"IMPACT OF ADMISSION GLYCEMIA ON 30-DAY MORTALITY IN NON DIABETIC PATIENT'S ADMITTED FOR MYOCARDIAL INFARCTION - A ONE YEAR CROSS SECTIONAL STUDY"

By

Dr. DHAREPPA G. CHOUGALA

DISSERTATION

Submitted to the

KLE UNIVERSITY, BELGAUM

KARNATAKA.

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE
In
GENERAL MEDICINE

Under the Guidance of

Dr. S. H. Asundi MD

Associate Professor

DEPARTMENT OF GENERAL MEDICINE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM – 590010
KARNATAKA

MAY 2009

KLE UNIVERSITY, BELGAUM

KARNATAKA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"IMPACT OF ADMISSION GLYCEMIA ON 30-DAY MORTALITY IN NON DIABETIC PATIENT'S ADMITTED FOR MYOCARDIAL INFARCTION- A ONE YEAR CROSS SECTIONAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. S. H. ASUNDI** $_{MD,}$, Associate Professor, Department of Medicine, J. N. Medical College, Belgaum-590010

Date:
Place: Belgaum

Dr. DHAREPPA G. CHOUGALA
Department of General Medicine,
J. N. Medical College, Belgaum-10

KLE UNIVERSITY, BELGAUM

KARNATAKA.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"IMPACT OF ADMISSION GLYCEMIA ON 30-DAY MORTALITY IN NON DIABETIC PATIENT'S ADMITTED FOR MYOCARDIAL INFARCTION- A ONE YEAR CROSS SECTIONAL STUDY"** is a bonafide research work done by **Dr. DHAREPPA G. CHOUGALA** in partial fulfillment of the requirement for the Degree of MD (MEDICINE)

Guide

Dr. S. H. ASUNDI MD
Associate Professor
Department of General Medicine,
J. N. Medical College,
Belgaum – 590 010
Karnataka

Date:

Place: Belgaum

KLE UNIVERSITY, BELGAUM

KARNATAKA

ENDORSEMENT BY H.O. D., PRINCIPAL/ HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"IMPACT OF ADMISSION GLYCEMIA ON 30-DAY MORTALITY IN NON DIABETIC PATIENT'S ADMITTED FOR MYOCARDIAL INFARCTION- A ONE YEAR CROSS SECTIONAL STUDY"** is a bonafide research work done by **Dr. DHAREPPA G. CHOUGALA** under the guidance of **Dr. S. H. ASUNDI** **MD** Associate Professor, Department of General Medicine, J. N. Medical College, Belgaum-590010.

Dr. V. A. KOTHIWALE **MD, Ph. D**
Professor& Head,
Department of General Medicine,
J. N. Medical College,
Belgaum- 590010
Karnataka.

Date:

Place: Belgaum

Dr. V. D. PATIL **MD (Paed)**
Principal,
J. N. Medical College,
Belgaum – 590 010
Karnataka

Date:

Place: Belgaum.

KLE UNIVERSITY, BELGAUM

KARNATAKA

C O P Y R I G H T

DECLARATION BY THE CANDIDATE

I hereby declare that KLE University, Belgaum, Karnataka, shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

(Dr. DHAREPPA G. CHOUGALA)

Date:

Place: Belgaum

A C K N O W L E D G E M E N T

It is indeed a great pleasure to recall the people who have helped me in the completion of my dissertation. To name all of them would be impossible, yet I attempt to show my gratitude to a select few, to whom I am greatly indebted.

I am extremely grateful to my respected teacher and guide, **Dr. S. H. Asundi** **MD** *Associate Professor, Department of General Medicine, J. N. Medical College, Belgaum, for his able guidance, supervision, invaluable suggestions, and kind help, rendered throughout the course of my study, and in the preparation of this dissertation.*

I would like to take this opportunity to express my most sincere and humble gratitude to **Dr. V. A. Kothiwale** **MD, Ph. D** **,** *Professor and Head of Department of General Medicine , J. N. Medical College, Belgaum for his inspiration, constant guidance, continuous supervision and critical review of this work at regular "thesis meetings."*

I express my sincere gratitude to ***Dr. V. D. Patil*** ***MD, DCH*** *Principal J. N. Medical College, Belgaum,* ***Dr. M. V. Jali*** ***MD,*** *Director and Chief Executive, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum for allowing me to utilize the facilities in above institution for the dissertation.*

I owe deep sense of gratitude and express my heartfelt thanks to ***DR. S. B. Kalagate*** ***MD*** *for his constant encouragement and support.*

My respectful regards and humble thanks to ***Dr. H.B. Rajshekar, Dr. Vijay Sommannavar, Dr. Rekha S Patil, Dr. Srinivas,*** *Professors, Department of General Medicine, J. N. Medical College, Belgaum, for their constant inspiration and help.*

My sincere thanks to ***Dr. Neeta Deshpande , Dr. Arathi Darshan , Dr. Mamata Patil,*** *Associate Professors, Department of General Medicine, J. N. Medical College, Belgaum, for their constant help.*

*My special thanks to****, Dr. Naveen Angadi, Dr. Prakash Babliche,*** *and* ***Dr. Dyanesh M****, Assistant Professors , for their encouragement and timely advice during the study.*

I express my sincere thanks to ***Dr S T Yavagal*** *MD, DM Professor & Head Department of Cardiology J N Medical College,* ***Dr S V Patted*** *MD, DM (Cardio),* *and* ***Dr Prabhu Halkati*** *MD, DM (Cardio) for their support and permission to include the study subjects from ICCU KLE's Dr Prabhkar Kore Hospital and MRC Belgaum and utilize the facilities.*

I thank all the ICCU staff for their immense cooperation in making this dissertation a success.

I sincerely thank my friends, batch mates and all the postgraduates in Medicine, for all the help and support they have given me throughout my post graduation.

I wish to offer my thanks to Department of Medical Education for their valuable information and support.

I express my sincere thanks to ***Dr Jyothi R Malagavi****,* ***Dr. Raghavendra B Nayak, Dr Ravikant Patil, Dr Rohan Bhise, Dr Madhav Prabhu*** *and* ***Mr Sanjeev Kumar R Chougala,*** *for their constant help, support, encouragement and cooperation in designing my dissertation.*

I will always fall short of words when I express my gratitude to my dear parents, ***Mr Gireppa H Chougala,*** *and* ***Mrs Bhagirati G Chougala,*** *also my uncle and aunt* ***Mr.Hanumanth S Chikkannavar*** *and* ***Mrs. Mahadevi. H. Chikkannavar*** *whose cherished blessings and countless sacrifices are behind whatever success I have achieved in my life, they are the reason for my being who I am.*

I am very thankful to my brothers ***Mr Basavaraj G Chougala****,* ***Master. Rutwik*** *and* ***Tushar***

Last but not the least, this acknowledgement is incomplete if I fail in my duty to thank all the subjects who have whole heartedly participated in the study and have made the study complete.

Date: **Dr. DHAREEPPA G CHOUGALA**

Place: Belgaum

LIST OF ABBREVIATIONS USED

ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
BP	Blood Pressure
CAD	Coronary Artery Disease
CK	Creatine Phosphokinase
CK-MB	MB Isoenzyme of Creatine Phosphokinase
cTnI	Cardiac-Specific Troponin I
cTnT	Cardiac-Specific Troponin T
DM	Diabetes Mellitus
ECG	Electrocardiogram
FFA	Free Fatty Acids
HTN	Hypertension
HbA1c	Glycosylated Hemoglobin
IGT	Impaired Glucose Tolerance
IHD	Ischaemic Heart Disease
LVEF	Left Ventricular Ejection Fraction
NSTEMI	Non-ST-segment Elevation Myocardial Infarction
PCI	Primary Percutaneous Coronary Intervention
RBS	Random Blood Sugar
rPA	Reteplase
STEMI	ST-Segment Elevation Myocardial Infarction
TNK	Tenecteplase
tPA	Tissue Plasminogen Activator
UA	Unstable Angina

ABSTRACT

Background and Objectives : In recent years, much attention has been given to the evidence that the concomitant occurrence of hyperglycaemia in patients admitted to intensive care units with an acute myocardial infarction (MI) enhances the risk of mortality and morbidity, whether the patient has diabetes or not. This study aims at exploring the association between the admission glycemic status and 30 day-mortality in acute myocardial infarction in non diabetics.

Methods: The study was conducted on 60 cases of AMI admitted at KLE's Dr Prabhakar Kore Hospital &MRC Belgaum during the year 2007-08. The cases were divided into 4 groups (group I to IV) based on admission RBS. There were 16 patients in group I (admission RBS < 120mg%), 12patients in group II (admission RBS 120- 140mg%), 14 patients in group III (admission RBS 140- 167mg%), 18 patients in group IV (admission RBS > 167mg%). All cases were subjected to investigation, and in-hospital complications were noted. They were also followed up for 30 days. In hospital complications and 30-day mortality was analyzed using appropriate statistical methods across the groups (I- IV).

Results: Of the 60 cases, all had ST segment elevation myocardial infarction. Age and sex were comparable between the groups but patients aged >60 years were more common in group IV. With progressive rise in admission RBS (Groups I to IV), there was a progressive drop in systolic BP (P= 0.042) and LVEF (P= 0.001), and greater occurrence of arrhythmias (P= 0.003) and subsequent development of cardiogenic shock (P= 0.006). Patients with high admission RBS were also found to have higher

admission Killip class (Killip class I - P= 0.018, Killip class II - P= 0.016) and increased incidence of subsequent deterioration of Killip class by ≥2 classes (P= 0.001) during the hospital stay. The 30 day- mortality occurrence increased as we progressed from group I to IV (P= 0.008).

Conclusion: In our study overall in hospital complications were more common in subjects with high admission RBS. There was a positive linear correlation between admission RBS and 30-day mortality.

Key words: Acute Myocardial Infarction; Diabetes Mellitus; Hyperglycemia.

CONTENTS

SL. NO.	TITLE	PAGE NO.
1.	INTRODUCTION	1-2
2.	OBJECTIVES OF THE STUDY	3
3.	REVIEW OF LITERATURE	4-35
4.	METHODOLOGY	36-39
5.	RESULTS	40-55
6.	DISCUSSION	56-62
7.	CONCLUSION	63
8.	SUMMARY	64-65
7.	BIBLIOGRAPHY	66-78
8.	ANNEXURES I. CONSENT FORM II. PROFORMA III. MASTER CHART	

LIST OF TABLES

No	TITLE	PAGE No
A	Major Risk Factors for AMI	11
B	Class I Recommendations for Use of an Early Invasive Strategy	25
C	Killip Classification	37
1	Distribution of Patients (N=60) across the groups depending on admission RBS	40
2	Socio demographic details	41
3	Personal History	42
4	General Physical Examination	43
5a	Blood Investigations	44
5b	Territory of infarct	46
5c	Killip class	47
6a	Arrhythmias	48
6b	Left ventricular function (LVEF at admission)	50
6c	Development of cardiogenic shock	51
6d	30-day mortality	52
7	Correlates of 30-day mortality as an Outcome	53
8	Independent Predictors of 30-day mortality (Logistic Regression)	54
9	Summary of Results	55

LIST OF GRAPHS & FIGURES

Sl. No.	Particulars	Page No.
1.	Fig. 1- Showing entry of monocytes and macrophages, smooth muscle proliferation and foam cell formation which are important steps in the process of atherosclerosis	15
2.	Fig. 2 The TIMI Risk Score for UA/NSTEMI, a simple but comprehensive clinical risk stratification score to identify increasing risk of death, myocardial infarction, or urgent revascularization to day 14	23
3.	Pie Diagram 1: Showing Disrtibution of Patients	40
4.	Graph 1: Showing Mean RBS at Admission	45
5.	Graph 2: Showing Incidence of Arrhythmias	49
6.	Graph 3: Showing Mean Left Ventricular Ejection Fraction	50
7.	Pie Diagram 2: Showing 30-Day Mortality	52

INTRODUCTION

In recent years, much attention has been given to the evidence that the concomitant occurrence of hyperglycaemia in patients admitted to intensive care units with an acute myocardial infarction (AMI) enhances the risk of mortality and morbidity, whether the patient has diabetes or not.[1] In some cases, the elevation of glucose could simply be a marker of pre-existing, but not yet detected, type 2 diabetes or impaired glucose tolerance (IGT).[2] This may mean that besides being causal, elevated glucose also could be a marker of existing insulin resistance and/or beta-cell failure that may contribute to the poor prognosis through other mechanisms. However, a positive association between hyperglycaemia at the time of the event and subsequent mortality from AMI has frequently been reported.[3,4,5,6] A strong correlation between glycaemia and shock or development of heart failure has also been reported.[7] Consequently, understanding the possible mechanisms through which hyperglycaemia worsens the prognosis of AMI, as well the effectiveness of its control during AMI, seems to be of great relevance.

Ischaemic heart disease causes more death and disability and incurs greater economic burden than any other illness the world over. With rapid urbanization and sedentary lifestyles the incidence of IHD is on an increase in India. By 2020 IHD is going to be the most common cause of death the world over. This burden compels us to evolve accurate parameters to determine the risk and pathophysiology of IHD.[8]

It is now accepted world wide that the most important factor influencing atherosclerotic plaque instability is inflammation. Elevated blood glucose levels per se adversely affect outcome through the cumulative effects of several mechanisms, including induction of endothelial dysfunction, oxidative stress.[7,8] hypercoagulability and impaired fibrinolysis. Acute hyperglycaemia in healthy subjects and in patients with impaired glucose tolerance or overt diabetes produces a rise in inflammatory markers. Following this line of thought, it might be speculated that the detrimental effect of stress hyperglycaemia in acute MI might also stem from its ability to increase inflammation.

Determination of blood sugar is a simple procedure, requires no expertise, is inexpensive and importantly, It is a correctable factor, having a bearing on morbidity and mortality. Thus this study aims at exploring the association between the admission glycemic status and 30-day mortality in acute myocardial infarction in non diabetics.

OBJECTIVES

To analyze the impact of admission glycemia on 30-day mortality in non diabetic patients with acute myocardial infarction.

REVIEW OF LITERATURE

Acute hyperglycemia: a "new prognostic marker" during myocardial infarction

Acute hyperglycemic response to stress has been recognized since Claude Bernard's observations more than a century ago.[9] This "diabetes of injury" exemplifies the obligatory metabolic rearrangements required to cope with critical stress. The concept evolved as glucose became identified as metabolic mirror of the severity and outcome of critical illness.

There is high variability in prevalence of stress hyperglycemia, defined as hyperglycemia in previously euglycemic patients that gets corrected once the acute process resolves. This occurs because of an inconsistently applied definition and the co-mingling of patients with new onset or unrecognized diabetes mellitus (DM). In one study hyperglycemia occured in about 27.43% of the cases with acute myocardial infarction and had normalized in 90.27% of these patients by the time of discharge from hospital.[10] Although hyperglycemia was once considered a compensatory response, it imposes a range of adverse effects including abnormal immune function,[11] and hemodynamic and electro myocardial disturbances.[12]

One-third of all individuals with hyperglycemia admitted to general hospital do not have a previous diagnosis of diabetes; in these patients, hyperglycemia is a risk factor for adverse outcomes during acute illness.[13]

The Myocardial infarction and Glycemic Status

Admission hyperglycemia may not be only the cause of more severe myocardial damage but also its consequence. Large infarcts are more likely to

cause catecholamine release, which effect fatty acid and glucose homeostasis. The catecholamine response is proportional to the severity of the infarct, as confirmed by the correlation between admission blood glucose and heart rate or Killip's class on admission.[14] In a study[15] concentrations of cortisol, epinephrine and norepinephrine were the main determinants of plasma glucose concentration measured in non diabetic patients with acute myocardial infarction.

The effect of acute hyperglycemia on AMI

In MI, an increased plasma glucose level has been demonstrated to be capable of inducing such electrophysiological alterations as to favour the occurrence of arrhythmias, whose outcome could be fatal.[16] This is consistent with the evidence that an acute increase of glycaemia in normal subjects produces a significant QT elongation,[12] a phenomenon confirmed in an in vitro model of a working heart from a rat.[17] Acute hyperglycaemia is independently associated with impaired left ventricular function,[18] and with a larger infarct size due to an increased incidence of the no-reflow phenomenon.[19] Moreover, studies in animals have shown that acute hyperglycaemia abolishes ischaemic pre-conditioning.[20] Finally, a worse myocardial performance has been demonstrated in patients with acute MI and concomitant hyperglycaemia.[21] The association of MI with increased thrombophilia is an old finding.[22] It has been reported that increased platelet activation after an MI is correlated with hyperglycaemia in non-diabetic patients.[23] The possible role of hyperglycaemia in the activation of blood coagulation has previously been reviewed.[24] It emerges that acute glycaemic variations are matched with a series of alterations in coagulation that are likely to cause a thrombosis. Acute hyperglycaemia induces a shortening of the fibrinogen half-life,[25] and increases in fibrinopeptide A,[26] fragments of pro-thrombin,[27] in

factor VII,[28] and in platelet aggregation,[29] which are all phenomena suggesting increased activation of thrombosis. A growing body of evidence suggests that MI is associated with local and systemic inflammation.[30] Indeed, inflammatory cells infiltrate nearly all plaques; culprit lesions of infarcted hearts appear to be particularly enriched in activated T-cells.[31] Although circulating immune markers are also chronically elevated in patients with chronic stable angina, a transient burst of T-cell activation can only be detected in patients with unstable angina and MI,[32] suggesting that immune factors might precipitate plaque complications such as thrombus formation and vasoconstriction at the site of the culprit lesion. A recent paper demonstrated an association between inflammatory immune markers and functional cardiac outcome in patients with a first uncomplicated MI.[33] Stress hyperglycaemia was found to be associated with amplified inflammatory immune reactions and worse functional cardiac outcome.[33] Interestingly enough, acute hyperglycaemia in healthy subjects and in patients with impaired glucose tolerance or overt diabetes produces a rise in inflammatory markers.[34,35,36] Following this line of thought, it might be speculated that the detrimental effect of stress hyperglycaemia in acute MI might also stem from its ability to increase inflammation. Endothelial dysfunction plays a key role in cardiovascular disease:[37] endothelial dysfunction is a common feature after an MI.[38] In patients with MI treated with thrombolysis, severe endothelial dysfunction in the infarct-related arteries is observed early.[39] Many studies have shown that an acute increase of glycaemia worsens endothelial function,[40,41] therefore suggesting that hyperglycaemia-induced endothelial dysfunction can also contribute to the damaging effect of hyperglycaemia during an AMI.

Oxidative stress as a pathogenic factor underlying the effect of acute hyperglycemia

Oxidative stress is a well-recognized pathogenic process for atherosclerosis and cardiovascular disease.[42] The processes through which acute hyperglycaemia works is probably through the production of free radicals.[43] Both indirect and direct evidence supports this concept. Indirect evidence is obtained through the use of antioxidants. The fact that antioxidants can hinder some of the effects acutely induced by hyperglycaemia, endothelial dysfunction,[44,45,46] activation of coagulation,[27] and inflammation,[35,36] suggests that the action of acute hyperglycaemia is mediated by the production of free radicals. Direct evidence is linked to the estimate of the effects of acute hyperglycaemia on oxidative stress markers. It has been reported that during glucose oral challenge, a reduction in the antioxidant defences,[47] and an increase in markers of oxidative stress is observed.[43] More interestingly, new data come from studies on a new compound namely nitrotyrosine. 3-Nitrotyrosine is thought to be a relatively specific marker of oxidative damage mediated by peroxynitrite,[48] and it has recently been demonstrated to be an independent predictor of cardiovascular disease.[49] Nitrotyrosine formation is detected during acute hyperglycaemia in the artery wall of monkeys,[50] and in working hearts from rats during hyperglycaemia,[51] but also in the plasma of healthy and diabetic subjects.[52,53] Compelling evidence is also accumulating which suggests a role for oxidative stress as a putative mechanism finally leading to plaque denudation and activation through increased endothelial cell apoptosis.[38] Thus, oxidative stress, irrespective of atherosclerotic disease stages, seems to represent a key phenomenon in acute

vascular disease progression.[38] Hyperglycaemia generating oxidative stress by itself, can therefore contribute to worsen such a condition.

Therapeutic prospects

The DIGAMI Study published in 1995 re-ignited interest in the use of insulin following acute MI.[54] It first reported on the feasibility of the use of an insulin–glucose infusion following MI in patients with a plasma glucose level of ≥11 mmol/L;[54] a later paper reported the 1 year mortality and morbidity results.[55] The final paper published in May 1999 reported the long-term mortality data.[56] DIGAMI showed that an insulin–glucose infusion followed by at least 3 months of multiple-dose insulin reduced long-term mortality in patients with diabetes who had an MI.[54,55,56] However, not all were convinced by the results, particularly the mechanisms of action and whether the benefits that occurred were solely from the insulin–glucose infusion used acutely.[57,58] The question concerning the use of insulin–glucose infusion during MI is still open; a recent trial did not show beneficial effect on total mortality in patients treated by primary angioplasty for acute MI.[59]

However, it is necessary to distinguish between a favourable metabolic effect of glucose–insulin infusion and the control of acute hyperglycaemia. In terms of metabolic efficacy it has been suggested that insulin, by itself, should have direct beneficial effect, particularly in reducing the level of free fatty acids (FFAs), which are known to be associated with a deterioration of clinical outcome and may have toxic effects of their own on the myocardium.[60,61] Incidentally, it is reasonable that the toxic effect of FFAs is also mediated through free radical generation.[62] However, it is remarkable that glucose exerts several

direct and powerful damaging effects, as described above, which are all able to worsen the prognosis of MI. Therefore, the true open question is whether hyperglycaemia, when present during a MI, has to be treated with intensive insulin therapy even in non-diabetic patients. While waiting for specific trials, it should be helpful to consider that intensive insulin therapy has already shown a beneficial effect in critically ill patients,[63] where normoglycaemia, rather than the infused insulin dose, is related to the beneficial effects of intensive insulin therapy.[64]

Ischemic Heart Disease

Introduction

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

Obesity, insulin resistance, and type 2 diabetes mellitus are increasing and are powerful risk factors for IHD. With urbanization in the developing world, the prevalence of risk factors for IHD is increasing rapidly in these regions such that a majority of the global burden of IHD is now occurring in low-income and middle-income countries. Population subgroups that appear to be particularly affected are men in South Asian countries, especially India. Given the projection of large increases in IHD throughout the world, IHD is likely to become the most common cause of death worldwide by 2020.

Patients with ischemic heart disease fall into two large groups: patients with chronic coronary artery disease (CAD) who most commonly present with stable angina and patients with acute coronary syndromes (ACSs). The latter group, in turn, is composed of patients with acute myocardial infarction with ST-segment elevation on their presenting electrocardiogram (STEMI) and those with unstable angina and non-ST-segment elevation MI (UA/NSTEMI).

Table A. Major Risk Factors for AMI

Cigarette smoking

Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)

Low HDL cholesterol [<1.0 mmol/L (<40 mg/dL)]

Diabetes mellitus

Family history of premature CHD

- CHD in male first-degree relative <55 years
- CHD in female first-degree relative <65 years

Age (men ≥45 years; women ≥55 years)

Lifestyle risk factors

- Obesity (BMI ≥30 kg/m^2)
- Physical inactivity
- Atherogenic diet

Emerging risk factors

- Lipoprotein(a)
- Homocysteine
- Prothrombotic factors
- Proinflammatory factors
- Impaired fasting glucose
- Subclinical atherogenesis

Coronary Atherosclerosis

Epicardial coronary arteries are the major site of atherosclerotic disease. The major risk factors for atherosclerosis [high plasma low-density lipoprotein (LDL), low plasma high-density lipoprotein (HDL), cigarette smoking, hypertension, and diabetes mellitus] disturb the normal functions of the vascular endothelium. These functions include local control of vascular tone, maintenance of an antithrombotic surface, and impairment of inflammatory cell adhesion and diapedesis. The loss of these defenses leads to inappropriate constriction, luminal thrombus formation, and abnormal interactions with blood leukocytes, especially monocytes, and platelets. Monocyte interaction ultimately results in the subintimal collections of fat, smooth-muscle cells, fibroblasts, and intercellular matrix (i.e., atherosclerotic plaques), which develop at irregular rates in different segments of the epicardial coronary tree (Fig. 1) and lead eventually to segmental reductions in cross-sectional area.

When a stenosis reduces the diameter of an epicardial artery by 50%, there is a limitation on the ability to increase flow to meet increased myocardial demand. When the diameter is reduced by ~80%, blood flow at rest may be reduced, and further minor decreases in the stenotic orifice area can reduce coronary flow dramatically and cause myocardial ischemia.

Segmental atherosclerotic narrowing of epicardial coronary arteries is caused most commonly by the formation of a plaque, which is subject to rupture or erosion of the cap separating the plaque from the bloodstream. Upon exposure

of the plaque contents to blood, two important and interrelated processes are set in motion: (1) platelets are activated and aggregate; and (2) the coagulation cascade is activated, leading to deposition of fibrin strands. A thrombus composed of platelet aggregates and fibrin strands traps red blood cells and can reduce coronary blood flow, leading to the clinical manifestations of myocardial ischemia.

The location of the obstruction influences the quantity of myocardium rendered ischemic and determines the severity of the clinical manifestations. Severe coronary narrowing and myocardial ischemia are frequently accompanied by the development of collateral vessels, especially when the narrowing develops gradually. When well developed, such vessels can, by themselves, provide sufficient blood flow to sustain the viability of the myocardium at rest but not during conditions of increased demand.

With progressive worsening of a proximal epicardial artery stenosis, the distal resistance vessels (when they function normally) dilate to reduce vascular resistance and maintain coronary blood flow. A pressure gradient develops across the proximal stenosis, and poststenotic pressure falls. When the resistance vessels are maximally dilated, myocardial blood flow becomes dependent on the pressure in the coronary artery distal to the obstruction. In these circumstances, ischemia, manifest clinically by angina or electrocardiographically by ST-segment deviation, it can be precipitated by increases in myocardial oxygen demand caused by physical activity, emotional stress, and/or tachycardia. Changes in the caliber of the stenosed coronary artery due to physiologic vasomotion, loss of endothelial control of dilation (as occurs in diabetes mellitus), pathologic spasm

(Prinzmetal's angina), or small platelet-rich plugs can also upset the critical balance between oxygen supply and demand and thereby precipitate myocardial ischemia.

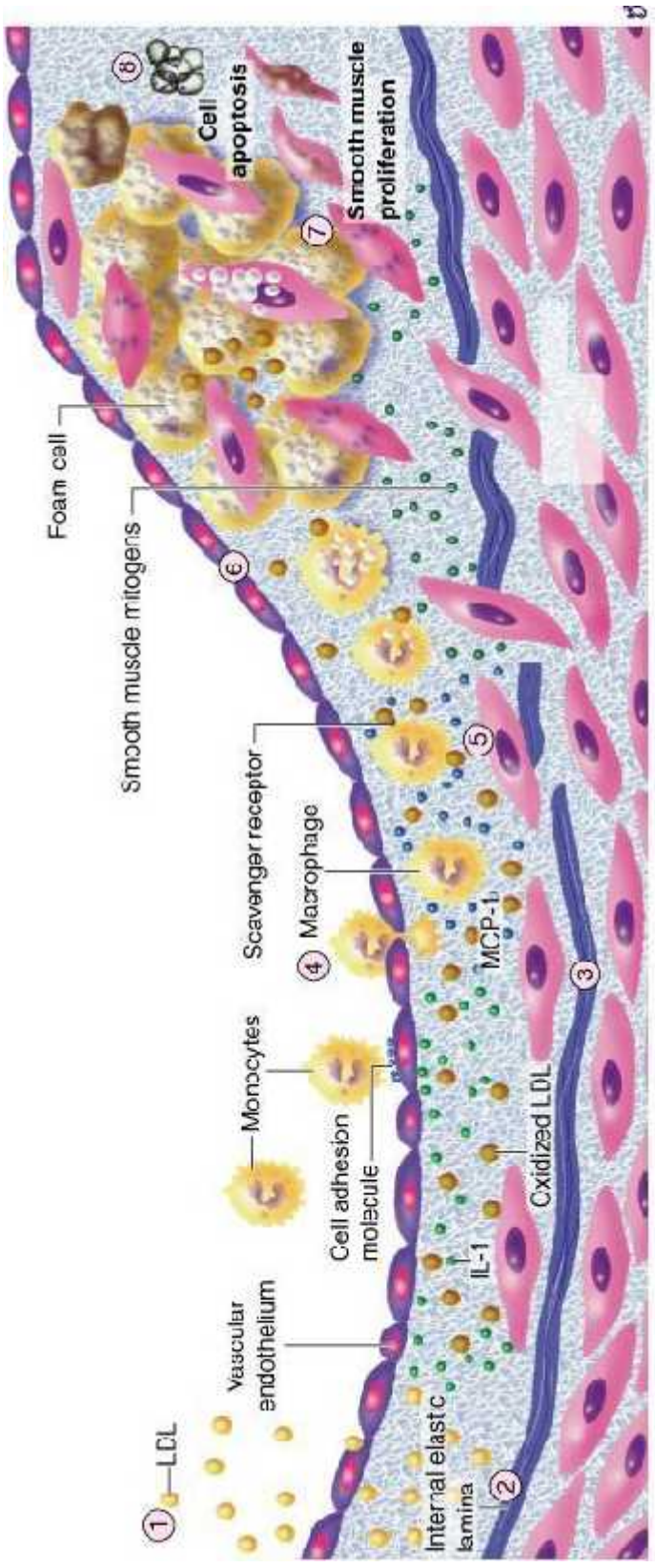


Figure 1 : Showing entry of monocytes and macrophages, smooth muscle proliferation and foam cell formation which are important steps in the process of atherosclerosis

STABLE ANGINA PECTORIS

Stable angina pectoris is characterized by chest or arm discomfort that may not be described as pain but is reproducibly associated with physical exertion or stress and is relieved within 5–10 min by rest and/or sublingual nitroglycerin.

Pathophysiology

Central to an understanding of the pathophysiology of myocardial ischemia is the concept of myocardial supply and demand. Under normal conditions, for any given level of a demand for oxygen, the myocardium will be supplied with oxygen-rich blood to prevent underperfusion of myocytes and the subsequent development of ischemia and infarction. An adequate supply of oxygen to the myocardium requires a satisfactory level of oxygen-carrying capacity of the blood (determined by the inspired level of oxygen, pulmonary function, and hemoglobin concentration and function) and an adequate level of coronary blood flow.

The normal coronary circulation is dominated and controlled by the heart's requirements for oxygen. This need is met by the ability of the coronary vascular bed to vary its resistance (and, therefore, blood flow) considerably while the myocardium extracts a high and relatively fixed percentage of oxygen. Normally, intramyocardial resistance vessels demonstrate an immense capacity for dilation. For example, the changing oxygen needs of the heart with exercise

and emotional stress affect coronary vascular resistance and in this manner regulate the supply of oxygen and substrate to the myocardium (metabolic regulation). The coronary resistance vessels also adapt to physiologic alterations in blood pressure in order to maintain coronary blood flow at levels appropriate to myocardial needs (autoregulation).

By reducing the lumen of the coronary arteries, atherosclerosis limits appropriate increases in perfusion when the demand for flow is augmented, as occurs during exertion or excitement. When the luminal reduction is severe, myocardial perfusion in the basal state is reduced. Coronary blood flow can also be limited by spasm, arterial thrombi, and, rarely, coronary emboli as well as by ostial narrowing due to aortitis.

Myocardial ischemia can also occur if myocardial oxygen demands are markedly increased and when coronary blood flow may be limited, as occurs in severe left ventricular (LV) hypertrophy due to aortic stenosis. The latter can present with angina that is indistinguishable from that caused by coronary atherosclerosis largely owing to subendocardial ischemia. A reduction in the oxygen-carrying capacity of the blood, as in extremely severe anemia or in the presence of carboxyhemoglobin, rarely causes myocardial ischemia by itself but may lower the threshold for ischemia in patients with moderate coronary obstruction. Abnormal constriction or failure of normal dilation of the coronary resistance vessels can also cause ischemia. When it causes angina, this condition is referred to as microvascular angina.

Clinical Presentation

The typical patient with angina is a man >50 years or a woman >60 years who complains of chest discomfort, usually described as heaviness, pressure, squeezing, smothering, or choking and only rarely as frank pain. Patients indicate a squeezing, central, substernal discomfort (Levine's sign). Angina is usually crescendo-decrescendo in nature, typically lasts 2 to 5 min, and can radiate to the left shoulder and to both arms, especially to the ulnar surfaces of the forearm and hand. It can also arise in or radiate to the back, interscapular region, root of the neck, jaw, teeth, and epigastrium. Episodes of angina are typically caused by exertion (e.g., exercise, hurrying, or sexual activity) or emotion (e.g., stress, anger, fright, or frustration) and are relieved by rest. The patient may be awakened at night distressed by typical chest discomfort and dyspnea. The threshold for the development of angina pectoris may vary by time of day and emotional state. Many patients report a fixed threshold for angina, which occurs predictably at a certain level of activity, such as climbing two flights of stairs at a normal pace. In these patients coronary stenosis and myocardial oxygen supply are fixed and ischemia is precipitated by an increase in myocardial oxygen demand. In other patients the threshold for angina may vary considerably within any given day and from day to day. In such patients variations in myocardial oxygen supply, most likely due to changes in coronary vascular tone, may play an important role. Exertional angina is typically relieved by rest in 1 to 5 min and even more rapidly by rest and sublingual nitroglycerin. Indeed, the diagnosis of angina should be at doubt if it does not respond to the combination of these two measures. Anginal “equivalents” are symptoms of myocardial ischemia other

than angina. These include dyspnea, fatigue, and faintness and are more common in the elderly and in diabetic patients.

Diagnosis of Stable Angina

Electrocardiogram

A 12-lead ECG recorded at rest is normal in about half the patients with typical angina pectoris, but there may be signs of an old myocardial infarction. Although repolarization abnormalities, i.e., ST-segment and T-wave changes as well as left ventricular hypertrophy and intraventricular conduction disturbances are suggestive of IHD, they are nonspecific, since they can also occur in pericardial, myocardial, and valvular heart disease or, in the case of the former, transiently with anxiety, changes in posture, drugs, or esophageal disease. Typical ST-segment and T-wave changes that accompany episodes of angina pectoris and disappear thereafter are more specific.

Stress testing in the absence of significant ECG changes the diagnosis of unstable angina involves recording the 12-lead ECG before, during and after exercise, usually on a treadmill. The ischemic ST-segment response is generally defined as flat depression of the ST segment >0.1 mV below baseline (i.e., the PR segment) and lasting longer than 0.08 s. Upsloping or junctional ST-segment changes are not considered characteristic of ischemia and do not constitute a positive test. Negative exercise tests in which the target heart rate (85% of maximal heart rate for age and sex) is not achieved are considered to be nondiagnostic. Since the overall sensitivity of exercise stress electrocardiography is only 75%, a negative result does not exclude CAD, although it makes the likelihood of three-vessel or left main CAD extremely unlikely. The development

of angina or severe (>0.2 mV) ST-segment depression at a low workload, i.e., before completion of stage II of the Bruce protocol, and/or ST-segment depression that persists for >5 min after the termination of exercise increases the specificity of the test and suggests severe IHD and a high risk of future adverse events.

Management

Each patient must be evaluated individually with respect to his or her expectations and goals, control of symptoms, and prevention of adverse clinical outcomes, such as MI and premature death. The degree of disability as well as the physical and emotional stress that precipitates angina must be carefully recorded in order to set treatment goals. The management plan should include the following components: (1) explanation of the problem and reassurance about the ability to formulate a treatment plan, (2) identification and treatment of aggravating conditions, (3) recommendations for adaptation of activity as needed, (4) treatment of risk factors that will decrease the occurrence of adverse coronary outcomes, (5) drug therapy for angina, and (6) consideration of revascularization.

UNSTABLE ANGINA AND Non ST- ELEVATION MI

The diagnosis of UA is based largely on the clinical presentation. UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features:

1. It occurs at rest (or with minimal exertion) usually lasting > 10 min,
2. It is severe and of new onset (i.e., within the prior 4 to 6 weeks), and/or

3. It occurs with a crescendo pattern (i.e., distinctly more severe, prolonged, or frequent than previously).

The diagnosis of Non ST- ELEVATION MI(NSTEMI) is established if a patient with the clinical features of UA develops evidence of myocardial necrosis, as reflected in elevated cardiac biomarkers.

Pathophysiology

UA/NSTEMI is most commonly caused by a reduction in oxygen supply and/or by an increase in myocardial oxygen demand superimposed on an atherosclerotic coronary plaque, with varying degrees of obstruction. Four pathophysiologic processes that may contribute to the development of UA/NSTEMI have been identified: (1) plaque rupture or erosion with superimposed nonocclusive thrombus, believed to be the most common cause—NSTEMI may occur with downstream embolization of platelet aggregates and/or atherosclerotic debris; (2) dynamic obstruction [e.g., coronary spasm, as in Prinzmetal's variant angina]; (3) Progressive mechanical obstruction [e.g., rapidly advancing coronary atherosclerosis or restenosis following percutaneous coronary intervention (PCI)]; and (4) secondary UA related to increased myocardial oxygen demand and/or decreased supply (e.g., tachycardia, anemia). More than one of these processes may be involved.

Clinical Presentation

The clinical hallmark of UA/NSTEMI is chest pain, typically located in the substernal region or sometimes in the epigastrium that frequently radiates to the neck, left shoulder, and left arm. Examination may be unremarkable. If the

patient has a large area of myocardial ischemia or a large NSTEMI, the physical findings can include diaphoresis, pale cool skin, sinus tachycardia, a third and/or fourth heart sound, basilar rales, and sometimes hypotension, resembling the findings of large STEMI.

DIAGNOSIS OF UNSTABLE ANGINA AND Non ST ELEVATION MI

Electrocardiogram

In UA, ST-segment depression, transient ST-segment elevation, and/or T-wave inversion occur in 30–50% of patients, depending on the severity of the clinical presentation. In patients with the clinical features of UA, the presence of new ST-segment deviation, even of only 0.05 mV, is an important predictor of adverse outcome. T-wave changes are sensitive for ischemia but less specific, unless they are new, deep T-wave inversions (≥ 0.3 mV).

Cardiac Biomarkers

Patients with UA who have elevated biomarkers of necrosis, such as CK-MB and troponin (a much more specific marker of myocardial necrosis), are at increased risk for death or recurrent MI. Elevated levels of these markers distinguish patients with NSTEMI from those with UA.

Cardiac Imaging

Echocardiography or radionuclide angiography should be carried out to assess left ventricular function in patients with unstable angina and in patients with a history of a prior myocardial infarction, pathologic Q waves, or clinical evidence of heart failure.

Risk Stratification and Prognosis

Patients with documented UA/NSTEMI exhibit a wide spectrum of early (30 days) risk of death, ranging from 1 to 10%, and of new or recurrent infarction of 3–10%. Assessment of "global risk" can be accomplished by clinical risk scoring systems such as that developed from in the Thrombolysis in Myocardial Infarction (TIMI) Trials, which includes seven independent risk factors: age ≥65 years, three or more risk factors for CAD, documented CAD at catheterization, development of UA/NSTEMI while on aspirin, more than two episodes of angina within the preceding 24 h, ST deviation ≥0.5 mm, and an elevated cardiac marker.

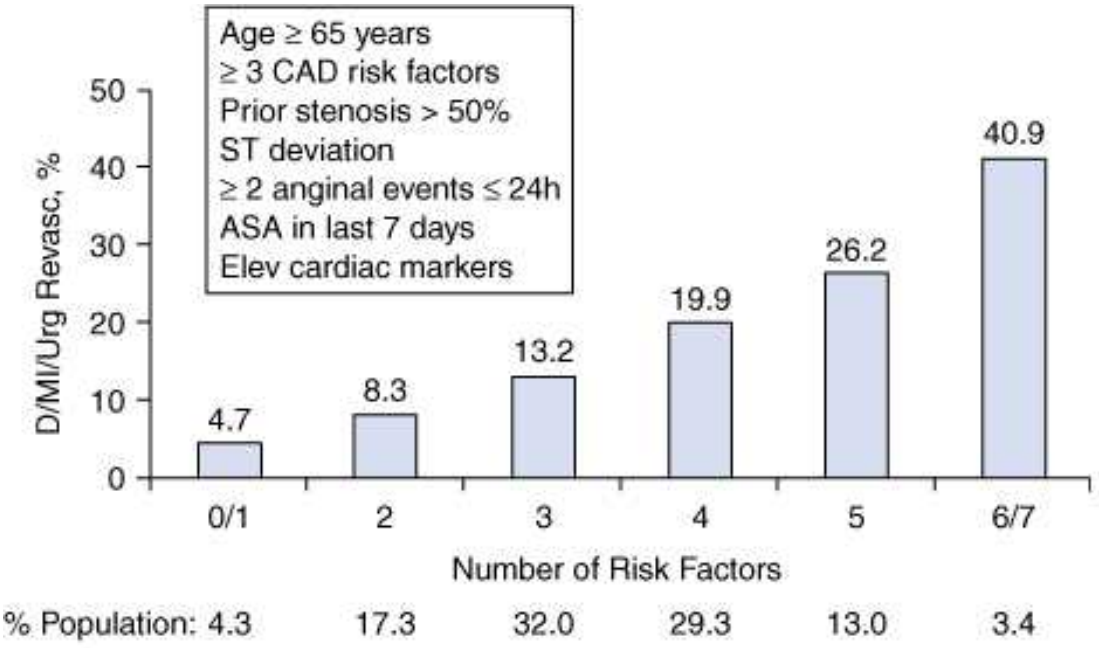


Fig. 2 The TIMI Risk Score for UA/NSTEMI, a simple but comprehensive clinical risk stratification score to identify increasing risk of death, myocardial infarction, or urgent revascularization to day 14. CAD, coronary artery disease; ASA, aspirin.

Management

Medical Treatment

Patients with UA/NSTEMI should be placed at bed rest with continuous ECG monitoring for ST-segment deviation and cardiac rhythm. Ambulation is permitted if the patient shows no recurrence of ischemia (discomfort or ECG changes) and does not develop a biomarker of necrosis for 12–24 h. Medical therapy involves simultaneous anti-ischemic treatment and antithrombotic treatment.

Invasive versus Conservative Strategy

Multiple clinical trials have shown the benefit of an early invasive strategy in high-risk patients, i.e., patients with multiple clinical risk factors, ST-segment deviation, and/or positive biomarkers (Table B). In this strategy, following treatment with anti-ischemic and antithrombotic agents, coronary arteriography is carried out within ~48 h of admission, followed by coronary revascularization (PCI or coronary artery bypass grafting), depending on the coronary anatomy.

In low-risk patients, the outcomes from an invasive strategy are similar to those obtained from a conservative strategy, which consists of anti-ischemic and antithrombotic therapy followed by "watchful waiting," in which coronary arteriography is carried out only if rest pain or ST-segment changes recur or there is evidence of ischemia on a stress test.

Table B. Class I Recommendations for Use of an Early Invasive Strategy
Class I (level of evidence: A) indications
Recurrent angina at rest/low-level activity despite Rx
Elevated TnT or TnI
New ST-segment depression
Rec. angina/ischemia with CHF symptoms, rales, MR
Positive stress test
EF < 0.40
Decreased BP
Sustained VT
PCI < 6 months, prior CABG

ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

STEMI usually occurs when coronary blood flow decreases abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis. Slowly developing, high-grade coronary artery stenoses do not typically precipitate STEMI because of the development of a rich collateral network over time.

Pathophysiology: Role of Acute Plaque Rupture

STEMI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. This injury is produced or facilitated by factors such as cigarette smoking, hypertension, and lipid accumulation. In most cases, STEMI occurs when the surface of an atherosclerotic plaque becomes disrupted (exposing its contents to the blood) and conditions (local or systemic) favor thrombogenesis. A mural thrombus forms at the site of plaque disruption, and the involved coronary artery becomes occluded. Histologic studies indicate that the coronary plaques prone to disruption are those with a rich lipid core and a thin fibrous cap. After an initial platelet monolayer forms at the site of the disrupted plaque, various agonists (collagen, ADP, epinephrine, serotonin) promote platelet activation. After agonist stimulation of platelets, thromboxane A_2 (a potent local vasoconstrictor) is released, further platelet activation occurs, and potential resistance to fibrinolysis develops.

In addition to the generation of thromboxane A_2, activation of platelets by agonists promotes a conformational change in the glycoprotein IIb/IIIa receptor. Once converted to its functional state, this receptor develops a high affinity for amino acid sequences on soluble adhesive proteins (i.e., integrins) such as fibrinogen. Since fibrinogen is a multivalent molecule, it can bind to two different platelets simultaneously, resulting in platelet cross-linking and aggregation.

The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of the disrupted plaque. Fluid-phase and clot-bound thrombin participate in an autoamplification reaction leading to further activation of the coagulation cascade. The culprit coronary artery eventually becomes occluded by a thrombus containing platelet aggregates and fibrin strands.

In rare cases STEMI may be due to coronary artery occlusion caused by coronary emboli, congenital abnormalities, coronary spasm, and a wide variety of systemic- particularly inflammatory diseases. Patients at increased risk of developing STEMI include those with multiple coronary risk factors and those with unstable angina

Clinical Presentation

Pain is the most common presenting complaint in patients with STEMI. The pain is deep and visceral; adjectives commonly used to describe it are heavy, squeezing, and crushing, although occasionally it is described as stabbing or burning. It is similar in character to the discomfort of angina pectoris but

commonly occurs at rest, is usually more severe, and lasts longer. Typically the pain involves the central portion of the chest and/or the epigastrium, and on occasion it radiates to the arms. Less common sites of radiation include the abdomen, back, lower jaw, and neck. The frequent location of the pain beneath the xiphoid and epigastrium and the patients' denial that they may be suffering a heart attack are chiefly responsible for the common mistaken impression of indigestion. The pain of STEMI may radiate as high as the occipital area but not below the umbilicus. It is often accompanied by weakness, sweating, nausea, vomiting, anxiety, and a sense of impending doom. The pain may commence when the patient is at rest, but when it begins during a period of exertion, it does not usually subside with cessation of activity, in contrast to angina pectoris.

However, pain is not uniformly present in patients with STEMI. The proportion of painless STEMIs is greater in patients with diabetes mellitus, and it increases with age. In the elderly, STEMI may present as sudden-onset breathlessness, which may progress to pulmonary edema. Other less common presentations, with or without pain, include sudden loss of consciousness, a confusional state, a sensation of profound weakness, the appearance of an arrhythmia, evidence of peripheral embolism, or merely an unexplained drop in arterial pressure.

Diagnosis of Myocardial Infarction

Myocardial infarction (MI) progresses through the following temporal stages: (1) acute (first few hours to 7 days), (2) healing (7 to 28 days), and (3) healed (≥29 days). When evaluating the results of diagnostic tests for STEMI, the temporal phase of the infarction process must be considered. The laboratory tests

of value in confirming the diagnosis may be divided into four groups: (1) ECG, (2) serum cardiac biomarkers, (3) cardiac imaging, and (4) nonspecific indexes of tissue necrosis and inflammation.

Electrocardiogram

During the initial stage, total occlusion of an epicardial coronary artery produces ST-segment elevation. Most patients initially presenting with ST-segment elevation ultimately evolve Q waves on the ECG. However, Q waves in the leads overlying the infarct zone may vary in magnitude and even appear only transiently, depending on the reperfusion status of the ischemic myocardium and restoration of transmembrane potentials over time. A small proportion of patients initially presenting with ST-segment elevation will not develop Q waves when the obstructing thrombus is not totally occlusive, obstruction is transient, or if a rich collateral network is present.

Previously it was believed that transmural MI is present if the ECG demonstrates Q waves or loss of R waves, and nontransmural MI may be present if the ECG shows only transient ST-segment and T-wave changes. However, electrocardiographic-pathologic correlations are far from perfect and terms such as Q-wave MI, non-Q-wave MI, transmural MI, and nontransmural MI, have been replaced by STEMI and NSTEMI.

Serum Cardiac Biomarkers

Certain proteins, called serum cardiac biomarkers, are released from necrotic heart muscle after STEMI. The temporal pattern of protein release is of diagnostic importance, but contemporary urgent reperfusion strategies necessitate making a decision (based largely on a combination of clinical and ECG findings)

before the results of blood tests have returned from the laboratory. Rapid whole-blood bedside assays for serum cardiac markers are now available and may facilitate management decisions, particularly in patients with nondiagnostic ECGs.

Cardiac-specific troponin T (cTnT) and cardiac-specific troponin I (cTnI) - are not normally detectable in the blood of healthy individuals but may increase after STEMI to levels >20 times higher than the upper reference limit (the highest value seen in 99% of a reference population not suffering from MI), the measurement of cTnT or cTnI is of considerable diagnostic usefulness, and they are now the preferred biochemical markers for MI. The cardiac troponins are particularly valuable when there is clinical suspicion of either skeletal muscle injury or a small MI that may be below the detection limit for CK and CKMB measurements, and they are therefore of particular value in distinguishing UA from NSTEMI. Levels of cTnI and cTnT may remain elevated for 7–10 days after STEMI.

Creatine phosphokinase (CK) rises within 4–8 h and generally returns to normal by 48–72 h. An important drawback of total CK measurement is its lack of specificity for STEMI, as CK may be elevated with skeletal muscle disease or trauma, including intramuscular injection. The MB isoenzyme of CK has the advantage over total CK that it is not present in significant concentrations in extracardiac tissue and therefore is considerably more specific. A ratio (relative index) of CKMB mass:CK activity ≥2.5 suggests but is not diagnostic of a myocardial rather than a skeletal muscle source for the CKMB elevation.

For the purposes of confirming the diagnosis of MI, serum cardiac markers should be measured on admission, 6 to 9 h after admission, and 12 to 24 h after admission if the diagnosis remains uncertain.

Many hospitals are using cTnT or cTnI rather than CKMB as the routine serum cardiac marker for diagnosis of STEMI, although any of these analytes remains clinically acceptable. It is not cost-effective to measure both a cardiac-specific troponin and CKMB at all time points in every patient.

Cardiac Imaging

Abnormalities of wall motion on two-dimensional echocardiography are almost universally present. In the emergency department setting, early detection of the presence or absence of wall motion abnormalities by echocardiography can aid in management decisions, such as whether the patient should receive reperfusion therapy [e.g., fibrinolysis or a percutaneous coronary intervention (PCI)]. Echocardiography may also identify the presence of right ventricular (RV) infarction, ventricular aneurysm, pericardial effusion, and LV thrombus. In addition, Doppler echocardiography is useful in the detection and quantitation of a ventricular septal defect and mitral regurgitation, two serious complications of STEMI. Several radionuclide imaging techniques are available for evaluating patients with suspected STEMI. However, these imaging modalities are used less often than echocardiography because they are more cumbersome and lack sensitivity and specificity in many clinical circumstances. Myocardial perfusion imaging with ^{201}Tl or ^{99m}Tc-sestamibi, which are distributed in proportion to myocardial blood flow and concentrated by viable myocardium, reveal a defect ("cold spot") in most patients during the first few hours after development of a transmural infarct. However, although perfusion scanning is extremely sensitive,

it cannot distinguish acute infarcts from chronic scars and thus is not specific for the diagnosis of acute MI. Radionuclide ventriculography, carried out with ^{99m}Tc-labeled red blood cells, frequently demonstrates wall motion disorders and reduction in the ventricular ejection fraction in patients with STEMI.

Other Prognostic Markers During Acute Coronary Syndromes

C-Reactive Protein

Among the growing list of additional markers that appear to be useful in assessing patients with UA/NSTEMI, CRP holds considerable promise. Elevated levels of high sensitivity (hs) CRP relate to increased risk of death, MI, and/or need for urgent revascularization,[65] Of note, because CRP is an acute-phase reactant, it is known to be elevated by an ACS. Thus, "elevated" levels of CRP in patients with ACS are approximately five times higher than for stable patients.[66] Among patients with negative troponin I at baseline who overall had a 14-day mortality of only 1.5 percent, CRP was able to discriminate a high- and low-risk group: mortality for patients with an elevated CRP was 5.8 percent versus 0.4 percent for patients without elevated CRP.[67] When using both CRP and troponin T, mortality could be stratified from 0.4 percent for patients with both markers negative, 4.7 percent if either CRP or troponin were positive, to 9.1 percent if both were positive.[67] Multiple other studies have yielded similar results.[67,68] Of note, however, CRP has not yet been shown in the setting of UA/NSTEMI to predict a differential benefit of a therapy.[69]

CRP measured after stabilization post-ACS strongly predicts outcome after 3 to 12 months.[69,70] Study of other inflammatory markers has offered

consistent evidence of an association between systemic inflammation and recurrent adverse events, including serum amyloid A,[68] monocyte chemoattractant protein (MCP)-1,[71] and interleukin-6.[72,73] These studies indicate that inflammation is related to the instability of patients and an increased risk of recurrent cardiac events.

CK-MB and the Troponins

There is a linear relation between the level of troponin T or I in the blood and subsequent risk of death—the higher the troponin level, the higher the mortality risk.[74] On the other hand, a higher risk of MI (or recurrent MI) was observed with *lower* degrees of troponin elevation in several studies; thus the overall rate of death or MI is equally high among patients with low or higher troponin values.[67]

Myeloperoxidase

Myeloperoxidase (MPO) is a heme protein expressed by leukocytes that generates hypochlorous acid, a potent pro-oxidant. One case-control study found an association of MPO levels with the presence of angiographically documented CAD, independent of other cardiovascular risk factors and of WBC count.[73] In patients presenting to the emergency department with chest pain,[75] and in patients with UA/NSTEMI, MPO serum levels predict increased risk for subsequent death or MI, independent of other risk factors and other cardiac markers. as well as mortality alone in other populations. Elevations of MPO have been seen throughout the coronary vasculature in patients with UA/NSTEMI. Thus, MPO

may be a marker of inflammation, but also suggests a direct role of leukocyte activation in the pathophysiology of vascular inflammation and ACS.

B-Type Natriuretic Peptide

B-type natriuretic peptide (BNP) is a neurohormone that is synthesized in ventricular myocardium and released in response to increased wall stress. It has many actions including natriuresis, vasodilation, inhibition of sympathetic nerve activity, and inhibition of the renin-angiotensin-aldosterone system. BNP has usefulness as a diagnostic and prognostic marker among patients with congestive heart failure, and in patients with acute MI.[76] BNP has prognostic value across the full spectrum of patients with ACS, including those with UA/NSTEMI: In OPUS-TIMI 16, patients with elevated levels of BNP (>80 pg/ml) or Ntpro BNP had a two- to threefold higher risk of death by 10 months.[77] This finding was confirmed in the TIMI 11 and TACTICS-TIMI 18 trials. Together, these data suggest that measurement of BNP in patients presenting with UA/NSTEMI adds importantly to our current tools for risk stratification.

White Blood Cell Count

Another, even simpler and universally available marker of inflammation is the white blood cell (WBC) count. Several studies of patients with acute MI and more recently with UA/NSTEMI,[67,75] have observed that patients with elevated WBC counts have higher risk of mortality and recurrent MI. This association was independent of CRP,[66] suggesting that no one marker, such as CRP, captures all the information regarding the influence of inflammation on outcomes.

Creatinine

Another simple tool for risk stratification is the use of creatinine and/or calculation of creatinine clearance. Several recent studies have found that elevated creatinine is associated with an adverse prognosis.[78,79] The risk appears to be independent of other standard risk factors, such as troponin elevation. This factor may also play a role in decreased drug clearance, indicating the need for adjustment of doses of medications such as low-molecular-weight heparin (LMWH).[80]

Need for the Study

A higher baseline glucose level at the time of presentation predicts significantly higher long-term mortality, independent of a history of diabetes, and is a risk factor that may be modifiable with aggressive treatment. Determination of blood sugar is a simple procedure, requires no expertise, is inexpensive and importantly, It is a correctable factor, having a bearing on morbidity and mortality. Thus this study aims at exploring the association between the admission glycemic status and 30 day-mortality in acute myocardial infarction in non diabetics.

METHODOLOGY

Materials and Methods:

I. **Source of Data:** KLE's Dr. Prabhakar Kore Hospital and MRC, Belgaum.

II. **Method of collection of data:**

A. **Study design:** One year cross sectional study

B. **Sample size:** 60 cases, divided into 4 groups depending on sextiles of blood glucose concentration at admission, namely Group I (≤120 mg %), Group II (120-140 mg %), Group III (140-167 mg %) and Group IV (>167 mg %).

C. **Duration:** One year (2007-08)

D. **Inclusion criteria**:

1. Patients with acute myocardial infarction proven by cardiac enzymes, Electrocardiography and symptoms suggestive of acute myocardial infarction.
2. Normal HbA1c (<7)

E. **Exclusion criteria**:

1. Known cases of diabetes
2. Patients who had received dextrose containing intravenous fluids before admission.
3. Post surgical, post trauma(up to 1 month)
4. Patients receiving drugs elevating blood sugar levels. (e.g.- corticosteroids)
5. Time from the beginning of symptoms to admission to the ICCU more than 48 hours

Informed consent was taken from all the patients who participated in the study. The study was conducted as per the guidelines of the institute, after departmental peer review and approval by Ethics committee.

III. Instruments/ Tools:

1. **Socio demographic and clinical data sheet**: This sheet was used to collect the patient's socio demographic data, including age, gender, educational status, residential status, socioeconomic status, past history, family history, personal history and details of general physical examination.
2. **Killip's class grading**: In 1967 prior to invasive monitoring, Killip and Kimball[81] devised a clinical classification based on physical findings present on admission, which provided a prognostic guide.

Table C. Killip Classification

Killip class	**Hospital mortality (%)**
I No congestive heart failure	6
II Mild congestive heart failure, rales, S_3, congestion on chest radiograph	17
III Pulmonary edema	38
IV Cardiogenic shock	81**

** It is important to note that with modern therapy, the mortality of those in cardiogenic shock has improved from 81 percent to approximately 60 percent.

IV. Procedure:

1. The study included all the consecutive non diabetic patients admitted to the ICCU with raised serum cardiac enzymes, any or all of symptoms suggestive of myocardial infarction for at least 30 minutes, ECG changes on at least two contiguous leads with pathological Q waves and persistent ST elevation or depression (>0.1 mV).
2. The time from the beginning of symptoms to admission to the intensive care unit has to be less than 48 hours.
3. All patients with glycemia measured on admission by a single standard calibrated glucometer and who had no history of or treatment for diabetes mellitus at entry, were included.
4. The patient's cardiovascular history, medication at the time of admission, risk factors, in-hospital clinical course, including Killip's class, and the initial diagnostic and therapeutic management was recorded. Furthermore, ECG of all patients was read and recorded (territory of infarct, STEMI, NSTEMI, Rhythm disturbances), left ventricular ejection fraction and regional wall motion abnormality was assessed by echocardiography at any time during the first 5 days, and recorded.
5. The end points of study were 30 days or till death during hospitalization. If the patient was discharged within 30 days, then contact address and telephone number was taken and follow up was done.
6. The patients were subjected to routine investigations as per protocol and in case patient refused the investigations required for this study, the cost of the investigations was borne by the principal investigator (Dr Dhareppa G. Chougala).

7. Patients were divided into 4 groups depending on sextiles of blood glucose concentration at admission, Group I (≤120 mg %), Group II (120-140 mg %), Group III (140-167 mg %) and Group IV (>167 mg %). Then comparison between the initial and 30 day-mortality data according to sextiles of blood glucose concentrations at admission, was done.

V. Investigations or Interventions Conducted on Patients:

1. Random blood sugar at admission
2. Electrocardiography
3. Cardiac enzymes (Troponin I and CK MB)
4. Echocardiography
5. Glycosylated hemoglobin (HbA1c)

VI. Statistical Methods:

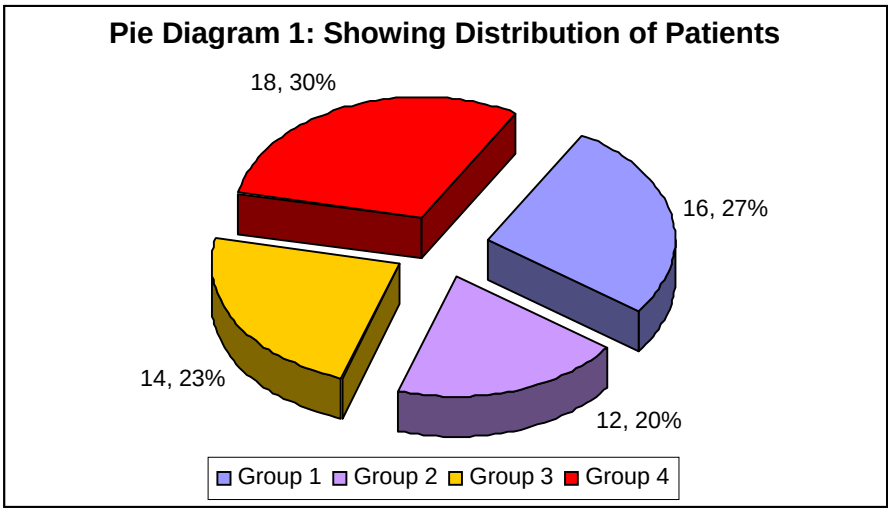
1. Data obtained was tabulated using version 13 of the Statistical Package for Social Sciences (SPSS, published SPSS Inc.) and subjected to appropriate statistical analysis.
2. Chi- square test and one way ANOVA with post hoc test were used to identify differences between 4 groups
3. Bivariate correlation using Pearson's method was used to identify different correlates of death as outcome.
4. Logistic regression was used to see the significant predictors of outcome as death.

RESULTS

1. Distribution of Patients (N=60) across the groups depending on admission RBS:

Variable	Group I	Group II	Group III	Group IV
Admission RBS	< 120mg%	120-140 mg%	140-167 mg%	>167 mg%
Number of patients	16	12	14	18

The above table shows the study patients are divided into four groups (I to IV) depending on the admission RBS. Group I- 16 patients, Group II- 12patients, Group III- 14 patients, Group IV- 18 patients respectively.



2. Socio demographic details:

Variable		Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		F/ χ2	P
		Mean / N	SD/ %	Mean / N	SD/ %	Mean / N	SD/ %	Mean / N	SD/ %		
Age		50.75	11.51	56.17	18.33	53.43	11.95	61.00	11.59 %	1.845	0.150
Age >60Yrs		5	31.25 %	4	33.33 %	4	28.57 %	13	72.22 %	8.80	0.032*
Sex	M	13	81.25 %	8	66.66 %	12	85.71 %	12	66.66 %	2.302	0.512
	F	3	18.75 %	4	33.34 %	2	14.29 %	6	33.34 %		

M= Male, F= Female

* statistically significant (95% Confidence Interval)

The above table shows that there is no significant difference in age and sex distribution between the groups. However, the number of patient's above 60 years was greatest in group IV. This was statistically significant.

3. Personal History:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N	%	N	%		
HTN	3	18.75%	6	50%	2	14.29%	9	50%	7.567	0.056
Smoking	9	56.25%	2	16.67%	10	71.43%	7	38.89%	8.816	0.032*
Alcohol	5	31.25%	2	16.67%	4	28.57%	2	11.11%	2.617	0.454

This table shows that there is statistically significant difference in number of smokers across the groups and there is no difference of Alcohol consumption and prevalence of HTN between the groups.

4. General Physical Examination:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		F	P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
BP Systolic	126.87	19.57	123.33	29.64	120.86	27.37	93.67	54.38	2.911	0.042*
BP Diastolic	82.25	13.80	73.33	28.71	74.00	24.86	60.78	42.94	1.464	0.234
Heart~~Pulse~~ Rate	88.75	13.03	82.67	18.63	89.00	20.48	79.17	34.54	0.652	0.585

Post Hoc test: BP- Systolic; Significant association between Group1 and Group 2, 3 & 4

BP- Diastolic; Significant association between Group1 and 4

This table shows, There is a statistically significant (P= 0.042) drop in the mean systolic BP as we move from Group I to Group IV. There occurred no statistically significant difference in the mean diastolic BP and heart rate~~pulse rate~~ at admission across the groups.

5. Investigations:

5 a~~A~~. Blood Investigations

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		F	P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Admission RBS	105.13	8.99	125.25	3.72	149.57	7.21	229.39	61.72	41.983	0.001*
CK-MB	20.94	20.86	37.42	46.34	32.14	39.30	31.46	32.13	0.572	0.636
HbA1c	5.70	0.49	5.58	0.79	5.58	0.81	5.82	0.98	0.330	0.804

Post Hoc Test:

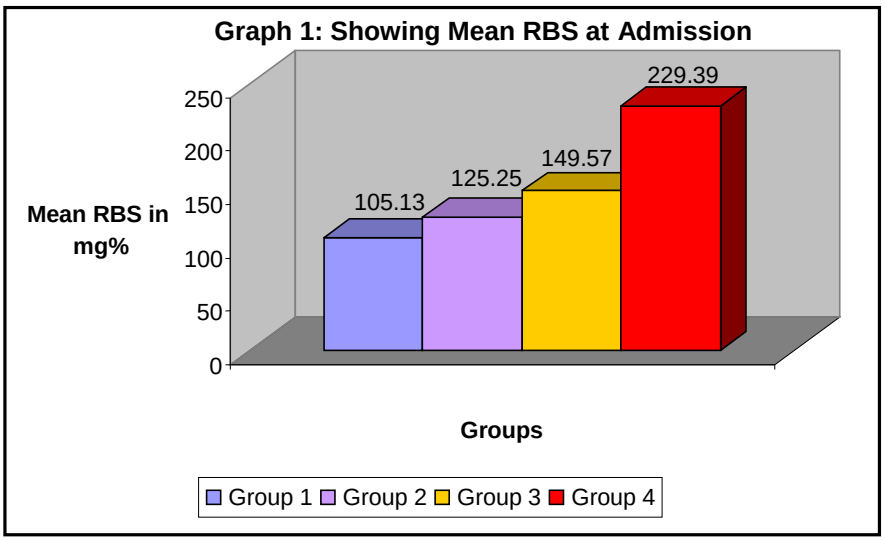
Admission RBS; Significant association between Group1 and Group 3 and 4

Significant association between Group2 and Group4

Significant association between Group3 and Group 4

Significant association between Group4 and Group 1, 2 and 3

This table shows statistical significance in admission RBS levels across the groups. And there is no difference in the HbA1c and CK-MB levels across the groups.


Graph 1: Showing Mean RBS at Admission
Mean RBS in mg%
250
200
150
100
50
0
105.13
125.25
149.57
229.39
Groups
Group 1
Group 2
Group 3
Group 4

5bB. Territory of infarct:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N	%	N	%		
Anterior wall	1	6.25%	3	25%	1	7.14%	2	11.11%	2.809	0.422
Antero-Septal	7	43.75%	3	25%	6	42.86%	7	38.89%	1.225	0.747
Inferior wall	8	50%	6	50%	7	50%	9	50%	0.000	1.000

This table shows there is no statistical significance in the territory of infarct and admission RBS levels

5cC. Killip class:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N/	%	N	%		
Killip class I	13	81.25%	6	50%	6	42.86%	5	27.78%	10.091	0.018*
Killip class II	3	18.75%	5	41.69%	8	57.14%	13	72.22%	10.369	0.016*
Killip class III	0	0	0	0	0	0	0	0		
Killip class IV	0	0	1	8.31%	0	0	0	0	4.068	0.254
Killip class Deteoriation By ≥ 2 classes in the hospital stay	0	0	0	0	1	7.14%	8	44.44	17.859	0.001*

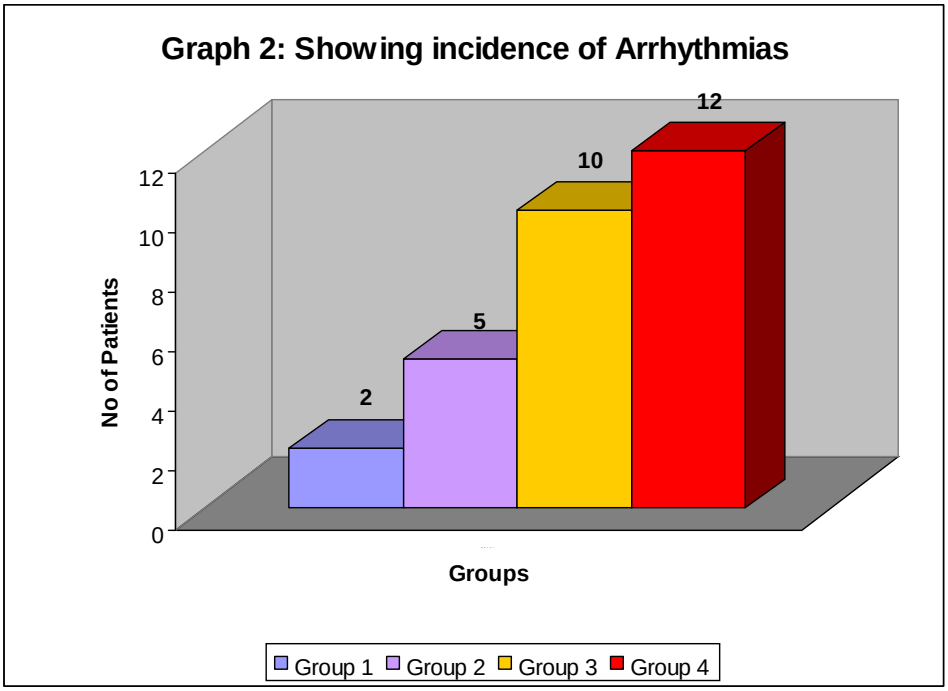
This table shows, statistically significant difference between groups in Killip's class I & II at admission. There is higher admission Killip's class as admission RBS value increases. This table also shows significant Killip's class deterioration by more than 2 classes during the hospital stay as admission RBS increases.

6. In Hospital Complications:

6a~~A~~. Arrhythmias:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N	%	N	%		
Atrial Tachyarrhythmias	1	6.25%	0	0	1	7.14%	1	5.56%	0.831	0.842
Ventricular Tachyarrhythmias	0	0	4	33.33%	5	35.71%	5	27.78%	6.939	0.074
Bradyarrhythmias/ Heart Block	1	6.25%	2	16.67%	4	28.57%	7	38.89%	5.558	0.135
Any arrhythmias	2	12.5%	5	41.67%	10	71.43%	12	66.67%	13.853	0.003*

This table shows that there is no significant occurrence of specific type of arrhythmias across the groups. However there is statistically significant difference in the increased incidence of arrhythmias (Brady + Tachy) with increase in admission RBS.


Graph 2: Showing incidence of Arrhythmias
No of Patients
0
2
4
6
8
10
12
2
5
10
12
Groups
Group 1
Group 2
Group 3
Group 4

6bB. Left ventricular function (LVEF at admission):

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		F	P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
LV EF (%)	50.78	6.17	46.67	6.85	42.86	7.52	41.28	5.69	6.903	0.001*

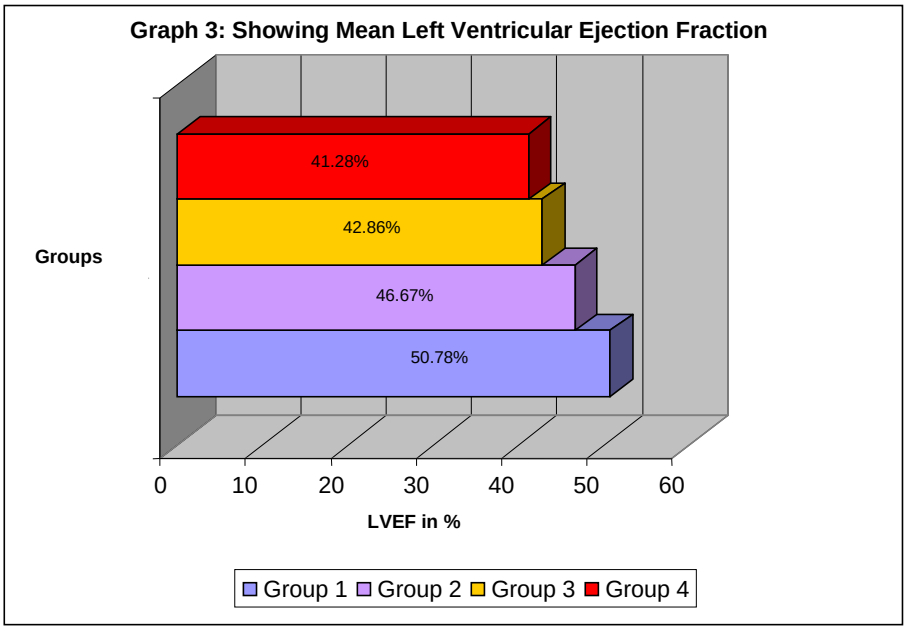
Post Hoc Test:

LVEF; Significant association between Group1 and Group3 and 4

Significant association between Group2 and Group 4

Significant association between Group4 and Group 1, 2 and 3

This table shows a statistically significant reduction of LV Ejection Fraction as admission RBS level increases.



6cC. Development of cardiogenic shock:

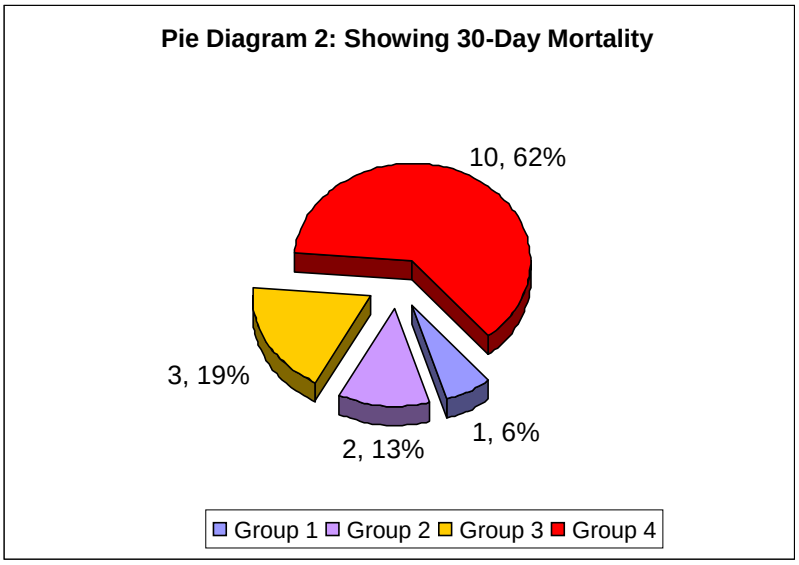
Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N	%	N	%		
Development of Cardiogenic Shock	0	0	1	8.33%	0	0	6	33.33%	12.291	0.006*

This table shows statistically significant difference in incidence of development cardiogenic shock across the groups. Higher risk of development of cardiogenic shock in subjects with high admission RBS.

6dD. 30--day -mortality:

Variable	Group 1 (N=16)		Group 2 (N=12)		Group 3 (N=14)		Group 4 (N=18)		χ 2	P
	N	%	N	%	N	%	N	%		
Death	1	6.25%	2	16.67%	3	21.43%	10	55.56%	11.902	0.008*

This table shows the incidence of 30--day- mortality, which linearly increases as admission RBS rises (across the groups). This is statistically significant (P= 0.008).



7. Correlates of 30-Day Mortality ~~Death~~ as an Outcome:

Variables	N	r (Pearson correlation)	P
Groups 1-4	60	0.415	0.001*
Age	60	0.181	0.166
Age ≥ 60 yrs	60	0.233	0.073
Sex	60	0.174	0.183
Known history of Hypertension	60	0.373	0.003*
History of Smoking	60	-0.035	0.789
History of Alcohol intake	60	-0.134	0.307
Systolic BP	60	-0.378	0.003*
Diastolic BP	60	-0.265	0.041*
Heart~~Pulse~~ Rate	60	-0.017	0.899
Atrial Tachy arrhythmias	60	0.035	0.793
Ventricular Tachy arrhythmias	60	0.202	0.122
Brady arrhythmias or Heart block	60	0.380	0.003*
Arrhythmias (Brady & Tachy)	60	0.473	0.001*
Development of Cardiogenic Shock	60	0.368	0.004*
Admission RBS	60	0.328	0.010*
CK MB	60	0.083	0.528
Anterior Wall Involvement	60	0.206	0.114
Anterolateral Wall Involvement	60	-0.134	0.307
Inferior Wall Involvement	60	0.000	1.000
Septal Involvement	60	-0.096	0.468
LV Ejection Fraction	60	-0.328	0.010*
Killip's Heart Failure Class	60	0.349	0.006*
HbA1c	60	0.114	0.386

This table shows; Groups 1-4, Personal History of HTN, Brady arrhythmias or Heart block, Arrhythmias, Cardiogenic Shock, Admission Random Blood Sugar, and Killip's Heart Failure Class have statistically significant positive correlation with death. Systolic BP, Diastolic BP and LV Ejection Fraction have statistically significant negative correlation with death.

8~~7~~. Independent Predictors of 30-Day Mortality (Logistic Regression)~~Logistic Regression~~:

Variable	B	Wald	df	p	Exp (B)	95.0% CI for Exp (B)	
						Lower	Upper
Hypertension	-1.707	3.948	1	0.047	0.181	0.034	0.977
Arrhythmia	-2.257	5.394	1	0.020	0.105	0.016	0.703
Cardiogenic Shock	-2.585	3.702	1	0.054	0.075	0.005	1.049
Killip's Class		5.167	2	0.075			
Killip's Class 1	18.630	000	1	1.000	1E+ 008	0.000	
Killip's Class 2	21.046	000	1	1.000	1E+ 009	0.000	

Overall percentage of the model is 86.7%

This above table shows, out of 10 variables which have statistically significant correlation with death as a outcome, only four variables; Personal History of HTN, Arrhythmia, Cardiogenic Shock and Killip's Class are the best predictors of death and overall this model has 86.7% predictability.

SUMMARY OF RESULTS

Table 9.

Variable	Group 1 (N=16) <120 mg%	Group 2 (N=12) 120-140 mg%	Group 3 (N=14) 140 -167 mg%	Group 4 (N=18) >167 mg%	F/ χ^2	P
Admission RBS						
Age	50.75	56.17	53.43	61.00	1.845	0.150
Age >60Yrs	5	4	4	13	8.80	0.032*
Sex- Male Female	13 3	8 4	12 2	12 6	2.302	0.512
HTN	3	6	2	9	7.567	0.056
Smoking	9	2	10	7	8.816	0.032*
Alcohol	5	2	4	2	2.617	0.454
BP Systolic	126.87	123.33	120.86	93.67	2.911	0.042*
BP Diastolic	82.25	73.33	74.00	60.78	1.464	0.234
Heart~~Pulse~~ Rate	88.75	82.67	89.00	79.17	0.652	0.585
Admission RBS	105.13	125.25	149.57	229.39	41.983	0.001*
HbA1c	5.70	5.58	5.58	5.82	0.330	0.804
Killip class Deterioration By ≥ 2 classes in the hospital stay	0	0	1	8	17.859	0.001*
Arrhythmias	2	5	10	12	13.853	0.003*
LV EF (%)	50.78	46.67	42.86	41.28	6.903	0.001*
Development of cardiogenic Shock	0	1	0	6	12.291	0.006*
30 day-mortality	1	2	3	10	11.902	0.008*

Formatted: Font: 12 pt, Not Bold
Formatted: Justified
Formatted: Font: Times New Roman, 12 pt, Not Bold
Formatted: Font: Times New Roman, Not Bold
Formatted: Font: Times New Roman
Formatted: Font: Times New Roman
Formatted: Font: Times New Roman

DISCUSSION

It is well known that hyperglycemia may occur in some people suffering from severe, stressful diseases or when exposed to other stress situations, although they have not been diagnosed as diabetics before. This was noticed in some individuals who had experienced acute myocardial infarction. In the present study we evaluated the impact of admission blood glucose on 30 day-mortality in non diabetic patients presenting with acute myocardial infarction.

In our study we included 60 cases of acute myocardial infarction, who presented within 48 hours of onset of symptoms with no known history of diabetes mellitus and were admitted in KLE's Dr Prabhakar Kore Hospital & MRC Belgaum during 2007-08. The patients were interviewed at admission for history, and physical examination findings were noted. At admission patient's blood glucose values, ECG, cardiac enzymes, HbA1C were done. The echocardiography was done for every patient. The patients were followed during the hospital stay and in-hospital complications were noted. Patient's were then followed up to 30 days. Death was the end point of the study. Admission RBS values, in hospital complications and 30 day-mortality data were analyzed.

Of the 60 patients that were studied all had ST elevation acute myocardial infarction. The 60 patients were divided into group I- IV based on admission RBS. There were 16 patients in group I (admission RBS < 120mg%), 12patients in group II (admission RBS 120- 140mg%), 14 patients in group III (admission RBS 140- 167mg%), and 18 patients in group IV (admission RBS > 167mg%).

The mean age of the patients in years was 50.75 (Group I), 56.17 (group II), 53.43 (Group III) and 61 (Group IV) respectively. There is no statistically significant difference in age distribution between the groups (P= 0.150). However, the number of patient's above 60 years was greatest in group IV. This was statistically significant (P= 0.032). This shows that as age advances, there is higher admission glycemic status, which is in accordance with the known fact that there is impaired glucose tolerance with advancing age. This finding is similar to previous studies.[4,82]

There were a total of 45 males and 15 females in our study. The number of males and females between the groups were comparable (P= 0.512). But in a previous study by Kadri et al[82] women had higher admission RBS compared to males of similar age.

In our study 20 patients had hypertension and were on treatment, 28 patients gave history of smoking, 13 patients consumed alcohol. There was no difference in the prevalence of hypertension and alcohol consumption between the groups. However there is a statistically significant difference (P= 0.032) in number of smokers across the groups, but there is no linear correlation of number of smokers to the admission RBS groups. So it is unlikely to be a confounding risk factor for death among the groups.

Mean systolic BP at admission was 93.67 mm Hg in group IV as compared to 126.87 mm Hg in group I, 123.33mm Hg in group II and 120.86 mm

Hg in group III. There was a statistically significant (P= 0.042) drop in the mean systolic BP as we move from Group I to Group IV. Probable explanation for this is that more patients in the higher admission blood glucose groups had a lower LV ejection fraction and poorer LV function. There occurred no statistically significant difference in the mean diastolic BP and heart rate at admission across the groups. Previous studies [82,83] have reported similar results with respect to mean systolic BP, but their observation was that a higher heart rate was associated with higher admission RBS values (probably due to raised sympathetic tone).

In our study the mean HbA1c was 5.70 in group I, 5.58 in group II, 5.58 in group III and 5.82 in group IV. As we move from group I to IV there is linear rise in the mean HbA1c values which suggest that there is some degree of preexisting impaired glucose tolerance in patients with higher admission RBS values. However there was no statistical significant difference (P= 0.802) in the HbA1c levels across the groups, which implies a similar glycemic status in all the study subjects prior to acute myocardial infarction (AMI). And all our study subjects had HbA1c within normal range and were comparable. Thus glucose values at admission were purely the result of acute stress. CK MB levels across the groups were not comparable, as estimation of enzymes was done at varying time interval, from the onset of symptoms. Troponin I was not compared as it was not estimated in few patients. Earlier studies[83,84] have an observation of higher level of enzymes correlated with higher admission RBS values.

In our study when territory of infract was analyzed with respect to admission RBS values, there was no correlation. There occurred similar location and number of infarcts in all the groups. Similar results were found in studies by Stranders et al[4] and Suleiman et al.[83] Kadri et al[82] in his study, found a statistically significant association between higher admission RBS values with anterior wall AMI. The probable mechanism involved is that there is higher sympathetic tone with anterior wall AMI with consequent rise in catecholamine and hyperglycemia.

At admission, 30 patient's were in Killip class I, 29 patient's in Killip Class II and only one patient in Killip class IV with no patient's having Killip class III. We observed that patient's in group III and group IV had higher admission Killip class, which was statistically significant (P= 0.018 for number of patents with Killip class I at admission between the groups and similarly for Killip class II is P= 0.016). Another observation was Killip class deterioration by ≥ 2 classes during the hospital stay occurred more commonly in group III and IV. Killip class was high in subjects with higher admission RBS values. When we statistically analyzed the number of subjects with Killip class deterioration by ≥ 2 classes during the hospital stay, among the groups, there is significant difference (P= 0.001). Similar result was reported by Kadri et al.[82]

In-hospital complications were more common in patients with raised admission glycemia, and the increase in complication rates was linear in the 3 upper groups of subjects. In addition, among the group without cardiogenic shock on admission, more patients with raised glycemia subsequently developed

cardiogenic shock. Mean LVEF in group IV was 41.28% as compared to 50.78%, 46.67%, 42.86% in group I, II, III respectively. This difference in the mean LVEF measured during the hospital stay across the groups is statistically significant (P= 0.001). There was lower LVEF in patient's with higher admission glycemia, which is in accordance with previous studies by Kadri et al[82] and Marfell et al.[33] There was higher risk of development of cardiogenic shock in subjects with high admission RBS. This observation is statistically significant (P= 0.006). This finding matches those of available studies[4,82]

There was no correlation between any specific type of arrhythmia (brady or tachy) and admission glycemic values. However higher admission RBS values were found to have higher incidence of arrhythmias (brady and tachy). This observation is statistically significant (P= 0.003). Kadri et al[82] reported higher incidence of atrial and ventricular fibrillations in subjects having higher admission RBS.

30-day mortality in our study was 6.25% in patients with group I, compared with 16.67% in patients in the group II, 21.43% in group III and 55.56% in group IV. This difference in the incidence of 30 day-mortality which linearly increases as admission RBS rises, is statistically significant (P= 0.008). Similar findings were reported by Kadri et al.[82]

In our study, when we carried out Pearson's correlation on death as out come with different variables, the results revealed (Table-7); Groups 1-4, known history of hypertension, brady arrhythmias or heart block, arrhythmias (brady and

tachy), cardiogenic shock, admission random blood sugar, and Killip's Class had statistically significant positive correlation with death. Systolic BP, Diastolic BP and Ejection Fraction had statistically significant negative correlation with death.

When the above significant positive and negative correlates were analyzed with logistic regression to see the independent predictors of 30-day mortality, results showed (Table - 8) that only four variables viz, known history of hypertension, cardiogenic shock, Arrhythmia (brady and tachy) and Killip's Class are the independent predictors of death, and overall this model has 86.7% predictability.

Finally the raised admission RBS is an important correlate of 30 day-mortality in our study. However we observed that it is not an independent predictor of death in our study. These results are in accordance with Foo et al[85] who studied a cohort of 2127 patients presenting with acute coronary syndromes. They observed that admission glycemia was related to in hospital mortality by univariate analysis. Its prognostic significance disappeared when left ventricular failure was included in the statistical models of their study. However Kadri et al[82] reported admission glycemia as an independent and powerful predictor of in hospital and late mortality in the presence or absence of left ventricular failure. Probable explanation as to why higher admission glycemia was not an independent predictor of mortality, though it was a positive correlate of death in our study is, smaller sample size (N=60). Also admission RBS values did not uniformly increase as we move from group I to IV. Infact, in group IV (RBS

>167 mg%), with 18 subjects, 10 subjects who expired had a lower admission RBS value as compared to those who survived in that group.

Several hypotheses (which are not mutually exclusive) have been put forward to explain the relation between stress hyperglycemia and poor outcome. Stress hyperglycemia may be a marker of extensive myocardial damage, reflecting a surge of stress hormones such as catecholamines and cortisol that produce or augment an insulin-resistant state.[15,23] Relative insulin deficiency and excess catecholamines reduce glucose uptake by the ischemic myocardium and promote lipolysis and increased circulating free fatty acids. The latter inhibit glucose oxidation (the "glucose–fatty acid cycle") and are toxic to ischemic myocardium, resulting in increased membrane damage, arrhythmias, and reduced contractility.[86,87,88,89] Alternatively, elevated blood glucose levels per se adversely affect outcome through the cumulative effects of several mechanisms, including induction of endothelial dysfunction,[28] oxidative stress,[7,8] hypercoagulability, and impaired fibrinolysis.[9] Lastly, admission hyperglycemia may not be only the cause of more severe myocardial damage, but also its consequence. Large infarcts are more likely to cause catecholamine release, which affect fatty acid and glucose homeostasis. In a study by Oswald et al[15] concentrations of cortisol, epinephrine and norepinephrine were the main determinants of plasma glucose concentration measured in non diabetic patients with acute myocardial infarction.

CONCLUSIONS

The conclusions arrived at from our study are, that higher admission RBS was seen in older subjects with AMI, with no difference in males and females of similar age. Subjects with higher admission RBS were found to have lower systolic blood pressure, lower LVEF, and more risk of development of cardiogenic shock. Arrhythmias occurred more commonly in subjects with high admission RBS, and also, these subjects had higher admission Killip class with risk of deterioration of Killip class by ≥2 classes during the hospital stay. There was a positive linear correlation between admission RBS and 30-day mortality.

SUMMARY

In the present study we evaluated the impact of admission glycemia on 30 day-mortality in non diabetic patient's admitted for myocardial infarction. The study was conducted on 60 cases of AMI admitted at KLE's Dr Prabhakar Kore Hospital & MRC, Belgaum during the year 2007-08. The cases were divided into group I to IV based on admission RBS. There were 16 patients in group I (admission RBS < 120mg%), 12 patients in group II (admission RBS 120- 140mg%), 14 patients in group III (admission RBS 140- 167mg%), and 18 patients in group IV (admission RBS > 167mg%). All cases were subjected to investigations, and in-hospital complications were noted. They were all followed up for 30 days.

The results are as follows:

1. Age and sex were comparable between the groups.
2. The admission RBS was higher in older subjects, more so in the subjects aged ≥ 60 years.
3. Subjects with history of smoking and alcohol consumption were not uniformly distributed between the groups.
4. The subjects with higher admission RBS were found to have lower systolic BP at the time of admission.
5. High admission RBS subjects had lower LVEF.
6. The subjects with high admission RBS were also found to have higher admission Killip class and increased incidence of subsequent deterioration of Killip class by ≥2 classes during the hospital stay.

7. In hospital complications were more common in subjects with high admission RBS. Development of cardiogenic shock and incidence of arrhythmias had a linear correlation with rise in admission RBS values.
8. In our study admission RBS, known history of hypertension, arrhythmias, development of cardiogenic shock during the hospital stay and Killip class at admission were positive correlates of 30 days mortality.
9. In this study systolic BP, diastolic BP and LVEF were negative correlates of 30 day-mortality.
10. In this study, personal history of hypertension, arrhythmia, cardiogenic shock and Killip's class were independent predictors of 30 day-mortality.
11. In our study there was a significant positive linear correlation between admission RBS and 30-day mortality.

BIBLIOGRAPHY

1. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 2000; 355: 773–778.
2. Norhammar A, Tenerz A, Nilsson G, Hamsten A, Efendíc S, Rydén L, et al. Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study. Lancet 2002; 359: 2140–2144.
3. Wahab NN, Cowden EA, Pearce NJ, Gardner MJ, Merry H, Cox JL. ICONS Investigators. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002; 40: 1748–1754.
4. Stranders I, Diamant M, van Gelder RE, Spruijt HJ, Twisk JW, Heine RJ, et al. Admission blood glucose level as risk indicator of death after myocardial infarction in patients with and without diabetes mellitus. Arch Intern Med 2004; 164: 982–988.
5. Wong VW, Ross DL, Park K, Boyages SC, Cheung NW. Hyperglycemia: still an important predictor of adverse outcomes following AMI in the reperfusion era. Diabetes Res Clin Pract 2004; 4: 85–91.
6. Hadjadj S, Coisne D, Mauco G, Ragot S, Duengler F, Sosner P, et al. Prognostic value of admission plasma glucose and HbA1c in acute myocardial infarction. Diabet Med 2004; 1: 05–310.

7. Zeller M, Cottin Y, Brindisi MC, Dentan G, Laurent Y, Janin-Manificat L, et al. Impaired glucose and cardiogenic shock in patients with acute myocardial infarction. Eur Heart J 2004; 355: 308-12.
8. Antman EM, Selwyn AP, Braunwald E, Loscalzo J. Ischemic Heart Disease. In Harrison's Principles of Internal Medicine. Editors: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J. 17th edition. Mc Graw Hill. Vol 2. 1514-27.
9. Bernard C. Lecons sur le diabete at la glycogenase animale. Paris: Bailliere; 1877.
10. Alajbegovic S, Metelko Z, Alajbegovic A, Suljic E, Resic H. Hyperglycemia and Acute Myocardial Infarction in a Nondiabetic Population. Diabetalogia Croatica 2003; 32: 169-74.
11. Perner A, Nielsen SE, Rask-Madsen J. High glucose impairs superoxide production from isolated blood neutrophils. Intensive Care Med 2003; 29:642-645.
12. Marfella R, Nappo F, De Angelis L, Siniscalchi M, Rossi F, Giugliano D. The effect of acute hyperglycemia on QTc duration in healthy men. Diabetologia 2000; 43: 1332-1333.
13. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab 2002; 87:978–982.
14. Karlsberg RP, Cryer PE, Roberts R. Serial plasma catecholamine response early in the course of clinical acute myocardial infarction: relation to infarct extent and mortality. Am Heart J 1981; 102: 24-9.

15. Oswald GA, Smith CC, Betteridge DJ, Yudkin JS. Determinants and importance of stress hyperglycemia in non diabetic patients with myocardial infarction. BMJ 1986; 293: 917-22.
16. Gokhroo R, Mittal SR. Electrocardiographic correlates of hyperglycemia in acute myocardial infarction. Int J Cardiol 1989; 22: 267–269.
17. D'Amico M, Marfella R, Nappo F, Di Filippo C, De Angelis L, Berrino L, et al. High glucose induces ventricular instability and increases vasomotor tone in rats. Diabetologia 2001; 44: 464–470.
18. Ishihara M, Inoue I, Kawagoe T, Shimatani Y, Kurisu S, Nishioka K, et al. Impact of acute hyperglycemia on left ventricular function after reperfusion therapy in patients with a first anterior wall acute myocardial infarction. Am Heart J 2003; 46: 674–678.
19. Iwakura K, Ito H, Ikushima M, Kawano S, Okamura A, Asano K, et al. Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. J Am Coll Cardiol 2003; 41: 1–7.
20. Kersten JR, Schmeling TJ, Orth KG, Pagel PS, Warltier DC. Acute hyperglycemia abolishes ischemic preconditioning in vivo. Am J Physiol 1998; 275: H721–H725.
21. Poulsen SH, Jensen SE, Tei C, Seward JB, Egstrup K. Value of the Doppler index of myocardial performance in the early phase of acute myocardial infarction. J Am Soc Echocardiogr 2000; 13: 723–730.
22. Chandler AB, Chapman I, Erhardt LR, Roberts WC, Schwartz CJ, Sinapius D, et al. Coronary thrombosis in myocardial infarction. Report of

a workshop on the role of coronary thrombosis in the pathogenesis of acute myocardial infarction. Am J Cardiol 1974; 34: 823–833.

23. Oswald GA, Smith CC, Delamothe AP, Betteridge DJ, Yudkin JS. Raised concentrations of glucose and adrenaline and increased in vivo platelet activation after myocardial infarction. Br Heart J 1988; 59: 663–671.
24. Ceriello A. Coagulation activation in diabetes mellitus: the role of hyperglycaemia and therapeutic prospects. Diabetologia 1993; 36: 1119–1125.
25. Jones RL, Peterson CM. Reduced fibrinogen survival in diabetes mellitus a reversible phenomenon. J Clin Invest 1979; 63: 485–493.
26. Ceriello A, Giugliano D, Quatraro A, Dello Russo P, Marchi E, Torella R. Hyperglycemia may determine fibrinopeptide A plasma level increase in humans. Metabolism 1989; 38: 1162–1163.
27. Ceriello A, Giacomello R, Stel G, Motz E, Taboga C, Tonutti L, et al. Hyperglycemia-induced thrombin formation in diabetes. The possible role of the oxidative stress. Diabetes 1995; 44: 924–928.
28. Ceriello A, Giugliano D, Quatraro A, Dello Russo P, Torella R. Blood glucose may condition factor VII levels in diabetic and normal subjects. Diabetologia 1988; 31: 889–891.
29. Sakamoto T, Ogawa H, Kawano H, Hirai N, Miyamoto S, Takazoe K, et al. Rapid change of platelet aggregability in acute hyperglycemia. Detection by a novel laserlight scattering method. Thromb Haemost 2000; 83: 475–479.
30. Mulvihill NT, Foley JB. Inflammation in acute coronary syndromes. Heart 2002; 87: 201–204.

31. Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med 1999; 340: 115–126.
32. Neri Serneri GG, Prisco D, Martini F, Gori AM, Brunelli T, Poggesi L, et al. Acute T-cell activation is detectable in unstable angina. Circulation 1997; 95: 1806–1812.
33. Marfella R, Siniscalchi M, Esposito K, Sellitto A, De Fanis U, Romano C, et al. Effects of stress hyperglycemia on acute myocardial infarction: role of inflammatory immune process in functional cardiac outcome. Diabetes Care 2003; 26: 3129–3135.
34. Marfella R, Esposito K, Giunta R, Coppola G, De Angelis L, Farzati B, et al. Circulating adhesion molecules in humans: role of hyperglycemia and hyperinsulinemia. Circulation 2000; 101: 2247–2251.
35. Esposito K, Nappo F, Marfella R, Giugliano G, Giugliano F, Ciotola M, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. Circulation 2002; 106: 2067–2072.
36. Ceriello A, Quagliaro L, Piconi L, Assaloni R, Da Ros R, Maier A, et al. Effect of postprandial hypertriglyceridemia and hyperglycemia on circulating adhesion molecules and oxidative stress generation and the possible role of simvastatin treatment. Diabetes 2004; 53: 701–710.
37. De Caterina R. Endothelial dysfunctions: common denominators in vascular disease. Curr Opin Lipidol 2000; 11: 9–23.
38. Valgimigli M, Merli E, Malagutti P, Soukhomovskaia O, Cicchitelli G, Macrì G, et al. Endothelial dysfunction in acute and chronic coronary

syndromes: evidence for a pathogenetic role of oxidative stress. Arch Biochem Biophys 2003; 420: 255–261.

39. Iraculis E, Cequier A, Gomez-Hospital JA, Sabaté M, Mauri J, Fernández-Nofrerias E, et al. Early dysfunction and long-term improvement in endothelium-dependent vasodilation in the infarct-related artery after thrombolysis. J Am Coll Cardiol 2002; 4: 257–265.
40. Giugliano D, Marfella R, Coppola L, Verrazzo G, Acampora R, Giunta R, et al. Vascular effects of acute hyperglycemia in humans are reversed by L-arginine. Evidence for reduced availability of nitric oxide during hyperglycemia. Circulation 1997; 95: 1783–1790.
41. Williams SB, Goldfine AB, Timimi FK, Ting HH, Roddy MA, Simonson DC, et al. Acute hyperglycemia attenuates endothelium-dependent vasodilation in humans in vivo. Circulation 1998; 97: 1695–1701.
42. Heinecke JW. Oxidative stress: new approaches to diagnosis and prognosis in atherosclerosis. Am J Cardiol 2003; 91(Suppl.):12A–16A.
43. Ceriello A. Acute hyperglycaemia and oxidative stress generation. Diabet Med 1997; 14: S45–S49.
44. Marfella R, Verrazzo G, Acampora R, La Marca C, Giunta R, Lucarelli C, et al. Glutathione reverses systemic hemodynamic changes by acute hyperglycemia in healthy subjects. Am J Physiol 1995; 268: E1167–E1173.
45. Beckman JA, Goldfine AB, Gordon MB, Creager MA. Ascorbate restores endothelium-dependent vasodilation impaired by acute hyperglycemia in humans. Circulation 2001; 103: 1618–1623.

46. Ceriello A, Motz E, Giugliano D. Hypertension and ascorbic acid. Lancet 2000; 355: 1272–1273.
47. Ceriello A, Bortolotti N, Crescentini A, Motz E, Lizzio S, Russo A, et al. Antioxidant defenses are reduced during oral glucose tolerance test in normal and non-insulin dependent diabetic subjects. Eur J Clin Invest 1998; 28: 329–333.
48. Beckman JS, Koppenol WH. Nitric oxide, superoxide, and peroxynitrite: the good, the bad, and ugly. Am J Physiol 1996; 271: C1424–C1437.
49. Shishehbor MH, Aviles RJ, Brennan ML, Fu X, Goormastic M, Pearce GL, et al. Association of nitrotyrosine levels with cardiovascular disease and modulation by statin therapy. JAMA 2003; 289: 1675–1680.
50. Pennathur S, Wagner JD, Leeuwenburgh C, Litwak KN, Heinecke JW. A hydroxyl radical-like species oxidizes cynomolgus monkey artery wall proteins in early diabetic vascular disease. J Clin Invest 2001; 107: 853–860.
51. Ceriello A, Quagliaro L, D'Amico M, Di Filippo C, Marfella R, Nappo F, et al. Acute hyperglycemia induces nitrotyrosine formation and apoptosis in perfused heart from rat. Diabetes 2002; 51: 1076–1082.
52. Marfella R, Quagliaro L, Nappo F, Ceriello A, Giugliano D. Acute hyperglycemia induces an oxidative stress in healthy subjects. J Clin Invest 2001; 108: 635–636.
53. Ceriello A, Taboga C, Tonutti L, Quagliaro L, Piconi L, Bais B, et al. Evidence for an independent and cumulative effect of postprandial hypertriglyceridemia and hyperglycemia on endothelial dysfunction and

oxidative stress generation. Effects of short- and long-term simvastatin treatment. Circulation 2002; 106: 1211–1218.

54. Malmberg K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenström A, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. J Am Coll Cardiol 1995; 26: 57–65.
55. Malmberg K, Ryden L, Hamsten A, Herlitz J, Waldenström A, Wedel H. Effects of insulin treatment on cause-specific one-year mortality and morbidity in diabetic patients with acute myocardial infarction. DIGAMI Study Group. Diabetes Insulin-Glucose in Acute Myocardial Infarction. Eur Heart J 1996; 17: 1337–1344.
56. Malmberg K, Norhammar A, Wedel H, Rydén L. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. Circulation 1999; 99: 2626–2632.
57. Frier BM. Diabetes and myocardial infarction. Diabetes Rev Int 1998;7:1–2.
58. Fisher BM. Diabetes mellitus and myocardial infarction: a time to act or a time to wait? Diabet Med 1998; 15: 275.
59. Van der Horst IC, Zijlstra F, van't Hof AW, Doggen CJ, de Boer MJ, Suryapranata H, et al. Zwolle Infarct Study Group. Glucose-insulin-potassium infusion in patients treated with primary angioplasty for acute

myocardial infarction: the glucose-insulin-potassium study: a randomized trial. J Am Coll Cardiol 2003; 42: 784–791.

60. Oliver MF, Yates PA. Induction of ventricular arrhythmias by elevation of arterial free fatty acids in experimental myocardial infarction. Cardiology 1971; 56: 359–364.
61. Kurien VA, Yates PA, Oliver MF. The role of free fatty acids in the production of ventricular arrhythmias after acute coronary artery occlusion. Eur J Clin Invest 1971; 1: 225–241.
62. Ceriello A, Motz E. Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes, and cardiovascular disease? The common soil hypothesis revisited. Arterioscler Thromb Vasc Biol 2004; 24: 816–823.
63. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in the critically ill patients. N Engl J Med 2001; 345: 1359–1367.
64. Van den Berghe G, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Schetz M, et al. Outcome benefit of intensive insulin therapy in the critically ill: Insulin dose versus glycemic control. Crit Care Med 2003; 31: 359–366.
65. James SK, Armstrong P, Barnathan E, Califf R, Lindahl B, Siegbahn A, et al. Troponin and C-reactive protein have different relations to subsequent mortality and myocardial infarction after acute coronary syndrome: A GUSTO-IV substudy. J Am Coll Cardiol 2003; 41:916-924.
66. Sabatine MS, Morrow DA, Cannon CP, Murphy SA, Demopoulos LA, DiBattiste PM, et al. Relationship between baseline white blood cell count

and degree of coronary artery disease and mortality in patients with acute coronary syndromes: A TACTICS-TIMI 18 (Treat Angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy—Thrombolysis in Myocardial Infarction 18 Trial)substudy. J Am Coll Cardiol 2002; 40:1761-1768.

67. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, et al. C-reactive protein is a potent predictor of mortality independently and in combination with troponin T in acute coronary syndromes: A TIMI 11A substudy. J Am Coll Cardiol 1998; 31:1460-1465.
68. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, et al. Serum amyloid A predicts early mortality in acute coronary syndromes: A TIMI 11A study. J Am Coll Cardiol 2000; 35:358-362.
69. Heeschen C, Hamm CW, Bruemmer J, Simoons ML. Predictive value of C-reactive protein and troponin T in patients with unstable angina: a comparative analysis. CAPTURE Investigators. Chimeric c7E3 AntiPlatelet Therapy in Unstable angina REfractory to standard treatment trial. J Am Coll Cardiol 2000; 35:1535-1542.
70. Lindmark E, Diderholm E, Wallentin L, Siegbahn A. Relationship between interleukin 6 and mortality in patients with unstable coronary artery disease: Effects of an early invasive or noninvasive strategy. JAMA 2001; 286:2107-2113.
71. de Lemos JA, Morrow DA, Sabatine MS, Murphy SA, Gibson CM, Antman EM, et al. Association between plasma levels of monocyte

chemoattractant protein-1 and long-term clinical outcomes in patients with acute coronary syndromes. Circulation 2003; 107:690-695.

72. Mueller C, Neumann FJ, Roskamm H, Buser P, Hodgson JM, Perruchoud AP, et al. Women do have an improved long-term outcome after non-ST-elevation acute coronary syndromes treated very early and predominantly with percutaneous coronary intervention: A prospective study in 1450 consecutive patients. J Am Coll Cardiol 2002; 40:245-250.
73. Zhang R, Brennan ML, Fu X, Aviles RJ, Pearce GL, Penn MS, et al. Association between myeloperoxidase levels and risk of coronary artery disease. JAMA 2001; 286:2136-2142.
74. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, et al. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med 1996; 335:1342-1349.
75. Brennan ML, Penn MS, Van Lente F, Nambi V, Shishehbor MH, Aviles RJ, et al. Prognostic value of myeloperoxidase in patients with chest pain. N Engl J Med 2003; 349:1595-1604.
76. Richards AM, Nicholls MG, Yandle TG, Frampton C, Espiner EA, Turner JG, et al. Plasma N-terminal pro-brain natriuretic peptide and adrenomedullin: New neurohormonal predictors of left ventricular function and prognosis after myocardial infarction. Circulation 1998; 97:1921-1929.
77. de Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatine MS, McCabe CH, et al. The prognostic value of B-type natriuretic peptide in

patients with acute coronary syndromes. N Engl J Med 2001; 345:1014-1021.

78. Malmberg K, Norhammar A, Wedel H, Ryden L. Glycometabolic state at admission: Important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: Long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. Circulation 1999; 99:2626-2632.
79. Pinto DS, Skolnick A, Kirtane AJ, Murphy SA, Barron HV, Giugliano RP, et al. U-shaped relationship of blood glucose with adverse outcomes among patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol 2005; 46:178-180.
80. Becker RC, Spencer FA, Gibson M, Rush JE, Sanderink G, Murphy SA, et al. Influence of patient characteristics and renal function on factor Xa inhibition pharmacokinetics and pharmacodynamics after enoxaparin administration in non-ST-segment elevation acute coronary syndromes. Am Heart J 2002; 143:753-759.
81. Killip T 3rd, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two-year experience with 250 patients. Am J Cardiol 1967; 20: 457–464.
82. Kadri Z, Danchin N, Vaur L, Cottin Y, Gueret P, Lablanche JM, et al. Major impact of admission glycemia on 30 day and one year mortality in non diabetic patients admitted for myocardial infarction: results from the nationwide French USIC 2000 study. Heart 2006; 92: 910-915.
83. Suleiman M, Hammerman H, Boulos M, Kapeliovich MR, Suleiman A, Agmon Y, et al. Fasting Glucose Is an Important Independent Risk Factor

for 30-Day Mortality in Patients With Acute Myocardial Infarction A Prospective Study. Circulation 2005; 111: 754-760.

84. Goyal A, Mahaffey KW, Garg J, Nicolau JC, Hochman JS, Weaver WD, et al. Prognostic significance of the change in glucose level in the first 24 h after acute myocardial infarction: results from the CARDINAL study. European Heart Journal 2006; 27:1289-1297.
85. Foo K, Cooper J, Deaner A, Knight C, Suliman A, Ranjadayalan K, et al. A single serum glucose measurement predicts adverse outcome across the whole range of acute coronary syndromes. Heart 2003; 89: 512-6.
86. Oliver MF, Kurien VA. Serum-free-fatty-acids and arrhythmias after acute myocardial infarction. Lancet 1969; 2: 1077–1078.
87. Lopaschuk GD, Stanley WC. Glucose metabolism in the ischemic heart. Circulation 1997; 95: 313–315.
88. Taegtmeyer H, McNulty P, Young ME. Adaptation and maladaptation of the heart in diabetes, part I: general concepts. Circulation 2002; 105: 1727–1733.
89. Depre C, Vanoverschelde JL, Taegtmeyer H. Glucose for the heart. Circulation 1999; 99: 578 –588.

INFORMED CONSENT

Title of the Study: "Impact of Admission Glycemia on 30 Day-Mortality in Non Diabetic Patient's Admitted for Myocardial Infarction - A One Year Cross Sectional Study"

Objectives and Purpose of the Study: This is a study to analyze impact of admission glycemia on 30 days mortality in non diabetic patients admitted for myocardial infarction. The principal investigator of the study is Dr. Dhereppa G. Chougala and guided by Dr. S. H. Asundi, Associate Professor of Medicine, J. N. Medical College Belgaum.

Procedure: If i agree to be part of the study, I will be asked the relevant history and will be subjected to relevant clinical examination. I will also undergo investigations like: Random blood sugar by glucometer, ECG, Echocardiography, cardiac enzymes and Glycosylated haemoglobin.

Risk and benefits: I have been explained by investigators, that there are no potential risks involved in this study and no benefits.

Alternatives: Taking part in this study is voluntary, I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or sponsor may stop my participation in this study anytime. If I choose not to take part in this study I will receive standard treatment for patients with my condition.

Privacy and confidentiality: All information collected about me during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify me in this research record.

Institutional / sponsor policy: Does not apply to this research.

Financial incentives for participants: I will not be charged any amount for investigations subjected to me. I will not receive compensation or reimbursement for taking part in this study.

Authorization to publish results: Information from this study may be published but my identity will be confidential in any publication.

Consent statement: I voluntarily agree to take part in this study by signing below. I may withdraw at anytime. I am not giving up any legal rights by signing this form. My signature below indicated that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of the participant or legally authorized representative:

Signature / Thumb print:

In case of the quires during study or in future you may contact following person:

Principal Investigator: Dr. Dhareppa G. Chougala Phone: 9845003369

Guide : Dr. S. H. Asundi Phone: 9448467727

Name of the witness: Signature:

Investigator name: Signature:

Date: Place:

PROFORMA

"Impact of Admission Glycemia on 30 Day-Mortality in Non Diabetic Patient's Admitted for Myocardial Infarction - A One Year Cross Sectional Study"

Name: **I. P. No.:**

Age: **Occupation:**

Address: **Marital Status:**

Date of Admission: **Date of Discharge:**

Chief Complaints:

1. Chest pain.

Onset

Duration

Referred to

Associated with

Relived by

Drug Intake:

Past History:

Hypertension

Diabetes

Angina

Myocardial Infarction

Congestive Cardiac Failure

PCI

Surgery- CABG

Any other

Trauma

Personal History:

Diet: Bowel:

Habits- Smoking/ alcohol/ Drug abuse Bladder:

Family History:

Myocardial Infarction

Stroke

Hypertension

Diabetes

Any other

General Physical Examination:

B.P: Heart Rate: Temperature: R.R:

Peripheral Pulses:

Pallor □ Cyanosis □ Edema □ Lymphadenopathy □ Clubbing □

Cardiovascular System:

Respiratory System:

Per abdomen:

Central Nervous System:

Complications: In-Hospital Course

Tachyarrhythmias: Atrial Tachyarrhythmias

Ventricular Tachyarrhythmias

Bradyarrhythmias/ Heart Block

Cardiogenic shock

Killip Class Deterioration by ≥2 Classes during hospital stay

Death

Investigations:

1. Random blood sugar at admission by glucometer
2. Cardiac enzymes
    - CK-MB
    - Troponin-I
3. ECG:
    - Territory of infarct:

      Anterior □ Anterolateral □ Inferior □ Septal □
    - ST EMI □ NST EMI □
    - RhythmDisturbances:

      Tachyarrhythmias □

      Bradyarrhythmias □
4. Echocardiography
    - Ejection Fraction
    - Regional wall:

      Motion abnormality
5. Heart failure class (Killip's class on admission)

   Class I □ Class II □

   Class III □ Class IV □
6. Glycosylated haemoglobin:

Mode of Treatment:

KEY TO MASTER CHART

ASMI	Antero septal Myocardial Infarction
AWMI	Anterior wall Myocardial Infarction
Car shock	Cardiogenic shock
CK-MB	MB Isoenzyme of Creatine Phosphokinase
D- BP	Diastolic Blood Pressure
F	Female
HbA1c	Glycosylated Hemoglobin
h/o	History of
HR	Heart Rate
HTN	Hypertension
IP No	Inpatient number
IWMI	Inferior wall Myocardial Infarction
KA	Killip class at admission
KD	Killip class deterioration by ≥ 2 classes
LVEF	Left Ventricular Ejection Fraction
M	Male
RBS @ adm	Random Blood Sugar at admission
S – BP	Systolic Blood Pressure
TOI	Territory of Infarct

12-Master Chart_560F800

Sl. No.	Group	Name	I. P. NO.	Age (years)	Sex	RBS @ Adm (mg%)	h/o Smoking	h/o Alcohol
31	3	Ramesh	256837	42	M	143	Yes	No
32	3	Mohammed	227658	47	M	144	Yes	No
33	3	Malasiddayya	239972	65	M	145	Yes	No
34	3	Mallappa	239833	57	M	145	Yes	No
35	3	Mahantesh	251252	50	M	145	Yes	No
36	3	Govind	260002	68	M	148	Yes	No
37	3	Bajirao	251893	42	M	154	Yes	Yes
38	3	Ravi	251257	42	M	154	Yes	Yes
39	3	Fathima	217256	48	F	155	No	No
40	3	Gangawwa	226063	72	F	157	No	No
41	3	Balachandra	216980	52	M	160	Yes	No
42	3	Shakeel	223735	48	M	162	Yes	Yes
43	4	Gudleppa	216438	85	M	168	No	No
44	4	Sangappa	219284	65	M	175	Yes	Yes
45	4	Kashappa	226899	70	M	178	Yes	No
46	4	Mallawwa	253517	65	F	178	No	No
47	4	Gangawwa	231377	60	F	186	No	No
48	4	Sanjay	241189	40	M	188	No	No
49	4	Rukmawwa	243302	75	F	189	No	No
50	4	Gururaj	240687	67	M	190	No	No
51	4	Gangawwa	221189	65	F	201	No	No
52	4	Mallappa	224459	65	M	205	No	No
53	4	Sunanda	257777	50	F	212	No	No
54	4	Prakash	226475	45	M	215	Yes	No
55	4	Ajambi	242830	60	F	246	No	No
56	4	Prathap	225979	48	M	278	No	No
57	4	Siddalingayya	224340	70	M	312	Yes	No
58	4	Salim	258740	45	M	324	Yes	No
59	4	Taranappa	235751	60	M	330	Yes	Yes

12-Master Chart_560F800

60	4	Manuvijay	235112	63	M	354	Yes	No

12-Master Chart_560F800

Sl. No.	Group	Name	I. P. NO.	S- BP	D- BP	HR	CK MB	HbA1c (%)	h/o HTN
31	3	Ramesh	256837	140	90	77	68	6	No
32	3	Mohammed	227658	90	0	60	8	4.8	No
33	3	Malasiddayya	239972	110	70	90	6	6.2	No
34	3	Mallappa	239833	130	90	82	7	4.2	No
35	3	Mahantesh	251252	80	60	114	8	6.8	Yes
36	3	Govind	260002	120	80	96	23	5.4	No
37	3	Bajirao	251893	130	80	110	8	6.6	No
38	3	Ravi	251257	130	80	110	40	6	No
39	3	Fathima	217256	136	86	114	13	5	No
40	3	Gangawwa	226063	190	110	60	11	5	No
41	3	Balachandra	216980	110	80	72	138	6	Yes
42	3	Shakeel	223735	90	60	100	26	5	No
43	4	Gudleppa	216438	80	50	42	6.8	6	Yes
44	4	Sangappa	219284	90	70	112	39	6.2	Yes
45	4	Kashappa	226899	50	0	46	12	5.4	No
46	4	Mallawwa	253517	130	80	70	10	5.7	No
47	4	Gangawwa	231377	70	40	130	10	6	No
48	4	Sanjay	241189	70	50	90	27	6	No
49	4	Rukmawwa	243302	110	80	66	22	5.4	Yes
50	4	Gururaj	240687	100	70	76	8	5.4	Yes
51	4	Gangawwa	221189	110	80	86	12.5	5.8	Yes
52	4	Mallappa	224459	130	90	110	11	5.2	Yes
53	4	Sunanda	257777	100	80	100	107	4.6	No
54	4	Prakash	226475	100	60	102	10	4.8	Yes
55	4	Ajambi	242830	60	0	60	16	5.6	Yes
56	4	Prathap	225979	70	50	80	78	5.4	No
57	4	Siddalingayya	224340	128	80	56	73	5.6	No
58	4	Salim	258740	100	90	93	18	6.3	No
59	4	Taranappa	235751	128	94	66	16	6.4	Yes

12-Master Chart_560F800

60	4	Manuvijay	235112	60	30	40	90	6	No

12-Master Chart_560F800

Sl. No.	Group	Name	I. P. NO.	TOI	KA	KD	Arrhythmias	LVEF%	Car Shock	Death
31	3	Ramesh	256837	A MI	1	No	Yes	50	No	No
32	3	Mohammed	227658	IW MI	2	No	Yes	45	No	No
33	3	Malasiddayya	239972	IW MI	2	No	Yes	45	No	No
34	3	Mallappa	239833	IW MI	1	No	No	60	No	No
35	3	Mahantesh	251252	AS MI	2	Yes	Yes	40	No	Yes
36	3	Govind	260002	AS MI	2	No	Yes	30	No	No
37	3	Bajirao	251893	AS MI	2	No	Yes	40	No	No
38	3	Ravi	251257	AS MI	2	No	No	40	No	No
39	3	Fathima	217256	AS MI	1	No	Yes	45	No	Yes
40	3	Gangawwa	226063	IW MI	1	No	Yes	45	No	No
41	3	Balachandra	216980	IW MI	2	No	Yes	35	No	Yes
42	3	Shakeel	223735	AS MI	1	No	No	40	No	No
43	4	Gudleppa	216438	AW MI	2	Yes	Yes	40	Yes	Yes
44	4	Sangappa	219284	AS MI	2	No	Yes	35	No	Yes
45	4	Kashappa	226899	AW MI	2	Yes	Yes	35	No	Yes
46	4	Mallawwa	253517	AS MI	1	No	No	40	No	No
47	4	Gangawwa	231377	AS MI	2	No	No	40	Yes	Yes
48	4	Sanjay	241189	IW MI	2	No	Yes	35	Yes	Yes
49	4	Rukmawwa	243302	AS MI	2	No	No	40	No	No
50	4	Gururaj	240687	IW MI	2	Yes	No	40	No	Yes
51	4	Gangawwa	221189	IW MI	2	Yes	Yes	40	No	Yes
52	4	Mallappa	224459	IW MI	2	No	Yes	40	No	No
53	4	Sunanda	257777	IW MI	2	No	No	38	No	No
54	4	Prakash	226475	AS MI	1	Yes	Yes	45	Yes	No
55	4	Ajambi	242830	IW MI	2	Yes	Yes	40	Yes	Yes
56	4	Prathap	225979	AS MI	2	Yes	Yes	40	No	No
57	4	Siddalingayya	224340	AS MI	1	No	No	40	No	No
58	4	Salim	258740	IW MI	1	No	Yes	55	No	No
59	4	Taranappa	235751	IW MI	1	No	Yes	55	No	Yes

12-Master Chart_560F800

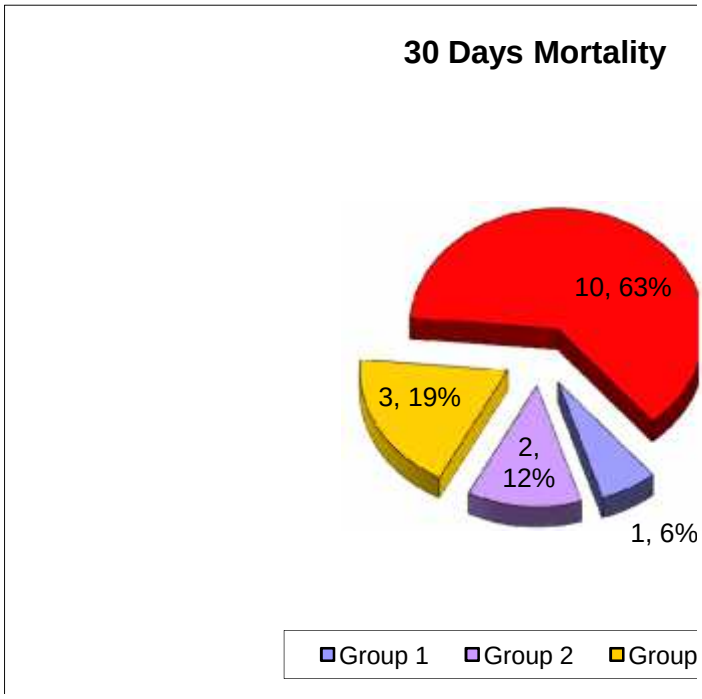
60	4	Manuvijay	235112	IW MI	2	Yes	Yes	45	Yes	Yes

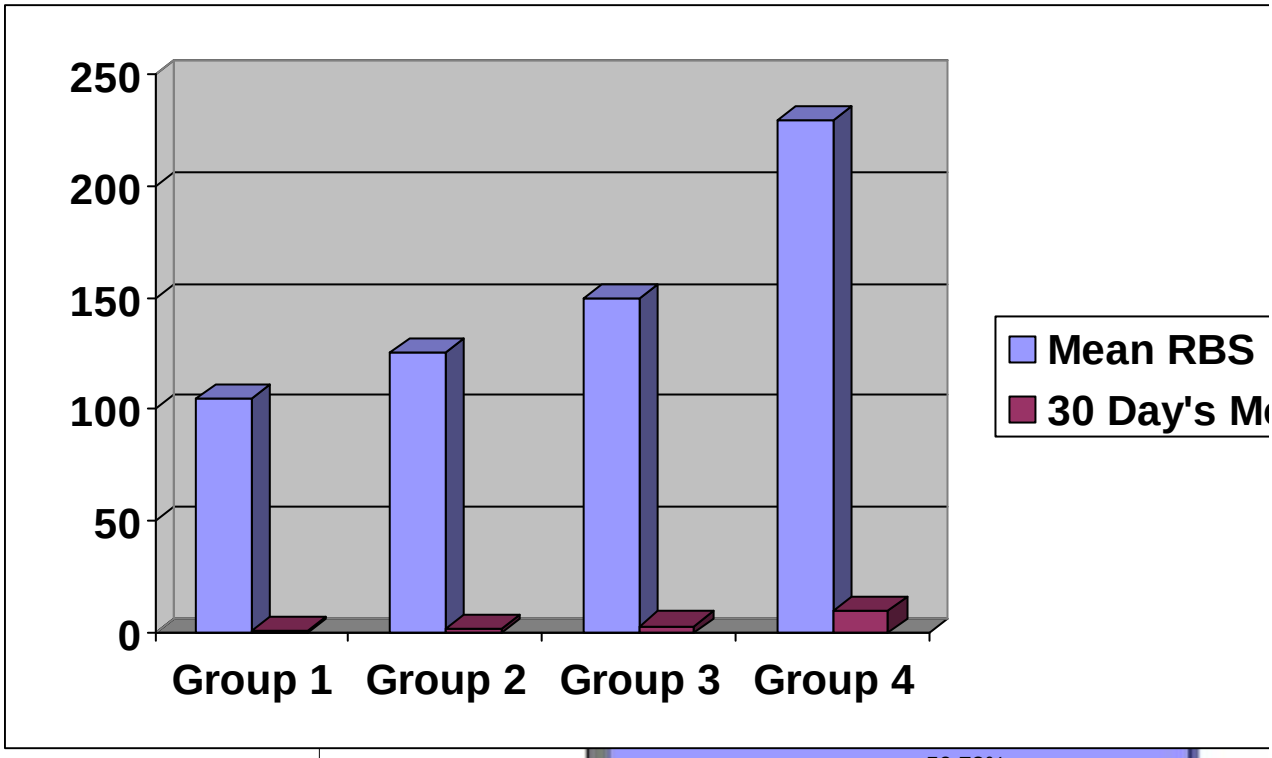
Sl. No.	Group	Name	I. P. NO.	Age	Sex	RBS @ Adm	Smoking	Alco Use
1	1	Sanadev	248162	35	0	83	1	1
2	1	Maruti	239213	62	0	90	1	1
3	1	Abida	250093	52	1	97	0	1
4	1	Vijay	255749	63	0	101	0	0
5	1	Bansilal	226608	35	0	105	0	0
6	1	Sambu	241596	46	0	105	1	0
7	1	Gajendrabau	233319	61	0	107	1	1
8	1	Goursab	248679	55	0	107	0	0
9	1	Rajendra	248460	35	0	107	1	0
10	1	Hirabai	219241	70	1	108	0	0
11	1	Ibrahim	249096	40	0	110	1	0
12	1	Bhagirathi	247490	58	1	110	0	0
13	1	Basanagouda	240261	47	0	113	1	1
14	1	Jogendra	239456	38	0	116	1	0
15	1	Jayant	243142	60	0	118	1	0
16	1	Rajashekar	261691	55	0	105	0	0
17	2	Shebarappa	249766	50	0	120	1	1
18	2	Durgappa	242505	58	0	120	0	0
19	2	Ranjana	252775	40	1	123	0	0
20	2	Yashodha	239842	65	1	125	0	0
21	2	Shankar	228622	65	0	122	0	0
22	2	Ramesh	256883	35	0	126	0	0
23	2	Dundavva	254746	95	1	126	0	0
24	2	Vishwanath	217695	58	0	126	1	0

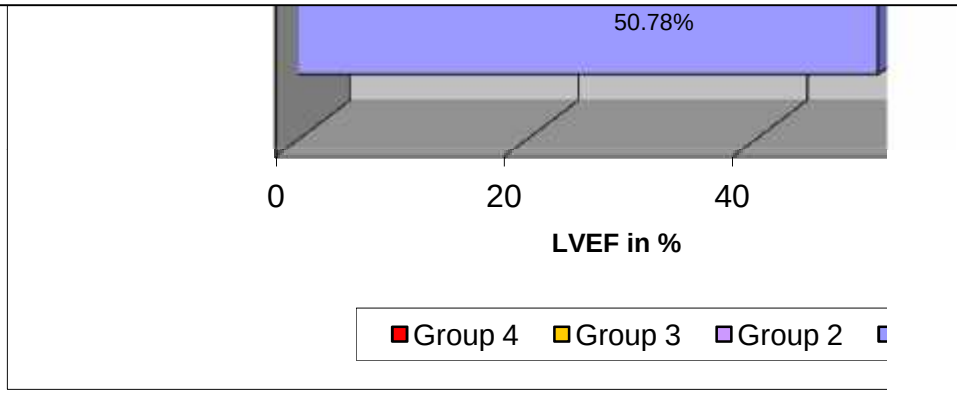
25	2	Gurayya	249472	81	0	130	0	0
26	2	Sher Pathan	228461	48	0	130	0	0
27	2	Manjunath	252414	35	0	131	0	1
28	2	Nirmala	247182	44	1	124	0	0
29	3	Sudhakar	226011	40	0	140	0	1
30	3	Bhimrao	224350	75	0	142	0	0
31	3	Ramesh	256837	42	0	143	1	0
32	3	Mohammed	227658	47	0	144	1	0
33	3	Malasiddayya	239972	65	0	145	1	0
34	3	Mallappa	239833	57	0	145	1	0
35	3	Mahantesh	251252	50	0	145	1	0
36	3	Govind	260002	68	0	148	1	0
37	3	Bajirao	251893	42	0	154	1	1
38	3	Ravi	251257	42	0	154	1	1
39	3	Fathima	217256	48	1	155	0	0
40	3	Gangawwa	226063	72	1	157	0	0
41	3	Balachandra	216980	52	0	160	1	0
42	3	Shakeel	223735	48	0	162	1	1
43	4	Gudleppa	216438	85	0	168	0	0
44	4	Sangappa	219284	65	0	175	1	1
45	4	Kashappa	226899	70	0	178	1	0
46	4	Mallawwa	253517	65	1	178	0	0
47	4	Gangawwa	231377	60	1	186	0	0
48	4	Sanjay	241189	40	0	188	0	0
49	4	Rukmawwa	243302	75	1	189	0	0
50	4	Gururaj	240687	67	0	190	0	0

51	4	Gangawwa	221189	65	1	201	0	0
52	4	Mallappa	224459	65	0	205	0	0
53	4	Sunanda	257777	50	1	212	0	0
54	4	Prakash	226475	45	0	215	1	0
55	4	Ajambi	242830	60	1	246	0	0
56	4	Prathap	225979	48	0	278	0	0
57	4	Siddalingayya	224340	70	0	312	1	0
58	4	Salim	258740	45	0	324	1	0
59	4	Taranappa	235751	60	0	330	1	1
60	4	Manuvijay	235112	63	0	354	1	0

Group 1	16	0	105.13	126.87	2	50.78	1
Group 2	12	0	125.25	123.33	5	46.67	2
Group 3	14	1	149.57	120.86	10	42.86	3
Group 4	18	8	229.39	93.67	12	41.28	10



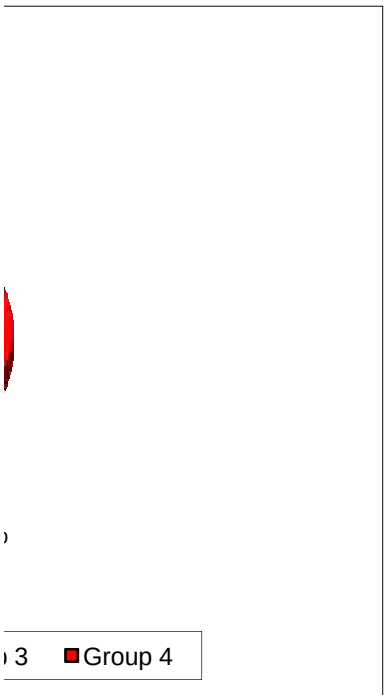

250
200
150
100
50
0
Group 1
Group 2
Group 3
Group 4
Mean RBS
30 Day's M

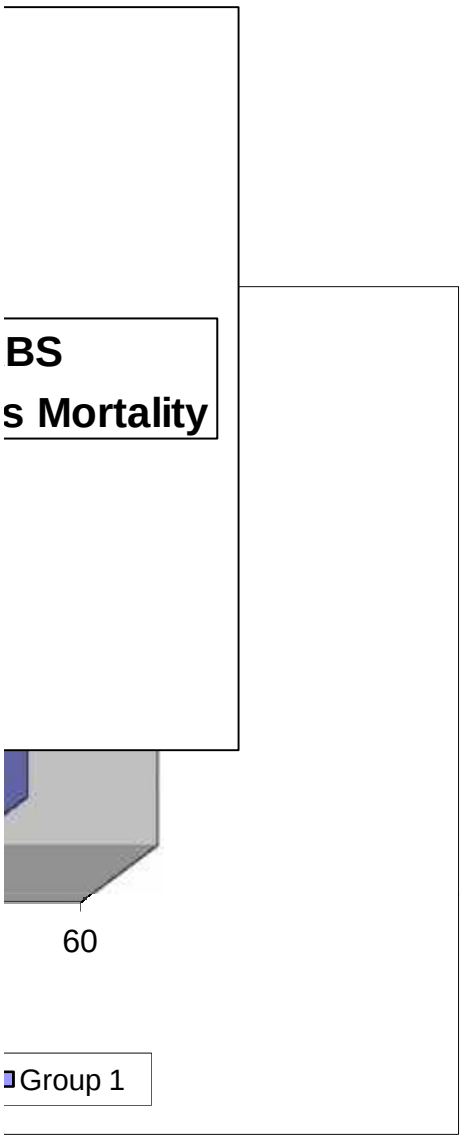

50.78%
0
20
40
LVEF in %
Group 4
Group 3
Group 2

Sl. No.	Group	Name	I. P. NO.	S- BP	D- BP	HR	CK MB	HbA1c	PH of HTN
1	1	Sanadev	248162	120	70	80	18	5.6	0
2	1	Maruti	239213	140	80	65	89	4.8	1
3	1	Abida	250093	110	70	94	38	6.2	0
4	1	Vijay	255749	160	110	96	29	6.2	0
5	1	Bansilal	226608	100	80	88	10	5.8	0
6	1	Sambu	241596	110	70	76	21	5.2	0
7	1	Gajendrabau	233319	130	80	96	7	6.2	0
8	1	Goursab	248679	110	70	110	29	6	0
9	1	Rajendra	248460	140	90	104	20	5.8	0
10	1	Hirabai	219241	100	60	105	10	5.6	1
11	1	Ibrahim	249096	130	80	78	9	5.6	0
12	1	Bhagirathi	247490	120	80	78	7	5.4	0
13	1	Basanagouda	240261	170	110	70	7	6	0
14	1	Jogendra	239456	130	90	90	10	4.8	0
15	1	Jayant	243142	130	90	95	28	6.5	1
16	1	Rajashekar	261691	130	86	95	10	5.5	0
17	2	Shebarappa	249766	110	70	76	27	4.6	0
18	2	Durgappa	242505	160	90	110	29	4.8	1
19	2	Ranjana	252775	160	100	80	52	6.1	0
20	2	Yashodha	239842	110	70	76	10	5.2	1
21	2	Shankar	228622	110	70	66	29	5.4	1
22	2	Ramesh	256883	140	80	86	158	6.6	0
23	2	Dundavva	254746	110	70	76	12	5.8	1
24	2	Vishwanath	217695	140	100	96	99	5	1

25	2	Gurayya	249472	170	110	60	8	5	1
26	2	Sher Pathan	228461	90	0	116	9	5	0
27	2	Manjunath	252414	100	70	94	7	6.8	0
28	2	Nirmala	247182	80	50	56	12	6.7	0
29	3	Sudhakar	226011	130	80	60	20	5.2	0
30	3	Bhimrao	224350	106	70	101	85	5.4	0
31	3	Ramesh	256837	140	90	77	68	6	0
32	3	Mohammed	227658	90	0	60	8	4.8	0
33	3	Malasiddayya	239972	110	70	90	6	6.2	0
34	3	Mallappa	239833	130	90	82	7	4.2	0
35	3	Mahantesh	251252	80	60	114	8	6.8	1
36	3	Govind	260002	120	80	96	23	5.4	0
37	3	Bajirao	251893	130	80	110	8	6.6	0
38	3	Ravi	251257	130	80	110	40	6	0
39	3	Fathima	217256	136	86	114	13	5	0
40	3	Gangawwa	226063	190	110	60	11	5	0
41	3	Balachandra	216980	110	80	72	138	6	1
42	3	Shakeel	223735	90	60	100	26	5	0
43	4	Gudleppa	216438	80	50	42	6.8	6	1
44	4	Sangappa	219284	90	70	112	39	6.2	1
45	4	Kashappa	226899	50	0	46	12	5.4	0
46	4	Mallawwa	253517	130	80	70	10	5.7	0
47	4	Gangawwa	231377	70	40	130	10	6	0
48	4	Sanjay	241189	70	50	90	27	6	0
49	4	Rukmawwa	243302	110	80	66	22	5.4	1
50	4	Gururaj	240687	100	70	76	8	5.4	1

51	4	Gangawwa	221189	110	80	100	12.5	5.8	1
52	4	Mallappa	224459	130	90	110	11	5.2	1
53	4	Sunanda	257777	100	80	100	107	4.6	0
54	4	Prakash	226475	100	60	102	10	4.8	1
55	4	Ajambi	242830	60	0	60	16	5.6	1
56	4	Prathap	225979	70	50	80	78	5.4	0
57	4	Siddalingayya	224340	128	80	56	73	5.6	0
58	4	Salim	258740	100	90	93	18	6.3	0
59	4	Taranappa	235751	128	94	66	16	6.4	1
60	4	Manuvijay	235112	60	30	40	90	6	0
				6888	4326	5097			




BS
s Mortality
60
Group 1

Sl. No.	Group	Name	I. P. NO.	TOI	Arrhythmias	LVEF%	Car Shock	Death
1	1	Sanadev	248162	AS MI	0	55	0	0
2	1	Maruti	239213	IW MI	0	55	0	0
3	1	Abida	250093	AW MI	0	60	0	0
4	1	Vijay	255749	IW MI	0	50	0	0
5	1	Bansilal	226608	IW MI	0	45	0	0
6	1	Sambu	241596	IW MI	0	55	0	0
7	1	Gajendrabau	233319	AS MI	0	60	0	0
8	1	Goursab	248679	AS MI	0	40	0	0
9	1	Rajendra	248460	AS MI	0	50	0	0
10	1	Hirabai	219241	IW MI	1	50	0	1
11	1	Ibrahim	249096	IW MI	0	55	0	0
12	1	Bhagirathi	247490	IW MI	0	55	0	0
13	1	Basanagouda	240261	IW MI	1	47.5	0	0
14	1	Jogendra	239456	AS MI	0	40	0	0
15	1	Jayant	243142	AS MI	0	45	0	0
16	1	Rajashekar	261691	AS MI	0	50	0	0
17	2	Shebarappa	249766	IW MI	0	50	0	0
18	2	Durgappa	242505	AW MI	1	55	0	0
19	2	Ranjana	252775	AW MI	1	45	0	1
20	2	Yashodha	239842	AW MI	0	40	0	0
21	2	Shankar	228622	IW MI	0	50	0	0
22	2	Ramesh	256883	AS MI	1	40	0	0
23	2	Dundavva	254746	AS MI	0	40	0	0
24	2	Vishwanath	217695	IW MI	1	40	0	1

25	2	Gurayya	249472	AS MI	1	60	0	0
26	2	Sher Pathan	228461	IW MI	0	50	0	0
27	2	Manjunath	252414	IW MI	0	40	1	0
28	2	Nirmala	247182	IW MI	0	50	0	0
29	3	Sudhakar	226011	IW MI	0	50	0	0
30	3	Bhimrao	224350	IW MI	1	35	0	0
31	3	Ramesh	256837	A MI	1	50	0	0
32	3	Mohammed	227658	IW MI	1	45	0	0
33	3	Malasiddayya	239972	IW MI	1	45	0	0
34	3	Mallappa	239833	IW MI	0	60	0	0
35	3	Mahantesh	251252	AS MI	1	40	0	1
36	3	Govind	260002	AS MI	1	30	0	0
37	3	Bajirao	251893	AS MI	1	40	0	0
38	3	Ravi	251257	AS MI	0	40	0	0
39	3	Fathima	217256	AS MI	1	45	0	1
40	3	Gangawwa	226063	IW MI	1	45	0	0
41	3	Balachandra	216980	IW MI	1	35	0	1
42	3	Shakeel	223735	AS MI	0	40	0	0
43	4	Gudleppa	216438	AW MI	1	40	1	1
44	4	Sangappa	219284	AS MI	1	35	0	1
45	4	Kashappa	226899	AW MI	1	35	0	1
46	4	Mallawwa	253517	AS MI	0	40	0	0
47	4	Gangawwa	231377	AS MI	0	40	1	1
48	4	Sanjay	241189	IW MI	1	35	1	1
49	4	Rukmawwa	243302	AS MI	0	40	0	0
50	4	Gururaj	240687	IW MI	0	40	0	1

51	4	Gangawwa	221189	IW MI	1	40	0	1
52	4	Mallappa	224459	IW MI	1	40	0	0
53	4	Sunanda	257777	IW MI	0	38	0	0
54	4	Prakash	226475	AS MI	1	45	1	0
55	4	Ajambi	242830	IW MI	1	40	1	1
56	4	Prathap	225979	AS MI	1	40	0	0
57	4	Siddalingayya	224340	AS MI	0	40	0	0
58	4	Salim	258740	IW MI	1	55	0	0
59	4	Taranappa	235751	IW MI	1	55	0	1
60	4	Manuvijay	235112	IW MI	1	45	1	1

Sex: 0= Male 1= Female

Killip Class:
1 to 4 Depending on Killip Class I to IV

Other Categorical Variables: 0= No 1= Yes

Sl. No.	Group	Name	I. P. NO.	S- BP	D- BP	HR
1	1	Sanadev	248162	120	70	80
2	1	Maruti	239213	140	80	65
3	1	Abida	250093	110	70	94
4	1	Vijay	255749	160	110	96
5	1	Bansilal	226608	100	80	88
6	1	Sambu	241596	110	70	76
7	1	Gajendrabau	233319	130	80	96
8	1	Goursab	248679	110	70	110
9	1	Rajendra	248460	140	90	104
10	1	Hirabai	219241	100	60	105
11	1	Ibrahim	249096	130	80	78
12	1	Bhagirathi	247490	120	80	78
13	1	Basanagouda	240261	170	110	70
14	1	Jogendra	239456	130	90	90
15	1	Jayant	243142	130	90	95
16	1	Rajashekar	261691	130	86	95
17	2	Shebarappa	249766	110	70	76
18	2	Durgappa	242505	160	90	110
19	2	Ranjana	252775	160	100	80
20	2	Yashodha	239842	110	70	76
21	2	Shankar	228622	110	70	66
22	2	Ramesh	256883	140	80	86
23	2	Dundavva	254746	110	70	76
24	2	Vishwanath	217695	140	100	96
25	2	Gurayya	249472	170	110	60
26	2	Sher Pathan	228461	90	0	116
27	2	Manjunath	252414	100	70	94
28	2	Nirmala	247182	80	50	56
29	3	Sudhakar	226011	130	80	60
30	3	Bhimrao	224350	106	70	101
31	3	Ramesh	256837	140	90	77
32	3	Mohammed	227658	90	0	60
33	3	Malasiddayya	239972	110	70	90
34	3	Mallappa	239833	130	90	82
35	3	Mahantesh	251252	80	60	114

36	3	Govind	260002	120	80	96
37	3	Bajirao	251893	130	80	110
38	3	Ravi	251257	130	80	110
39	3	Fathima	217256	136	86	114
40	3	Gangawwa	226063	190	110	60
41	3	Balachandra	216980	110	80	72
42	3	Shakeel	223735	90	60	100
43	4	Gudleppa	216438	80	50	42
44	4	Sangappa	219284	90	70	112
45	4	Kashappa	226899	50	0	46
46	4	Mallawwa	253517	130	80	70
47	4	Gangawwa	231377	70	40	130
48	4	Sanjay	241189	70	50	90
49	4	Rukmawwa	243302	110	80	66
50	4	Gururaj	240687	100	70	76
51	4	Gangawwa	221189	120	80	100
52	4	Mallappa	224459	130	90	110
53	4	Sunanda	257777	100	80	100
54	4	Prakash	226475	100	60	102
55	4	Ajambi	242830	60	0	60
56	4	Prathap	225979	70	50	80
57	4	Siddalingayya	224340	128	80	56
58	4	Salim	258740	100	90	93
59	4	Taranappa	235751	128	94	66
60	4	Manuvijay	235112	60	30	40

Sex: 0= Male

Killip Class:
1 to 4 Dependin

Other Categorical Va

1= Female

ıg on Killip Class I to IV

ıriables: 0= No 1= Yes