CLINICAL AND ECHOCARDIOGRAPHIC FINDINGS OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AMONG HYPERTENSIVE PATIENTS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM

By

Tulizo Shemu Sanga

A Dissertation Submitted in Partial fulfillment of the Requirements for the Degree of Master of Science (Cardiology) of the Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for the Msc degree award of a dissertation entitled ***Clinical and Echocardiographic findings of left ventricular diastolic dysfunction among hypertensive patients at Muhimbili National Hospital, Dar es Salaam,*** in partial fulfillment of the Requirements for the degree of Master of Science (Cardiology) of the Muhimbili University of Health and Allied Sciences.

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Prof. E. Maro

(Supervisor)

Date: …….

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LIST OF ABBREVIATIONS

ACEI	-	Angiotensin Converting Enzyme Inhibitor
ARB	-	Angiotensin Receptor Blocker
AV	-	Aortic Valve
BMI	-	Body mass index
BSA	-	Body surface area
CCB	-	Calcium Channel Blocker
DBP	-	Diastolic blood pressure
DHF	-	Diastolic heart failure
DT	-	Deceleration time
ECHO	-	Echocardiogram
FS	-	Fractional shortening
IVRT	-	Isovolumic relaxation time
LVM	-	Left ventricular mass
LVMI	-	Left ventricular mass index
LVOT	-	Left Ventricular Outflow Tract
LV	-	Left Ventricle
LVEF	-	Left Ventricular Ejection Fraction
LA	-	Left Atrium
MUHAS	-	Muhimbili University of Health and Allied Sciences
MV	-	Mitral Valve
NOMA	-	Norad's Programme for masters Studies
NY	-	New York
NYHA	-	New York Heart Association
PA	-	Postero-anterior
PND	-	Paroxysmal Nocturnal Dyspnoea
PP	-	Pulse pressure
PV	-	Pulmonary Valve
RVOT	-	Right Ventricular Outflow Tract
RA	-	Right Atrium
RV	-	Right Ventricle

RWT	-	Relative wall thickness
SBP	-	Systolic Blood pressure
TV	-	Tricuspid Valve
VSD	-	Ventricular Septal Defect
WC	-	Waist circumference

ABSTRACT

Hypertension is the commonest of the cardiovascular risk factors, whose prevalence in Tanzania is high between 20-30%, among rural and urban residents respectively. Uncontrolled hypertension leads to a number of structural changes in the heart which eventually cumulates into interstitial fibrosis, myocardial wall thickness and functional alteration such as diastolic dysfunction.

Diastolic dysfunction is thought to be responsible for as many as 74% of cases of HF in hypertensive patients. Despite this likelihood; it is rarely diagnosed in clinical practice except by default.

Diastolic heart failure is common in sub-Saharan African hypertensive patients. However less is known about the prevalence of subclinical left ventricular (LV) diastolic dysfunction in asymptomatic and symptomatic hypertensive patients in Tanzania.

Objectives: To describe the clinical and echocardiographic features of Left ventricular diastolic dysfunction among hypertensive patients at Muhimbili National Hospital.

Methods: LV geometry and diastolic function were assessed by echocardiography in 200 hypertensive patients attending Muhimbili National Hospital in Dar es Salaam, Tanzania. The demographic parameters including age, sex, and body surface area, systolic and diastolic blood pressure were taken. Patients were categorized into groups of in-patients and outpatients. Ethical clearance was sought from the Research and Publications Committee of MUHAS and permission to conduct the study was obtained from the Ethics committee department of MNH. Patients were enrolled after informed verbal and written consent. Data entry and analysis has been done using the SPSS windows version 16

Results:

Two hundred participants were recruited into the study during the study period. One hundred and eight (54%) were females.The mean age of the study population was 52±13.5 years, which varied from 23-86 years, with men being older than women, with higher body surface area and heights than women.

LV diastolic dysfunction was found in 58.5 % of participants, 50% were in grade 1 diastolic dysfunction. The overall prevallence of left ventricular hypertrophy was 86% in this population of patients, concentric LVH dominated in both patient groups constituting 60.4% , eccentric hypertrophy was seen in 17.6% and concentric remodeling in 8%. Fourteen percent had normal left ventricular geometry. Concentric left ventricular geometry was the predominant geometry among the in-patients with diastolic dysfunction

In-patient hypertensive group had statistically significant larger LV internal diameters and wall thicknesses, and they had higher LV mass as well as higher prevalence of LVH (all $p<0.01$.

higher E/E' ratio was independently found to be associated with in-patient status, adjusting for lower age, larger LA size, higher mitral valve A velocity and lower IVRT (multiple $R^2=0.26$, $p<0.001$).

Conclusion: The prevalence of diastolic dysfunction is high among this population of patients with hypertension . Concentric left ventricular hypetrophy is high among hypertensives in this population and is a predominant geometry in patients with diastolic dysfunction. Elevated left ventricular filling pressures were independetly associated with inpatient status.

Recommendations:The higher prevalence of cardiac hypertrophy and left ventricular diastolic dysfunction among hypertensives in our study support the need for improved attainment of blood pressure goals in these patients. Aggressive Screening for end organ demage should be warranted in this population.

CHAPTER ONE

1. INTRODUCTION AND LITERATURE REVIEW

1.1. The global burden of hypertension

The global prevalence of hypertension defined as an average systolic BP of 140mmHg or greater, a diastolic BP of 90mmHg or greater, or the use of antihypertensive medication was estimated to increase by 60% to a total of 1.56 billion by 2025, which is 29% of the world wide adult population.[1] During the same period 75% of the world's hypertensive population will be residing in the third world countries [1, 2]

Overall the prevalence of hypertension in all regions increases with age more steeply in women. Increasing obesity and sedentary life style has a significant reparcation on hypertension. By age of 60, more than half of the adults in most regions of the world will be hypertensive. These alarming figures highlights that hypertension is set to remain the single most important preventable cause of premature death worldwide over the next two decades with the highest rates in Latin America and the Caribbean, former Socialist republics and Sub Saharan Africa.[3]

The reported prevalence of hypertension varied around the world, with the lowest prevalence in rural India (3.4% in men and 6.8% in women) and the highest prevalence in Poland (68.9% in men and 72.5% in women). Awareness of hypertension was reported for in 46% of the studies and varied from 25.2% in Korea to 75% in Barbados; treatment varied from 10.7% in Mexico to 66% in Barbados and control (blood pressure < 140/90 mmHg while on antihypertensive medication) varied from 5.4% in Korea to 58% in Barbados.[4,5]

Hypertension is an important public health challenge in both economically developing and developed countries. [6, 7] significant numbers of individuals with hypertension are unaware of their condition and, among those with diagnosed hypertension, treatment is frequently inadequate, measures are required at a population level to prevent the development of hypertension and to improve awareness, treatment and control of hypertension in the community.[8]

According to the Framingham Study, hypertension accounts for about a quarter of heart failure cases.[3] In the elderly population, as many as 68% of heart failure cases are attributed to hypertension. Community-based studies have demonstrated that hypertension may contribute to the development of heart failure in as many as 50-60% of patients. In patients with hypertension, the risk of heart failure is increased by 2-fold in men and by 3-fold in women. Improved surveillance of all diseases within sub-Saharan Africa is needed in order to place non-communicable diseases properly within the context of the overall burden of disease.[8, 9, 10, 11]

In Tanzania, a two linked cross-sectional population-based surveys done to describe the prevalence, detection, treatment and control of hypertension in an urban and rural areas, high prevalence of hypertension in both rural and urban areas of between 27-37%. In both areas, just under 20% of hypertensive subjects were aware of their diagnosis, approximately 10% reported receiving treatment and less than 1% were controlled (blood pressure < 140/90 mmHg). Hypertensive subjects were older, had greater body mass indices and waist: hip ratios, and had more risk factors for hypertension and its complications (smoking, heavy alcohol consumption, physical inactivity, obesity and diabetes) than the nonhypertensives. High prevalence of hypertension in rural and urban areas of Tanzania, with low levels of detection, treatment and control exists in this country. This demonstrates the need for cost-effective strategies for primary prevention, detection and treatment of hypertension and the growing public health challenge of non-communicable diseases in this area of Sub-Saharan Africa.[9, 12]

1.2. Classification of hypertension

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) simplifies the classification of blood-pressure levels and outlines how to use this new classification scheme for hypertension prevention and management.[13]

BP Scheme for Adults (in mm Hg)

Normal: systolic BP <120 and diastolic BP <80

Pre-hypertension: SBP 120-139 or DBP 80-89

Stage 1 hypertension: SBP 140-159 or DBP 90-99

Stage 2 hypertension: SBP ≥160 or DBP ≥100

For patients age 50 or older, elevated SBP is a stronger cardiovascular risk factor than elevated DBP. Within the BP range of 115/75 mm Hg to 185/115 mm Hg, each increment of 20/10 mm Hg doubles cardiovascular risk. Pre-hypertension warrants management with lifestyle modification (e.g., low-salt diet, regular physical activity).[1314]Traditionally, investigators have focused on abnormalities of systolic function to explain the signs and symptoms of heart failure. However, increasingly, abnormalities of diastolic function are being viewed as influential in precipitating heart failure and determining prognosis.[5] In the United States, 5 million patients have heart failure and 500,000 new cases occur annually. In half of the patients, the primary cause of heart failure is diastolic dysfunction, with preservation of the left ventricular ejection fraction (LVEF) [15, 16]

Of the 619 patients included in the NY Heart failure Registry who had an LVEF of 50% or more were hospitalized for heart failure, 73% were women with a mean age of 70 years and the common co morbid conditions were hypertension in 78%, increased left ventricular (LV) mass in 82%, diabetes mellitus in 46%, and obesity in 46%.[17]

Doppler echocardiography is the most practical method for assessing filling patterns and myocardial relaxation and for estimating LV filling pressures at rest and with exertion by recording flow velocities from the atrioventricular valves, central veins, and myocardial tissue. [19] [21, 22]

In uncontrolled hypertension, the thickness of the LV wall is frequently increased and the left atrium (LA) is usually enlarged because of the chronic increase in LV filling pressures. The increases LV wall thickness may be due to hypertension, hypertrophic cardiomyopathy, infiltrative cardiomyopathy or obesity.

1.3. Normal left ventricular diastolic function

Diastolic function is determined by two factors: the process of myocardial relaxation an active process that requires metabolic energy and the elasticity or distensibility of the left ventricle which is a passive process. [23] Relaxation of the contracted myocardium starts just prior to aortic valve closure. The rapid pressure decay and the concomitant "untwisting" of the left ventricle produces a suction effect that augments the left atrial-to-left ventricular pressure gradient, thereby promoting rapid early diastolic filling. . [24]

Loss of normal LV diastolic relaxation and distensibility, due to either structural like LVH or functional like ischemia, impairs LV filling. This results in increases in LV diastolic, left atrial, and pulmonary venous pressures. The net effect is a relative shift of LV filling from early to the later part of diastole with a greater dependence on atrial contraction.

Cardiac function is critically dependent upon diastolic physiologic mechanisms to provide adequate LV filling (cardiac input) in parallel with LV ejection (cardiac output). These processes must function under a variety of physiologic conditions, both at rest and during exercise.

The normal cycle of cardiac contraction and relaxation requires a precise, transient increase and decrease in the intracellular concentration of calcium ions. The sarcoplasmic reticulum helps orchestrate the movement of calcium during each contraction and each relaxation[24] The contraction of cardiac muscle is initiated by the cellular action potential that causes the opening of L-type sarcolemmal calcium channels through which calcium ions enter the cytosol. This influx of calcium ions result in the lease of more calcium ions from the adjacent sarcoplasmic reticulum through ryanodine receptor channels, a process called calcium- induced calcium release. These calcium ions bind to troponin c, which ultimately disinhibits the interaction of acting and myosin and results in the formation of cross-bridges.[25]

Myocardial relaxation is accomplished primarily by the removal of calcium ions from troponin by an enzyme in the sarcoplasmic reticulum, called sarcoplasmic reticulum calcium adenosine triphosphatase (SERCA2), and the sarcolemmal sodium-calcium exchanger. In humans, approximately 75% of calcium ions are removed by SERCA2 and 25% by the sodium –calcium exchanger.[26]

1.4. Diastolic dysfunction

Diastolic dysfunction and diastolic heart failure are not synonymous terms [27].Diastolic dysfunction indicates a functional abnormality of diastolic relaxation, filling, or distensibility of the left ventricle, regardless of whether the left ventricular ejection fraction is normal or abnormal and whether the patient is asymptomatic or has symptoms and signs of heart failure. On the other hand diastolic heart failure denotes the signs and symptoms of clinical heart failure in a patient with a normal LVEF and evidence for LV diastolic dysfunction.

Heart failure is now the leading cause of hospitalization for people aged 65 and over in the United States; Ninety percent of new cases of heart failure in the Framingham Heart Study[31] had a history of previous hypertension.

In the last 10 years or so, it has become apparent that approximately half of the patients who present with classic signs and symptoms of heart failure appear to have normal ventricular function, typically defined by the finding of an ejection fraction of >50% on echocardiography. This group has been variously described as having diastolic dysfunction, diastolic heart failure, or "heart failure with a normal ejection fraction (HFNEF). [27]

This condition, while undoubtedly of major importance, remains a murky area for several reasons. First, assessment of diastolic function is difficult and ideally requires cardiac catheterization; while noninvasive measures are used, they are nonspecific. Second, there are no reliable animal models of diastolic heart failure. Third, there is no treatment that is specifically aimed at improving diastolic function. In an 11page document outlining practice guidelines for the evaluation and management of heart failure, published recently by the American Heart Association and American College of Cardiology (AHA/ACC), diastolic failure received less than a page[27]

Clinical conditions responsible for primary diastolic dysfunction include Hypertension, Cardiomyopathy (Hypertrophic, Infiltrative and Restrictive), Coronary artery diseases, Diabetes mellitus, obesity, sleep apnea and Constrictive pericarditis. Data are limited with respect to the relationship among objective measures of diastolic dysfunction, symptoms and signs of heart failure with outcome and therapy.[28, 29]

A major reason for paucity of randomized controlled trials in heart failure patients is the difficulty in defining and measuring diastolic function. Although hemodynamic data obtained by heart catheterization can be used to measure diastolic function, the invasive nature of this assessment limits its applicability to most patients. Therefore, Doppler echocardiography is the method of choice in routine clinical practice to asses for diastolic dysfunction.[36].

Doppler assessment of diastolic function is complex and requires expert interpretation, furthermore, loading conditions affects mitral inflow pulsed wave Doppler parameters, making the differentiation between normal and pseudo normal diastolic function particularly difficult. Therefore in addition to mitral inflow parameters, pulmonary venous (PV) flow Doppler and changes in mitral inflow parameters during Valsava maneuver and currently tissue Doppler studies are used to distinguish pseudo normal from normal diastolic function.[30].

1.5. Diastolic heart failure from left ventricular diastolic dysfunction

LV diastolic dysfunction is a progressive condition and is characterized by an increasing resistance dependence on ventricular preload. Over time the increasing resistance to ventricular filling results in a failure of the Frank Starling mechanism.[31]

Predisposing conditions for DHF are older age, female gender, diabetes, obesity, arterial hypertension and left ventricular (LV) hypertrophy. Often, the full- blow picture of DHF emerges when a precipitating factor is superimposed on a state of subclinical LV diastolic dysfunction.[32]

1.5.1. Epidemiology of diastolic heart failure

Diastolic HF is thought to be responsible for as many as 74% of cases of HF in hypertensive patients.[33]. Despite this likelihood, it is rarely diagnosed in clinical practice except by default. This is a problem because the symptoms, such as dyspnea and fatigue, are nonspecific. Over the past decade, there has been a steady rise in the prevalence of heart failure in those with preserved left ventricular ejection fraction (diastolic heart failure) [34]. Based on their wide experience in the Framingham Heart Study, Vasan and Levy[33] have proposed three diagnostic categories: definite, probable, and possible. The diagnosis of definite diastolic failure requires the strong clinical evidence of HF, a normal EF and objective evidence of diastolic function, defined as “abnormal LVEF”

The prevalence of diastolic heart failure increases with age.[27] By the seventh decade of life, the incident cases of heart failure with a preserved LV systolic function approach, and by the eighth decade of life exceed those with a reduced LV ejection fraction. [35] The development of diastolic dysfunction in elderly adults may be independent of left ventricular mass, heart rate, contractility, or systemic blood pressure[36, 37] Diastolic dysfunction and DHF is more common in women than men.[38,39,40,41] In a chart study of over 19,000 Medicare beneficiaries hospitalized with the principal discharge diagnosis of HF, 35 percent had a normal ejection fraction. [42] Among patients with normal ejection fraction, 79 percent were women, while among those with decreased ejection fraction, 49 percent were women.

1.6. Clinical manifestations

Asymptomatic diastolic dysfunction is more prevalent than symptomatic disease, [36] when present; the symptoms of DHF do not appear to differ significantly from those of systolic HF. This was illustrated in a report in which 59 patients aged at least 60 years with symptoms of HF and an LVEF $\geq$ 50 percent (DHF) were compared with 60 patients of the same age with an LVEF $\leq$ 35 percent (systolic HF) and with 28 age-matched healthy controls. [45] The patients with DHF had similar, although generally less severe, manifestations (reduced exercise capacity, neurohumoral activation, and diminished quality of life).

Exercise intolerance seen in diastolic heart failure may be caused by elevation in left atrial and pulmonary venous pressures and/or impaired stroke volume leading to dyspnea and fatigue. [46.47] Diastolic dysfunction may also be a cause of exercise intolerance in patients without overt diastolic heart failure, but the underlying mechanisms are not well defined. A cross-sectional study of 2867 patients undergoing exercise echocardiography found that diastolic dysfunction was independently associated with reduced exercise capacity. [48]

Patients with diastolic heart failure have particular difficulty in tolerating certain kinds of hemodynamic stress: They tolerate atrial fibrillation poorly, since the loss of atrial contraction can dramatically reduce left atrial emptying, LV filling, and LV stroke volume. They do not tolerate tachycardia well, since the increase in heart rate shortens the duration of diastole and truncates the important late phase of diastolic filling. Elevations in systemic blood pressure, especially the abrupt, severe, or refractory elevations often seen with renovascular hypertension, increase left ventricular wall stress, which can impair or delay myocardial relaxation in patients with diastolic heart failure.[49]

The acute induction or worsening of diastolic dysfunction by ischemia raises left atrial and pulmonary venous pressure. This explains why many patients with coronary heart disease have respiratory symptoms with their anginal pain, including wheezing, a limited ability to take a deep breath, shortness of breath, and overt pulmonary edema. Episodes of hemodynamic decompensation may result in overt pulmonary edema,"Two population-based studies have compared the prognosis of systolic and diastolic failure. One of the studies evaluated all 216 patients who were diagnosed with HF in Olmsted County, Minnesota in 1991[50] Of the patients who had their systolic function evaluated, the EF was normal in 43%. The prognosis was similar in the patients with diastolic and systolic failure. The second study is the Framingham Heart Study, [51] where it was found that half of 73 HF patients had normal systolic function. Mortality was high in both groups but higher in those with systolic HF.[51]

Diastolic dysfunction may be a function of age independent of BP and LV mass.[52] Elderly patients with borderline systolic hypertension (systolic pressures between 140-159 mm Hg) have been found to have signs of diastolic dysfunction on echocardiography without any impairment of systolic function.[53]

While diastolic failure typically presents in the elderly, abnormalities of diastolic function have been described in young, healthy subjects with a family history of hypertension. An example comes from a study conducted by Aeschbacher et al, [14] which followed a cohort of 25-year-old males for 5 years, half of whom had a family history and half who did not. It was revealed that family history of hypertension hypertrophy associated with left ventricular pressure or volume overload, and suggests that abnormalities of diastolic function seen in pathologic hypertrophy are due to factors other than cardiac hypertrophy itself.

1.7. Pathophysiology of hypertensive diastolic dysfunction.

The histological features of hypertensive cardiac remodeling are myocytes hypertrophy and myocardial fibrosis. These changes are basically adaptive responses to pressure overload. It is considered that when hypertension persists. Disproportionate LV hypertrophy and myocardial fibrosis develop and in turn result in diastolic and eventually systolic dysfunction. Given that recent studies have demonstrated the substantial involvement in the inflammatory process in the pathogenesis of various cardiovascular diseases, such as atherosclerosis. Inflammatory changes may play a role in cardiac remodeling in the hypertensive heart as well. In this view the regulation of inflammation is a possible therapeutic strategy for targeting diastolic dysfunction in hypertensive hearts.[55, 56]

1.8. Myocardial Remodelling in Hypertensive Hearts

Myocyte hypertrophy and myocardial fibrosis are important adaptive mechanisms in response to pressure overload onto the LV[57]. Hypertension increases wall stress of the left ventricle.

Increased wall stress is compensated by a parallel increase in the contractile units of the cardiac myocytes, leading to hypertrophy and resultant LV wall thickening, with resultant degree of myocardial fibrosis which prevents the ventricular deformation by raised stress and transmits the force to the entire ventricle.

Prolonged increase in cardiac work results in excessive myocyte hypertrophy and disproportionate myocardial fibrosis, which are responsible for increased myocardial stiffness and impaired pumping capacity in hypertensive patients[58] Evidence suggests that myocardial stiffening depends mainly upon myocardial fibrosis rather than LV wall thickening and myocyte hypertrophy in spontaneously hypertensive rats (SHRs)[59,60,61] , experimental renovascular hypertensive rats[62] and Dahl salt-sensitive rats [63] In these experimentally induced pressure-overload models and in patients with hypertension, there is an increase in the quantity of interstitial collagen, particularly fibrillar collagen (*i.e.*, collagen type I and collagen type III), in the hearts [64]. Accumulation of fibrillar collagen increases viscoelasticity and passive stiffness of the hypertrophied myocardium. Changes in the distribution and microstructure of collagen, as well as imbalance of type I *vs.* type III collagens, affect myocardial stiffness and diastolic properties as well. [65]. Figure 1.

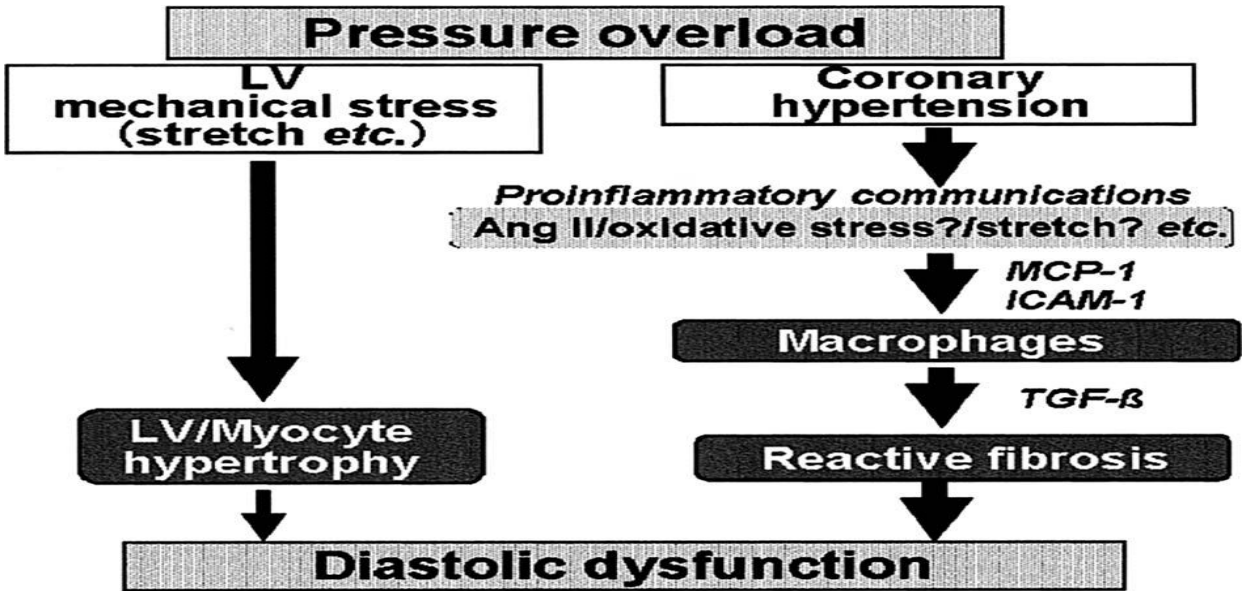


Figure. 1. Schematic showing the role of perivascular inflammation in myocardial remodeling and diastolic dysfunction in pressure overloaded hearts.

1.9. Measurements of diastolic dysfunction

The ideal measurement of diastolic dysfunction requires cardiac catheterization and high-fidelity micro manometer catheters, which is, of course, impractical for routine clinical evaluation. Cardiac catheterization would show an increased end-diastolic pressure and normal systolic function. Several different noninvasive measures of diastolic dysfunction have been proposed, [66] the indices that are supposed to indicate diastolic dysfunction are also not straightforward. Thus the traditional method has been the E:A ratio of flow across the mitral valve measured by the Doppler technique.[67] More recently, two other echo techniques have been introduced: measurements of pulmonary vein velocity and Tissue Doppler imaging, but they also show multiple patterns that differ in subtle ways - Hemodynamic determinants of the mitral annulus diastolic velocities by tissue Doppler.[68,]Furthermore, in many cases, the patterns may vary according to extrinsic factors such as heart rate and BP.

1.10. Echocardiography evaluation of diastolic function

Echocardiography provides a comprehensive and reliable non invasive way of assessing structural and hemodynamic parameters of the heart. In patients with hypertension quantification of cardiac chambers and assessment of ventricular systolic and diastolic functions are essential parts of echocardiography examination. In heart failure patients, echocardiography has emerged as the preferred diagnostic method for assessing the anatomy and function of the heart. It is the single most useful test in the evaluation, it is excellent for serial studies, and allows an assessment of both global and regional LV functions, as well as cardiac motion analysis.[69] Ejection fraction (LVEF), severity of LV remodeling, and changes in diastolic inflow properties.

1.10.1. Left Ventricular Functional parameters

Echocardiography can measure several parameters as an expression of systolic function of the heart. These parameters are LVEF, fractional shortening, stroke volume and cardiac index, systolic tissue velocity of the mitral annulus and myocardium, strain, and regional wall motion analysis.

1.10.2. Left Ventricular Ejection Fraction

This is a well-accepted expression of global LV function. It is a simple measure of how much end-diastolic volume is ejected from the LV with each contraction. LVEF has been found to be a strong predictor of clinical outcome in almost all major cardiac conditions, and it is used to select optimal management strategies. Objectively the LVEF is obtained using volumetric measurements as described by the following equation: LVEF= (LVEDV-LVESV)/ (LVEDV) Where, LVEDV and LVESV are LV end-diastolic volume and end-systolic volume, respectively. LVEF can also be calculated from LV dimensions measured with M-mode or 2D echocardiography. M-mode or 2D echocardiographic measurement of LV dimensions from the mid ventricular level. The following formula is used to calculate LVEF:

$$LVEF = LVEDD^2\text{-}LVESD^2/LVEDD^2$$

Where, LVEDD and LVESD are end-diastolic dimension and end-systolic dimension, respectively. This equation is a percentage change in LV area, or fractional shortening of the LV short axis, which equals LVEF if the apical long-axis dimension remains the same from diastolic phase to systolic contraction.

1.10.3. Assessment of LV Diastolic Function

Echocardiography is an alternative technique to cardiac catheterization in the evaluation of patients with diastolic dysfunction which include M-mode, 2-D and Doppler echocardiography studies.[70, 71]An increased relationship of left atrial size and stage of diastolic dysfunction has been described.[72] the basic parameters of the transmitral flow vary with age and within the spectrum of diastolic filling.[73, 74] The normal E/A ratio is usually greater than one. In diastolic dysfunction, it passes from a reversed E/A ratio through a "pseudo-normal" pattern (E/A ratio greater than 1) to the most abnormal restrictive pattern.

Therefore it is difficult to use this single parameter to evaluate correctly diastolic dysfunction. An increased pulmonary atrial reversal flow, reversal velocity or width and valsalva manouvre may aid to differentiate pseudo-normal from normal diastolic function corresponding to elevated left atrial or left ventricular diastolic pressures.[75] Four stages of diastolic abnormalities have been described and have been shown to correlate with diastolic impairment and symptom class.[76]

The normal pattern seen in normal people with E/A ratio greater than 1, mitral valve deceleration time is between 150-220ms. The first stage of diastolic dysfunction is the delayed relaxation phase seen in patients with delayed left ventricular relaxation but with relatively normal compliance and filling pressures.[77] E/A ratio is less than 1, deceleration time prolonged (more than 220ms) and isovolumic relaxation time greater than 100ms. This pattern is seen in the aged, [72], [78] ischemia, [79] hypertrophic cardiomyopathy, and secondary hypertrophy, and obese diabetic.[80]

The second stage is the pseudo-normal stage which is difficult to recognize because it is similar to the normal pattern. Abnormalities of relaxation and compliance and elevated filling pressures are present. Transmitral E/A ratio is between 1 and 2, a deceleration time between 150-220ms and IVRT between 60-100ms. The left atrial size is usually increased and left ventricular function may be impaired or wall thickness increased.

Restrictive filling pattern stage III is seen in the presence of severely reduced left ventricular compliance and elevated filling pressures and ongoing delayed relaxation. E/A ratio is usually greater than 2, deceleration time is less than 150ms and IVRT less than 60ms. The Irreversible restrictive filling pattern (Stage IV) is associated with a poor prognosis. Additional prognostic information can be obtained in patients with restrictive filling patterns evaluated under different haemodynamic conditions. Patients are graded into mild, moderate and severe diastolic abnormalities in accordance with the pattern of diastolic dysfunction demonstrated in them.

1.10.4. Tissue Doppler imaging

Tissue Doppler imaging (TDI) is a novel use of ultrasound to image the motion of tissue with Doppler echocardiography. Given the limitations of preload dependency, atrial fibrillation, tachycardia and regurgitant valvular lesions, tissue Doppler imaging (TDI) has taken the "front-stage" in the transthoracic echocardiographic assessment. Echocardiography records and displays the velocities of the moving targets, [81] their normal velocity ranges from 10cm/s in the venous circulation to150cm/s in the arterial circulation. However, the velocities of myocardial tissue are much lower (1-20cm/s), but their amplitudes are greater than those produced by blood.[82] Therefore, tissue Doppler ultra-sound instruments have been modified to record the low velocities of myocardial tissue and hence a reliable measure of diastology.

Early Ea or E' of the mitral annulus measured with TDI is a good indicator of LV myocardial relaxation,[83] this is one of the most important components of myocardial diastolic function, the others being LV compliance and filling pressure. In the normal heart with normal myocardial relaxation, E' increases with an increasing transmitral gradient, increasing preload, exercise, and dobutamine infusion.[84] However when myocardial relaxation is impaired because of ageing or disease process, E' Is affected less or even unchanged by pre load or transmitral gradient. Velocities of longitudinal mitral annulus motion are best obtained from apical views.

Although various locations of the mitral annulus can be interrogated with TDI, the septal (medial) and lateral mitral annulus are the most frequently used locations. E' from the lateral annulus is normally higher >15cm/s than that from the medial >10cm/s.[86]

Late diastolic velocity (Aa or A') of the mitral annulus at the time of atrial contraction increases during early diastolic dysfunction, as is the case for the mitral inflow A wave, but decreases as atrial function deteriorates . A' has been correlated with LA function.[85] Tissue Doppler e= is a more sensitive parameter for abnormal myocardial relaxation than mitral variables. Several studies in animals and humans demonstrated significant correlations between e and e'. Most patients with e'= (lateral) 8.5 cm/s or e'= (septal) 8 cm/s have impaired myocardial relaxation. However, for the most reliable conclusions, it is important to determine whether e'= is less than the mean minus 2 standard deviations of the age group to which the patient belongs.

In the presence of impaired myocardial relaxation, the time interval *T* lengthens and correlates well with LV minimal pressure. However, this approach has more variability than a single velocity measurement and is needed in few select clinical scenarios.[87, 88] A limitation of TDI is that the E/e' ratio is not helpful for estimating LV filling pressures in normal subjects and patients with mitral valve disease including heavy mitral annular calcification and also not reliably useful in patients with mitral valve disease. Importantly In patients with constrictive pericarditis an inverse relationship between E/e' and PCWP is observed [89].

1.10.5. Grading of diastolic dysfunction (diastolic filling pattern)

Grade 1 (mild dysfunction) -impaired relaxation with normal filling pressure

Grade 2 (moderate dysfunction)-pseudo normalized mitral inflow pattern

Grade 3 (severe reversible dysfunction) -reversible restrictive (high filling pressure)

Grade 4 (severe irreversible dysfunction)-irreversible restrictive (high filling pressure)

1.10.6. Left Ventricular Dimensions and left ventricular Geometry

LV dimensions are measured from 2D-guided M-mode echocardiograms of the LV at the level of mitral leaflet tips or the papillary muscle using the parasternal view. If no significant regional wall motion abnormalities are present, the LV dimensions measured at the mid ventricular level can be used to calculate global LVEF.

The thicknesses of the ventricular posterior wall and the ventricular septum (from the leading edge to the trailing edge) are measured from the same M-mode echocardiogram. The long-axis and short-axis dimensions of the ventricle can also be obtained directly from systolic and diastolic frames of the 2D parasternal long-axis view and apical view. The LV end-diastolic and end-systolic dimensions are measured at the level of tips of the mitral leaflets as the largest and the smallest LV dimensions, respectively. From the LV dimensions the LV geometry can be calculated and defined with the LVM indexed for height or for body surface area. Different geometries have been described from Normal geometry, Concentric remodeling, eccentric LVH and Concentric LVH. These are of prognostic importance in patients with hypertension.

1.10.7. Left Atrial Size and Volume

LA dimension is determined from the parasternal long-axis view at end-systole. However, the size of the LA may be underestimated from the parasternal view because the chamber may enlarge longitudinally. Therefore LA size should also be measured from apical views (from the tip of the mitral valve to the posterior wall of the LA). However, LA volume is a better measure of LA size and provides better prognostic value. Four different methods are available for determining LA volume: (a) prolate ellipse, (b) biplane area-length, (c) biplane Simpson, and (d) 3D echocardiography.

Table 1: The reference values for cardiac parameters in centimeters.

Chamber	**WOMEN**				**MEN**			
	Normal	**Mild**	**Moderate**	**Severe**	**Normal**	**Mild**	**Moderate**	**Severe**
LVID(cm)	3.9-5.3	5.4-5.7	5.8-6.1	≥6.2	4.2-5.9	6.0-63	6.4-6.8	≥6.9
RV (cm)	2.7-3.3	3.4-3.7	3.8-4.1	≥4.2	2.7-3.3	3.4-3.7	3.8-4.1	≥4.2
LA (cm)	2.7-3.8	3.9-4.2	4.3-4.6	≥ 4.7	3.0-4.0	4.1-4.6	4.7-5.2	≥5.3
RA(cm)	2.9-4.5	4.6-4.9	5.0-5.4	≥5.5	2.9-4.5	4.6-4.9	5.0-5.4	≥5.5
LVEF%	≥55	45-54	30-44	<30	≥55	44-54	30-44	<30

CHAPTER TWO

2.1. PROBLEM STATEMENT

Traditionally, investigators have focused on abnormalities of systolic function to explain the signs and symptoms of heart failure. However abnormalities of diastolic function are increasingly being viewed as influential in precipitating heart failure and determining prognosis. In the US, 5 million patients have heart failure and 500,000 new cases occur annually. Epidemiological studies have shown that approximately 50 percent of patients who develop clinical heart failure have a normal or preserved left ventricular systolic function (HF-PSF), suggesting that diastolic dysfunction may be responsible for their clinical manifestation[3, 4, 5]

As our understanding evolves of the profound adverse clinical consequences of clinically overt diastolic dysfunction, [46, 47] the prevalence of asymptomatic diastolic dysfunction in the general community is not insignificant, a finding being noted in approximately 25-30% of individuals over 45 years of age. Hypertension is an important public-health challenge worldwide. The estimated total number of adults with hypertension in 2000 was 972 million; 333 million in economically developed countries and 639 million in economically developing countries!. The number of adults with hypertension in 2025 is predicted to increase by about 60% to a total of 1.56 billion (1.54-1.58 billion) [1, 2, 13]

According to the Framingham Study, hypertension accounts for about a quarter of heart failure cases,[31] in the elderly population, as many as 68% of heart failure cases are attributed to hypertension. Hypertension is the leading cause of heart failure globally and diastolic dysfunction starts setting earlier than the systolic dysfunction in these patients contributing to morbidity and mortality.[47, 48]early detection is likely to halt the progression of diastolic dysfunction into overt diastolic heart failure.

2.2. RATIONALE OF THE STUDY

Hypertension is set to remain the single most important preventable cause of premature death worldwide over the next two decades. Despite a higher prevalence of hypertension in Tanzania, [8] the magnitude of symptomatic and asymptomatic diastolic dysfunction is not known. Studies indicate that diastolic dysfunction has the worst prognosis in heart failure among African hypertensives. People of African origin have also been known to have more severe forms of hypertension than in the comparable Caucasian population. [17]

As our understanding of diastology increases and with availability of non invasive techniques at our hands, there has been an increase in the asymptomatic diagnosis of diastolic dysfunction especially so in patients with hypertension.[56]There is a need to describe the magnitude and characteristics of the existing diastolic impairment among hypertensive patients in Tanzania using non invasive echocardiographic parameters, which will open the ways towards possible interventions to prevent progress into diastolic heart failure.

OBJECTIVES

Broad objective

To describe the clinical and echocardiographic features of diastolic dysfunction among adult hypertensive patients referred at Muhimbili National Hospital.

Specific objectives

1. To determine the prevalence of diastolic dysfunction among hypertensive patients at MNH
2. To describe the left ventricular geometry among hypertensive patients with diastolic dysfunction at MNH
3. To determine the clinical findings and covariates of left ventricular diastolic dysfunction among hypertensive patients at MNH

CHAPTER THREE

METHODOLOGY

3.1. Study design

Descriptive cross-sectional study

3.2. Study site

The study was been conducted at Echocardiography room recruiting patients from wards and outpatient clinics of Muhimbili National Hospital Dar es Salaam who are referred for Echocardiography due to hypertension from January to March- 2011.The diagnoses of hypertension were made by the principal investigator and the physicians taking care of the patients at clinics and wards at Muhimbili National Hospital.

Dar es Salaam is the largest city in Tanzania with a population of about 3.5 million, *estimated*.2003. Muhimbili National Hospital (MNH) is a tertiary referral and teaching hospital, situated in Dar es Salaam city. It serves patients referred from the three municipal hospitals (Temeke, Kinondoni and Ilala) as well as patients from other regional hospitals in the country. It has admission bed occupancy of about 1500 patients a week. It also serves about 1000 outpatients per day.

3.3. Study subjects

All adult hypertensive patients (18 years and above), referred for echocardiography from inpatients and outpatients care units at Muhimbili national hospital

3.4. Study period

January -March 2011

3.5. Sample size and sampling procedure

To determine the minimum sample size required, the following formula was used (Adapted from Kirkwood, 1988)

$$n = \frac{Z^2 * p * (100 - p)}{\varepsilon^2}$$

Where: n = minimum required sample size.

p = proportion of patients with diastolic dysfunction among hypertensive in tertiary hospital-Nigeria

ε = Margin tolerable error (5%)

Z = Standard normal distribution at 5% level of significance (1.96).

$$n = \frac{1.96^2 * 85 * (100 - 85)}{} = 196.$$

Those who gave consent for participation were consecutively recruited for the study. 200 subjects consecutively were enrolled.

3.6. Sampling procedure

Consecutive recruitment sampling was used in this study. Recruited participants were interviewed on their socio-demographic details such as age, sex, etc. Physical examination and Echocardiography was carried out for each participant.

Inclusion criteria

1. Diagnosis of hypertension by a physician/ cardiologist or being on antihypertensive treatment
2. Consent to participate into the study
3. Age from 18 years and above

Exclusion criteria

1. Hypertensives with atrial fibrillation, ventricular fibrillations and acute coronary syndromes
2. Hypertensives with known valvular lesions, RHD and congenital heart diseases.
3. Documented or suspected cardiomyopathies
4. Athletes
5. Patients with abnormal EF, EF< 50%

3.7. Procedures

3.7.1. Clinical and demography

A structured questionnaire was used for interview. The socio-demographic characteristics, history and duration of hypertension with or without treatment were ascertained. Height and weight were measured and used to calculate body mass index. Waist circumference was measured at the level of the umbilicus and used as a measure of central obesity

3.7.2. Blood Pressure measurement

Blood pressure was measured at the right brachial artery using a standard mercury sphygmomanometer and appropriate cuff size following the joint European Society of Hypertension and European Society of Cardiology guidelines.[13] After 5 minutes rest in the sitting position, a set of three readings were done 5 minutes apart. The average of the last two readings was taken as the patient's clinic blood pressure. Mean arterial pressure (MAP) was been calculated as MAP=DBP+ (SBP-DBP)/3, where SBP is systolic blood pressure and DBP is diastolic blood pressure

3.7.3. Echocardiography

The examination was performed by the principal investigator assisted by two experienced cardiologists using a PHILIPS (SONOS 7500) Echocardiographic machine with a 3.50MHz transducer and read by a third independent observer.
All data was recorded with patients in the left lateral position during end-expiration apnea. All recordings were performed at a high sweep speed (100m/s) and with simultaneous electrocardiographic ECG recording and included; complete m-mode, 2-dimensional, and Spectral Doppler with tissue Doppler echocardiographic examinations, emphasis was on evaluation of LV diastolic and systolic functions, LV size and mass.

The M-mode, 2D, and Doppler echocardiographic evaluations were performed. A minimum of 10 to 15 beats were recorded for all 2 dimensional, M-mode and Doppler parameters. Echocardiographic images of all patients was printed in papers and recorded on VHS videotapes. A cardiac ejection fraction was calculated automatically by an echocardiograph machine in all patients EF Teichholz). Fractional shortening = LVIDd-LVIDs/LVIDd. Patients with ejection fraction less than 50% was classified as having systolic dysfunction

3.8. M-Mode and 2D Echocardiography

3.8.1. Cardiac Structure and LV geometry

Left atrial and aortic route diameters, left ventricular end-diastolic and end-systolic diameters (LVIDd and LVIDs, respectively), and interventricular septum and posterior wall diastolic thickness (IVSd and PWd, respectively) were all measured in the parasternal long-axis view during M-mode tracing according to the recommendation of the American Society of Echocardiography.[96] Left ventricular mass (LVM) in grams was calculated by the Devereux[97] formula LVM = 0.832[(LVIDd +IVSd +PWd)3- LVIDd3] + 0.69.

LVM index (LVMi) was calculated as follows: LVMi=LVM/$m^{2.7}$, where m is height in meters. Relative wall thickness (RWT) was calculated as the ratio (IVSd +PWd)/ LVIDd. LV geometric pattern was considered normal if LVMi is <49.2 g/$m^{2.7}$ for men and <46.7 g/$m^{2.7}$ for women with RWT is <0.42. Concentric remodeling was diagnosed when LVMi is <49.2 g/$m^{2.7}$ for men and 46.7 g/$m^{2.7}$ for women with RWT is >0.44; concentric hypertrophy was defined as LVMi >49.2 g/$m^{2.7}$ for men and >46.7 g/$m^{2.7}$ for women with RWT>0.42; eccentric hypertrophy was detected when LVMi is >49.2 g/$m^{2.7}$ for men and >46.7 g/$m^{2.7}$ for women with RWT is <0.42. BSA was computed from body weight and height by the echo machine.

3.8.2. Assessment of LV diastolic function

Doppler Indexes of Diastolic Function

Assessment of diastolic function was obtained by pulsed-wave Doppler of transmitral flow and tissue doppler patterns on medial(septal) and lateral annulus recorded in the apical 4-chamber view.

LV relaxation and filling was recorded at the level of the mitral valve tips. The leading edge of the mitral flow pattern was traced to derive peak early (E) and atrial (A) velocities, E/A ratio and E deceleration time. Isovolumic relaxation time was measured from the leading edge of the aortic valve closure spike to the leading edge of the mitral valve opening spike. The septal and lateral early diastolic mitral annular velocities (E') were measured by spectral tissue Doppler imaging in apical four-chamber view. The ratio of E to E'septal (medial) velocity (E/E' ratio) was taken as an estimation of LV filling pressure.[19]

The following variables were also measured; Deceleration time of the E wave (DtE); and duration of the A wave (dA). When atrial contraction occurs before the mitral deceleration has decreased to zero, DtE was calculated as the time between peak E wave and the deceleration slope extrapolated to zero baseline. Left ventricular isovolumetric relaxation time (IVRT) was also measured as the interval between the aortic valve closure click and the start of mitral flow[100]

Patients were categorized into groups of normal LV diastolic function and, mild, moderate or severe LV diastolic dysfunction, respectively, based on combined LV inflow pattern and tissue Doppler imaging of mitral annulus as previously validated. [20, 21] Mild LV diastolic dysfunction (impaired relaxation without evidence of elevated filling pressure) was considered present when the E/A ratio was low for age (<1 for patients younger than 50 years or <0.75 for patients older than 50 years), the E deceleration time was >140msec and the E/E' ratio $\leq$10. Moderate LV diastolic dysfunction (pseudo normal LV filling) was considered present if E/A ratio was 0.75-1.5, E deceleration time >140 ms and E/E' $\geq$10. Severe LV diastolic dysfunction (restrictive LV filling) was considered present if E/A ratio was high for age (i.e. >2.9 for patients younger than 18 years, > 2 for patients 18 – 50 years and >1.5 for those >50 years of age), coexisting with a short deceleration time (<140msec) and with elevated LV filling pressure (E/E' $\geq$ 15).[20, 22] Pulmonary venous flow and Valsalva maneuver was not performed in this study, so further categorization into reversible or irreversible restrictive LV filling was not possible [99].

3.9. Definition of terms

Hypertension is defined as history of hypertension according to the seventh Joint National Committee on Prevention, Detection, Evaluation and Treatment of high blood pressure (JNC VII) as a systolic blood pressure of 140 mm Hg or greater, diastolic blood pressure of 90 mm Hg or greater in untreated patients measured on at least 2 occasions or taking antihypertensive medication.

Diastolic dysfunction will be defined by Doppler E/A<1, E'/A'<1,, DT>240, or E/E'>15

Left ventricular hypertrophy was defined as an increase in the mass of the left ventricle. In males the LV mass indexed for height$^{2.7}$ >49.2 and in women >46.7 g/m$^{2.7}$ was taken as presence of LVH.

A BMI of less than 18..5, 18.5- 24.9 kg/m^2 , 25 -29.9 kg/m^2 and ≥30 kg/m^2 will be defined as underweight normal weight, overweight and obese respectively.

Outpatients- these were the patients seen at outpatient for hypertension treatment and follow up being symptomatic or asymptomatic but not necessitating admission in ward

In-patients: patients who were admitted in hospital wards due to severe hypertension or hypertensive crises which necessitated hospital control.

3.10. Data management & statistical analysis

All filled questionnaires were checked daily for completeness and consistencies. Then data was coded before entering into computer using Statistical Package for Social Sciences (SPSS) version 18. Data was cleaned with consistence checks and analyzed using the same SPSS package.Frequency distributions and two way tables were used to summarize the data. Data is presented as mean ± standard deviation for continuous variables and for categorical variables. Groups of patients were compared using χ^2 test at 5% tolerable error, unpaired Student's t-test or one way ANOVA.

Bivariate correlations were assessed by Pearson's correlation coefficients. Uni- and multivariate linear and logistic regression analyses were used to test the association between higher E/E' and admission status in the total study population and in groups of patients with diastolic dysfunction separately independent of other parameters. Results are presented as beta coefficients and significant level for the linear models and as odds ratios (OR) and 95% confidence intervals (CI) for the logistic models. A 2-tailed *P* value of ≤0.05 was considered statistically significant in both univariate and multivariate analyses.

3.11. Ethical considerations

Ethical clearance was sought from the Research and Publications Committee of MUHAS and permission to conduct the study was obtained from the Ethics department of MNH. Patients were enrolled after informed verbal and written consent. Patients who did not consent to participate in the study were not been deprived their rights to receive medical care at our institution. Confidentiality was adhered to when filling in the data. Patients identified to have a serious conditions requiring immediate attention were treated and followed through as appropriately according to the existing protocols

CHAPTER FOUR

RESULTS

4.1. Demographic and baseline clinical characteristics of the study population

During the study period a total of two hundreds referred hypertensive patients fulfilled the inclusion criteria and were recruited into the study, out of which 108(54%) were women. The mean age of the study population was 52±13.5 years, but varied from 23-86 years, with men being older (M=55.5, SD= 14 vs women M=48.9, SD 12, p<0.001) higher body surface area (M=1.83, SD=0.2, vs women M=1.77, SD=0.17, p=0.006) and heights (M=167, SD=8 vs women 161, SD=8, p<0.001) than women. Interestingly women had significantly higher mean body mass indices than men (M=28.7, SD=5.7, vs men M=26.8, SD=3.8, p=0.009)

The study population was divided into in-patients (n=61) and out-patients (n=139). Clinical and demographic characteristics of the total study population and patient status groups are shown in Table 2.

The mean diastolic pressure was found to be significantly higher among the in-patient group (M = 91, SD = 7) than outpatients (M = 87, SD = 8) p=0.002, the in-patients were on higher proportions of antihypertensive treatment; (95.1% among in-patients vs 74.1% in outpatients, p=0.001) and an average number of drug used was higher among in-patients than outpatients.(p=0.001) . There were no statistically significant differences in weight, height, BSA,radial pulse rates, pulse pressure ,systolic blood pressure and waist circumference between the in-patient and outpatient groups in this study.

Majority of the study participants 80.5% were on different forms of medications for hypertension. Table 2

Table 2: Demographic and clinical characteristics of In-patients and outpatients hypertensive's at Muhimbili National Hospital

Variable	Total population N=200	In-patients N=61	Outpatients N=139	p-value
Age(years)	52.0 ± 13.5	58.3±12.1	49.2 ± 13.2	<0.001
Weight (kg)	74.2 ± 12.9	75.6 ± 14.2	73.5 ± 12.3	0.290
Height (cm)	164 ± 9	164.3 ± 8.9	163.2± 8.5	0.409
BSA (m^2)	1.79 ± 1.7	1.82 ± 0.18	1.79 ± 0.16	0.281
BMI (kg/m^2)	27.8 ± 4.9	28.1 ± 5.8	27.7 ± 4.6	0.530
Waist circumference(cm)	84 ± 17	85.3± 20	83 ± 16	0.374
Pulse rate (beats/min)	75 ± 9	76 ± 14	74 ± 7	0.271
Systolic BP (MmHg)	145 ± 14	147 ± 12	144 ± 14	0.800
Diastolic BP (MmHg)	88 ± 8	91 ± 7	87 ± 8	0.002
Pulse pressure(MmHg)	57 ± 9	57 ± 8	57 ± 9	0.844
On treatment (%)	80.5	95.1	74.1	0.001
Number of drugs	1.4±1.0	1.7±0.8	1.2±1.0	0.001
Beta-blockers (%)	48.5	55.7	69.5	0.114
CCB% (%)	37.0	39.25	60.8	0.03
ARB% (%)	18.0	38.9	61.1	
ACEI (%)	33.0	40.9	59.1	0.025

ACE- Angiotensin converting enzyme inhibitors, ARB-Angiotensin receptor blockers, CCB- Calcium channel blockers

4.2. Echocardiographic characteristics of the study patients

During the study period,the hypertensive group of patients who were admitted in wards were found to have statistically significant larger LV internal diameters and wall thicknesses, and they had higher LV mass as well as higher prevalence of LVH (all $p<0.01$), however there were no statistically significant differences in relative wall thickness and fractional shortening between the two groups. (Table 4). As demonstrated, the vast majority of patients irrespective of the patient status had concentric LV geometry.

Of note, the overall prevallence of left ventricular hypertrophy was 86% in this population of patients, concentric LVH dominated in both patient groups constituting 60.4% , eccentric hypertrophy was seen in 17.6% and concentric remodeling in 8%. Fourteen percent had normal left ventricular geometry. Concentric left ventricular geometry was the predominant geometry among the in-patients with diastolic dysfunction. However, among out-patient, eccentric LVH followed by concentric remodeling were more prevalent.

Table 4: Echocardiographic findings among in-patient and outpatient hypertensive patients

Variable	Total population N=200	In-patients N=61	outpatients N= 139	p-value
IVSD (cm)	1.59±0.28	1.67±0.20	1.55±0.29	0.002
PWd (cm)	1.48±0.27	1.56±0.21	1.44±0.29	0.001
IVSs (cm)	1.69±0.29	1.73±0.30	1.65±0.28	0.040
PWs (cm)	1.59±0.3	1.63±0.29	1.55±0.29	0.680
LVIDd (cm)	4.46±0.64	4.71±0.65	4.37±0.56	0.001
LVIDs (cm)	3.15±1.86	3.62±3.23	2.9±0.55	0.016
RWT	0.68±0.18	0.68±0.17	0.67±0.18	0.690
FS (%)	31.69±6.16	30.74±6.9	32.10±5.64	0.065
EF %	60.42±8.3	57.39±9.3	61.8±7.5	<0.001
LVM (gm)	302.0±104	338±108	272±103	0.002
LVMI/ht ($g/m^{2.7}$)	78.5±30	89.58±32	73.32±29	0.0001

Looking at diastolic LV function; echocardiographic parameters, in-patients had larger LA diameter, lower E' velocity and higher E/E' ratio (all $p<0.05$), reflecting higher filling pressures among in-patients. There were no differences among these groups in transmitral filling pattern including early deceleration time and E/A ratio and Isovolumic relaxation time (IVRT). Furthermore, 24.6% of in-patients compared to 0.7% of out-patients had an elevated E/E' ratio>15, ($p=0.001$) reflecting elevated filling pressure ($p<0.001$). All patients with E/E' ratio >15 also had concentric LVH geometry. Table 5

Table 5: Left ventricular diastolic parameters among in-patients and outpatient hypertensive's

Variable	Total population N=200	In-patient N= 61	Outpatient N=139	p-value
E	56±19	60 ± 21	54 ±18	0.056
A	63±20	68 ±20	61 ± 44	0.036
E/A ratio	0.95±0.4	0.96±0.4	0.95±0.36	0.932
E-decel. time	194±50	195 ± 51	194 ± 50	0.948
E'medial	7.3±2	6.32±2.1	7.68±.2	<0.001
E'lateral	8.9±2.5	8.1±2.6	9.4±2.4	<0.001
E'Average	8.1±2.3	7.2±2.3	8.5±2.14	<0.001
E/E'medial	8.62±5.21	10.7±5.6	7.7±4.6	0.001
E/E' average	7.4±3.3	9.2 ±4.4	6.7±2.4	<0.001
A'	8.4±2	8.2±2.3	8.6±2.6	0.25
E'/A'	1.0±0.9	1.0±0.3	1.1±1.2	0.82
IVRT	115±42	118±38	114±45	0.53
LA size	4.1±0.51	4.34±0.05	3.92±0.43	<0.001

4.3. Echocardiographic correlates of diastolic dysfunction with elevated LV filling pressures

Univariate correlates of higher E/E' ratio in the total study population is presented in Table 4. There is statistically significant correlation between E/A ratio, E deceleration time and IVRT with E/E'. Other important correlates in univariate analysis were age and LA size (Table 6). Interesting, no significant correlation was found between EF, LVM, RWT and body weight with E/E'.

Table 6: Univariate correlates of higher medial E/E' ratio among the study population

Variable	Pearson Correlation coefficiency (r)	P-value
Age	0.14	0.048
LA size	0.27	<0.001
Medial E'	-0.42	<0.001
MvE	0.48	<0.001
DTE	-0.16	0.021
MVA	0.16	0.021
E/A	0.30	<0.001
IVRT	-0.29	<0.001

Based upon the identified univariate correlations, multivariate linear regression analysis was used to identify independent covariates of higher E/E' ratio. In the total study population, higher E/E' ratio was associated with in-patient status independent of lower age, larger LA size, higher mitral valve A velocity and lower IVRT (multiple R^2=0.26, p<0.001) (Table 7).

Table 7: Independent covariates of higher E/E' ratio in multivariate linear regression analysis

Variable	Beta coefficient	P-value
Age(years)	-0.01	0.893
LA size (cm)	0.26	<0.001
DTE (m/s)	-0.06	0.326
IVRT(m/s)	-0.38	<0.001
MVA(cm/s)	0.19	0.006
In-patient status	0.15	0.030

Multiple R^2=0.26, p<0.001

4.4. Clinical correlates of diastolic dysfunction

The overall prevalence of diastolic dysfunction was found to be 58%, normal diastolic function was seen in 83(41.5%) of the study patients. Majority of those with impaired diastolic function (50.5%) had grade one diastolic dysfunction (impaired relaxation).

Patients with normal diastolic function and those with grade one diastolic dysfunction were predominantly seen in New York Heart failure Classes I and II, however many of those in grade 3 and 4 diastolic dysfunction were in advanced class of heart failure (30% vs 2.5%)p<0.001.

There is statistically significant association between higher level of blood pressure and higher grade of diastolic dysfunction, participants with poorly controlled hypertension were predominantly found In the grade 3 and 4 of diastolic dysfunction, where by those who are controlled to mild hypertension were in the groups with normal and grade 1 diastolic dysfunction. p=0.002. Table 8.

Table 8. Distribution of patients with diastolic dysfunction Vs Level of hypertension control and New York heart Association classes

	Diastolic function parameters			
Bp(mmHg)	Normal	Grade 1dysfunction Impaired relaxation	Grade3&4 dysfunction (increased LV filling	P-value
Mild Hypertension	33(39.8%)	20(19.8%)	1(6.2%)	
Moderate hypertension	37(44.6%)	46(45.5%)	10(62.5%)	0.002
Severe hypertension	13(15.7%)	35(34.7%)	5(31.2%)	
NYHC				
Class I-II (%)	77(47.8)	80(49.7)	4(2.5)	<0.001
Class III-IV	6(15.4)	21(53.8)	12(30.8)	
Total	83(41.5)	101(50.5)	16(8.0)	

DISCUSSION

Prevalence of diastolic dysfunction among hypertensives

This study was undertaken among hypertensive patients who were attended at Muhimbili National Hospital. The aim of the study was to determine the prevalence and determinants of diastolic dysfunction among adult hypertensive patients, the participants of this study were aged between 23 and 86 years. High prevalence of diastolic dysfunction 58.5% is reported in this group of hypertensive patients. Findings from this study are comparable to reports from studies done in Nigeria where a prevalence of 82.86% and 85.0% has been reported. [101, 102] It is however higher than what is reported among the European populations where a prevalence of between 46-48% have been reported. [103, 104, 105] The differences observed may be attributable to the higher prevalence of left ventricular hypertrophy among the Tanzanian hypertensives which may be responsible for more cases of early diastolic dysfunction seen among the participants in this study. Africans have also been known to have more severe forms of hypertension than in the comparable Caucasian population. [106]

Fifty eight percent (116/200) of study participants had diastolic dysfunction in this study, of which 86% (100/166) had early diastolic dysfunction with 14% (16/100) having late diastolic dysfunction. Higher proportion of participants with early diastolic dysfunction might be due to the fact that many of the participants were recently diagnosed to have hypertension with varying levels of blood pressures on treatment. However the Valsava maneuver was not done during the current study which might have missed some patients with pseudo normalization of the left ventricular filling pressure. Pseudo-normalization result may be classified as early diastolic dysfunction.

The prevalence rate of severe form of diastolic dysfunction (with increased filling pressures) was significantly higher among admitted (inpatient) participants. Mean diastolic pressure was also higher among admitted participants (91±7 vs 87±8, p=0.002). This is in agreement with previous studies that have documented increased prevalence of diastolic dysfunction and left ventricular hypertrophy in patients with higher blood pressures.[107, 108]

Consistent with the finding of higher mean diastolic blood pressure, admitted participants were on average higher number of antihypertensive drugs. Similar findings were reported by Giuseppe et al in a study which was conducted on the prevalence of LVH in patients without and with blood pressure control.[109]

Left ventricular geometry and its correlates

It is now well established that LVH determined by echocardiography is a strong predictor of poor prognosis in cardiovascular disorders independent of traditional risk factors.[110, 111, 113] Prevalence of left ventricular hypertrophy from this study was 86% (172/200). Out of which eccentric LVH 20.5% (35/172), concentric LVH 69.8% (120/172), and concentric remodeling constituting 9.3% (16/172). These findings compares to those of Wachtell et al[111] in the LIFE multicentre study group which reported prevalence of LVH to be 42-78%. Contrary to our findings eccentric LV geometry was the predominant abnormal geometry in Wachtell study.

LVMI indexed to ht $^{2.7}$ was used as convention for LVM in this study. Two recent publications have compared the prognostic implications of different normalizations for LVH. Report from the Strong heart Study group showed that the presence of LVH identified by LV mass normalized for height to allometric powers to be associated with higher incidence of cardiovascular events than LVH detected by normalization for body surface area.[112]

Left ventricular hypertrophy in Africans

It is clear that hypertension and hypertensive complications such as stroke and end stage renal disease are more common in blacks than whites.[113] Deveraux and colleagues in the meta- analysis of the 9 prior echocardiographic studies that addressed people of African decency in LVH in hypertensives concluded that relative wall thickness but not Left ventricular mass index was consistently increased in blacks as compared with whites[114]

According to Kizer and colleagues in an analysis of the Hypertension Genetic Epidemiology Network(Hyper-GEN) study revealed that blacks has confirmed the predominance of concentric and not eccentric LVH, a pattern that would be expected if LVH was a consequence of hypertension[115] Left ventricular hypertrophy is a cardinal manifestation of pre clinical cardiovascular disease that strongly predicts cardiovascular events in hypertensive patients as well as in the general population.[116,117] Previous publications have suggested that the assessment of lv geometry may add prognostic information in hypertensive patients beyond assessment of left ventricular mass,[118]

The findings of higher prevalence of cardiac hypertrophy (86%) among hypertensive patients in our study support the need for improved control of blood pressure goals in these patients. Screening for end organ damage should be warranted in this population. Electrocardiography has been found to be an insensitive and less specific test among patients of African decency for detection of LV hypertrophy; this makes echocardiographic evaluation such valuable tool in this population[119, 120]

Echocardiographic diastology parameters and clinical correlates

Diastolic dysfunction among the admitted participants was statistically associated with larger LA diameter, lower E' velocity and higher E/E' ratio, >>15 i.e. (24.6% among in-patients vs 0.7% of outpatients) $p<0.05$). This reflects higher left ventricular filling pressures among in-patients. These findings concurs with other studies, [126] Nagueh et al, while evaluating on the relationship between Mitral E/E' prime and left ventricular filling pressure using tissue Doppler imaging, revealed that [121] E/E' ratio relates well to mean Pulmonary capillary wedge pressure[122] Further more, higher E/E' ratio was found to be an independent predictor of more than mild form of diastolic dysfunction $R2=0.26$, $p<0.001$).

Tissue Doppler assessment of diastolic function with E/E' ratio has been validated, when E/E' exceeds 15, LV filling pressures are elevated and when the ratio is lower than 8 LV filling pressures are low.[123] E/E' is a powerful predictor of survival after myocardial infarction and E/E'>15 is superior as a predictor of prognosis than clinical or other echocardiographic variables.[124] The close correlation between E/E' and filling pressures has been confirmed in heart failure patients with depressed or preserved EF and in patients with slow relaxation or pseudo normal early mitral flow velocity filling patterns.[125]

CONCLUSIONS

The prevalence of diastolic dysfunction is high among this population of patients with hypertension as reported in this in this study. Many of them having concentric left ventricular hypertrophy.

Admitted symptomatic hypertensive patients were found to have severe form of diastolic dysfunction with higher left ventricular filling pressures and predominant concentric Left Ventricular hypetrophy with poorly controlled hypertension.

Diastolic dysfunction was highly correlated with larger left atria diameter, lower E' velocity and higher E/E' ratios, this was a reflection of higher filling pressures in this group of patients.

Higher E/E' ratio is observed to be an independent predictor of more than mild diastolic dysfunction in hypertensive patients.

LIMITATIONS OF THE STUDY

Valsalva maneuver and pulmonary venous flow were not performed, hence pseudo normalization, the reversibility and non reversibility of the grade 4 diastolic dysfunction was not categorized.

Majority of patients were already on treatment limiting the categorization and staging of their hypertensive status.

This is a hospital based study of a selected group, limiting generalization of the findings to the general population.

Cardiologists were not blinded in this study during physical examinations and investigations.

RECOMMENDATIONS

1.The higher prevalence of cardiac hypertrophy among hypertensives in our study support the need for improved controll of blood pressure in these patients

2. This study calls for concerted effort at appropriate diagnostic evaluation of diastolic dysfunction by echocardiography with spectral and tissue Doppler in patients with essential hypertension to prevent future upsurge in the incidence of subsequent diastolic heart failure.

3. A large prospective community based study at primary level is recommended in order to study and generalize the sub clinical diastolic parameters in untreated hypertensives.

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APPENDICES:

Appendix I:

QUESTIONNAIRE: ENGLISH VERSION

CLINICAL AND ECHOCARDIOGRAPHIC FINDINGS OF LEFT VENTRICULAR DIASTOLIC FUNCTION AMONG HYPERTENSIVE PATIENTS AT MUHIMBILI NATIONAL HOSPITAL

1. **Demographic Characteristics:**

Serial Number…… Sex 1.Male… 2.Female……

Date of birth……. (Age……yrs)

District …… Tel……..

2. History

1. Have you been diagnosed to have high blood pressure? 1. YES…… 2. NO……

2. If yes, how long since you have been diagnosed to have high blood pressure? …… (Months)

3. Are you on any treatment for high blood pressure? 1. YES…… 2. NO ……

4. If yes on which drugs: ACEI 2.ARB 3.BB 4.DIURETICS 5. CALCIUM ANT 6.Others (specify)……

5. For how long have you been on treatment …… (Months)

In the past one month;

6. Have you experienced awareness of heart beats 1. YES…….. 2. NO ……..

7. Have you experienced difficulty in breathing 1. YES…….. 2. NO ……

8. Have you experienced undue tiredness 1. YES ……. 2. NO …

9. Have you experienced swelling of your legs 1. YES ……. 2. NO ……..

10. Have you experienced waking up at night due to air hunger? 1. YES…. 2.NO……

11. Have you experienced cough at night? 1. YES….. 2. NO……

12. Have you experienced shortness of breath on ordinary exertion?1. YES 2. NO…

13. Do you experience marked limitation of physical activities, comfortable only at rest?

1. YES…….. 2. NO…….

14. Do you experience marked limitation of activities even at rest

1.YES…… 2. NO……

3. Physical Examination

15. Body weight (Kg)…… 16. Height (M)……

17. Body Surface area (BSAm2) 18. Body Mass Index (BMI)…….

19. Waist circumference … (cm) 20. Radial pulse (Rate, per minute) ….

21. Cyanosis 1.Present……2.Absent……

22. Peripheral pulses 1.Present……2.Absent…….

23. Apex beat 1.Normal……...2.abnomal (specify)..

17. S3 sound 1.Present…….2.Absent…3 gallop…

18. S4 sound 1.Present ……..2.Absent ….

19. Pulmonary rales/ wheezes 1.Present……..2.Absent……

20. Neck vein Distension (JVP) 1. Present…… 2. Absent….....

21. Hepatojugular reflux 1.Positive ……2.Negative…….

22. Blood Pressure (mmHg) Systolic ……. Diastolic……pulse pressure…

23. Hepatomegally 1.Present…..... 2.Absent……..

24. Bilateral ankle oedema 1.Present……..2.Absent…….

25. Ascites 1.Present……. 2.Absent……

26. Murmur 1. YES…... 2. NO…...

27. If there is a murmur; Grade: I……. II…… III…… IV……. V…… VI……

28. Type of Murmur

1. Mitral……2.Aortic…….3.ASD……4.VSD…5.Tricuspid……6.Pulmonary……..

29. Functional state of Heart failure (NYHA class) 1. I -II, 2. III- IV

30. **ECHOCARDIOGRAPHY**

15. SYSTOLIC FUNCTION AND LV GEOMETRY

Left Ventricle :

IVS (s)	Cm,	IVS (d)	Cm,	AR=	cm
LVID(s)	Cm	LVID(d)	Cm	FS =	%
LVPW(s)	Cm.	LVPW (d)	Cm	LVEF=	%
LVM =		LVMi=		RWT = (IVSd+PWd)/LVDd	

Conclusion.

Left ventricular geometry; 1. normal 2. Concentric remodeling 3. concentric hypertrophy 4. eccentric hypertrophy

ECHO Diagnosis

1. Normal……..... 2. LVH due to HT……..

3. Dilated cardiomyopathy..... 4. Hypertrophic Cardiomyopathy.....

5. Restrictive Cardiomyopathy…..... 6. Congenital Heart Disease……

7. Pericardial Effusion..... 8. Pulmonary pressure (RVSP) ……

9. Chamber sizes 1. LA…… 2.LV…..3.RA…….4.RV…….5.Aortic root……

10. Others (Specify)……..11. Associated commobidities…….

15. DIASTOLIC FUNCTION

I	Left Atrial size, antero-posterior (cm)	
Ii	Left Atrial size, planimetry (cm^2)	
Iii	Mitral E-wave (cm/sec)	
Iv	E-wave deceleration time (sec)	
V	Mitral A-wave (cm/sec)	
Vi	Mitral A-wave (duration)	
Vii	Mitral E/A	
viii	Lateral mitral E'(DTI)	
Vix	Medial mitral E' (DTI)	
x	Average E'	
Xi	E/E'	
Xii	Average A'	
Xiii	E'/A'	
Xiv	IVRT	

Conclusion; Diastolic function

1. Normal 2.Grade 1 3.Grade 2 4. Grade 3 5. Grade 4

QUESTIONNAIRE (SWAHILI VERSION)

DODOSO:

Nambari ya mtiririko…… Tarehe …….

Nambari ya faili……

Jinsia

1.Me……...2.ke…….

Tarehe ya kuzaliwa…… (Umri wako ……miaka)

Wilaya ukaayo …… Nambari ya simu……..

2. Historia

1. Je umekwisha wahi kugunduliwa na ugonjwa wa shinikizo la damu?

1. ndiyo…… 2. hapana……

2. kama ndiyo, nilini uligunduliwa kuwa na ugonjwa huo? ……..

3. Je unatumia dawa zozote za ugonjwa huo? 1. ndiyo…… 2. Hapana

4. Kama ndiyo, je ni dawa gani unatumia 1. ACEI 2.ARB 3.BB 4.DIURETICS 5. CALCIUMANT 6.nyingine(taja jina)…

5. kwa muda gani sasa umekuwa katika matibabu ya shinikizo la damu? ……

Ndani ya mwezi mmoja uliopita ;

6. Je umesikia mapigo ya moyo kwenda haraka? 1. Ndiyo….. 2.Hapana

7. Je umesikia kuishiwa na pumzi? 1. Ndiyo….. 2.Hapana

8. Je umejisikia kuchoka kusiko kawaida? 1. Ndiyo ……. 2.Hapana .

9. Je umeona kuvimba kwa miguu yako? 1. Ndiyo……. 2.Hapana

10.Je umesikia kuamka usiku kwa kuishiwa na hewa?

1. Ndiyo…. 2.Hapana..

11.Je umekuwa ukikohoa usiku ? 1.Ndiyo….. 2.Hapana..

12. Je umekuwa ukisikia kuishiwa na pumzi kwa kufanya kazi za kawaida?

1. Ndiyo.... 2. Hapana…..

13. Je umejisikia kuzidiwa sana na pumzi hata kwa kufanya kazi za kawaida ?

1. ndoyo…….. 2.Hapana….

14. Je umekuwa unajisikia kuzidiwa kabisa nahi ya pumzi hata ukiwa umeketi kitako

1. ndiyo…….. 2. Hapana…….

Vizio vya mwili

15. uzito (Kg)……

16. Kimo (M)……

17. Eneo la mzunguko wa mwili (BSAm2)

18. kizio cha uzito kwa urefu cha mwili (BMI)…….

19. unene wa kiuna ……. (cm)

20. Kiwango cha mapigo ya moyo mkononi (idadi/kwa dakika) …….

21. Cyanosis 1.Present……2.Absent……

22. Peripheral pulses 1.Present……2.Absent……

23. Apexbeat

1.Normal……...2.abnomal(specify)

Appendix II:

CONSENT FORM (ENGLISH VERSION)

Clinical and echocardiographic features of left ventricular diastolic dysfunction among hypertensive patients at Muhimbili national hospital, "a tissue doppler imaging study"

Goodmorning/ afternoon,

My name is is Dr Tulizo Shemu Sanga, a postgraduate student in Msc Cardiology.

We are conducting a study on adult hypertensive patients (from eighteen years and above) admitted and those attending services at Muhimbili National hospital. The study will involve more than 200 patients. I would like to involve you in this study if you would consent and fulfill the inclusion criteria.

Study Aim:

To determine the clinical and echocardiographic characteristics of left ventricular diastolic dysfunction of the hearts, among patients attending service at Muhimbili National hospital and know the magnitude and beharviour of the problem.

Involvement:

You will be asked, after consenting, to answer questions posed to you by a researcher before you are put on the echocardiography machine for measurement of your heart.

Confidentiality:

All information collected in this questionnaire will be confidential.

Side effects:

We are not expecting any major effect on your health from your involvement in this study.

Withdrawal from the study:

Your participation in this study is voluntary; you therefore have a right to withdraw from the study anytime. Your withdrawal from the study will not interfere anyhow with your right for care from us.

Benefits:

Your participation in the study will enable you to know if you have any cardiac disease because of your hypertension as a complication of it or from any other cause and ultimately advice you and put you on the management plan accordingly and be followed on regular basis at our cardiac clinic.

Contacts:

If you have questions on your rights as a study participant you are asked to consult Prof Abood, The Chairman of Ethical and Research committees of Muhimbili University of Health and Allied Sciences (office landline 022 2152489, P.O BOX 65001, Dar es Salaam).

Do you have any question?

I _____I have read/ information have been read to me from this questionnaire, my questions are clearly answered. I have voluntarily agreed to participate in the study.

Signature of the participant _____

Signature of the researcher: _____

Date: _____

Appendix II:

CONSENT FORM (SWAHILI VERSION)

IDHINI YA KUSHIRIKI KATIKA UTAFITI

Nambari ya Usaili……

Ndugu, hujambo?

Mimi naitwa..**Dr. Tulizo shemu Sanga**, Ni tabibu mwanafunzi wa udhamili Chuo Kikuu cha Tiba Muhimbili. Nafanya utafiti kuhusu ***"ugonjwa wa shinikizo la damu kwa wagonjwa wanaotibiwa na kufanyiwa kipimo kikubwa cha moyo katika hospitali ya taifa muhimbili"***

Madhumuni ya Utafiti

Katika utafiti huu, lengo ni kusajiri wagonjwa watakaoonekana kuwa na Shinikizo la damu na kufanyiwa kipimo kikubwa cha moyo kiitwacho ***echocardiography*** ili kujua ni kwa kiasi gani moyo umeathirika kutokana na kuwa na shinikizo la damu na madhara yake kwa afya ya muhusika

Ushiriki wa wagonjwa

Kama unakubali kushiriki katika utafiti huu utaombwa kujibu maswali kadhaa na pia kufanyiwa kipimo cha moyo.

Utunzaji wa siri

Taarifa zote zitatunzwa kwa siri na mtafiti.

Madhara na athari

Hakuna madhara yoyote yanayotegemewa kutokana na ushiriki kwenye utafiti huu.Kipimo hiki ni salama kwa afya yako na wala hakitoi mionzi inayohatarisha afya.

Uhuru wa kushiriki

Ni hiari ya mgonjwa kushiriki kwenye utafiti huu na pia anaweza kujitoa wakati wowote. Hata hivyo kutoshiriki au kujitoa kwenye utafiti hakumnyimi mgonjwa haki yake ya kupata huduma za matibabu. Mgonjwa aliyejitoa kushiriki utafiti akiamua kurudi atapokelewa na kuendelea kupata huduma zote kwa mujibu wa utaratibu uliopo.

Faida za utafiti

Mgonjwa atafaidi kwa kuhudumiwa na mtafiti pindi mgonjwa anapohitaji utaalamu maalum wa magonjwa ya moyo.

Pia afya ya mshiriki itafuatiliwa kwa ukaribu na mtafiti kwenye kliniki maalum ya magonjwa ya moyo katika hospitali ya Taifa Muhimbili

Ni matumaini kwamba taarifa za utafiti huu zitasaidia kuboresha tiba kwa wagonjwa wengine siku za baadaye.Kuna kamati ya kusimamia udhibiti wa utafiti ambayo hutoa taarifa za matokeo ya utafiti ambayo hutoa elimu kubwa kuhusu tatizo hili.

Taarifa

Endapo utahitaji kupata maelezo kuhusu haki zako au kutoa taarifa ya madhara ambayo unahisi yametokana na kipimo hiki cha moyo, wasiliana na Prof.Abood, mwenyekiti wa kamati ya utafiti,S.L.P 655001, Dar es Salaam. Namba: 2150302-6.

Je unakubali kushiriki kwenye utafiti? (weka alama) Ndiyo..... Hapana.....

Mimi…….nimeelezwa/nimesoma maelezo haya.Maswali yangu yamejibiwa.

Nimekubali kushiriki kwenye utafiti huu

Sahihi ya mgonjwa……

Sahihi ya ndugu/shahidi…….

Sahihi ya Mtafiti……..Tarehe……