DISSERTATION ON

A STUDY ON THE PREVALENCE OF METABOLIC SYNDROME AND ITS VASCULAR COMPLICATIONS IN ELDERLY WITH METABOLIC SYNDROME WITH OR WITHOUT DIABETES

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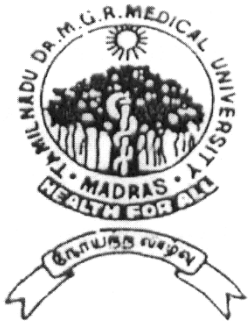

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CERTIFICATE

This is to certify that this dissertation entitled **"A STUDY ON THE PREVALENCE OF METABOLIC SYNDROME AND ITS VASCULAR COMPLICATIONS IN ELDERLY WITH METABOLIC SYNDROME WITH OR WITHOUT DIABETES"** submitted by **Dr. ARAVINDH, M.** appearing for Part II M.D. Branch I General Medicine Degree examination in September 2006 is a bonafide record of work done by him under my direct audience and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I solemnly declare that the dissertation titled "A STUDY ON THE PREVALENCE OF METABOLIC SYNDROME AND ITS VASCULAR COMPLICATIONS IN ELDERLY WITH METABOLIC SYNDROME WITH OR WITHOUT DIABETES" is done by me at Madras Medical College & Govt. General Hospital, Chennai under the guidance and supervision of Prof. V. Sundaravadivelu, M.D

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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CONTENTS

INTRODUCTION

The concept of the metabolic syndrome has existed for at least 80 years.[1] Initially constellation of risk factors like hypertension, hyperglycemia, and gout were included as a component of metabolic cardiovascular risk factor by Kylin in 1920.[2] Later, in 1947, Vague found that upper body (android) adiposity was associated with metabolic abnormalities associated with type 2 diabetes and cardiovascular disease.[3]

Later constellation of metabolic abnormalities includes glucose intolerance (type 2 diabetes, impaired glucose tolerance, or impaired fasting glycaemia), insulin resistance, central obesity, dyslipidaemia, and hypertension as a component of metabolic syndrome, which is also known as syndrome X,[4] or Insulin resistance syndrome.[5]

Subsequently, the National Cholesterol Education Program Adult Treatment Panel 3 have formulated definition of metabolic syndrome includes the essential components-glucose intolerance, obesity, hypertension, and dyslipidaemia which provide a tool for clinicians researchers. [6]

Both metabolic syndrome and diabetes are associated with increased prevalence of cardiovascular disease when they co-exist. We examined the role of metabolic syndrome alone without diabetes as a risk factor for cardiovascular disease in our study population.

THE OBJECTIVES OF THE STUDY

1. To estimate the prevalence of metabolic syndrome in the elderly

2. To estimate the prevalence of vascular diseases (coronary heart disease/ stroke/ peripheral arterial disease) in elderly with the metabolic syndrome with or without diabetes when compared with subjects without metabolic syndrome.

3. To estimate whether metabolic syndrome alone without diabetes is an independent risk factor for vascular diseases in elderly.

4. To find the strength of correlation of metabolic syndrome components with vascular diseases.

REVIEW OF LITERATURE

METABOLIC SYNDROME

The concept of metabolic syndrome is the most significant development in the management of CV disease for the past two decades. There is clearly an association of insulin resistance (IR) and hyperinsulinemia with metabolic risk factors that are involved in the etiology of atherosclerotic disease.

IR syndrome provides an important concept for screening and aggressively treating patients for multiple CV risk factors with a variety of drugs some of which are efficacious in the treatment of insulin resistance itself.

Insulin resistance represents a major underlying abnormality driving cardiovascular disease, the major cause of morbidity and mortality globally. Previously physicians often treated co-existing diabetes, hypertension or dyslipidemia as separate diseases without

considering the impact of treatment for one on the other. Gerald Reaven drew attention to a constellation of features associated with coronary heart disease.[7]

Currently, insulin resistance is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as such as it does in a normal population.

Components of metabolic syndrome:

Resistance to insulin-stimulated glucose uptake

Glucose intolerance

Hyperinsulinemia

Increased VLDL triglyceride

Decreased HDL cholesterol

Hypertension

Central obesity

Microalbuminuria

High plasminogen activator inhibitor - 1

Hyperleptinemia

Hyperuricemia

Insulin resistance and Diabetes

Genes and the environment play a role in the development of type 2 diabetes. The early prediabetic phase begins in young adulthood and can be identified as insulin resistance in peripheral tissues. Initially, insulin levels are elevated in response to the resistance, but as glucose desensitization develops, insulin secretion decreases. This eventually leads to clinical non-insulin— dependent diabetes.

Both the insulin resistance and the decreased insulin secretion are genetically programmed. This program is modified by a variety of environmental factors, especially diet and activity.[8] overt diabetes will develop when insulin cannot be increased to overcome insulin resistance. In comparison with thin patients, many obese patients without diabetes produce 5 to 8 times more insulin (500 U/day) to overcome insulin resistance.

Insulin resistance and Obesity

Several large studies provide convincing evidence of the link between obesity per se and coronary heart disease. More recently, in the analysis of the Nurses' study, a body mass index of 25— 28.9 was associated with a twofold increase in CV disease; the risk rose to almost fourfold once the BMI exceeded 29.[9] Strong evidence now links obesity with left ventricular hypertrophy, hypertension, alterations in haemostatic factors, and alteration in lipid profiles.[10] Visceral adiposity plays a greater role in the development of diabetes, IGT, and atherosclerosis than generalized obesity. Regional adiposity is closely associated with morbidity and mortality than general obesity.

San Antonio Heart Study

A combination of three or more risk factors for CHD in the same cardiac patient was more prevalent than either one factor alone or two factors in combination. Hyperinsulinemia might provide the common etiologic link. This forms one of the epidemiological evidence of metabolic syndrome and coronary artery disease

Clinical diagnosis of metabolic syndrome

Risk Factor	Defining Level
Abdominal Obesity (waist circumference)	
Men	>102 cm (40 inch)
Women	> 88 cm (32 inch)
Triglycerides	≥150mg/dl (1.7mmol/L)
HDL cholesterol Men	< 40 mg/dl (1.0 mmol/L)
HDL cholesterol Women	< 50 mg/dl (1.1 mmol/L)
Blood Pressure	≥130 / 85 mmHg
Fasting Plasma glucose	≥110 mg/dl
Diagnosis is established when >3 of these risk factors are present	

International Association for the study of obesity and the International Obesity Task Force redefined overweight as BMI >23 and obesity as BMI >25 in Asians. Central obesity was defined as >80 cm for women and >90 for men.[11]

METABOLIC SYNDROME AND DIABETES

Today, India has a primary position in the global diabetes epidemiology map as it is the home of nearly 33 million diabetic subjects which is the highest number in the world. This is both, due to a rising prevalence of the disease and the large population in the country. Initially study conducted by the ICMR showed prevalence was 3%. But there was gradual increase in prevalence of diabetes.

A recent study in Southern India showed that the prevalence had increased from 2.1% to 6.3%[12].This increase in mainly contributed by the urban population which has undergone significant changes in the lifestyle pattern.

The preclinical stages of diabetes, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are also steadily increasing. It indicates the potential for a future increase in diabetes as these conditions deteriorate when the environmental factors are adverse.

The major risk factors associated with diabetes are positive family history, age, obesity, especially upper body adiposity, physical inactivity and insulin resistance. Urban environment increases obesity, physical inactivity and causes unhealthy diet habits all of which lead to increased insulin resistance. Indians have a racial predisposition and a high familial aggregation of diabetes, effect of which is precipitated by the above environmental factor.

A series of studies have indicated that Indians have several peculiar features such as low risk thresholds for susceptibility for diabetes. These include a young age at onset, low normal range for body adiposity < 23.0 kg/m^2, presence of central adiposity despite having normal and high insulin resistance.

Indian have a high genetic susceptibility for diabetes and the above factors act adversely in such individuals. Because of the above facts screening for the metabolic syndrome is essential in preventing both diabetes and its complication.

Dysglycemia is commonly associated with the metabolic syndrome, characterized by the clustering of CHD risk factors like obesity, hypertension and dyslipidaemia in a single individual. These risk factors increase the risk of development of type 2 diabetes and also have a multiplicative effect on the risk for development of CHD. Recognition and treatment of the metabolic syndrome would help in prevention of type 2 diabetes and CHD.

The normal values proposed by the American diabetes association is as follows

Category	Fasting Plasma Glucose (mg/dl)	2hr Post Glucose Plasma glucose (mg/dl)
Normal	< 110	< 140
IFG	110 - 125	< 140
IGT	< 110	140-199
Diabetes	> 126	> 200

Impaired fasting glucose

The IFG denotes an abnormally high fasting glucose concentration which falls short of diagnosis of diabetes (plasma glucose 110-125 mg/dl.[13] The defects in insulin action in glucose metabolism include deficiencies in the ability of the hormone to suppress glucose production by the liver and kidney, and to mediate glucose uptake and metabolism in insulin sensitive tissues (i.e., muscle and adipose tissue).

The relation between impaired fasting glucose or impaired glucose tolerance and insulin resistance is well supported by human, non-human primate, and rodent studies to compensate for defects in insulin action, insulin secretion and/or clearance must be modified to sustain euglycaemia. If this compensation fails, a defect in insulin secretion predominates.

Insulin resistance in pancreatic islet beta cells implies that, signals that generate glucose-dependent insulin secretion have been adversely modified, and fatty acids are prime candidates. Although

free fatty acids can stimulate insulin secretion; increasing and prolonged exposure to excessive concentrations results in fall in insulin secretion.[14] The mechanism for this alteration has been attributed to lipotoxicity through several potential different mechanisms.[15]

IGT and IFG are not synonymous in terms of pathophysiology and in the development of the long term complications. The term prediabetes is a practical and convenient term for impaired fasting glucose and impaired glucose tolerance, which places individuals at risk of developing diabetes and its complications. Both IGT and IFG appear well before type 2 diabetes is diagnosed thereby presenting an opportunity for intervention to reduce the future burden of diabetes.

Not all individuals with prediabetes will necessarily progress to diabetes. A significant proportion of people who are diagnosed with IGT will revert to normoglycemia. IFG and IGT are associated with the metabolic syndrome which includes obesity, dyslipidaemia of the high triglyceride and/ or low HDL cholesterol and hypertension.

Identifying people with prediabetes particularly in the context of the metabolic syndrome indicates those who would benefit from cardiovascular risk modification. While people with isolated IFG/IGT do not have risk for micro vascular disease, they have a higher risk for the development of diabetes and cardiovascular disease.

IGT is more strongly associated with CHD outcomes. However, individuals identified as having both IFG and IGT are at higher risk for diabetes as well as CHD. Lifestyle interventions have been shown to be highly effective in delaying or preventing the onset of diabetes in people with IGT.

In the NHANES III data, it was found that impaired fasting glucose had twice the prevalence of CHD compared with normal glucose levels and diabetes had three times the prevalence.[16]

In a recent study from North India the prevalence of IFG was found to be 11.7% in the population. Individuals with IFG had a clustering of cardiovascular risk factors and the prevalence of the Metabolic Syndrome as per NCEP ATP III criteria was 61% in this

group with IFG compared with 16% in those with normoglycemia ($p<0.001$).[17]

The major risk factors (cigarette smoking, hypertension and dyslipidaemia) contribute to the cardiovascular risk in diabetic populations. For each CHD risk factor analyzed in the MRFIT trial the risk of CHD was approximately three-fold greater in the diabetic than in the non-diabetic population.[18]

METABOLIC SYNDROME AND DYSLIPIDAEMIA

NATIONAL CHOLESTEROL EDUCATION GUIDLINE classify the lipids and their normal values are

Classification of plasma lipids

Total cholesterol (mg/dl)

< 200 - Desirable

200 – 239 - Borderline high

≥ 240 - High

HDL cholesterol (mg/dl)

< 40	- Low (<50 for Females)
> 60	- High

LDL cholesterol (mg/dl)

< 100	- Optimal
100 – 129	- Near optimal
130 – 259	- Borderline high
160 – 189	- High
≥ 190	- Very high

Triglycerides (mg/dl)

< 150	- Normal
150 – 199	- Borderline high
200 – 499	- High
≥ 500	- Very high

In general, with increases in free fatty acid flux to the liver, increased production of apo B containing triglyceride rich VLDL occurs.[19] The effect of insulin on this process is complex. In the setting

of insulin resistance, increased flux of free fatty acids to the liver increases hepatic triglyceride synthesis; but under physiological conditions, insulin inhibit VLDL secretion into systemic circulation.[20] This response in part is an effect of insulin on the degradation of apo B. Yet insulin is also lipogenic, increasing transcription of many genes related to triglyceride biosynthesis.

Additionally, insulin resistance could also reduce the concentration of lipoprotein lipase in peripheral tissues (i.e. in adipose tissue more than muscle).[21] This alteration in lipoprotein lipase, however contribute less to the hypertriglyceridemia than does the overproduction of VLDL. Nevertheless hypertriglyceridemia is an excellent reflection of insulin resistant condition and is an important diagnostic criterion for metabolic syndrome.

The other major lipoprotein disturbance in the metabolic syndrome is a reduction in HDL cholesterol. This reduction is a consequence of changes in HDL composition and metabolism. In the presence of hypertriglyceridemia, a decrease in the cholesterol content of HDL results from decreases in the cholesteryl ester content of the

lipoprotein core with variable increases in triglyceride making the particle small and dense, a function in part of cholesteryl ester transfer protein.[22] This change in lipoprotein composition also results in an increased clearance of HDL from the circulation.[23] The relation of these changes in HDL to insulin resistance is probably indirect, arising in concert with the changes in triglyceride-rich lipoprotein metabolism.

In addition to HDL, the composition of LDL is also modified in similar way. In fact, with fasting serum triglycerides > 2 mmol/l, almost all patients have a predominance of small dense LDL.[24] This change in LDL composition is attributable to relative depletion of unesterified and esterified cholesterol, and phospholipids with either no change or an increase in LDL triglyceride.[25]

Small dense LDL is more atherogenic than buoyant LDL because it is more toxic to the endothelium; it is more able to transit through the endothelial basement membrane; it adhere well to glycosaminoglycans; it has increased susceptibility to oxidation; it is more selectively bound to scavenger receptors in macrophages.[26]

In some studies this alteration is an independent risk factor for cardiovascular disease.[27] However most of the time it is related to concomitant changes in other lipoproteins and other risk factors.[28]

Dyslipidaemia is present in over 50% of the diabetic population and constitutes a major risk factor for CHD, particularly as it persists despite the treatment of hyperglycemia. Diabetic dyslipidaemia is characterized by moderate hypertriglyceridemia and low levels of HDL cholesterol. The levels of total cholesterol and LDL cholesterol are similar to that in the non-diabetic population. However, the distribution of LDL particles in diabetic subjects is shifted towards smaller denser particles that are thought to be particularly atherogenic.

Hypertriglyceridemia is a major determinant of the distribution of LDL particles - the higher the fasting triglyceride level, the greater the preponderance of the small dense LDL in the total LDL concentration.[29]

Triglycerides are also associated with increased concentration of important procoagulant factors such as plasminogen activator inhibitor- 1. Thus elevated triglyceride levels directly influence the thrombus formation.

Non-HDL cholesterol (Total cholesterol- HDL cholesterol) is a secondary goal of therapy in patients with triglycerides > 200 mg/dl and therapeutic cutoff point for non-HDL cholesterol are 30mg/dl more than for LDL cholesterol.

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METABOLIC SYNDROME AND HYPERTENSION

The relation between insulin resistance and hypertension is well established,[30] And relates to several different mechanisms. First, it is important to note that insulin is a vasodilator when given intravenously to people of normal weight,[31] with secondary effects on sodium reabsorption in the kidney.[32] Evidence indicates that sodium reabsorption is increased in white people but not Africans or Asians with the metabolic syndrome.[33] In the setting of insulin resistance, the

vasodilator effect of insulin can be lost, [34] but the renal effect on sodium reabsorption preserved.[35]

Fatty acids themselves can mediate relative vasoconstriction.[36] Insulin also increases the activity of the sympathetic nervous system,[37] an effect that might also be preserved in the setting of the insulin resistance.[38] However, when assessed by concentration of fasting insulin, HOMA or the HOMA insulin resistance index (HOMA-IR),[39] insulin resistance contributes only modestly to the increased prevalence of hypertension in the metabolic syndrome.[40] When blood pressure measures > 130/85 mm Hg, it forms one of the clinical diagnostic criteria for metabolic syndrome under NCEP ATP 3 guidelines.

Metabolic syndrome and obesity

Obesity is an important modifiable risk factor for cardiovascular disease, including diabetes type 2, hypertension, hypercholesterolemia, coronary heart disease, and stroke.[41] The rising prevalence of type 2 diabetes, and metabolic syndrome in the developing countries, appears

to be mainly related to the increasing number of overweight and obese individual all over the world.[42] Accordingly, both World Health Organization and the National Heart, Lung and Blood Institute has defined obesity as a body mass index of more than 30 kg/ m^2 and BMI value between 25 and 30 is defined as over weight or pre obese.

Classification of overweight in Adults (WHO)

Classification	BMI	Risk of co-morbidities	Asia Pacific Guidelines
Underweight	< 18.5	low	< 18.5
Normal range	18.5- 24.9	average	18.5- 23
Overweight	> 25		
Pre-obese	25- 29.9	increased	23-24.9
Obese class 1	30- 34.9	moderate	25- 30
Obese class 2	35-39.9	severe	> 30
Obese class 3	> 40		

Obesity is defined as the presence of abnormally large amount of adipose tissue.

Measurement of adipose tissue is done by clinically as follows [43]

1. BMI: It is a measure of the ratio between weight (kg) and height (m^2). It clearly relates body fat independent of height. The only pitfall in BMI calculation, that it does not take musculature and differential adipose tissue into account.

2. Skin-fold thickness: It is used to measure fat distribution. Disadvantages are observer's error and failure to accommodate the fat contour.

3. Measurement of body circumference: Waist- hip ratio higher than 0.72 are abnormal. The only pitfall is to evolve standards for a particular ethnic group.

4. Waist circumference: It is used to identify body weight component of metabolic syndrome. It is measured at 1 cm above navel at minimal respiration. Waist circumference greater than 102 cm for male and greater than 88 cm for female is used as one of clinical diagnosing criteria for metabolic syndrome.

5. Because ATP 3 criteria for Waist circumference might not be appropriate for Asian population, the cutoff value for metabolic syndrome is changed to more than 90 cm for men and more than 80 cm for women.[44]

For several definition of the metabolic syndrome, waist circumference is included. Mechanistically, a distinction between a large waist due to increases in subcutaneous adipose tissue versus visceral fat is debated. This distinction can be made with computed tomography or magnetic resonance imaging.[45]

With increases in intra-abdominal or visceral adipose tissue, a higher rate of flux of adipose tissue-derived free fatty acids to the liver through the splanchnic circulation would be expected, whereas increases in abdominal subcutaneous fat would release lipolysis products into the systemic circulation and avoid more direct effects on hepatic metabolism (i.e., glucose production, lipid synthesis, and secretion of prothrombotic proteins such as fibrinogen and plasminogen activator inhibitor 1).[46]

Despite these potential differences in mechanisms related to excessive abdominal adipose tissue distribution, the clinical diagnosis of the metabolic syndrome does not distinguish between increases in subcutaneous and visceral fat.

Yet, perhaps by a mechanism related to free fatty acid flux and metabolism, the relative predominance of visceral rather than subcutaneous adipose tissue with increasing waist circumference in Asians and Asian Indians[47] renders the relative prevalence of the syndrome higher than in African- American men in whom subcutaneous fat predominates.[48]

However, there is evidence that the elevated postprandial free fatty acid release in upper body obese women originates from the non-splanchnic upper body fat, and not from the visceral depot.[49] These results suggest that visceral fat might be a marker for, but not the source of, excess postprandial free fatty acids in obesity.

VASCULAR ENDOTHLIAL DYSFUNCTION

Endothelial dysfunction occurs very early in the process of atherogenesis, which impairs normal vasodilator response. Endothelial dysfunction is therefore an important factor not only in atherosclerosis but also in hypertensive heart disease; Dysfunction allows platelets to adhere to the vessel wall and in turn causes contraction by thromboxane A2 and serotonin. Platelet-derived growth factor induces migration of smooth muscle cells. Endothelial cells produce growth promoters and inhibitors. The balance between them is maintained in normal endothelial function, under conditions of dysfunction the smooth muscle cells proliferate and migrate.[50]

Some vascular trees are more prone to the development of endothelial dysfunction like coronary arteries and aorta branches while some are relatively protected like the internal mammary artery and the brachial artery. The recognized known cardiac risk factors including age, gender, hypertension, hyperlipidaemia, diabetes mellitus, smoking, mental stress, and hyperhomocysteinaemia have been associated with

endothelial dysfunction. Some of the above mentioned risk factors are component of metabolic syndrome.

It is well known endothelial dysfunction can be detected well before the development of angiographically significant atherosclerotic plaque.[51] Abnormalities in peripheral endothelial function correlate with the presence of coronary vasomotor dysfunction.

The correlation in endothelial function in both the coronary and the peripheral vasculature suggests that a common pathway contributed to endothelial dysfunction in both vascular beds.[52]

METABOLIC SYNDROME AND CORONARY ARTERY DISEASE

The twin epidemics of diabetes mellitus and heart disease are a major threat to the well-being as. It is believed that a combination of factors, genetic and environmental including newer risk factors like the *metabolic syndrome* and hypercoagulability in addition to traditional risk factors like smoking, hypertension and hypercholesterolemia is the culprit behind the explosive rise in the incidence of these diseases. CAD

in DM is not only 2-4 times more frequent than non-diabetics and also has a worse prognosis.

Many patients have sub clinical or asymptomatic CAD which can have devastating consequences. Tight glycaemic control alone only has a marginal effect in controlling CAD. This can be treated by a multifactorial approach which includes not only adequate glycaemic control but also control of dyslipidemia, hypertension which form part of metabolic syndrome.[53]

The unprecedented increase in diabetes and cardiovascular disease (CVD) prevalence is evident from the report of WHO which shows that India tops the world with the largest number of subjects. According to recent WHO reports presently India has 32 million diabetic subjects and this is projected to increase to 100 million i.e. a rise by 250 % by the year 2035; in addition there is also a growing incidence of *metabolic syndrome*. This syndrome is a deadly combination of hypertension, diabetes mellitus, and dyslipidemia with abdominal obesity and often leads to heart disease.

The cause of this is both bad genes and defective environmental influences. Hence, in the coming decades the burden of CVD related to DM will increase significantly. Most diabetic's die of CVD and atherosclerosis accounts for almost 80**%** of all diabetic mortality**.**[54] Presence of DM increases the risk of cardiovascular disease (CVD) 2-4 folds. Type 2 DM represents more than 90% of the diabetic population. However type 1 DM also have an independently higher risk of CVD and their disease develops at younger age.

All the manifestations of CAD are at least two-fold more common in patients with DM than in nondiabetic individuals. Conversely, the prevalence of DM in CAD is approximately 20%**.**[55] There is evidence from Indian data as well that CAD is more common in diabetic subjects. Studies conducted in south India by Mohan et al and Ramchandran et al in Chennai showed a prevalence of diabetes varying from 12-16%.

In a study done at MV Diabetes Centre, Madras; the prevalence of CAD was assessed in a large cohort of 6597 NIDDM patients.[56] Overall 17.8% of patients had CAD. Its prevalence was not significantly different in males and females, The Chennai Urban Population Study (CUPS)

reported that overall CAD prevalence was 11%. 12% of this population was diabetic. Among these 21.4% had CAD, more than the double that of non-diabetics. All these data suggest that the epidemic of type 2 DM and CAD has already assumed alarming proportions.

Cardiovascular risk factors

Diabetes mellitus and coronary artery disease share many common risk factors. According to Reaven, diabetes and CAD are constituents of the metabolic syndrome in which insulin resistance plays a contributory role. There is a clustering of several metabolic disorders like dyslipidemia, HTN, hyperglycemia and central abdominal obesity.

In addition, a number of other risk factors for CAD such as atherothrombotic factors, fibrinolytic factors, coagulation factors inflammatory markers have also been described in diabetic patients.

Risk factors more common in Asians

1. Decreased physical activity
2. Increased central obesity

3. Hyperinsulinemia and increased insulin resistance
4. Decreased beta cell function
5. Increased prevalence of NIDDM
6. Increased lipoprotein (a)
7. Increased TG
8. Decreased HDL

The metabolic syndrome is a constellation of abnormalities including glucose intolerance, hyperinsulinemia, dyslipidemia, obesity [central or generalized], hypertension and Microalbuminuria, often combined with haemostatic and fibrinolytic abnormalities.

The WHO definition of this syndrome includes [57]

1. Impaired glucose regulation or diabetes
2. Insulin resistance
3. Raised arterial pressure > 160/90
4. Raised plasma triglyceride > 150 mg/dl and/or low HDL Cholesterol <35 mg/dl in men and <39 mg/dl in women.
5. Central obesity (males waist to hip ratio > 0.9 females waist to hip ratio > 0.85**)** and / or BMI / 30 kg/m^2

6. Microalbuminuria

To satisfy the criterion of metabolic syndrome a patient needed to have either criterion (1) or (2) positive along with at least 2 of the 4 remaining criteria.

Two major studies on the metabolic syndrome include a recent population-based study by Isomaa and Coworkers in Finland and Sweden concluded that the metabolic syndrome was present in 10% of subjects with normal glucose tolerance, 50% of subjects with impaired fasting glucose or impaired glucose tolerance and 80% of subjects with type 2 diabetes. The risk of coronary artery disease and stroke was markedly increased (nearly three-fold) in those with the syndrome.

It is clear that an excess of established risk factors for heart disease in not the only explanation for the increased CAD among Asians. Perhaps a constellation of cardiovascular risk factors typical of these observed in insulin resistant status operates in Indians; notably increased

triglycerides, decreased HDL, hyperinsulinemia, central obesity and a high prevalence of type 2 diabetes (as part of the metabolic syndrome or independently).

Recent findings suggest that part of this risk is inherited, probably linked to lipoprotein (a) and genetic polymorphism. This when combined with environmental influence of westernization including obesity, decreased physical activity, dietary changes, increased LDL cholesterol and diabetes can be transformed into very potent risk factor for IHD. This may be mediated through an increased thrombotic tendency related to increased plasminogen activator inhibitor-1 (PAl-1) and reduced tissue plasminogen levels.

Treadmill test is most widely used for both diagnosing ischemic heart disease and as well as estimating their prognosis by using 12 lead electrocardiography. It predicts the likelihood of coronary artery disease in 98% of persons with typical angina. The positive response to ischemia is flat ST segment depression of >0.1mV below baseline (PR segment)

last longer than 0.08s. Negative test does not exclude the coronary artery disease although it makes the three-vessel (or) left main coronary artery disease unlikely.

METABOLIC SYNDROME AND STROKE

Stroke is the second leading cause of death worldwide.[58] In India community surveys have shown a crude prevalence rate for hemiplegia in range of 200 per 100000 persons nearly 1.5% of all medical and around 20% of neurological cases.[59] In India, peak year of occurrence of stroke between 55-65 years.[60]

Risk factors for stroke

1. Systemic arterial hypertension
2. Diabetes
3. Hyperlipidaemia (particularly, low HDL and high LDL)
4. Smoking
5. Older age

6. Family history of thrombotic stroke are proven atherosclerosis risk factors for ischemic stroke

Of these above mentioned risk factors, first three forms the components of the metabolic syndrome. Among this hypertension is the most significant risk factor for ischemic stoke.[61] So all hypertensive patients to be treated. Whether or not tight control of blood sugar in patients with diabetes lowers stroke risk is uncertain.[62]

But one Meta analysis of incidence of stroke in Asian population showed a positive relation between increasing cholesterol levels and non-hemorrhagic stroke[63] and several trials have confirmed that statin drugs reduce the risk of stroke even in patients without elevated LDL or low HDL.[64]

PERIPHERAL ARTERIAL DISEASE

The term peripheral arterial disease generally refers to atherosclerosis when it obstructs the blood supply to the lower or upper extremities. It is an important manifestation of systemic atherosclerosis, and is a strong marker for risk of major cardiovascular and cerebrovascular events,

The risk factor most correlated with the onset and progression of peripheral arterial disease is cigarette smoking, followed by diabetes mellitus. Abnormalities in lipid metabolism are also associated with an increased prevalence of peripheral arterial disease; Relative risk for peripheral arterial disease is about 1.1 for each 10 mg /dl increase in total cholesterol with similar increases for development of claudication.[65]

Peripheral Vascular Disease of the lower extremity is an important cause of morbidity and affects 10 million people in India.[66]

Unique Features of Peripheral Vascular Disease in Indians

1. Presentation at younger age (mean age 45 years)
2. Increased association of diabetes and presence of typical Diabetic Peripheral Vascular Disease
3. Strongest correlation with presence of Coronary Artery Disease (CAD) and Cerebrovascular Disease (CVD).

Peripheral vascular disease in diabetes

Diabetes Mellitus is an important risk factor of lower extremity arterial disease (LEAD) in India. Smoking and insulin resistance are frequently present in patients with diabetes and contribute an additional risk for vascular disease.

In population based and epidemiology based studies, [67] It is estimated that 20-30% of diabetic patients over 65 years of age have peripheral arterial disease. In 75% cases peripheral vascular disease is asymptomatic, in 25% cases peripheral vascular disease is symptomatic with intermittent claudication, coldness and numbness of feet, weakness of lower limb, dependent rubor, non healing ulcer and gangrene.

Clinical presentation of lower limb vascular disorders

1. Intermittent Claudication

It is characterized by pain or fatigue in the affected leg on walking and relieved by rest. It occurs when the oxygen demand of the skeletal muscle exceeds the blood supply during exercise and is due to activation of local receptors by accumulated lactic acid. Claudication has been graded using different classifications. The commonly used classification is

Fontaine classification [68]

Stage	Symptoms
I	Asymptomatic
II	Intermittent claudication
II a	Pain free, claudication on walking > 200 meters
II b	Pain free, claudication on walking < 200 meters
III	Rest and nocturnal pain
IV	Necrosis, gangrene

2. Rest Pain

Clinical Methods

1. Palpation of peripheral pulses

Absence of peripheral pulses is an important finding. Absent posterior tibial, popliteal or femoral pulses with / without bruits indicate significant occlusive peripheral vascular diseases especially if associated with symptoms like claudication. Physical examination often reveals decreased pulsations. Capillary refilling, increased venous filling time (>20 seconds), atrophic changes, loss of hair, discoloration of skin and decreased temperature are common clinical findings.

2. Ankle brachial index

It is the ratio of the systolic blood pressure measurement of the ankle to that of the brachial artery.

a) A normal ABI should be less or equal to 1.1

b) An index of < 0.9 is abnormal and indicates occlusive PVD, especially in presence of absent peripheral pulses.

c) ABI less than or equal to 0.8 indicates PVD regardless of symptoms.

d) Because of the presence of calcific medial sclerosis which prevents

the compression of the calcified vessel, diabetics present a challenge to the sensitivity of this method.

Duplex Imaging

Gray scale and color flow imaging are useful in localizing the diseased segment while spectral imaging is used to assess the severity of the lesion. A two fold or greater increase in peak systolic velocity at the site of stenosis indicates 50% or more stenosis. Doppler signals are absent if artery is totally occluded.

MATERIALS AND METHODS

A sample of 120 cases of elderly (60 years & above) men and women were selected by systematic sampling methods from our medical out patients department, Government General Hospital, 20 cases were excluded since they had hemorrhagic stroke and selected cases were analyzed for the presence of metabolic syndrome and vascular complications present in that group.

The patients having three or more of the following criteria (according to the National Cholesterol Education Guidelines Adult Treatment Panel (ATP) 3 report) were defined as having the metabolic syndrome:

1. Waist circumference > 102 cm in men and > 88 cm in women
2. Hypertriglyceridemia: ≥ 150 mg/dl (≥ 1.7 mmol/l).
3. Low HDL: < 40 mg/dl in men (<1.0 mmol/l)

   and < 50 mg/dl in women (<1.3 mmol/l)

5. High blood pressure: ≥ 130/85 mmHg or use of antihypertensive medication.
6. High fasting plasma venous glucose: ≥ 110 mg/dl (≥ 6.1 mmol/l) or treatment for diabetes.

Because the ATP 3 criteria for HDL cholesterol and waist circumference might not be appropriate for Asian population, additional calculations for the prevalence of the metabolic syndrome were done based on a recommended regional cutoff for HDL cholesterol of less than 40 mg/dl (1.0 mmol/l) for both men and women and waist circumference greater than 90 cm for men and greater than 80 cm for women.[69]

The 1997 American Diabetes Association criteria were used to define diabetes.[70] we considered a subject to have diabetes when the fasting plasma venous glucose was ≥ 126 mg/dl (≥ 7mmol/l) in two consecutive assessments or if they were on treatment for diabetes.

For each enrolled subject, the personal and family medical histories were obtained. On the study day, height and weight were measured twice during the examination. Weight was measured to the nearest 100 g with bare foot. Height was measured to the nearest mm with a stadiometer. Body mass index (BMI) was calculated by the formula

$$BMI = \text{Weight (kg)} / \text{Height (m)}^2$$

Overweight was defined as a BMI of 23 kg/m^2 or greater, according to Asia Pacific guidelines. Blood pressure was measured was measured with patient in the sitting position after a 5 min rest, with mercury sphygmomanometer (cuff size 12.5 × 40 cm). The systolic BP and diastolic BP were read to the nearest 2 mmHg. Disappearance of Korotkoff's sounds (phase 5) was the criterion for diastolic BP. Standard 12 lead ECG was obtained from each patients. Echocardiogram was obtained for each patient to show the features of ischemia changes. Waist

circumference was measured at 1 cm above the navel at minimal respiration.[71]

The definition of vascular disease included coronary heart disease, stroke, and/ or peripheral arterial disease. The presence of vascular disease was established based on physical examination and personal medical history. Prevalent coronary heart disease was diagnosed by the presence of history of hospitalization for myocardial infarction, coronary bypass artery grafting, or percutaneous transluminal angioplasty, or by the presence of stable angina, positive exercise tolerance test (The development of 0.10 mV (1 mm) or greater of J point depression measured from PQ segment with a flat ST segment depression of 0.10 mV or greater at 80 m sec after J point in three consequent beats is the evidence of ischemia) or coronary angiography with at least one substantial coronary artery stenosis.

Subjects were considered to have a stroke if they had been discharged from a hospital with this diagnosis. Only those with

confirmation of a non-hemorrhagic stroke by a CT scan were included. Peripheral arterial disease was established by physical examination and the presence of intermittent claudication, and Duplex imaging. If a subject had more than one vascular disease manifestation he/she was considered only once (adjustment for overlap).

The study groups were classified into four groups i.e.) metabolic syndrome with diabetes, metabolic syndrome without diabetes, no metabolic syndrome with diabetes, no metabolic syndrome without diabetes. Initially prevalence of metabolic syndrome in the study group was assessed, and then vascular disease prevalence was assessed by comparing with non-metabolic syndrome group.

STUDY DESIGN:

To evaluate the presence of metabolic syndrome and assess the prevalence of vascular diseases in elderly with the metabolic syndrome with or without diabetes when compared with subjects without metabolic syndrome, a cross-sectional study design was chosen.

Laboratory methods

Overnight fasting (at least 10 hours) blood specimen were obtained for measurement of serum lipids and plasma glucose. Concentration of total cholesterol, HDL- cholesterol, and triglycerides were assessed enzymatically with commercially available reagents. Concentration of LDL- cholesterol was calculated by use of the Friedewald equation for participants who had triglycerides (< 400 mg/dl)

$$LDL = TC – HDL\text{-}c – TGL/5$$

Serum creatinine, blood urea, serum electrolytes, and other biochemical evaluation were performed according to routine standards, at biochemical lab attached to Institute of Biochemistry, Govt. General Hospital.

STATISTICAL ANALYSIS

Statistical analysis was carried out for 100 subjects [45 metabolic syndrome, 55 no metabolic syndrome] after categorizing each variable. Base line data was collected from patients with vascular disease and metabolic syndrome and without metabolic syndrome. Age, sex, lipid profile, non HDL cholesterol, components of the metabolic syndrome such as waist circumference, systemic BP > 130/85, fasting glucose > 110, Triglycerides >150, Low HDL < 40 mg/dl were analyzed.

The significance of difference in means between two groups and the significance of difference in proportions were analyzed by Z test. The prevalence of vascular disease in the metabolic syndrome were analyzed and compared with non-metabolic syndrome group. Statistical significance was taken when two-sided p value < 0.05. Statistical analysis was carried out using standard formulae by Microsoft Excel 2003. The correlation between metabolic syndrome components and vascular disease was done by spearman's rho methods.

Observations

Table 1

Prevalence of vascular diseases in Total met syn group

	All Subjects	Met syn all	No Met syn all	P value
	n =100	n = 45	n = 55	
Male (%)	56	51.1	60.0	0.368
WC (%)	52	86.7	23.6	<0.00001
High FGL (%)	44	68.9	23.6	<0.00001
AH (%)	47	75.6	23.6	<0.00001
High TGL (%)	47	91.1	10.9	<0.00001
Low HDL (%)	44	66.7	25.5	<0.00001
DM (%)	34	53.3	18.2	<0.00001
CHD (%)	31	55.6	10.9	<0.00001
Stroke (%)	25	44.4	9.1	<0.00001
PAD (%)	2	4.4	0.0	0.161
Vas D (%)	42	71.1	18.2	<0.00001
Vas D > 1 (%)	16	33.3	1.8	<0.00001

WC- waist circumference; AH- arterial hypertension

Table 2

Prevalence of vascular diseases in met syn with DM group

	All Subject	Met syn + DM	No Met syn +DM	P value
	n =100	n = 24	n = 10	
CHD (%)	31	66.7	30.0	<0.034
Stroke (%)	25	58.3	30.0	<0.108
PAD (%)	2	4.2	0.0	<0.316
Vas D (%)	42	87.5	50.0	<0.026
Vas D > 1 (%)	16	41.7	10.0	<0.020

Table 3

Prevalence of vascular diseases in met syn without DM group

	All Subject	Met syn +no DM	No Met syn + No DM	P value
	n =100	n = 21	n = 45	
CHD (%)	31	42.9	6.7	<0.0006
Stroke (%)	25	28.6	4.4	<0.0124
PAD (%)	2	4.8	0.0	<0.270
Vas D (%)	42	52.4	11.1	<0.0002
Vas D > 1 (%)	16	23.8	0.0	<0.006

Table 4

Lipid profile in met syn and no met syn group

Lipid fraction	Met syn	No met syn	P value
Total cholesterol	214.07± 18.24	195.09± 11.19	<0.0001
HDL	39.27± 4.29	42.05± 4.13	<0.0008
Triglycerides	177.53± 22.89	147.47± 11.77	<0.0001
LDL	139.29± 17.82	123.54± 13.63	<0.0001

The prevalence of metabolic syndrome in our study group was 45%. The prevalence of metabolic syndrome in men was 51.1%. The prevalence of metabolic syndrome in women was 48.9%. Both genders had same prevalence of metabolic syndrome ($p = 0.5$) and was not statistically significant.

The overlap adjusted prevalence of vascular disease in all participants was 42%. All subjects with the metabolic syndrome (n

=45) had a vascular disease prevalence of 71.1%, significantly higher than that of people (n = 55) without metabolic syndrome (18.2%, $p < 0.0001$).

Participants without both the metabolic syndrome and DM (n = 45) had the lowest vascular disease prevalence (11.1%), while subjects with DM but without the metabolic syndrome (n = 10) had a vascular disease prevalence of 50% ($p < 0.05$). This was nearly similar to that of people (n = 21) with the metabolic syndrome without DM (52.4%), but significantly lower than that of participants (n = 24) with both the metabolic syndrome and DM (87.5%, $p < 0.05$).

The concomitant presence of CHD, stroke and PAD in the metabolic syndrome group, with or without DM, (33.3%) was higher than in those without the metabolic syndrome (1.8%). Thus, the sum total of CHD, stroke and PAD was higher in the metabolic syndrome group than in those without the metabolic syndrome. In the metabolic syndrome group, having more than one of CHD, stroke or PAD, the prevalence of vascular disease, when counted as a presence of CHD,

stroke and/or PAD was 71.1%. In contrast, this figure was 18.2% for those without the metabolic syndrome.

All the lipid values of subjects with the metabolic syndrome were significantly different from those of subjects without the metabolic syndrome. A substantial percentage (71.1%) of patients with the metabolic syndrome had high LDL-C levels > 130 mg/dl (> 3.4 mmol/l) and even more (82.2%) had a non- HDL-C > 160mg/dl (> 4.1mmol/l).

The prevalence of vascular disease in the metabolic syndrome group was 71.1%. Among the vascular diseases coronary artery disease had the highest prevalence; PAD had least prevalence and stroke prevalence in between.

Among the component factors of metabolic syndrome, waist circumference (> 90 cm in male, >80 cm in female) had the highest prevalence than other factors. Highest BMI was prevalent in the metabolic syndrome with diabetes group.

The prevalence of vascular disease in the metabolic syndrome alone group without diabetes was significantly ($p < 0.0002$) higher than that of group without metabolic syndrome and no DM but similar to that of group without metabolic syndrome and with DM. Thus the presence of metabolic syndrome alone without DM has increased the risk of developing vascular diseases.

We assessed the strength of correlation of the metabolic syndrome components with the vascular diseases. We found that waist circumference, fasting glucose, triglyceride, arterial hypertension were positively correlating with vascular events, and HDL was inversely correlated with vascular events. Arterial hypertension strongly correlated with stroke, TGL strongly correlated with CHD and HDL was inversely correlated with both CHD and stroke.

Fig.1

Sex distribution

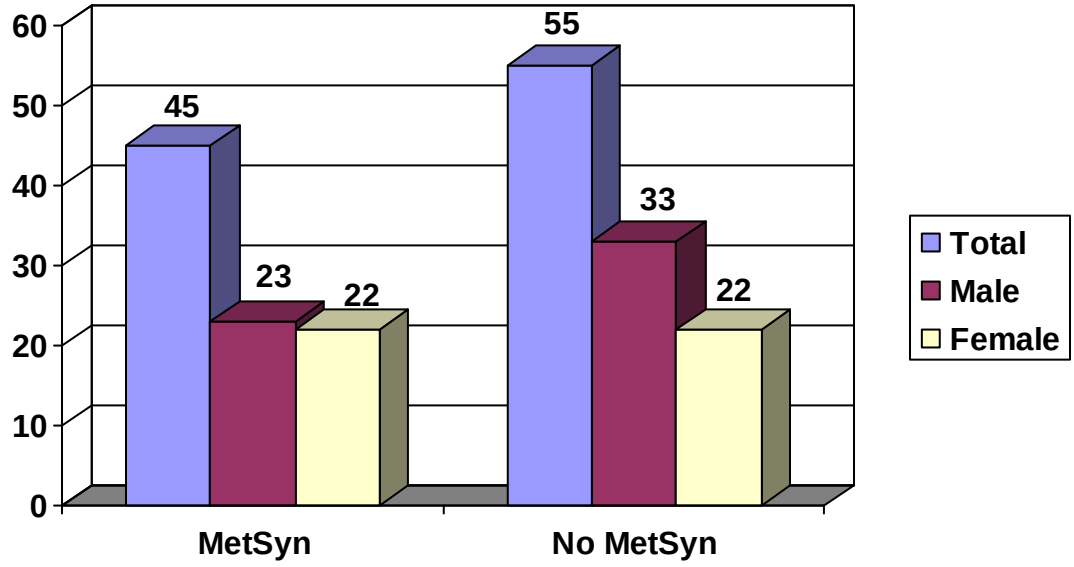


Fig. 2

Prevalence of diabetes

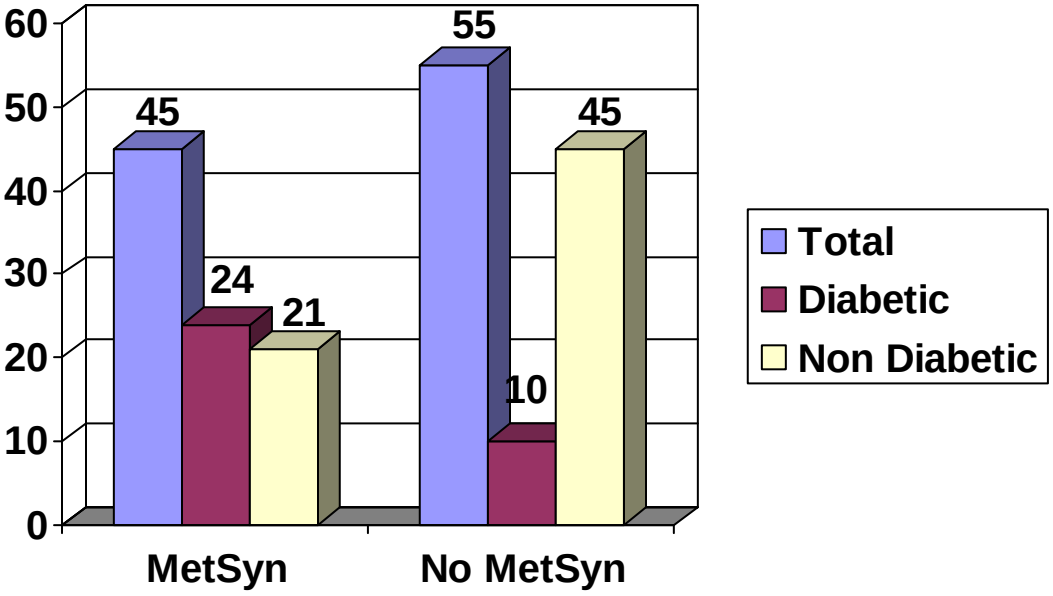


Fig. 3

Prevalence of Central obesity

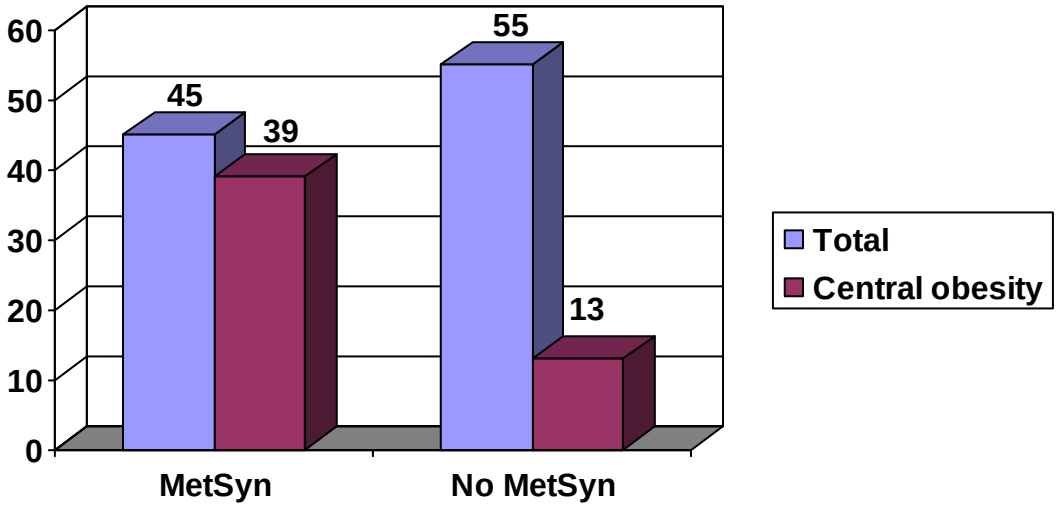


Fig. 4

Prevalence of obesity (BMI >23)

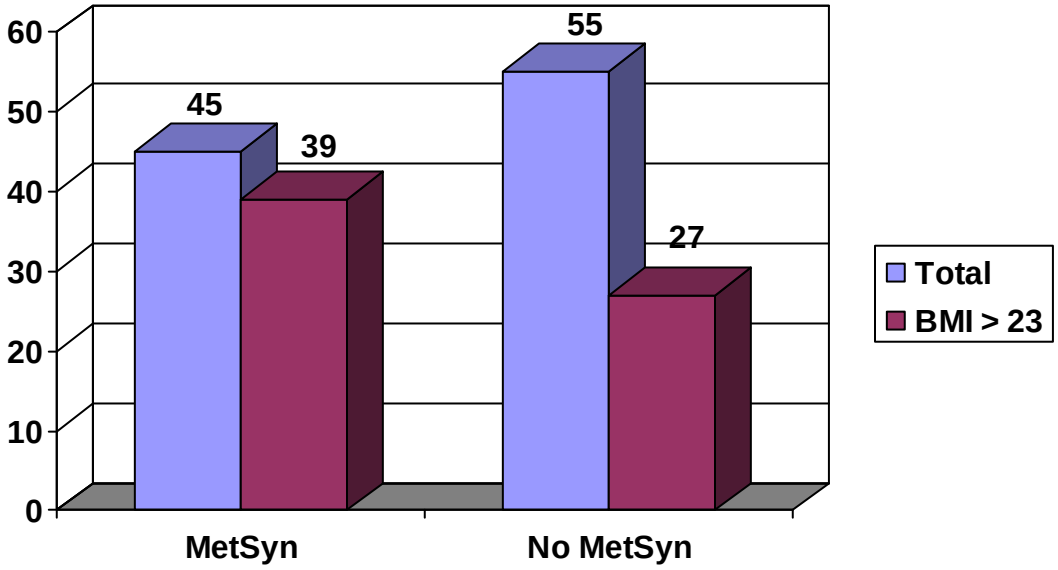


Fig. 5

Prevalence of High triglyceride

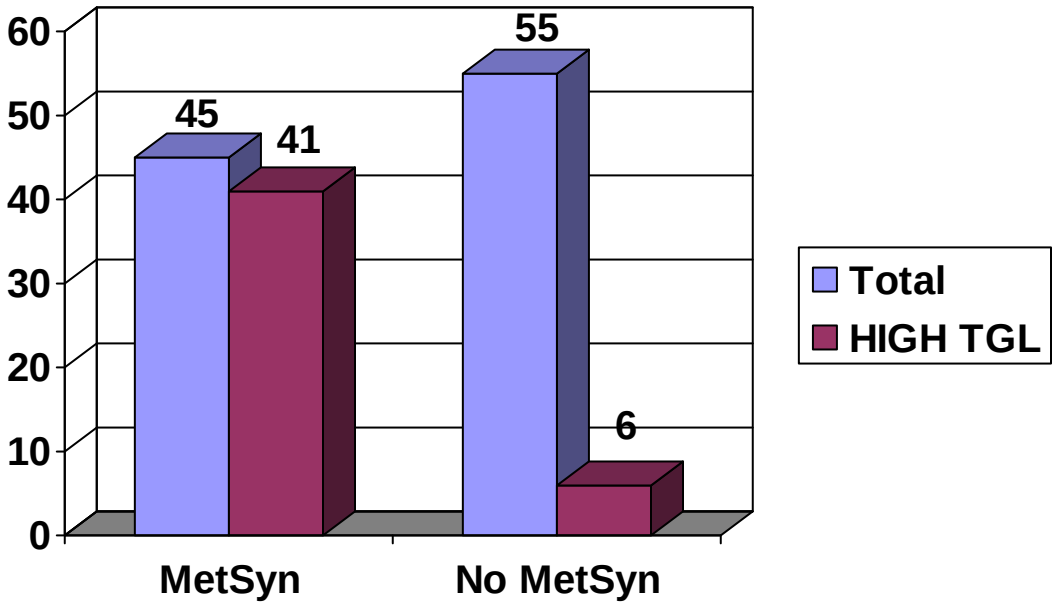


Fig. 6

Prevalence of Low HDL

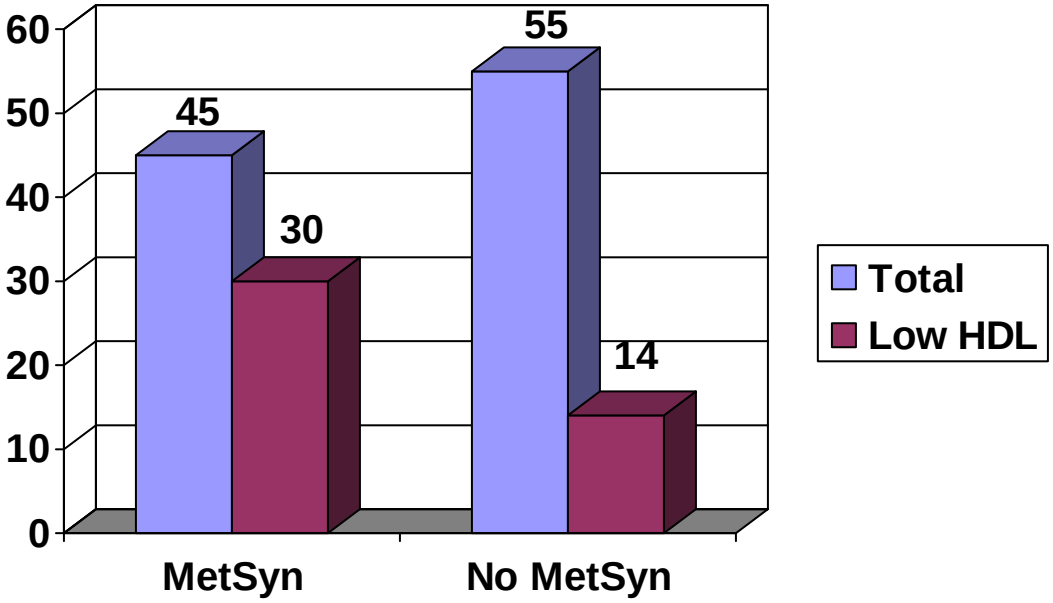


Fig. 7

Prevalence of systemic hypertension

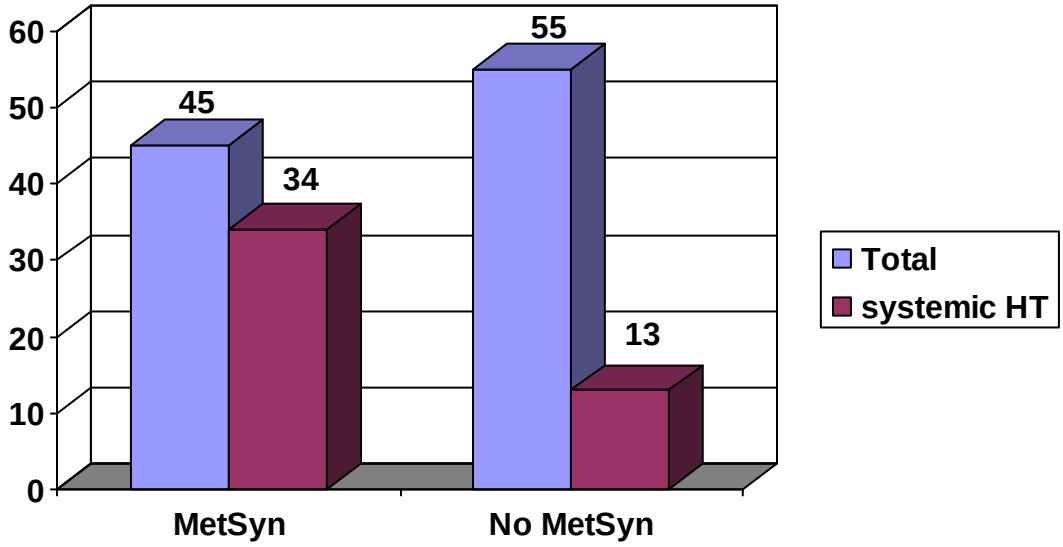


Fig. 8

Prevalence of vascular diseases

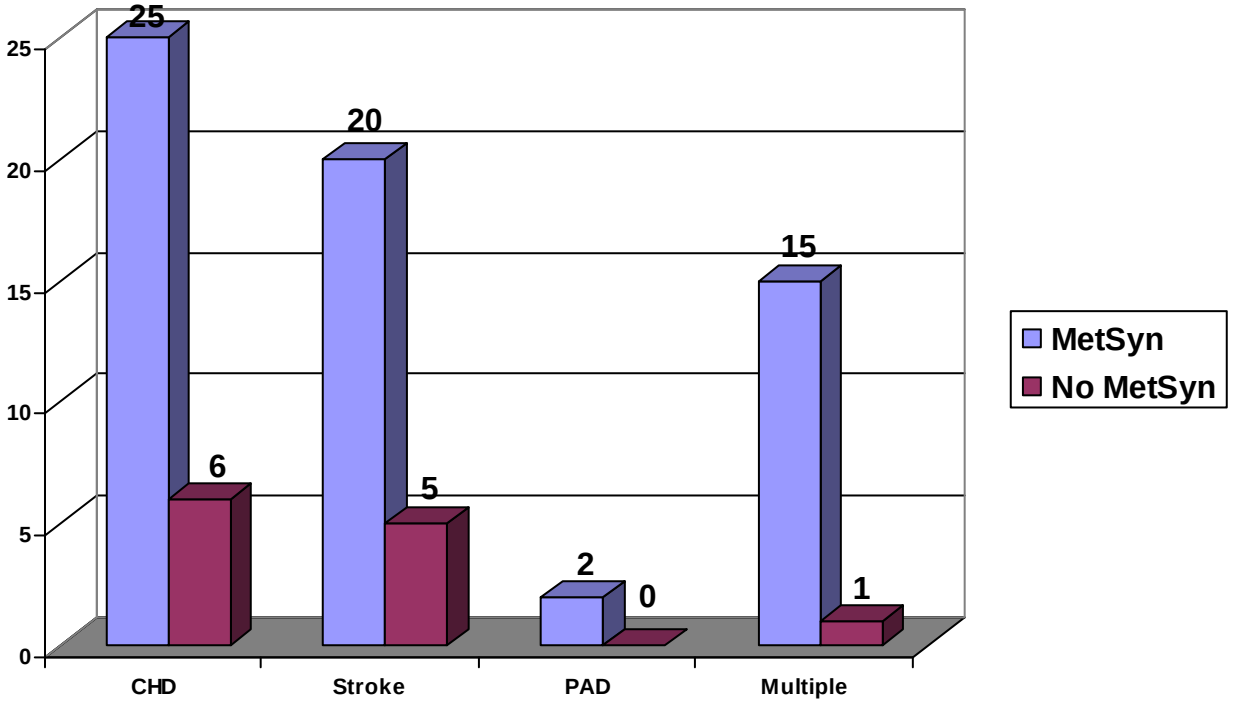


Fig. 9

Prevalence of CHD

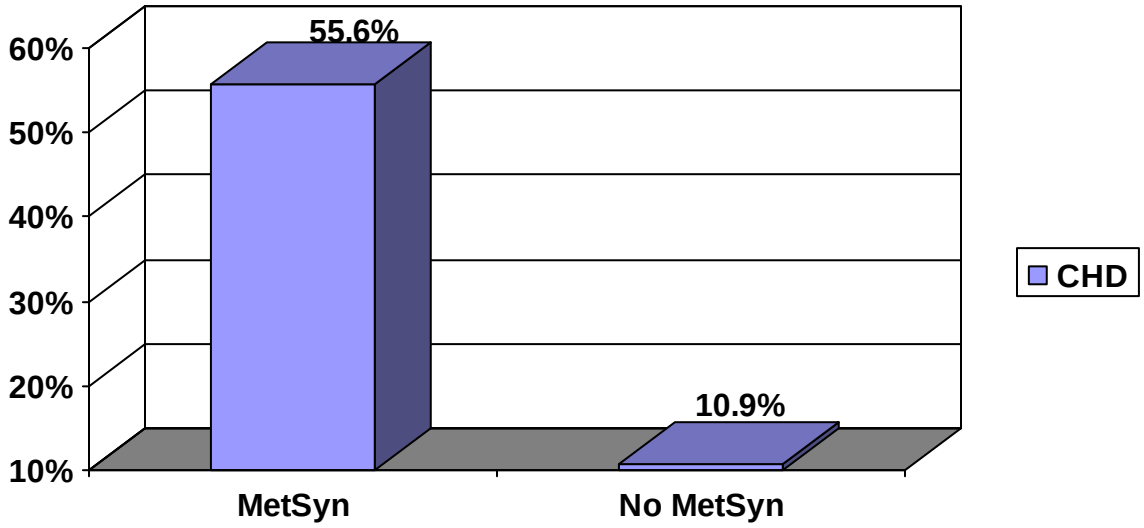


Fig. 10

Prevalence of Stroke

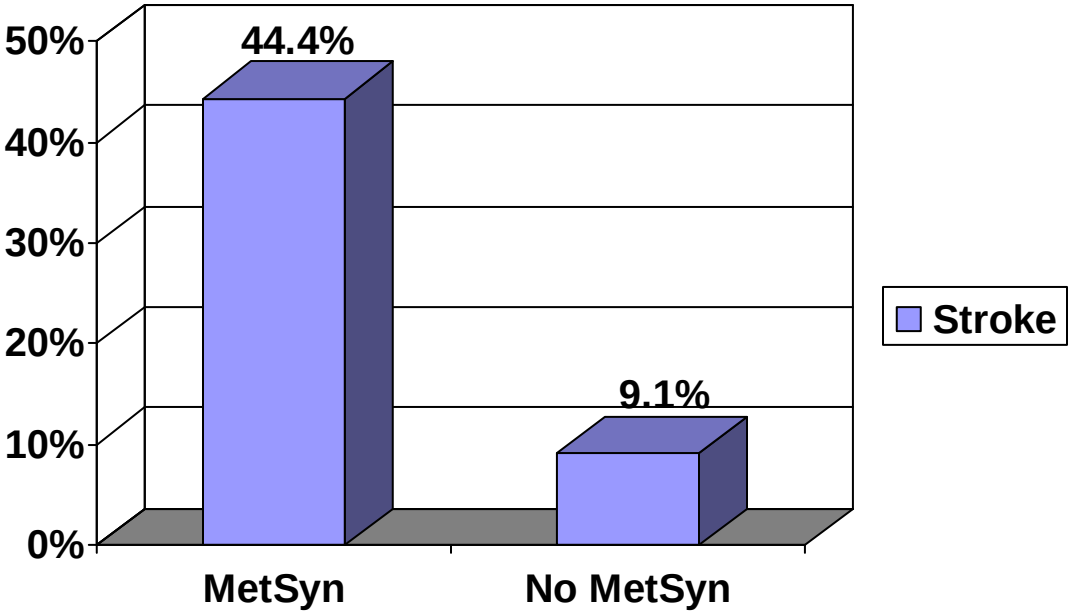


Fig. 11

Prevalence of Peripheral arterial disease (PAD)

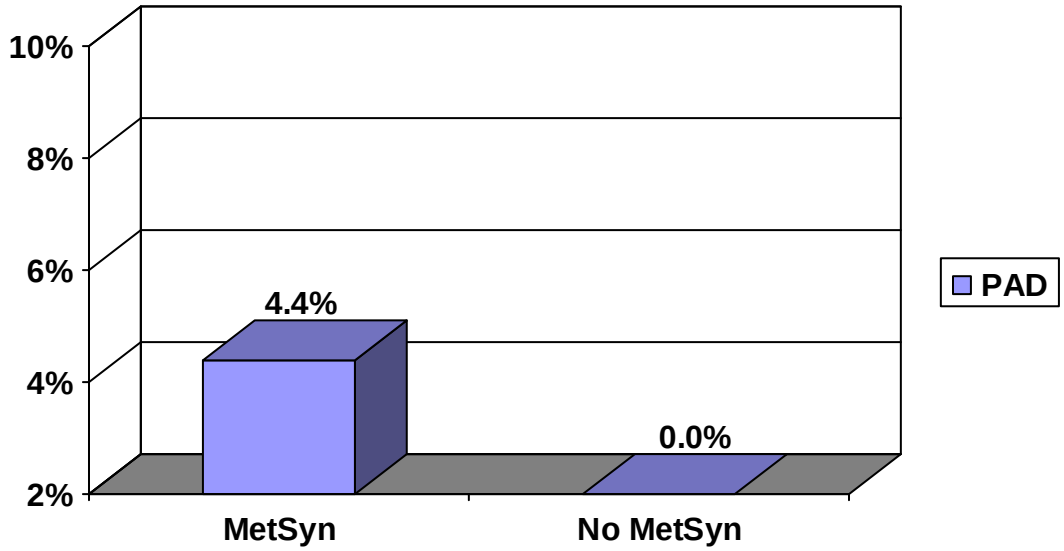


Fig. 12

Prevalence of more than 1 vascular disease

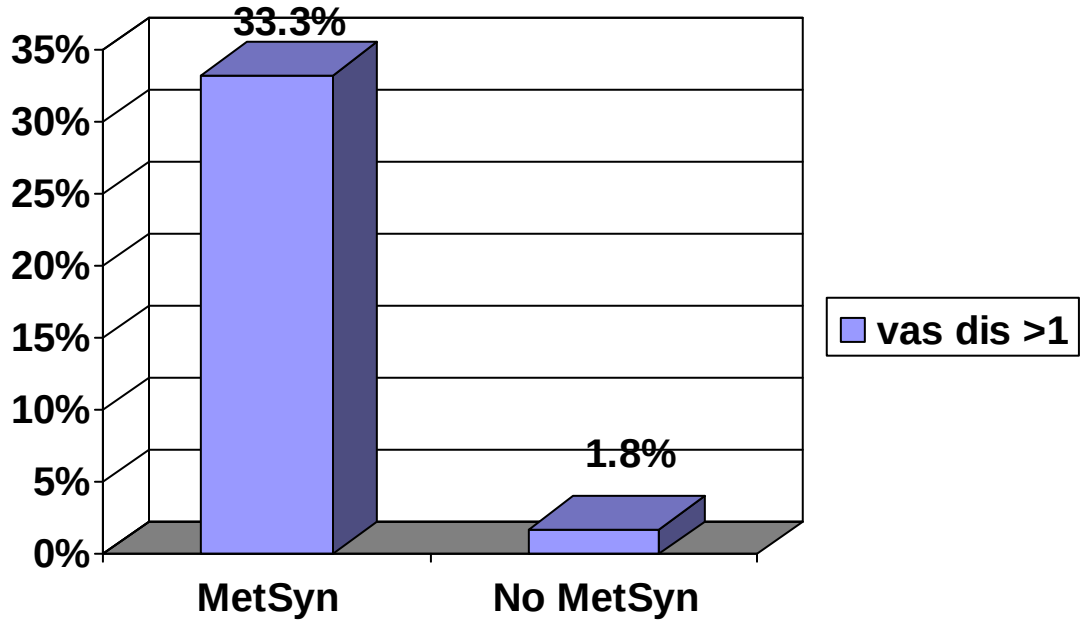


Fig. 13

Prevalence of LDL more than 130 mg/dl

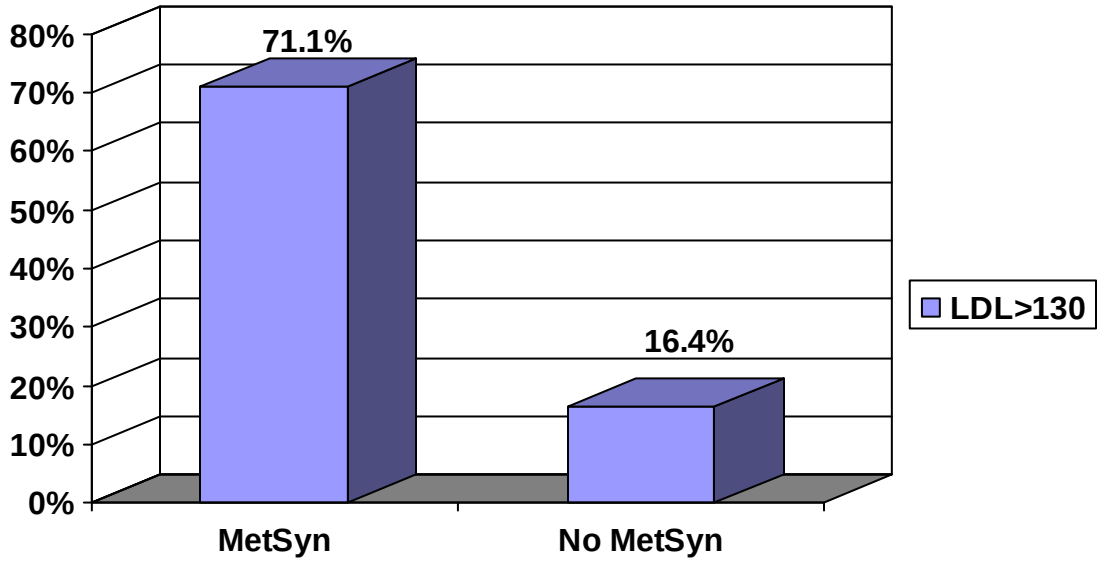


Fig. 14

Prevalence of CHD and Stroke in metsyn with DM and No DM

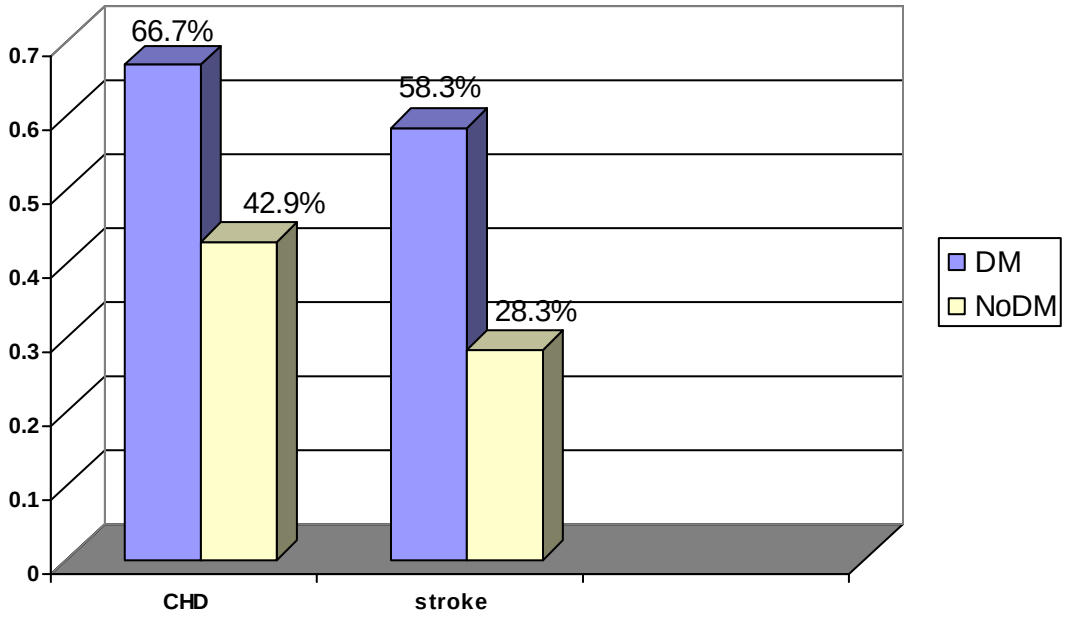
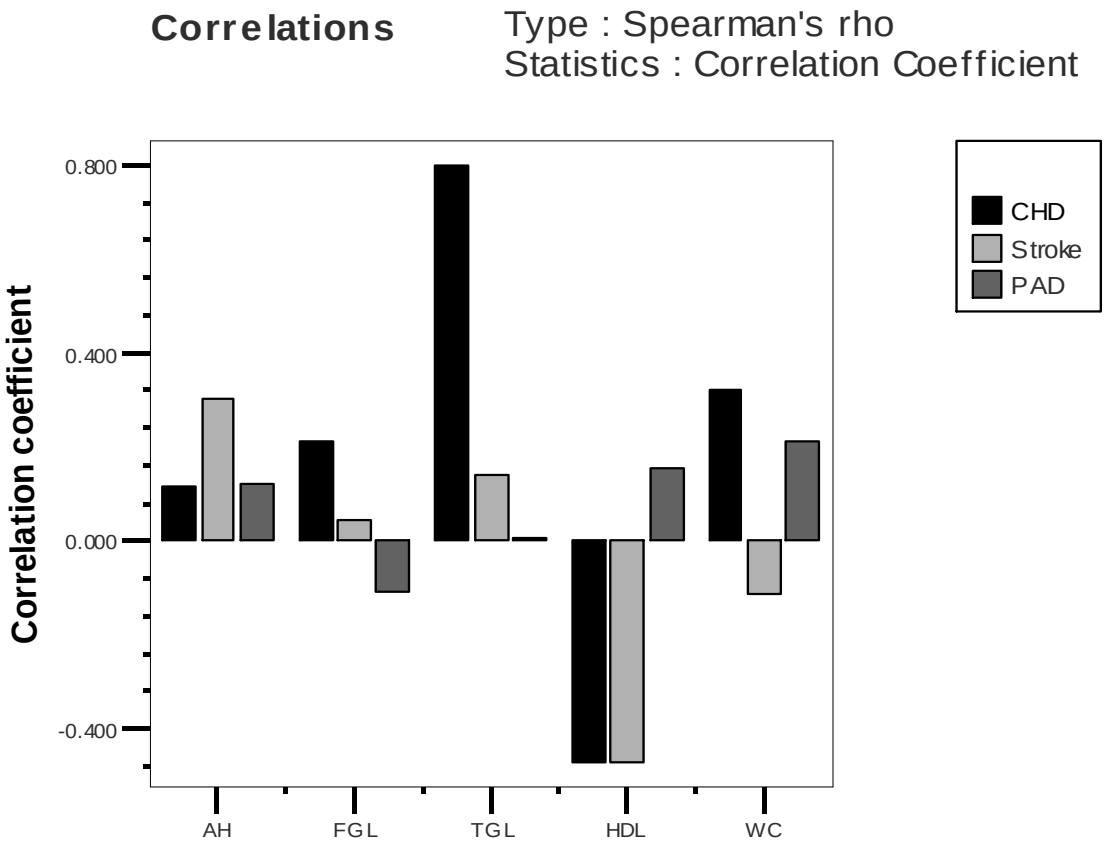


Fig. 15

Correlation of vascular events with MetSyn components



AH-Arterial hypertension

FGL- Fasting glucose

TGL- Triglycerides

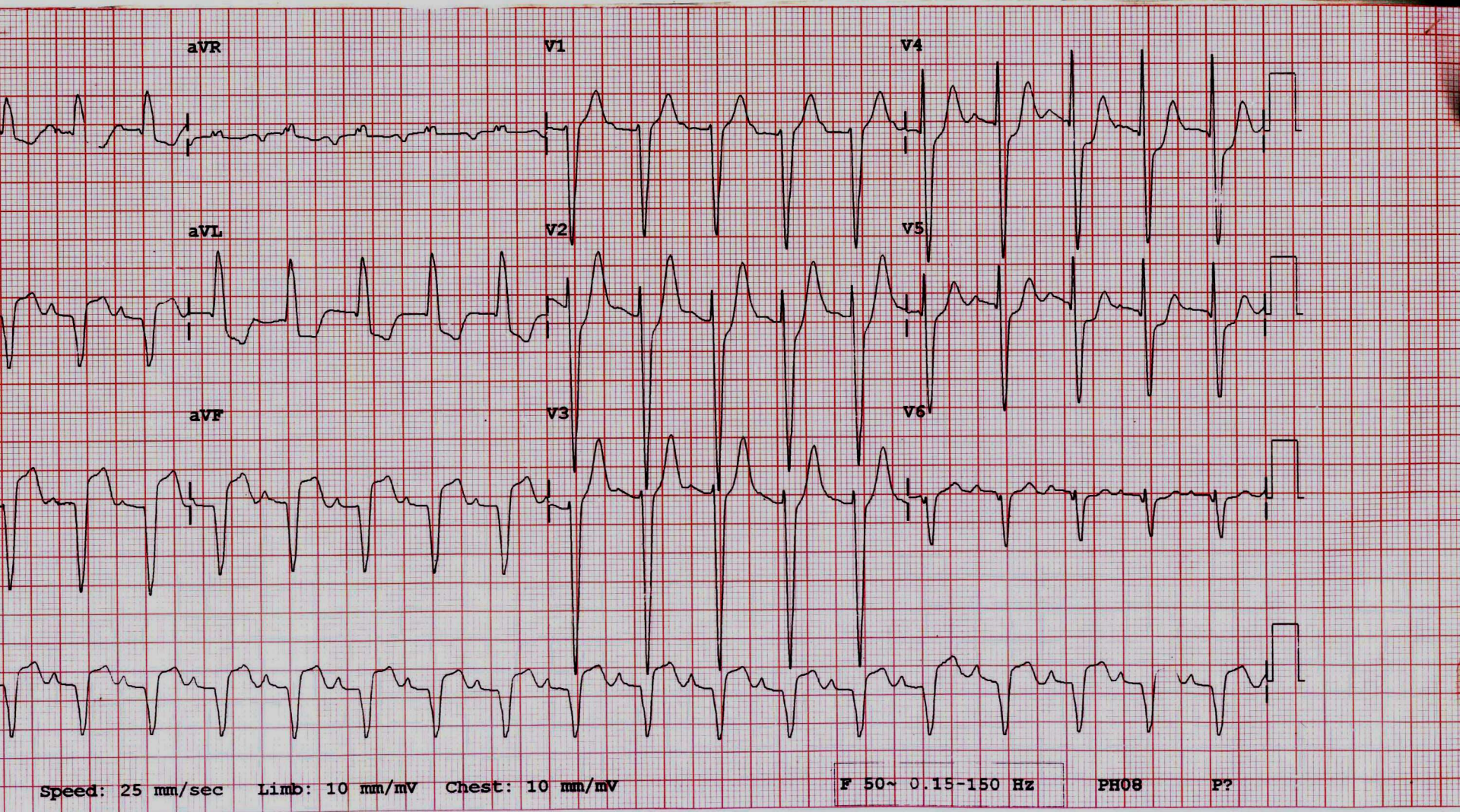
HDL- High density lipoprotein

WC- Waist circumference

PAD- Peripheral arterial disease

CHD- coronary artery disease

DEPARTMENT OF CARDIOLOGY
Government General Hospital
Name Mr. Sivalingam Age 73/M
Date 10.01.06 Time.
M.R.D. No.



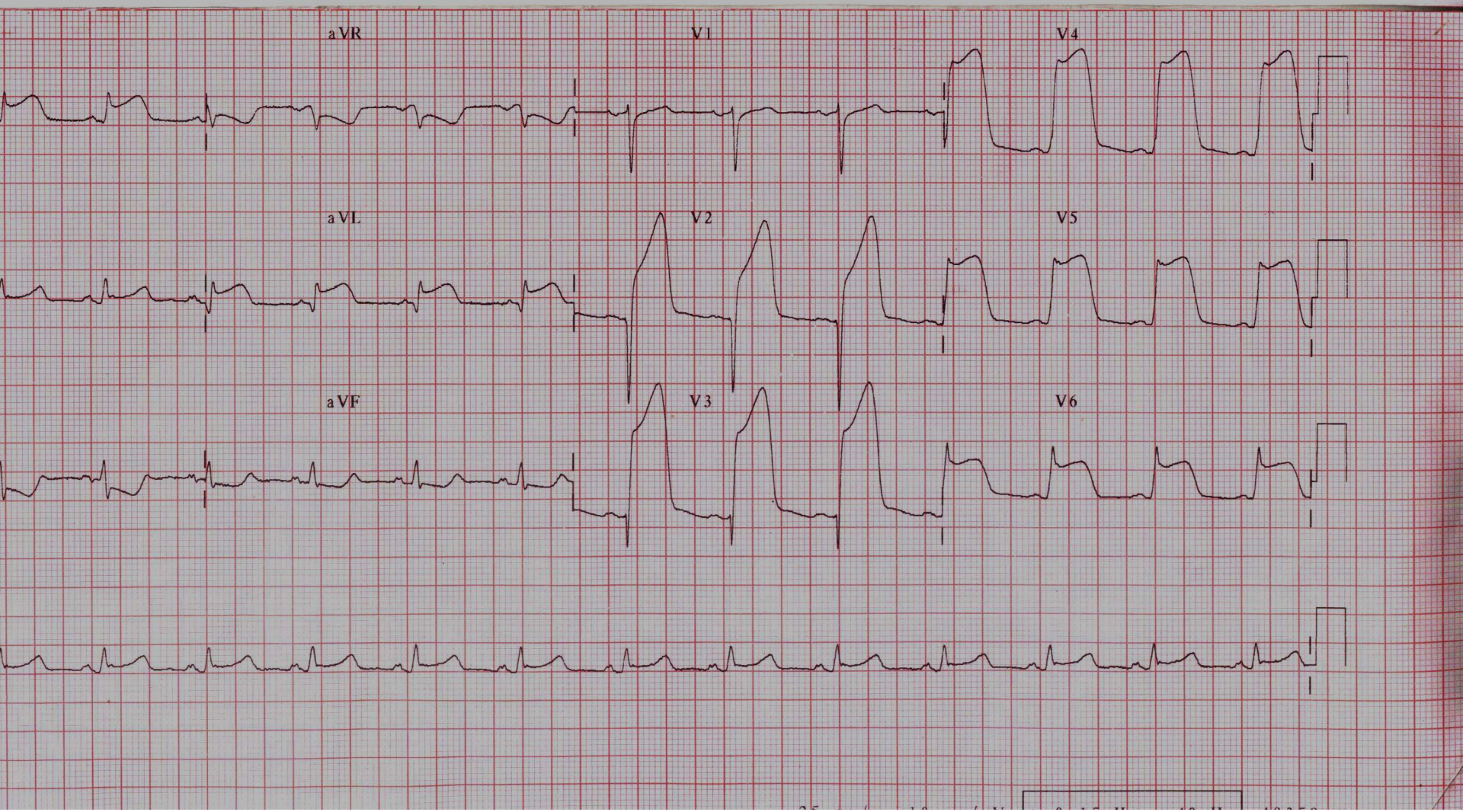
CARDIOLOGY

Government General Hospital

Name Mr. Ramamoorthy. 65/m

Date 22.2.06 Time.

M.R.D.No.



DEPARTMENT OF CARDIOLOGY
GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

First Name : MR SAMUTHARAPANDIAN
Birth Date : / /1945 Age : 61 Y Gender : M
Height : 155 cm Weight : 58 kg
BSA : 1.56 Target HR : 159

Technician : N.S
Code : PROF.VJ

Required by:
Indications : Diabetes

Therapy :

	MAX VALUES		TIME
SPEED	5.4	Km/h	6:09
SLOPE	14.0	%	
	10.1	METS	
HR	112	bpm	2:24
	70.5 %	Target HR	
RPP	198	mmHg*bpm/100	
BP	180	mmHg	3:16
ST+ (V3)	2.0	mm	4
ST- (V4)	-3.3	mm	6:29

Protocol	Test	Stress	Recovery
Bruce	16:35	6:09	8:15

		DURATION	SPEED Km/h	SLOPE %	METS	HR bpm	BPs/BPd mmHg	STMax (V4)
Stand	01	0:31				62	140/ 80	0.6
WarmUp	01	1:39	1.0	0.0	1.5	92	140/ 80	1.1
Exe	01	3:00	2.7	10.0	4.7	109	__/__	-0.8
	02	3:00	4.0	12.0	7.1	108	180/ 80	-2.9
	Peak	0:09	5.4	14.0	10.1	109	180/ 80	-3.0
Recov	01	8:12	0.0	0.0	1.0	69	160/ 80	-0.4
Post	01	0:03	0.0	0.0	1.0	69	__/__	-0.4

Reasons for end : CHEST PAIN

Symptoms : ANGINA

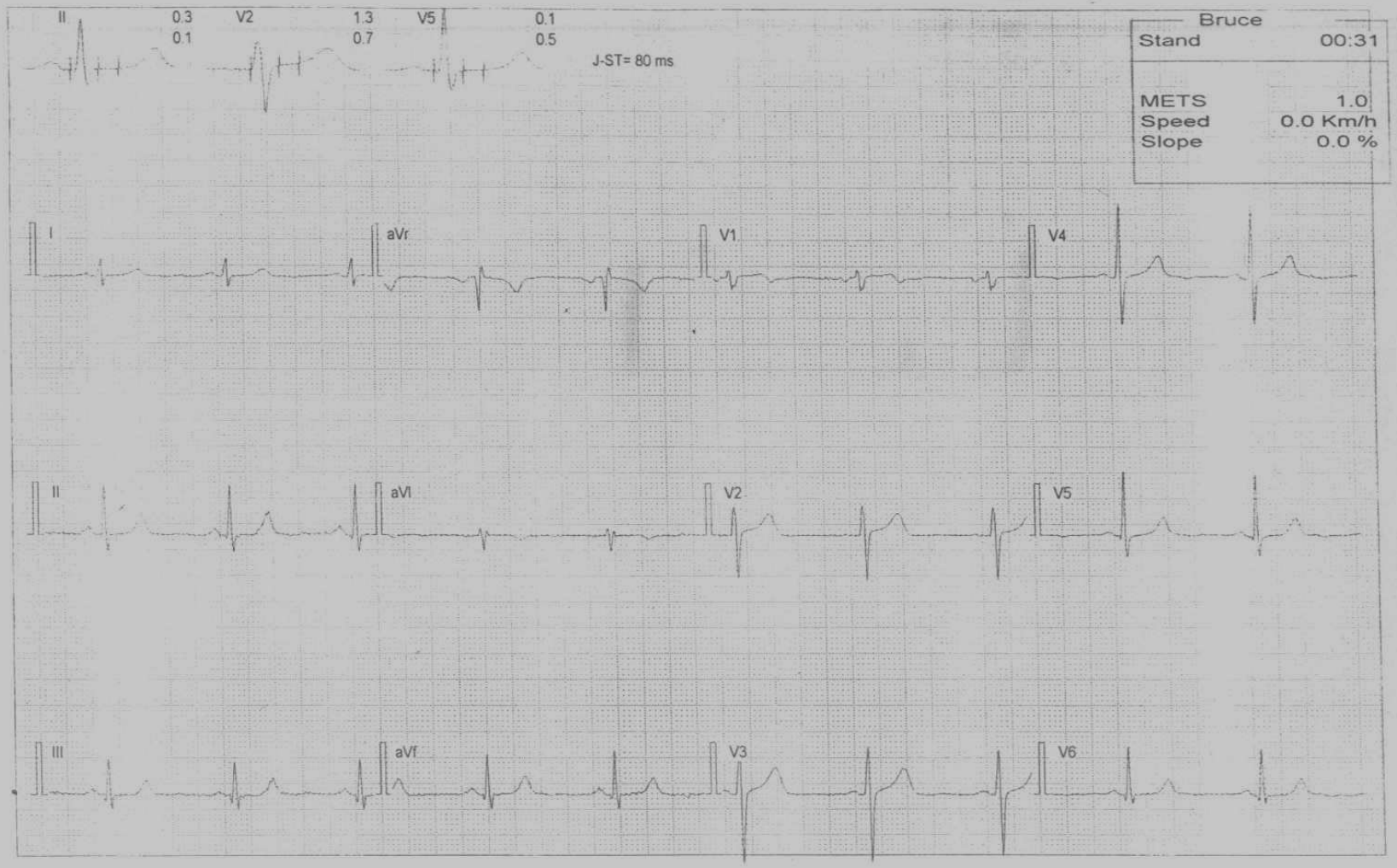
Conclusions : ACHIEVED 70% THR AT 10.1 METS WORKLOAD
NORMAL HR BP RESPONSE
DEVELOPED ANGINA AT 7.1 METS
FUNCTIONAL CAPACITY MODERATE
2mm DOWNSLOPING ST DEPRESSION IN LEADS V3 TO V6 AND LEAD II,III,AVF WHICH PERSIST 8min DURING RECOVERY PERIOD

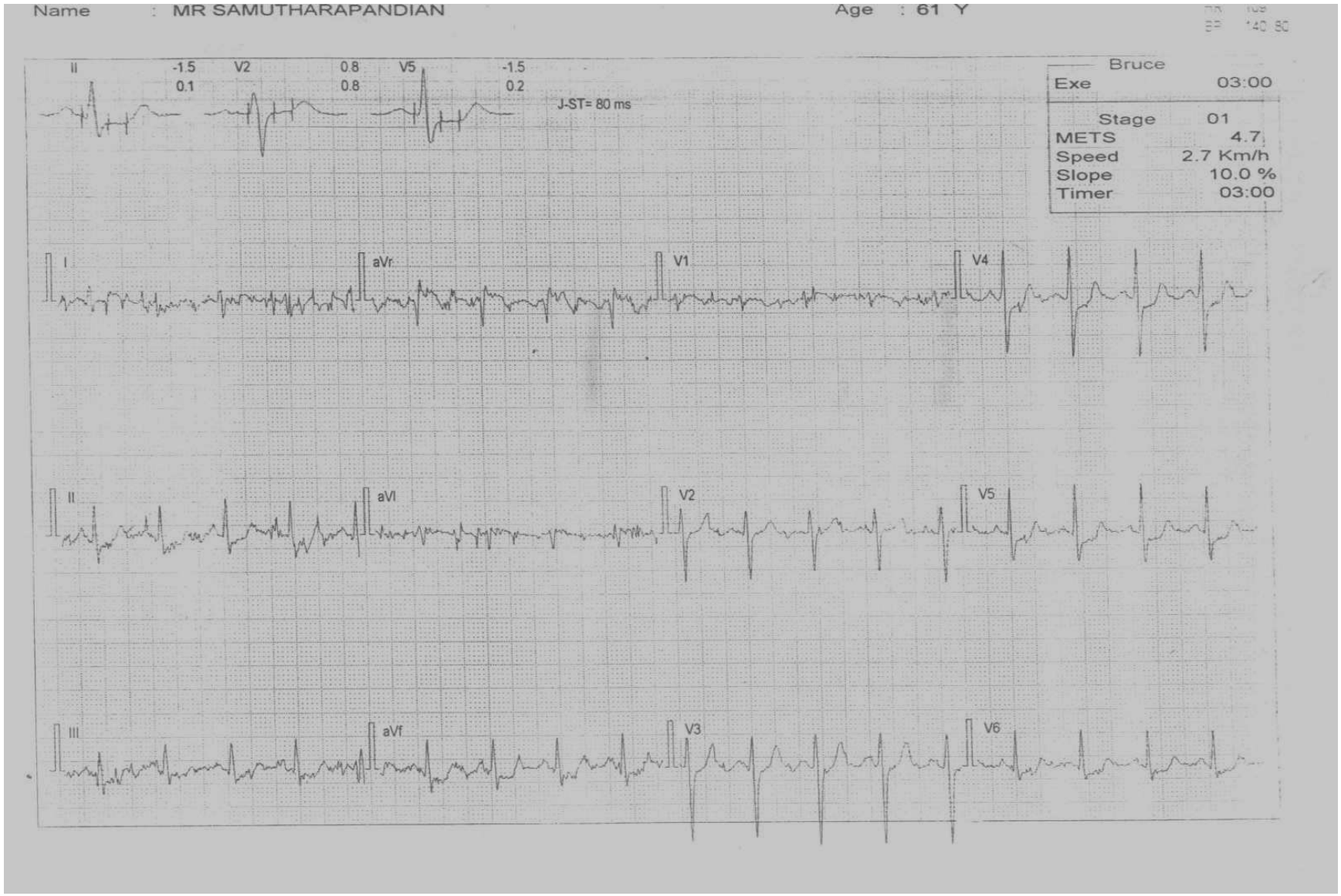
TMT IS POSITIVE FOR INDUCIBLE ISCHEMIA

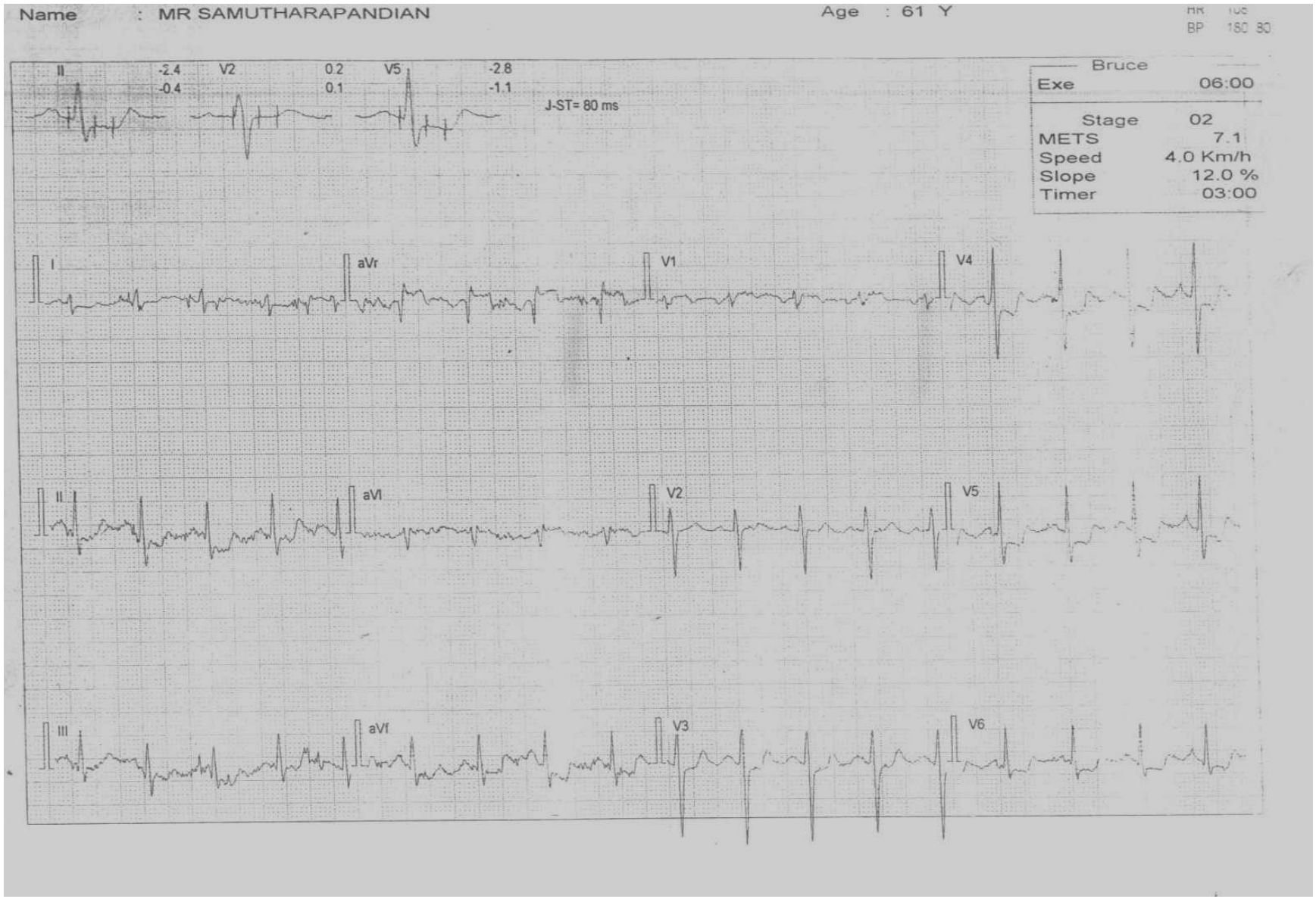
Reported by : DR. P. JAYASANKAR

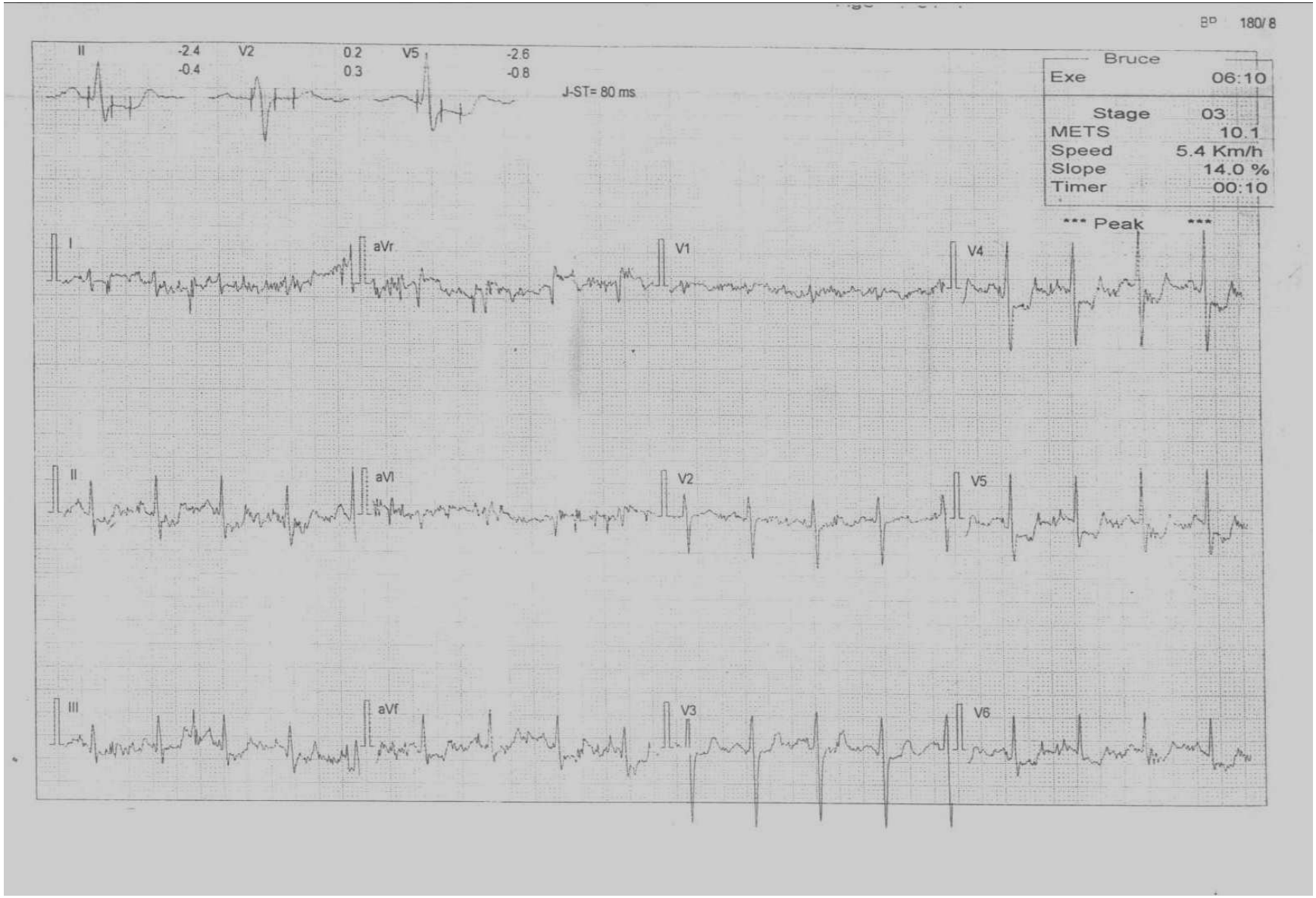
Patient ID : 338
Name : MR SAMUTHARAPANDIAN

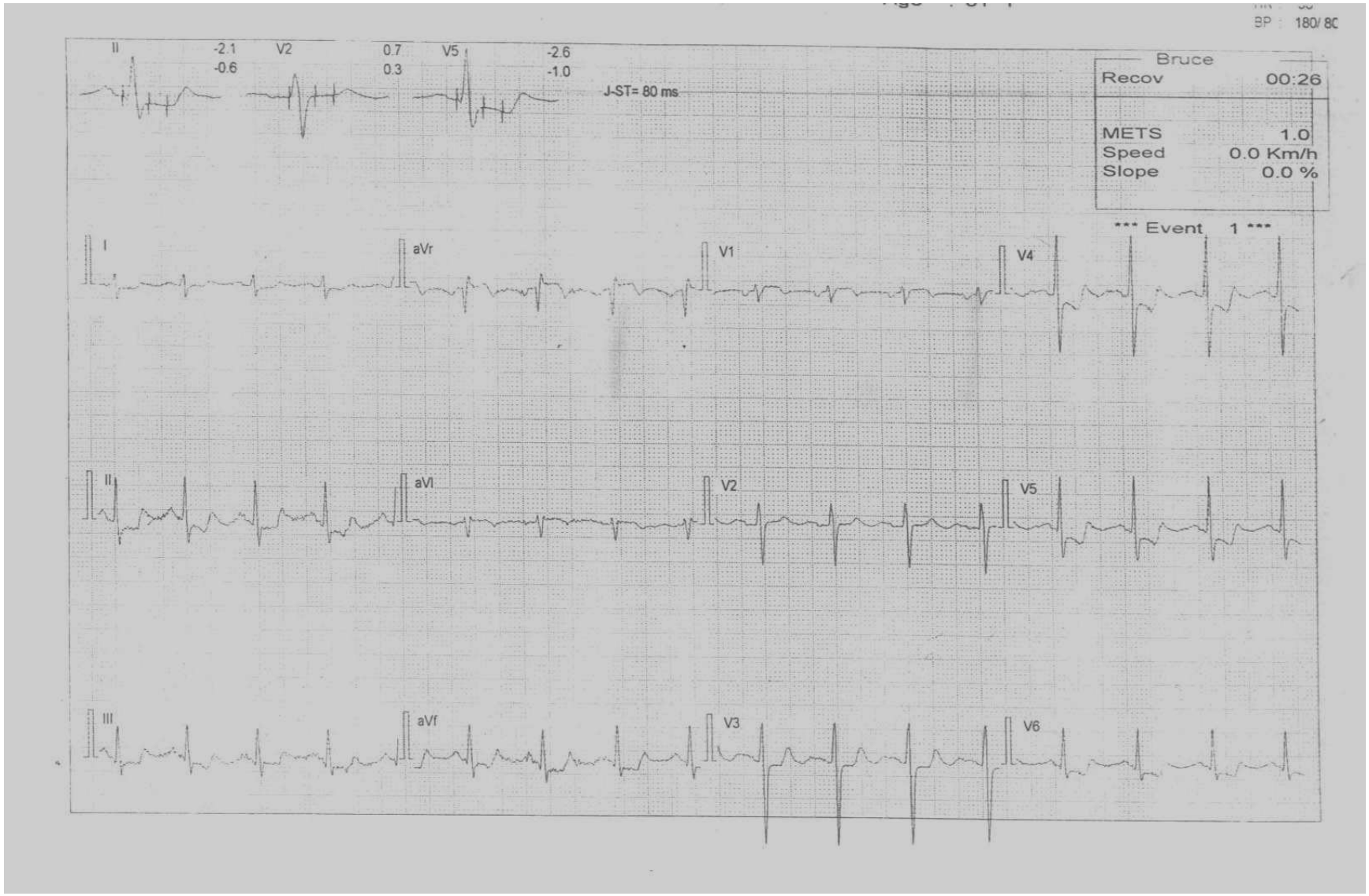
GOVT.GEN.HOSPITAL 10:26:29 01/Mar/2006
Age : 61 Y HR 62
BP 140/80




Name : MR SAMUTHARAPANDIAN
Age : 61 Y
II -1.5 V2 0.8 V5 -1.5
0.1 0.8 0.2
J-ST= 80 ms
Bruce
Exe 03:00
Stage 01
METS 4.7
Speed 2.7 Km/h
Slope 10.0 %
Timer 03:00
I aVr V1 V4
II aVl V2 V5
III aVf V3 V6

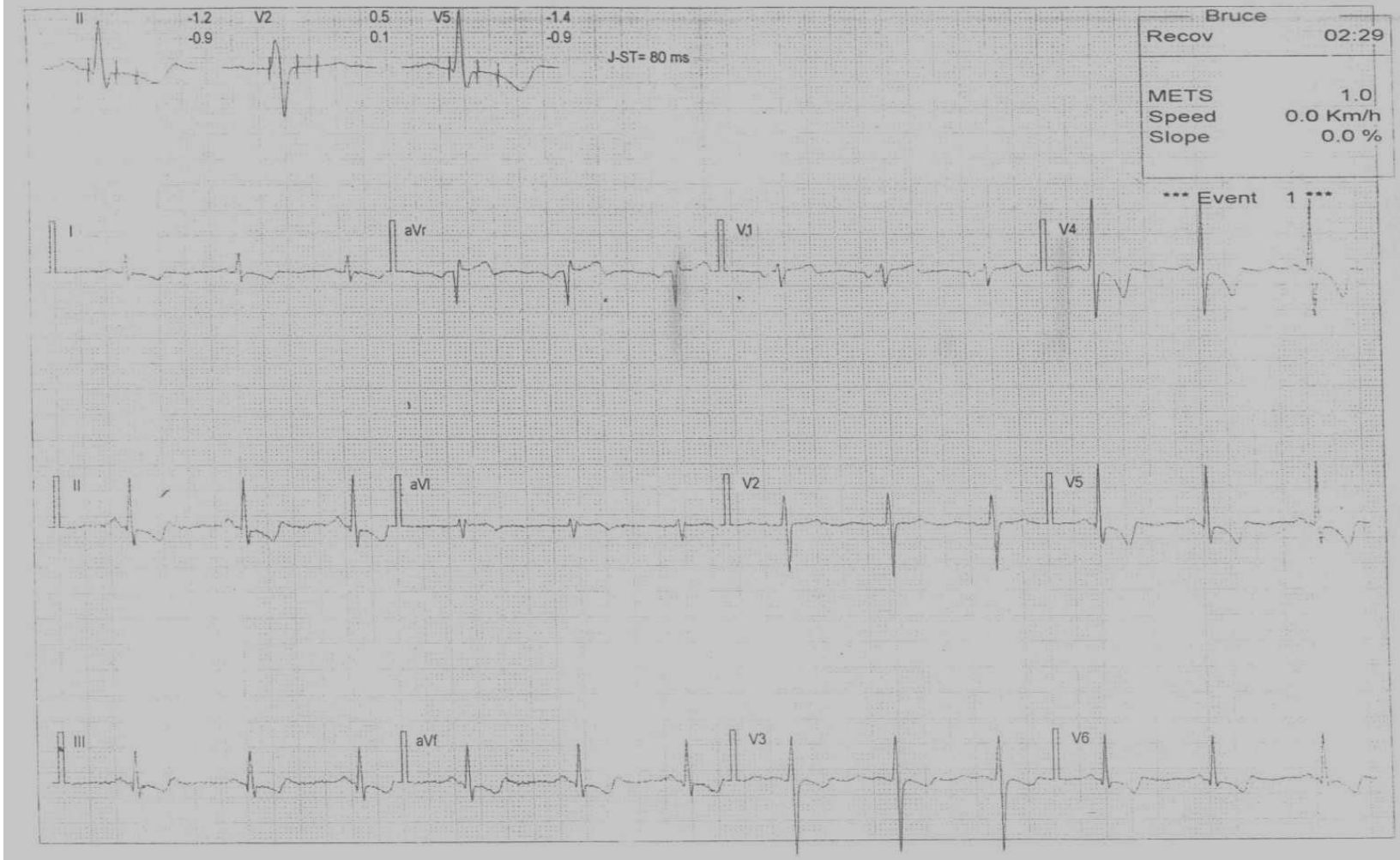

Name : MR SAMUTHARAPANDIAN
Age : 61 Y
BP 180 80
II -2.4 -0.4
V2 0.2 0.1
V5 -2.8 -1.1
J-ST= 80 ms
Bruce
Exe 06:00
Stage 02
METS 7.1
Speed 4.0 Km/h
Slope 12.0 %
Timer 03:00
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

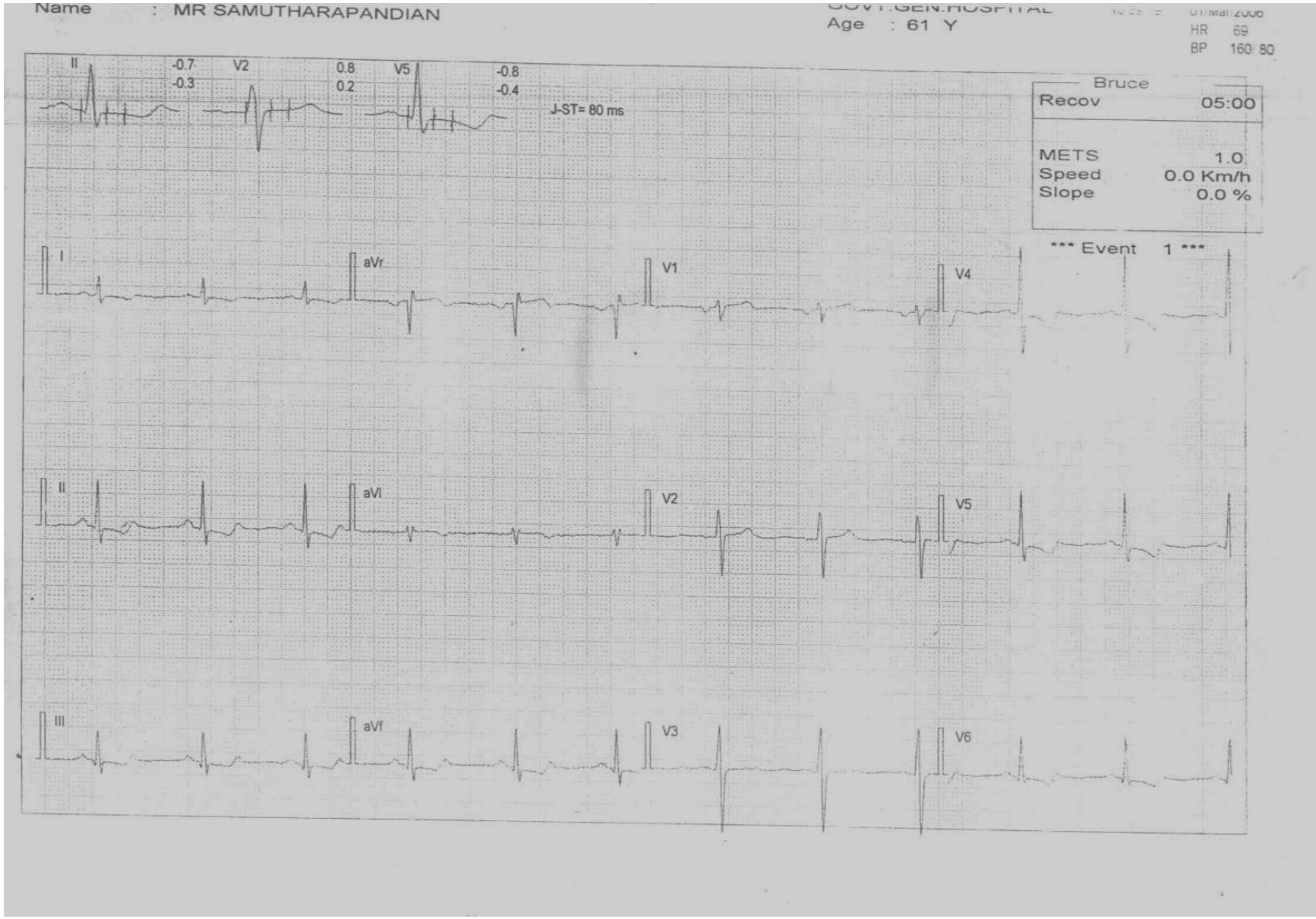

BP 180/8
II -2.4 -0.4
V2 0.2 0.3
V5 -2.6 -0.8
J-ST= 80 ms
Bruce
Exe 06:10
Stage 03
METS 10.1
Speed 5.4 Km/h
Slope 14.0 %
Timer 00:10
*** Peak ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6


BP 180/8C
II
-2.1
-0.6
V2
0.7
0.3
V5
-2.6
-1.0
J-ST= 80 ms
Bruce
Recov 00:26
METS 1.0
Speed 0.0 Km/h
Slope 0.0 %
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

Patient ID : 338
Name : MR SAMUTHARAPANDIAN

GOVT.GEN.HOSPITAL 10:36:48 01 Mar/2006
Age : 61 Y HR 73
BP 160/ 80

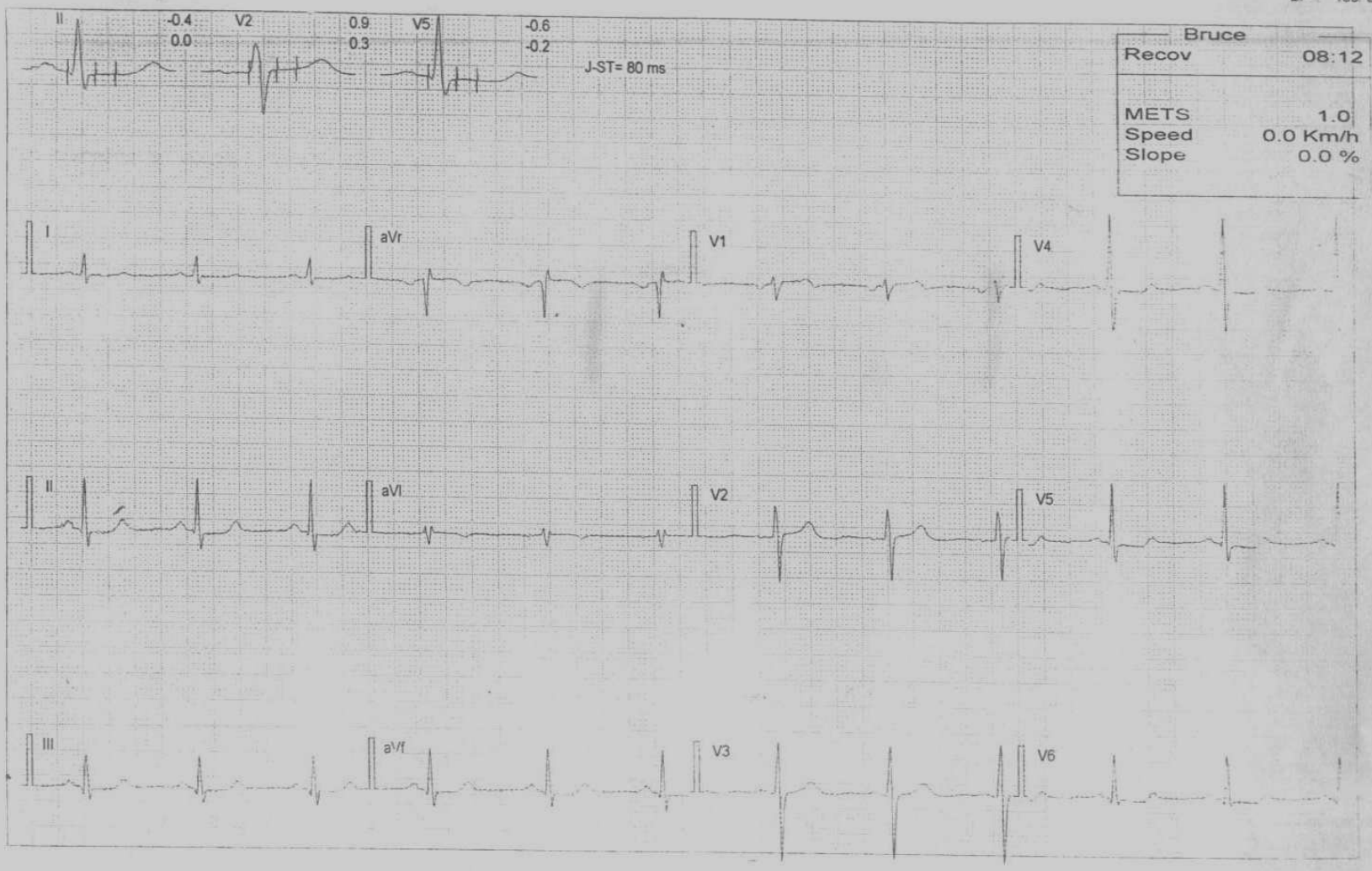


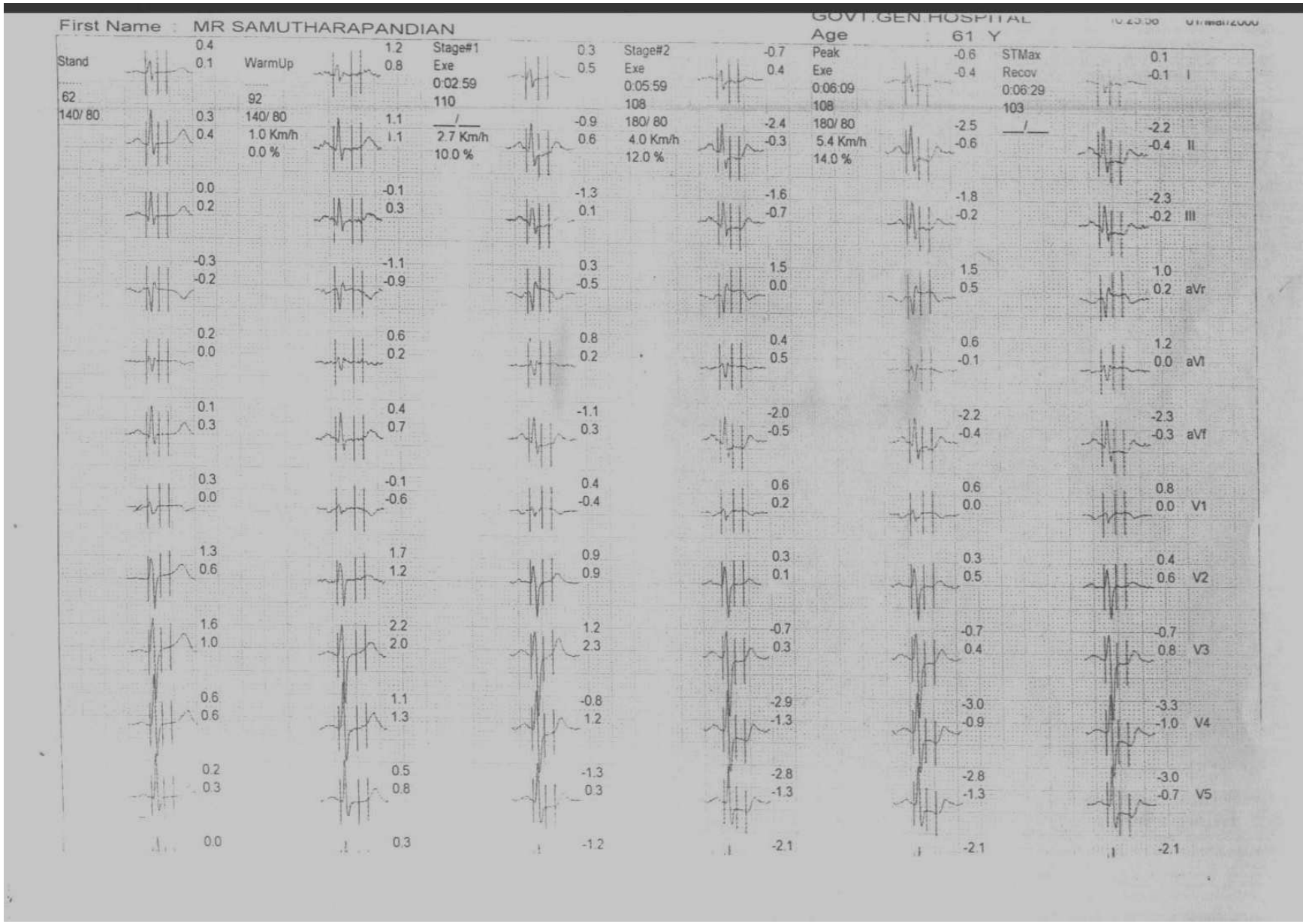

Name : MR SAMUTHARAPANDIAN
Age : 61 Y
HR 69
BP 160/80
II
-0.7
-0.3
V2
0.8
0.2
V5
-0.8
-0.4
J-ST= 80 ms
Bruce
Recov 05:00
METS 1.0
Speed 0.0 Km/h
Slope 0.0 %
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

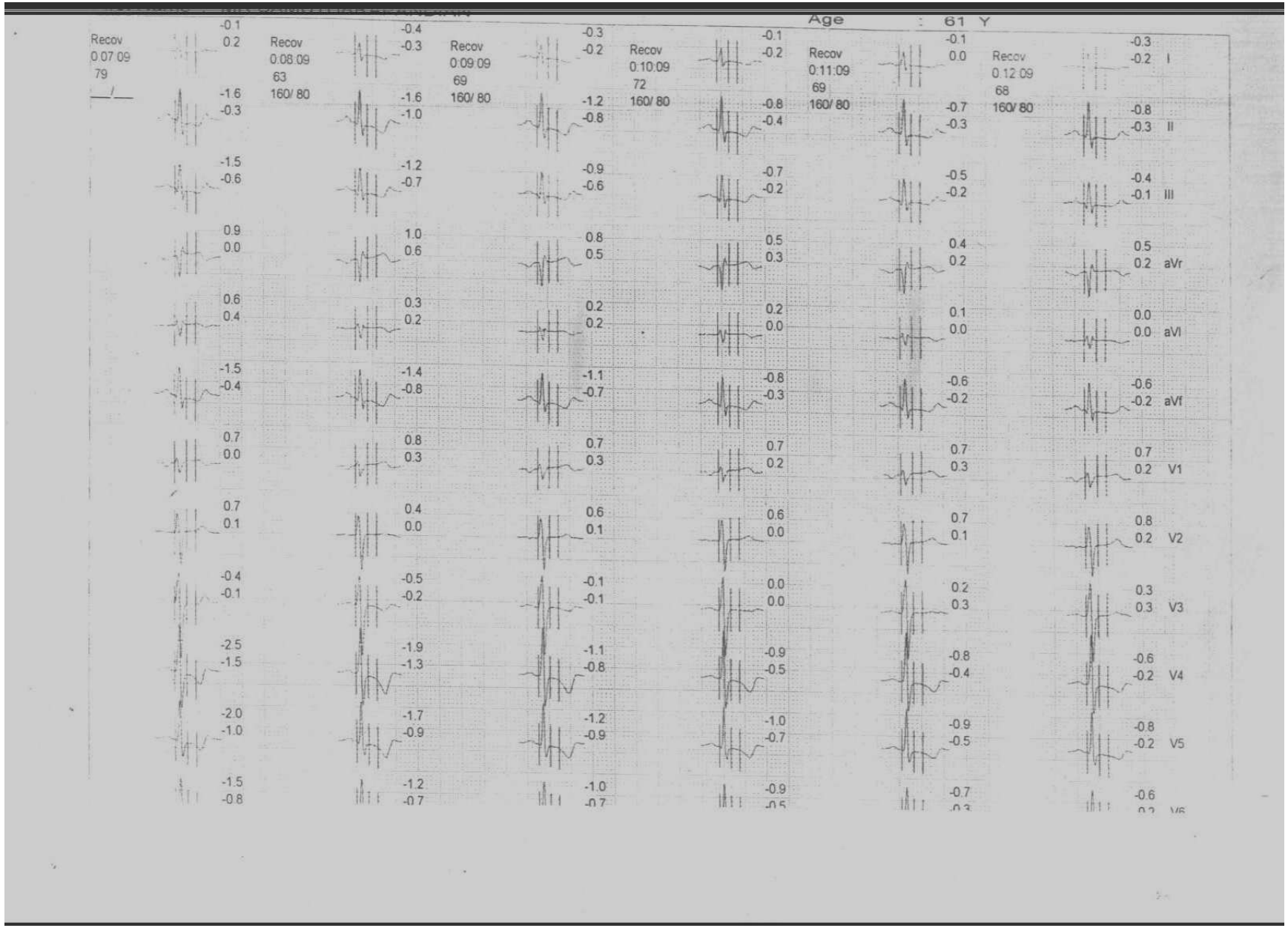
Patient ID : 338
Name : MR SAMUTHARAPANDIAN

GOVT.GEN.HOSPITAL
Age : 61 Y

10:42:30 01/Mar/2006
HR 69
BP 160/80




First Name : MR SAMUTHARAPANDIAN
GOVT.GEN HOSPITAL
Age : 61 Y
Stand
62
140/ 80
WarmUp
92
140/ 80
1.0 Km/h
0.0 %
Stage#1
Exe
0:02:59
110
2.7 Km/h
10.0 %
Stage#2
Exe
0:05:59
108
180/ 80
4.0 Km/h
12.0 %
Peak
Exe
0:06:09
108
180/ 80
5.4 Km/h
14.0 %
STMax
Recov
0:06:29
103
I
II
III
aVr
aVl
aVf
V1
V2
V3
V4
V5


Age : 61 Y
Recov 0.07:09 79
Recov 0.08:09 63 160/ 80
Recov 0:09:09 69 160/ 80
Recov 0.10:09 72 160/ 80
Recov 0:11:09 69 160/ 80
Recov 0.12:09 68 160/ 80
I
II
III
aVr
aVl
aVf
V1
V2
V3
V4
V5
V6

10:14:22 20 Mar/2006

DEPARTMENT OF CARDIOLOGY
GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

Patient ID : 399
First Name : MR. STANISLAUS
Birth Date : / /1936 Age : 70 Y Gender : M
Height : 160 cm Weight : 50 kg
BSA : 1.50 Target HR : 150

Technician : N.S
Code : PROF.ABG

Required by:
Indications : Chest pain

Therapy :

	MAX VALUES		TIME
SPEED	2.7	Km/h	2:35
SLOPE	10.0	%	
	4.7	METS	
HR	127	bpm	2:30
	84.7 %	Target HR	
RPP	130	mmHg*bpm/100	
BP	150	mmHg	4:20
ST+ (V1)	1.3	mm	2:20
ST- (V5)	-3.0	mm	2:45

Protocol	Test	Stress	Recovery
Bruce	11:35	2:36	7:49

		DURATION	SPEED Km/h	SLOPE %	METS	HR bpm	BPs/BPd mmHg	STMax (V5)
Stand	01	0:32				93	130/ 70	-0.4
WarmUp	01	0:37	1.0	0.0	1.5	110	130/ 70	-0.4
Exe	Peak	2:36	2.7	10.0	4.7	126	___/___	-2.6
Recov	01	7:48	0.0	0.0	1.0	82	150/ 70	-0.7
Post	01	0:00	0.0	0.0	1.0	82	___/___	-0.5

Reasons for end : ANGINA FATIGUE

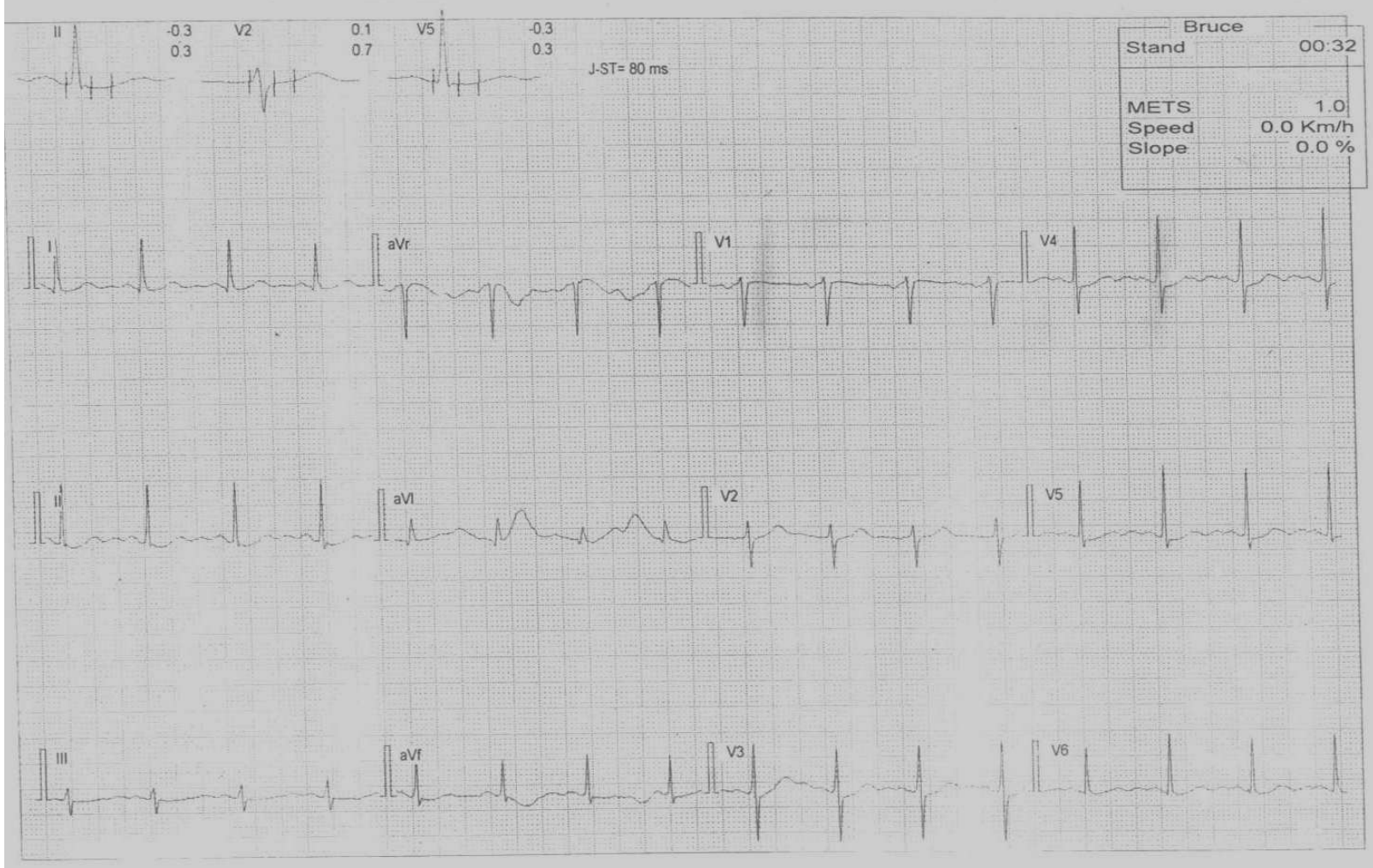
Symptoms : ANGINA FATIGUE

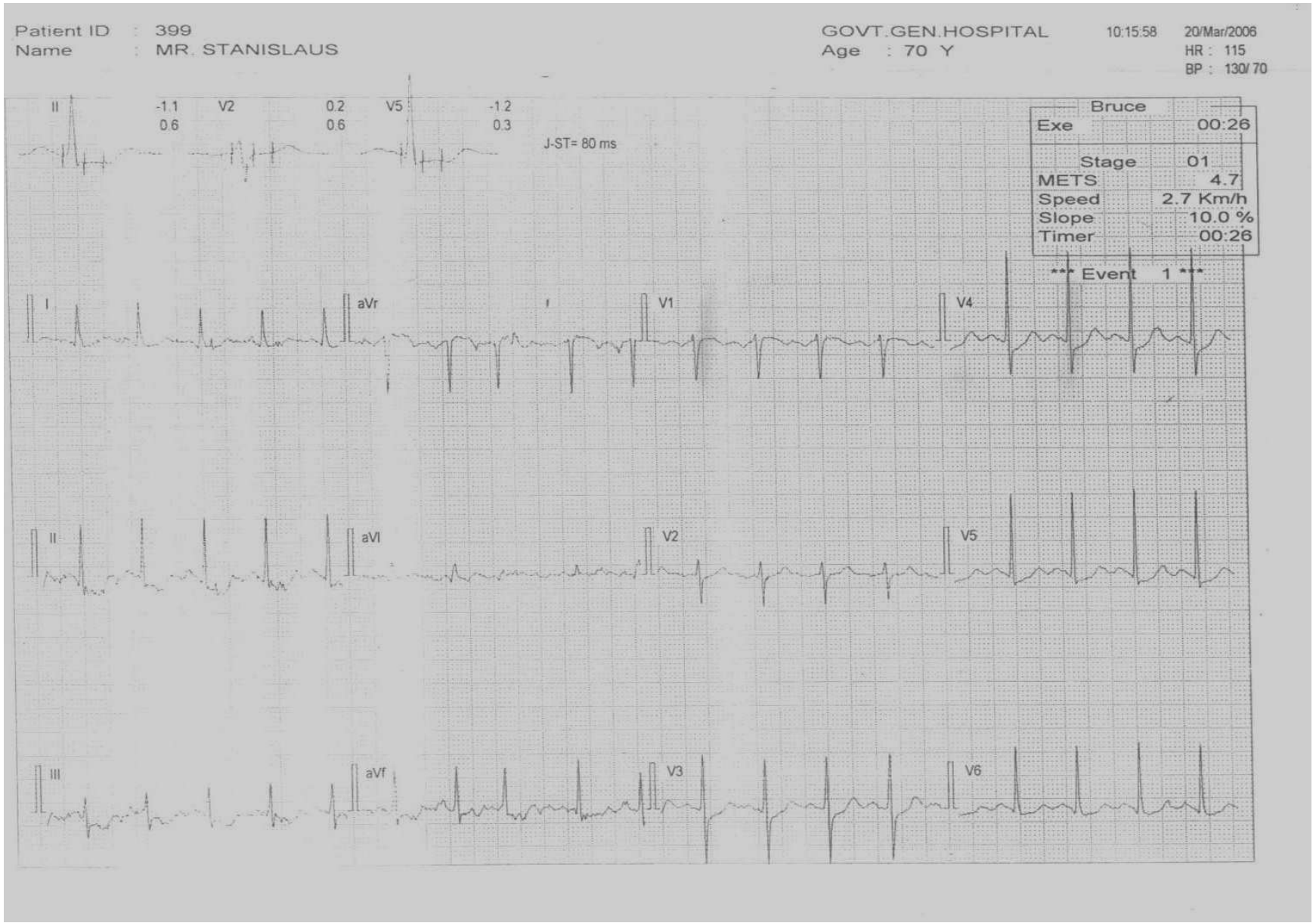
Conclusions : ACHIEVED 84% THR AT 4.7 METS WORKLOAD
FUNCTIONAL CAPACITY POOR
ANGINA AT STAGE 1 NO ARRYTHMIA
NORMAL HR BP RESPONSE
ST DEPRESSION 2 MM INFERO LATERAL
LEADSTMT IS POSITIVE FOR INDUCIBLE
ISCHEMIA

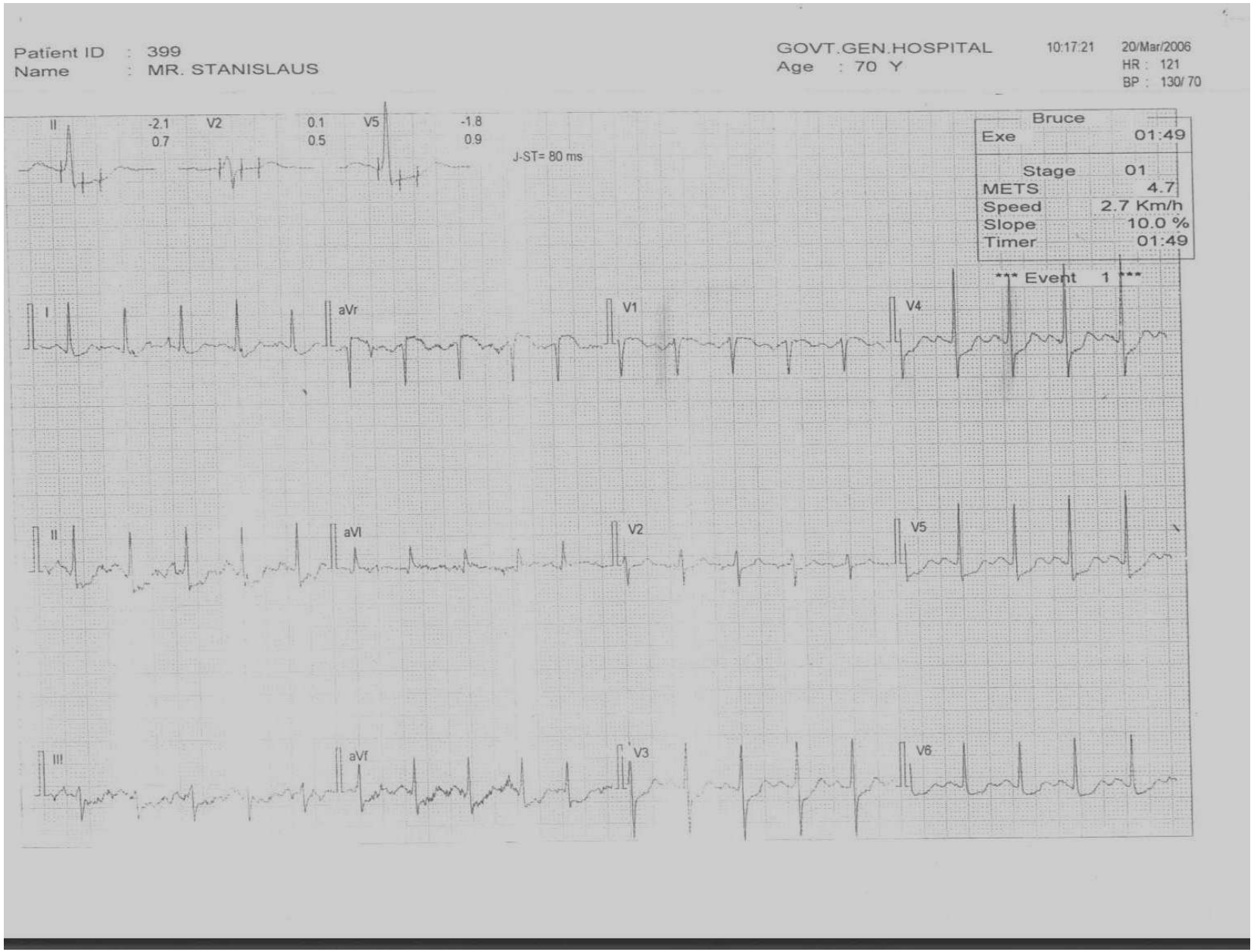
Reported by : DR M KATHIRESAN

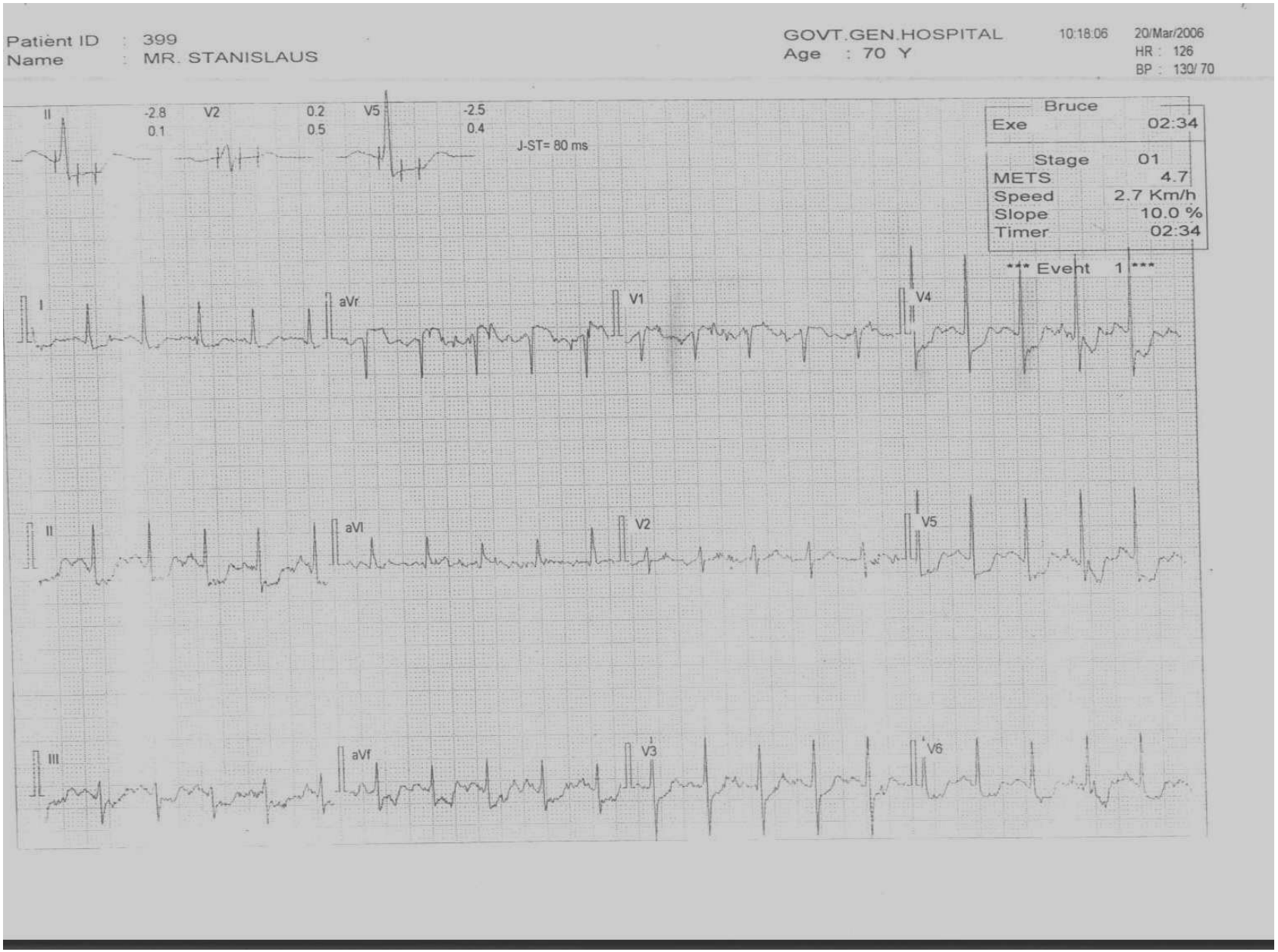
Patient ID : 399
Name : MR. STANISLAUS

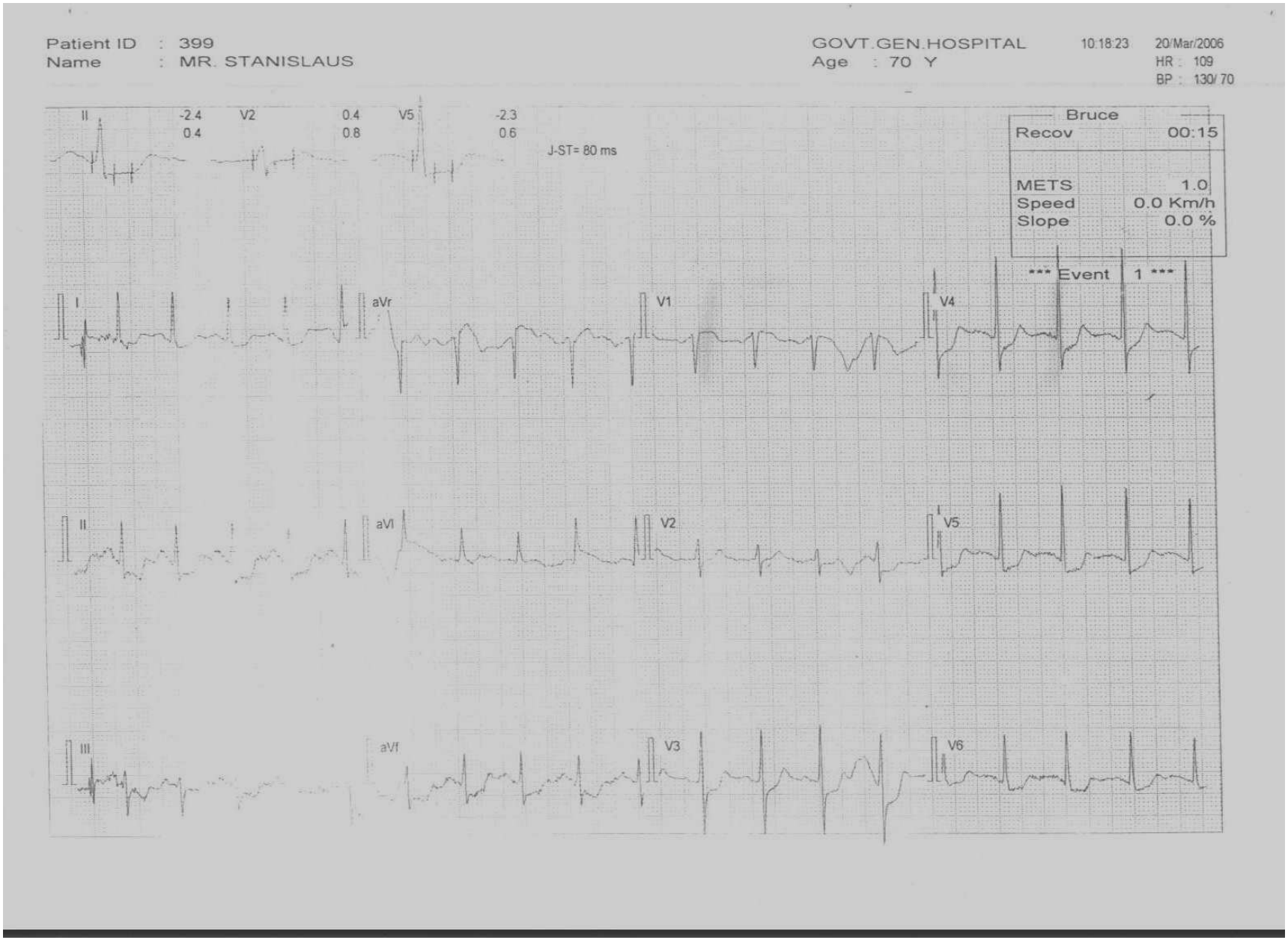
GOVT.GEN.HOSPITAL 10:14:54 20/Mar/2006
Age : 70 Y HR : 93
BP : 130/ 70

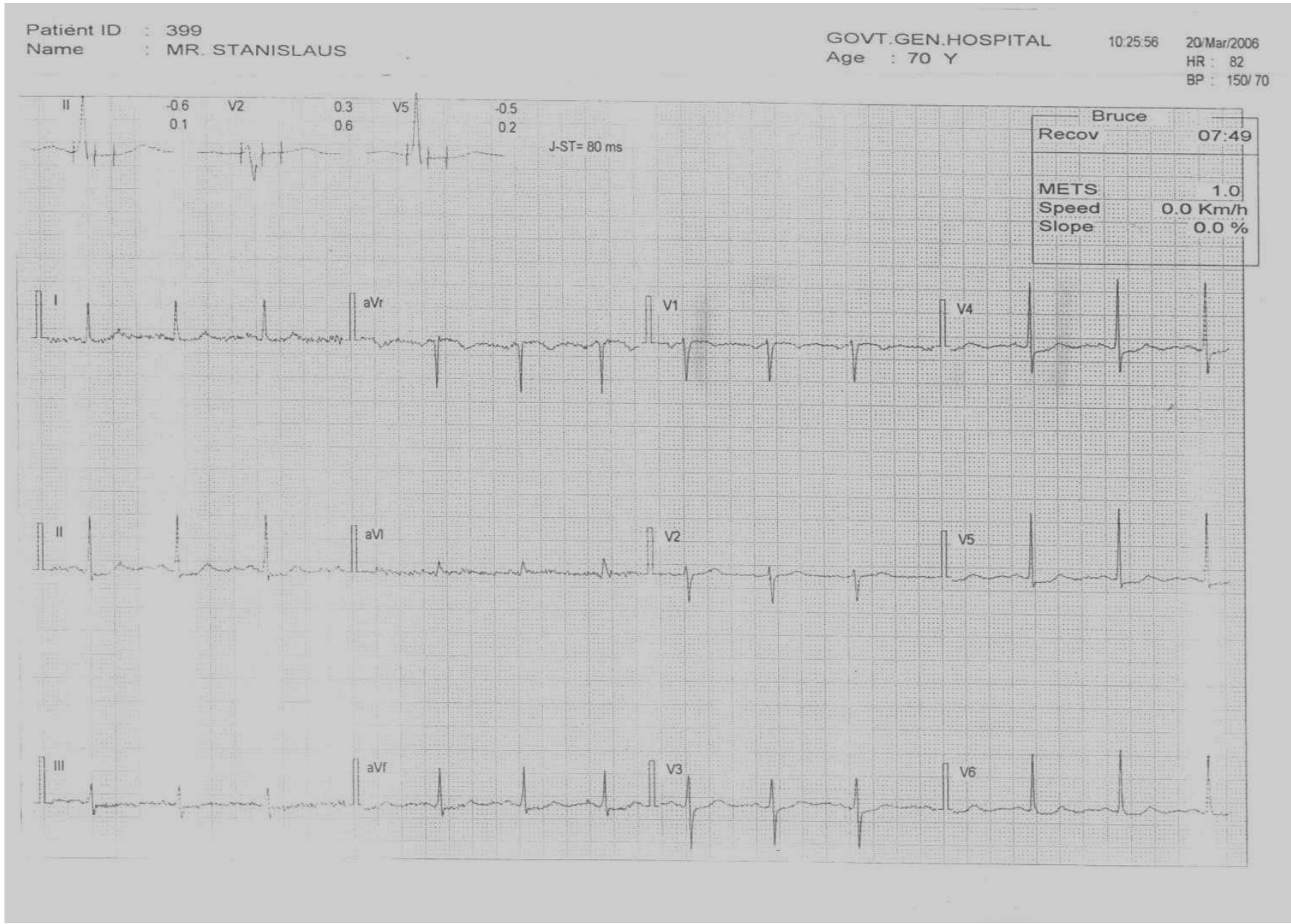


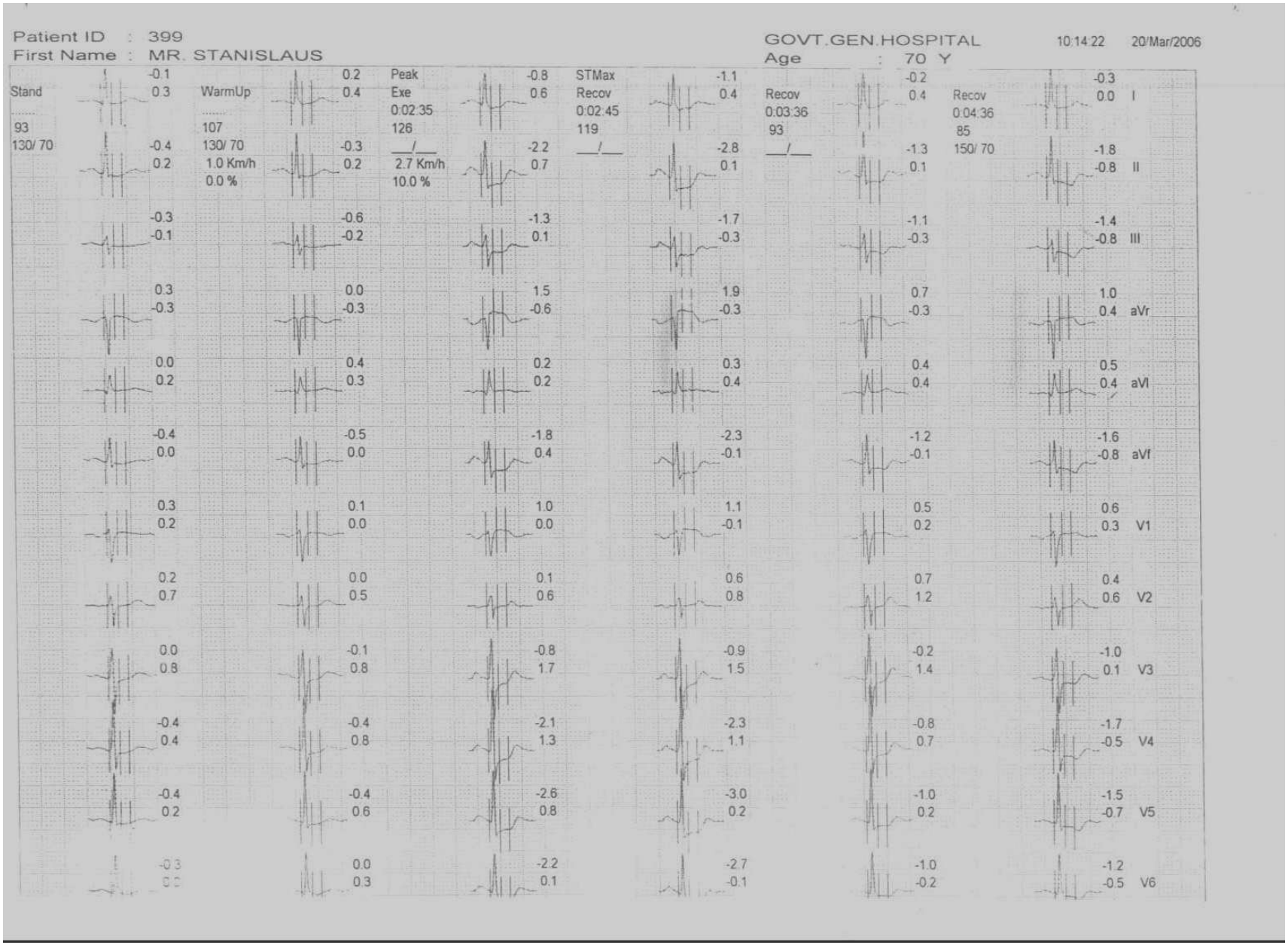

Patient ID : 399
Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:15:58
20/Mar/2006
HR : 115
BP : 130/ 70
II
-1.1
0.6
V2
0.2
0.6
V5
-1.2
0.3
J-ST= 80 ms
Bruce
Exe 00:26
Stage 01
METS 4.7
Speed 2.7 Km/h
Slope 10.0 %
Timer 00:26
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

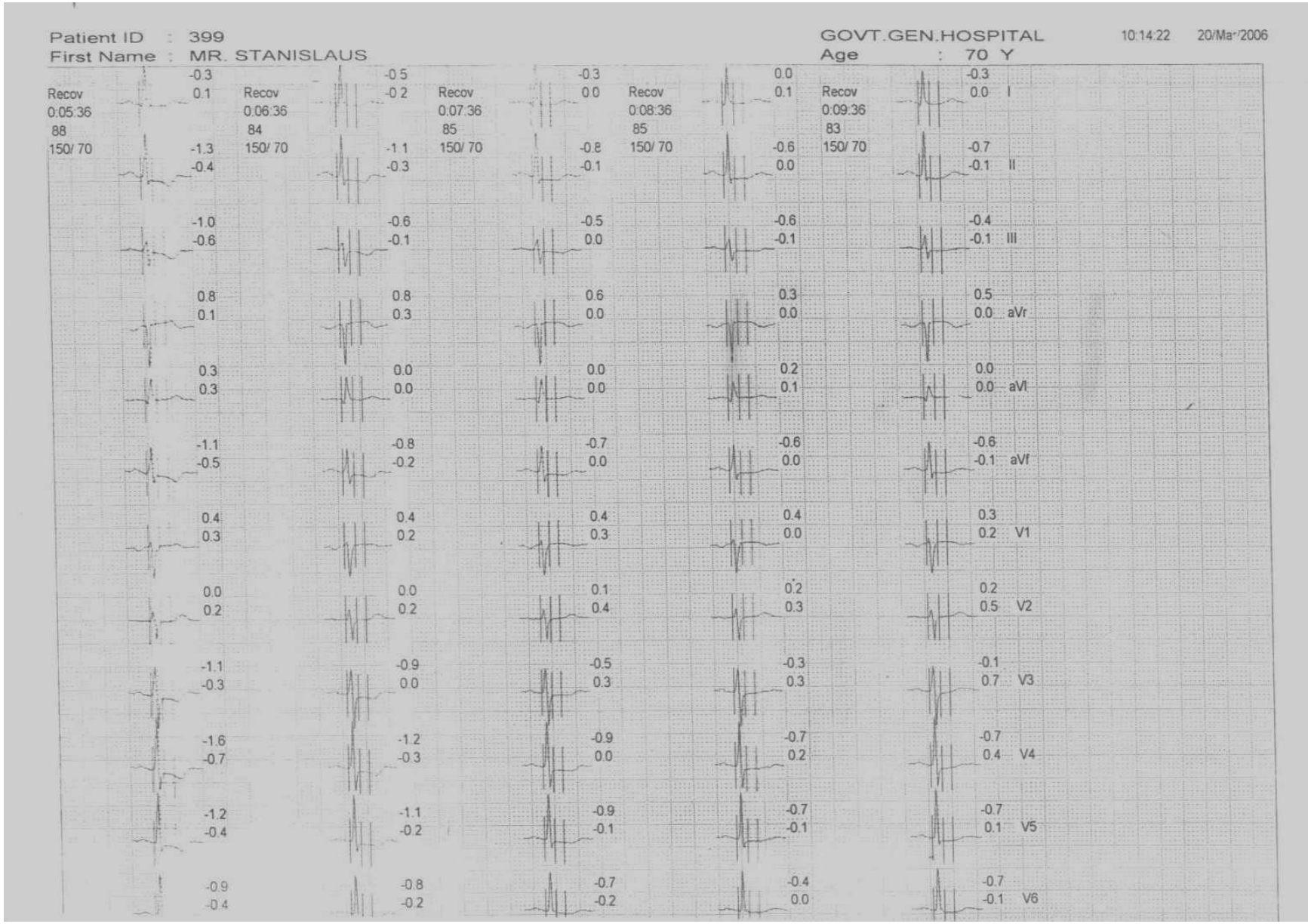

Patient ID : 399
Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:17:21
20/Mar/2006
HR : 121
BP : 130/ 70
II
-2.1
0.7
V2
0.1
0.5
V5
-1.8
0.9
J-ST= 80 ms
Bruce
Exe 01:49
Stage 01
METS 4.7
Speed 2.7 Km/h
Slope 10.0 %
Timer 01:49
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

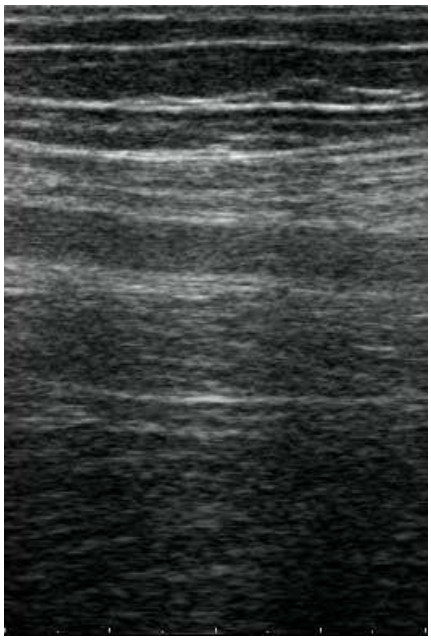

Patient ID : 399
Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:18:06
20/Mar/2006
HR : 126
BP : 130/ 70
II
-2.8
0.1
V2
0.2
0.5
V5
-2.5
0.4
J-ST= 80 ms
Bruce
Exe 02:34
Stage 01
METS 4.7
Speed 2.7 Km/h
Slope 10.0 %
Timer 02:34
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6


Patient ID : 399
Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:18:23
20/Mar/2006
HR : 109
BP : 130/ 70
II
-2.4
0.4
V2
0.4
0.8
V5
-2.3
0.6
J-ST= 80 ms
Bruce
Recov 00:15
METS 1.0
Speed 0.0 Km/h
Slope 0.0 %
*** Event 1 ***
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6

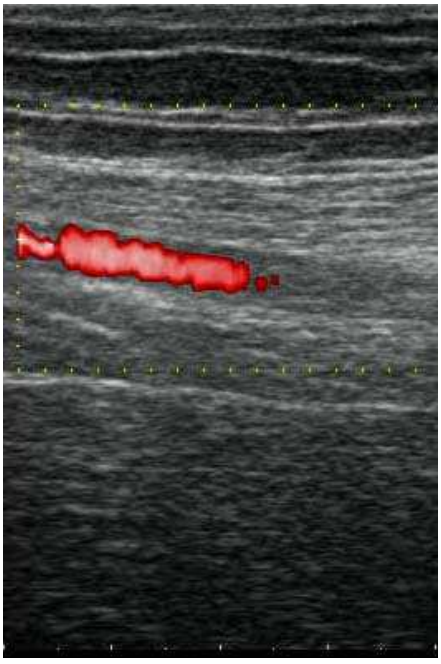

Patient ID : 399
Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:25:56
20/Mar/2006
HR : 82
BP : 150/ 70
II
-0.6
0.1
V2
0.3
0.6
V5
-0.5
0.2
J-ST= 80 ms
Bruce
Recov 07:49
METS 1.0
Speed 0.0 Km/h
Slope 0.0 %
I
aVr
V1
V4
II
aVl
V2
V5
III
aVf
V3
V6


Patient ID : 399
First Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:14:22 20/Mar/2006
Stand
93
130/ 70
WarmUp
107
130/ 70
1.0 Km/h
0.0 %
Peak
Exe
0:02:35
126
2.7 Km/h
10.0 %
STMax
Recov
0:02:45
119
Recov
0:03:36
93
Recov
0:04:36
85
150/ 70
I
II
III
aVr
aVl
aVf
V1
V2
V3
V4
V5
V6

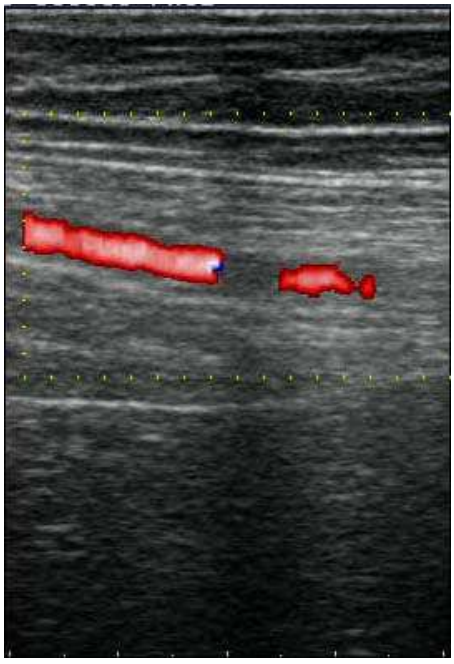

Patient ID : 399
First Name : MR. STANISLAUS
GOVT.GEN.HOSPITAL
Age : 70 Y
10:14:22
20/Mar/2006
Recov
0:05:36
88
150/ 70
Recov
0:06:36
84
150/ 70
Recov
0:07:36
85
150/ 70
Recov
0:08:36
85
150/ 70
Recov
0:09:36
83
150/ 70
I
II
III
aVr
aVl
aVf
V1
V2
V3
V4
V5
V6



2D DOPPLER



PROXIMAL ARTERIAL FLOW



OBSTRUCTION WITH DISTAL ARTERIAL FLOW

DISCUSSION

Our results suggest that in our study population, the metabolic syndrome prevalence in the elderly was 45%; in contrast with the population (adult) based METS-GREECE Multicenter study which had a prevalence of 23.6%. This was due to the clustering of the metabolic syndrome in the elderly group and increasing prevalence of metabolic syndrome with age. In accordance with METS-GREECE Multicenter study, our study identifies a substantial additional vascular risk (CHD/stroke/PAD) in men and women, even in those without diabetes.

Furthermore, the overlap adjusted prevalent vascular disease in those with the metabolic syndrome but no diabetes were significantly greater than that of those in the non-metabolic syndrome group, underlining the high risk associated with the Metsyn. These findings in accordance with METS-GREECE Multicenter study, suggest that the metabolic syndrome should probably be added to the list of coronary heart disease equivalents, even in the absence of diabetes.

The prevalence of increased vascular disease in subjects with the metabolic syndrome may be explained by the components that define the metabolic syndrome in association with other, not routinely measured factors. For example, impaired fibrinolysis, oxidative stress hypercoagulability, high LDL-C levels, increased small dense LDL particles, inflammation and hyperinsulinemia. It was also reported that the Metsyn is associated with higher levels of oxidized LDL-C, apolipoprotein-B, urate, leptin, fibrinogen, leucocytes, erythrocyte sedimentation rate and soluble endothelial adhesion molecule and lower apolipoprotein-A concentrations.

Apart from the five components of the metabolic syndrome, other two factors play an important role for coronary heart disease risk. This was partly due to increased levels of LDL-C, small dense LDL particles and elevated non-HDL cholesterol. All these parameters cannot be assessed in each patient in everyday clinical practice. However, LDL-C and non-HDL-C (total cholesterol minus HDL-C) are easily calculated.

Although LDL-C is not considered as a component of the metabolic syndrome, many of patients have raised levels of LDL-C. In our study, 71.1% of the subjects with the metabolic syndrome had a LDL-C > 130 mg/dl (> 3.4 mmol/l), this finding more in accordance with METS-GREECE Multicenter study which had 64% of the subjects with LDL-C > 130 mg/dl and the importance of LDL-C is that it forms primary treatment target in the management of dyslipidemia.

The contribution of high LDL-C levels to vascular disease risk in subjects with the Metsyn was highlighted by retrospective analysis of the landmark statin trails. The placebo data from the Scandinavian Simvastatin Survival Study (4s) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/Tex-CAPS) showed that the relative risk of major coronary events associated with the metabolic syndrome, after excluding DM was 1.5 (95% CI = 1.2-1.8) and 1.4 (95% CI = 1.04-1.9) respectively, in comparison to subjects without the metabolic syndrome.

These data demonstrate that the metabolic syndrome is associated with an increased vascular risk in hypercholesterolemic

patients with CHD in 4s and in those with average LDL-C levels and low HDL-C but without CHD in AFCAPS/TexCAPS. This argues for whether elevated LDL-C might be considered modifying components of the metabolic syndrome, especially in the presence of elevated triglycerides (indicating small dense LDL particles with increased atherogenicity).

In individuals with triglycerides >200 mg/dl (> 2.3 mmol/l), probably the majority of subjects with the metabolic syndrome, non-HDL is a secondary treatment target. Non-HDL-C includes cholesterol in LDL and triglyceride-rich lipoproteins. In our study, 82.2% of subjects with the metabolic syndrome had a non-HDL-C level >160 mg/dl (>4.1 mmol/l), in accordance with METS-GREECE Multicenter study which had 69% of subjects with non-HDL-C level >160 mg/dl.

In the Lipid Research Clinics follow-up study, non-HDL-C level was a better predictor of CHD death than LDL-C. In the GREACE study, non-HDL-C level was a better predictor of risk for clinical vascular events in untreated patients than LDL-C, in these instances non-HDL-C should be the primary treatment target. Therefore, non-

HDL-C may be incorporated in the definition of the metabolic syndrome.

Several studies including METS-GREECE Multicenter study and data from our study group suggest that the metabolic syndrome, even in the absence of diabetes, is associated with an increased vascular risk. This will reset the LDL-C and non-HDL-C treatment targets and may result in additional clinical benefit in these subjects.

Study limitations

The study is a hospital based study and may not be representative of general population. As a cross-sectional study, the present analysis is limited in its ability to elucidate causal relationships between risk factors and outcome. Some subgroups like no Metsyn but with diabetes are small in number.

CONCLUSIONS

1. The prevalence of metabolic syndrome in our study group was 45% and vascular disease (coronary artery disease/stroke) prevalence was markedly increased in the presence of the metabolic syndrome in the elderly.

2. Those with both the metabolic syndrome and diabetes had the highest prevalence of coronary artery disease and stroke, followed by those with the metabolic syndrome but without diabetes in the elderly.

3. The metabolic syndrome is significantly associated with vascular disease risk, even in the absence of diabetes in the elderly; probably metabolic syndrome alone without diabetes can be considered as a coronary heart disease-risk equivalent in future guidelines.

4. Among metabolic syndrome components, Arterial hypertension strongly correlated with stroke, Triglycerides strongly correlated with coronary artery disease and High density lipoprotein was inversely correlated with both coronary artery disease and stroke.

5. Both raised levels of low density lipoprotein and non-high density lipoprotein (not a component of metabolic syndrome) are strongly correlated with coronary artery disease in the metabolic syndrome group, and hence these can be considered as modifying components of metabolic syndrome

SCOPE FOR FUTURE STUDIES

This study conducted in our Indian population has significant observation and had potential therapeutic implications. Our study concluded that Met syn without DM can be considered as a coronary heart disease-risk equivalent in future guidelines. This initiative would reset treatment targets and whether it potentially provides additional benefit in patients with the Met syndrome, which can be elucidated by further studies.

In Met syn group, majority of patients had elevated lipid values. We can asses the effectiveness of hypolipidemic drug therapy in this Met syn group and can elucidate whether Met syn is also a major factor in response to therapy, like it influences the risk of CHD by further future studies.

PROFORMA

Name:

Age:

Sex:

Occupation:

OP No:

Address:

DM Y/N

Hypertension Y/N

Drugs used

H/o hospitalization for Myocardial infarction

H/o stable angina

H/o coronary bypass artery grafting

H/o percutaneous transluminal angioplasty

H/o cerebrovascular accident

H/o intermittent claudication

Co morbid condition:

Smoker: Type/ quantity/ duration

Alcohol: Type/ quantity/ duration

Family H/o DM/HT/ CAD/ CVA

Examination

Height weight BMI waist circumference

Pulse peripheral pulses carotids Equal/unequal

BP (upper limb)

CVS RS Abd CNS

INVESTIGATIONS

Blood glucose- Fasting postprandial

Urine Alb sugar deposit

Lipid profile

TC TGL HDL LDL

ECG

ECHO

CT Brain

Stress ECG

Coronary angiography

Duplex imaging

Inclusion criteria

1. Age ≥ 60 yr (both sexes)

Exclusion criteria

1. Hemorrhagic stroke (on CT brain)

S.No	Name	Age	Sex	Height	Weight	BMI	AH	SBP	DBP	FGL	TC	TGL	HDL	LDL	non HDL	WC	DM	CHD	Stroke	PAD
1	alagami	65	f	155	60	24.97	y	150	80	130	200	168	45	121	155	78	y	n	n	n
2	alagar	62	m	168	78	27.64	n	128	82	132	230	202	33	157	197	93	y	y	y	n
3	anadi	61	f	165	56	20.57	y	140	100	98	186	158	44	110	142	98	n	n	n	n
4	anandraj	60	m	167	69	24.74	n	128	82	128	230	204	38	151	192	93	y	y	n	n
5	devan	69	m	168	68	24.09	y	140	88	98	224	206	34	149	190	91	n	y	n	n
6	devi	71	f	155	55	22.89	y	132	90	98	186	148	46	110	140	82	n	n	n	n
7	duraiyammal	62	f	145	46	21.88	y	140	100	88	198	152	47	121	151	69	n	n	n	n
8	ganapathi	62	m	170	68	23.53	y	140	92	128	230	204	44	145	186	92	y	y	n	n
9	girigori	75	m	166	70	25.40	y	150	90	140	220	200	38	142	182	92	y	y	y	n
10	jayaraj	77	m	162	68	25.91	y	160	70	122	230	200	38	152	192	91	y	y	y	n
11	kali	68	m	162	60	22.86	n	128	70	98	166	168	38	94	128	98	n	n	n	n
12	kaliyammal	68	f	162	68	25.91	y	140	88	128	208	160	38	138	170	78	y	n	y	n
13	kanthamal	70	f	152	62	26.84	y	180	100	140	230	202	32	158	198	103	y	y	y	n
14	samutharapandian	61	m	155	58	24.14	y	170	100	132	220	204	38	141	182	91	y	y	y	n
15	krisnan	67	m	173	68	22.72	n	130	84	125	192	152	48	114	144	91	y	n	n	n
16	kumari	66	f	156	58	23.83	n	126	80	130	202	158	41	129	161	82	y	n	n	n
17	lakshmi devi	62	f	156	58	23.83	n	120	78	120	210	152	42	138	168	88	n	n	n	n
18	mani	72	m	168	68	24.09	y	140	90	92	220	200	36	144	184	91	n	y	y	n
19	murugan	68	m	164	62	23.05	y	148	98	92	220	200	38	142	182	92	n	y	y	n
20	natarajan	62	m	166	76	27.58	y	130	90	116	200	152	42	128	158	108	n	n	n	n
21	natchiar	60	f	152	55	23.81	n	120	74	132	230	204	38	151	192	86	y	y	n	n
22	padma	65	f	148	54	24.65	n	128	80	124	214	148	38	146	176	86	y	n	y	n
23	pappa	60	f	152	52	22.51	n	140	100	114	163	156	48	84	115	93	n	n	n	n
24	parvatam	67	f	140	58	29.59	y	150	90	120	200	160	39	129	161	85	y	n	y	n
25	parvathi	61	f	160	62	24.22	y	132	94	102	198	160	37	129	161	84	n	n	n	n
26	pattu	68	m	168	70	24.80	y	170	100	88	200	160	39	129	161	92	n	n	y	y
27	periyasamy	60	m	162	62	23.62	y	150	88	62	200	147	39	132	161	92	n	n	y	n
28	raja	72	m	172	70	23.66	y	150	100	118	230	156	36	163	194	91	n	n	n	n

Metabolic syndrome group

29	ramamoorthy	65	m	179	78	24.34	y	160	100	100	230	198	35	155	195	91	n	y	n	n
30	raman	68	m	178	74	23.36	y	170	10	96	220	204	38	141	182	92	n	y	y	n
31	ramathilagam	64	f	155	58	24.14	n	128	82	112	210	178	38	136	172	83	n	y	n	n
32	ramayi	65	f	152	58	25.10	y	140	100	128	230	168	38	158	192	77	y	n	y	n
33	ramayiyammal	65	f	158	60	24.03	y	170	100	138	220	202	33	147	187	82	y	y	y	n
34	sakunthala	60	f	154	63	26.56	y	160	100	140	250	170	40	176	210	94	y	y	n	n
35	sanmugam	68	m	168	74	26.22	y	138	86	132	220	166	42	145	178	92	y	y	n	n
36	saraswathi	66	f	158	60	24.03	y	140	90	126	210	148	38	142	172	78	y	n	y	n
37	saroja	63	f	152	60	25.97	y	140	100	116	220	200	37	143	183	83	y	y	y	n
38	saroja	65	f	158	60	24.03	y	140	88	112	220	152	35	155	185	92	n	y	n	n
39	sarojini	75	f	145	50	23.78	y	180	90	112	230	200	32	158	198	83	y	y	y	n
40	satchu	68	f	151	50	21.93	y	140	70	100	212	152	47	135	165	82	n	n	n	n
41	sivalingam	73	m	178	80	25.25	y	140	96	120	222	200	34	148	188	92	y	y	y	n
42	subbu	63	m	168	73	25.86	y	140	80	120	240	204	46	153	194	92	y	y	n	n
43	stanislaus	70	m	160	50	19.53	y	138	86	92	200	162	39	129	161	92	n	y	y	n
44	sunder	78	m	178	78	24.62	n	126	80	112	222	204	38	143	184	92	n	y	n	n
45	sunderajan	78	m	172	78	26.37	y	150	80	126	240	200	43	157	197	96	y	y	n	y

Metabolic syndrome group

S.No	Name	Age	Sex	Height	Weight	BMI	AH	SBP	DBP	FGL	TC	TGL	HDL	LDL	NON-HDL	WC	DM	CHD	Stroke	PAD
1	aiagar	70	m	168	62	21.97	y	140	100	100	190	148	32	128	158	80	n	n	n	n
2	alagarsamy	66	m	165	68	24.98	n	120	80	130	196	135	42	127	154	78	y	n	n	n
3	andal	68	f	156	58	23.83	n	126	82	100	178	148	42	106	136	87	n	n	n	n
4	babu	60	m	178	74	23.36	y	140	90	100	190	138	42	120	148	88	n	n	n	n
5	chandra	66	f	156	54	22.19	n	120	78	110	190	148	42	118	148	78	n	n	n	n
6	chinnamal	62	f	158	54	21.63	n	124	84	100	194	146	44	121	150	76	n	n	n	n
7	devaki	70	f	140	45	22.96	n	120	80	112	230	148	38	162	192	75	y	n	y	n
8	durairaj	60	m	173	70	23.39	y	140	80	77	188	146	32	127	156	89	n	n	n	n
9	ekambaram	75	m	176	65	20.98	n	130	90	110	181	123	47	109	134	77	n	n	n	n
10	gopalsamy	70	m	168	72	25.51	n	120	80	150	230	148	32	168	198	87	y	y	y	n
11	govindan	70	m	168	66	23.38	n	126	82	102	188	146	44	115	144	88	n	n	n	n
12	hari	72	m	168	66	23.38	n	126	84	102	198	148	44	124	154	88	n	n	n	n
13	indurani	65	f	152	52	22.51	y	160	100	102	198	148	39	129	159	66	n	y	n	n
14	iyappan	71	m	168	66	23.38	n	128	84	98	198	148	44	124	154	88	n	n	n	n
15	jeyachandran	63	m	174	72	23.78	n	120	84	82	200	148	42	128	158	88	n	n	n	n
16	kandan	70	m	178	72	22.72	n	128	82	100	188	148	44	114	144	88	n	n	n	n
17	karupu	64	m	167	64	22.95	y	140	100	100	198	148	39	129	159	78	n	n	y	n
18	kothainayagi	60	f	145	48	22.83	n	130	80	112	192	148	40	122	152	75	n	n	n	n
19	krisnan	63	m	168	60	21.26	n	118	82	100	190	136	42	121	148	88	n	n	n	n
20	kumar	66	m	165	65	23.88	n	108	84	92	180	148	42	108	138	89	n	n	n	n
21	kuppu	75	m	172	64	21.63	n	120	80	100	182	136	44	111	138	86	n	n	n	n
22	lakshmi	63	f	160	58	22.66	n	126	80	126	200	158	42	126	158	78	y	n	n	n
23	lakshmiyammal	70	f	150	55	24.44	y	140	90	128	220	148	42	148	178	78	y	y	n	n
24	murugesan	62	m	172	70	23.66	n	124	80	96	188	140	48	112	140	88	n	n	n	n
25	muthusamy	70	m	164	60	22.31	n	130	80	94	200	148	48	122	152	89	n	n	n	n
26	nellamal	62	f	158	59	23.63	n	130	80	90	200	146	32	139	168	85	n	y	n	n
27	padma	69	f	156	56	23.01	n	120	70	100	198	142	42	128	156	88	n	n	n	n
28	padmavathi	62	f	158	54	21.63	n	110	80	100	182	148	46	106	136	78	n	n	n	n
29	palani	60	m	165	55	20.20	n	124	84	88	200	136	45	128	155	89	n	n	n	n
30	panchanathan	66	m	170	70	24.22	n	120	80	130	222	148	38	154	184	86	y	y	n	n

No Metabolic syndrome group

31	pandiyammmal	73	f	158	56	22.43	n	126	80	100	198	146	42	127	156	92	n	n	n	n
32	parameswari	62	f	160	58	22.66	n	124	84	100	188	140	42	118	146	72	n	n	n	n
33	perumal	63	m	172	60	20.28	n	110	80	110	179	221	46	89	133	82	n	n	n	n
34	pitchi	71	m	168	66	23.38	n	128	80	114	192	138	48	116	144	88	n	n	n	n
35	pitchiyandi	62	m	150	50	22.22	n	106	78	106	196	148	46	120	150	92	n	n	n	n
36	rajeswari	63	f	143	47	22.98	y	134	84	75	206	148	42	134	164	78	n	n	n	n
37	ramu	72	m	168	66	23.38	n	120	70	82	200	148	48	122	152	89	n	n	n	n
38	rani	72	f	156	54	22.19	n	130	78	92	190	152	38	122	152	74	n	n	n	n
39	rathinam	75	f	144	45	21.70	y	130	86	112	190	148	44	116	146	76	y	n	n	n
40	ravi	76	m	170	68	23.53	n	130	80	114	200	158	46	122	154	88	y	n	n	n
41	sangeta	70	f	154	52	21.93	n	130	80	100	188	148	43	115	145	88	n	n	n	n
42	sankar	65	m	172	70	23.66	n	128	80	92	200	148	42	128	158	94	n	n	n	n
43	sanmugam	73	m	172	70	23.66	n	128	70	112	179	160	47	100	132	88	n	n	n	n
44	selvi	63	f	158	53	21.23	n	118	78	96	188	136	44	117	144	88	n	n	n	n
45	sivaprakasam	60	m	154	56	23.61	n	130	80	96	200	148	38	132	162	98	n	y	n	n
46	subbu	70	m	160	58	22.66	y	140	90	100	190	148	38	122	152	78	n	n	n	n
47	sundaran	74	m	176	62	20.02	n	130	80	124	200	148	39	131	161	85	y	n	y	n
48	sundari	66	f	158	60	24.03	n	120	70	130	200	148	42	128	158	78	y	n	n	n
49	tamilarasi	71	f	160	58	22.66	y	150	94	88	200	148	42	128	158	78	n	n	n	n
50	tamilselvi	68	f	155	56	23.31	n	128	82	96	188	154	50	107	138	78	n	n	n	n
51	vadivelu	66	m	158	58	23.23	y	150	90	102	199	148	38	131	161	88	n	n	y	n
52	valli	72	f	155	56	23.31	y	138	90	98	196	146	42	125	154	78	n	n	n	n
53	varatharajan	60	m	162	56	21.34	y	150	90	82	196	148	38	128	158	72	n	n	n	n
54	velu	60	m	168	66	23.38	n	128	70	96	178	146	42	107	136	88	n	n	n	n
55	venkat	66	m	166	66	23.95	n	126	80	98	200	146	46	125	154	88	n	n	n	n

No Metabolic syndrome group

ABBREVIATIONS

AH - Arterial Hypertension

BMI - Body Mass Index

CHD - Coronary Heart Disease

CAD - Coronary Artery Disease

DM - Diabetes Mellitus

DBP - Diastolic Blood Pressure

FGL - Fasting Glucose

HDL - High Density Lipoprotein

LDL - Low Density Lipoprotein

PAD - Peripheral Arterial Disease

SBP - Systolic Blood Pressure

TC - Total Cholesterol

TGL - Triglyceride

WC - Waist Circumference

BIBLIOGRAPHY

1. cameron AJ, shaw JE, zimmet PZ. The metabolic syndrome; prevalence in worldwide population. Endocrinol metab clin north Am 2004; 33: 351-75.

2. Kylin E. studien. Hypertonie-hyperglykamie-hyperkaemiesyndrome. Zentralblatt fur innere Medizin(44). 1923.

3. VagueJ.La differenciation sexuelle, facteur determinant des formes de l obesite. Presse Med.1947; 30: 339-40.

4. Reaven GM.Banting lecture 1988. Role of insulin resistence in human disease. Diabetes1988; 37: 1595-607.

5. DeFronzo RA,Ferrannini E. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidaemia and atherosclerotic vascular disease. Diabetes care 1991; 14: 173-94.

6. Executive summary of the third report the NCEP expert panel on detection, evaluation and treatment of high blood cholesterol in adult. JAMA 2001; 285: 2486-97.

7. Reaven GM Banting lecture 1988; Role of insulin résistance in human diseases 1988: 1595-1607.

8. Kahn CR. Insuin action , diabetogens, and the cause of type 2 diabetes. Diabetes 1994; 43: 1066-1084.

9. Willlett WC .Weight, weight change and coronary heart disease in women. JAMA 1995: 27: 1461-1465.

10. Jung RT. Obesity as a disease. Br Med Bull 1997; 35: 307-321.

11. WHO,Western pacific Region. The Asia pacific perspective. Redefining Obesity and its treatment. WHO/ IASO/ IOTF,2000.

12. Epidemiology of diabetes in India. API medicine update2005; chapter 36.

13. The Expert committee report on diagnosis and classification of diabetes. Diabetes care 1997; 20: 1183-97.

14. Lee Y, Hirose H, Ohneda M, Beta cell lipotoxicity in the pathogenesis of NIDDM of obese rats. Proc Natl Acad Sci USA 1994; 91:1087-82.

15. Yaney GC, Corkey BE, Fatty acid metabolism and insulin secretion in pancreatic beta-cells. Diabetologia 2003; 46: 1297-312.

16. Ford ES, Prevalence of the metabolic syndrome among US adults. findings from the third national health and nutrition examination survey. J Am Med Asso 2002; 287:356-59.

17. Chaturvedi V, PrabhakaranD, Cardiovascular risk associated with impaired fasting glucose in urban north India. Diabetologia 2003; 46 supple 2: A 142 (abstract).

18. Tamler J, Vaccaro O, Diabetes, other risk factors, and 12 yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. Diabetes care 1993;16: 434-44.

19. Lewis GF, Uffelman KD. Interaction between freee faty acids and insulin in the acute control of VLDL production in human. J Clin Invest 1995; 95:158-66.

20. Lewis GF, Steiner G. Acute effects of insulin in the control of VLDL production in humans. Diabetes Care 1996; 19: 390-93.

21. Eckel RH, Yost TJ. Alteration in lipoprotein lipase in insulin resistance. Int J Obes Relat Met Disord 1995; 19 (suppl): s16-s21.

22. Murakami T, Longhi R, et al. triglycerides are major determinants of cholesterol esterification/transfer and HDL remodeling in human plasma. Arterioscle Thromb Vasc Biol 1995; 15: 1819-28.

23. Brinton EA, Eisenberg S. Increased apo A1 and A2 fractional catabolic rate in patients with low HDL levels with or without hypertriglyceridemia. J Clin Invest 1991; 87: 536-44.

24. Manzato E, Zambon. Level and physiochemical properties of lipoprotein subclass in moderate hypertriglyceridemia. Clin Chim Acta 1993; 219: 57-65

25. Kwiterovich PO Jr. clinical relevance of the biochemical, metabolic, and genetic factors that influence LDL heterogeneity. Am J Cardiol 2002; 90: 30i-47i

26. Packard CJ. LDL subfractions and athergenicity: an hypothesis from the university of glassgow. Curr Med Res Opin 1996; 13: 379-90.

27. Zambon A, Hokanson JE. Evidence for a new pathophysiological mechanism for coronary artery disease regression: hepatic lipase mediated changes in LDL density. Circulation 1999; 99: 1959-64.

28. sacks FM, Campos H. Cardiovascular endocrinology: low density lipoprotein size and cardiovascular disease :a reappraisal. J Clin Endocrinol Meta 2003; 88: 4525-32.

29. Abdel-Maksoud MF, Hokanson JE. The complex role of triglycerides in cardiovascular disease. Semin Vasc Med 2003; 2: 325-34.

30. Ferrannini E, Buzzigoli G, et al. Insulin resistance in essential hypertension. N Eng J Med 1987;17: 350-57.

31. Steinberg HO, Brechtel G. Insulin –mediated skeletal muscle vasodilatation is nitric oxide dependent. A novel action of insulin to increase nitric oxide release. J Clin Invest 1994; 94; 1172-79.

32. DeFronzo RA, Cooke CR. The effect of insulin on renal handling of sodium, potassium, calcium, and phosphate in man .J Clin Invest 1975; 55: 845-55.

33. Barbato A, Folker EJ, et al. metabolic syndrome and renal sodium handling in three ethnic groups living in England. Diabetologia 2004; 47:40-46.

34. Tooke JE, Hannemann MM. Adverse endothelial function and the insulin resistance syndrome. J Intern Med 2000; 247: 425-31.

35. Kuroda S, Fujii T, et al. Role of insulin resistance in the genesis of sodium sensitivity in essential hypertension. J Hum Hypertens 1999; 13: 257-62.

36. Tripathy D, Dhindsa S, et al. Elevation of free fatty acids induces inflammation and impairs vascular reactivity in healthy subjects. Diabetes 2003; 52; 2882-87.

37. Anderson EA, Hoffman RP, Mark AL. hyperinsulinemia produces both sympathetic neural activation and vasodilatation in normal humans. J Clin Invest 1991; 87: 2246-52.

38. Egan BM. Insulin resistance and the sympathetic nervous system. Curr Hypertens Rep 2003; 5: 247-54.

39. Matthews DR, Hosker JP. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentration in man. Diabetologia 1985; 28: 412-19.

40. Hanely AJ, Karter AJ, Festa A, et al. Factor analysis of metabolic syndrome using directly measured insulin sensitivity. The insulin resistance atherosclerosis study. Diabetes 2002; 51: 2642-47.

41. Krauss RM, Winston M, Grundy SM. Obesity: impact on cardiovascular disease. Circulation 1998; 98: 1472-76.

42. “Diabetes and obesity” Time to act- jointly published by International Diabetes Federation & International association for the study of obesity. 2004.

43. Management of adolescent obesity. API medicine update 2005; chapter 67.

44. The World Health Organization Western Pacific Region, the International Association for the study of obesity, and the

International obesity Task Force. The Asia-Pacific perspective: redefining obesity and treatment. Melbourne: Health communication Australia, 2000.

45. Lee S, Ross R. Interindividual variation in abdominal subcutaneous and visceral adipose tissue: influence of measurement site. J Appl Physiol 2004; 97: 948-54.

46. Aubert H, Alessi MC. Weak and non-independent association between plasma TAF 1 antigen levels and the insulin resistance syndrome. J Thromb Haemost 2003; 1: 791-97.

47. Bajaj M, Banerji MA. Type 2 diabetes in south Asians: a pathophysiologic focus on the Asian- Indian epidemic. Curr Diab Rep 2004; 4: 213-18.

48. Tanaka S, Horimai C. Ethnic differences in abdominal visceral fat accumulation between Japanese, African-Americans, and Caucasians: a meta analysis. Acta Diabetol 2003; 40 (suppl 1): s 302-s 304.

49. Guo Z, Jensen MD, Johnson CM. Regional postprandal fatty acid metabolism in different obesity phenotypes. Diabetes 1999; 48: 1586-92.

50. Vane J, Botting R. Regulatory function of the vascular endothelium. N Engl J Med 1990; 323: 27-36.

51. Neutnfl T, Hassan A, et al. Systemic endothelial dysfunction is related to the extent and severity of coronary artery disease. Atherosclerosis: 1997; 129: 111-118.

52. Anderson T, Gerhard M, et al. Close relation of endothelial function in the human coronary and peripheral circulation. J Am Coll Cardiol 1995; 26: 1235-1241.

53. Coronary artery disease in diabetes mellitus. API medicine update2005; Chapter 3.

54. Kannel WB. Metabolic risk factors for coronary heart disease in perspective from the Framingham study. Am Heart J 1987; 114: 413-9.

55. Haffner SM, Letho S, Laakso M. Mortality from coronary heart disease in subjects with and without prior myocardial infarction. Am J Med 1999; 23: 43s-45s.

56. Mohan V, Premalatha G.Ischaemic heart disease in south India NIDDM patients-A clinic based study on 6597 NIDDM patients. Int J Diab Countries 1995; 15: 64-67.

57. Alerti KG, Zimmet PZ, for the WHO consultation. Definition and diagnosis of complications. Part 1 diagnosis and classification of

diabetes mellitus provisional report of a WHO consultation. Diab Med 1998; 15: 539-553.

58. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global burden of disease study. Lancet 1997; 349: 1269-76.

59. Dalal PM. API Text Book of medicine 7th Ed. 203 page 796.

60. Dalal PM. Editorial. JAPI 2004; 52: 695.

61. Harrison's Principles of Internal Medicine; chapter 349: page 2379.

62. Harrison's Principles of Internal Medicine; chapter 349: page 2380

63. Eastern stroke and CHD collaborative research group. BP, cholesterol and stroke in Eastern Asia 1998; 352: 1801-7.

64. Harrison's Principles of Internal Medicine; chapter 349: page 2380.

65. Executive summary of atherosclerotic vascular disease conference proceedings for health care professionals from a special writing group of the American heart Association. Circulation 2004; 109; 2617-2625.

66. Duttta R; Vascular disease management plaqued by lack of awareness & Research, Express Health Care Management, 1:2, Jan 1.15, 2003. API medicine update2005; chapter 19.

67. Ochard TJ. Strandness DE: Assessment of peripheral vascular in diabetes. Report and recommendations of an international workshop. Circulation, 1993; 88: 819.

68. Over view of peripheral vascular disease. API medicine update2005; chapter 19: page 93.

69. The World Health Organization Western Pacific Region, the International Association for the study of obesity, and the International obesity Task Force. The Asia-Pacific perspective: redefining obesity and treatment. Melbourne: Health communication Australia, 2000.

70. Expert Committee on the Diagnosis and the classification of Diabetes mellitus. Report of the expert Committee on the Diagnosis and the classification of Diabetes mellitus. Diabetes Care 1997; 20: 1183-97.

71. Prevalence of the metabolic syndrome and overweight among adults in china. Lancet 2005; 365: 1398-405.