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PREVENTING SUDDEN CARDIAC DEATH – THE ROLE OF NON-INVASIVE ASSESSMENT OF HEART FUNCTION

By

M.O. BALOGUN
Professor of Medicine

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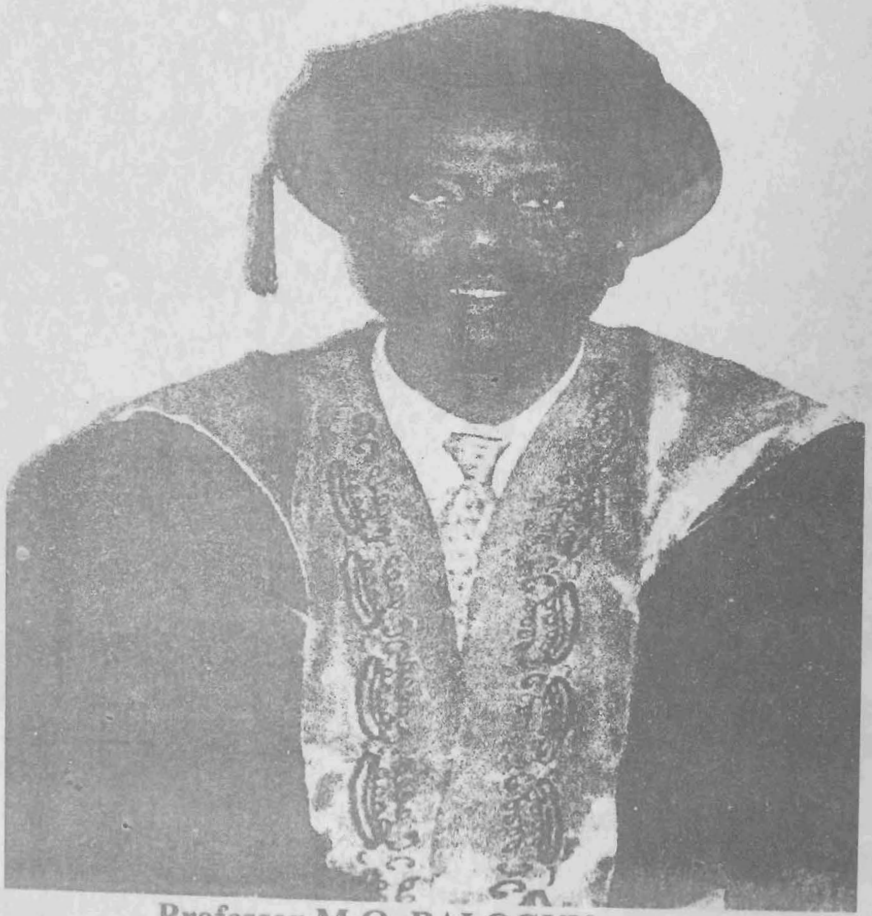

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Introduction

Cardiovascular disease (CVD) is the leading cause of death in developed and many developing countries being responsible for the deaths of 17 million people each year. This constitutes about one-third of global deaths annually (WHO Report 2002). Nearly 85% of the global mortality and disease burden from CVD is borne by low and middle-income countries. Data from the Global Burden of Disease Study suggest that CVD and infections and parasitic diseases have similar burdens of mortality for developing countries as far back as 1990. It is interesting to note that far more CVD deaths (Table 1) occur in developing than developed countries (Murray and Lopez 1996).

While in developing economies, the major health concerns have been focused on infections, parasitic, nutritional and perinatal diseases, (with 9.17 million deaths in 1990), CVD ranks a close second (with 9.08 million deaths in 1990) and an epidemic of cardiovascular disease may be inevitable due to progressive urbanization, industrialization, improving control of communicable diseases and gradual increase in life expectancy.

This illustrates the double burden of communicable and non-communicable diseases (NCD) that developing countries face (Murray and Lopez 1997).

It was with this in mind that the Federal Ministry of Health of Nigeria in December 1988 set up a National Expert Committee on Non-Communicable Diseases (NCD) with the principal objectives of identifying the risk factors involved in the diseases and formulating a suitable programme for early detection and effective control. In their report, CVD was recognized as one of the major non-communicable diseases in Nigeria (NEC 1992).

Appropriate Diagnostic Technology in the Management of Cardiovascular Diseases

Cardiovascular diseases in the adult African include hypertension and hypertensive heart disease, cardiomyopathies, valvular heart disease, pericardial disease, coronary heart disease, congenital heart disease, diabetic heart disease, thyrotoxic heart disease, sickle cell heart disease, pulmonary vascular disease, peripheral vascular disease, and cardiac infections. Heart failure may result from any of these diseases.

Table 1. Deaths in Developed and Developing Countries from Top Ten Causes in 1990

	Deaths in Thousands in Region		
Cause of Death	Developed	Developing	World
CV disorders	5245	9082	14327
Infectious and Parasitic Diseases	163	9166	9329
Malignant neoplasms	2413	3611	6024
Respiratory Infections	389	3992	4380
Unintentional injuries	552	2682	3233
Respiratory disorders	500	2435	2935
Perinatal disorders	82	2361	2443
Digestive disorders	424	1426	1851
Intentional injuries	282	1569	1851
Genitourinary disorders	167	568	735

Source: Murray and Lopez, 1996.

Until the 1950s the main cardiac investigation was the 3-lead electrocardiogram (ECG), but 12 leads increased in popularity in the past 20 years. The initial exercise test was carried out with the inefficient Master two-step test. Now the bicycle ergometer and the treadmill are the most popular modes of exercise test worldwide. Echocardiography was pioneered in Sweden by the cardiologist Inge Edler of Lund in association with the physicist Helmuth Hertz in 1954. Cross-sectional echocardiography was developed in the 1970s, as was Doppler ultrasound, largely as a result of the work of Liv Hatle of Norway (Julian, 2002).

While the overall objectives of the WHO Cardiovascular Diseases Programme were to prevent and control CVDs in the community, one of the specific tasks of the Programme was to monitor advances and developments in technology for management of CVDs. Major advances in invasive and non-invasive cardiological diagnostic and therapeutic techniques had taken place in recent years. However developing economies are limited in their ability to acquire these resources due to financial constraints and will have to apply the concept of appropriate health technology.

Appropriate health technology means methods, procedures, techniques, and equipment that are scientifically valid, adapted to local needs, and acceptable both to those who use them and to those for whom they are used, and that can be acquired, maintained, and utilized with resources the community or the country can afford (WHO 1988). While clinical history and physical examination are highly important components of cardiovascular diagnosis and evaluation, many symptoms of CVD are common to those of disease in other organ systems and thus are of variable specificity. Moreover, CVD may be severe in the absence of symptoms, while severe symptoms may be present where disease is mild.

The risk of sudden death and the economic burden of cardiac care increase with inaccurate diagnosis and delayed treatment. Early and accurate diagnosis using appropriate technology is therefore essential.

Diagnostic technologies have a variety of uses (WHO 1988):

- Diagnosis, assessment and management of acute or chronic illness;
- Identification of asymptomatic disease or risk;
- Population studies;
- Assessment of disability;
- Teaching, training physicians and other health care personnel about disease and health care; and
- Research.

Cardiac Care Unit

While cardiology practice had been in existence since the inception of the Obafemi Awolowo University Medical School, an organized Cardiac Care Unit (CCU) of the Obafemi Awolowo University (OAU)/ Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife was first established under the leadership of Prof G. O. A. Ladipo, my mentor and teacher, in 1983. Other members of the CCU during this period were Prof J. J. Andy (also my teacher), Dr S. Lawal, Dr P. O. Ogunnowo and myself.

Prof A. A. Ajayi, now retired, a clinical pharmacologist, whose research thrust was in the area of cardiovascular pharmacology, was actively collaborating with the unit.

With the retirement of Prof G. O. A. Ladipo in 1989, the leadership mantle of the unit fell on my shoulders. The other members of the unit currently include Dr A. O. Akintomide, Dr R.A. Adebayo, Dr O. E. Ajayi and Dr S. A. Ogunyemi.

Recently the Cardiac Care Unit was expanded, upgraded, and equipped with the state of the art technology for accurate diagnosis and appropriate treatment of CV disorders. This was made possible under the visionary leadership of Dr S. F. Kuku, the Chairman of the Board, and Prof O. Akinola, the Chief Medical Director and other members of the Management Board of the OAUTHC. Some of these equipment are shown in figures 1-3.

Figure 1: The Echocardiographic Equipment

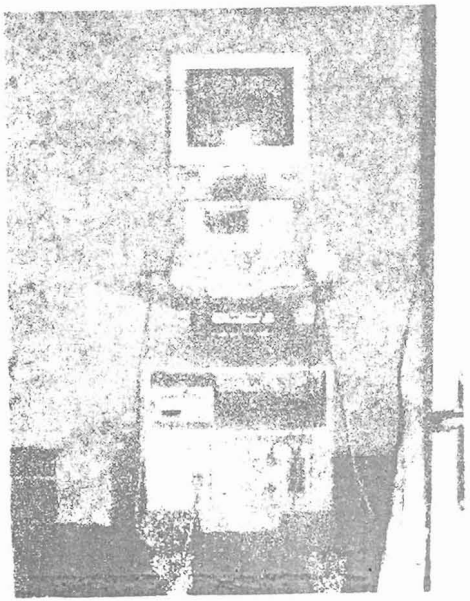


Figure 2: A Patient Having An Echocardiogram

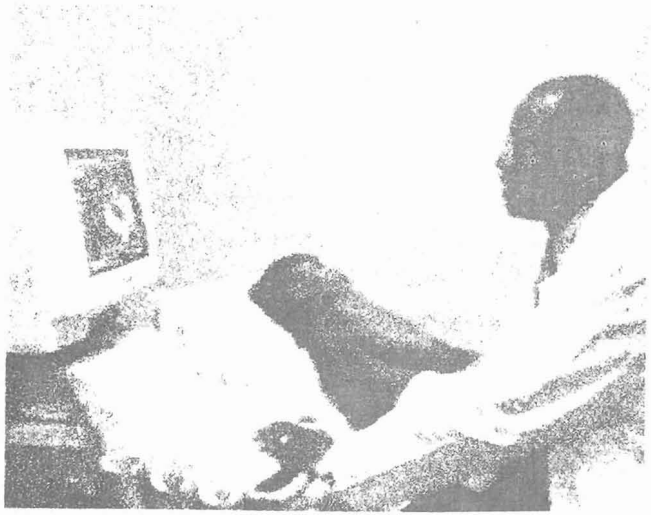
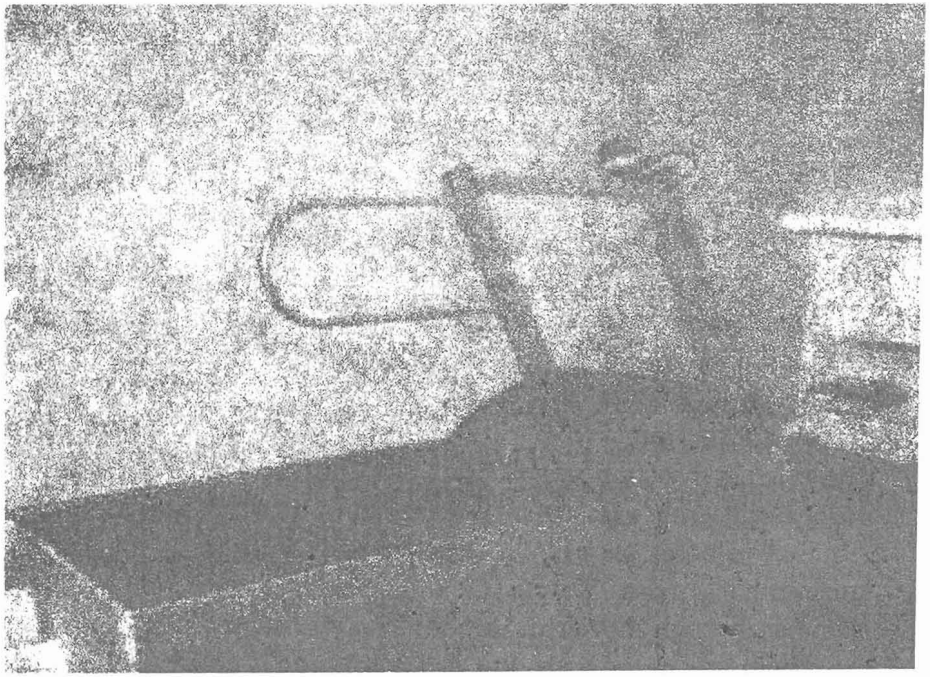


Figure 3: The Treadmill Exercise Testing Equipment.



Our research efforts had focused on non-invasive assessment of cardiac function and therapies of heart diseases in order to improve cardiac function and my humble contributions to these efforts commenced in June 1983.

This Inaugural lecture creates an opportunity for me to present before you our findings and how we have influenced the lives of our patients.

By the Grace of God I have the privilege of being the first alumnus Provost of the College of Health Sciences, having been the first alumnus Dean for four years and now I stand to present the first Inaugural Lecture from the Department of Medicine.

Cardiac Function

The primary function of the heart is to impart energy to blood in order to generate and sustain a satisfactory blood pressure. This is required in order to provide an adequate perfusion of organs. By contracting its muscular walls, the heart pumps blood from the cardiac chamber through the valves into the major outflow vessels and into the other parts of the body. For example blood is propelled from the left ventricle through the aortic valve into the aorta from where blood is distributed to the rest of the body.

The stroke volume (SV) is the volume of blood ejected each time the heart beats and the heart rate (HR) is the number of beats per minute. The product of the SV and HR equals the cardiac output (CO).

CO = SV x HR (litres/minute)

Changes in stroke volume or heart rate or both will alter the cardiac output.

Cardiac function has two important components:

(1) Systolic function and
(2) Diastolic function.

Systolic Function

The systolic function of the myocardium is a reflection of the interaction of myocardial preload, afterload, and contractility (Tibby and Murdoch, 2003).

Non-invasive indices of systolic function determined in clinical practice include oxygen uptake, ejection fraction, fractional shortening, cardiac index, end-systolic volume index, end-systolic volume, end-diastolic volume, end-diastolic volume index, mean velocity of circumferential fibre shortening, mitral E-point septal separation and Doppler derived flow velocity integrals.

Diastolic Function

Diastolic function reflects the events during the two phases of diastole including the (1) isovolumic relaxation phase and (2) the filling phase.

The filling phase can be further divided into the process of early rapid filling, the period of diastasis and the period of atrial systole (Balogun, 2001). The non-invasive indices of diastolic function include assessment of mitral and tricuspid early and late filling patterns, isovolumic relaxation time, deceleration time, pulmonary venous flow velocity curves and tissue doppler velocities (Balogun *et.al* 1994, Balogun 2001).

There are various investigative techniques available for the assessment of cardiac function and these include invasive as well as non-invasive techniques. Non-invasive methods include exercise stress testing, echocardiography including doppler echocardiography, cardiac magnetic resonance imaging, nuclear ventriculography, computed x-ray tomography and impedance cardiography. Haemodynamic measurements are taken during the assessment of cardiac function because of the relationship between pressure, flow and resistance.

Exercise Testing

Exercise testing is an established non-invasive diagnostic, prognostic and evaluative technique in cardiovascular medicine.

Exercise, a common physiological stress, can elicit CV abnormalities not present at rest and can be used to determine the adequacy of cardiac function. Two types of exercise can be applied as a stress to the CV system: Isometric (static) or isotonic (dynamic). Dynamic exercise is preferred for testing because it puts a volume stress rather than a pressure stress on the heart and it can be graduated. Isometric exercise (e.g., handgrip) on the other hand imposes greater pressure than volume load on the left ventricle in relation to the body's ability to supply oxygen. However, most activities usually combine, in varying degrees, both types of exercise (Fletcher *et.al* 1990).

There is an increasing public awareness of the benefits of exercise as evidenced by the increasing number of fitness clubs in our cities. The exercise enthusiasts claim prophylactic and therapeutic benefits.

There are many who have neglected exercise completely and prefer instead to watch others do it and may prefer to pay handsomely to that end. The occasional widely reported exercise related death reinforces any excuse for physical inactivity. For the sedentary individual, there is a risk involved in the sudden, unregulated and injudicious use of strenuous exercise, especially if such an individual is a middle-aged adult who may have subclinical heart disease. Legend has it that in 490 BC, PHEIDIPPIDES, the original marathon man, died minutes after running 26miles, 385 yards to Athens to announce a victory over Persia in the BATTLE OF MARATHON. Many years ago, a 45 year old runner given to overextending himself entered a long-distance race wearing a T- shirt imprinted with the message, "You have not run a good marathon unless you have dropped dead. - Pheidippides."

Ironically, a week after entering the race, the middle aged runner with the T-shirt collapsed during a long run, dead from coronary heart disease. It turned out that he had long ignored warning symptoms of chest pain (Brody, 1990).

The most comprehensive studies on the effects of physical activity on CV risk including blood pressure (BP) have been reported by Paffenberger *et.al* 1983. Sedentary alumni were at 35% greater risk for the development of hypertension (HT) while exercising alumni had significantly lower blood pressures than sedentary alumni. Other studies reported similar findings of the benefit of physical fitness in reducing the risk for CV disease (Blair *et.al* 1984; Kannel and Sorlie 1979; Pekkanen *et.al* 1987)

While epidemiological evidence supports the view that maintenance of a high physical activity level is in itself an effective preventive against the development of coronary heart disease, exercise testing is advisable before an individual 40 years of age or older begins exercise training or exercise programmes (Fletcher *et.al* 1990).

Objectives of Exercise Testing

The objectives of exercise testing include:

(1) To diagnose coronary artery disease and investigate physiological mechanisms underlying cardiac symptoms (angina, arrhythmias, inordinate blood pressure rise, functional valve incompetence)

(2) To evaluate cardiovascular functional capacity for work, sport or participation in a rehabilitation programme or to estimate response to medical or surgical treatment.

(3) To evaluate responses to conditioning and /or preventive programmes.

(4) To increase individual motivation for entering and adhering to exercise programmes (Committee on Exercise 1972).

Cardiovascular Responses To Exercise

Normal subjects

In 1984, I started conducting a cardiovascular screening survey of residents in Ile-Ife. One hundred and twenty four healthy Nigerians (80 males; 44 females) aged 20-59 years, without contraindications to exercise, were selected amongst those who volunteered to undergo exercise testing in order to assess their level of CV fitness. There was a decline in participation with increasing age, and greater response by males than females to participate. Seventy-seven percent of subjects were sedentary. No active females above the age of 29 years volunteered (Balogun and Ladipo, 1989).

Maximum oxygen uptake ($VO_{2\ max}$) is equal to maximum cardiac output times maximum arteriovenous oxygen difference. Resting cardiac output (5 to 6 Litres/minute) increases to as high as 20 to 25 L/min during peak exercise, an increase proportional to the workload and exercise demand. Because of the linear relation between VO_2 and CO during exercise, oxygen consumption reflects cardiac output. Since cardiac output is equal to the product of stroke volume and heart rate, VO_2 is directly related to heart rate.

The VO_2 is therefore a good indicator of CV fitness (Lim *et al* 1996). Its importance is based on the fact that it defines in otherwise healthy and motivated subjects the functional limits of the CV system. The VO_2 max may be expressed in metabolic equivalents (METs). The MET is a unit of sitting resting VO_2 which is 3.5 ml O_2 per Kg of body weight per minute.

While it is ideal to measure the $VO_{2\,max}$ directly during exercise testing, direct measurements are cumbersome as well as difficult and equipment may not be readily available. The $VO_{2\,max}$ however can be predicted from the duration of work performed on the treadmill.

With the Bruce protocol, there is a high correlation between the duration of exercise and O_2 uptake (Bruce *et . al*, 1973). In the evaluation of cardiovascular fitness, reference data, obtained from

the CV responses of normal individuals to exercise, are usually provided. Such data, based on adequate samples, are available for Caucasians in the developed countries. My interest in this area of research was stimulated because of the lack of published data for black Africans. In view of the variability of absolute values of maximal O_2 uptake published for different population groups, and the possibility of difference in CV responses to exercise in these groups, it became necessary to provide normal reference values for black Africans with which values in diseased states can be compared.

In Nigerians, the duration of exercise (DOE) and estimated VO_2 max during treadmill exercise decreased linearly with increase in age with a significantly high correlation between age and VO_2 max ($r = -0.82$) and between age and DOE in seconds ($r = -0.8$) ($p < 0.0001$). Regression equations were derived separately based on level of activity of subjects and also for DOE in relation to age.

DOE (secs) = 962-9.54 (age in years) (Balogun and Ladipo 1989; Balogun *et. al* 1997).

The 50 – 59 year old subjects were performing at between 60 – 70 % of subjects in the 20 –29 age group. Exercise capacity was significantly higher in male than female subjects and in active than sedentary subjects .Men have a 10% to 14 % greater haemoglobin level, greater muscle mass and less fat than women and these attributes contribute to the increased exercise capacity in men.

The anticipation of exercise increases the heart rate (HR) through activation of the sympathetic nervous system. As exercise begins, the HR increases rapidly because of a further reduction of vagal tone, followed later by a further increase in sympathetic tone and circulating catecholamine levels. During dynamic exercise, HR increases linearly with workload and VO_2. Heart rate response is influenced by several factors, including age. As observed in other populations, our studies showed an age related decline in maximal heart rate. There was a significant negative correlation of maximal

heart rate (MHR) with age during exercise (r= - 0.51). Average values of MHR (beats/min) expected in healthy Nigerian men and women can be predicted from the regression equation below:
MHR = 207 – 0.620 (age in years) (Balogun and Ladipo 1989).
Our studies showed that the MHR correlated significantly with DOE on the treadmill or bicycle (Balogun *et al,* 1997).

The systolic blood pressure (SBP) rises with increasing dynamic work as a result of increasing CO whereas DBP usually remains about the same. Maximum SBP during exercise increases with age in males and females in our studies on normal subjects.

The rate-pressure product (RPP) is a haemodynamic predictor of myocardial oxygen consumption during exercise and its peak value is related to the magnitude of the load imposed on the left ventricle (Kitamura *et .al,* 1972). Normal individuals usually develop a peak value of 200 to 400 (mm Hg X beats/min X 10^{-2}) (Balogun and Ladipo, 1988a).

There is a linear relation between myocardial oxygen consumption and coronary blood flow. Angina pectoris usually occurs at the same double product rather than at the same external workload.

Exercise Mode/Protocol

Many exercise protocols are in use but no single test is universally applicable to a wide range of patients and subjects. The Bruce protocol is the most widely used protocol on the treadmill and the Astrand protocol on the bicycle ergometer in our exercise laboratory. Different modes of dynamic exercise testing including simple walking tests, step tests, field-testing, bicycle ergometer and treadmills are often used. Various factors determine the choice of exercise mode. The bicycle ergometer and treadmill are now the most commonly used dynamic exercise testing devices. While bicycle ergometers predominate in mainland Europe, treadmills are favoured in the United States and United Kingdom. There was no data on the comparative

circulatory responses to both bicycle ergometer (BE) and treadmill (TD) exercise and the preferred mode of exercise testing in our population. We therefore conducted a study comparing these two modes of exercise.

The DOE, MHR, Peak SBP, and Peak RPP values were significantly higher with the TD than BE ($p< 0.0001$). However these haemodynamic values were significantly higher at sub-maximal exercise on BE than TD.

The TD, therefore imposes a greater haemodynamic burden on the myocardium than the BE at peak exercise indicating that the TD might have a higher sensitivity for the detection of coronary artery disease.

None of the subjects considered the TD as a " very hard " mode while 25% considered BE as ''very hard ''. Eighty-five percent of subjects preferred the TD while 15% preferred the BE for their future exercise testing and for their personal physical exercise programme (Balogun et al 1997).

Exercise Responses in Groups at Risk for Developing Hypertension

An exaggerated BP response to exercise in normotensive subjects (absolute SBP values of 200 to 230 mm Hg) may be a marker for future development of hypertension (Wilson and Meyer 1981; Dlin *et al* 1983; Balogun and Ladipo 1988a) and for left ventricular hypertrophy (LVH) (Gottdierer *et al* 1990).

Wilson and Meyer 1981 found that normotensive individuals with an elevated exercise BP response (> 225 mm Hg) followed for an average of 32 months had over twice the risk for the development of hypertension as subjects without this response. Dlin *et al* 1983 found that 10.6 % of subjects with an exaggerated BP response during exercise testing (defined as a SBP > 200 mmHg or a rise of diastolic BP of at least 10 mmHg if this value exceeded 90 mmHg) developed

hypertension; none of the subjects who did not show an exaggerated exercise BP response developed hypertension over the mean 5-year follow-up period. We carried out, for the first time in Black Africans, an evaluation of the BP response to exercise in normotensive subjects with hypertensive parents and compared values with properly matched normotensives who were certain their parents were normotensive. The SBP and RPP values were significantly higher in subjects with parental hypertension compared with those with normotensive parents ($p < 0.01$).

Twenty-seven percent of subjects with parental hypertension had exercise SBP > 200 mmHg compared to none in the normotensive parental group. We therefore considered this a hypertensive response and this group a high-risk group (Balogun and Ladipo, 1988a). The subjects who participated in this study are to be re-evaluated in 2004. These findings indicate that even in the absence of baseline hypertension, the BP response during exercise testing may suggest an increased likelihood for developing hypertension in the future. Identification of such patients may allow preventive measures that would delay or prevent the onset of this disease. In addition to a possible role in predicting the evolution of hypertension, the response to exercise testing has also been assessed as a way to predict susceptibility to end organ damage especially LVH.

In a large prospective study involving the follow up of 4907 middle-aged apparently normal men in the Paris civil service for an average of 17 years, Filipovsky *et al* 1992, provided strong evidence that exaggerated SBP (> 230 mm Hg) after 5 minutes of exercise was associated with increased mortality after controlling for age, smoking, total cholesterol levels, body mass index, LVH on ECG, and athletic activities.

Exercise Responses in Essential Hypertension

Hypertension is a major cause of morbidity and mortality among adult Nigerians. Generally the prevalence of hypertension (HT) in adults in

Nigeria is of the order of 8-10% of rural and 10-12% of urban communities. Blood pressure rises with age in most populations of the world including Nigeria. However, there are pockets of population in Nigeria such as some villages outside Kaduna and the isolated Koma community in Adamawa State in which the BP does not appear to rise with age (NEC, 1992). Hypertension is more severe, develops much earlier, results in a higher mortality at a younger age more commonly from cerebrovascular accident than from coronary artery disease in blacks than whites (Saunders 1991).

Hypertension affects approximately 1 billion individuals worldwide. Recent data from the Framingham Heart Study (Vasan *et al* 2002) suggest that individuals who are normotensive at 55years of age have a 90% lifetime risk for developing HT.

Hypertension is a leading risk factor for stroke, congestive heart failure, renal failure, angina and myocardial infarction at all ages and in both sexes.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (2003) provides a new guideline for hypertension prevention and management.

The new proposed classification is presented in Table 2.

This classification is for adults aged 18 years or older. In contrast with the classification provided in the JNC VI report, a new category designated prehypertension has been added, and stages 2 and 3 hypertension have been combined. Patients with prehypertension are at an increased risk for progression to hypertension; those in the 130/80 to 139/89 mmHg BP range are at twice the risk to develop HT as those with lower values (Vasan *et al* 2001). Lifestyle modifications, including weight reduction, dietary modifications, and increased physical activity through exercise, are required in patients with elevated BP in other to decrease the risk of CV complications (JNC 7 report).

Table 2. Classification of Blood Pressure for Adults ≥ 18 Years

BP Classification	Systolic BP, mmHg		Diastolic BP,mmHg
Normal	< 120	and	<
80Prehypertension	120 - 139	or	80 –
89Stage 1 hypertension	140 – 159	or	90 –
99Stage 2 hypertension	≥160	or	≥100

In children and teenage populations, the prevalence of hypertension ranges between 0% and 13.9% (Bertrand *et. al* 1981; Abu-Bakare and Oyaide 1983). We found a prevalence of 4% using the 95th centile BP of 133/92 mm Hg as the cut off value (Balogun *et. al* 1990a) and we found that the strong determinants of BP in children were weight, Quetelet index and triceps skinfold thickness (Balogun *et. al* 1990b). Clearly lifestyle modifications are required in children who have evidence of elevated BP.

Dynamic exercise, such as walking and running, is performed as part of many daily activities in hypertensives. In controlled circumstances, formal exercise testing has shown that the CV responses of hypertensives are significantly different from the responses of age and sex matched normal subjects. Our studies have shown significant reduction in work capacity, as evidenced by significantly lower DOE, VO_2 max, and significantly higher functional aerobic impairment (FAI), in hypertensives compared with controls (Balogun and Ladipo 1988b; Balogun and Ladipo 1990). The FAI represents the percent difference of estimated VO_2 max from that predicted in health for a person of the same sex, age and habitual activity status. Treated hypertensives significantly exercised longer on the treadmill than untreated patients.

Most of the treated patients were on drugs capable of regressing LVH and whether this contributed to improved cardiac function was not addressed in our studies. Exercise capacity in hypertensives is reduced as much as 30% compared with age-matched normotensive controls. Our studies also showed that maximal heart rate (MHR) and the rest – maximal change in heart rate (Δ HR) were significantly lower in hypertensives than normotensives. The BP response to exercise was significantly higher in hypertensives than normotensives, and in untreated than treated hypertensive patients. A striking rise of SBP to 230mm Hg or above was observed in 45% of hypertensive males. The reduction in BP response with treatment was more noticeable with the diastolic than the systolic BP values. It was also observed that the drop in diastolic BP at peak exercise was more noticeable in normals than hypertensives and in treated than untreated hypertensives. This tends to support the observation that HTs maintain a higher total peripheral resistance (TPR) at all levels of exercise as shown from invasive measurements (Amery *et .al,* 1967) than normal subjects and this can be modified by treatment. The mean PRPmax was significantly higher in hypertensives than normotensives, and lower in treated than untreated hypertensives. The benefit of treatment of hypertensives is further emphasized by the reduction in blood pressure response to exercise and the reduced myocardial oxygen consumption during maximal exercise. It is probable that the reduced MHR with exercise in our hypertensive population contributed in part to impairment of exercise capacity by a limitation in maximal exercise CO (Balogun and Ladipo 1990). These observations should be taken into consideration whenever exercise prescription is required for hypertensive patients.

Non-invasive Assessment of Cardiac Function in Hypertensive Heart Disease

Hypertensive heart disease is the association of arterial hypertension with LVH. Our findings indicate that impaired exercise

performance in African hypertensives occurs with the onset of ventricular hypertrophy (Balogun and Ladipo, 1988b; Balogun *et. al,* 1988). Our patients had either radiological evidence of enlargement or electrocardiographic signs of LVH including voltage criteria with evidence of myocardial strain (ECG-LVH) or both.

Both the Framingham study and the Glasgow blood pressure clinic study have shown that ECG-LVH is an important risk factor for the CV complications of HT (Kannel 1983, Dunn *et. al* 1990). In the Framingham study patients with LVH and strain had an 8-fold increase in CV deaths and a 6-fold increase in coronary mortality. In the Glasgow study voltage LVH without strain was found to be associated with an increase in mortality, which could not be explained on the basis of an increase in blood pressure alone. Furthermore, they observed that LVH with ST-T changes was associated with a particularly high mortality rate, yielding a risk similar to that carried by ECG evidence of previous myocardial infarction. The authors therefore, concluded that the excess risk associated with LVH, with or without ST-T changes, could not be explained by age, increased BP at referral to the clinic, or cigarette smoking habit, when these factors were considered either separately or in combination when analyzed by regression analysis. This shows that ECG-LVH has an adverse effect on survival even in patients who are free of coronary artery disease (Sullivan *et. al* 1993). Whether ECG-LVH carries the same impact on mortality in African hypertensives as observed in Caucasian hypertensives, remains to be determined through epidemiological studies (Balogun and Dunn, 1996).

We have suggested from our findings that voltage LVH on ECG may be an early marker of impaired exercise capacity (Balogun and Eniola, 1995).

Although the specificities of the available criteria for ECG-LVH are typically high (> 90 %), the sensitivities are lower and in the range of 20-60 % (Devereux *et. al,* 1984). Echocardiography has a

higher degree of sensitivity and a much-improved predictive accuracy in the detection of LVH (Levy *et. al,* 1990). Studies have indicated that echocardiographic derived LVH (Echo-LVH) has important prognostic implications in the hypertensive patient for all the CV complications of HT (Koren *et. al,* 1991).

The Prevalence of LVH in Hypertension

The prevalence of LVH increases with age and is significantly higher in hypertensives than normotensives. Many factors are known to influence the development of LVH and some of these include the height of the blood pressure, the renin-angiotensin-aldosterone system and the sympathetic nervous system (Balogun and Dunn, 1990).

In the Framingham study of almost 5000 subjects ECG-LVH was found in 2.9% of men and 1.5% of women, while Echo-LVH was detected in 14.2% of men and 17.6% of women (Levy *et. al* 1990). The prevalence may be as high as 90% in patients hospitalized for hypertension (Devereux *et. al* 1987).

The increased risk of CV complications associated with LVH may be due to several mechanisms including myocardial ischaemia, accelerated atherosclerosis, sudden cardiac death and impaired ventricular function.

Hypertensive patients with LVH are at an increased risk for CAD both because of intrinsic perfusion abnormalities associated with the LVH and also because of the associated CAD (Balogun *et. al,* 1990c, Pringle *et. al,* 1989).

Sudden Cardiac Death and LVH

Sudden cardiac death may be defined as natural death due to cardiac causes initiated by abrupt loss of consciousness within one hour of the onset of the terminal symptoms, occurring in an individual

who may or may not have recognized pre-existing heart disease, but in whom the time and mode of death are unexpected.

LVH is one of the most powerful risk factors for sudden cardiac death and mechanisms postulated to explain this include associated CAD, myocardial ischaemia, an arrhythmic potential of LVH, LV dysfunction and possibly antihypertensive therapy (Dunn, 1990). Several studies have suggested that there is an increased prevalence of ventricular arrhythmias in patients with LVH. We assessed the prevalence of exercise-induced arrhythmias (EIAR) in asymptomatic Nigerian hypertensives with and without voltage ECG-LVH. None of the subjects studied had either high-grade ventricular ectopic activity or non-sustained ventricular tachycardia during treadmill exercise. The prevalence of EIAR was 15% in hypertensives and was slightly more common in those with voltage ECG-LVH who were carefully matched with those without voltage ECG-LVH. The clinical significance of this finding remains to be determined and therefore warrants further study (Balogun and Eniola 1995). Mild to moderate alcohol intake do not seem to predispose to EIAR and did not significantly impair exercise capacity in alcohol drinking Nigerian HTs compared with those who were not (Balogun *et. al,* 1990d).

An association between alcohol consumption and hypertension has been found in several studies of general population (Arkwright *et. al,* 1982, Klatsky *et. al,* 1977). Nigerian hypertensives who were heavy alcohol drinkers were found to be very prone to heart failure (Falase *et. al,* 1983).

Alcohol has been shown to exert a dose-related toxic effect on cardiac muscle, impairing cardiac function in asymptomatic alcoholic patients
(Urbano-Marquez *et. al* 1989).

LVH and Cardiac Dysfunction

Systolic function may be normal in hypertensive patients with LVH and may, in fact, be increased in the early stages (Balogun and Dunn 1991), but becoming impaired in the late stages with increased and persistent severity of hypertension (Lawal and Falase 1988, Adesanya and Sanderson 1981). Abnormalities of diastolic function are present in HT even before LVH develops, but in addition, other factors also contribute, in particular, age and body weight Abnormalities of diastolic function have been demonstrated using radionuclide studies, digitized M-mode echocardiography and Doppler echocardiography and these are described in detail elsewhere (Balogun 2001). In hypertensive LVH, the abnormalities are predominantly in the relaxation phase. In a preliminary study, 58% of hypertensive Nigerians had impaired relaxation on Doppler assessment of diastolic function (Balogun *et.al* 1999). In a follow up study, Dr Ajayi and I observed relaxation abnormalities of up to 70% in hypertensives and age, elevated BP and LVH were contributory. Restrictive diastolic dysfunction was present in only 3% (Ajayi and Balogun unpublished observation). It has been shown that exercise capacity is better correlated with diastolic function than systolic function (Davies *et.al* 1992).

Various studies have shown that antihypertensive agents which inhibit the sympathetic nervous system (SNS) or the renin-angiotensin aldosterone system (RAAS) are more commonly associated with regression of LVH than agents which do not (Dunn *et.al* 1984). The aggregate results of 46 monotherapy trials reviewed by Liebson 1990 suggest that angiotensin converting enzyme inhibitors (ACEIs), Beta adrenergic receptor blockers (BB) and calcium antagonists (CCB) reduce ventricular mass more consistently than diuretics or peripheral vasodilators. Methyldopa is also a powerful regressor of LVH. Systolic and diastolic functions are preserved at rest and during situations of stress. Diuretics have been shown to be less effective and minoxidil

and trimazosin may actually lead to an increase in cardiac mass, in spite of BP reduction with these drugs. There are racial differences in cardiac structure and function in hypertension, and blacks have been shown to have significantly higher LVH and more impairment of diastolic function than whites matched for age, sex, body mass index, duration and degree of hypertension (Mayet *et. al* 1994) although this has not been demonstrated consistently.

Most of the studies have been carried out predominantly in white populations. Also there are racial differences in the response to antihypertensive therapy with black patients responding less well to ACEIs and BBs than whites unless these are combined with CCBs or diuretics or some other drug combinations (Ajayi *et.al* 1996, Abengowe *et. al* 1997, Abengowe *et.al* 1998). This is further compounded by the cost of newer antihypertensive agents making compliance difficult (Olasemo *et.al* 1996). The findings from studies carried out in predominantly Caucasian populations may not be extrapolated to the African hypertensive. These findings on drug regression of LVH and its impact on cardiac function require confirmation in the black African hypertensive through well conducted, adequately funded, clinical trials, hopefully, in the near future.

There is also the need to explore non-pharmacological means of LVH regression, such as has been observed with weight reduction in obese patients (Macmahon *et.al* 1986).

Heart Weight

Normal values for the whole heart average 325g in adult men and 275g in adult women. When expressed as a percentage of body weight, normal limits of heart weight in healthy adults have been estimated as 0.4-0.45%.

Left ventricular mass is about 23-68 g; right ventricular mass about 23-68g and the interventricular septal mass is about 17-61g. (Geigy Scientific Tables, 1990). Figures 4-6 show different views of the heart.

Figure 4: Shows the Anterior View of the Heart

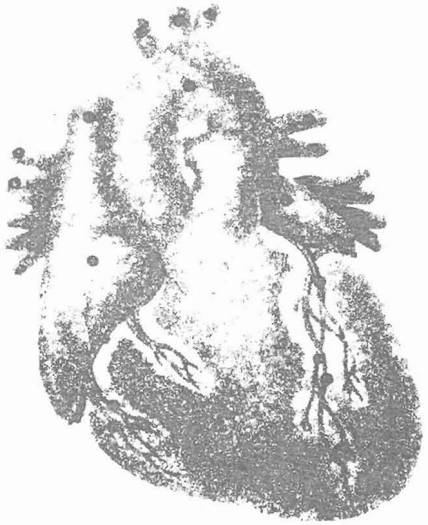


Figure 5: Shows the Posterior View of the Heart

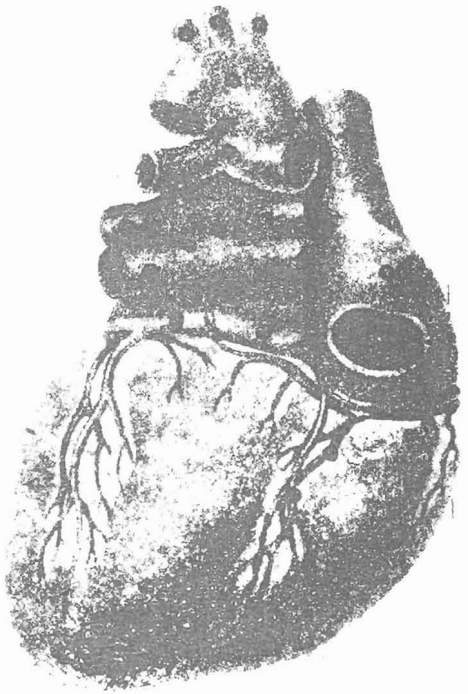


Figure 6: Shows the Sagittal View of the Heart

Cardiac Function in Diabetes

The prevalence of diabetes is increasing rapidly and about 100 million people are affected worldwide. It is predicted that this number will increase to 200-225 million within the next 20-25 years (Clark and Perry 1999).

There are a number of reasons for this dramatic increase. The aging of the general population, lack of physical exercise combined with an unhealthy diet are significant factors. As developing countries continue to adopt the bad habits of developed economies, the incidence will rise. About 90% will have type 2 diabetes, which develops with age and has a strong relation to macrovascular complications. The burden of diabetes mellitus (DM) in Nigeria is enormous and the prevalence is 2.7% (NEC 1992) and about 75% of these are non-insulin dependent diabetes mellitus. (Osuntokun *et.al* 1971). The substantial risk of CV disease in patients with DM has been recognized for some time, with 80% of mortality being due to macrovascular complications. The outcome has worsened for female DM patients than the males over the years. One reason for the poor outcome for DM patients is probably the divided care they receive. They are generally cared for by endocrinologists, although the main manifestations of their disease are cardiovascular which cardiologists treat. Cardiological referrals may then take place only when complications have developed. It is therefore important for endocrinologists and cardiologists to meet to plan patients' treatment protocols. The risk of CV disease in the DM population is high. A diabetic patient is at as high a risk for a cardiac event as a patient who has suffered a myocardial infarction. About 50-70% of patients with non-insulin dependent diabetes (NIDDM or Type 2 DM) will have hypertension. About 35-75% of complications of DM are thought to be due to hypertension, the presence of which further increases the CV risk in diabetes. In our own studies in Nigerians with NIDDM,

41.7 % had concomitant hypertension (Ikem *et.al* 2001). The prevalence of proteinuria in this study was 53.8 % and this correlated significantly with SBP (p = 0.0001; Ikem *et. al* 2002). In patients with type 1 or type 2 DM and microalbuminuria, which may progress to proteinuria there is, advanced structural damage in the kidney.

In one study of patients with essential HT we found the prevalence of microalbuminuria to be 17.4% and this correlated positively and significantly with SBP, ECG voltage LVH, cardio-thoracic ratio, and echocardiographic LV mass (Olatunde *et.al* 2002). There is no doubt that microalbuminuria has emerged as an important marker of elevated BP and CV disease in HT and DM. We conducted a study in young normotensive Caucasian IDDM patients in order to determine whether abnormalities of

(1) Blood pressure, as assessed by ambulatory BP (ABP) monitoring, and

(2) Diastolic function as assessed by Doppler echocardiography could precede the appearance of microalbuminuria.

The IDDM patients had significantly higher 24 hour mean arterial pressure and maximal BP during reported daily physical activity than controls during ABP monitoring. Abnormal diastolic function was observed but this did not correlate with the ABP variables (Balogun *et.al* 1994).

Our studies have also shown that estimated VO_2 max progressively reduced from normals, DM, HT to combined HTDM ($p < 0.0001$ ANOVA) using the bicycle ergometer (Okokhere *et.al* 2000). The results showed that HT and DM impair exercise capacity during dynamic exercise and their concomitant existence synergistically increases this impairment in Nigerians. The myocardial oxygen consumption normalized per unit time or workload increased progressively from DM, to HT and to combined HTDM showing additional CV risk for CHD. Submaximal exercise blood pressure

response was significantly higher in the HT and HTDM groups than the other groups. The inotropic and chronotropic capacities were different in the patient groups than controls. Babalola and Ajayi 1992 had reported similar findings although the HR and BP responses were not described. They found the greatest depression in systolic function amongst the HTDM group. In view of the above observations, aggressive management is required in patients with HTDM.

Recent guidelines support the aggressive treatment of hypertension in DM (Chobanian *et.al* JNC 7, 2003). Combinations of 2 or more drugs are usually needed to achieve the target BP goal of less than 130/80 mm Hg. The ACEIs and the angiotensin receptor blockers (ARBs) reduce albuminuria and progression of nephropathy. ACE inhibitors may be beneficial even before the development of microalbuminuria in DM.

Sickle Cell Disease

Sickle cell anaemia (SCA) is the commonest symptomatic haemoglobinopathy in Nigeria with a prevalence of 2% and the most troublesome in terms of frequency and severity of clinical manifestations (NEC 1992). The heart is largely involved in SCA and patients may develop high output congestive heart failure. Many Echo studies of ejection phase indices of LV systolic function have reached conflicting results (Adebiyi *et.al* 1999, Simmon *et.al* 1988, Adebayo *et.al* 2001, Balfour *et.al* 1988) with evidence of normal systolic function in some and depressed function in others. Diastolic function may be impaired in SCA. Lewis and coworkers 1991 demonstrated abnormal LV diastolic function (Predominantly due to impaired relaxation) with Doppler echo in SCA patients in the absence of symptoms of heart failure or LV systolic dysfunction. We have similarly observed LV diastolic dysfunction in Nigerian patients with SCA (Adebayo *et.al* 2001) despite their normal systolic function. The cardiovascular responses to exercise in SCA differ from normals

(Adebayo *et.al,* 2002a, Adebayo *et.a,l* 2002b, Akinola and Balogun 1995) irrespective of the mode of exercise used. Walking is a familiar mode of exercise for patients with SCA and we had demonstrated, either using the 12-minute fast-paced walking (FPW) exercise test or a modified treadmill protocol, reduced chronotropic capacity and a significant limitation of exercise capacity. With the FPW, post exercise DBP was significantly lower in SCA than controls. It has been suggested that the abnormal diastolic function in SCA may be responsible for the exercise intolerance and failure of LVEF to increase appropriately during exercise (Balfour *et.al*, 1988). It has been suggested that the sickle cell trait with haemoglobin AS (SCT) may be a risk factor for sudden cardiac death (SCD) in blacks. Kark and associates (1987) observed a significantly higher death rate of 32.2/ 100,000 for sudden unexplained deaths amongst black recruits with SCT compared with a rate of 1.2/100,000 in black recruits with normal haemoglobin, and a rate of 0.7/100,000 for non-black recruits with normal haemoglobin. Many of these deaths were associated with exercise. It is fascinating that there have been so many reports of sudden death in persons with SCT, but relatively few in patients with SCA; presumably this difference is caused by a greater limitation of physical activity in the latter group (Saunders 1991).

Thyrotoxic Heart Disease

The heart is a major target organ for thyroid hormone action and marked changes occur in cardiac function in thyrotoxic patients (Woeber, 1992).

Thyrotoxicosis is frequently associated with hypertension especially systolic hypertension and thyrotoxic patients may develop cardiac complications such as congestive heart failure and cardiac arrhythmias. The mean SBP of thyrotoxics in the report by Adetuyibi (1976) was 144.3 ± 19.9 mm Hg. Atrial fibrillation is the most common clinically significant tachyarrhythmia occurring in 9 to 22 % of

thyrotoxics in Caucasian studies (Kahaly *et.al* 1998) but only 4-5% in local studies (Adetuyibi 1976, Famuyiwa 1987, Kolawole *et.al* 1999a). Patients over 60 years of age who have thyrotoxicosis of long duration are at increased risk of congestive heart failure, as are patients with pre-existing cardiac disease. Valvular heart disease, especially mitral regurgitation, may play a more substantial role in thyrotoxic heart disease than previously recognized (Cavros *et.al* 1996,Kolawole *et.al* 1999b, Kolawole and Balogun 2001) and it has been shown that mitral valve prolapse occurs with increased frequency compared with the general population (Noah *et.al* 1988). It is important therefore that echocardiographic assessment of valve function and cardiac function be carried out in patients with thyrotoxicosis. Cardiac failure can arise as a result of diastolic dysfunction despite the presence of normal systolic function (Kolawole and Balogun 2001, Mintz *et.al* 1989).

Obesity

Obesity has become a major health, social and economic problem in the western world in more than 20 years. More than 50% of American adults are now overweight, and nearly a quarter are obese (Flegal *et.al* 1998) and blacks are known to have higher weight levels than whites. In the UK 32% of adult females and 45% of males are now overweight and the prevalence of obesity continues to rise (Erens and Primatesta 1998). In Ghana, the prevalence rates of obesity are 23.4 % in females and 14.1% in males (Amoah 2003), The body mass index (BMI), which is the weight in kilograms divided by the square of the height in metres, is widely used to define degrees of overweight. Overweight is defined as a BMI of 25-29.9 kg/m^2 and obesity as a BMI greater than or equal to 30 kg/m^2. The weight of Ghanaian males was comparable to that of Nigerian males (Okosun *et.al* 1998). Both environmental and genetic factors affect the expression of obesity across the lifespan. Obesity is a risk factor for several chronic diseases, including hypertension, dyslipidaemia, type

2 DM, CAD, sleep apnoea, musculoskeletal problems, gallbladder disease, stroke and some cancers. The Adult Treatment Panel III guideline (NCEP 2002) for cholesterol management defines the metabolic syndrome as the presence of 3 or more of the following conditions: abdominal obesity (waist circumference > 102cm (>40 in) in men or >89 cm (> 35 in) in women, glucose intolerance (fasting glucose ≥110 mg/dl or ≥6.1 mmol/L), BP of at least 130/85 mm Hg, high triglycerides (≥ 150mg/dL or ≥1.70 mmol/L), or low high density lipoprotein cholesterol [< 40 mg /dL (< 1.04 mmol/L) in men or < 50 mg/dL (< 1.30 mmol/L) in women]. Intensive lifestyle modification should be pursued in all individuals with the metabolic syndrome, and appropriate drug therapy should be instituted for each of its components as indicated. Congestive heart failure is a common complication of obesity, even in the absence of HT or CAD. Such patients can have significantly higher LV cavity size, LVH and end-systolic wall stress. LV systolic and diastolic dysfunction may occur and substantial weight loss can improve LV systolic function and diastolic function as well as improve symptoms. The LVH and reduced heart rate variability present in obesity are markers of sudden cardiac death. Dietary intervention, lifestyle modification and increased exercise are important strategies for weight management in obesity.

Congestive Heart Failure

Heart failure may be defined as the pathophysiological state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the metabolic requirements of the body and/or the heart is able to do so only from an elevated filling pressure.

Congestive heart failure (CHF) is a chronic, disabling and lethal disease of global health significance with high rates of morbidity and mortality. It is characterized by an age-related incidence, which rises sharply after the age of 75 years. It is estimated that about 15 million

people are afflicted worldwide, affecting between 0.4 and 2% of the world's population, prevalence similar to that of DM. The prevalence in the United Kingdom, Scandinavia and the United States is about 0.4-2% overall and 10% in elderly subjects. The annual incidence increases with age from about 0.2% in persons 45 to 54 years to 4.0% in men 85 to 94 years, with the incidence approximately doubling with each decade of age. Women lagged slightly behind men in incidence at all ages. The commonest complication of HT in Africans is heart failure (Balogun, 2002). In one study, hypertensive heart failure (HHF) accounted for 29% of all adult cases presenting at the cardiac unit (Carlisle and Ogunlesi, 1972). In our study, HHF constituted 59% of cases seen over a three year period (Adewole *et.al*, 1996) while in a study from Zaria 102 cases were seen between 1993 and 1994 (Danbauchi *et.al* 1996). In our preliminary echocardiographic study 67% of heart failure patients had HHF (Balogun *et.al*, 1999).

Mortality of CHF is high, there has been a 50% mortality 5 years after the onset of symptoms. There is a 2-year mortality rate of about 30% in patients with moderate CHF (NYHA Classes II and III) which increases to about 75% in severe CHF (NYHA Class IV). In seven separate studies which involved almost 900 patients, the overall one year mortality was between 34% and 58% (Kannel *et.al* 1988, Packer 1985). CHF is a malignant condition with mortality rates comparable to that of cancer. Morbidity is also high and this is reflected in the high hospital admission rates resulting in a major economic burden on health care systems consuming 1-2% of health care expenditure in a number of industrialized countries (McMurray *et.al*, 1998).

The very complex syndrome of CHF is characterized by anatomic and biochemical alterations of the myocardium, changes in systolic and diastolic function, activation of various neurohumoral systems and derangements in organ blood flow and function.

The chest X-ray and the ECG may show indirect evidence of cardiac dysfunction. A normal ECG should alert the clinician to the possibility that the diagnosis of CHF is incorrect. Common abnormalities associated with chronic LV dysfunction include left atrial enlargement, left bundle branch block, LVH and ST-T abnormalities. The chest X-ray may show cardiomegaly and evidence of pulmonary congestion or oedema.

We have reported a higher resting supine heart rate, SBP, and DBP in patients with HHF compared with age- and sex-matched normotensive volunteers and patients with essential hypertension. During exercise testing with the treadmill, the increase in SBP and HR was markedly impaired, an outcome associated with reduced exercise capacity in patients with HHF. The estimated VO_2 max in such patients (3.5 METs) was reduced by 50% compared with normotensive persons (7.2 METs) and by 40% compared with patients with hypertension (6.2 METS) (Balogun *et.al* 1988).

Depressed systolic function and perhaps impaired diastolic function contributed to the reduced exercise capacity in these patients. Various studies have shown that the ventilatory and chronotropic responses to exercise as well as workload are powerful and independent predictors of heart failure mortality. We and others have shown that echocardiographic indices of systolic function may predict functional capacity and exercise tolerance in CV disease in contrast to the findings of Franciosa *et.al* 1981. The impact of diastolic function was not assessed and our patients were free of CAD and therefore these differences might explain the contrast in our findings (Ajayi *et.al* 1990, Ajayi and Akinwusi 1993).

Systolic and diastolic function can be assessed using echocardiography, radionuclide ventriculography, nuclear ventriculography, and cardiac magnetic resonance imaging. The type used depends on the availability of and institutional experience with the use of these equipment.

Every patient suspected of having heart failure should have an assessment of cardiac function using non-invasive methods especially echocardiography. There are widespread inaccuracies in diagnosis when clinical methods alone are used. In many patients in whom the diagnosis was made in the primary care setting prove not to have the condition on further investigation.

Echocardiography is an established and important technique for the diagnosis of a wide range of CV disorders, even in emergency situations, and findings are known to influence management decisions (Balogun *et.al* 1993, Balogun *et.al* 1999). The echo indices of systolic function have been mentioned earlier. The survival of patients with CHF and a normal ejection fraction (EF) is substantially better than in those with a low EF. The diagnosis of clinically significant systolic dysfunction is made if the EF is less than 40%. Confirmatory evidence can be obtained from other measurements such as the mitral E-point septal separation (mitral EPSS), fractional shortening (FS), aortic root motion and Doppler derived stroke distance. If the mitral EPSS is greater than 7 mm, it is indicative of an EF below 45%. The end-systolic volume index is easy to measure and is a very powerful predictor of survival. Systolic function can also be visually assessed by experienced echo specialists. Patients with LV systolic dysfunction may be without symptoms. There is the need to use echo more widely in patients with CV disease. Tissue Doppler, strain, and strain rate echocardiography and three-dimensional echocardiography are newer techniques for the evaluation of systolic function.

Thirty to fifty per cent of patients with heart failure have normal systolic function, implicating diastolic dysfunction as a major pathophysiological abnormality (Ommen and Nishimura 2003; Balogun, 2001).

Fifty to fifty-three per cent of our heart failure patients assessed using Doppler echocardiography, had impaired diastolic relaxation, while 10-38 % had restrictive diastolic dysfunction (Balogun *et.al*-1999).

The therapeutic strategy in patients with pure diastolic heart failure differ from that in patients with systolic heart failure, therefore, making it mandatory for the assessment of diastolic function in heart failure.

There is a progression of diastolic dysfunction that has been described for different disease states. Understanding the relation between various Doppler velocity curves and LV filling abnormalities has allowed a non-invasive approach to identify the severity of diastolic dysfunction in patients. This requires an integration of findings from mitral flow velocity patterns, isovolumic relaxation time, deceleration time, pulmonary flow velocity curve, tissue Doppler velocities and colour M-mode flow propagation. Different grades of diastolic dysfunction (I, II, III, IV) can be determined and findings can be used for diagnosis, prognosis, and determination of therapy in patients with suspected diastolic dysfunction. Abnormal relaxation pattern is grade I diastolic dysfunction, while the pseudonormal pattern is grade II, and the restrictive pattern is grade III-IV diastolic dysfunction. An individual patient may progress or regress between grades I, II, and III diastolic dysfunction depending upon the state of compensation in filling pressures at the time of the echo examination. However, in severe end stage disease, the restrictive pattern persists despite manipulation of filling pressures and may be irreversible (grade IV) (Ommen and Nishimura).

Left atrial reservoir, conduit, and booster pump function can also be assessed using Doppler echo. Right ventricular diastolic function may be assessed also with Doppler and we are currently looking at whether this can be predicted by LV diastolic indices.

Valve Function

An assessment of the patient's valvular function should be undertaken by a mixture of imaging and Doppler ultrasound as this may be responsible for heart failure. The valves should be inspected

in all available views. Abnormal valves should be assessed by continuous wave Doppler. The application of the modified Bernoulli equation (gradient = 4V2) is required for the determination of the peak and mean pressure gradients and valve area. Mitral valve area can be estimated from the rate of diastolic pressure decline and the continuity equation may be required for the calculation of Valve area in the setting of a low cardiac output. Doppler ultrasound is extremely sensitive for the detecting of regurgitant lesions. Clinically unsuspected mitral and aortic regurgitant jets are frequently seen and may be readily detected using colour flow mapping or spectral Doppler. Mitral regurgitation is very frequently seen in patients with dilated ventricles, and is often more extensive than can be appreciated by auscultation alone. Pulmonary artery pressure and right ventricular pressures can also be estimated Echocardiography gives additional information on unsuspected abnormalities responsible for CHF (Balogun *et.al* 1996, Langhorne *et.al* 1993, Balogun *et.al* 1993). The following figures 7-10. illustrate the clinical utility of the echocardiogram in the diagnosis of patients with heart failure

Figure 7: Parasternal Long Axis of a 16 year old Female Patient with Heart Failure

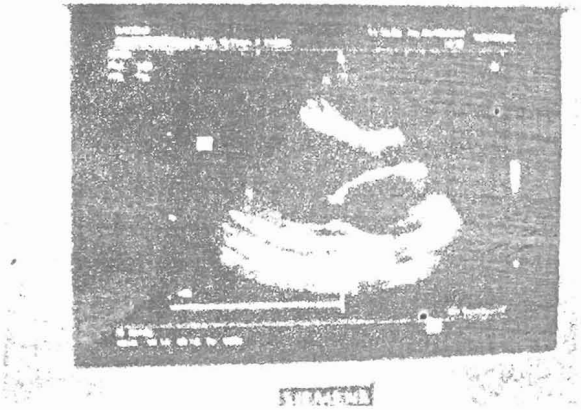


Figure 8: Colour Flow Doppler Showing Severe Mitral Regurgitation

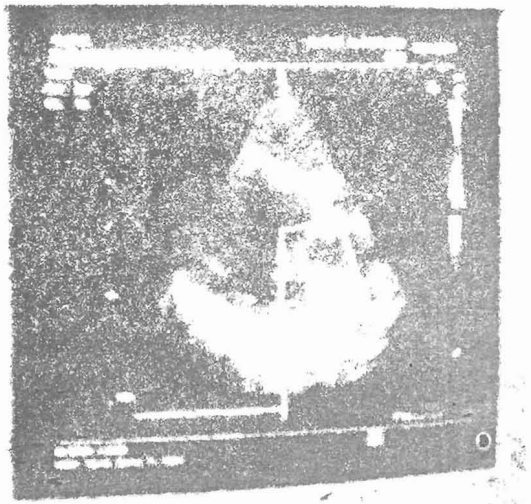


Figure 9: Apical Four Chamber View Showing Dilated Chambers and Mitral Regurgitation

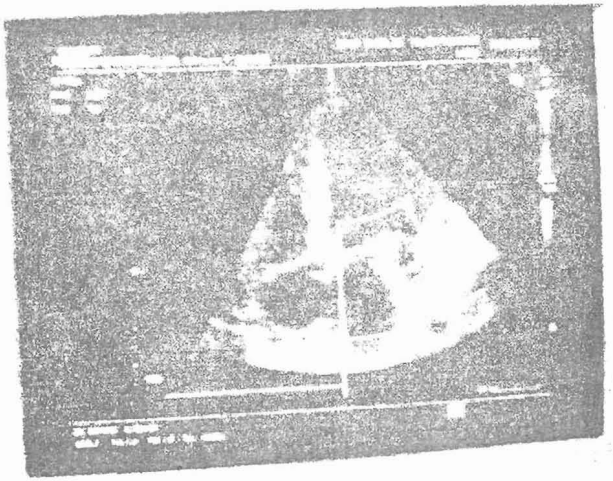
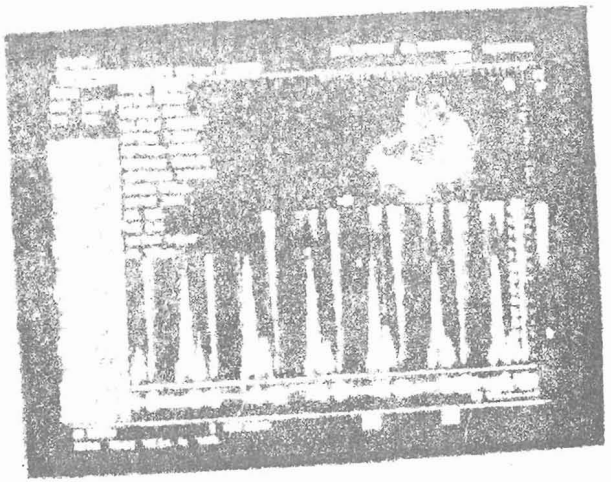


Figure 10: Restrictive Diastolic Dysfunction in the same Patient



Therapeutic Strategies that Improve Survival

In CHF, considerable advances have recently been made and it is important that patients receive appropriate care to improve their prognosis. While diuretics and digoxin are effective therapeutic strategies in the management of heart failure especially systolic HF, they have not been found to improve survival in large scale studies. The introduction of ACEIs has proved to be a major advance for HF patients. Large trials (CONSENSUS, SAVE, SOLVD, V-HEFT II) have shown that they improve the symptoms and signs of all grades of CHF, improve exercise tolerance, reduce progression of HF from mild to severe, reduce hospitalization and improve survival in all grades of CHF (Betkowski and Hauptman, 2000). In Nigerians with CHF, we have shown that ACEIs are beneficial, reduce intrahospital mortality and duration of hospitalization, ameliorate symptoms and improve exercise tolerance (Ajayi *et.al* 1989a, Ajayi *et.al* 1989b, Ajayi and Balogun 1990, Adewole *et.al* 1996). Patients with high risk of intrahospital mortality (NYHA IV, hyponatraemia) require early aggressive therapy (Balogun *et.al* 1995 Adewole *et.al* 1996). In the under 70s, the ATLAS study showed a clear mortality benefit from the use of high dose lisinopril. ACE inhibitors have been shown to be beneficial in patients with asymptomatic LV dysfunction. Recently from the HOPE study, ramipril was found to significantly reduce the rate of development of heart failure in patients at high risk of CV events who had normal EF. Certain inotropic drugs and adrenergic agonists should be avoided in heart failure because they have been associated with increase in mortality in CHF. Antiarrhythmic agents should be avoided in asymptomatic patients with CHF. Low dose amiodarone has been shown to reduce mortality in severe CHF.

Combination Therapy

In our studies, alpha-adrenergic blockade with prazosin in combination with enalapril was found to significantly increase exercise tolerance compared with enalapril alone with a marked and rapid clinical amelioration of symptoms (Ajayi *et.al,* 1996). In the RALES study, the addition of spironolactone to diuretics and ACEIs, resulted in a striking reduction in mortality in HF patients with systolic dysfunction.

Large trials (CIBIS II, COPERNICUS, MERIT-HF) have shown that beta-blocker treatment in patients with NYHA class II, III, and IV heart failure results in substantial reductions in mortality and improvements in LV function (McMurray, 1999). Current evidence from trials (Val-Heft, ELITE II) generally indicate that the angiotensin II receptor blockers are no more effective than the ACEIs in reducing mortality in patients with CHF due to LV systolic dysfunction. However, they should be prescribed for patients who develop an intractable cough on ACEIs or as add-on therapy for further blockade of the renin-angiotensin system (Betkowski and Hauptman 2000). The dihydropyridine calcium antagonists have been demonstrated to be safe in treating angina and hypertension in patients with heart failure when used in addition to ACEIs, diuretics or digoxin. Newer therapeutic options continue to be evaluated in the management of CHF with the overall goal of achieving further reduction in mortality. The references on these landmark trials that have influenced our practice will be supplied on request.

Conclusion and Recommendations

Mr. Vice-Chancellor sir, Ladies and Gentlemen, I have tried in this lecture to present some of the issues that have engaged my research time over the years. Cardiovascular disease is the leading cause of mortality worldwide. The principal forms of CVD, coronary artery disease and stroke, ranked first and second among the 15 leading

causes of death in 1990 and are expected to maintain these ranks in 2020. In sub-saharan Africa however, CVD is not yet the number one killer. Our concern is based on the emerging evidence of adverse trends in CVD risk factors and mortality from sub-Saharan Africa (SSA) especially in the urban areas. Addressing and reversing these trends are highly important issues and should be on the Government agenda. To support heart-healthy choices, emphases must be placed on policy development, systems change and the creation of environmental factors including: strengthening legislation and regulatory mechanisms controlling the leading risk factors such as tobacco, physical inactivity, and poor nutrition. All preventive strategies including primordial, primary, and secondary prevention strategies must be integrated and coordinated. A unique opportunity exists for primordial prevention in SSA. Heart-healthy and stroke free initiatives including health education, and surveillance of risk factors and their modification, should be developed and integrated into diverse community settings including schools, worksites, communities, and healthcare systems. Health promotion, risk factor control and disease prevention should be integrated within the primary healthcare setting.

In secondary and tertiary care settings, risk factors for CVD should be properly assessed with appropriate technology, and the appropriate evidence-based therapeutic strategies are instituted in order to reduce complications and the risk of sudden cardiac death. Individuals with family history of HT and exaggerated BP response to exercise deserve special attention and primary prevention strategies. Food manufacturers and restaurants must reduce sodium in the food supply by 50% over the next decade. Addition of table salt to meals served should be discouraged. Hypertension is a leading risk factor for CHF, stroke, CAD and renal failure at all ages and in both sexes. It is important to control BP with antihypertensive drugs as treatment has been shown to reduce mortality. Life-style modifications are important and exercise, dietary changes and weight management are

recommended. Motivating individuals to adhere to drug therapy and lifestyle modifications are major public health challenges. Family support is crucial and physicians must also build trust and increase communication with patients and their families. LVH must be aggressively treated with drugs that are known to regress hypertrophy. Heart failure and stroke should be prevented with therapeutic strategies that are evidence based. Heart failure should be aggressively treated according to evidence-based therapeutic strategies.

It is recommended that anyone who plans to begin an exercise programme more vigorous than walking should have a physical examination. Individuals under age 40, who have a normal examination, no symptoms of CVD, no major CAD risk factors, and no murmurs, hypertension or other physical evidence of CVD, and a normal ECG, do not need an exercise test. Individuals 40 years of age or older or those who have abnormal physical examination and/ or 2 or more CV risk factors have a higher prevalence of occult heart disease and should therefore have a symptom-limited, maximum exercise test. The risks of serious complications of physical activity are highest during vigorous exercise and in individuals with heart disease.

Patients with heart disease may also require an echocardiography or other appropriate tests. I therefore recommend fast pace walking because it is well tolerated, has a low impact on the musculo-skeletal system, a minimum risk of complications, and it provides excellent results. Walking appears to be as beneficial as more vigorous activities. Some benefit is apparently derived from as little as 20 to 30 minutes of low-intensity exercise performed three times per week on non-consecutive days at a minimum intensity of 50-60% of maximum oxygen uptake. Moderate intensity, at 75 % of age-predicted maximum heart rate and at less than or equal to 75% of maximum oxygen uptake, is beneficial. Swimming, stationary cycling, and treadmill walking may also be appropriate. The risk of sudden cardiac death is increased with unsupervised jogging, squash and

competitive high intensity forms of exercise in subjects at least 40 years of age.

Patients with CVD should have exercise prescription from appropriately certified personnel. Exercise requires certain precautions for safety purposes.

(1) It should be avoided when feeling unwell, and immediately after eating.

(2) Adjust exercise to the weather and drink adequate fluids (Not beer) to maintain hydration.

(3) Understand personal limitations.

(4) Be alert for symptoms .

(5) Start slowly with warm up exercises, progress gradually, and avoid stopping abruptly by doing cool down exercises.

Mr. Vice-Chancellor, Ladies and Gentlemen, I thank God for giving me the opportunity to give this lecture and I thank my family, friends and colleagues for their support and encouragement. I thank you for your attention and may God bless you all. Amen.

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