PATTERN OF PRESENTATION AND MANAGEMENT OF ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION TO A TERTIARY CARE CENTRE IN A DISTRICT CAPITAL IN SOUTH INDIA

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF DM – BRANCH II CARDIOLOGY EXAMINATION OF THE TAMILNADU DR.MGR MEDICAL UNIVERSITY, CHENNAI, TO BE HELD IN JULY/AUGUST 2009.

CERTIFICATE

This is to certify that the thesis titled **"Pattern of presentation and management of acute ST-segment elevation myocardial infarction to a tertiary care centre in a district capital in South India"** is the bonafide work of the candidate Dr. S. Ramakrishnakumar in partial fulfillment of DM – Branch II (Cardiology) Examination of The Tamilnadu Dr. M.G.R. Medical University, Chennai to be held in July/August 2009.

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CONTENTS

ABSTRACT

Pattern of presentation and management of acute ST-segment elevation myocardial infarction (STEMI) to a tertiary care centre in a district capital in South India

Background: Cardiovascular disease (CVD) is the leading cause of death worldwide and by 2010, 60% of world's heart disease is expected to occur in India. The prevalence of diabetes and obesity has increased. Rates of primary percutaneous coronary intervention (PCI) have increased in western population. Mortality rates from STEMI are declining worldwide. We sought to study the pattern of presentation and management of patients presenting with acute STEMI to a tertiary care centre in a district capital in South India**.**

Methods: 150 consecutive patients presenting with acute STEMI to a tertiary care centre were enrolled. The demographic, socioeconomic, risk factor, clinical and laboratory profile of patients presenting with STEMI were recorded. The reperfusion strategy, use of guideline based acute medical therapy, in-hospital and 30 day outcomes were recorded for these patients.

Results: The mean age of study population was 57 ± 12 years. There were 117(78%) males and 33(22%) females. 84(56%) belonged to the middle class, 20(13.3%) and 46(30.7%) belonged to the upper and lower socioeconomic class respectively. The median pre-hospital delay was 4 hours. The median door-to-needle time was 45 minutes. The median door-to-

balloon time was 92 minutes. 73(48.7%) had diabetes, 64(42.7%) had hypertension, 51(34%) were smokers. The mean body mass index was 23.9 ± 2.8. The mean ejection fraction was 45 ± 9%. 76(50.7%) had anterior wall myocardial infarction and 68(45.3%) had inferior wall myocardial infarction. 130 (86.7%) underwent thrombolysis and 11(7.3%) underwent primary PCI. Streptokinase was the thrombolytic agent used in 124(95.4%) and tenecteplase in the rest. 89(59.3%) had >50% ST segment resolution post reperfusion. 28(18.7%) underwent coronary angiography during index hospitalization. Acute pharmacotherapy was widely used: Aspirin (98.7%), clopidogrel (97.3%), beta-blocker (88%), Angiotensin converting enzyme inhibitors (ACEI) (88.7%) and statins (94%). The in-hospital outcomes were death (12%), re-infarction (0.7%), recurrent angina (8%), arrhythmia (7.3%), LV systolic dysfunction (60.7%), stroke (1.3%), cardiogenic shock (3.3%), rescue PCI (5.3%), adjunct PCI (2.7%). The mean duration of hospital stay was 2.6 ± 2 days. The 30 day outcomes were death (0.7%0, re-infarction (2.7%0, recurrent angina (12%), and heart failure (11.3%).

Conclusion: Patients presenting with STEMI are younger in comparison to western population. The proportion of women presenting with STEMI and prevalence of diabetes mellitus has increased. Women have significantly higher prevalence of diabetes than men. The pre-hospital delay is longer than Western population. Thrombolysis is the most commonly used reperfusion therapy. In-hospital mortality rates are declining but still higher than the western population. Use of guideline based prescription of acute medical therapy has increased.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide and has reached epidemic proportions. The prevalence of CVD shows remarkable geographic variation. Mortality associated with CVD is declining in Western Europe and North America[1] , but the burden of CVD in developing countries continues to rise and is expected to be the major cause of death in adults from low and middle income countries worldwide[2] . Moreover South Asians have a greater prevalence of coronary risk factors than the rest of the world, and coronary artery disease (CAD) often manifests at an early age which creates pressure on society and the economy [3] .

Over the last decade, western countries have shown decrease in mortality due to ST-segment elevation myocardial infarction (STEMI). More women and elderly are presenting with STEMI [4]. Among the risk factors, there has been significant increase in incidence of diabetes and obesity [5]. There were marked geographic differences in extent of pre-hospital delay in patients with STEMI [6]. More number of people are treated by primary percutaneous coronary intervention (PCI) compared to thrombolytic therapy [7].

Major risk factors are the same around the world. Tobacco use, dyslipidemia and hypertension are the main determinants of population attributable risk (PAR) worldwide. As the Indian economy grows there is a possibility for further increase in cardiovascular disease. The prevalence of overweight and obesity is increasing, and more importantly, rates of diabetes are increasing even more rapidly. A moderate increase in body mass index makes south Asians more prone for insulin resistance and related diseases [8] .

Earlier studies done in India and study done in this same institution have shown significantly prolonged pre-hospital delay. Studies done in Indian population have shown that the patients presenting with acute coronary syndrome are younger and they present more often with STEMI as compared to that of developed countries[9] . Moreover the use of lipid lowering therapies, beta blockers and angiotensin converting enzyme inhibitors (ACEI) were lower. Fewer patients had an invasive approach with coronary revascularization. Especially, in poor people, substantial underutilization of evidence – based treatments were seen. Indian hospitals have access to the most modern technologies on par with the rest of the world. They can provide the latest and the best medical care as long as the patient can afford it. But, focus on advanced technology can interrupt delivery of inexpensive drugs that can reduce mortality and morbidity in acute coronary syndromes. In fact widespread use of these drugs in the hospital and at discharge from hospital has been the major cause of improved outcomes in acute coronary syndromes in developed countries [10] . It has been shown that initiatives to enhance quality through consistent delivery of these therapies can achieve remarkable improvements in survival[11] . The strategies to improve outcomes of acute coronary syndrome are not expensive. Most of the decline in USA is believed to be due to secondary to improving risk factor profiles, effective primary and secondary treatment of acute coronary syndrome with beta blockers, statins, aspirin and ACEI. In fact, expensive intervention such as revascularization accounts only for 5% of this benefit [12]

This study was done to assess the pattern of presentation and management of patients with acute STEMI to a tertiary care centre in a district capital in South India in the current era. It would also evaluate the extent of pre-hospital delay in seeking medical care in patients presenting to a tertiary care centre with acute STEMI. It would also be informative to know of any change in risk factor profile of patients presenting with STEMI in the current era. This would also assess the type of the reperfusion strategy used and assess appropriate use of

pharmacotherapy as per current guidelines. The in-hospital and 30 day outcomes also need to be assessed in the present era due to greater advancements in the treatment of acute myocardial infarction (AMI), better knowledge of the pathology and complications of myocardial infarction, better pharmacotherapy available and greater availability of primary PCI.

AIMS AND OBJECTIVES

AIMS:

The aim is to study the pattern and presentation of ST-segment Elevation Myocardial Infarction to a tertiary care centre in a district capital in South India

OBJECTIVES:

1. To study the demographic, socioeconomic, risk factor and clinical profile of patients presenting with acute ST-segment elevation myocardial infarction.
2. To study the time delay associated with presentation and management of acute ST-segment elevation myocardial infarction.
3. To study the in-hospital outcomes in patients presenting with acute ST-segment elevation myocardial infarction.
4. To study the 30 day outcomes in patients presenting with acute ST-segment elevation myocardial infarction.
5. To compare and contrast the patient characteristics, presentation and management of acute ST-segment elevation myocardial infarction with that of data obtained from 1999 – 2003 in the same institution.

REVIEW OF LITERATURE

Global and regional burden of cardiovascular disease

CVD has become the leading cause of death and loss of disability adjusted life years in many developing countries and will soon attain that status in several others [13] . The projected increase in the proportion of all deaths that are due to cardiovascular causes, from about 25 percent in 1990 to more than 40 percent in 2020, signals the advance of the epidemic of CVD. Coronary heart disease (CHD) is the leading cause of death in adults in the United States, accounting for about one-third of all deaths in subjects over age of 35 [13] . The death rate is higher in men than in women (three times higher at ages 25 to 34, falling to 1.6 times at ages 75 to 84) and in blacks compared to whites, an excess that disappears by age 75.

Although age-adjusted cardiovascular death rates have declined in several developed countries in past decades, rates of CVD have risen greatly in low-income and middle-income countries. The fact that 80% of deaths from CVD worldwide and 87% of related disability currently occur in low-income and middle income countries indicates the magnitude of the problem[14] . The Indian subcontinent is home to 20 per cent of the world's population and may be one of the regions with the highest burden of CVD in the world. The high burden of mortality from cardiovascular causes in developing countries is estimated to increase to 19 million by 2020 [15] . This is only partially explained by their large population. In India, ischemic heart disease may not be largely explained by traditional risk factors [16] .

Over the past 40 years, the prevalence of CHD in urban India has increased by a factor of six to eight, to about 10 percent among persons 35 to 64 years of age. Coronary deaths in India

are expected to reach 2 million by 2010. At the turn of the century, it was reported that CHD mortality was expected to increase approximately 29 percent in women and 48 percent in men in developed countries between 1990 and 2020. The corresponding estimated increases in developing countries were 120 percent in women and 137 percent in men [17] .

In non-Western countries, deaths due to CVD tend to occur a decade or two earlier than they do in Western countries; nearly half occur before 70 years of age, whereas only one fifth occur so early in the West — a difference attributable to both the earlier occurrence of cardiovascular events and the lower level of clinical care available [18] . As a result, the Indian subcontinent suffers from a tremendous loss of productive working years due to CVD deaths: an estimated 9.2 million productive years of life were lost in India in 2000, with an expected increase to 17.9 million years in 2030 (almost ten times the projected loss of productive life in the United States) [19] .

Of the 24 million people expected to die of CVD in 2020, about 9.3 million will be between 30 and 69 years of age. Most of them will be in non-Western countries. A huge increase in the prevalence of diabetes will further increase the burden of CVD. India also has the highest number of diabetics in the world[20] . India, where nearly 20 million people had diabetes in 1995, will see atleast a tripling of that number by 2025.

The huge burden of CVD in the Indian subcontinent is the consequence of the large population and the high prevalence of CVD risk factors. Moreover, the projected increase in deaths and disability from CVD is expected to follow closely an explosion in the prevalence of traditional risk factors. Driving this steep rise in CVD risk factor burden is the rapid increase in the proportion of urban inhabitants (currently at 30% with a projected rise to 43% in 2021)[21] . Urbanization is characterized by a marked increase in the intake of energy-dense foods, a decrease in physical activity, and a heightened level of psychosocial stress, all of

which promote the development of diabetes, hypertension, and dyslipidemia[17] .

Risk factors and cardiovascular disease

A risk factor can be defined as a characteristic that is associated with increased or decreased likelihood of subsequent development of CVD. The concept of risk factor can be used to study the cause or pathophysiology of CVD, to estimate the total cardiovascular risk, to understand the dynamics of the CVD epidemic within and between populations. Absolute cardiovascular risk is the probability that a person or a group of persons will develop CVD over a fixed period of time. Relative risk is generally expressed as a ratio comparing a person or a group of persons with another person or group of persons that differ in terms of exposure. Relative risk is of great scientific interest. It says about the strength of association. However, in terms of public health, absolute risk is also very important - a given relative risk reduction will end up in many more end points avoided if applied to a group of subjects at high absolute risk than one at low absolute risk.

Risk factors can be identified by means of cross sectional or case-control studies. In the INTERHEART study[22] it was reported that a limited set of risk factors – abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits, vegetables and alcohol, and regular physical activity account for most of the risk of myocardial infarction worldwide in both sexes and at all ages in all regions. The levels of these risk factors have increased steeply in most non – Western countries over the past two decades. Although there are some differences among the ethnic groups in the interactions between the genes and environment , the available evidence indicates that the main risk factors for CVD are relevant to all populations and that most of the risk is environmentally determined.

Age

Age is one among the strongest cardiovascular risk. Its relationship with cardiovascular mortality is exponential. It is an important factor to consider in total cardiovascular risk estimation, but its non modifiable nature limits its use in the management of cardiovascular risk. Given the nature of its association with CVD, it explains the paradox that if prevention of CVD is successful in a given generation, total cardiovascular mortality will increase by preventing premature deaths, a larger proportion of the population will grow old and enter the elderly age group where death is attributed to CVD in a majority of cases. In fact, the number of people >60 years of age is expected to double by 2025 and to triple by 2050 globally[23] . The proportion of this aged population is likely to increase more in the Asian-Pacific region; thus, half of the world's cardiovascular burden is predicted to occur in this area[24] .

Sex

Total cardiovascular risks in women tend to resemble those of men of 10 years younger. Thus, risk is merely deferred by 10 years and ultimately more women than men die from CVD. The apparent protection of women from CVD is a myth – 40% of women die from CVD, compared with 3% of deaths from breast cancer. Of 17.5 million persons worldwide dying from CVD each year, over 8.6 million are women. Ischemic heart disease (IHD) presents later in women, who are therefore older and more likely to suffer from co-morbidities such as diabetes and hypertension. Women with diabetes develop CVD at the same time in life as men, canceling out the 10-year protection effect afforded by female hormones. Specific hormone-related risk factors include polycystic ovarian syndrome, premature menopause,

and gestational diabetes or hypertension. Female sex hormones are potent modulators of cardiac risk factors at virtually every level of the atherosclerotic process. CHD and stroke are rare before menopause. However, hormone replacement therapy has failed to show any benefit in terms of CVD risk reduction in women, mainly because of associated adverse effects. Current risk estimation systems underestimate the problem, especially by not accommodating older women. There is therefore a pressing need to to ensure that cardiovascular trials are specifically designed to incorporate sufficient numbers of women to allow gender specific efficacy analyses to be undertaken.

Family history of cardiovascular disease

It is defined as history of premature CVD in a first degree male relative <55 years of age and female relative <65 years. Although the odds ratio for an acute myocardial infarction in people with a family history was about 1·5, the PAR rose from 90% with the nine potentially modifiable risk factors to 91% with the addition of family history[22] . This finding suggests that a large part of the effect of family history might be mediated through known risk factors, which could be affected by both shared lifestyles and genetic factors rather than through independent pathways.

A special group of non modifiable risk indicators relate to existing CVD in a given person. Patients with established CVD are at high risk of recurrent events, but indicators of existing vascular damage in asymptomatic subjects can also help in the identification of high risk groups in the community. Different techniques such as the ankle-brachial index, the intima-media thickness of the carotid artery, calcium deposits in the coronary arteries identified by CT scan and left ventricular wall motion abnormalities identified by echocardiography have been recommended to identify this high risk group. These tests can be of help in developing

strategies for prevention of CVD.

Modifiable risk factors

They can in principle be prevented, changed or controlled. Modifiable risk factor per se does not equate with reversibility of CVD. Major modifiable risk factors include sedentariness, smoking, dietary imbalance, impaired glucose tolerance and diabetes mellitus, hypertension, dyslipidemia and obesity. Other factors which are of importance includes psychosocial factors (perceived stress at work, symptoms of depression, low socioeconomic status), indicators of chronic inflammation and hemostatic factors.

Tobacco smoking

In long term smokers, smoking is responsible for 50% of all avoidable deaths and one half of these are due to CVD. The adverse effect of smoking is related to the amount of tobacco smoked daily and to the duration of smoking. The relative mortality from vascular disease has been found higher in female smokers than in male smokers and this difference remains significant after adjustment for major cardiovascular risk factors[25] . The impact of atherosclerotic progression in greater in subjects with diabetes and hypertension and risk of future cardiovascular risk is high if smoking starts before age of 15 years. Passive smoking has now been shown to increase the risk of CAD and other smoking related diseases[26] . Regular exposure to secondhand smoke increases risk of risk of coronary heart disease by 25%[27] .

In the INTERHEART study, it was estimated that smokers and former smokers are at almost twice the risk of a myocardial infarction compared with never smokers[22] . Smoking accounted for about 36% of PAR of acute myocardial infarction worldwide and about 44% in men.

Smoking even five cigarettes per day increased risk. A strong and graded relation was noted between numbers smoked and risk of myocardial infarction, with the risk increasing at every increment, so that individuals smoking greater than 40 cigarettes per day had an odds ratio of 9.16. This finding suggests that there is no safe level of smoking and that if quitting is not possible, the risk of myocardial infarction associated with smoking could be significantly reduced by a reduction in the numbers smoked. A meta analysis on the effect of smoking cessation on mortality after a myocardial infarction showed a mortality benefit with combined odds ratio in those who quit of 0.54. The mortality benefit was consistent regardless of sex, duration of follow up, study site and time period[28] .

Smoking increases the risk of atherosclerosis and the occurrence of superimposed thrombotic phenomenon. The latter effect may be more important as stopping smoking leads to a quicker reduction in the risk of subsequent coronary heart disease events in patients with established coronary heart disease than in asymptomatic individuals. In patients with established heart disease, the risk falls within 2 to 3 years to the level of those coronary heart disease patients who never smoked, whereas in asymptomatic individuals up to 10 years are needed to reach the risk level of those who never smoked.

In 2002, a national survey of tobacco use reported that the Indian subcontinent had an alarming rate of current tobacco use of 56 per cent among Indian men aged 12-60 yr[29] . Reddy and colleagues also recently observed in a survey of sixth and eighth graders attending school in an urban setting that the prevalence of tobacco use (any history of use or current use) was 2-3 times higher among sixth graders compared with eighth graders, suggesting a concerning new wave of smoking among India's youth that forebodes serious future public health consequences for the Indian subcontinent[30] . Little data have existed regarding the association between the use of other forms of tobacco and the risk of CVD. However, a recent analysis of data from the INTERHEART case-control study of risk factors

for acute myocardial infarction has documented that there is an increased risk of myocardial infarction associated with all forms of smoked and smokeless tobacco[31] .

Impaired glucose tolerance and diabetes

Epidemiological studies have consistently shown a linear relationship between nonfasting glucose values and risk of developing CVD. This is confirmed by 2-hour oral glucose tolerance test values[32] and assay of glycated hemoglobin HbA1c[33]. The relationship between hyperglycemia and CVD should be considered a continuum.

In diabetes, the relative risk of CVD is of the order of 2 to 3 in men and of 3 to 5 in women, while in people with impaired glucose tolerance the relative risk is 1.5 compared with people with normal glucose tolerance[34] . The INTERHEART study estimated that 15% of heart attacks in Western Europe and 9% of heart attacks in Central and Eastern Europe were due to diagnosed diabetes[22] .

Subjects with type I diabetes have a 2 to 3 fold high increase in the risk of developing CVD. This increased risk is almost entirely confined to patients developing diabetic nephropathy. All type 2 diabetes patients are at increased risk of CVD even in the absence of diabetic nephropathy. Finnish data published in 1998 suggested that the risk of developing a myocardial infarction in patients with type 2 diabetes was of the same order as for patients without diabetes who had already suffered a first myocardial infarction[35] . This finding had a decisive influence on the drafting of treatment guidelines, in which diabetes was labeled as a “CVD equivalent” in terms of assessment. Diabetes also remains an important risk factor for mortality in patients with established CVD[36] .

Impact of type 2 diabetes on CVD risk is influenced by a number of factors, including duration of diabetes, age and sex[37] . The relative impact of type 2 diabetes on cardiovascular risk is

stronger in women than in men. The Indian subcontinent has a higher prevalence of diabetes mellitus than any other region in the world, and 2-3 times the reported prevalence in Western countries[38] . In India alone, an estimated 19.3 million people had diabetes in 1995, and this is expected to almost triple to 57.2 million in 2025 [39] . The Indian Council of Medical Research (ICMR) estimates that the prevalence of diabetes is 3.8 per cent in rural areas, compared with 11.8 per cent in urban areas[21] .

Hypertension

Hypertension is highly prevalent (20-40% among urban and 12-17% among rural adults)[40], and was affecting an estimated 118 million inhabitants in India in 2000; this number is projected to almost double to 214 million in 2025[41] .

Hypertension has been identified as a risk factor for CHD, heart failure, cerebrovascular disease and renal failure in both men and women[42] . Both systolic and diastolic blood pressures show a continuous and graded independent relationship with the risk of stroke and coronary events. Death from both CHD and stroke increases progressively and linearly from blood pressure levels as low as 115mmHg systolic and 75mmHg diastolic upward[42] . Increased risks are present in all age groups ranging from 40 to 89 years old. For every 20mmHg systolic or 10mmHg diastolic increase in blood pressure, there is a doubling of mortality from both CHD and stroke[42] . The apparently simple direct relationship between increasing systolic blood pressure and diastolic blood pressure and cardiovascular risk is confounded by the fact that systolic blood pressure rises throughout adult age in the vast majority of populations, whereas diastolic blood pressure peaks at about age 60 in men and 70 in women, and falls gradually thereafter. This observation helps to explain why a wide pulse pressure has been shown to in some observational studies to be a better predictor of

adverse cardiovascular outcomes than either systolic blood pressure or diastolic blood pressure individually. The contribution of pulse pressure is pronounced after age of 55 years of age[41] . Because risk factors may interact positively with each other, the overall cardiovascular risk of hypertensive patients may be high even if blood pressure is only modestly raised. A high systolic blood pressure may be associated with a lower risk for developing cardiovascular risk than a low systolic blood pressure, depending on the cholesterol level and smoking status – e.g. Mortality is < 10% with a systolic blood pressure of 180mmhg, but in a non smoker with a total cholesterol of < 5mmol/L while mortality is > 10% despite a lower systolic blood pressure of only 120mmHg in the presence of smoking and cholesterol elevation. (Data based on SCORE project)[42] .

Long term observational data provide evidence that in hypertensive patients in whom treatment effectively controls blood pressure, coronary, cerebrovascular, and overall cardiovascular morbidity remains higher than that of normotensive controls. This may be accounted for by factors such as irreversible organ damage at the time treatment is started, indicating the need for early identification and management of blood pressure elevation.

Dyslipidemia

The ICMR surveillance project reported a prevalence of dyslipidemia (defined as a ratio of total to HDL cholesterol >4.5) of 37.5 percent among adults aged 15-64 yr, with an even higher prevalence of dyslipidemia (62%) among young male industrial workers[21] . The INTERHEART investigators reported that the prevalence of dyslipidemia (abnormal apolipoprotein ApoB/ApoA1 ratio) among controls without acute myocardial infarction was higher among study participants living in the five South Asian countries (45%) compared with participants from the other 47 countries represented in the study (35%). As in the overall

INTERHEART population, abnormal ApoB/ApoA1 ratio was the single largest contributor to the PAR for acute myocardial infarction in South Asian countries. The impact of dyslipidaemia on the burden of CHD has been otherwise understudied at a population level in native South Asians, despite its large contribution to CHD in other world populations.

The prevalence of dyslipidemia is increased in patients with premature CHD: as high as 75 to 85 percent compared to approximately 40 to 48 percent in age-matched controls without CHD [43, 44] . In the worldwide INTERHEART study of patients from 52 countries, dyslipidemia (defined as a raised apo B to apo A-1 ratio) accounted for 49 percent of the population attributable risk of a first MI.

Over the entire range of total and LDL cholesterol concentrations there is a strong, continuous , graded, and independent positive association with risk of cardiovascular disease. This association applies to women as well as men, and to old as well as younger people. The relationship is exponential, indicating that a given absolute difference in total or LDL cholesterol from any point in the distribution is associated with constant percentage difference in coronary heart disease risk. This association is considerably modified by other risk factors such as age, sex, smoking, blood pressure, diabetes and low HDL cholesterol.

CAD is rare in populations with total cholesterol less than 3 to 4 mmol/L (115-155 mg/dl0, even in the presence of other risk factors. Conversely, CAD is inevitable in untreated patients with the severest forms of familial hypercholesterolemia, even in the absence of other risk factors. The results of epidemiological studies, as well as trials with angiographic or clinical endpoints confirm that the reduction of LDL cholesterol must be of prime importance in both primary and secondary prevention of CVD. A meta-analysis of 38 primary and secondary prevention trials found that for every 10 percent reduction in serum cholesterol, CHD mortality

would be reduced by 15 percent and total mortality risk by 11 percent[45] .

Hypertriglyceridemia is also associated with the risk of developing cardiovascular risk, but the association is not as strong as it is for hypercholesterolemia. Although the risk of CVD does increase with hypertriglyceridemia, the risk is associated with more strongly with moderate than with severe hypertriglyceridemia, probably because the former is often due to accumulation in plasma of triglyceride rich atherogenic intermediate density lipoprotein (IDL) and small very low density lipoprotein (VLDL), whereas the latter can be due to nonatherogenic large VLDL and chylomicrons.

Low concentrations of high density lipoproteins (HDL) are clearly associated not only with early development of atherosclerosis, but also with poor outcome in those who already have CVD. The combination of moderately elevated triglycerides and low concentrations of HDL cholesterol termed as mixed dyslipidemia is very common in type 2 diabetes and people with metabolic syndrome. It is characterized by a triad of increased concentrations of IDL and VLDL, the presence of small dense LDL, and low concentrations of HDL. An increase in 1% in HDL is associated with 3% - 5% decrease in risk for women, but only a 2% decrease for men[46] .

Other lipoproteins

Lipoprotein A or Lp (a) – It is a low density lipoprotein to which an additional protein called apolipoprotein (a) is attached. It has no known physiological role and high concentrations of Lp (a) (arbitrarily >30mg/dl) are largely resistant to modification. They identify persons at increased risk of atherosclerotic disease.

Apolipoprotein B (apo B) – It is the major protein component of LDL, IDL, VLDL and truncated forms of chylomicrons. Almost all apolipoprotein B is in atherogenic lipoproteins. Concentrations of apo B are therefore a direct measure of the concentration of atherogenic lipoproteins in plasma. The measurement is a useful indicator of risk of atherosclerosis, particularly in patients with hypertriglyceridemia and in people with normal concentrations of LDL cholesterol. Values > 150mg/dl are clearly associated with increased risk[22]

Apolipoprotein A1 – It is the major apoprotein of HDL. Low concentrations of apolipoprotein A1 are, like low HDL cholesterol, associated with higher risk of cardiovascular risk.

The apolipoprotein B/A1 ratio – This ratio beyond doubt is one of the strongest risk markers. This is emphasized in INTERHEART study. This ratio showed a graded relation with myocardial infarction risk, with no evidence of a threshold, with an odds ratio of 4.73 for the top versus the lowest decile of ApoB/ApoA1 ratio. On the other hand it has been shown that the prognostic power does not change when total cholesterol/HDL ratio is replaced by the apo B/apo A1 ratio[47] .

Total cholesterol/HDL ratio – This ratio if > 5 indicates increased risk and is particularly useful in the middle range of the cholesterol distribution (190-250mg/dl). However, this ratio does not predict cardiovascular events better than simple total cholesterol measurement[42] .

Psychosocial factors

There is increasing evidence that psychosocial factors contribute independently to the risk of coronary heart disease even after statistical control for the effects of standard risk factors [22, 48,

[49] . Low socioeconomic status, lack of social support and social isolation, stress at work and in family life and negative emotions including depression and hostility have been shown to influence both the risk of contracting CHD and the worsening of clinical course and prognosis in patients with CHD [50, 51] . In addition to increasing the risk of first event and worsening the prognosis in CHD, these factors may act as barriers to treatment adherence and efforts to improve lifestyle, as well as promoting health and well being in patients and populations[52] . Psychosocial factors may contribute to the early development of atherosclerosis as well as to the acute precipitation of myocardial infarction and sudden cardiac death. The link between psychologic stress and atherosclerosis may be both direct, via damage of the endothelium, and indirect, via aggravation of traditional risk factors such as smoking, hypertension, and lipid metabolism[53] .

Obesity

Obesity is a major risk factor for the development of fatal and nonfatal cardiovascular events[54] . Body mass Index (BMI – kg/height in m^2) has been extensively used to define overweight or obesity. In adults, overweight is defined by an increased BMI ranging from 25 to 29.9 and obesity by BMI $\geq$ 30. Increasing BMI is highly associated with CVD. Increased body mass index (BMI) is associated with a higher risk of acute myocardial infarction[55] . This association is, however, attenuated or disappears after adjustment for metabolic factors, indicating the important indirect role of overweight and obesity. Other indicators apart from BMI have been proposed to assess body fat distribution. The waist-hip ratio (WHR) and waist circumference (WC) are now frequently used. Both the World Health Organisation (WHO) report on obesity[56] and the American national Heart, Lung and Blood Institute (NHLBI) expert panel on obesity[57] recommend the use of WC as an additional indicator of cardiovascular risk. WC >102cm in men and >88cm in women is the threshold at which weight reduction is

advised. Waist and hip circumference is measured with a nonstretchable standard tape measure. Waist measurements are obtained over the unclothed abdomen at the narrowest point between the costal margin and iliac crest, and hip circumferences over light clothing at the level of the widest diameter around the buttocks[22] . In healthy subjects, WC is a better predictor of acute coronary events than BMI[58] .

Obesity paradox

In patients with AMI, high BMI appears to have an unexplained protective effect on survival [59-60] . In patients with CAD, BMI does not adequately discriminate between body fat and lean body mass and may thus help to explain the controversy known as the obesity paradox[61] . The major impact of younger age in the apparent protection conferred by obesity also has been reported in most recent studies[59,62] .Young age may drive an increased use of medications and procedures, a factor that may have a favorable impact on outcomes.

Lifestyle factors

A diet rich in calories, saturated fat, and cholesterol contributes to other risk factors that predispose to CHD. Weight gain promotes the major cardiovascular risk factors and weight loss improves them. Epidemiologic data indicate that moderate alcohol intake has a protective effect on coronary heart disease[63, 64] . In addition to the amount of exercise, the degree of cardiovascular fitness (a measure of physical activity), as determined by duration of exercise and maximum oxygen uptake on a treadmill, is also associated with a reduction in CHD risk and overall and cardiovascular mortality[65] . After adjustment for age, peak exercise capacity, measured in metabolic equivalents (METs), was a stronger predictor of mortality than other established cardiovascular risk factors among men with and without CVD. For each one MET increase in exercise capacity, there was a 12 percent improvement in

survival[66] . Exercise may have a variety of beneficial effects including an elevation in serum HDL-cholesterol, a reduction in blood pressure, less insulin resistance, and weight loss.

There is growing evidence suggesting that fruit and vegetable consumption is inversely related to the risk of CHD and stroke[67] . The INTERHEART study found that lack of daily consumption of fruits and vegetables accounted for 14 percent of the PAR of a first AMI. High fiber intake is also associated with a reduction in the risk of CHD and stroke compared to low intake. In two studies of male and female health professionals, a 10 g increase in total daily dietary fiber intake was associated with a relative risk for MI of 0.81[68] .

Universal definition of myocardial infarction[69]

From the epidemiological point of view, the incidence of myocardial infarction in a population can be used as a proxy for the prevalence of CAD in that population. It is an indicator of one of the leading health problems in the world, and it is an outcome measure in clinical trials and observational studies. With these perspectives, myocardial infarction may be defined from a number of different clinical, electrocardiographic, biochemical, imaging, and pathological characteristics.

A universal definition for myocardial infarction would be of great benefit to future clinical studies in this area since it will allow for trial-to-trial comparisons as well as accurate meta-analyses involving multiple investigations. The definition of myocardial infarction employed in trials will determine the characteristics of patients entering the studies as well as the number of outcome events. Consistency among investigators and regulatory authorities with regard to the definition of myocardial infarction used in clinical investigations is essential.

In general, the conceptual meaning of the term myocardial infarction has not changed, although new sensitive diagnostic methods have been developed to diagnose this entity. Thus, the current diagnosis of acute myocardial infarction is a clinical diagnosis based on

patient symptoms, ECG changes, and highly sensitive biochemical markers, as well as information gleaned from various imaging techniques.

Criteria for acute myocardial infarction

The term myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

• Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following:

1. Symptoms of ischemia
2. ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block [LBBB])
3. Development of pathological Q waves in the ECG
4. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

• Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood.

• For percutaneous coronary interventions (PCI) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 3 × 99th percentile URL have been designated as defining PCI-related myocardial infarction. A

subtype related to a documented stent thrombosis is recognized.

• For coronary artery bypass grafting (CABG) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 5 × 99th percentile URL plus either new pathological Q waves or new LBBB,

or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium have been designated as defining CABG-related myocardial infarction.

• Pathological findings of an acute myocardial infarction.

Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior myocardial infarction:

• Development of new pathological Q waves with or without symptoms.

• Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischemic cause.

• Pathological findings of a healed or healing myocardial infarction.

Clinical classification of different types of myocardial infarction

TYPE 1 - Spontaneous myocardial infarction related to ischemia due to primary coronary event such as plaque erosion and / or rupture, fissuring, or dissection.

TYPE 2 - Myocardial infarction secondary to ischemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension or hypotension.

TYPE 3 - Sudden unexpected cardiac death, including cardiac arrest, often with symptoms

suggestive of myocardial ischemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and / or at autopsy, but death occurring before blood samples could be obtained, or at time before the appearance of cardiac biomarkers in the blood.

TYPE 4a – Myocardial infarction associated with PCI.

TYPE 4b – Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy.

TYPE 5 – Myocardial infarction associated with CABG.

Reperfusion strategy in STEMI

Prompt and complete restoration of flow in the infarct-related artery by thrombolysis or percutaneous coronary intervention is the mainstay of management of acute ST-segment elevation myocardial infarction. Regardless of the mode of reperfusion, the overreaching concept is to minimize total ischemic time, which is defined as the time from onset of symptoms of STEMI to initiation of reperfusion therapy.

Thrombolysis in STEMI

Reperfusion therapy is underutilized in patients with STEMI. Despite improvements in care, up to one-third of patients presenting with STEMI within 12 hours of symptom onset still receive no reperfusion therapy acutely. In analyses of data from the NRMI-2 database[70] , and the GRACE (Global Registry of Acute Coronary Events) study[71] , factors associated with eligible patients not receiving reperfusion therapy included age ≥75 years, female gender, presentation without chest pain, and a history of CVD. In addition, the EDQMI (Emergency Department Quality in Myocardial Infarction) study found that failure to identify high-risk electrocardiogram (ECG) findings in patients with acute MI was associated with greater odds

of ideal candidates not receiving reperfusion therapy[72]. The 2004 ACC/AHA guidelines provide recommendations on selecting a reperfusion strategy for patients with STEMI. The first step is to determine time from onset of symptoms, the presence of high-risk attributes, the relative risks associated with fibrinolysis, and estimated total time required for achieving PCI balloon inflation; these factors logically determine treatment selection. An invasive strategy is generally preferred if first door-to-balloon time can be realistically achieved within 90 min if there is high risk from STEMI or fibrinolysis is contraindicated[73] . The first of these criteria sets an important benchmark, and it should be noted that the goal of performing primary PCI within 90 minutes of first medical contact represents the longest time that should be considered acceptable rather than the ideal time frame[74] . Yet registry data have shown that a door-to-balloon time of <90 minutes is not achieved in the majority of patients undergoing primary PCI, particularly if transfer is required[75, 76]. These data suggest that many STEMI patients are being denied the optimal treatment for prompt reperfusion. Fibrinolysis is preferred if <3 hours have elapsed from symptom onset, there is an anticipated delay that decreases the potential advantage of PCI, or an invasive strategy is not an option (e.g., owing to vascular access difficulties or lack of access to a skilled PCI laboratory with skilled operators)[73] .Thus, within 3 hours of symptom onset, in the absence of delays to initiating an invasive strategy, the ACC/AHA guidelines indicate that there is no preference for either PCI or fibrinolysis[73]. A recent pooled analysis suggested a consistent advantage of primary PCI over fibrinolysis regardless of time from symptom onset to presentation[77]. However, Gersh and Antman[78] have commented that this conclusion is controversial, and cautioned that analyses such as this should not be used as justification for exclusively choosing a strategy of primary PCI without taking into account a realistic estimate of the time needed to implement this strategy in all clinical settings.

The early-open-artery theory suggests that benefits of reperfusion in patients with STEMI are

directly related to the speed and completeness with which patency of the infarct-related coronary artery is re-established. Mortality has been shown to be lower among patients in whom TIMI flow grade 2 to 3, compared with TIMI flow grade 0 to 1, was achieved within 90 minutes after AMI[79]. This is strongly supported by clinical studies confirming the important relationship between achieving prompt antegrade coronary flow of the infarct artery and improved clinical outcomes, for both primary PCI[80-84] and fibrinolysis[85-87]. An analysis by Boersma et al. indicated that the 35-day mortality benefit associated with early treatment equated to 1.6 lives per 1,000 patients per hour of delay from symptom onset to treatment, with even more of an impact of time in the early hours[86]. However, the recent Occluded Artery Trial showed that PCI provided no delayed benefit over optimal medical therapy alone in stable patients with persistent total occlusion of the infarct-related coronary artery 3 to 28 days after AMI who met criteria for high risk[88], indicating that there is no indication to open an occluded vessel outside the therapeutic window in an asymptomatic patient following STEMI.

In theory the ideal figure for the use of thrombolytic therapy is the sum of patients eligible on ECG criteria minus those who have clear contraindications for treatment, either because of perceived risk of bleeding or if the delay after the onset of symptoms is excessive. In practice this figure is not easily determined because neither cardiographic appearances nor contraindications are categorical variables and are subject to individual interpretation. In one UK based study[89] of 13628 patients with a final diagnosis of definite myocardial infarction 75.7% were considered eligible for thrombolytic therapy. Of these 85.9% were administered thrombolytic therapy and 14.1% were considered late for thrombolytic therapy or had clinical contraindications.

The most common thrombolytic agents have been streptokinase (first generation thrombolytic agent) and alteplase (tissue type plasminogen activator, t-PA, second generation thrombolytic agent). In the meantime, third generation thrombolytic agents have reached clinical practice.

Many of them are derivatives of alteplase, the current gold standard for thombolytic therapy in acute coronary syndromes with STEMI. The most prominent among them are reteplase, tenecteplase, and lanoteplase. Reteplase (recombinant plasminogen activator, r-PA) is a single chain deletion mutant of alteplase that is expressed in Escherichia coli and, therefore, is expressed as an unglycosylated protein. Reteplase includes 355 amino acids with a total molecular weight of 39 kDa. The molecule consists of cringle 2 and the protease domain of the alteplase molecule. Because of the deletion of the fibronectin finger region, the binding of reteplase to fibrin is significantly reduced in comparison with that of alteplase. Although kringle 2 (known to stimulate protease in the presence of fibrin) is part of the reteplase molecule, reteplase is stimulated in the presence of fibrin to a lower extent than alteplase, suggesting that the fibronectin finger is involved in the stimulation of the protease as well. Reteplase, in comparison with alteplase, is characterised by reduced fibrin selectivity. In the absence of fibrin, reteplase and alteplase do not differ with respect to their activity as plasminogen activators, nor do they differ with respect to their inhibition by the plasminogen activator inhibitor type 1 (PAI-1). Tenecteplase is also called the TNK-mutant of alteplase. The molecule does not constitute a deletion mutant of alteplase (as reteplase does). Instead, it consists of the alteplase molecule with the exception of three point mutations. At position 103 of the polypeptide the amino acid threonine has been replaced by asparagine leading to a new glycosylation site. The carbohydrate chain that is linked to this site enlarges the molecule, thereby reducing its elimination and prolonging its plasma half life. At position 117, asparagine has been replaced by glutamine. By the exchange of this amino acid the carbohydrate side chain that facilitates hepatic elimination has been removed. Hence, plasma half life is further prolonged. Finally, at position 296–299 the amino acids lysine, histidine, arginine, and arginine have been replaced by four amino acids alanine. Consequently, the inhibition by PAI-1 is reduced 80 times in comparison with alteplase. In the

ASSENT-1 (assessment of safety and efficacy of a new thrombolytic agent) trial in patients with AMI,, single bolus tenecteplase proved to be as safe as the gold standard of thrombolytic therapy, the accelerated regimen of alteplase (initial bolus followed by an infusion over 90 minutes)[90]. In the TIMI-10B (thrombolysis in myocardial infarction) trial single bolus administration of 40 mg tenecteplase achieved the same rate of patency at 90 minutes after the initiation of thrombolytic therapy as alteplase in the accelerated regimen did[91] . In the ASSENT-2 trial tenecteplase and alteplase were equal with respect to total mortality after 30 days [92].

The plasminogen activator lanoteplase (novel plasminogen activator, n-PA) is another deletion mutant of the alteplase molecule that also exhibits an additional, single point mutation. In comparison with alteplase the fibronectin finger region and the epidermal growth factor domain have been deleted in the lanoteplase molecule. In addition, in kringle 1, at position 117 the amino acid asparagine has been replaced by glutamine. Because of this point mutation the glycosylation site that is responsible for facilitated hepatic elimination is lost. Consequently, the plasma half life of lanoteplase is increased. The plasma half life of lanoteplase is about 10 times that of alteplase and may reach 45 minutes. In the thrombolytic treatment of an acute myocardial infarction lanoteplase can be administered as a single bolus. In the InTIME-1 (intravenous n-PA for treatment of infarcting myocardium early) trial, treatment with 120 kU lanoteplase per kg body weight resulted in a higher patency rate of the infarct related coronary artery at 90 minutes than treatment using alteplase in the accelerated regimen[93] . However, with respect to overall mortality at 30 days lanoteplase and alteplase were equally effective (InTIME-2 trial)[94].

Combination therapy

In the field of reperfusion therapy in acute myocardial infarction, the term "combination therapy" is most often used to describe the combined use of reduced dose plasminogen activators and full dose glycoprotein (Gp) IIb/IIIa inhibitors. The latter block the Gp IIb/IIIa receptors at the surface of activated platelets and, subsequently, platelet aggregation, the major mechanism in reocclusion. Since the activated receptor constitutes the final common pathway of platelet activation, the Gp IIb/IIIa inhibitors form the most potent antiplatelet therapy now available. Among them abciximab, eptifibatide, and tirofiban have proven their clinical efficacy.

In the TIMI 14 trial alteplase at half dose (15 mg as an initial bolus, 35 mg as an infusion over 60 minutes) combined with abciximab at full dose (0.25 mg/kg as an initial bolus, 10 µg/min as an infusion over 12 hours) yielded the highest patency rate 90 minutes after the initiation of treatment (TIMI 3 flow in 76% of treated patients) without increasing the risk of severe bleeding complications[95] . In the SPEED (strategies for patency enhancement in the emergency department) trial a patent coronary artery could be achieved more often with the combination of reteplase in half dose (a double bolus of 5 U each, 30 minutes apart) and abciximab in full dose than with reteplase in full dose alone[96]. However, in the GUSTO V trial the higher patency rate of this regimen could not be translated into reduced mortality after 30 days[97]. In the ASSENT 3 trial half dose tenecteplase combined with abciximab was compared with full dose tenecteplase alone[98]. With respect to the primary end point (a composite end point combining 30 day mortality, in-hospital re-infarction, or in-hospital refractory ischemia), the combination therapy was superior to monotherapy with plasminogen activator but without Gp IIb/IIIa inhibitor, although with higher bleeding rates with combination therapy. Double-bolus eptifibatide (180/2/180) plus half-dose TNK tended to improve angiographic flow and ST-segment resolution compared with TNK monotherapy but was associated with more

transfusions and non-cerebral bleeding[99] .

Primary PCI in STEMI

Treatment of acute STEMI has undergone a major revolution over the past 15 years, with the recognition that intracoronary thrombosis is the final mechanism of vessel occlusion and the understanding that the prompt reestablishment of vessel patency offers significant clinical benefits[100, 101]. Widely used thrombolytic regimens currently achieve complete reperfusion by 90 minutes in about 55% to 60% of cases and partial reperfusion in an additional 20 % to 25%[102]. Atleast 10% of vessel opened by thrombolysis either reocclude or cause recurrent angina during hospitalization owing to persistence of an underlying high grade atherosclerotic stenosis.

Primary PCI refers to the use of angioplasty to achieve reperfusion in patients with ST elevation myocardial infarction instead of thrombolysis. Primary PCI generally yields significantly higher rates of complete reperfusion than does thrombolytic therapy. In addition, the underlying coronary stenosis, a substrate for recurrent ischemia is relieved early in the course of the infarction. The potential of theses attributes of PCI to improve clinical outcome beyond that achievable with thrombolytic therapy has led to randomized control clinical trials directly comparing these two approaches.

Initially suitable only for highly selected low risk patients, percutaneous coronary revascularization has evolved into a vital component of the management of acute coronary syndromes (ACS). Remarkable advances in catheters, stents, adjunctive pharmacologic therapy, imaging and operative techniques have expanded the application of percutaneous coronary intervention to patients with clinically and anatomically complex coronary heart disease.

The largest single trial of this type GUSTO II B compared direct angioplasty and accelerated

tissue plasminogen activator (tPA) therapy in 1138 patients[103]. The primary end point (a composite of death, non fatal reinfarction or nonfatal disabling stroke at 30 days) occurred in 9% of the angioplasty group and 13.7% in the tPA group (p=0.03) for a 33% risk reduction. A secondary analysis at 6 months still favoured angioplasty, although the difference between the 2 strategies was no longer statistically significant (primary end point occurred in 14.7% of angioplasty patients and 16.1% of tPA patients).

A meta analysis of GUSTO II B and 9 other randomized trials comparing direct angioplasty and various thrombolytic regimens also supports the superiority of direct PCI when practiced in centres with on site coronary catheterization[104] . The widely used end point of 30 day mortality or re-infarction was significantly lower among patients treated with direct PCI than among those given thrombolytic therapy.

There has been a concern regarding the safety of stents in the highly thrombotic setting of STEMI. Direct angioplasty with stenting has been tested against balloon angioplasty alone in randomized trials[105, 106] . In the Stent PAMI study[105] , the prespecified primary 6 month end point (a composite of death, nonfatal myocardial infarction, stroke or target vessel revascularization) occurred less frequently with stenting than without stenting (12.6% vs. 20.1%, P<0.01).

It has been suggested that vigorous plaque and thrombus compression associated with primary PCI in general and stent deployment in particular may increase athero and thromboembolic plugging of downstream microvessels. Such a phenomenon could paradoxically increase infarct size. This has led to the investigators testing the administration of glycoprotein IIb/IIIa inhibitors during PCI. Studies have shown that the addition of glycoprotein IIb/IIIa inhibitors during stent based primary PCI do indeed improve coronary blood flow and reduce infarct size[107-109].

A comprehensive review by Keeley and colleagues included 23 trials in a meta analysis[110]. It

showed that Primary PTCA was better than thrombolytic therapy at reducing overall short-term death (7% *vs.* 9%; p=0·0002), non-fatal reinfarction (3% *vs.* 7% ; p<0·0001), stroke (1% *vs.* 2% ;p=0·0004), and the combined endpoint of death, non-fatal reinfarction, and stroke (8% *vs.* 14% ; p<0·0001). The results seen with primary PTCA remained better than those seen with thrombolytic therapy during long-term followup, and were independent of both the type of thrombolytic agent used, and whether or not the patient was transferred for primary PTCA.

2007 focused update of the ACC/AHA 2004 Guidelines for the management of patients with STEMI states that all patients diagnosed to have STEMI presenting to a hospital with PCI capability should be treated with primary PCI within 90 minutes of first medical contact as a systems goal (Class IA). STEMI patients presenting to a hospital without PCI capability and who cannot be transferred to a PCI centre and undergo PCI within 90 minutes of first medical contact should be treated with fibrinolytic therapy within 30 minutes of hospital presentation as a systems goal unless fibrinolytic therapy is contraindicated (Class IB)[111] .

METHODOLOGY

This is an observational study done in 150 consecutive patients who presented with acute STEMI between November 2008 to January 2009 to the accident and emergency department and chest pain unit of a tertiary care centre in a district capital in South India.

Inclusion criteria

Patients aged > 18 years and presenting within 7 days of acute ST-segment elevation myocardial infarction were included.

Exclusion criteria

Patients aged < 18 years

Patients presenting after 7 days of acute ST-segment elevation myocardial infarction

Patients presenting with non ST-segment elevation myocardial infarction or unstable angina.

Demographic profile

Demographic data including age, sex and socioeconomic status of the patients were recorded. Socioeconomic score was obtained according to modified Kuppuswamy's socioeconomic status scale and the patients were stratified into 5 groups accordingly[112]. Patient's symptoms at the time of presentation were noted. The place of first medical contact was recorded as whether it was the local practitioner / the government hospital or the accident and emergency unit/ chest pain unit of the tertiary care centre.

Assessment of time delays in presentation of STEMI

Pre-hospital delay was defined as the time between the onset of symptoms suggestive of acute coronary disease and arrival at the accident and emergency department / coronary care unit[113]. The time delay from onset of symptom to that of presentation to any hospital was recorded. If the patient had presented to the local practitioner/government hospital initially, the time delay of transport form the first referral center to the tertiary care hospital was also recorded. The pre-hospital delay was taken as the total time delay from onset of symptoms to final presentation at the accident and emergency unit or the chest pain unit of the tertiary care centre. The door-to-needle time for thrombolytic therapy and door-to-balloon time were recorded for primary PCI. The time delay for transfer from the accident and emergency department of the tertiary care centre to the chest pain unit was also recorded. All patients who were thrombolysed elsewhere but presenting to the tertiary care hospital for further

management within 7 days of STEMI were also included in the study.

Risk factor profile

The risk factor profile of patients including diabetes, hypertension, smoking status, past history of ischemic heart disease, family history of ischemic heart disease, dyslipidemia and postmenopausal status in case of female sex was recoded. Smoking status was recorded as non smoker or former smoker or current smoker. Current smokers were defined as individuals who smoked any tobacco in the previous 12 months and included those who had quit within the past year. Former smokers were defined as those who had quit more than a year earlier. Non smokers were who never smoked in their lifetime.

The body mass index was calculated after measuring the height and weight of patients whenever possible.

Clinical and laboratory profile

The clinical parameters including pulse rate, blood pressure and Killip class at the time of presentation was recorded. 12 lead ECG was taken within 10 minutes of presentation or as early as possible to the tertiary care centre. Following criteria was used for the definition of STEMI: chest pain of >20 min duration and ST segment elevation >1 mm in at least two standard limb leads or >2 mm in at least two contiguous precordial leads or the presence of new onset left bundle branch block in the electrocardiogram. CK-MB and Troponin I were subsequently done to confirm diagnosis of acute myocardial infarction. 12 lead ECG was repeated 90 minutes after thrombolysis and immediately after primary PTCA to calculate ST segment resolution. ST segment resolution >50% was taken as a marker for reperfusion as per 2004 ACC/AHA guidelines[114]. The location of MI was determined as per the electrocardiogram. Laboratory profile including hemoglobin, total and differential white cell

counts, AC, PC , lipid profile within 24 hours of myocardial infarction, cardiac enzymes – troponin I and CK-MB, creatinine was measured. 2D echocardiography was done during the course of hospital stay and cardiac internal dimensions, ejection fraction, diastolic function were recorded and presence or absence of mechanical complications assessed.

Management strategy

All patients were given options of primary PCI and thrombolysis whenever appropriate and treatment strategy was initiated after patients consent for the appropriate strategy. Patients were treated conservatively if they were not eligible for thrombolysis and were not willing for a primary PCI. If the patient opted for thrombolysis, it was done using either streptokinase or tenecteplase which was decided after giving the options of both to the patient and according to financial affordability. Primary PCI was done using standard protocol and stents implanted whenever indicated.

All patients were given standard pharmacotherapy which included aspirin, clopidogrel, beta blockers and angiotensin converting enzyme inhibitors (if not contraindicated) and statins. Other drugs such as nitrates, diuretics, digoxin and angiotensin receptor blockers were used appropriately as per clinical needs. Temporary pacemaker insertion was done when deemed appropriate. Patients were given anticoagulant therapy whenever clinically indicated and the type of anticoagulant therapy was recorded.

Assessment of in-hospital outcomes

All patients were monitored in hospital for clinical outcomes including mortality, recurrent angina, re-infarction, arrhythmias, heart failure, stroke, bleeding, mechanical complications and requirement of rescue PCI. Coronary angiography and PCI (adjunct PCI) was done during the hospital stay whenever deemed necessary and at the affordability of the patient.

Duration of hospital stay was recorded.

Assessment of outcomes at 30 days

Patients were followed up at the end of 30 days in the outpatient department and 30 day outcomes which included mortality, recurrent angina, re-infarction, heart failure, arrhythmias and stroke were recorded. Patients who did not follow up in the outpatient department at the end of 30 days were contacted by telephone or by post and 30 day outcomes obtained.

Statistical analysis

All data were analyzed using SPSS Software (17.0 versions). Categorical variables were compared by the likelihood ratio Chi-square test or Fisher's exact test. Continuous variables are presented as mean ± SD and assessed by independent sample T tests. Predictors of pre-hospital delay were analyzed by logistic regression. A probability value of <0.05 was considered statistically significant.

RESULTS

Over a 3 month period 150 consecutive patients with ST-segment elevation myocardial infarction were enrolled into this study. The results of demographic, socioeconomic, risk factor, clinical and laboratory profile, pattern of presentation and management, in-hospital and 30 day outcomes are presented below.

Table 1: Demographic Characteristics

	Total 150 (100)	Male 117 (78)	Female 33 (22)	p
Age in years	57±12	56±12	60±10	0.10
Socioeconomic Status				
Upper	20 (13.3)	14(12)	6(18.2)	0.52
Upper middle	21 (14)	17(14.5)	4(12.1)	0.94
Lower middle	63 (42)	48(4.1)	15(45.5)	0.79
Upper lower	33 (22)	26(22.2)	7(21.2)	0.93
Lower	13 (8.7)	12(10.3)	1(3)	0.39

Data are number (%) or mean ± SD.

Table 2: Place of first medical contact

	N (%)
Local practitioner / primary/ secondary care hospital	107 (71.3)
A&E of tertiary care centre	19 (12.7)
Chest Pain Unit of tertiary care centre	24 (16)

A&E – accident and emergency unit

Table 3: Pre-hospital delay, door-to-needle time, door-to-balloon time

	Total	Male	Female	p
Time to first contact	308 ±577	249 ±459	520±854	0.01
Pre-hospital delay	403±589	3522±92	39±9335	0.08
D2N time	55±51	49±52	39±47	0.88
D2B time	87±32	83±34	95±29	0.56
A&E to CPU	63±44	60±44	71±42	0.34
Local Hospital to CMC	158±151	147±145	192±165	0.17

All data are Mean ± SD (in minutes), D2N – door-to-needle time, D2B- door-to-balloon time, A&E – accident and emergency unit of tertiary care centre, CPU – chest pain unit of tertiary care centre.

The median pre-hospital delay was 4 hours. The median door-to-needle time was 45 minutes. The median door-to-balloon time was 92 minutes. The mean pre-hospital delay in hours was 6.7±9.8 hours. The mean pre-hospital delay in hours for men and women were 5.5±7.9 hours and 10.8±13.9 hours respectively (P=0.003). After excluding all patients who presented later than 12 hours, the mean pre-hospital delay was 4.5±3.1 hours and the mean pre-hospital delay in men and women was 4.3±3.1 hours and 5.2±3.2 hours respectively(P=0.205)

Skewness and Kurtosis value for pre-hospital delay was 4.761 (SE 0.198) and 27.9 (SE 0.394) respectively.

Table 4: Comparison of door to needle time among patients presenting initially to A&E / Chest Pain Unit of tertiary care centre

	A&E of tertiary care centre	Chest Pain Unit of tertiary care centre	p
Frequency (Percentage)	17	19	
Door to needle time Mean ±SD	65.3±39.1	32.1±39.1	0.017

A&E – accident and emergency unit of tertiary care centre

Table 5: Characteristics associated with prolonged Pre-hospital delay

Characteristics	Pre-Hospital Delay		P value	OR (95% CI)
	≤ 6 Hours n=100	≥ 6 Hours n=50		
Women	16(16)	17(34)	0.012	2.7(1.2-5.9)
Age in years (mean ±SD)	58±12	56±11	0.385	
Diabetes Mellitus	49(49)	24(48)	0.908	1.04(0.53-2.05)
Hypertension	46(46)	18(36)	0.243	1.51(0.75-3.05)
Smoking	33(33)	18(36)	0.715	0.8(0.43-1.79)
Family history of IHD	4(4)	1(2)	0.520	2.04(0.22-18.7)
Past history of IHD	7(7)	0(0)	0.05	1.53(1.36-1.73)
Location of MI			0.84	
Anterior wall	49(49)	27(54)	0.68	
Inferior wall	47(47)	21(42)	0.68	
Lateral wall	4(4)	2(4)	1.0	
BMI			0.771	
<18.5	4(4.5)	3(6.7)	0.91	
18.5-24.9	52(59.1)	28(62.2)	0.87	
25-29.9	27(30.7)	13(28.9)	0.98	
>30	5(5.7)	1(2.2)	0.63	

Table 6: Symptom at presentation

	Frequency (percentage)	Male n(%)	Female n(%)	p
SYMPTOMS				
Chest pain	147 (98)	116(99.1)	31(93.9)	0.059
Dyspnoea	24(16)	16 (13.7)	8(24.2)	0.144
Palpitation	4(2.7)	4(3.4)	0(0)	0.28
Giddiness	12(8)	10(8.5)	2(6.1)	0.64
Syncope	2(1.3)	1(0.9)	1(3)	0.33
Sweating	44(29.3)	32(27.4)	12(36.4)	0.31
Vomiting	14(9.3)	17(15)	2(6)	0.31

Table 7: Risk factor profile

Risk factors	Frequency (percentage)	Male n (%)	Female n (%)	p
Diabetes Mellitus	73(48.7)	49(41.9)	24(72.7)	0.002
Hypertension	64(42.7)	46(39.3)	18(54.5)	0.18
Smoking	51(34)	50(42.7)	1(3)	0.00
Family History of IHD	5(3.3)	4(3.4)	1(3)	0.91
Past History of IHD	7(4.7)	6(5.1)	1(3)	0.61
Dyslipidemia	1(0.7)	1(0.9)	0(0)	0.59
Post Menopausal		0(0)	29(88)	-
No risk Factors	21(14)	20(17.1	1(3)	0.04

Figure 1. Risk factor profile

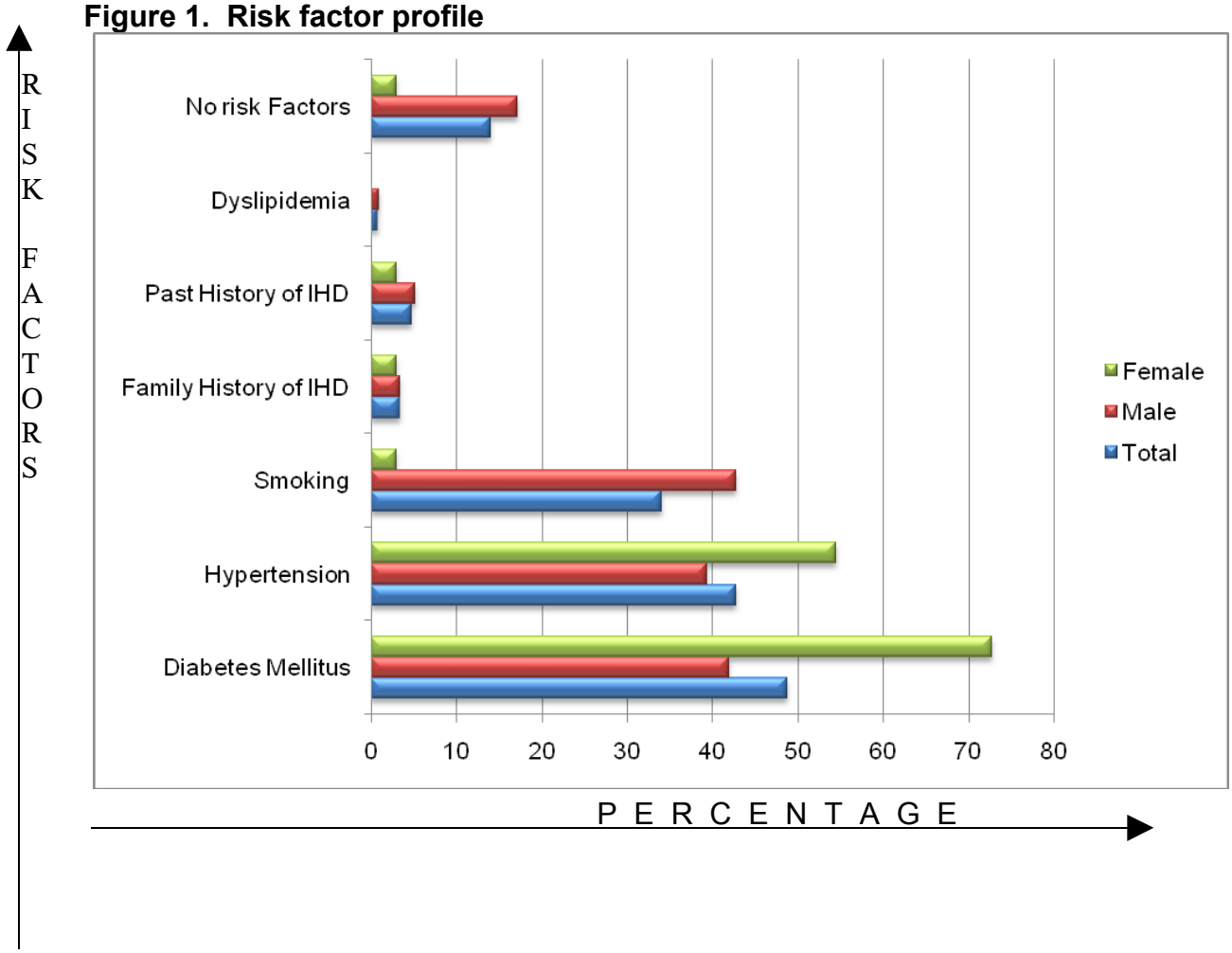


Table 8: Body mass index

BMI	Frequency (%)	Male	Female	p
Mean	23 ± 6	23.9±2.8	23.9±3.9	0.976
<18.5	7 (5.2)	5(4.8)	2(7.1)	0.98
18.5-24.9	80 (60.1)	63(60)	17(60.7)	0.94
25-29.9	40 (30.0)	33(31.4)	7(25)	0.66
>30	6 (4.5)	4(3.8)	2(7.1)	0.81

BMI of 23.0 has been identified as the cut off in Asians for predicting the risk of CVD. The number of patients who had a BMI of greater than 23.0 was 85(56%).

Table 9: Location of myocardial infarction

	N (%)
ANTERIOR	76 (50.7)
ASMI	33(22)
EXTENSIVE AWMI	43(28.7)
INFERIOR	68(45.3)
INFERIOR	9(6.0)
INFERIOR+RVMI	26(17.3)
INF+RV+PWMI	10(6.7)
INF+PWMI	23(15.3)
LATERAL	6(4.0)
LATERAL	3(2.0)
PW + LWMI	3(2.0)

The most common location of acute myocardial infarction involved the anterior wall. Inferior wall myocardial infarction, either isolated or associated with right ventricular and / or posterior wall was observed in 45.3%. Lateral wall myocardial infarction was rare.

Table 10: Killip class & Ejection fraction.

KILLIPS	Frequency (%)	Male	Female	p
I	122(81.3)	100 (85.5)	22(66.7)	0.02
II	8(5.3)	5(4.3)	3(9.1)	0.51
III	8 (5.3)	4(3.4)	4(12.1)	0.12
IV	12 (8.0)	8(6.8)	4(12.1)	0.53
EF	45 ± 9	45.1± 9	46.3 ± 8	0.51

Data are number (%) or mean ± SD.

Table 11: Laboratory profile

	Mean± SD	Male	Female	p
Hemoglobin	13. ±72.3	14. ±51.9	11.3±1.9	0.00
Total count	13108±4818	1305±84956	13279±4392	0.81
AC	160±65	15±662	17±474	0.18
PC	18±686	181±81	206±100	0.16
Creatinine	1.0±80.33	1.07±0.27	1.1±50.50	0.22
Troponin	34. ±857	30±55	51±61	0.07
CKMB	98±95	96±95	103±95	0.70
Total Cholesterol	190±43	188±37	199±59	0.19
TG	161±106	15±281	191±168	0.08
HDL	35±9	34±7	37±14	0.07
LDL	12±237	121±33	12±749	0.45
Newly detected DM	8(5.3)	8(7.1)	0	0.12
Newly detected Dyslipidemia	106(70.7)	85(76.6)	21(65.6)	0.21

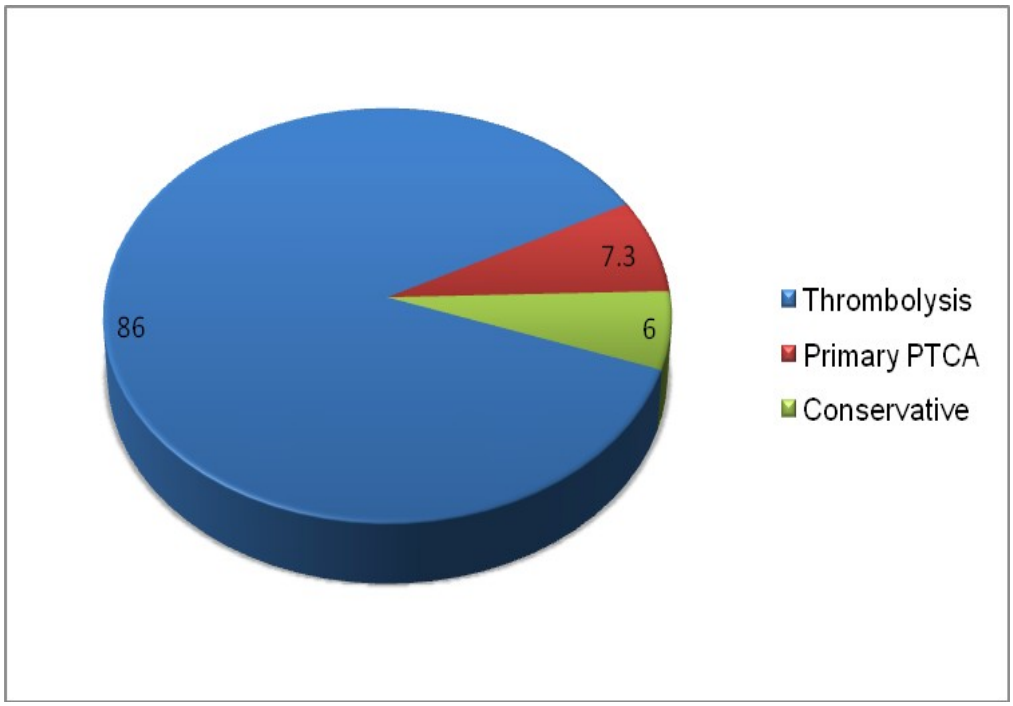
Data are number (%) or mean ± SD.

Women had significantly lower levels of hemoglobin. Troponin levels at time of presentation were significantly higher in females. About 70% were newly diagnosed to have dyslipidemia based on LDL level > 100mg/dl.

Table 12: Management strategy

	N (%)
Reperfusion Strategy	
Thrombolysis	130 (86.7)
Primary PTCA	11(7.3)
Conservative	9(6)
Thrombolytic Agent Used	130(100)
Streptokinase	124(95.4)
Tenecteplase	6(4.6)

Figure 2. Management strategy*



* - Number in pie chart represents percentages

Table 13: Comparison of management strategy with respect to pre-hospital delay

	Pre-Hospital Time delay in hours		
Management Strategy	<6	6-12	>12
Thrombolysis	93 (88.6)	30(93.8)	7(53.8)
Primary PTCA	9(8.6)	2(6.3)	0(0)
Conservative	3(2.9)	0(0)	6(46.2)

Data are number (%) of patients

Table 14: Effect of pre-hospital delay and reperfusion strategy on ECG ST-segment resolution.

ECG ST RESOLUTION	< 50	> 50	p
N (%)	53 (35.3)	89(59.3)	
Pre-hospital delay			0.02
<6 hours	33(62.3)	66(74.2)	0.19
6-12 hours	11 (20.8)	20(22.5)	0.97
>12 hours	9(17)	3(3.4)	0.01
Reperfusion strategy			0.09
Thrombolysis	47(38.2)	76(61.8)	0.76
Primary PTCA	1(9.1)	10(90.9)	0.09

Table 15: Coronary angiography findings

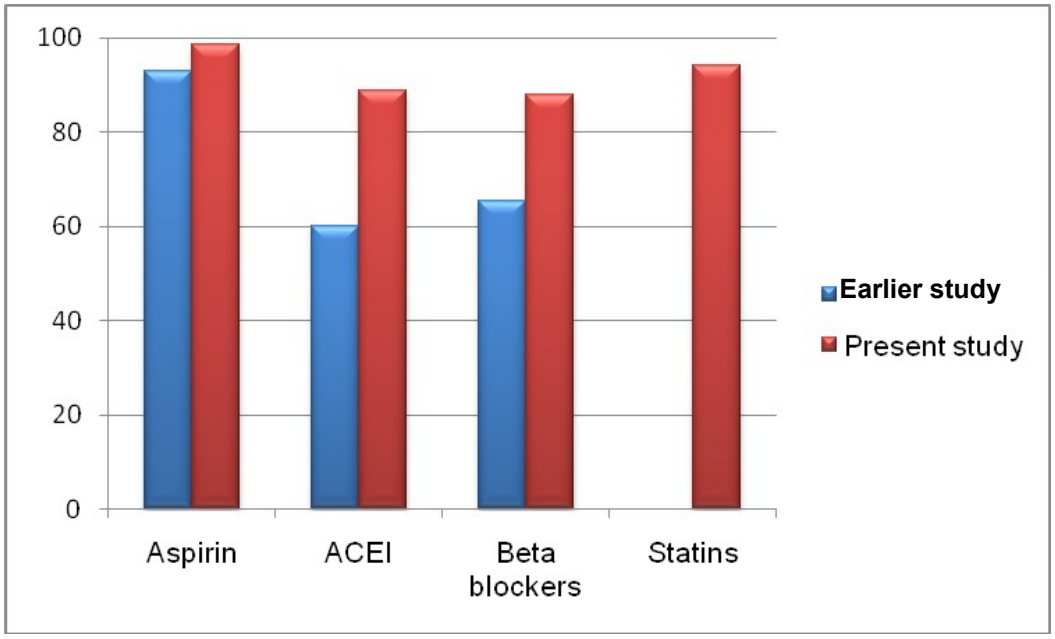
	N (%)
CAG at index admission	28 (18.7)
No of vessels involved	
SVD	16(59.3)
DVD	7(25.9)
TVD	4(14.8)
Type of stent used	24(85)
DES	3(12.5)
BMS	21(87.5)

SVD- single vessel disease, DVD – double vessel disease, TVD- triple vessel disease
DES – drug eluting stent, BMS – bare metal stent

Table 16: Pharmacotherapy

	N (%)
Aspirin	148 (98.7)
Clopidogrel	146(97.3)
ACEI	133(88.7)
Beta blockers	132(88)
Statins	141(94)
Nitrates	43(28.7)
Diuretics	43(28.7)
ARB	1(0.7)
TPI	5(3.3)
Digoxin	4(2.7)
Anticoagulants	**47(31.3)**
Heparin	7(4.7)
LMWH	32(21.3)
Fondaparinux	8(5.3)
None	103(68.7)

Figure 3. Comparison of prescription of medical therapy between earlier study* and present study

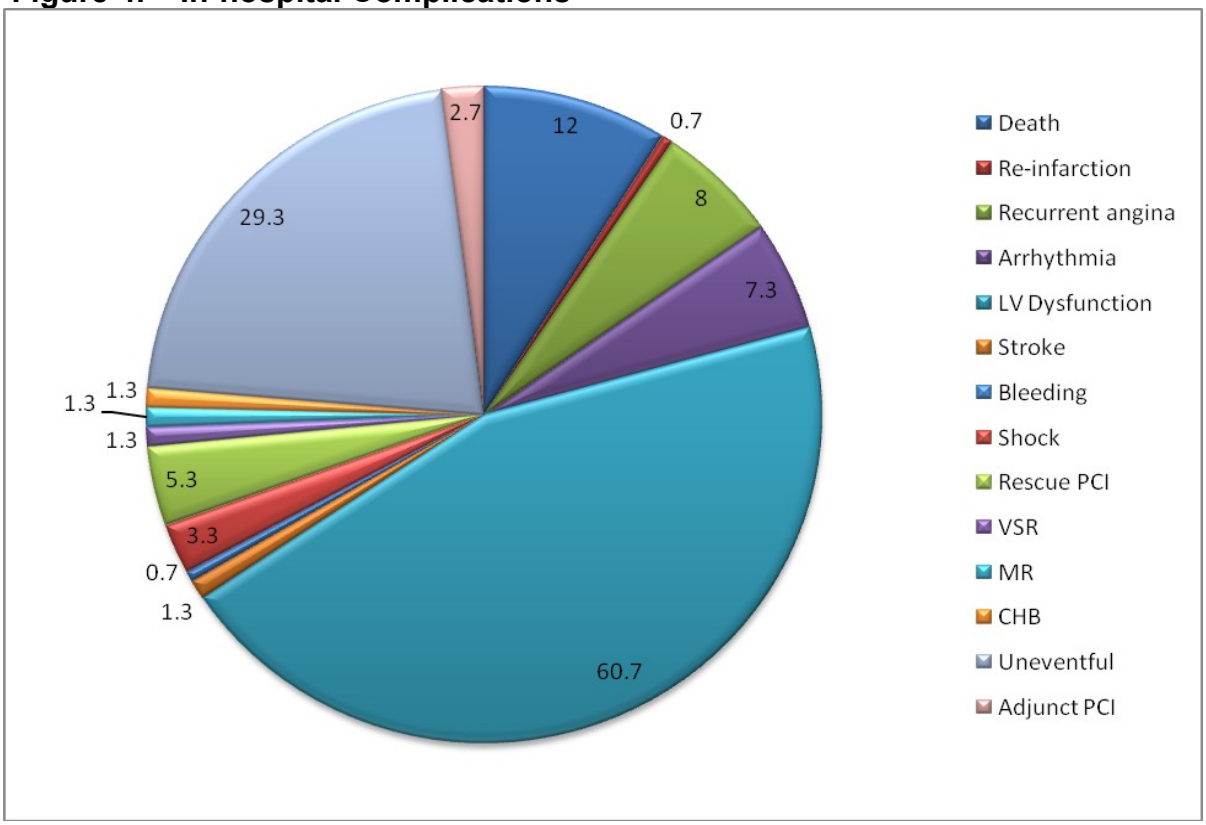


* - Jose et al [115]

Table 17: In-hospital Complications

Complications	N (%)
Death	18(12)
Re-infarction	1(0.7)
Recurrent angina	12(8)
Arrhythmia	11(7.3)
LV Dysfunction	91(60.7)
Stroke	2(1.3)
Bleeding	1(0.7)
Shock	5(3.3)
Rescue PCI	8(5.3)
VSR	2(1.3)
MR	2(1.3)
CHB	2(1.3)
Uneventful	44(29.3)
Adjunct PCI	4(2.7)

Figure 4. In-hospital Complications*



* - Number in pie chart represents percentages

Table 18: Duration of hospital stay

	Duration of Hospital stay in days		
Management Strategy	Mean±SD	Median	Range
Thrombolysis	2.5±2	2	1-17
Primary PTCA	3.6±2.2	3	1-9
Conservative	3.4±1.7	3	1-6
Overall	2.6 ±2		

Table 19: Characteristics of patients with in-hospital mortality

	Total N=18	P
Age (Mean±SD)	60±12	0.19
Male	12 (67)	0.35
Diabetes Mellitus	9 (50)	0.91
Hypertension	7 (39)	0.73
Smoking	4 (22)	0.26
Pre Hospital delay >6 hrs	5 (28)	0.59
Management Strategy		1.0
Thrombolysis	16 (88)	0.76
Primary PCI	1 (6)	0.75
Conservative	1 (6)	0.95
ECG ST resolution <50%	9 (50)	0.002
Ejection Fraction (in %)	34.6±8.1	<0.002

Data are number (%) or Mean±SD

The mean ejection fraction in those who survived is 46.1±8.4%. The mean age in those who survived is 56.6±11.4 years.

Table 20: Causes of In-hospital Mortality

Cause Of Death	Total N=18 (100)	Male N=117(100)	Female N=33(100)
Heart Failure	11(61)	6(5.1)	5(15)
Arrhythmias VT/VF	3(16.6)	2(1.7)	1(3)
Suspected Myocardial rupture	2(11.1)	2(1.7)	0(0)
Re-infarction/ CHB	1(5.5)	0	1(3)
Ventricular Septal Rupture	1(5.5)	1(0.8)	0(0)

Data are number (%)

Table 21: Thirty Day outcome

Outcome	N (%)
Death	1(0.7)
Re-infarction	4(2.7)
Arrhythmias	-
Angina	18(12)
Heart Failure	17(11.3)
Stroke	-
Uneventful	93(62)
Lost to follow up	4(2.7)

Table 22: Baseline characteristics, management strategy and treatment outcomes by socioeconomic strata

Characteristics	Upper 20(13.3)	Middle 84(56)	Lower 46(30.7)	P
Diabetes Mellitus	13(65)	33(39.3)	27(58.7)	0.031
Hypertension	9(45)	35(41.7)	20(43.5)	0.955
Smoking	3(15)	29(34.5)	19(41.3)	0.115
Place of first visit				0.044
Local Hospital	18(90)	60(71.5)	20(63.3)	
A & E	0 (0)	8(9.5)	11(23.3)	
Chest pain Unit	2 (10)	16(19)	6(13.3)	
Pre Hospital delay >6 hours	9(45)	26(31)	15(32)	0.484
Management Strategy				0.133
Thrombolysis	17(85)	70(83.3)	43(93.5)	
Primary PTCA	2(10)	9(10.7)	0(0)	
Conservative	1(5)	5(6)	3(6.5)	
Coronary Angiogram	4(20)	22(26.2)	2(4.3)	0.004
In hospital Mortality	4(20)	8(9.5)	6(13)	0.377
BMI >25	9(56.3)	24(30.8)	13(33.3)	0.146
Duration of Hospital stay <3d	13(65)	44(52.4)	31(67.4)	0.208
Pharmacotherapy				
Aspirin	19(95)	84(100)	44(97.8)	0.18
Clopidogrel	19(95)	82(97.6)	45(97.8)	0.78
ACEI	17(85)	73(86.9)	43(93.5)	0.45
Beta blockers	18(90)	70(83.3)	44(95.7)	0.11
Statins	19 (95)	78(92.9)	44(95.7)	0.71
Anticoagulation	8(40)	26(31)	13(28.3)	0.636

Table 23: Comparison of baseline characteristics, management strategy and in-hospital outcomes of patients enrolled in earlier study* vs. the present study

Characteristics	Earlier Study N=1320 (100)	Present Study N=150 (100)
Age	56±13	57±12
Males	1106 (83.8)	117(78)
Females	214 (16.2)	33 (22)
Time Delay		
< 6 hrs	679 (51.5)	100 (66.67)
> 6 hrs	641 (48.5)	50 (33.33)
Smoking	569(43.1)	51 (34)
Diabetes Mellitus	531(40.2)	73 (48.7)
Hypertension	504(38.2)	64 (42.7)
Past History Of MI	154(11.7)	7 (4.7)
Family History Of MI	128(9.7)	5(3.3)
Location Of MI		
Anterior wall MI	752 (57)	76 (50.7)
Inferior wall MI	517 (39)	68 (45.3)
Reperfusion Therapy		
Thrombolysis	1093(82.8)	130 (86.7)
Primary PCI	0	11 (7.3)
Aspirin	1225 (92.8)	148 (98.7)
ACEI	791 (60.0)	133 (88.7)
Beta blockers	863 (65.4)	132 (88)
Statins	0	141 (94)
In Hospital outcome		
Death	223 (16.9)	18 (12)
Re-infarction	61 (4.6)	1(0.7)

Data are number (%) or mean± SD

*- Jose et al [115]

DISCUSSION

The demographic characteristics, clinical and risk factor profile, pattern and presentation of management of 150 consecutive patients presenting to a tertiary care centre in a district capital in South India with a diagnosis of STEMI were assessed in this study. The in-hospital and 30 day outcomes were also evaluated.

Demographic, symptom and risk factor profile (Table 1, 6, 7 & Figure 1))

The mean age of presentation of STEMI was 57 ±12 years with the majority of them being males. The mean age did not differ significantly among males and females. There is no change in the mean age of presentation over the past decade. In the study done by Jose et al,[115] which included patients from 1999-2003 and the CREATE registry[9] which enrolled patients from 2001-2005, the mean age has been 56 ±13 years and 57.5 ± 12 years. Patients enrolled in this study presented a decade earlier in comparison to the Western data where the mean age of presentation has increased from 64.1 years to 66.4 years[4, 116] . As STEMI occurs earlier in this set of population, it can lead to tremendous loss of productive years and can have an adverse outcome on the economy as well as national health.

Compared to a decade ago, more women have presented with STEMI (16.2% vs. 22%). But, this proportion is considerably lower than the western countries, where the proportion has increased from 32.4% to 37 % (P<0.0001)[4]. This may be explained by the increased emphasis on clinical recognition of acute ischemic syndromes in females[117,118]. The appropriate use of 12 lead ECG and use of cardiac enzymes, especially troponins, has lead to better recognition of acute coronary syndromes in women in developed countries. In

contrast, women in developing countries lack awareness of the risk of cardiovascular disease as majority of public health expenditure is devoted to maternal and child health[119]. Moreover, the use of 12 lead ECG and application of cardiac enzymes would be far less prevalent in developing countries leading to underdiagnosis in women.

Chest pain was the most common symptom at presentation among both males and females, but there was a trend for females to present with lesser frequency in comparison with males. Sweating and dyspnoea were the next most common symptoms. There was no significant difference among the sexes based on the symptom of presentation. Studies assessing gender differences in symptom of presentation in acute coronary syndrome, have found that while men tend to present more with chest pain and diaphoresis, women report significantly greater number of symptoms than men and have significantly more jaw and back pain, nausea and / or vomiting, dyspnoea, indigestion and palpitation[120, 121.]

In comparison to data derived from Western population[4,116], diabetes Mellitus was more prevalent (48.7% vs. 22.4%), while hypertension was less prevalent (42.7% vs. 56.9%). Smoking was equally prevalent in both groups. There was lesser number of people who presented with family history or past history of ischemic heart disease. Prevalence of patients presenting with history of prior CABG or prior PCI has increased in the Western population, as revascularization procedures are more widely used in the West. The increased prevalence of diabetes in patients presenting with STEMI is reflective of the epidemic rise in proportion of the people with diabetes, obesity and metabolic syndrome. Compared to men, women who presented with STEMI had significantly higher prevalence of diabetes ($P = 0.002$). Almost 90% of the women were postmenopausal. There was no difference in the prevalence of other risk factors apart from smoking which was almost non existent among women. The increased prevalence of diabetes among women presenting with STEMI is reflective of the fact, that they are older at the time of presentation and hence more likely to have higher prevalence of

diabetes, hypertension and obesity. The presence of diabetes negates the protective effect of hormones in females.

Only 14% of the study population had reported no risk factor at the time of presentation of STEMI. Even among these, nearly three fourth of them were found to have dyslipidemic (LDL cholesterol > 100mg/dl) on evaluation of lipid profile at time of hospitalization for STEMI. This supports the fact shown by Canto et al [122] and Greenland et al [123], where approximately 90% of the coronary events could be explained by the presence of at least one of the established four risk factors and only 10% had to investigate for other markers of cardiovascular risk .

Pre-hospital delay (Tables 2, 3, 4 & 5)

Patients enrolled in this study took much longer to present to the first medical contact from the onset of symptom and for definitive treatment to the tertiary care centre. The mean time delay to first medical contact was 308 ± 577 minutes (5.63 ± 9.62 hours) and pre-hospital delay was 6.7 ± 9.8 hours. The median prehospital delay was 4 hours. After exclusion of patients who presented later than 12 hours after symptom onset, the pre-hospital delay was 4.5 ± 3.1 hours. Wide geographical variation in the extent of pre-hospital delay has been reported before. The shortest time was observed in Australia/New Zealand/USA and CANADA (median of 2.2 hours), the longest delay was seen in Argentina /Brazil (median 4.0 hours) [124]. Factors associated with greater pre-hospital delay were identified to be elderly age, female sex, diabetes mellitus, past history of acute myocardial infarction (AMI). After adjustment of confounding variables, only age, DM and past history of AMI emerged as strong predictors associated with greater pre-hospital delay[125]. 45% of patients studies in Worcester Heart attack study had presented within 2 hours [125]. However, the proportion of patients who presented within 2 hours constitute only 20% of this study group. There were no factors which were predictive of a shorter pre-hospital delay (<2 hours). Hence, based on

the mean pre-hospital delay, we categorized patients into 2 groups- those presenting within 6 hours and those after 6 hours. About 1/3 of the patients took longer than 6 hours to present to tertiary care centre. Among these patients, women and patients with past history of ischemic heart disease were more likely to present greater than 6 hours. Univariate logistic regression analysis showed that female sex was the only risk factor associated with prolonged pre-hospital delay {P= 0.012, OR (95% CI) 2.7 (1.2 -5.9)}.

Rosenfeld et al reported that difficulty in interpreting the severity of symptoms was the factor most predictive in women patients who delay seeking care [126]. Health care workers and women themselves fail to recognize the early signs of acute coronary syndrome. Women are less likely to be correctly assessed and cared for when symptoms are present. Women also tend to underreport the symptoms and may present with atypical symptoms[127] . Moreover, women who present with acute myocardial infarction are older, have greater co- morbidities, and are dependent on others for seeking medical care. The other reasons for patients reaching hospital late include financial constraints, a lack of awareness of the importance of the symptoms, and different types of health-care providers that prevent rapid access to secondary and tertiary care hospitals [9]. The mean delay from first medical contact to the tertiary care centre was 102.5 minutes. This delay could be shortened by prompt diagnosis and referral to the tertiary care centre, training professionals at the primary and secondary level hospitals to manage low risk STEMI patients and refer only the high risk patients to tertiary care center, especially if undue prolonged transfer time is expected. Western centers are well equipped for pre-hospital thrombolysis. But, in developing countries, lack of efficient emergency medical services and trained paramedic professionals does not provide this option. Educating people about cardiovascular risk factors and symptoms, making 12 lead ECG and cardiac enzymes widely and cheaply available, training of professionals to diagnose promptly, assess risk and refer patients appropriately for reperfusion therapy would reduce

the pre-hospital delay.

The recommended door-to-needle time and door-to-balloon time is 30 minutes and 90 minutes respectively. The median door-to-needle time is prolonged, but the door-to- balloon time was near optimally achieved. The median door to needle time was 45 minutes which is longer compared to that achieved in US registries[128]. The median door- to-needle time and door-to-balloon time in NRMI registry in 2006 was 29 minutes and 79 minutes respectively. On segregation of patients into those presenting to the accident and emergency department initially and those to chest pain unit of the tertiary care centre initially, the door-to-needle time was significantly shorter in those presenting to the chest pain unit directly(mean time – 32.1 +/- 39.1 minutes, P = 0.017). This was due to the efficient triage system in place in the chest pain unit where the patient in attended to immediately by trained staff, a 12 lead ECG taken within 10 minutes of hospital arrival and availability of a cardiologist round the clock. Moreover, there was a mean time delay of 60 ± 44 minutes associated with transferring patients from the accident and emergency unit to the chest pain unit before initiating thrombolysis. This emphasizes the rationale and need for set up for such chest pain units which could shorten the time delays associated with management of STEMI..

Socioeconomic status (Table 1, 22)

Patients across all the socioeconomic strata presented with STEMI. Though, the lower middle class presented in greater numbers, it was not statistically significant. CREATE registry[9] had showed increased prevalence of diabetes and hypertension in the rich, higher prevalence of smoking in the poor. However, in this study, we did not find similar results. Diabetes was significantly less prevalent in the middle class in comparison to the upper and lower socioeconomic strata. There was no difference in prevalence of hypertension or smoking, though relatively lesser number of upper class people smoked. Most of the upper class

people presented to the local practitioners initially after onset of symptoms, in comparison to the middle and lower class people(P = 0.044). This may possibly be due to the fact that the upper class people may have been in regular follow up with their family physicians and may have presented to them initially, while those in lower class may not be affordable to be in regular follow up and may never have visited a local practitioner for minor illness. Patients across all the socioeconomic strata presented with similar pre-hospital delays. Thrombolysis was the preferred modality of reperfusion across all the socioeconomic groups. Even though, this tertiary care centre was PCI capable and there was availability of experienced physicians and supporting staff, 24 hours a day, 7 days a week, only about 10% of the upper and middle class underwent primary PCI, while none among the lower class had primary PCI. This is because of the prohibitive costs associated with PCI and lack of awareness among the lower class regarding the benefits of PCI. Compared to Western countries, there is a lack of appropriate use of insurance cover and lack of health program initiatives from the government. The use of coronary angiography was significantly restricted to only among the upper and middle class. About $2/5^{th}$ of the upper group underwent coronary angiography while less than 5% in the lower class had it done during the hospital stay. This practice pattern was similar to that reported by Xavier et al. in the CREATE registry. There was no significant difference across the groups with regards to pharmacotherapy. Most of them received appropriate guideline based therapy and the use of guideline based acute medical therapy was much higher in comparison to that reported by Jose et al and Xavier et al. We did not find any difference in mortality across the various socioeconomic groups. There was no difference in the total duration of hospital stay either. This was essentially because of the fact that patients across all groups received appropriate guideline based therapy promptly without any disparity among the groups. CREATE registry had showed significant difference in treatment strategy among the different socioeconomic strata which ultimately reflected in

the greater mortality among the lower socioeconomic strata. It had showed that the differences in mortality across socioeconomic strata in India are not due to differences in risk factors, but almost entirely to differences in treatments and related factors. If all patients had access to similar health care facilities, reached hospital rapidly, and received similar treatments, mortality would be reduced, especially for patients in the lower socioeconomic strata. This was very much evident in present study as people across all the strata presented with similar time delays and received similar appropriate treatment and hence did not differ in mortality rates after STEMI. This emphasizes the fact, that prompt recognition of symptom, rapid referral and initiation of treatment, making appropriate reperfusion therapy available at affordable cost, and implementing guideline based therapy with prescription of low cost but effective pharmacotherapy would definitely result in reduction in mortality and also bridge the gap between the socioeconomic strata.

Clinical and laboratory profile (Tables 8, 9, 10, 11)

The mean body mass index was 23 ± 6. The proportion of those who were overweight or obese was 35%. This is similar to that seen in NRMI registry and CREATE registry. There was no significant difference among prevalence of overweight and obesity among males and females. The cut off for body mass index differs in Asian population, where the risk of cardiovascular disease starts occurring at a lower BMI cut off. A cut off above 23.0 identifies people at higher risk for cardiovascular risk. Applying this cut off, the proportion of overweight or obese increases to about 56%.

More than 80% presented in Killips class I. More males than females presented in Killips class I (P= 0.02). Less than 10% presented in Killps class IV. The mean ejection fraction was 45 ± 9%. There was no significant difference in ejection fraction among males and females. There was no significant difference in mean ejection fraction with respect to pre-

hospital delay.

An equal proportion of patients with presented with anterior and inferior wall myocardial infarction. Extensive anterior wall MI was the most common location of MI. Inferior wall MI was more often associated with right ventricular myocardial infarction and posterior wall myocardial infarction. Isolated inferior or lateral wall MI was not common.

The mean hemoglobin was significantly lower in women. Troponin levels were significantly more among women. This could be due to delayed presentation among women and hence greater time delay from onset of symptoms to collection of blood sample. Serum creatinine was elevated in about 10%. There was a trend towards higher mean triglyceride levels in women and lower mean HDL cholesterol levels in men. The mean LDL cholesterol levels were higher and above the prescribed LDL goal of < 100mg/dl for patients with established cardiovascular disease. About 5% were newly detected to have diabetes and about 70% were found to have LDL levels greater than 100mg/dl.

Management strategy (Tables 12, 13, 14 and Figure 2)

Thrombolysis was the most frequently used reperfusion strategy and streptokinase was the thrombolytic agent used in 95% of them. Tenecteplase was used in the rest. Compared to the CREATE registry, greater proportion of patients received thrombolytic therapy (58.5% vs. 86.7%). Primary PTCA was utilized in this study only in 7% of patients. This proportion is similar to that observed in the CREATE registry. This is in sharp contrast to the Western data, where the proportion undergoing thrombolysis has fallen from 52.5% to 27.6% and proportion undergoing primary PCI has increased from 2.6% to 43.2% over the past 15 years. The proportion of reperfusion eligible patients who did undergo any form of reperfusion therapy is very high in this study. 94% received either thrombolysis or primary PCI. The management strategy in this study was primarily dependent on the financial affordability of

patients. The decreased use of primary PCI in this study is due to the prohibitive costs associated with primary PCI in comparison to thrombolytic therapy, inadequate insurance cover and lack of government health programmes to support such high end technologies. The numbers of PCI capable hospitals are very few and not all of them offer services 24 hours of the day. Thrombolysis remains a cheap and effective option to primary PCI in India. It is widely available, easily administratable and can achieve results similar to primary PCI especially if initiated within 2 hours of symptom onset. The crux of the issue is to reduce the pre-hospital and door-to-needle time for improving outcomes after thrombolysis. In the NRMI 2006 registry, improvement in door-to-needle time has resulted in 16.5% adjusted relative improvement in mortality associated with thrombolytic therapy [128]. Thrombolysis remained the preferred treatment strategy across all groups of time delay, even after presenting later than 12 hours from symptom onset. Primary PCI was performed in all patients presenting with 12 hours of pre-hospital delay. The proportion of patients receiving no reperfusion therapy increased with greater pre-hospital delay. None of the patients underwent emergency CABG. ST-segment resolution post reperfusion is a simple clinical marker of effective reperfusion therapy. In this study, about 60% of patients had >50% ST resolution post reperfusion therapy. The proportion of patients having better ST resolution declined with longer pre-hospital delay. Patients who presented within 12 hours had significantly better ST resolution. There was trend towards better ST segment resolution with primary PCI in comparison to thrombolysis. Almost 90% in of those who underwent primary PCI achieved >50% ST resolution compared to only 62% among thrombolysis. But, this was not statistically significant, probably due to much reduced numbers undergoing primary PCI.

Coronary angiography (Table 15)

Less than 2/5 of patients underwent coronary angiogram during index hospitalization. This

compares well with CREATE registry, where about 22% underwent coronary angiography. The rate of coronary angiography is far less in comparison to Western countries, where almost 80% undergo cardiac catheterization prior to discharge. Use of coronary angiography was largely restricted to upper and middle socioeconomic strata. There was no difference among males and females in undergoing coronary angiography. Among the patients, who underwent coronary angiography, PCI with stenting was done in 85% of patients. PCI was not done in 3 of them due to severe triple vessel disease and one of the patients had a recanalised coronary artery. 60% had single vessel disease, while less than 15% had triple vessel disease. Bare metal stent was implanted in 87% of those who underwent PCI.

Pharmacotherapy (Table 16, Figure 3)

There was tremendous improvement in prescription of guideline based acute medical therapy. Both aspirin and clopidogrel were used in almost 99% of patients. Much greater improvement in prescription has been observed for beta-blockers, ACEI and statins. Compared to Jose et al and CREATE registry where prescription of beta-blocker and ACEI were seen only in 60% of patients, almost 90% of them received these drugs in this study. The largest gain has been observed for statins which was prescribed in nearly 94% of patients. This rate is much higher than that shown in CREATE registry where statins were prescribed only in 50% of patients. The pattern of prescription of acute medications is well comparable with western data and in fact higher with respect to statins and ACEI [129]. This is due to greater awareness of evidence based treatments among the treating physicians and the wider use of internet for quick and complete access to the current and latest in field of cardiovascular medicine. Less than a third of patients were prescribed anticoagulants. Though ACC/AHA guidelines state class IA indication for routine use of anticoagulation post thrombolysis and for patients undergoing PCI, use of anticoagulants in this study was not routinely prescribed in all patients after

thrombolysis and was limited to patients who were conservatively managed (received no form of reperfusion) or underwent PCI (primary /rescue or adjunct) and in those who had recurrent angina. This was due to shorter period of hospital stay in uncomplicated patients and additional financial burden associated with prescription of anticoagulants. There was no observed difference in prescription pattern among males and females.

In-hospital complications and 30 day outcomes (Tables 17, 18, 19, 20, 21 and Figure 4)

In-hospital mortality observed was 12% which has declined from about 17% as observed by Jose et al,[115] between the years 1999 – 2003. This could be due to the greater improvement in the guideline based prescription of low cost but effective acute medical therapy, especially statins, beta-blockers and ACEI. Moreover, greater proportion of patients received reperfusion therapy due to the reduction in pre-hospital delay and achievement of shorter door-to-needle time. Worldwide there has been a decline in in-hospital mortality from STEMI over the past 15 years. The overall mortality in STEMI has reduced from 11.5 % to 8 % [4]. Among patients undergoing thrombolysis, mortality has reduced from 7% in 1994 to 6% in 2006. Mortality among patients undergoing primary PCI has decreased from 8.6% in 1994 to 3.1% in 2006. European registries show a greater reduction in in-hospital mortality[116]. Observed in-hospital mortality in STEMI in GRACE registry, declined from 8.4% in 1999 to 4.6% in 2005 [130]. In-hospital mortality observed in this study is higher in comparison to the Western data. This may be due to the fact that primary PCI was utilized in fewer patients, with thrombolysis being the mainstay of therapy. The greatest benefits of thrombolysis have been obtained in patients who present within 2 hours of symptom onset. There was greater observed pre-hospital delay with only 20% of study population presenting within 2 hours, majority presenting only by 6 hours from symptom onset. There was greater prevalence of diabetes in this study group and higher incidence of mortality has been described in patients

with diabetes who present with STEMI. Invasive and intensive therapy could not be extended to all eligible patients due to financial constraints. Moreover, this institution being a tertiary care centre, there could be a referral bias with more high risk and sicker patients being referred from primary and secondary level hospitals. Use of acute medications and timely reperfusion therapy (shorter door-to- needle and shorter door-to-balloon time) accounted for up to 21% of the relative reduction in annual mortality [129]. The other reasons stated for decline in mortality rates in western countries are improved public awareness campaigns, improvements in emergency medical services, more rapid triage of patients with chest pain syndromes in emergency departments, and geographic changes in hospital location[128].

The baseline characteristics of those who died in-hospital due to STEMI were similar for age, sex and risk factors, pre-hospital delay and type of reperfusion strategy used. People who died had poor ECG ST-segment resolution compared to those who survived. (P=0.002). The mean ejection fraction was also significantly lower among those who died in-hospital. (P<0.002). The degree of ST-segment resolution has been shown to be predictive of short-, medium, and long-term outcome[131]. Heart failure and cardiogenic shock accounted for 60% of the in-hospital mortality. Fatal arrhythmias accounted only for 16% of the deaths. Suspected myocardial rupture accounted for about 10% of the deaths. All the suspected ruptures occurred in those who received thrombolysis. Greater use of primary PCI could have reduced the deaths due to myocardial rupture.

Apart from LV systolic dysfunction, defined as ejection fraction less than 50% which was observed in about 2/3 of the study population, the other in-hospital outcomes were relatively uncommon. Re-infarction was less than 1% and stroke occurred in 1.3%. Both the cases of stroke were observed in patients who received thrombolysis. The proportion of those presenting with cardiogenic shock were much less (3.3%). Rescue PCI and adjunct PCI was done in 5.3% and 2.7% respectively. The in-hospital outcomes are comparable with the

GRACE registry. Nearly half of the patients had an uneventful recovery after STEMI. Compared to that observed by Jose et al, all in-hospital outcomes occurred relatively less frequently.

The mean duration of hospital stay was shorter (2.6 ± 2 days.) The mean duration of hospital stay was similar across all the treatment groups. The observed duration of hospital stay is much shorter than that observed by Jose et al. (5.3 ± 3.4 days).

Most of the patients were free of outcomes at the 30 day follow up. Only 4 patients were lost to follow up. There was only one reported death. Heart failure and recurrent angina were observed equally among 12%. The re-infarction rate was 2.7%. Compared to the Euro heart survey, 30 day mortality, re-infarction rates are lower but heart failure and recurrence of angina are higher.

Comparison between earlier study [115] and present study (Table 23)

The results of the earlier and present study are summarized in table 23. A total of 1320 patients diagnosed with STEMI were enrolled between 1999-2003. The mean age is similar in both the study. The proportion of women presenting with STEMI has increased. The mean pre-hospital delay has considerably shortened with more number of people presenting within 6 hours. The prevalence of diabetes has increased, while smoking has become less prevalent. The proportion of patients having past history of IHD has decreased. Thrombolysis has remained the mainstay of reperfusion therapy. The use of guideline based prescription has shown tremendous increase with most of the patients receiving acute medical therapy at rates comparable to the western registries. The in-hospital mortality rate has reduced, but still remains higher in comparison to that in western registries. The reduction in mortality is explained by the shorter pre-hospital delay, increased use of guideline based therapy and due

to increased proportion of patients undergoing any form of reperfusion therapy. There is ample scope for further reduction in mortality by patient education and control of risk factors and increasing the awareness of symptoms of cardiovascular disease, reducing the pre-hospital delay to increase the proportion of patients receiving reperfusion therapy, greater and judicious use of primary PCI at PCI capable centres and increase in the practice of use of guideline based therapies.

LIMITATIONS

1. This is only an observational study and not a randomized control study. Hence, it cannot be used to compare outcomes among patient subsets.

2. The number of patients enrolled is very small and the time period of study was short and limited. Hence, the results are not generalizable.

3. The causes for time delay from onset of symptom to initial presentation to the physician have not been evaluated. Similarly, the causes for time delay at the local hospital for initial evaluation and subsequent transfer to tertiary care hospital have not been evaluated.

4. The mean hospital stay was shorter in our study population due to early discharge of uncomplicated patients. It is likely that we might have missed a few mechanical complications like ventricular septal defect and papillary muscle rupture.

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SUMMARY OF MAIN FINDINGS

1. The mean age of patients presenting with STEMI is at least a decade younger in comparison to Western populations.
2. The proportion of women presenting with STEMI has increased over the past decade.
3. Chest pain is the commonest symptom of presentation among both men and women, but it is reported at a significantly higher rate in men.
4. The prevalence of diabetes has increased and women have significantly higher prevalence of diabetics than men.
5. The mean pre-hospital delay is longer in comparison to Western populations.
6. The door-to-needle time is achieved more often if patients present directly to the chest pain unit of the tertiary care centre.
7. About half of the patients present with anterior wall MI and almost similar number present with inferior wall MI.
8. Most of the patients presenting with STEMI undergo reperfusion, and thrombolysis is the most commonly used reperfusion strategy.
9. Streptokinase is the most common thrombolytic agent used
10. Less than a third of patients undergo coronary angiography during index hospitalization.
11. Most of the patients are prescribed guideline based acute medical therapy and the use of these therapies is higher compared a decade ago and is similar to that in Western populations.
12. In-hospital mortality rates have declined compared to a decade ago but is higher than in western populations.
13. Duration of hospital stay has shortened compared to that a decade ago.

14. Heart failure and recurrent angina are the most frequently reported adverse outcomes at 30 day follow up.
15. There was no significant difference between the different socioeconomic strata with regard to reperfusion therapy, pharmacologic therapy, and in-hospital outcomes, but the lower socioeconomic group was less likely to undergo primary PCI or coronary angiography.

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STUDY PROFORMA

Pattern of presentation and management of STEMI in a tertiary care centre in a district capital in South India

Name : Sl.No.

Age / Sex : Hospital No.:

Address :

Phone :

SES :

Occupation : Profession / Semi-profession / Clerical-Shop owner – Farmer / Skilled worker/ Semi-skilled worker / unskilled worker / Unemployed

Educational status: Professional or Honors / Graduate or Post graduate / Intermediate or Post high school diploma / High school certificate Middle school certificate / Primary School / Illiterate

Income: ≥ 13500 / 6750 – 13499 / 5050 – 6749 / 3373 – 5049 / 2025 – 3374/ 676 – 2024 / ≤ 675

Date of admission : Date of Discharge :

Time from symptom onset to hospital :

Presentation to CPU / Accident and Emergency :

Referred by Primary level hospital/ secondary level hospital / local practitioner :

Symptoms: Chest pain / Dyspnea / palpitation / fatigue / syncope / others

Risk Factors:

Diabetes mellitus: duration: type: I / II OHA / Insulin / both / diet

Hypertension

Dyslipidemia

Smoking

Family history of IHD

Past history of MI

Post menopausal

On Examination:

Height: Weight: BMI:

Pulse Rate: BP: mmHg RS: CVS :

Killips Class I / II / III / IV

Other relevant system exam

ECG :

ECG ST resolution (post lysis):

Location of MI: ASMI Ext AWMI IWMI

IWMI+RVMI IW+RV+PWMI LWMI LW + PWMI

ECHO: LVIDD/S: EDV/ ESV: EF: %; MV E/A:

DECT: msec RWMA : MR:

Blood inv: HB: TC /DC : AC/PC: Creatinine:

Lipid profile: CKMB: Troponin:

Reperfusion strategy: Thrombolysis / Primary PTCA / Conservative

Door to needle time : min

Agent used : STK / Urokinase / Tenecteplase

Primary PTCA : SVD / DVD / TVD / LM / Recanalised vessel

Door to balloon time : min.

Stents used : DES / BMS

Other therapy : Aspirin / Clopidogrel / ACEI / Beta blockers / Statins / ARB / Nitrate / Diuretics / TPI

Anticoagulant therapy : Heparin / LMWH / Fondaparinux

In-hospital outcomes : Death / Re-infarction / Recurrent angina / Arrhythmias / LV systolic dysfunction/ Stroke / Bleeding / Cardiogenic shock / Pericarditis / Rescue PCI / adjunct PCI/ VSR / MR / Complete heart block / Uneventful / Others

CAG in index admission : Yes / No

Duration of hosp. stay :

30 day outcome : Death / Re-infarction / Heart failure / Arrhythmia / Recurrent angina / Stroke/ Uneventful / Others

GLOSSARY

CVD - Cardiovascular disease

STEMI - ST-segment elevation myocardial infarction

PCI - Percutaneous coronary intervention

ACEI - Angiotensin converting enzyme inhibitors

AMI - Acute myocardial infarction

PAR - Population attributable risk

IHD - Ischaemic heart disease

ACS - Acute coronary syndrome

AWMI - Anterior wall myocardial infarction

ASMI - Antero septal myocardial infarction

IWMI - Inferior wall myocardial infarction

LWMI` - Lateral wall myocardial infarction

PWMI - Posterior wall myocardial infarction

A&E - Accident & Emergency unit

CPU - Chest pain unit

Master chart

Hospno - Hospital number

SES - Socioeconomic status (1-upper, 2-upper middle, 3-lower middle, 4-upper lower, 5-lower)

TIMED1 - Time to first medical contact in minutes

TIMED2 - Window period in minutes

TIMED3 - Door-to-needle time

TIMED4 - Door-to-balloon time

TIMED5 - Transfer delay from accident and emergency unit to chest pain unit

TIMED6 - Delay to transfer from first medical contact to tertiary care centre

TIMED7 - Pre-hospital delay in minutes

PLACEFIR - Place of first medical contact (1-local hospital, 2- A&E, 3-CPU)

CHESTPAI - Chest pain (1-yes, 2-no)

PALPITAT - Palpitation (1-yes, 2-no)

RFDIABET - diabetes mellitus (1-yes, 2-no)

HYPERTEN - Hypertension (1-yes, 2-no)

FAMILYHI - Family history of coronary artery disease (1-yes, 2-no)

PASTIHD - Past history of ischaemic heart disease (1-yes, 2-no)

DYSLIP - Dyslipidemia (1-yes, 2-no)

POSTMEN - Postmenopausal (1-yes, 2-no)

NONE - No risk factor (1-yes, 2-no)

BMI - Body mass index

PR - Pulse rate

BPS - Systolic blood pressure

BPD - Diastolic blood pressure

ECGSTRES - ECG ST resolution (1-<50, 2->50)

LOCATION - Location of infarct (1 - ASMI, 2 - Ext AWMI, 3 - IWMI, 4–IWMI+RVMI, 5–IWMI+RVMI+ PWMI,

6 - IWMI +RVMI+PWMI+LWMI, 7-LWMI, 8-

LWMI+PWMI)

EF - Ejection fraction

CREAT - Creatinine

TROPO - Troponin I

TCH - Total cholesterol

TG - Triglyceride

HDL - High density lipoprotein

LDL - Low density lipoprotein

DMNE - Newly detected diabetes (1-yes, 2-no)

DYSLIPI - Newly detected Dyslipidemia (1-yes, 2-no)

REPERFS - Reperfusion strategy (1-thrombolysis, 2-primary PCI, 3-conservative)

THROMBO - Thrombolytic agent used (1-streptokinase, 2-urokinase, 3-tenekteplase)

PRIMA - Coronary artery disease (1-single vessel disease, 2-double vessel disease, 3-triple vessel disease, 4-recanalised vessel)

CAGINDEX - Coronary angiogram in index hospitalization (1-yes, 2-no)

ASPIRIN - Aspirin (1-yes, 2-no)

CLOPID - Clopidogrel (1-yes, 2-no)

ACEI - ACEI (1-yes, 2-no)

BETABLOC - Beta-blockers (1-yes, 2-no)

ARB - Angiotensin receptor blockers (1-yes, 2-no)

TPI - Temporary pacemaker insertion (1-yes, 2-no)

DIG - Digoxin (1-yes, 2-no)

DIURETI - Diuretics (1-yes, 2-no)

NITRATE - Nitrates (1-yes, 2-no)

STATINS - Statins (1-yes, 2-no)

ANTICOAG - Anticoagulant agent used (1-heparin, 2-lmwh, 3-fondaparinux, 4-none)

INHOSPIT – In-hospital mortality (1-yes, 2-no)

REINFARC – Reinfarction (1-yes, 2-no)

RECURREN - Recurrent angina (1-yes, 2-no)

ARRYTHMI – Arrhythmia (1-yes, 2-no)

LVDYSFN - LV systolic dysfunction (EF < 50%) (1-yes, 2-no)

PERICARD - Pericarditis (1-yes, 2-no)

RESCUEPC - Rescue PCI (1-yes, 2-no)

VSR - Ventricular septal rupture (1-yes, 2-no)

MR - Mitral regurgitation (1-yes, 2-no)

CHB - Complete heart block (1-yes, 2-no)

UNEVENT - Uneventful in-hospital stay (1-yes, 2-no)

ADJUNCT - Adjunct PCI (1-yes, 2-no)

DOHSTAY – Duration of hospital stay

THDDEATH - Mortality at 30 day follow up (1-yes, 2-no)

REINFAR – Reinfarction at 30 day follow up (1-yes, 2-no)

ARRHYT - Arrhythmia at 30 day follow up (1-yes, 2-no)

REANGINA - Recurrent angina at 30 day follow up (1-yes, 2-no)

HEARTFAI - Heartfailure at 30 day follow up (1-yes, 2-no)

STROKET - Stroke at 30 day follow up (1-yes, 2-no)

UNEVENTF - Uneventful at 30 day follow up (1-yes, 2-no)