	126	7.7	1.3	220	44	RWMA + ; 35%	5	3	expired(H)
50	Lakshmi	66	F	A	A	A		AWMI	5.5	232	7.2	3.1	330	54	RWMA+;62%	4	1	follow up
51	perumal	78	M	A	A	P	smoker	AWMI	6.1	88	8.5	1.9	240	39	RWMA + ; 28 %	6	2	expired(H)
52	stephan raj	76	M	A	P	A		AWMI	5.6	97	9	1.5	154	26	RWMA+ ; 54%	3	1	follow up
53	kumaresan	72	M	P	A	A		IWMI	9.9	191	10.2	2.4	230	60	RWMA + ;39%	5	2	follow up
54	issac	56	M	P	P	A	smoker	AWMI	8.5	69	9.6	1.9	340	23	RWMA + ; 49 %	8	3	follow up
55	kosalai	65	F	A	A	P		AWMI	5.4	98	9.9	2.3	245	35	RWMA+ ;38%	4	2	follow up
56	Annaselvam	71	M	P	P	A		IWMI	6.9	65	10.6	2.7	340	40	not done	7	4	expired(H)
57	sheela	53	F	A	A	A		AWMI	5.8	213	10	1.1	111	35	RWMA + ; 60%	3	1	follow up
58	ramachandan	75	M	P	A	A	smoker	inf & RV	8.1	80	10.9	2.2	370	47	RWMA + ; 32 %	5	3	follow up
59	Alphonsa	62	F	P	A	A		AWMI	6.8	91	11	0.9	54	15	RWMA+ ;55%	4	1	follow up
60	manikandan	68	M	A	A	A		IWMI	5.4	385	9.4	0.8	165	20	RWMA + ; 48 %	3	1	follow up
61	pichandi	70	M	A	P	A	alcoholic	AWMI	5.6	208	8.9	1.12	98	29	RWMA +; 52%	5	1	follow up
62	david	71	M	P	P	A		AWMI	9.2	318	9.3	2.1	225	49	RWMA + ;22 %	7	2	expired(H)
63	yesudhas	62	M	A	A	A	smoker	IWMI	5.6	79	9.7	1.8	330	21	RWMA + ; 44%	3	1	follow up
64	balammal	58	F	A	P	A		AWMI	5.6	212	8.9	2.3	285	36	RWMA+ ; 62%	4	1	follow up
65	bagavathiammal	59	F	A	A	A		AWMI	6.2	154	9	0.98	212	28	RWMA + ; 45%	5	1	follow up
66	kannimariyal	50	F	P	A	A		IWMI	8.4	167	9.5	1.4	320	21	RWMA + ; 32 %	4	2	follow up
67	shreekumari	73	F	A	P	A		AWMI	6.3	118	10.2	1.7	568	54	RWMA + ; 25%	5	1	follow up
68	rajan	59	M	A	A	P	smoker	IWMI	6.1	74	8.7	0.94	130	29	RWMA + ; 34 %	4	2	follow up
69	thanappan	57	M	P	P	A		AWMI	8.6	85	9.6	2.4	452	34	not done	9	2	expired(H)
70	ramesh	73	M	P	A	A		IWMI	7.8	90	9.5	1.3	340	15	RWMA + ;40%	4	1	follow up

71	lasar	79	M	A	A	P		AWMI	5.5	136	10.3	0.56	160	37	RWMA + ; 39 %	4	1	follow up
72	Jeyan	59	M	P	A	A		IWMI	9.2	145	9.7	3.5	289	38	RWMA +;51%	7	2	expired (F)
73	nadankan	57	M	A	A	A	smoker	AWMI	5.3	140	10	2.2	187	26	RWMA + ; 40%	5	2	follow up
74	arumuga peumal	77	M	A	A	A	smoker	AWMI	5.8	150	7.2	1.85	249	31	RWMA + ; 25%	4	1	follow up
75	thangappan	73	M	P	A	A		AWMI	7.3	78	8.8	0.95	547	65	RWMA +; 43%	5	1	follow up
76	kumar	56	M	P	P	A		IWMI	9	218	10.6	1.01	355	38	RWMA + ;28 %	6	2	expired(H)
77	muthusamy	61	M	A	A	A		AWMI	6.6	90	7.6	0.67	250	24	RWMA +; 33 %	7	2	follow up
78	mariappan	60	M	P	A	A	smoker	AWMI	8.5	71	11.2	2.3	760	69	RWMA + ; 21%	3	1	follow up
79	thangam	45	F	A	A	A		AWMI	5.9	65	10.3	3.3	552	34	RWMA + ; 32%	4	1	follow up
80	vimala rani	55	F	P	A	A		IWMI	6.7	87	9.4	1.09	567	79	RWMA+;39%	5	1	follow up
81	arulthangam	63	F	P	A	A		inf,RV, PW	7.1	67	10.7	0.78	340	35	not done	9	4	expired (H)
82	robert	70	M	A	P	A		AWMI	7.2	86	8.7	0.69	766	85	RWMA + ; 29%	3	1	follow up
83	maria arputham	71	F	A	A	P		AWMI	5.8	316	7.4	1.07	145	87	RWMA + ;19%	8	3	follow up
84	benjamin	61	M	A	A	A	smoker	IWMI	5.2	191	8.9	2.3	530	75	RWMA + ; 40%	3	1	follow up
85	ramaiyan	58	M	A	A	A		AWMI	5.7	117	9.4	2.9	270	35	RWMA + ; 55%	4	1	follow up
86	Fency	55	F	P	P	A		AWMI	8	175	10	1	350	43	RWMA + ; 42 %	6	2	follow up
87	rani	60	F	A	A	A		IWMI	6.2	190	7.9	1.21	740	90	not done	5	1	expired(H)
88	leela	72	F	A	P	A		AWMI	5.9	87	8.1	0.98	670	50	RWMA +; 33 %	7	1	follow up
89	mary	71	F	P	A	A	alcoholic	AWMI	6.8	134	10.4	2.3	544	62	RWMA + ; 42 %	6	1	follow up
90	ponmalar	77	F	P	A	P		AWMI	7.5	55	9.6	1.9	360	43	RWMA +; 49%	8	2	follow up
91	sundaresan	63	M	A	A	A		IWMI	5.6	278	8.1	1.8	560	80	RWMA + ; 32 %	7	1	follow up
92	velammal	67	M	A	A	A		IWMI	5.9	289	10.5	1.6	330	65	RWMA +; 49%	5	1	follow up
93	natarajan	55	M	P	P	A		AWMI	8.8	200	8.5	1.87	87	20	RWMA + ; 35%	4	1	expired (F)
94	seethalaksmi	56	F	P	A	P		AWMI	7.7	184	10.7	1.4	56	15	RWMA + ; 41 %	6	2	follow up
95	murugan	59	M	A	A	A		IWMI	5.3	71	9.6	2.3	540	38	RWMA + ; 44%	5	1	follow up
96	sreekishnan	73	M	P	P	A	smoker	IWMI	9.2	61	10.8	2.2	89	25	not done	7	3	expired (H)
97	nikkolas	49	M	A	A	A		LWMI	5.8	59	9.8	0.65	320	56	RWMA + ; 32 %	3	1	follow up
98	singaram	55	M	A	A	A		AWMI	6.3	90	9.6	3.9	89	28	RWMA +;48 %	4	1	follow up
99	subbaiya	56	M	A	A	P		AWMI	6.5	98	9.3	1.7	390	56	RWMA + ; 41 %	5	1	follow up
100	Thiru	90	M	A	P	A	smoker	AWMI	6.4	87	7.9	1.8	654	65	not done	6	1	expired (H)

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Office of the Dean,
Kanyakumari Govt. Medical College,
Asaripallam 629 201.
Dated 09.04.2015

Sub: Medical Education – Kanyakumari Govt. Medical College, Asaripallam – Ethical Committee approval - permission granted to II Year PG Students – Regarding.

Ref: 1. G.O. (D) No. 648 H&FW (MCA) Dept. dated 20.06.2009.
2. Individual application dated 30.01.2015
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In accordance with the powers delegated in the Govt. order cited, permission is granted to the following PG Candidates of MD General Medicine of Kanyakumari Govt. Medical College, Asaripallam to do the Project work regarding their dissertation on the following subjects.

1. ROLE OF HIGH SPECIFIC CRP AND TROPONIN T IN ACUTE ISCHAEMIC STROKE – BY Dr. U. Nagarajan, MD (General Medicine)
2. PULMONARY FUNCTION TESTS IN TYPE -2 DIABETICS AND NON-DIABETICS – A COMPARATIVE STUDY – with specification of Exclusive criteria Investigation of Echo/FB/PPBS- By Dr. M. Ilamaran (MD General Medicine)
3. PROGNOSTIC SIGNIFICANCE OF MEAN PLATELET VOLUME IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION – with inclusion of comparative study between diabetic and Non-diabetic patients – By Dr. M. V. Indhuja (MD General Medicine) in the department of Thoracic Medicine, Biochemistry, Neurology, Microbiology and Pathology of Kanyakumari Govt. Medical College, Asaripallam with effect from...13:....04.2015 during their study period.

DEAN

09/04/15

To
The II Year MD (General Medicine) PG Students –
1. Dr. U. Nagarajan,
2. Dr. M. V. Indhuja
3. Dr. M. Ilamaran

through HOD of Medicine, KGMC, Asaripallam

Copy to
1. The HOD of Medicine, Thoracic Medicine, Neurology, Biochemistry, Microbiology and Pathology.
2. RMO/ARMO/MS/DS-KGMCH, Asaripallam

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7.	One legal expert	:	Mrs. Shahila Pravin, Advocate, 9442112719. E-mail Id :shahilapravin@gmail.com
8.	One Social Scientist / Representation of Govt. Voluntary Agency	:	Dr. A. Burlington IMA Secretary / Rotarian, 43A5/06, North Street, Ranithottam, Nagercoil – 629001. 9443204537.
9.	One Business man	:	Thiru. S. Rajamoni, Sujha Surgicals Nagercoil E.mail Id : sujhasur@rediffmail.com
10.	One lay person	:	Mrs. D. Grena, Positive People Welfare Society in Kanyakumari District. Phone No. 04652-296123 8012502668.

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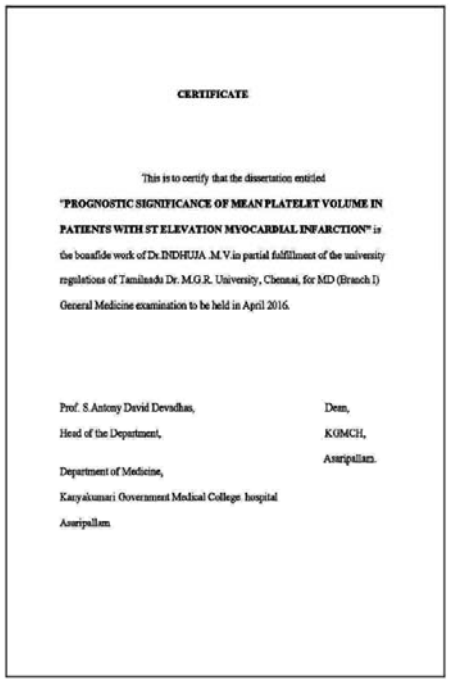

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Prof. S.Antony David Devadhas,
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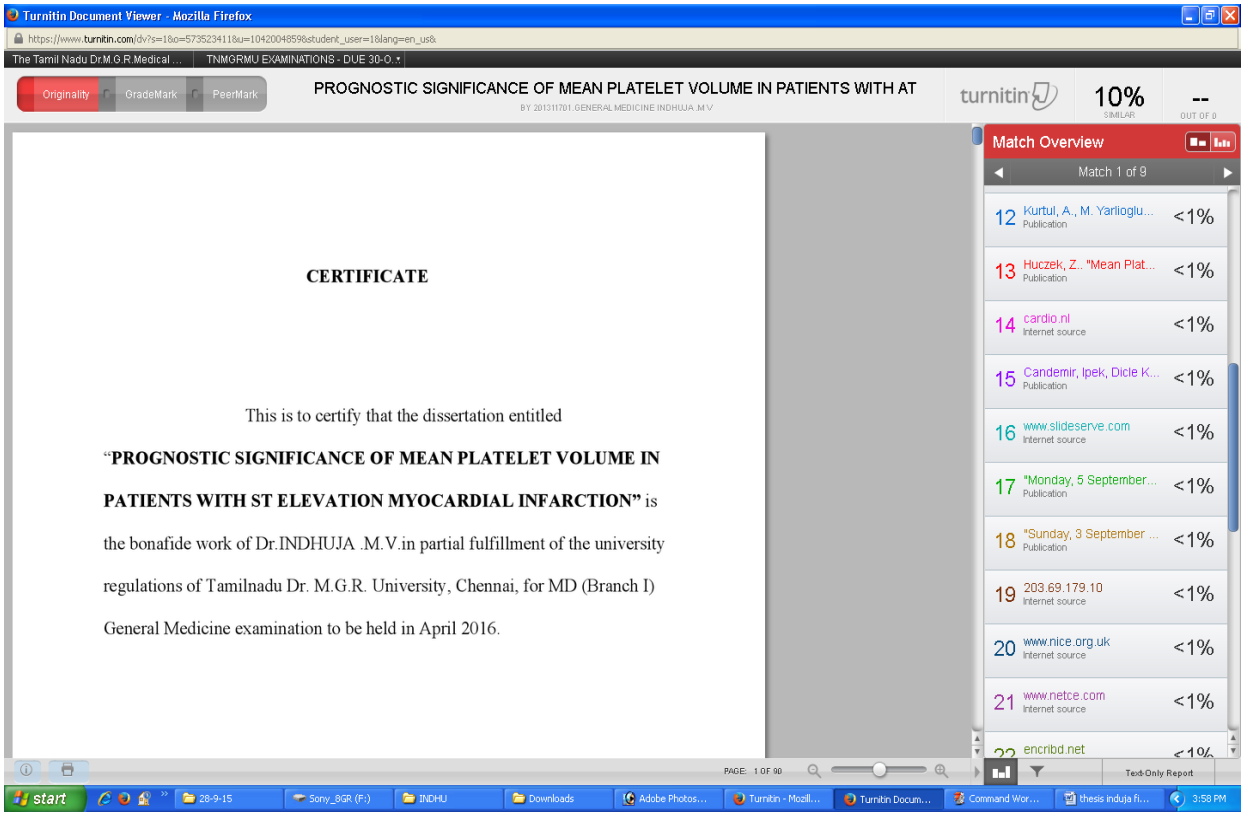
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