PATTERNS OF CAROTID DOPPLER FINDINGS AND ASSOCIATED FACTORS AMONG ADULT PATIENTS WITH ISCHEMIC STROKE AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET.

BY

ONWONG'A KERUBO MERCYLINE

THIS RESEARCH THESIS IS SUBMITED TO THE SCHOOL OF MEDICINE. COLLEGE OF HEALTH SCIENCES, IN PARTIAL FULLFILMENT FOR THE AWARD OF MASTER OF MEDICINE IN RADIOLOGY AND IMAGING OF MOI UNIVERSITY SCHOOL OF MEDICINE

DECLARATION

Declaration by the Candidate

This thesis is my original work and has not been presented for a degree or any academic credit in any other University or examining body. No part of this project may be reproduced without the prior written permission of the author and/or Moi University.

ONWONG'A MERCYLINE KERUBO

SM/ PGR/02/2016

Department of Radiology and Imaging, Moi University

Signature ………………………………………. Date ……………………

Declaration by Supervisors:

This thesis has been submitted for examination with my approval as a University supervisor.

Dr. Joseph Abuya

Senior Lecturer,

Department of Radiology and Imaging,

Moi University School of Medicine.

Signature ………………………………………. Date ……………………

Dr. Ouma Victor

Consultant Radiologist.

Department of Radiology and Imaging

Moi Teaching and Referral Hospital

Signature……………………………………… Date………………………….

DEDICATION

I dedicate this work to my husband Dr. Bosire Momanyi for his undying support and to my son Leeroy Okioma and daughter Leandra Machoka who give me the motivation to work hard.

ACKNOWLEDGEMENT

I wish to thank my supervisors, Dr. Joseph Abuya and Dr.Victor Ouma for their contributions, corrections and advice given to facilitate the successful completion of this project. I also wish to acknowledge Mr. Alfred Keter, my biostatistician for his invaluable assistance.

LIST OF ABBREVIATIONS

CCA	Common Carotid Artery
CIMT	Carotid Intima Media Thickness
CVA	Cerebrovascular Accident.
CVD	Cerebrovascular Disease
ECA	External Carotid Artery
EDV	End Diastolic Volume.
ICA	Internal Carotid Artery
MTRH	Moi Teaching and Referral Hospital.
NASCET	North American Symptomatic Carotid Endarterectomy Trial
PSV	Peak Systolic Volume
TIA	Transient Ischemic Attack
WHO	World Health Organization

DEFINITION OF TERMS.

Atheromatous plaque; An abnormal accumulation of material in the inner layer of the wall of an artery. The material may consist of macrophage cells, lipids, calcium, and variable amounts of fibrous connective tissue. The accumulated material forms a swelling in the arterial wall which may intrude into the lumen of the artery, narrowing it and restricting blood flow.

Carotid Intima Media Thickness(CIMT)- is the measurement of the thickness of the tunica intima and tunica media. This is obtained using a linear array probe in B – Mode, where the far wall is measured as the distance between two echoic lines separated by anechoic space.

Doppler Ultrasound- This is a non-invasive technique used to assess the flow of blood in vessels. The vessels studied were the common carotid, the internal carotid, and the external carotid arteries.

End diastolic volume (EDV)- This is an index measured in spectral Doppler ultrasound. On a Doppler waveform, the EDV corresponds to the point marked at the end of the cardiac cycle, just prior to the systolic peak.

Peak systolic velocity(PSV) This is an index measured in spectral Doppler ultrasound. On a Doppler waveform, the peak systolic velocity corresponds to each tall “peak” in the spectrum window.

Stroke; An abrupt onset of neurologic deficit due to vascular cause.

ABSTRACT

Background: Acute ischemic stroke is a major cause of death worldwide. About 80% of strokes are thromboembolic in origin, with carotid plaque as an embolic source. Carotid Doppler ultrasound is valuable to assess the localization, extent, and severity of extracranial carotid stenosis. It is a safe, accurate, and affordable alternative to Computed Tomography Angiography. However, limited studies have been done in our population.

Objectives: To describe the patterns of carotid Doppler ultrasound, the proportion of Internal Carotid Artery(ICA) stenosis, and its associated factors among ischemic stroke patients at Moi Teaching and Referral Hospital.

Methods: This was a cross-sectional study conducted among patients who presented with a CT diagnosis of acute ischemic stroke from September 2018 to August 2019. A census methodology was used and a total of 71 participants were recruited.

A data collection form was utilized to record age, gender, history of known risk factors such as diabetes, hypertension, and smoking and findings of carotid Doppler ultrasound. The 7.5 MHz linear array transducer of the Mindray M7 machine was used (Doppler angle <60º). The Mindray M7 is an ultrasound machine with superior image quality and exquisite Doppler capability. Stratification of ICA stenosis was done based on the United States Society of radiologists in ultrasound consensus criteria of 2004. Continuous variables were summarized using means and standard deviations. Categorical variables were summarized in frequency, percentages and bar graphs. Chi-square test and Fischer's exact test were done to assess the relationship between stenosis and associated factors. Mann Whitney U test was used to determine association between distribution of age and stenosis. P value of less than 0.05 was considered significant

Results: Of the participants studied, 42/71(59.2%)were male. The mean age was 64.2 years (SD=11.0). Increased Intima Media Thickness (>1 mm) was seen in 43/142(30.3%) of the common carotid arteries. 41 plaques were identified. The commonest site of plaque was the ICA 21/41(51.3%) followed by the carotid bulb 9/41 (21.9%) and the CCA 9/41 (21. 9%), where 28/41(68.3%) were characterized as homogenous, 7/41(17.1%) heterogeneous and 6/41(14.6%) were calcified. Mild ICA stenosis was seen in 20/71(28.2%) patients followed by 5/71(7%) with moderate stenosis, 2/71(2.8%) had severe stenosis while 1/71(1.4%) had near total occlusion. There was a statistically significant relation between diabetes, hypertension and smoking with ICA stenosis, P-values of <0.001, 0.025 and 0.032 respectively. Individuals with stenosis had a higher age (mean rank= 38.27) compared with those without stenosis (mean rank = 34.52). However, age and gender did not show any significant association with stenosis.

Conclusion: ICA was the most common site for plaque formation, with homogenous plaques being the most common. The proportion of patients with significant stenosis was low. Having Diabetes, hypertension and a smoking history was associated with carotid artery stenosis

Recommendation: Routine screening of patients above 50 years with a history of diabetes, hypertension and smoking is recommended. Prospective studies be done to further assess the strengths of association.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE: INTRODUCTION

1.1 Background Information

Stroke is defined as an abrupt onset of neurologic deficit due to vascular cause (Chung, 2017). Ischemic stroke is characterized by sudden loss of blood circulation to an area in the brain. It is caused by a thrombotic or embolic occlusion of a cerebral artery (Chung, 2017).

Carotid arteries are the main suppliers of blood to the brain, face and neck. They include the right and the left carotid arteries which branch in the neck into internal carotid artery (ICA) which supplies the brain with blood and the external carotid arteries (ECA) which supplies the neck and face. It is these arteries that are affected by stenosis thereby causing ischemic stroke (Dublin & Al-Dhahir, 2019).

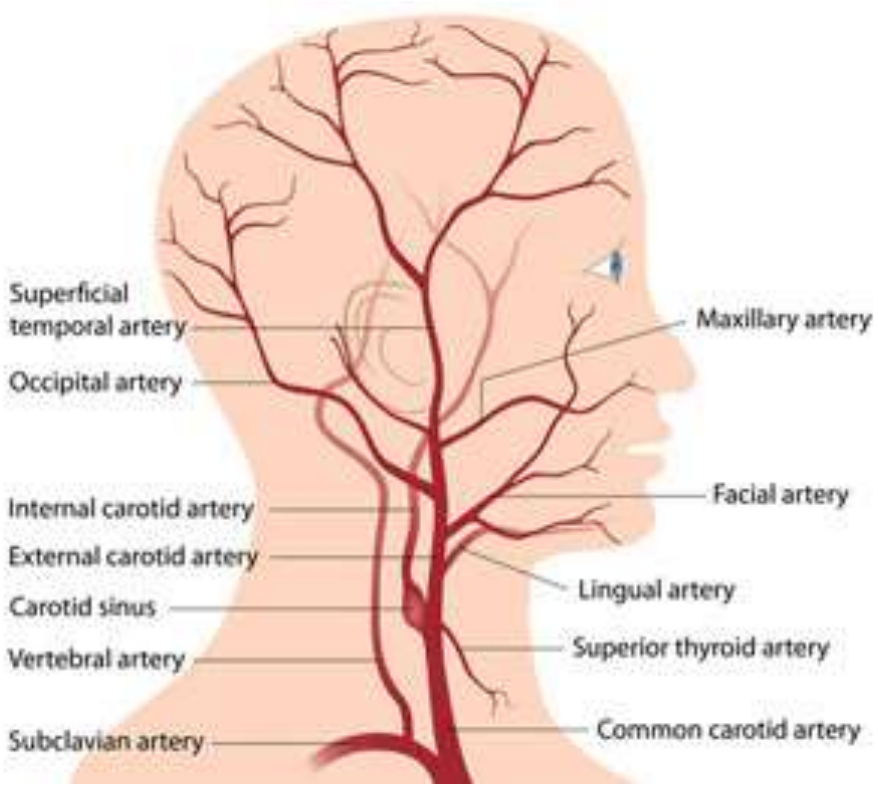


Figure 1: Right Carotid arteries
Adapted from:(Prestige Primary Care of Texas, 2020)

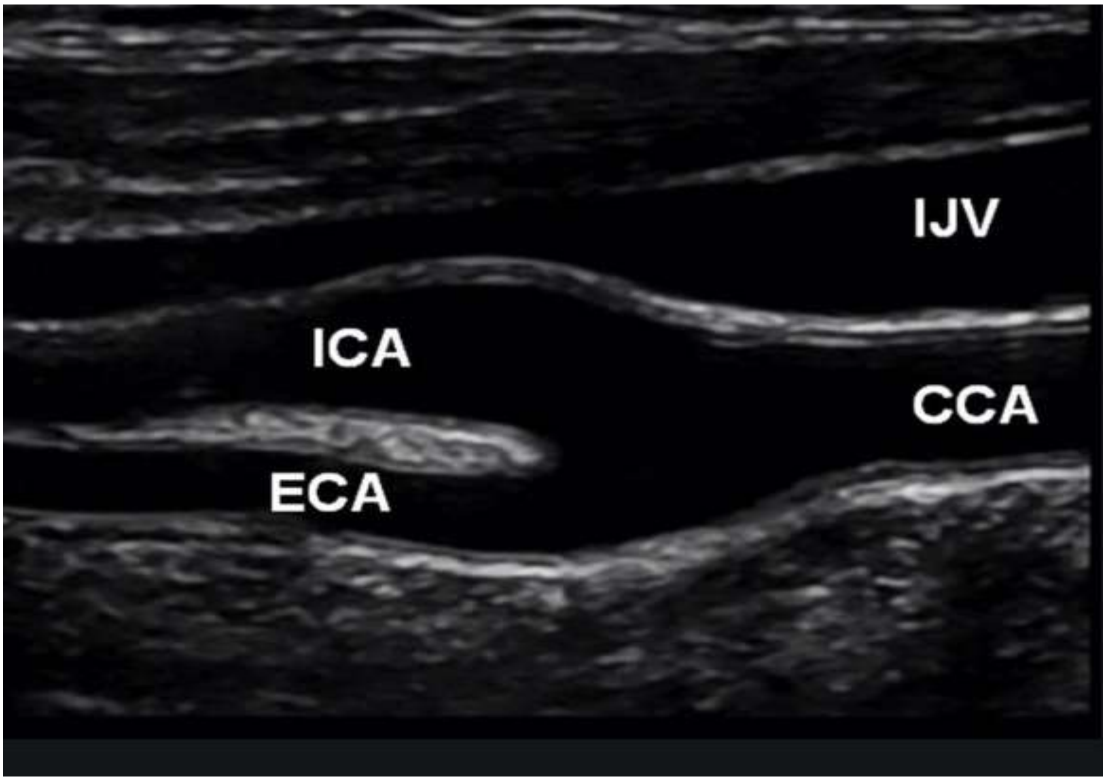


Figure 2: Normal carotid ultrasound, gray scale.
Adapted from : (Polak & Pellerito, 2012)

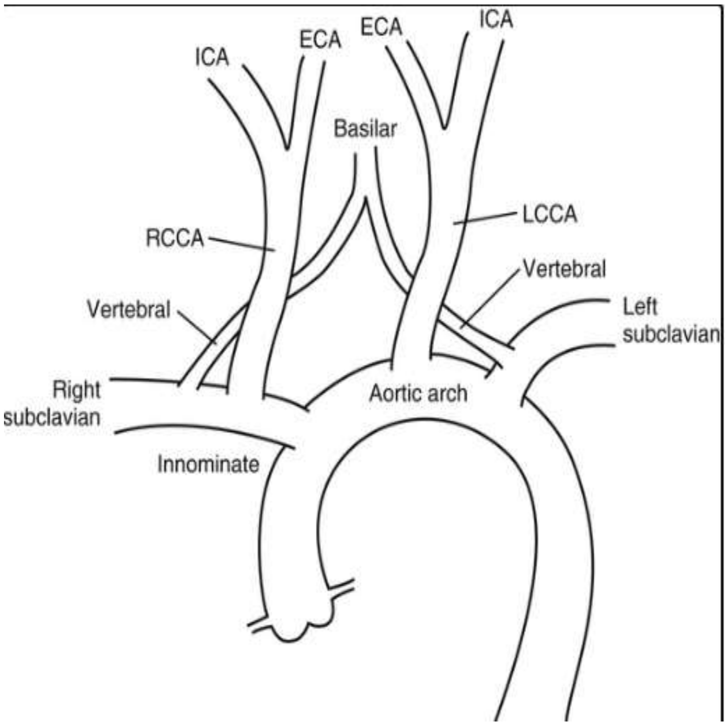


Figure 3: Schematic of the carotid vessels anatomy.
Adapted from (Ho & Reddy, 2010)

Ischemic stroke is more common than hemorrhagic stroke and is a leading cause of death in the world (WHO, 2012). The prevalence of deaths due to stroke in Kenya in 2014 stood at 4.3% (WHO, 2014).

Studies have shown that there is a close relationship between carotid artery disease and ischemic cerebrovascular disease. Atherosclerosis of intra and extra cranial carotid vessels account for about 80% of strokes, the remaining are due to intracranial hemorrhage and subarachnoid hemorrhage (Fernandes, Keerthiraj, Mahale, Kumar, & Dudekula, 2016). The global inter-stroke study, which was population based, reported hypertension as the most significant risk factor for stroke occurrence with population attributable risk (PAR) of 34%. Other risk factors included current smoking PAR of 18·9%, waist-to-hip ratio 26·5% and diabetes mellitus 5.4% (O'donnell et al., 2010) .

The risk of stroke is usually significantly high in the first three months after a transient ischemic attack (TIA). About 20% of strokes are heralded by TIAs (Calanchini et al., 1977). Approximately 20 -30% of stroke cases occur secondary to carotid bifurcation thrombus or plaque embolus (Timsit et al., 1992).

The highest risk of stroke appears to be among patients who have a high degree of carotid artery stenosis, a history of diabetes and presence of asymptomatic carotid artery plaques or a combination of all three. Accurate diagnosis of hemodynamically significant stenosis is therefore critical to identify patients who would benefit from intervention. The value of a safe, noninvasive, and low-cost screening test is therefore of a great advantage (Fernandes et al., 2016).

Several studies have shown carotid endarterectomy to have significant potential of reducing stroke risks hence reduce mortality in patients who have stenosis higher than 60% or 70% in the ICA compared to those who receive optimized medical therapy (E.

G. Grant et al., 2015). This justifies the need to identify individuals with stenosis of more than 70% for appropriate carotid endarterectomy.

Patients with carotid bruits and plaque risk factors and those with ischemic stroke symptoms necessitate referral for carotid arteries evaluation using either Magnetic Resonance Imaging (MRI), CT angiography or ultrasound. However, among all these imaging techniques, ultrasound is the least expensive, least invasive and most available in resource limited facilities. With its appropriate performance, ultrasound can detect surgical lesions represented by ICA stenosis of greater or equal to 70%. Another advantage is that these ultrasound findings does not necessitate confirmatory scanning with CT angiography or MRI if the procedure is carried out correctly, except in rare complex cases with poor visualization (Scoutt, Kirsch, & Hamper, 2010).

While carotid angiography is the gold standard for diagnosing carotid artery atherosclerosis, it is expensive, invasive and carries risk of reaction to contrast (Budoff & Shinbane, 2016). Magnetic resonance angiography on the other hand is quite expensive though it is thought to yield better results especially for flow quantification (Johnson, Wilkinson, Wattam, Venables, & Griffiths, 2000).

Duplex sonography combining high-resolution imaging and Doppler spectrum analysis has proved to be a screening tool of choice in evaluation of carotid artery disease. Carotid sonography has largely replaced angiography for suspected extracranial carotid atherosclerosis (Rothwell, Villagra, Gibson, Donders, & Warlow, 2000). If timely medical therapy, and or endarterectomy of the carotid arteries is performed, many stroke cases may be prevented.

Carotid artery Doppler ultrasound remains a safe, affordable and accurate method of evaluating the degree of carotid artery disease (Johnson et al., 2000). When color

Doppler and gray scale imaging are used, it is possible to grade stenosis and describe plaque characteristics (Budoff & Shinbane, 2016).

Gray scale imaging enables the identification of the characteristics, extent and location of atherosclerotic plaque in the ICA, ECA and common carotid artery (CCA). Abnormality in the blood flow can be detected using the color and spectral Doppler sonography. The flow of blood in terms of velocity in the proximal ICA and mid CCA is observed. External carotid artery (ECA) is evaluated in determining the differences in appearances of the ICA and ECA to ensure correctness in observation (Budoff & Shinbane, 2016).

While using Doppler sonography in the carotid artery examination, ultrasound machine with spectral or color Doppler capability and gray scale imaging with high resolution is needed. Mostly, high frequency of 7.5 to 10 MHz is used for spatial resolution optimization (Murray, Nahar, Kalashyan, Becher, & Nanda, 2018).

Color Doppler and grey scale imaging is key in the identification of irregular or hypoechoic plaque, believed to have rapid progression increasing the risk of thromboembolism. Spectral Doppler offers the physiologic information that is useful in giving leads to other distal and proximal conditions in addition to the provision of PSV measurements utilized in the ICA stenosis grading (Scoutt et al., 2010).

Ultrasound evaluation of carotid arteries

Detailed evaluation of the carotid artery using ultrasound includes the use of velocity criteria to estimate ICA stenosis, plaque evaluation and analysis of the waveform. Correlation of the velocity criteria with the color and grey scale amount of plaque estimation and the ICA and CCA distal and proximal waveform is recommended when evaluating ICA stenosis. The observed discrepancies need to be explained (Ho & Reddy, 2010).

When examining the patient, he/she is placed in the supine position with the neck slightly turned to the contralateral side and extended. However, anterior or posterior approach can be utilized. During the examination, plaque burden is first evaluated and the echotexture characterized as either echogenic, hypoechoic or heterogeneous (Scoutt et al., 2010).

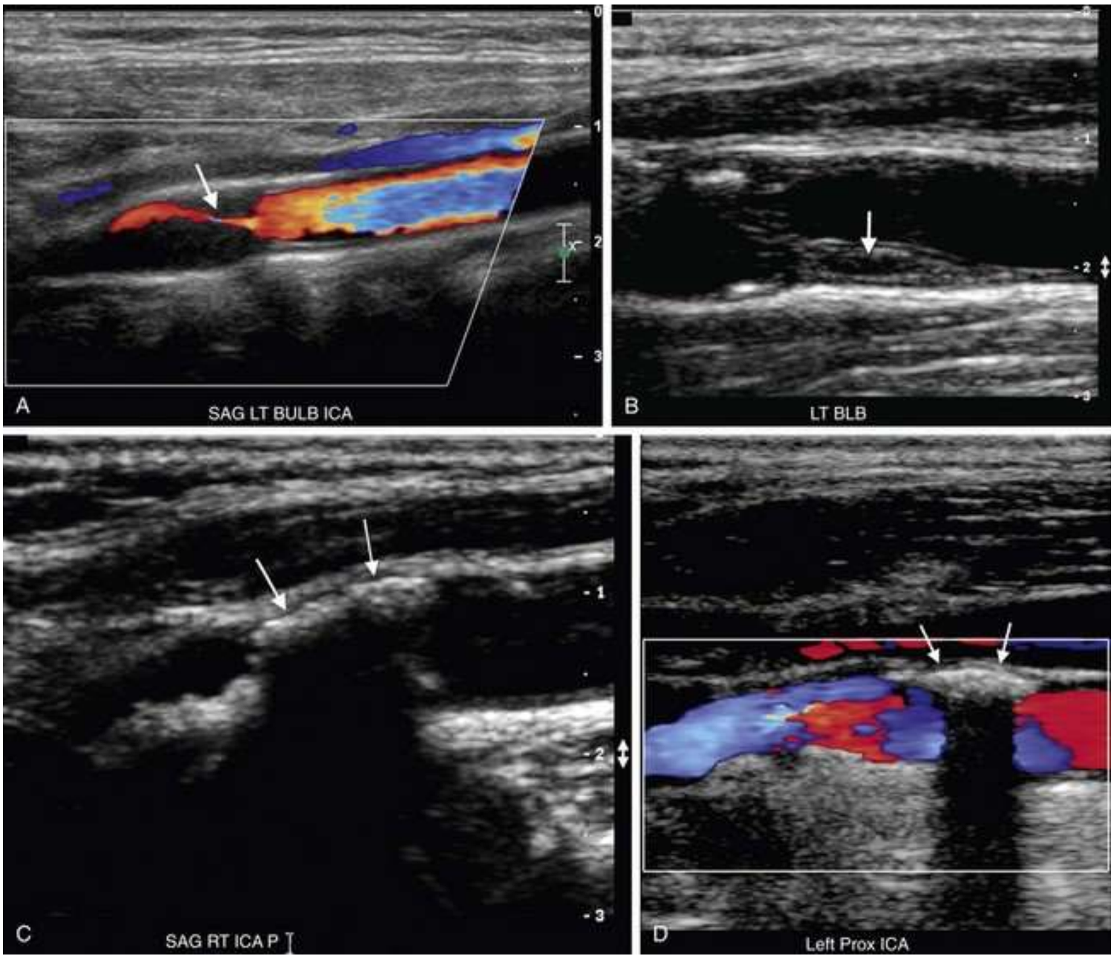


Figure 4: Carotid artery plaque echotexture
Adapted from: (Ho & Reddy, 2010)

A: Color Doppler image demonstrating a large amount of homogeneous hypoechoic plaque in the left ICA. There was luminal narrowing thus increasing resistance

B: focal hypoechoic area (arrow) within a heterogeneous plaque in the left carotid bulb. C: Homogeneous echogenic shadowing plaque (arrows) in the proximal right ICA.

D: Homogeneous echogenic shadowing plaque (arrows) in the left proximal ICA.

In addition, the plaque surface contour is described as either being irregular or smooth, with the percentage arterial diameter reduction caused by plaque being estimated

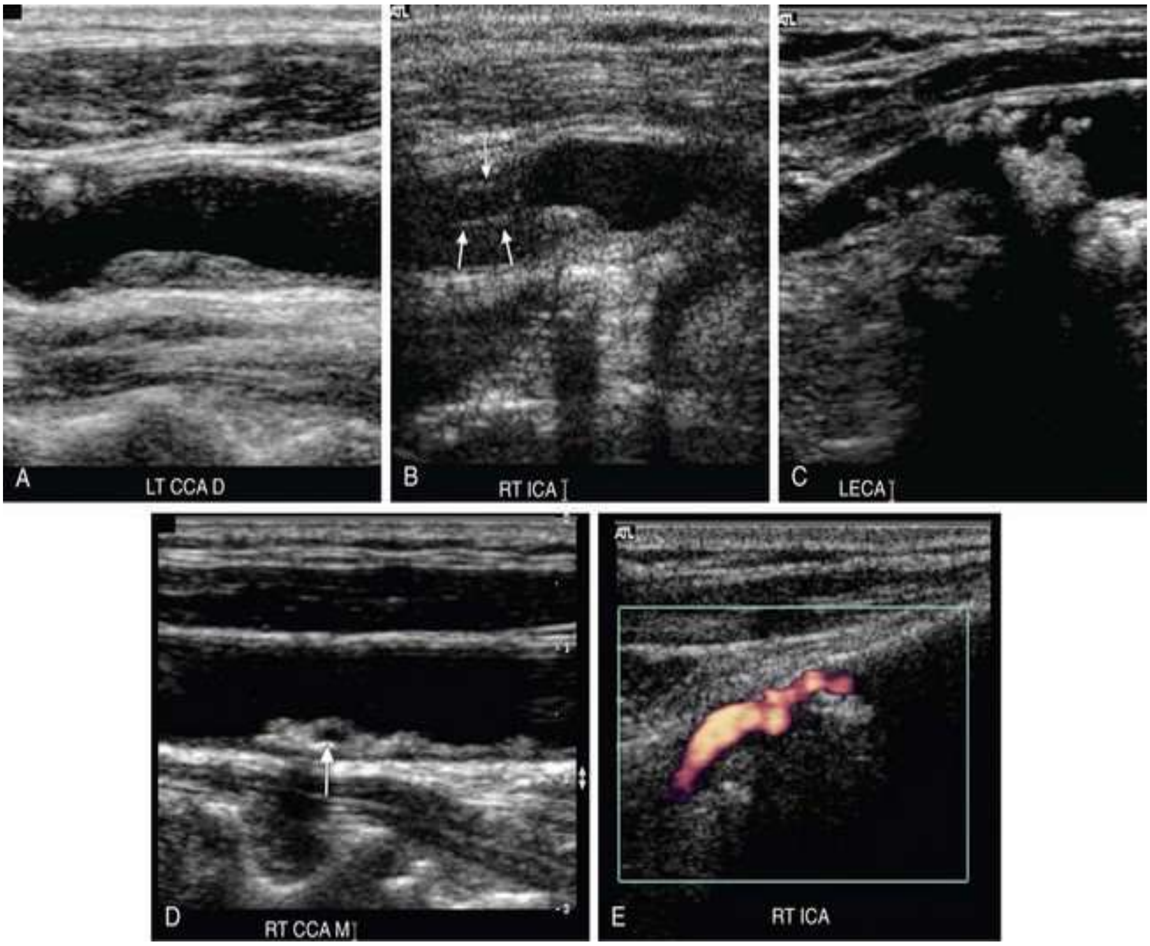


Figure 5: Carotid plaque surface contour
Adapted from: (Ho & Reddy, 2010)

A: Longitudinal gray-scale image of the distal left CCA showing plaque with a smooth surface contour and heterogeneous echotexture.

B: Longitudinal gray-scale image showing a large amount of hypoechoic plaque with a smooth surface contour (arrows) along the posterior and anterior walls of the right ICA and bulb.

C and D: Irregular surface contour from two different patients.

E: Image of right ICA showing an irregular residual lumen, revealing an irregular plaque surface.

For optimal plaque evaluation, color Doppler and gray scale imaging are conducted in both the entire transverse and longitudinal planes of ICA and CCA and the ECA origin. The focal zone is usually set at the vessels far wall. Harmonic or spatial compounding is used to improve the grey scale resolution.

Adjustment to the gray scale gain is done so that the vessel wall and the plaque are depicted with ease with the artifactual echoes being left out of the vessel lumen. Setting the gain low results in the plaque appearing artifactually hypoechoic. To optimize the color gain, the gain is slowly increased to a point where color speckles are observed in the nearby soft tissues. The decrease in gain is then done to a point where color pixels are seen in the vessel lumen alone. Setting the gain too high results in the color pixels bleeding over plaque resulting in obscured visual of the plaque burden hence stenosis being overlooked. While on the other hand, very low gain results in reduced sensitivity to blood flow hence false positive results in stenosis and occlusion diagnosis.

In instances where the lumen of the vessel is shadowed by plaque, hence not visible, it is important to use a curved array transducer or to approach the vessel from varied angles (Ho & Reddy, 2010).

To quantify stenosis with accuracy, PSV measurement on the spectral Doppler tracing need to be done accurately even though the degree can be estimated from the color Doppler and gray scale images (Murray et al., 2018).

Normal carotid arteries have thin and regular echogenic walls that do not have intraluminal thrombus or plaque or areas of mural calcification. The color fills the lumen vessel homogeneously. In cases of widened carotid bulb, peripheral flow reversal and blood flow pattern that is helical is considered normal, especially in patients that are younger as a result of separation of boundary layers

A number of factors determine what is considered to be normal CCA PSV including age, heart rate, systolic blood pressure, cardiac output and stroke volume. Generally, normal CCA PSV ranges between 70- 100cm/s with gradual decrease with distal sampling (Scoutt et al., 2010).

In the case of waveforms, their patterns vary in ICA, CCA and ECA. The ECA diastolic flow in normal cases is symmetric right to left and is usually less than CCA or ICA flow. On the other hand, ICA has a wave flow pattern with low resistance and continuous forward and high distal flow velocity, while CCA had intermediate distal flow showing brief flow reversal during early diastole. To eliminate the challenges of stenosis misinterpretation in ECA as the one of significant ICA stenosis, it is key to differentiate between ECA from ICA. ECA is identified by visualization of branches in the neck. The ICA gives no branch vessels in the neck (Ho & Reddy, 2010).

Irregular surface plaque and hypoechoic plaque have increased risks of thromboembolic events due to their high likelihood of rapid progression.

In the diagnosis of significant ICA stenosis > 70%, PSV > 230 cm/s and an ICA/CCA PSV ratio > 4.0 were recommended by the Society of Radiologists in Ultrasound consensus conference to be highly accurate (E. G. Grant et al., 2003).

Factors associated with ischemic stroke.

The incidence of stroke has been shown to increase after 60 years of age according to previous studies (Park JB et al, 2001).

Hypertension is another important factor. Hypertension causes atherosclerosis due to continuous endothelial trauma, ultimately leading to plaque formation and contributes to plaque growth (Steinman et al, 2004).

Diabetes mellitus can actually induce atherosclerosis development or accelerate its progression further. Diabetes mellitus comprises a group of disorders of carbohydrate metabolism that share a common main feature of chronic hyperglycemia that results from defects in insulin action, insulin secretion or both. Insulin is an anabolic hormone and its deficiency results in abnormalities in metabolism of proteins, lipids and carbohydrates (poznyak et al, 2015).

There is a clear association between the presence of carotid atherosclerosis and mortality among diabetic patients. Patients with diabetes and carotid stenosis ≥50% have a 2.5-fold increase in risk of cardiovascular death compared to patients without diabetes (Genkel et al, 2019).

Chronic cigarette smoking is a strong predictor for severe extracranial carotid atherosclerosis. Smoking induces oxidative stress, vascular inflammation platelet coagulation, vascular dysfunction, and impairs serum lipid profile in both current and chronic smokers, active and passive smokers, and results in detrimental effects of the cardiovascular system (Siasos et al, 2014). A cardiovascular health community based study done in 1998 showed that with increased smoking, there was a significantly higher internal and common carotid wall thickening and internal carotid artery stenosis: current smokers> former smokers> never smokers; for instance, the unadjusted percent stenosis was 24%, 20% and 16% respectively. Notably, the prevalence of clinically significant ICA stenosis (>50%) increased from 4.4% I never smoker to 7.3% in former smokers to 9.5% in current smokers (Tell, G .S et al, 1994)

1.2 Problem Statement

Stroke has been shown to be the third leading cause of morbidity and mortality causing approximately 5.8 million deaths in the year 2005 of which two thirds were in low-income and middle-income countries. About 80% of strokes are thromboembolic in origin and the embolus arises from carotid artery plaques (Haq et al., 2017).

The carotid arteries are a common site of formation of atherosclerotic plaques, and these are easily dislodged to the intracranial vessels, OR cause occlusion of the ICA thereby resulting in stroke.

The highest risk of stroke has been reported in patients with a high degree of carotid stenosis, presence carotid artery plaques, a history of diabetes or a combination of all three (Haq et al, 2017).

About 9-15% of ischemic strokes are related to internal carotid artery stenosis of >50%. However, the extent to which ICA stenosis < 50% causes ischemic cerebrovascular events is uncertain (Eihfnawy et al ,2019). Evidence is accumulating that low grade ICA stenosis also bears a high risk of ischemic stroke if medical treatment is not implemented and optimized. (Coutinho et al, 2016).

The incidence of extracranial ICA occlusion that has been associated with ischemic stroke in the US was found to be 3-4% (Flaherty et al, 2015).

The ipsilateral stroke rate per annum, associated with mild to moderate asymptomatic ICA stenosis is 0.1- 1.6%, compared to 2-3.3% associated with severe ICA stenosis.

While digital subtraction angiography is the gold standard for diagnosis of carotid atherosclerosis, it is expensive, invasive and carries the risk of reaction to contrast. (Fernandez et al, 2016)

Carotid ultrasound is a safe and accurate alternative, however, limited studies have been done in our population.

There is need for knowledge of the patterns of carotid atherosclerotic disease on Ultrasound in acute ischemic stroke and its associated factors (Baidya et al, 2015).

With sub-Saharan Africa undergoing epidemiological transition, stroke and other vascular diseases contribute greatly to the disease burden in the region. Nearly two thirds of the global burden of acute ischemic stroke is in developing countries (Feigin et al., 2015). In Kenya, an audit report of stroke cases showed a prevalence of 3,042 cases per 100, 000 admissions with the mean age of stroke patients being 61 years (Ogeng'o & Olabu, 2010) which was 10 years younger when compared to data from European countries and United States of America. Around 30% of all stroke patients in SSA are of the young adult age group (Feigin et al., 2015).

In Kenya, 85% of the stroke cases were ischemic stroke with hemorrhagic stroke constituting 8% of the stroke cases. This was high compared to global study where ischemic stroke accounted for 78% of the cases while 22% had cerebral hemorrhagic stroke. In Kenyan studies, the main risk factors for the occurrence of stroke were hypertension, diabetes, dyslipidemia, atrial fibrillation, obesity and HIV (Jowi & Mativo, 2008).

Proper Knowledge of acute ischemic stroke and its associated complications and risk factors can prevent the burden of this disease and its recurrence (Baidya, 2015). But this is hindered due to limited information available. Doppler sonography has been reported to be effective in the evaluation of patients, though literature on this evaluation in Africa is limited in spite of vital impact of the disease in the society.

While understanding of the characteristics of the carotid arteries of patients with ischemic stroke including, plaque and percentage stenosis is key in determining the type of treatment and management for the patients, limited information exists regarding this hence limiting the choice of treatment and management decisions. Data on patterns of carotid artery Doppler findings in patients with ischemic stroke in Sub-Saharan Africa is scarce and little work in terms of research has been done in this area.

In Kenya, there is a dearth of data on the characteristics of carotid arteries of patients with ischemic stroke and the grading of stenosis as evaluated using radiological imaging with only one study having been carried out at KNH with no study on the same at MTRH. The study at KNH only looked at the proportion of stenosis among patients with ischemic stroke, there was no further evaluation of other grey scale features of the carotids and the study did not attempt to draw any associations between stenosis and known cardiovascular risk factors.

1.3 Justification

Ischemic stroke is a major cause of morbidity and mortality worldwide (Feigin et al., 2015). Screening, identification, and management of carotid artery atherosclerosis as a risk factor for ischemic stroke can therefore help in early intervention, and ultimately, prevention of ischemic strokes.

Early detection of atheromatous changes in the carotid artery has the potential of reducing stroke related morbidity and mortality. Various vascular techniques can now be used to evaluate Carotid atherosclerosis which includes Carotid Doppler Ultrasonography, transcranial Doppler, CT angiography, Magnetic Resonance angiography, contrast enhanced Magnetic Resonance angiography (Carroll, 1991).

Among the tests Carotid Doppler ultrasound is a noninvasive, cost effective and easily available mode of investigation to identify the patients with significant stenosis and other changes due to atherosclerosis (Hunink, Polak, Barlan, & O'leary, 1993).

Since the noninvasive tests are used for preliminary screening before doing Carotid endarterectomy the value of the tests lies in their ability to accurately identify patients with significant stenosis. However newer studies of older technologies and the emergence of new noninvasive tests justify a revaluation of published data about noninvasive testing of Carotid arteries.

Doppler sonography is useful in evaluating and determining carotid artery atherosclerosis and its risk assessment hence informing the intervention measures. Correct diagnosis is vital in making choices on the need for surgical procedures on the patient (Fernandes et al., 2016). Being non-invasive and of affordable cost makes color Doppler sonography attractive. Carotid Doppler sonography is affordable and its sensitivity is close to that of angiography (Nedelmann et al., 2009).

Doppler sonography has no ionizing radiation and has the advantage of having the ability to characterize plaque into different risk groups. Accurate evaluation of the carotid arteries can result in many stroke cases and the associated complications being prevented (Chamarthi, Lava Kumar, Nirusha, Pravallika, & Kejriwal, 2017). With limited information on this in Kenya, this study seeks to contribute by providing information concerning the pattern of carotid artery disease in patients with ischemic stroke using the color Doppler sonography.

The purpose of this study is to evaluate the various changes in Carotid arteries by Doppler Ultrasonography in patients who had already suffered a stroke, which in turn determine the value of using Carotid Doppler Ultrasonography as a modality of test to screen for atherosclerosis and the risk of developing stroke in people with risk factors for stroke. This will in turn help in formulation of management protocols of patients who have suffered stroke or have suffered other symptoms of a subclinical ischemic event, e.g. transient ischemic attack, amaurosis fugax, among others. .

1.4 Significance of the study

The information obtained in this study will be vital in informing practices in the health sector. It will also provide relevant data that will inform decisions and policy on the diagnosis and management of carotid atherosclerosis in stroke patients. This being a less explored area with limited information in Africa, the study will inform and provide baseline data and help identify gaps that will be useful to students and scholars interested in this field of study. The data, once available, has the potential to guide the process of developing screening and management protocols for patients at risk of ischemic stroke.

1.5 Scope of the study

This study will cover conditions identified during carotid artery color Doppler sonography among stroke patients with more emphasis on carotid stenosis and the risk factors for those diseases as identified from the patients' history and records.

1.6 Research Questions

The study sought to answer the following questions.

- What are the patterns of Carotid Doppler Ultrasound findings, the proportion of Internal Carotid Artery stenosis, and its associated factors in patients presenting with ischemic stroke at MTRH?

1.7 Objectives

1.7.1 Broad Objective

- To describe the patterns of carotid atherosclerosis using ultrasound, the proportion of ICA stenosis, and its associated factors among ischemic stroke patients at MTRH.

1.7.2 Specific Objectives

1. To describe the carotid artery Doppler ultrasound findings in patients with ischemic stroke at MTRH.
2. To determine the proportion of patients with internal carotid artery stenosis amongst patients with ischemic stroke presenting at MTRH.
3. To determine the factors associated with internal carotid artery stenosis in patients with ischemic stroke at MTRH.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This section covers information on Doppler sonography of carotid artery in ischemic stroke patients from peer review journals.

2.2 Doppler Ultrasound of the carotid arteries

Doppler ultrasound techniques are based on the Doppler equation which was described by Christian Johann Doppler in 1842. The underlying principle is that when sound or light waves are moving between a transmitter and a receiver which are stationary in relation to each other, then the receiver will register the same frequency as the transmitter emitted. If there is relative movement towards each other then the receiver will register a slightly higher frequency (shorter wavelength) than was transmitted; conversely if there is relative motion apart, then the receiver will register a slightly lower frequency (longer wavelength). These small changes are known as Doppler shifts and can easily be measured by modern ultrasound equipment through direct comparison of the returning frequency with the transmitted frequency.

The derivation of the Doppler equation used in medical ultrasound is;

$$Fd = Ft - Fr = 2FtvcosQ/c$$

Fd- is the frequency or Doppler shift, Ft is the transmitted frequency, Fr is the received frequency. v is the velocity of the reflector (usually blood in the vessels). Q is the angle between the direction of flow of blood and c is the mean velocity of sound in tissues, 1540m/s. using modern ultrasound equipment the only variable which is unknown is the velocity of the reflecting blood cells (Middleton, Foley, & Lawson, 1988).

2.2.1 Duplex Doppler

These machines combine real time imaging with pulsed Doppler. This allows the operator to identify a specific segment in a particular vessel and to place the gate, or sample volume, at a specific location so that the source of the Doppler signal is known. In addition to transmitting the Doppler information as an audio signal, it can also be displayed as a spectral trace, or waveform scrolling across the screen.

Vessels have different wave forms or Doppler signatures which depend primarily on the size of the vessel and the type of capillary bed they are supplying. Internal Carotid artery supplies the relatively low resistance cerebral circulation and therefore has high diastolic flow in comparison to the external Carotid artery which supplies the higher resistance circulation of the scalp and face resulting in significantly lower diastolic flow. The waveform characteristics can change significantly in response to physiological stimuli as shown by the increased diastolic flow that is seen in femoral arteries on exercising the leg muscles (Zwiebel, 2000).

2.2.2 Colour Doppler

In colour Doppler systems the pulses along each scan line are divided on return to the transducer, some are used to provide imaging information and the rest are used to calculate the mean Doppler shift within small pixels of the image. The mean shift information is then coded on a colour scale and displayed as a colour map over the grayscale image. The choice of colours is arbitrary: usually shades of blue and red are used to represent flow towards and away from the transducer, with paler shades of the colour representing higher velocities (Duffy, 1993).

2.3 Colour duplex evaluation of carotid stenosis

The detection of Carotid stenosis and occlusions with colour Duplex sonography relies mainly on the combination of B mode and colour encoded flow imaging. The B mode image defines the outer boundary of the vessel wall and the lumen reducing material while the colour image demonstrates the flow pattern. Doppler frequency analysis serves mainly to confirm the imaging findings and may be necessary for quantification (Bongartz, 1996).

The severity of the Carotid stenosis may be evaluated by measuring the diameter or area of residual lumen and diameter or area of the original lumen. Thus the percentage of luminal reduction can be calculated. The accurate measurement of the Carotid Stenosis is dependent on good quality images and on the attainment of the true cross section of the vessel. Cross sectional images of diagnostic quality cannot always be obtained if there are tortuous vessels and calcified plaques. In such cases severity of stenosis must be estimated from Doppler spectral information (Erickson et al., 1989).

Colour Doppler ultrasound facilitates Doppler spectral analysis by rapidly identifying areas of flow disturbances. The highest velocity shifts can frequently be identified by colour flow Doppler aliasing. Colour Doppler ultrasound facilitates this by placing the pulsed wave Doppler sample volume in the region of the most striking colour abnormalities. Power Doppler ultrasound showing better edge definition and relative angle dependent flow imaging offers the potential for better visual assessment of degree of stenosis (Carroll, 1991).

2.4 Grading of stenosis

Carotid stenosis usually begins to cause velocity changes when the stenosis exceeds 50% diameter reduction (reduction of 70% cross sectional area) (Carroll, 1991). Flow velocity increases as severity of stenosis increases. Velocity increases are focal and more pronounced immediately distal to a stenosis. The point of maximum velocity can be easily determined on a color Doppler image. Commonly used methods of acoustic estimation of the degree of stenosis include the following (E. G. Grant et al., 2003).

1. Measurement of peak systolic velocities and end diastolic velocities
2. Measurement of ratios (internal Carotid artery peak systolic velocity /Common Carotid peak systolic velocity)
3. Some laboratories characterize degree of stenosis in terms of exact percentages. The ranges and measurements vary from laboratory to laboratory. Factors that affect measurements include the equipment used, the person performing the ultrasound, and the sites sampled for measurement.

In most cases, ICA grading is based on velocity criteria built on percept that flow volume is equal to vessel area multiplied by PSV. With volume flow being relatively constant, vessel lumen diameter and PSV are inversely associated. Hence, with decrease in diameter of vessel, PSV increases to maintain the flow volume.

Spencer and Reid, showed that if the diameter of the vessel reduces by > 50%, there is an exponential rise in the PSV at the stenosis site, maintaining volume flow until stenosis is nearly 70%. When stenosis is in excess of 70%, the volume flow reduces with exponential PSV increase, When the ICA stenosis is > 96%there is high gradient across the stenosis for the pressure resulting from the velocity elasticity and myocardial contractility to enable blood flow through the residual lumen, hence drop in PSV until velocity is zero and occlusion of the vessel occurs (Spencer & Reid, 1979).

Stenosis grading has changed over time with the North American Symptomatic Carotid Endarterectomy Trial (NASCET) grading being commonly used (NASCET, 1991). However, long before the NASCET recommendations, the calculation of percentage ICA stenosis was calculated by comparing residual ICA lumen width with estimated ICA diameter measured at the stenosis site. But considering that ICA out wall can only be observed on angiogram if it is calcified, ICA diameter measures from the angiogram are mostly estimates hence high intra and inter observer variability and challenges in reproducibility. The NASCET ICA percentage stenosis measurement was angiographically standardized by carrying out a comparison of ICA residual lumen width at the narrowest point with lumen diameter of the normal distal ICA; at a point beyond any post-stenotic dilation (Ho & Reddy, 2010).

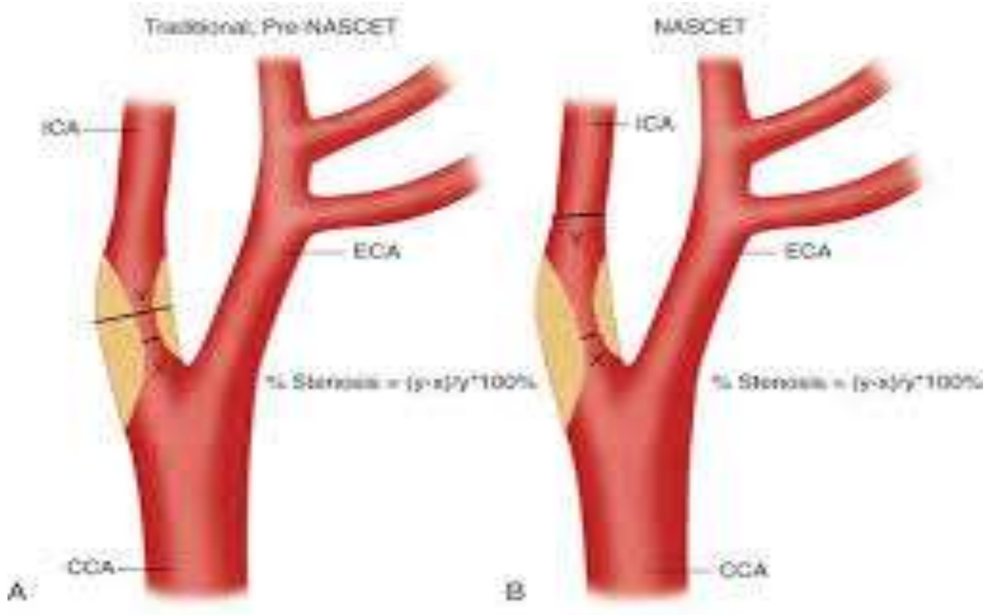


Figure 6: Carotid arteries
Adopted from: (Ho & Reddy, 2010)

There has been attempts to correlate EDV, PSV and PSVR measurements criteria for stenosis with angiographically computed stenosis percentage with varied outcomes being reported (Moneta et al., 1993; Sabeti et al., 2004). It has been found that the velocity criteria is more accurate with positive predictive value for stenosis of more than 70% but less reliable for moderate stenosis grading (< 50%). It has been shown that it is sometimes difficult to differentiate ICA stenosis by 10% increments (Sabeti et al., 2004). Hence, to ensure accuracy, focus is placed on whether stenosis is more than or less than a given stenosis percentage.

In most instances, stenosis is categorized as < 50%, 50-69%, 70-96% and >96% and carotid endarterectomy is recommended in individuals with stenosis of > 70%. In a study by Grant et al., reported varied accuracy in threshold of PSV and PSVR values but their specificity and sensitivity were inversely proportional. Lower thresholds having higher sensitivity were recommended when Doppler is used for screening. However, higher threshold are recommended in case Doppler is used for diagnosis purposes without angiography imaging being done for confirmatory purposes to ensure high specificity (E. Grant et al., 1999).

The Society of Radiologists in Ultrasound (SRU) experts' panel developed guidelines for ICA stenosis grading using Doppler ultrasound. According to their recommendations, PSVR of less than 2.0 and PSV < 125cm/s are indicative of stenosis <50%, PSVR of 2.0- 4.0 and PSV of 125-230 cm/s is indicative of 50%-69% stenosis, PSVR greater than 4.0, EDV greater than 100cm/s and PSV > 230cm/s are indicative of 70-96% stenosis (E. G. Grant et al., 2003).

With stenosis of more than 96%, there is PSV velocity reduction to the point of vessel occlusion with velocity dropping to zero (Spencer & Reid, 1979). With this in mind, it was recommended that the reduction in diameter by plaque be correlated with velocity based stenosis percentage estimates (E. G. Grant et al., 2003).

However, the use of this criteria is affected by incorrect Doppler angle choices. A high angle results in errors in PSV calculation. Another challenge results from high colour gain leading to bleeding and obscuring stenosis and plaque. In cases of low gain, the colour might not reach the wall of the vessel falsely creating hypoechoic plaque appearance. In case of tortuous carotid arteries as is common among the elderly patients, there might be increased PSV without the presence of stenosis. This calls for caution in diagnosis of stenosis based on PSV elevation alone without plaque evidence (Ho & Reddy, 2010).

2.5 Plaque assessment using ultrasound

Colour Doppler and grey scale imaging of the transverse and longitudinal planes are needed when evaluating plaque. This is used in the estimation of the percentage reduction in the diameter caused by plaque which is then correlated with the measurements of PSV. The surface texture and echotexture is also assessed with plaque being characterized as either echogenic or hypoechoic. Irregular hypoechoic plaque is linked to increased neurological events risk and that of increased progression of plaque (Polak et al., 1998).

Echogenic plaque is depicted well on grayscale imaging. The echogenic plaques that are associated with posterior acoustic shadowing are considered as calcified. Hypoechoic may not be visible, but the hypoechoic plaque is well observed on colour Doppler as a signal void. This is also the case with surface irregularities which are well observed on colour Doppler. However, Doppler is not very accurate in plaque ulceration identification. This is also the case with the use of angiography, hence histologic diagnosis being key in plaque ulceration. While color Doppler is important for hypoechoic plaque identification, it does not replace the need for gray scale as the plaque may be obscured by color blooming especially during systole resulting in underestimation of the burden of plaque (Scoutt et al., 2010).

Analysis of waveform

The use of spectral Doppler waveform offers detailed information regarding the carotid artery than that given by the measure measurement of PSV. The analysis of the morphology and contour of the waveform gives physiological details regarding the distal cerebral circulation and other proximal vessels and such information cannot be visualized directly on ultrasound examination. This helps deduce the presence of distal or proximal diseases associated with the cardiovascular system (Ho & Reddy, 2010).

Any changes in the waveforms may offer inference to rare iatrogenic conditions in the neck like pseudoaneurysm, and carotid dissections. Doppler waveform abnormalities can be grouped into changes affecting the diastole, systole or the whole cardiac system, for analysis purposes. Abnormalities associated with systolic peak stenosis are mainly associated with changes in the systolic peak configuration (Scoutt et al., 2010).

a) Artifacts in ultrasound

At least 18 artifacts have been identified in Carotid ultrasound; most of them occur during imaging (E. G. Grant et al., 2003).

The common artifacts include the following:

• Reverberations: If 2 or more reflectors are in the sound path, multiple reflections occur and may result in unreal images on the screen.

• Refraction: A refracting object bends the ultrasonic waves so that a reflector is improperly positioned on the screen.

• Shadowing: A strong reflector reduces the quantity of ultrasound that is intended to pass beyond it; the object behind the reflector is "shadowed"; in the case of a plaque, the artifact proves to be helpful in identifying it.

• Enhancing: Enhancing is the opposite of shadowing.

• Aliasing: This occurs during spectral analysis and colour flow imaging. During spectral analysis, the spectrum is "wrapped" around the screen so that the top of the waveform is seen at the bottom. This problem can be corrected by increasing the pulse repetition frequency (PRF), increasing the Doppler angle, shifting the baseline, lowering the emitted frequency, or using a continuous wave device.

2.5 Grey scale and Doppler sonography findings of the carotid arteries in patients with ischemic stroke.

In a study by Haq et al., Doppler sonography was used to evaluate carotid arteries in ischemic stroke patients. Out of the 50 patients studied, 28 patients had ischemic stroke on right side and 21 had ischemic stroke on left side. One had bilateral involvement. On right side, 13 patients had anterior circulation infarct, 11 patients had posterior circulation infarct and four had watershed zone involvement. On the left side, 11 patients had anterior and five had posterior circulation stroke and five patients had watershed zone infarct. MCA territory was most commonly involved in anterior circulation stroke. Out of 21 MCA stroke patients, 10 had right-sided and 11 had left-sided stroke (Haq et al., 2017).

In a study by Sethi and Gupta, a total of 36 plaques were observed out of which 19 (53%) were echogenic, 13 (36%) were calcified and 4 (11%) were hypoechoic. Two of the vessels were completely occluded. Ulceration was not detected on B-mode in any of the plaques. On B-mode imaging no ulceration was observed. On color flow imaging two of the plaques showed evidence of ulceration. 5.5% of plaques showed evidence of ulceration on color flow imaging. Of the 36 plaques 11 were located in common carotid artery, 7 in internal carotid artery and 18 at the bifurcation (Sethi, Solanki, & Gupta, 2005).

Overall 50% of the plaques were located at the bifurcation, 19.4% in internal carotid and 30.6% in the common carotid artery. Hypoechoic plaque was missed on B-mode imaging. Both color and spectral waveform analysis similarly classified four vessels in 40-59% stenosis group. Both Color spectral waveform analysis respectively similarly classified two vessels, one each in 60-79% and 80-99% stenosis group. (Color flow imaging diagnosed two vessels as completely occluded, both of which were assigned same stenosis category by duplex imaging. Power Doppler was used in two patients with complete occlusion on conventional duplex scanning and color flow imaging. In both patients findings of color flow imaging and spectral analysis were confirmed on power Doppler imaging (Sethi et al., 2005).

Garg et al., Color Doppler was used to Evaluate extracranial Carotid Arteries. Severe stenosis i.e. ≥ 70% was found in 7 males (3.4%) and 1 woman (0.6%). Near occlusion was observed in 2 men and one woman. Same was observed for total occlusion. The commonest lesion was atherosclerotic plaque. Majority of the plaques were low echogenic 142 (40%), followed by calcified plaque 99 (28%), moderately echogenic 24 (7%) and 89 (25%) hyperechogenic plaque. Maximum cases of plaque were observed on the right side (44%) followed by bilateral (30%) and left side (26%).

Analysis of the site of involvement showed maximum plaque at bifurcation (35% on right side and 41% on left side). No significant pattern was observed for involvement of CCA, ICA and ECA across left and right side (Garg, Kashikar, & Phatak, 2016).

In a similar study carried out by (Fernandes et al., 2016), to evaluate carotid arteries in stroke patients 50 patients were recruited in the study. Among the 50 patients, 40% had right sided stroke, 36% had left sided stroke, and 4% had bilateral involvement while the rest had TIA. In another study by Baidya among 50 patients with ischemic stroke among young adults in India to look at their radiological presentation, it was reported that 26 of the patients had the stroke localized on the left side while in the remaining 24, it was based on the right side (Baidya, 2015).

2.6 Prevalence of carotid artery stenosis

In a study carried out in India by Haq and colleagues to evaluate carotid artery in patients 50 with ischemic stroke, 31 had carotid artery stenosis of which 12 were female and the rest were male. Size of carotid stenosis was measured using percentage area reduction and it was found that the majority of those with carotid stenosis were between the ages of 51- 60 years. Of those with stenosis, 12 had stenosis less than 50% while the rest had stenosis greater than 50% (Haq et al., 2017).

Garg et al carried-out color Doppler evaluation of extracranial carotid artery and found the percentage of stenosis to increase with age and was more prevalent in male than female. Among the total 1043 cases under study, 33.9% (354) patients had stenosis. Those with significant stenosis (> 50%) were 17.8% (63) with the majority, 82.20% (291) having mild stenosis. severe stenosis (>70%) was shown in seven male (3.4%) and in one female (0.6%). The prevalence of severe stenosis was shown to be low with mild stenosis being high. Stenosis was also more severe in men than women (Garg et al., 2016).

Similarly, Sethi et al. carried out Doppler imaging evaluation of carotid arteries among 63 patients with ischemic stroke in India. It was reported that 22 of the patients with subcortical infarcts had mild stenosis (<40%) . out of the total 126 vessels examined with color Doppler sonography, 90 had 0 stenosis, 30 had 1- 39% stenosis, 4 had 40-59% stenosis, 1 had 60-79% stenosis, 1 80- 99% while 2 had 100% stenosis (Sethi et al., 2005).

O'Leary and colleagues determined the distribution of detectable carotid artery disease by sonography. The percentage diameter stenosis for every internal carotid artery was estimated by the reader using Doppler data and image. Peak systolic flow Doppler velocity of less than 1.5 m/sec were taken to show absence of significance lumen stenosis (50%). Data from gray scale imaging were applied in estimating the percentage of diameter stenosis which was taken to be; 0% absent, 1- 24% mild, 25-49% moderate. Peak flow Doppler velocity of between 1.5 to 2.5 m/sec represented stenosis of 50% to 74% while velocity flow of 22.5 indicated 75% stenosis including totally occluded internal carotid arteries (O'Leary et al., 1992).

The different measures of the thickness of the wall of carotid artery were summarized into two variables with one being for common carotid and the other for the internal carotid artery to be able to quantify the extend and degree of thickening. The common carotid artery maximum thickness was taken to be the mean of maximum (m) wall thicknesses for near (N) and far (F) wall (W) on both the left (L) and right (R) sides: mLNW+mLFW+ mRNW+mRFW/4. The same definition was adopted for the internal carotid artery and the three scans average was taken. Maximum stenosis was taken to be the largest stenosis seen on left or right side. Using maximum stenosis as continuous variable, it was coded as the midpoint of the interval to 0%, 1-25%, 26-50%, 51-75%, or 76-100% (O'Leary et al., 1992).

From this study, it was found that stenosis increased significantly with age with the prevalence of severe stenosis (75- 100%) being low at 2.3% in men and 1.1% in women. Moderate stenosis (50-74%) was also rare occurring in 5.3% of men and 4.0% of women only. Mild stenosis (1-49%) was the most prevalence being seen in 70% of the men and 60% of women. Men had significantly higher stenosis at all ages as compared to women of the same ages. Of the participants, only 25% of men and 38% of women had vessels without plaque deposition (O'Leary et al., 1992).

Detectable carotid stenosis was present in 75% of men and 62% of women, although the prevalence of >50% stenosis was low, 7% in men and 5% in women. Maximum stenosis and maximum wall thickness measurements increased with age and were uniformly greater at all ages in men than in women. Maximum internal carotid artery and common carotid artery wall thicknesses were greater in men than in women at every age, and both increased linearly with age. Wall thickness measurements of the internal carotid artery were uniformly greater than those of the common carotid artery (O'Leary et al., 1992).

In the study by Haq et al., it was reported that Internal Carotid Artery (ICA)/ Common Carotid Artery (CCA) Peak Systolic Velocity (PSV) predicted stenosis efficiently where by a ratio of 3 (greater than 60%) indicates significant stenosis (Haq et al., 2017).

2.7 Risk factors of carotid artery atherosclerosis

Haq and colleagues reported that hypertension was associated with carotid atherosclerosis and increased Carotid Intima Media Thickness (CIMT). Hyperlipidemia was shown to be positively correlated with carotid disease and increased CIMT. Multiple logistic regression analysis showed that hyperlipidemia, diabetes and smoking were shown to be statistically significant associated with carotid stenosis and CIMT (Haq et al., 2017). Fernandes et al. also reported smoking and hypertension to be the common significant risk factors for ischemic stroke in their study (Fernandes et al., 2016).

Sethi et al, reported that Male sex , Presence of hypertension, post-menopausal state, smoking, diabetes mellitus, history suggestive of peripheral arterial disease, systolic, blood pressure, previous CVA were determined to be statistically significant risk factors for stenosis (Sethi et al., 2005).

O' leary and colleagues reported that stenosis and stroke had highly significant associations with all three ultrasound measures used with the strength of association being varied. There was strongest correlation between history of coronary heart disease and the maximum internal carotid artery wall thickness (O'Leary et al., 1992).

Relations of the continuous risk factors with wall thickness and percent stenosis were computed using the partial correlation coefficient after adjustment for age and sex. The largest correlations were seen for systolic blood pressure, whereas diastolic blood pressure was not associated with maximum common wall thickness and only weakly correlated with the other measures. Total and LDL cholesterol and trigryceride levels were all positively associated with carotid abnormalities, whereas HDL cholesterol was negatively associated with them. Glucose and insulin levels were positively associated with the ultrasound measures. Left heart ventricular mass measured by echocardiography was positively associated with all three measures (O'Leary et al., 1992).

Relations of dichotomous variables were assessed by logistic regression analysis. Coronary disease was reported and confirmed in 25.6% of subjects. The prevalence of coronary disease was examined by both stenosis grade and quartile of wall thickness of the internal and the common carotid arteries. Maximum stenosis was highly associated with coronary disease. The prevalence of coronary disease increased from 17.8% in those with 0% stenosis to 45.8% in those with 75% stenosis. The odds ratio for coronary disease comparing those with stenosis to those with 0% stenosis increased from 1.50 for those with 1-24% stenosis to 3.90 for those with 75% (O'Leary et al., 1992).

Similar results were obtained for maximum wall thickness, although the differences between categories were less striking for the common wall thickness. The differences between categories were impressive for the internal wall thickness, even though nearly all subjects represented in the three highest stenosis categories are grouped together in the highest wall thickness quartile.

Multiple logistic regression was used to assess independent relations of carotid measures to prevalent coronary disease. A model of predicting the risk of coronary disease that included maximum stenosis, the two measures of wall thickness, age, and sex showed that after adjustment for age and sex, both the maximum internal wall thickness and the maximum common carotid wall thickness were significant correlates of coronary disease. The likelihood of coronary disease was estimated to increase by 36% for a 1-SD (0.69-mm) increase in the maximum internal wall thickness. The relation was somewhat weaker for the maximum common carotid wall thickness with a 1-SD (0.22-mm) increase estimating a 9% increase in risk. Maximum stenosis did not add significantly to the prediction of risk of prior coronary disease, however (O'Leary et al., 1992).

Prior stroke was reported and confirmed in 4.7% of participants. All three carotid ultrasound measures were associated with a history of stroke. The incidence of prior stroke was 3.3% in those with 0% stenosis and increased to 10.8% in those with 75% stenosis. The odds ratio for prior stroke comparing those with stenosis to those with 0% stenosis increased from 1.33 for those with 1-24% stenosis to 3.60 for those with 275% stenosis (O'Leary et al., 1992).

When ultrasound measures were included in a multiple logistic regression model for the prediction of prior stroke, adjusting for age and sex, both measures of wall thickness were significantly associated with a history of stroke and had similar risk ratios associated with a 1-SD change in wall thickness. Each of the wall thickness measures showed about a 20% increase in risk for a 1-SD change ($p<0.005$). As in the instance of prior coronary disease, maximum stenosis did not add significantly to the prediction of risk of prior stoke once adjustment was made for age, sex, maximum common carotid artery wall thickness, and maximum internal carotid artery wall thickness (O'Leary et al., 1992).

CHAPTER THREE: METHODOLOGY

3.1 Study Site

The study was conducted at the Moi Teaching and Referral hospital, radiology and imaging department, in the ultrasound room. Patients were referred from the internal medicine department.

The hospital is located in Eldoret town, the headquarter of Uasin Gishu county. It is 350km North West of the Kenyan capital Nairobi. It's the second National referral hospital which also serves as a teaching hospital for Moi University school of Medicine (MUSOM), School of Nursing, School of Public Health, and the School of Dentistry and Kenya Medial Training Centre, (KMTC). It is also an internship Centre for medical, nursing and clinical officers.

Its catchment includes the western part of Kenya and the North Rift which is about 20 million people. The hospital has a bed capacity of over 700 patients, with several departments which include, surgery, pediatrics, medicine, obstetrics and gynecology, radiology and imaging, accident, and emergency department, among others.

Radiology Department is composed of both diagnostic and interventional radiology. It has three CT scan machines, one MRI machine and five ultrasound machines. The staff comprises of consultant radiologists, registrars, radiographers, and other support staff. (www.mtrh.or.ke/).

3.2 Study Design

This was a facility based cross-sectional study done over a period of one year from September 2018 to august 2019. This is an observational type of study design where the exposure and outcome are measured at the same point in time. The design is fast and relatively affordable. It is also key when determining the burden of a condition in the population under study as was the case in this study where the prevalence of stenosis was sought. However, causal relationship cannot be inferred from cross sectional studies. (Setia, 2016)

3.3. Study Population

Study population included all adult patients who presented with acute ischemic stroke, and the diagnosis confirmed on CT at MTRH

3.4 Eligibility Criteria

3.4.1 Inclusion criteria.

For all patients who presented with a CT diagnosis of acute ischemic stroke, consent was obtained and were included in the study were included.

For patients who were unconscious or semi-conscious, consent was obtained from the next of kin

3.4.2 Exclusion criteria

i. Patients with documented valvular heart disease. (having been confirmed on echocardiography/ECG)

3.5 Sample Size

Literature shows that the proportion of patients with carotid artery atherosclerosis among those with ischemic stroke in a study carried out in India was 24.0% (Fernandes et al., 2016). Thus in order to study the patterns of carotid artery disease among the patients with ischemic stroke we determined the sample size. In order to be 95% sure that we report the proportion of patients with carotid artery disease to within plus or minus 5% of the reported value of 24.0% we determined the sample size using the following formula (Israel, 1992).

$$n = \left(\frac{Z_{1-a/2}}{d}\right)^2 \times P \times (1-P)$$

$$= \left(\frac{1.96}{0.05}\right)^2 \times 0.24 \times (1-0.24)$$

$$= 281$$

Where

Z_c is the quantile of the standard normal distribution corresponding to c x 100%, c = (1-a/2), a = type I error equal 5%;

d is the margin of error, equal to 5%;

P is the proportion of patients with carotid artery atherosclerosis among those diagnosed with ischemic stroke.

Under an infinite population size a total of 281 patients with ischemic stroke would need to be recruited in the study. However, the population size to be sampled is finite with an average of one ischemic stroke patients diagnosed every day in the radiology clinic. This gives an average total of 240 (=1 x 20 days a month x 12 months) ischemic stroke in 12 months. Thus correcting our sample size for this finite population size gives

n/1+n/N = 281/1+281/240

Hence a sample size of 130 ischemic stroke patients

However, for the study period, from September 2018 to August 2019, 75 ischemic stroke cases were referred to radiology department for a carotid artery ultrasound.

Hence a census methodology was used to recruit all eligible participants into the study, and a sample size of 71 patients was attained during the study period.

3.6 Study Procedure

Clinicians in the medical wards were sensitized about the study. The clinicians would send the patients to the radiology department for carotid ultrasonography. Patients presenting with a confirmed diagnosis of ischemic stroke on CT and sent for carotid sonography. Patients who met the eligibility criteria were selected as participants in the study. Informed consent was sought and patients enrolled into the study. A semi-structured questionnaire was administered by the principal investigator and further information obtained from the patient's records.

Clinical history was then taken from each of the patients and patient's kins. Information about their past medical history as regards diabetes, hypertension and heart disease was also obtained from the patient files and recorded. The diagnosis of hypertension and diabetes was made by the primary physician.

A study participant was considered to have hypertension if he/ she was receiving medications for high blood pressure, OR was newly diagnosed.

For the newly diagnosed patients, the diagnosis of hypertension was made by clinicians based on the American Heart Association guidelines (2017) where a blood pressure of > 130/80 mmHg on two occasions at-least one week apart, was regarded as hypertension.

A study participant was considered to have diabetes if he/she was receiving medications for diabetes mellitus or was newly diagnosed.

The diagnosis for diabetes was also made by the clinicians based on the American Diabetes Association guidelines (2015), where 4 criteria were used for diagnosis as described; hemoglobin A1c ≥ 6.5% OR fasting plasma glucose ≥ 7.0 mmol/l OR random plasma glucose ≥ 11.1 mmol/l, OR a 2- hour plasma glucose of ≥ 11.1 mmol/l during oral glucose tolerance test using a load of 75g anhydrous glucose dissolved in water.

A positive smoking history was considered when a patient self-reported smoking as at the time the history was taken as indicated in the records by the clinician

A standard carotid Doppler ultrasound exam was then conducted by the principal investigator. this was done using a real time scanner. Mindary M7 machine with 7.5-10 MHz linear array transducer, with grey scale and Doppler capability was used.

Carotid arteries were examined with patient in the supine position. Neck exposure was enhanced by tilting and rotating the head away from the side being examined, and ipsilateral shoulder being dropped as far as possible. The examiner was seated at the right side of the patient. The posterolateral and far posterolateral transducer positions were used to examine the carotid arteries in long axis (longitudinal). Short axis (transverse) views of the carotid arteries were obtained from an anterior, lateral or posterolateral approach. All the examinations were performed by the same operator or a trained assistant with a Doppler angle of ≤60°.

On gray scale, carotid intima media thickness(CIMT) presence or absence of plaque, location of plaque and plaque characteristics such as echo pattern, calcification, any ulceration, or intra-plaque hemorrhage were evaluated.

On Doppler study, PSV and EDV of CCA, ICA and ECA was evaluated. The society of radiologists in ultrasound (SRU) consensus criteria of 2004 in the United States was used to determine the degree of stenosis of the internal carotid artery. The SRU criteria involves estimating the percentage of stenosis using ICA PSV, ICA/CCA PSV ratios, and degree of stenosis at most stenotic portion

Details of the ultrasound protocol are in the appendix.

The images were archived and later reviewed by the principal investigator and two consultant radiologists and a consensus of the findings recorded. Patients were given a hard copy of the results. all information was kept confidential in a secure cabinet accessible by the principal investigator.

Standard references were used for interpretation. The following were considered as the normal reference ranges for this study.

CIMT- < 1mm

ICA PSV <125 cm/sec.

ICA EDV < 40 cm/sec.

ICA/ CCA ratio < 2.0

The Society of radiologists in ultrasound criteria was used in the stratification of ICA stenosis as represented below.

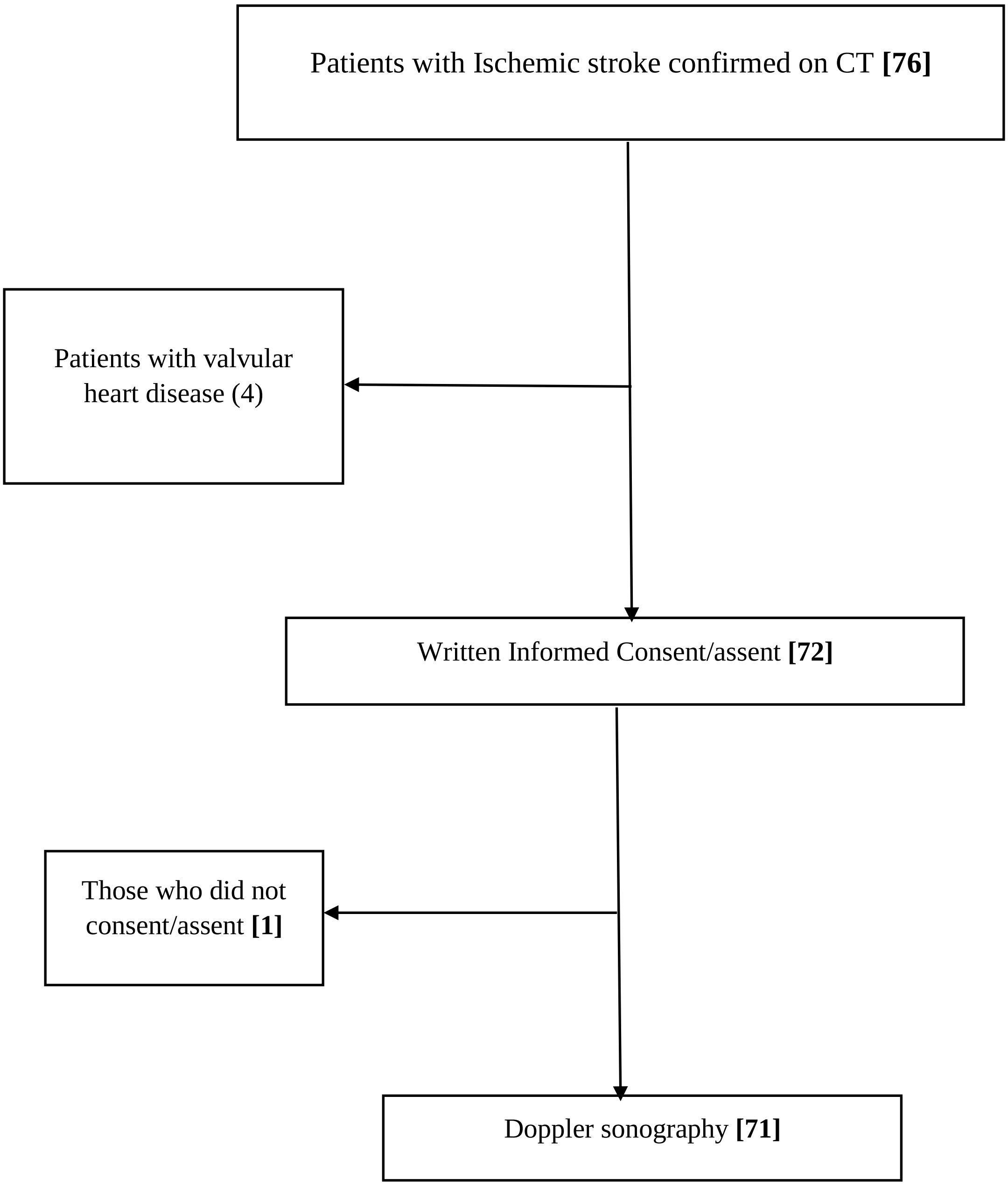
Table 1: SRU Criteria

	Primary parameters		**Secondary parameters**	
Degree of stenosis, %	ICA PSV, cm/sec	Plaque estimate , %	ICA/CCA PSV ratio	ICA EDV cm/sec
Normal	< 125	None	<2.0	<40
<50	<125	<50	<2.0	<40
50-69	125-230	≥50%	2.0-4.0	40-100
>70 but less than near occlusion	>230	≥50%	>4.0	>100
Near occlusion	High, low, or undetectable	visible	variable	Variable
Total occlusion	undetectable	Visible, no detectable lumen	Not applicable	Not applicable.

Society of radiologists in ultrasound(SRU) Consensus criteria.

Adopted from E.G.Grant et al, 2003

3.7 Study Schema



3.8 Data Collection, Entry and Management

Data collected was recorded in a data collection form.

Data entry was done into a standard database created using Microsoft excel. The

participant data was anonymized of the patient identifying information and the database was encrypted with password to ensure that confidentiality is maintained. The password was accessible to the investigator alone. The entered data was checked for consistency, missing data among other integrity issues, and cleaned appropriately. After data entry and data cleaning was finalized encrypted backups of the database were created using removable storage devices such as memory sticks and hard drives that were stored in separate safe locations were created. This helped cushion against data loss.

The cleaned copy of the database was then available for analysis.

3.9 Quality control

The ultrasound was performed by the principle investigator at the MTRH ultrasound rooms. The images were reviewed by the principle investigator and at least two consultant radiologist and a consensus of the findings recorded.

3.10 Data Analysis

The data entered in MS Excel was imported to IBM Statistical Package for Social Sciences (SPSS) Version 23.0 where it was coded and analyzed. Descriptive statistics including measures of central tendency such as the mean and the median were used to summarize the continuous variables such as age and CIMT. The corresponding measures of dispersions including the standard deviation for the mean and Interquartile range (IQR) for median were reported. Categorical variables such as patterns of carotid artery, sex, history of hypertension, diabetes among others were summarized using frequencies and the corresponding percentages.

Inferential analysis was carried to assess the factors associated with stenosis. Chi-square test and Fischer's exact test were done to assess the association between presence of stenosis and diabetes, hypertension and smoking and gender. Mann Whitney U test was conducted to determine the association between the distribution of age and stenosis. A P value < 0.05 was taken to be statistically significant.

3.10.1 Data Presentation and Dissemination

The data was presented in form of charts, tables, and graphs. The results were presented to department of radiology and imaging, Moi University School of medicine.

3.11 Limitations

1. There was difficulty in examination of the carotids in semi-conscious patients with a large body habitus and a short neck. This necessitated the use of a pillow behind the patients back to aid in extension of the neck to expose the area under study, and this would have made the patients quite uncomfortable.
2. The study was hospital based and therefore there would be limited generalizability to the rest of the population.
3. Cholesterol levels were not included in this study. This would have added value to this study.

3.12 Ethical Considerations

Ethical approval was granted by Moi University/ MTRH Institutional Research Ethics Committees (IREC), approval no: The purpose and nature of the study was explained to respondents and their concerns addressed. Both oral and written consent were sought from the respondents. Their autonomy was respected. For incompetent respondents, the consent was sought from their guardians. No one was coaxed or forced to participate in the study and respondents were free to withdraw from the study at any time and stage of the study.

Personal Information gathered was kept confidential without identifiers to protect the privacy of the respondents. All necessary measures were taken to ensure the confidentiality of the respondents and information that can point to a given respondent was generalized or omitted from the study report.

3.13 Pre-test

A pre-test study was carried out in ten conveniently selected patients with confirmed CT features of Ischemic stroke at MTRH to test the reliability and validity of the study tools. As there were no changes to the study and the tool after the pre-test, the patients included in the pre-test were included in the final study.

CHAPTER FOUR: RESULTS

4.1 Introduction

A total of 71 patients who were diagnosed with acute ischemic stroke on CT scan between September 2018 to September 2019 at radiology department in MTRH were included in this study.

4.2 Results

4.2.1 Demographic information

Of the 71 participants, 42 (59.2%) were male while the rest, 29 (40.8%) were female. (**Figure 1)**

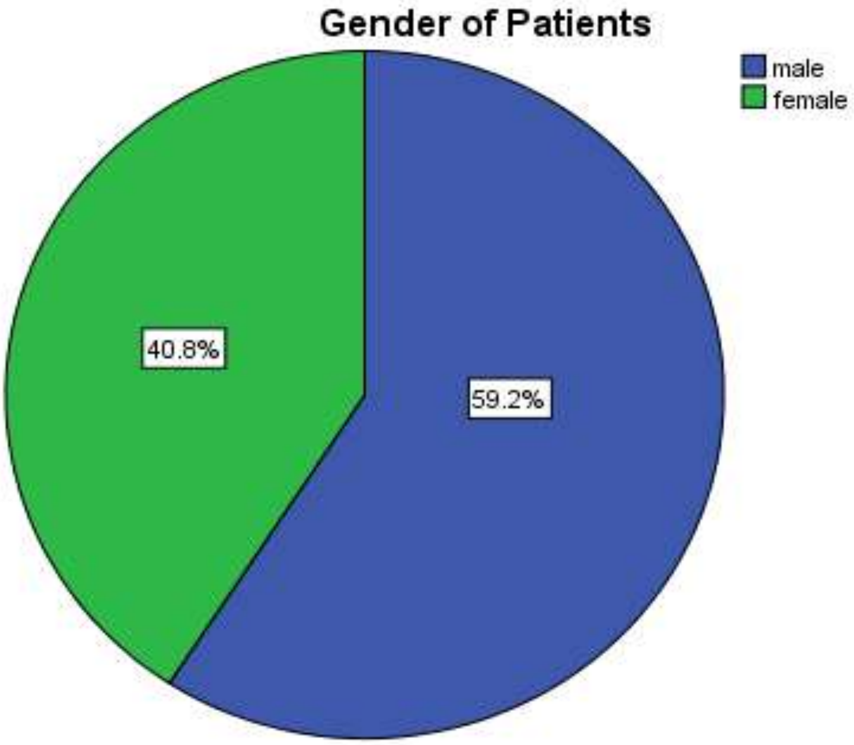


Figure 7: Gender of patients

The mean age of the study participants was 64.21 ± 11.05 (SD) years with a median of 67 years IQR (58-72). The youngest participant was 27 years while the eldest was 84 years. Most, 39 (54.93%) were between the age of 50- 69 years, 26 (36.62%) 70-89 years, 4 (5.63%) 30 - 49 years and 2 (2.82%) less than 30 years of age. (**Table 1)**

Table 2: Age distribution of patients

Age	**Frequency**	**Percent (%)**
Less than 30 years	2	2.8
30 - 49 years	4	5.6
50 - 69 years	**39**	**54.9**
70 - 89 years	**26**	**36.6**

The distribution of the participants' age according to their gender was as shown in **Table 3** below

Table 3: Age distribution according to gender of the patients

Age	Male (42)	Female (29)
Less than 30 years	1 (2.4%)	1 (3.4%)
30- 49 years	1 (2.4%)	3 (10.3%)
50- 69 years	25 (59.5%)	14 (48.3%)
70- 89 years	15 (35.7%)	11 (37.9%)

4.2.2 Territory of infarction

On the territory of infarction, 26 (36.6%) were in the right MCA, 25 (35.2%) left MCA, 8 (11.3%) right ACA, 5 (7.0%), left ACA, 8(11%) 3 (4.2%) lacuna, 2 (2.8%) left cerebellar and 2 in the right cerebellar. **(Table 4).**

Table 4: Territory of infarction

Territory	Frequency	Percent (%)
right MCA territory	26	36.6
left MCA territory	25	35.2
Lacuna infarct	3	4.2
Left Cerebellar infarct	2	2.8
Right Cerebellar infarct	2	2.8
Left ACA territory	5	7.0
Right ACA territory	8	11.3
Total	**71**	**100.0**

Hence, most, 51 were in the MCA territory, 13 ACA territory, 4 cerebellar and 3 lacuna territory. **(Figure 2).**

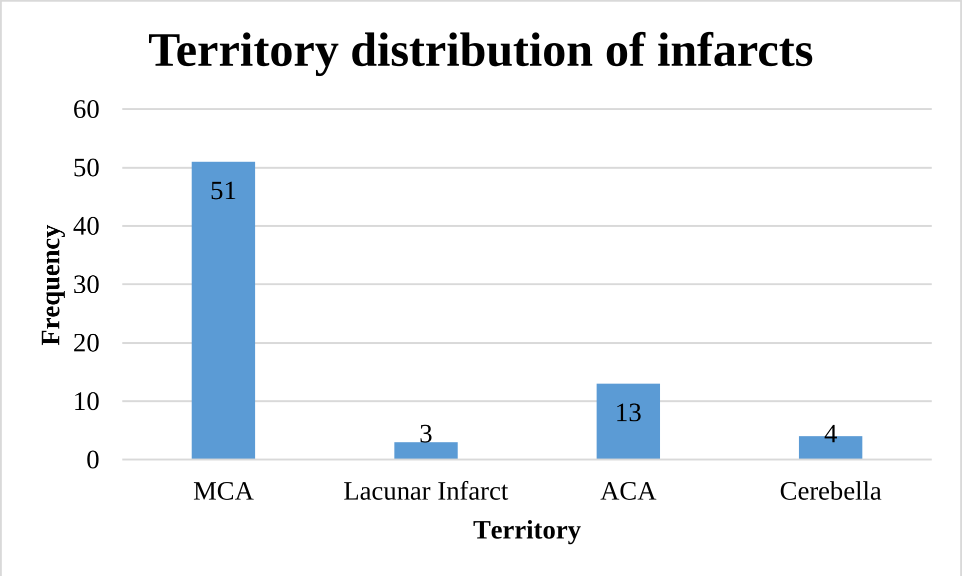


Figure 8: Territory distribution of infarction

Carotid Artery Stenosis among patients with ischemic stroke

A total of 65 (91.5%) had less than 125 cm/sec ICA PSV on the right carotid, 4 (5.6%) had 125-230 cm/sec, 1 (1.4%) had greater than 230 cm/sec while 1 (1.4%) had undetectable ICA PSV on the right carotid. On the left carotid, 67 (94.4%) had a PSV of less than 125 cm/sec, 3 (4.2%) had 125-230 cm/sec, and 1 (1.4%) had PSV greater than 230 cm/sec . **(Figure 3).**

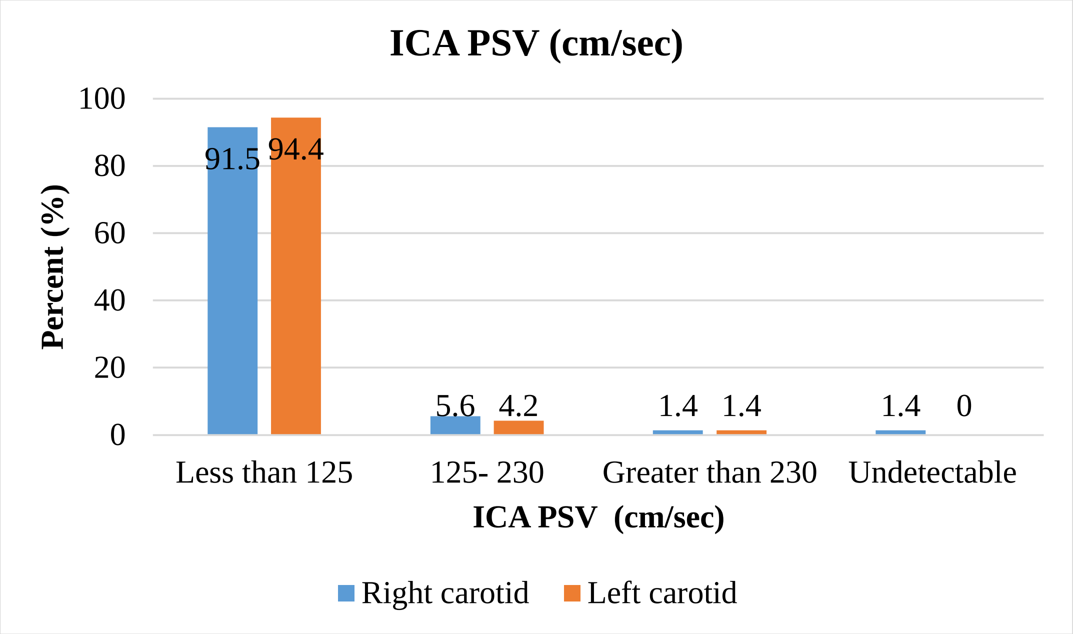


Figure 9: ICA EDV

On ICA EDV, 65 (91.5%) had less than 40 cm/sec, 5 (7.0%) had 40- 100 cm/sec and 1 (1.4%) had undetectable ICA EDV on the right carotid, while on the left carotid ICA EDV, 66 (93.0%) had less than 40 cm/sec, 3 (4.2%) had 40-100 cm/sec and 2 (2.8%) had undetectable ICA EDV. **(Table 5).**

Table 5: ICA EDV

ICA EDV (cm/sec)	Right carotid	Left carotid
Less than 40	65 (91.5%)	66 (93.0%)
40- 100	5 (7.0%)	3 (4.2%)
Undetectable	1 (1.4%)	2 (2.8%)

On the ICA/CCA PSV ratio, 65 (91.5%) had less than 2.0, 5 (7.0%) had 2.0 – 4.0 on the right carotid, and 1 (1.4%) was not applicable. On the left carotid, 66 (93.0%) had less than 2.0, 4 (5.6%) 2.0- 4.0 and 1 had greater than 4. **(Figure 4).**

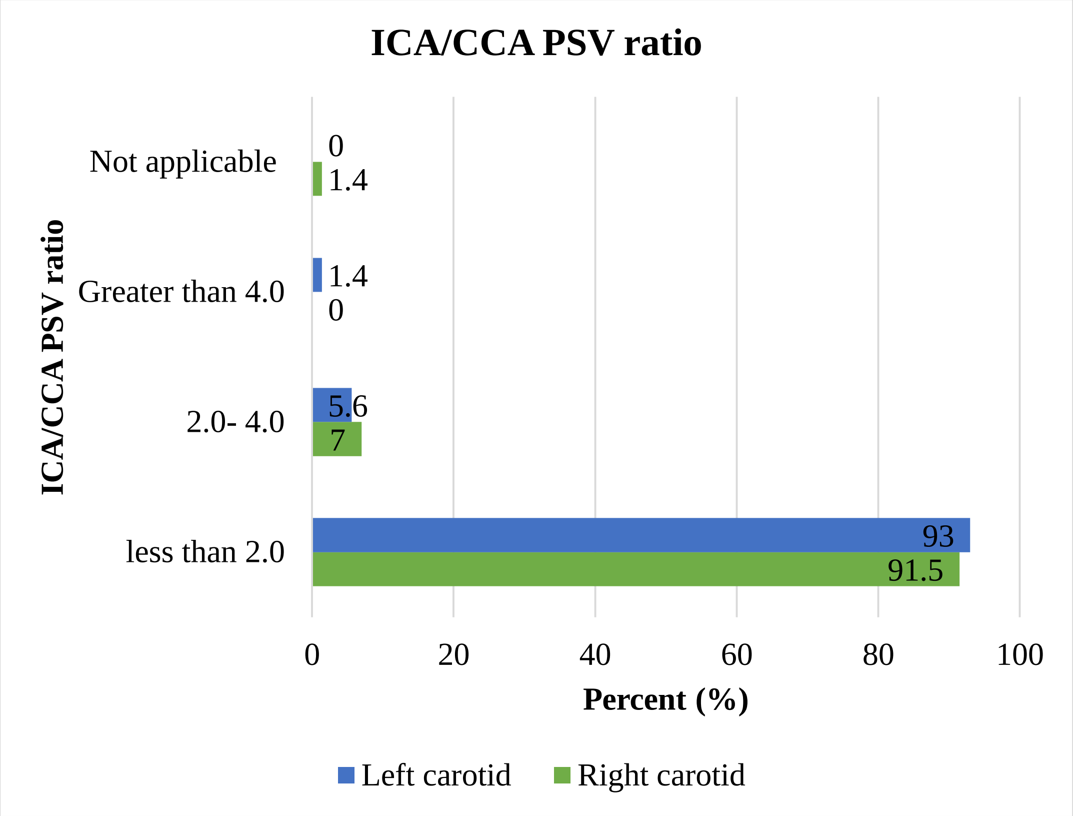


Figure 10: ICA/CCA PSV ratio

Among the patients, 67 (94.4%) and 65 (91.5%) of the patients had stenosis less than 50% on the left carotid and right carotid respectively. Only 4 (5.6%) had stenosis of 50-69% on the right carotid and 3 (4.2%) on the left carotid. Only one patient had near occlusion stenosis **(Table 5).**

Table 6: Degree of stenosis

Degree of stenosis	Right carotid	Left carotid
< 50%	65 (91.5%)	67 (94.4%)
50- 69%	4 (5.6%)	3 (4.2%)
70- 89%	1 (1.4%)	1 (1.4%)
Near occlusion	1 (1.4%)	0

The side with greatest degree of stenosis was taken to represent the magnitude of stenosis in that patient while the presence of plaque was used to differentiate between those who did not have stenosis and those with mild stenosis. Among the 71 patients, 43 (60.6%) did not have stenosis, 20 (28.2%) had mild stenosis (> 50%), 5 (7.0%) moderate stenosis (50- 69%), 2 (2.8%) had severe stenosis (70-89%) while one (1.4%) had critical stenosis (Near occlusion). **(Figure 6).**

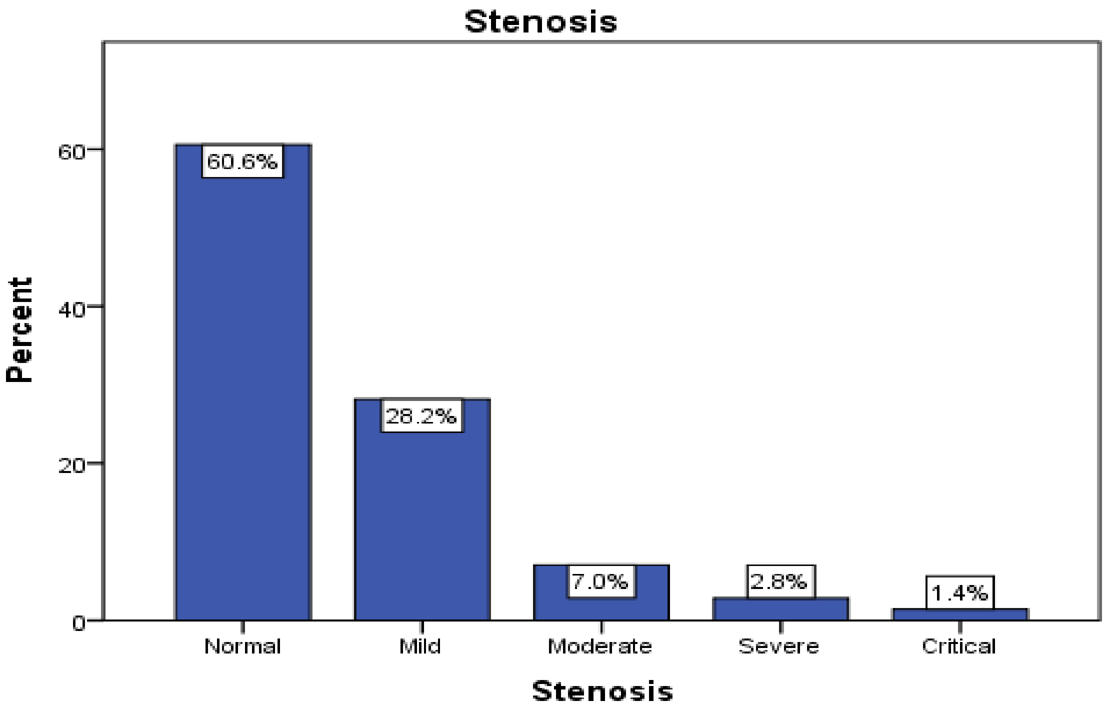


Figure 11: Classification of degree of stenosis

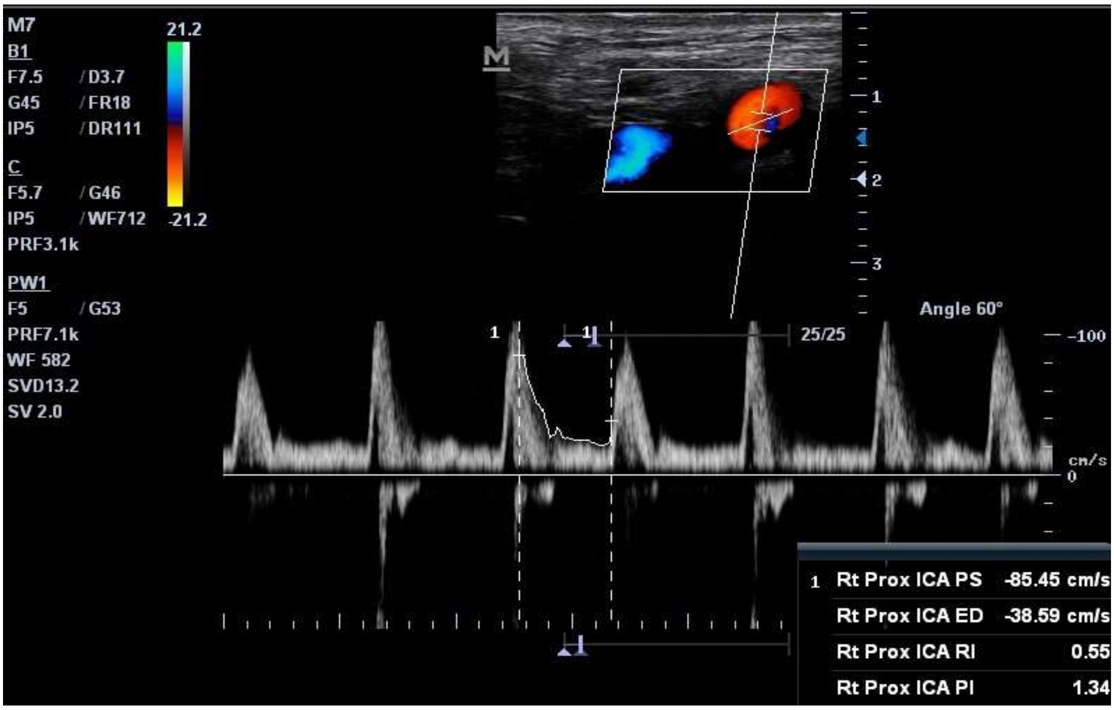


Figure 12: normal ICA Doppler waveform.

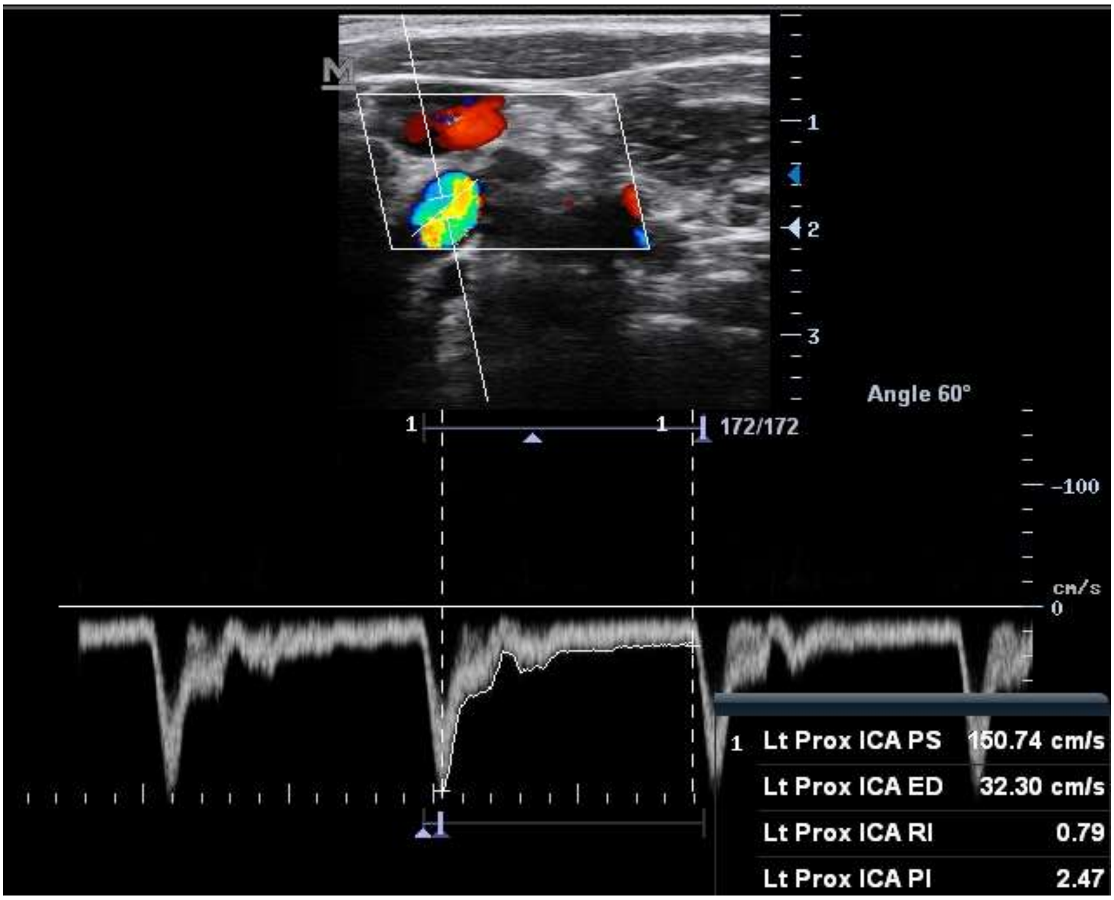


Figure 13; increased ICA PSV

According to the gender of the respondent, 24 (57.1%) of male patients did not have stenosis, while 19 (65.5%) of the female did not have it. The proportion of mild stenosis was high among female (31.0%) when compared to men (26.2%). The proportion of Moderate (9.5%) and severe stenosis (4.8%) in men was higher than that in female (3.4% and 0 respectively). **(Table 6).**

Table 7: Classification of stenosis according to gender of the patients

Stenosis	Male (n= 42)	Female (n= 29)
No Stenosis	24 (57.1%)	19 (65.5%)
Mild	11 (26.2%)	9 (31.0%)
Moderate	4 (9.5%)	1 (3.4%)
Severe	2 (4.8%)	0
Critical	1 (2.4%)	0

CIMT

The mean right CIMT was 0.62± 0.48 for right carotid and 0.63± 0.53cm for left carotid. **(Table 8).**

Table 8: CIMT values

Statistics		**CIMT(mm)- Right carotid**	**CIMT(mm)- Left carotid**
N		71	71
Mean		.6163	.6280
Median		.7000	.7000
Mode		1.10	1.30
Std. Deviation		.48278	.52966
	25	.0900	.0800
Percentiles	50	.7000	.7000
	75	1.1000	1.2000

For men, the mean CIMT was 0.61± 0.50 cm for right carotid and 0.62± 0.54 cm for the left carotid, while for females, the mean right carotid CIMT was 0.63 ± 0.46cm and 0.65± 0.52cm for the left carotid. There was no significant differences in mean CIMT between male and females

Table 9: CIMT and Gender

Group statistics	Gender of Patients	N	Mean	Std. Deviation	t test	P Value
CIMT(mm)- Left carotid	male	42	.6148	.54070	-0.254	0.800.
	female	29	.6472	.52212		
CIMT(mm)- Right carotid	male	42	.6048	.49945	-0.245	0.800.
	female	29	.6331	.46576		

Among the participants, 23(32.4%) had Increased CIMT while the remaining 48 (67.6%) had normal CIMT on the right carotid.

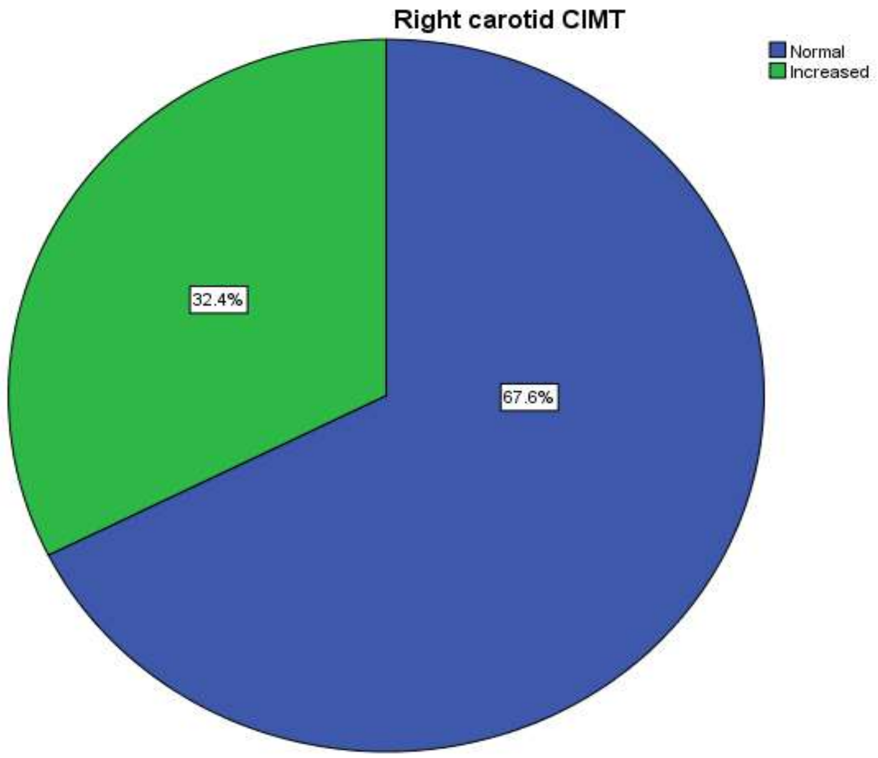


Figure 14: CIMT Distribution

On the left carotid, 20 (28.2%) had increased CIMT while 51 (71.8%) had normal CIMT on left carotid.

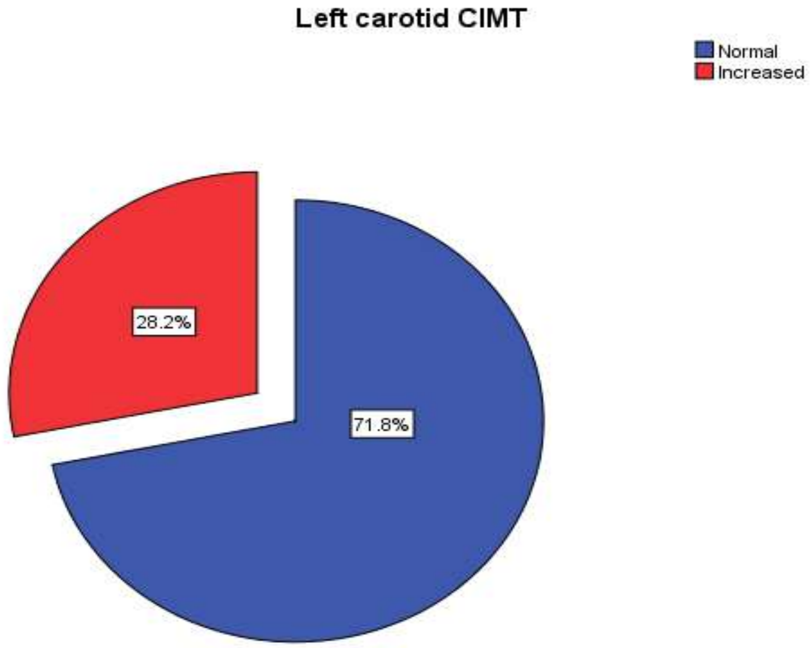


Figure 15: Left CIMT distribution

A CIMT of ≤ 1 mm was considered normal, while a CIMT of >1 mm was considered increased.

Table 10: Carotid IMT

	Normal <= 1mm	Increased > 1mm
Right CCA IMT	48 (67.6%)	23 (32.4%)
Left CCA IMT	51 (71.8%)	20 (28.2%)

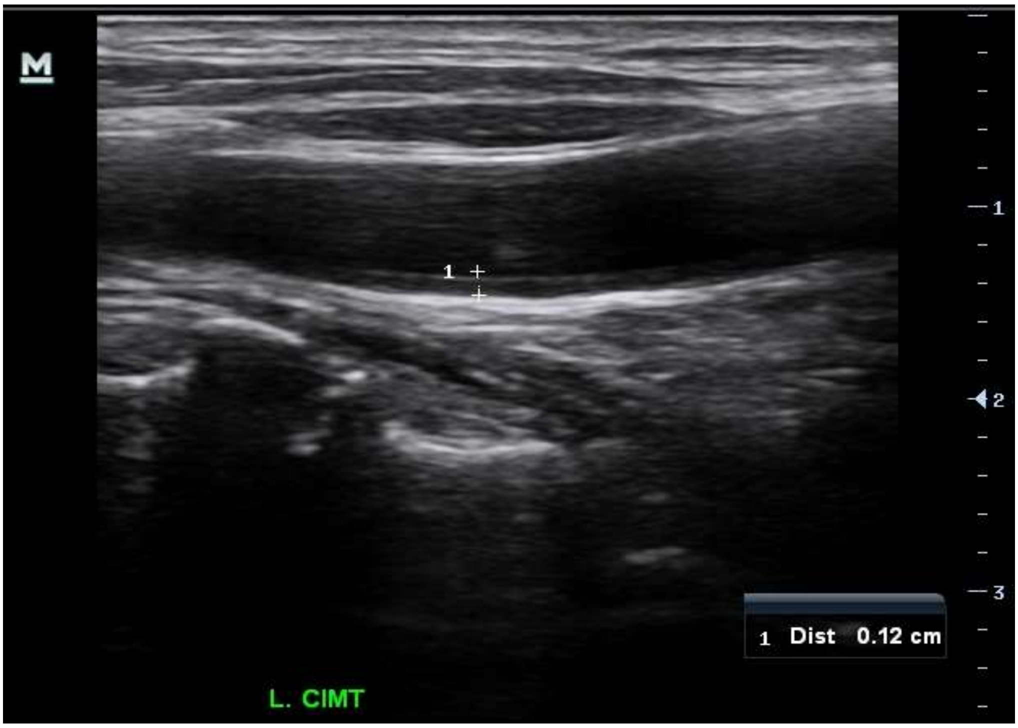


Figure 16: Enlarged CIMT

There were 41 plaques identified. In some patients, there could be more than one plaque in more than one site along the entire extracranial carotid system.

Of these, 28 (68.3|%|) were homogenous, 7 (17.1%) non-homogeneous and 6 (14.6%) calcified.

Table 11: Plaque and plaque characteristics

	Plaque Characteristics			
Site of plaque	**homogeneous**	**non homogeneous**	**calcified**	**Total**
right CCA	4	2	2	8
Right ICA	10	2	2	14
Right Carotid bulb	4	0	0	4
Right carotid bulb	2	0	0	2
Left ICA	5	2	0	7
Right carotid bifurcation	1	0	0	1
Left Carotid Bulb	1	0	2	3
Left CCA	0	1	0	1
Right CCA Bifurcation	1	0	0	1
Total	**28**	**7**	**6**	**41**

Most of the cases of plaque was detected in the right ICA (14).

Table 12: Plaque site

Plaque site	Frequency (n)	Percent (%)
right CCA	8	19.5
Right ICA	14	34.2
Right Carotid bulb	6	14.6
Left ICA	7	17.1
Right carotid bifurcation	1	2.4
Left Carotid Bulb	3	7.3
Left CCA	1	2.4
Right CCA Biforcation	1	2.4
Total	41	100.0

Table 13: Plaque site

	Right	**Left**
Plaque site	N (%)	N (%)
CCA	8 (19.5)	1 (2.4)
ICA	**14 (34.2)**	**7 (17.1)**
Carotid Bulb	6 (14.6)	3 (7.3)
ECA	1 (2.4)	1 (2.4)

Table 14: Plaque characteristics

Plaque characteristic	Frequency (n)	Percent (%)
Homogenous	28	68.3
Non-homogenous	7	17.1
Calcified	6	14.6
Total	**41**	**100**

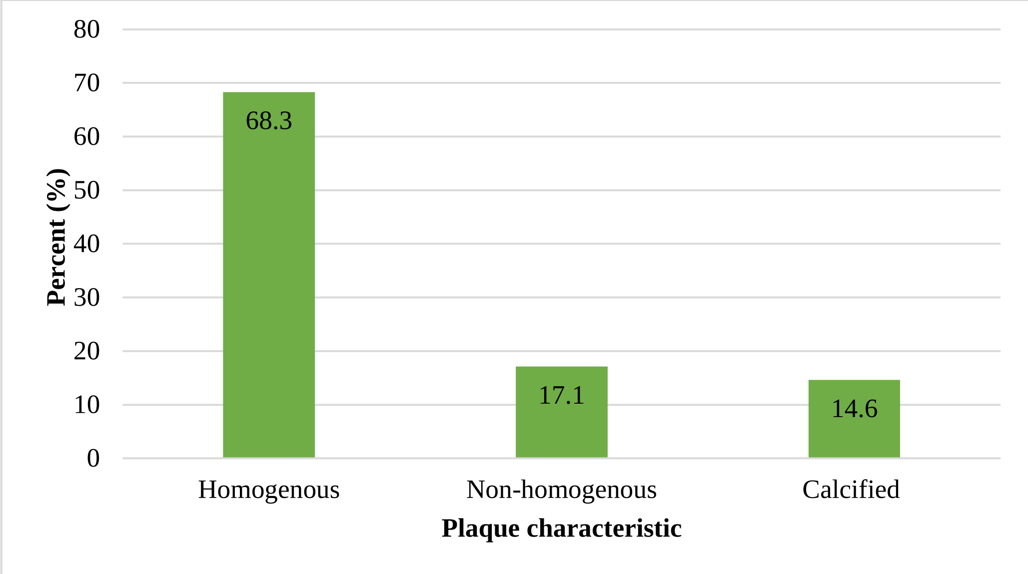


Figure 17: Plaque characteristics

4.2.4 Factors associated with stenosis

Of the respondents, 6 (8.5%) had a history of smoking. **(Figure 10).**

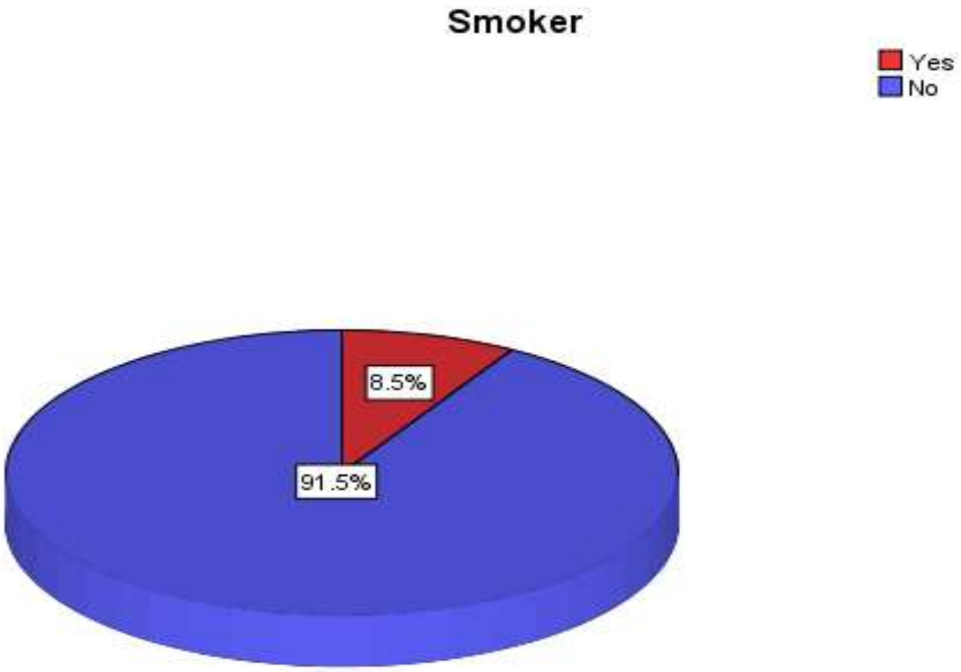


Figure 18: Patients who had a history of smoking

The distribution of the patients with regards to stenosis and smoking is shown in **table 9** below.

Table 15: Distribution of stenosis with regards to smoking characteristic

	Smoker	
Stenosis	**Yes**	**No**
Normal	1 (2.3%)	42 (97.7%)
Mild	5 (25.0%)	15 (75.0%)
Moderate	0 (0)	5 (100%)
Severe	0 (0)	2(100%)
Critical	0 (0)	1(100%)
Total	**6 (8.5%)**	**65 (91.5%)**

Most, 44 (62.0%) had hypertension. **(Figure 11).**

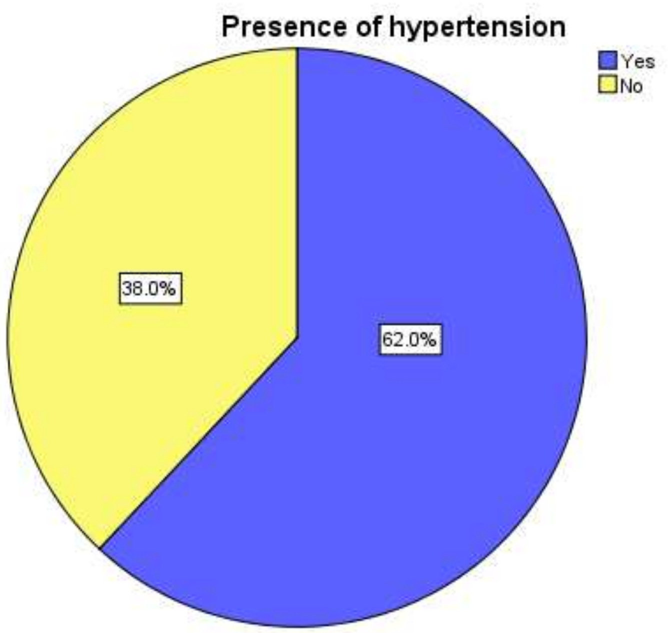


Figure 19: Presence of hypertension

The proportion of patients with significant stenosis was high among those who had hypertension. **(Table 10).**

Table 16: Distribution of patients with regards to stenosis and hypertension

	Presence of hypertension	
Stenosis	**Yes**	**No**
Normal	22 (51.2%)	21 (48.8%)
Mild	16 (80.0%)	4 (20.0%)
Moderate	3 (60.0%)	2 (40.0%)
Severe	2 (100%)	0 (0)
Critical	1 (100%)	0 (0)
Total	**44 (62.0%)**	**27 (38.0%)**

Among the participants, 25 (35.2%) had diabetes. **(Figure 12)**

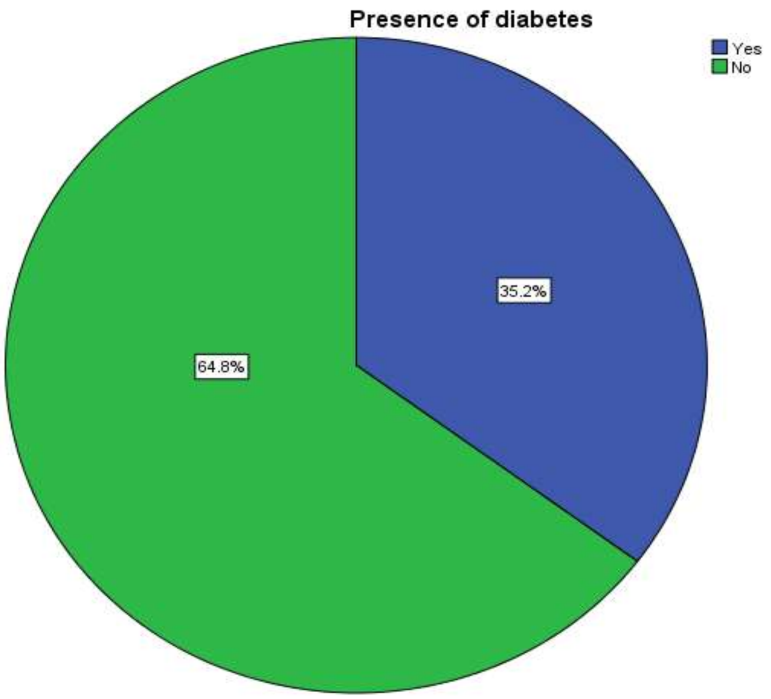


Figure 20: Presence of diabetes

The proportion of the patients with significant stenosis was high among patient without diabetes. **(Table 17).**

Table 17: Cross tabulation of patient's stenosis and diabetes

Stenosis	Presence of diabetes	
	Yes	No
Normal	8 (18.6%)	35 (81.4%)
Mild	12(60.0%)	11 (40.0%)
Moderate	3 (60.0%)	2 (40.0%)
Severe	1 (50.0%)	1 (50.0%)
Critical	1 (100%)	0 (0)
Total	25 (35.2%)	46 (64.8%)

There was statistically significant association between having diabetes (P-value<0.01), hypertension (P-value= 0.025) or being a smoker (P-value= 0.032) with presence of stenosis. **(Table 18).**

Table 18: Association between stenosis and its risk factors

No	Risk factor	Presence of stenosis (n=28)	Normal (n=43)	X^2	df	p-value
1	Have diabetes	17 (60.6%)	8 (18.6%)	13.181	1	< 0.001
2	Have hypertension	22 (78.6%)	22 (51.2%)	5.406	1	0.025
3	Smokers	5 (17.9%)	1 (2.3%)			0.032*
4	Gender					
	Male	18 (64.3%)	24 (55.8%)	0.504	1	0.622
	Female	10 (35.7%)	19 (44.2%)			

*Fishers exact test was used.

There was no significant association between CIMT and stenosis.

Table 19: Cross-tabulation of increased CIMT and stenosis

Characteristic	Presence of Stenosis		df	X^2	P value
	Yes (n=28)	No (n=43|)			
Increased right carotid CIMT	23 (82.1%)	30 (69.8|%)	1	0.679	0.461
Increased left carotid CIMT	19 (67.9%)	25 (58.1|%)	1	0.679	0.410

Smoking was significantly associated with right carotid CIMT (P value < 0.05).

Table 20: Cross-tabulation of patient characteristics and CIMT

Characteristic	Right Carotid CIMT		df	X^2	P value
	Increased (n=53)	Normal (n=18)			
Presence of diabetes	20 (37.7%)	5 (27.8%)	1	0.584	0.572
Presence of hypertension	36 (67.9%)	8 (44.4%)	1	3.143	0.096
Smoking	2 (3.8|%)	4 (22.2%)			0.033*
	Left carotid CIMT				
	Increased (n=44)	Normal (n=27)			
Presence of hypertension	28 (63.6%)	16 (59.2%)	1	0.136	0.712
Presence of diabetes	15 (34.1%)	10 (37.0%)	1	0.064	0.801
Smoking	2 (4.5%)	4 (14.8%)			0.192|*

***Fischer's exact test**

Mann-Whitney U test was used to determine the association between age of the participants and presence of stenosis. Individuals with stenosis had higher age in general (Mean rank= 38.3) compared with those who were normal (Mean rank= 34.5). However, there was no statistically significant differences in the mean distribution of age with stenosis ((U = 538.5, p = 0.455) **(Figure 13).**

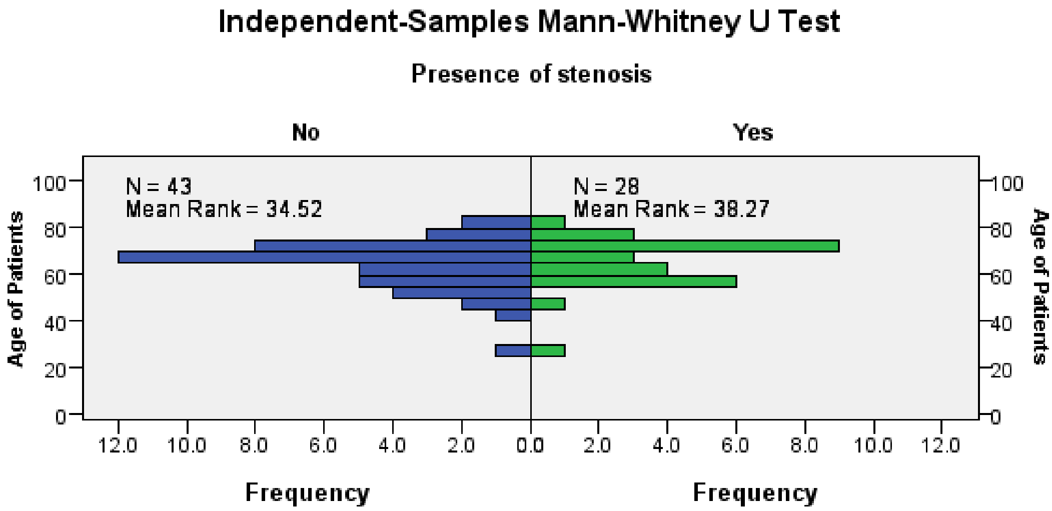


Figure 21: Mann-Whitney U test

SAMPLE IMAGES.

Figure 22:Calcified non-occlusive plaque in the left carotid bifurcation in a 62-year-old female who had a left sided ACA territory stroke

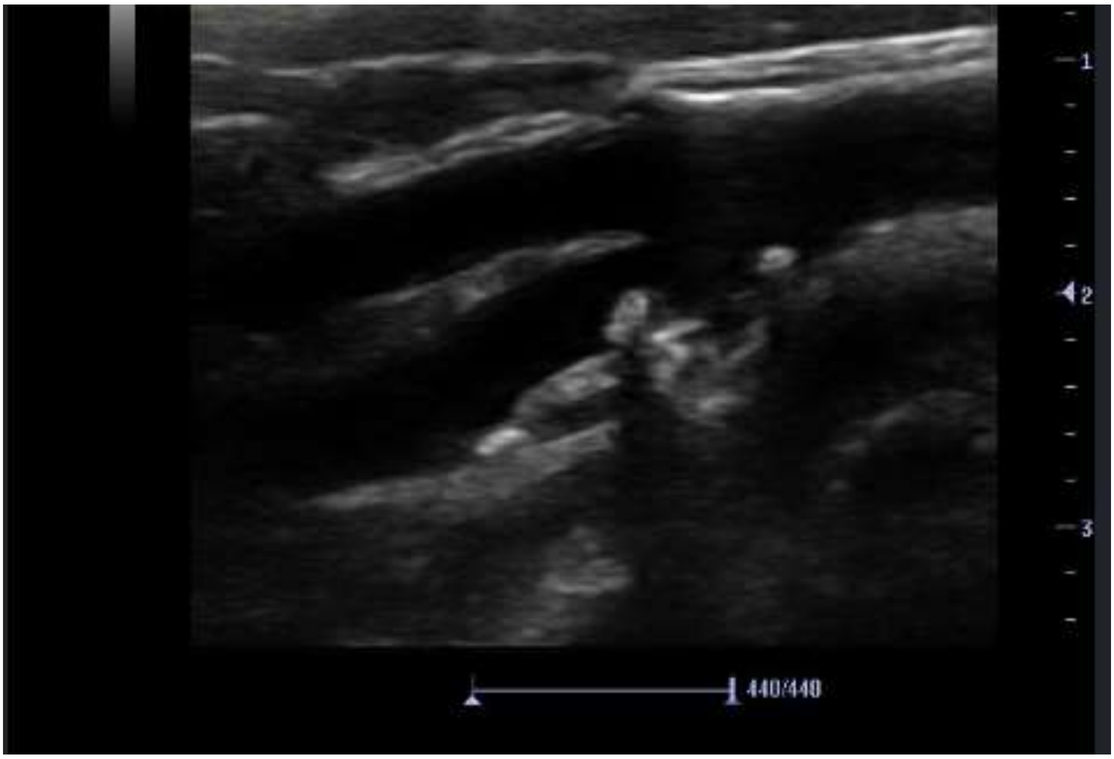
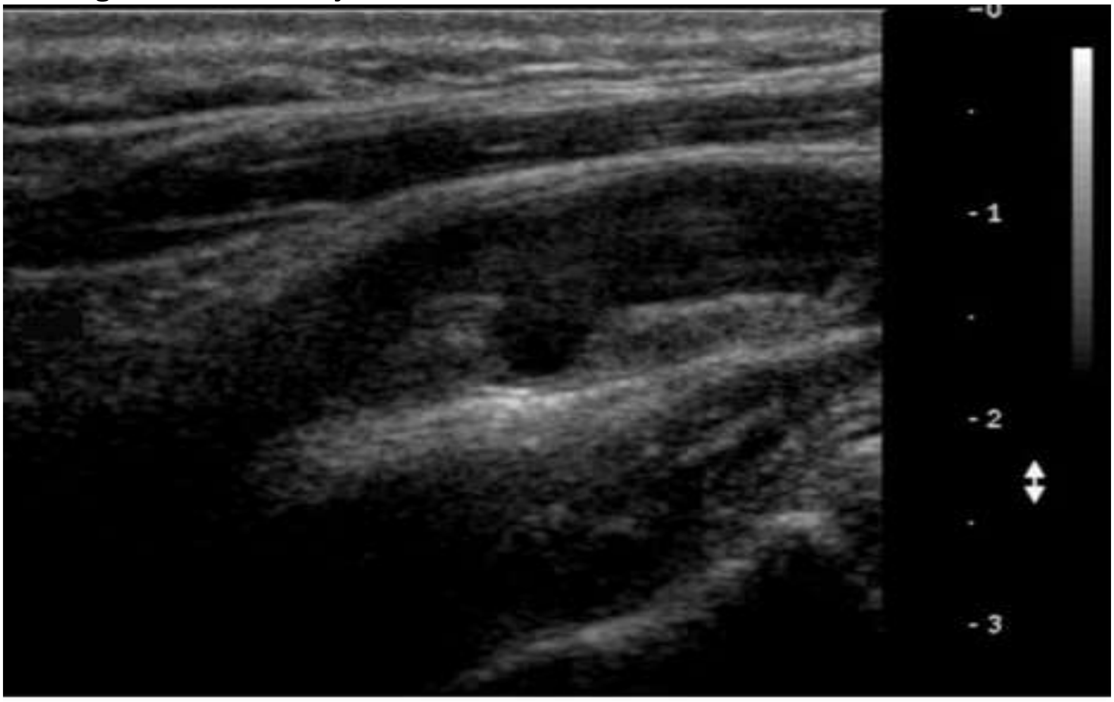


Figure 23 :Heterogenous plaque in the left proximal ICA in a 70 year old man with right MCA territory stroke.



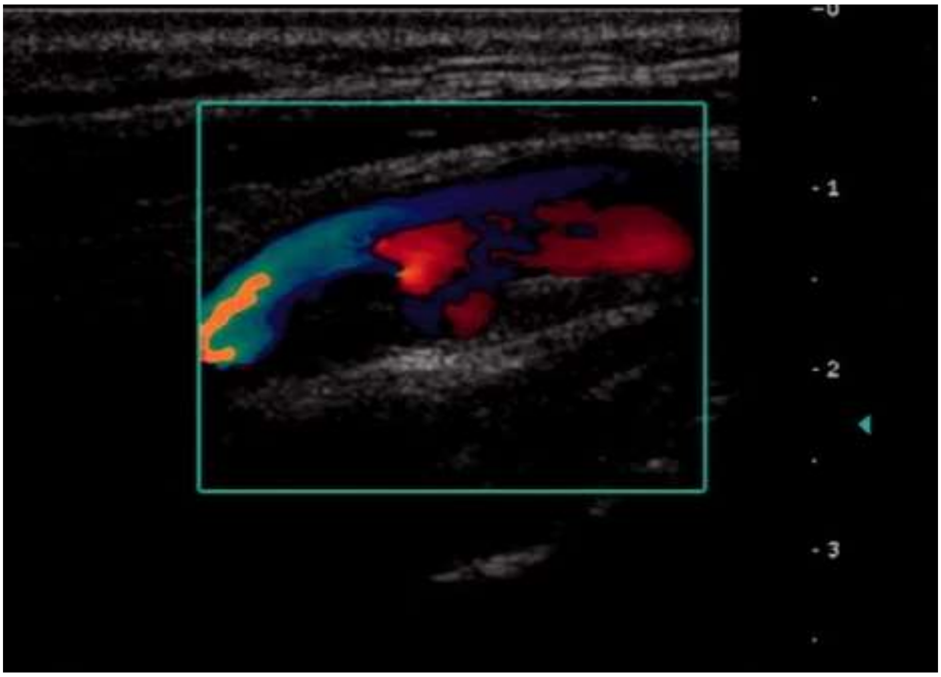


Figure 24:Grey scale (above) and color doppler(below) images showing Homogeneous plaque in the right ICA in a 67 year old man with right MCA territory stroke

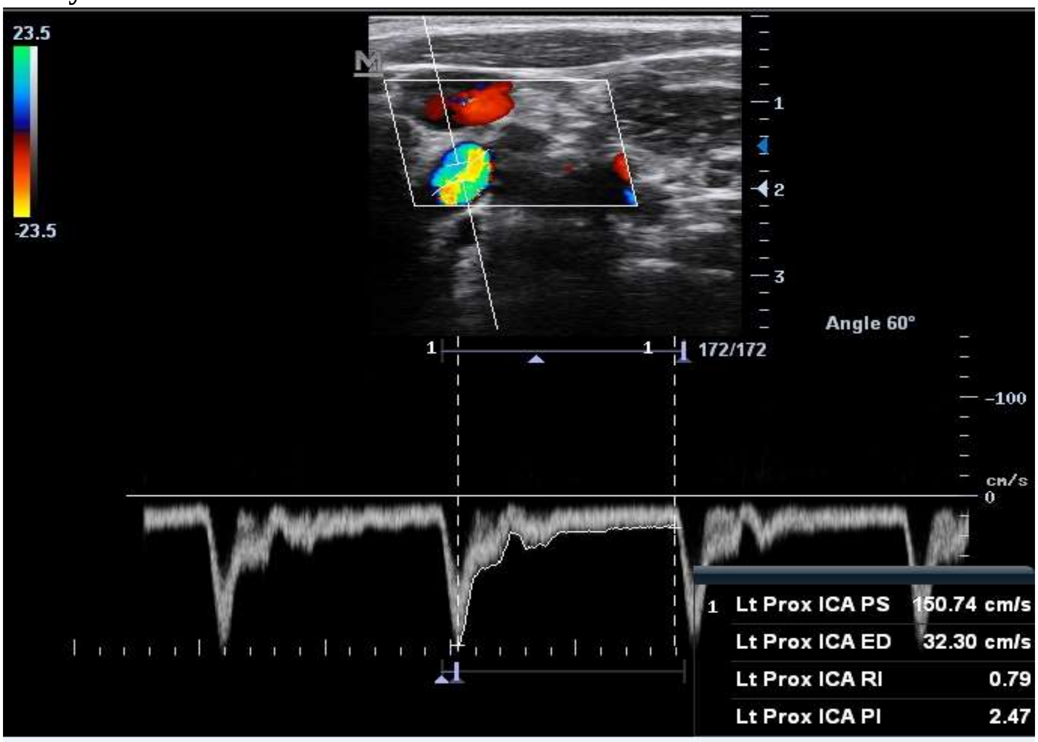


Figure 25 :Spectral Doppler showing Increased Peak systolic velocity in the left ICA suggestive of 50-69% stenosis in a 78 year old female with left MCA territory stroke.

Figure 26 :76-year-old female with a large MCA territory stroke showing a large heterogeneous plaque in the carotid bifurcation, and extending into the proximal ICA and ECA

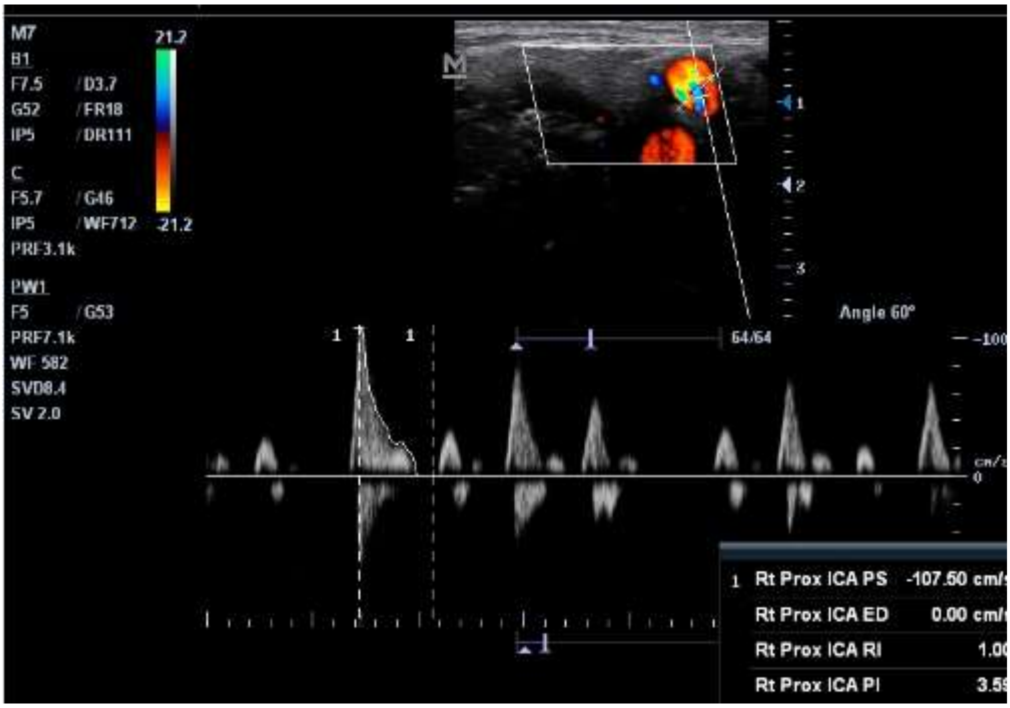


Figure 27:73-year-old woman with left MCA territory stroke showing a high resistance waveform pattern in the proximal right CCA

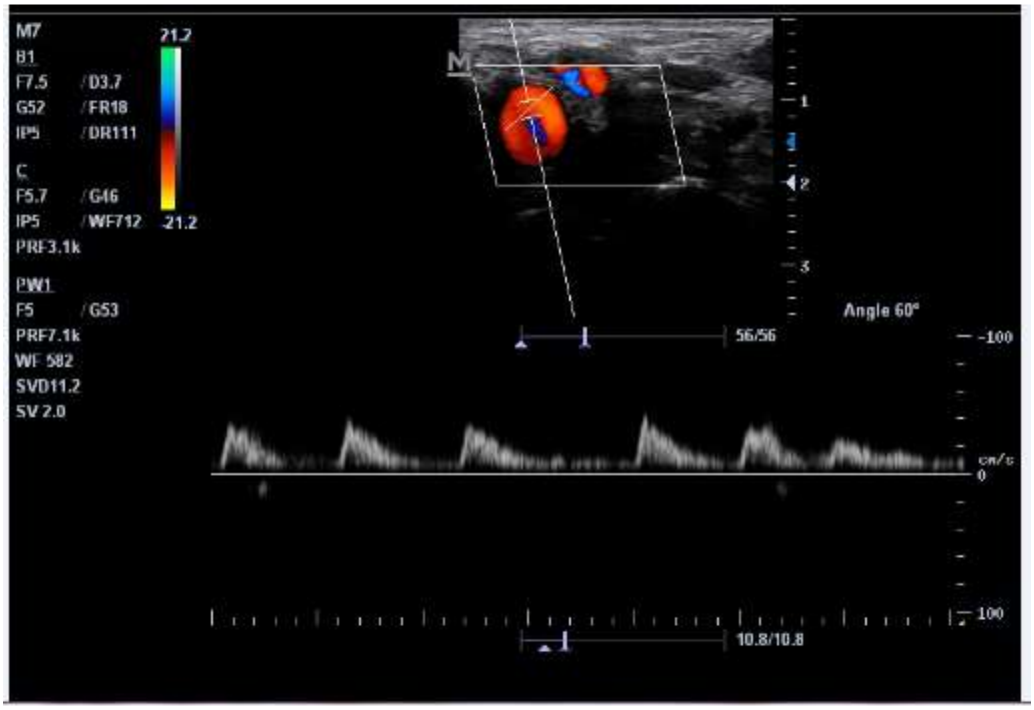


Figure 28:66 year old female with stenosis of the proximal right ICA showing diminished peak systolic amplitude in the mid ICA, distal to the stenotic potion. .

CHAPTER FIVE: DISCUSSION

5.1 Introduction

In this section, the results of the study are discussed by putting them into perspective and compared with those of previous studies.

There is limited information regarding carotid artery atherosclerosis among ischemic stroke patients locally, despite stroke contributing enormously to the morbidity and mortality burden due to non-communicable conditions in Kenya. We have one study, which was carried out at Kenyatta National Hospital; however, no such study has been conducted at MTRH, the second largest public referral facility in the country after KNH. Further, the KNH study only sought to ascertain the proportion of patients with carotid artery stenosis among patients with ischemic stroke. Other parameters of carotid ultrasonography were not studied, e.g. CIMT, carotid plaques and plaque characteristics among others.

In the Western countries and in India, similar studies have been conducted with the results being key in informing the diagnosis and management of ischemic stroke patients. There appears to be a higher risk of large artery stroke in patients who have a high degree of stenosis and presence of carotid plaque or a combination of both (Rothwell et al., 2000).

The process of diagnosing significant stenosis correctly is important to determine ischemic stroke patients who can greatly benefit from an intervention involving surgical procedure (carotid endarterectomy). Hence, it is advantageous to identify and utilize a low-cost, safe screening modality (Fernandes et al., 2016).

This study therefore sought to evaluate the carotid arteries using Doppler sonography in patients with ischemic stroke presenting at MTRH. This was done with a goal of establish the proportion of patients with carotid artery stenosis amongst patients with ischemic stroke and evaluate the characteristics of the carotid arteries of these patients on Doppler sonography, and the factors associated with carotid artery stenosis in stroke.

5.2 Discussion

5.2.1 Demographic information

The number of men was slightly higher than that of female in the study, as was the case in a study conducted at KNH where 62.7% of the patients with ischemic stroke were male (Mwazo, 2007). Similarly, the number of men was reported to be high (72%) among cerebral ischemic stroke patients in a study conducted in South India with a study population of 50 patients (Fernandes et al., 2016). These findings are also in agreement with findings of population based studies in which men have been reported to have more cases of ischemic stroke than females (Di Carlo et al., 2003; Kapral et al., 2005; Simpson, Wilson, Hannaford, & Williams, 2005). Overall, the incidence rate of stroke was found to be 1.25 times higher in males compared to females and was seen to increase steadily with age for both males and females. Research demonstrated that women are older at time of their first stroke (mean age-72.5 years) compared with males (68.6 years) (Alayna a samai, Sheryl martin-schild-2015)

The median age of the patients in our study was 67 years and the mean age was 64 years, which was more than that of patients with ischemic stroke in the study conducted at KNH where the median age was 54 years with a mean of 60. However, as is the case in this study, majority of the patients were aged 50 years and above (Mwazo, 2007). It is also important to note that the KNH study had age limit restrictions for its recruited patients, only patients above 45 years were recruited. As was the case in this study, In South India, most of the patients with stroke were aged 60-79 years (58%) (Fernandes et al., 2016).

Age differences has been noted with regards to gender of individuals with ischemic stroke with the average age of female being 4 years older than that of men at the first time of diagnosis of ischemic stroke (Gargano, Wehner, & Reeves, 2009). However, there was no significant differences in age of the patients concerning their gender. This might be due to the small study population and because the study did not establish the age at onset of the condition.

5.2.2 Doppler ultrasound findings of the carotid arteries in patients with ischemic stroke

Carotid intima media thickness(CIMT) is an indirect sonographic assessment of the degree of atheromatous vascular disease of the end organs. CIMT is associated with media layer adaptive hypertrophy(Touboul et al., 2004). Increased Carotid intima media thickness measurements have been found to be associated with the risk of stroke, and may be used as a diagnostic marker for predicting stroke events.(Kumar et al., 2020)

Increased carotid intima media thickness was seen in 30.3% of cases in this study, while 69.7% of participants had normal CIMT. This compared well with a study in India where the proportion of participants with increased IMT was 29.0 % and normal IMT in 58.8 % of cases.(Osawa et al., 2020). In contrast, a study done in Iran by Alrubaye in 2020 found that 58.8% of cases had increased CIMT, while 41.2 % has normal CIMT (Alrubaye, Ali-Hussaini, Hassan al-timimi, & Al-Saadi). This difference could be attributed to the fact that in the Iranian study, ultrasound was only done to the carotid arteries ipsilateral to the side of stroke in each patient.

In this study, the mean CIMT in males was 0.60 and 0.61 cm in the right and left carotid arteries respectively. The mean CIMT in females was 0.63 and 0.64 in the right and left carotid arteries respectively, the difference in distribution among the genders was however not statistically significant. In a study by Haq and colleagues, the mean CIMT in males, 0.091 was higher than that in females 0.082 with the differences being statistically significant (P-value <0.05) (Haq et al., 2017). This could be attributed to a higher percentage of males with smoking history (28%) in the Indian study, compared to only 8% in this study.

In this study, 28 (39.4%) of the patients had carotid plaques. This compared well with a study in Burkina Faso where the frequency of carotid plaques was 23.9% (Dabilgou et al., 2019). It was however lower than what was found in India where 39(78%) of the 50 carotid ischemic stroke patients evaluated had carotid plaques (Fernandes et al., 2016). In the study by Fernandez, the proportion of patients who had co-morbidities and significant history was much higher, (HTN- 66.0%, DM-44.0%, smoking 28.0%) compared to this study where 61.0% had hypertension, 35.2% had diabetes and 8.4% had a history of smoking. The difference could also be attributed to racial and geographical differences between India and Africa.

The commonest site for plaque formation was the ICA, 17(41.46%). This was similar to a study done by(Yadav et al., 2020) and (Fernandes et al., 2016) who also found that the commonest site of plaques was the ICA at 45.8% and 30% respectively.

The findings in this study differed with a study by Haq in India who found the carotid bulb to be the commonest site for plaque formation (38.7%)(Haq et al., 2017)

Carotid plaques frequently occur within 2 cm of the bifurcation and the proximal segments of the ICA. Sudden and rapid change in velocity and direction of blood in this region leads to increase in stress faced by the arterial walls and thus having a higher propensity to get damaged (Eyding, Geier, & Staub, 2011).

Doppler sonography has the advantage of being able to determine plaque composition. It is able to identify characteristics of plaque that have prognostic importance due to their usefulness in determining the surgical or medical therapy to adopt for a given patient (Iemolo, Martiniuk, Steinman, & Spence, 2004). Homogeneous plaque was the most prevalent plaque type (68.3%). This was followed by non-homogeneous plaques (17.1%) and calcified plaques (14.1%). This compared well with the study in Burkina Faso which found 85.2% , 10.2% and 4.5 % for the homogenous, non-homogenous and calcified plaques respectively(Dabilgou et al., 2019). However, the study by Fernandez in India found a higher proportion of calcified plaques at 30.1% and heterogeneous plaques at 17.9%(Fernandes et al., 2016). Heterogeneous plaques are unstable and carry a high risk of embolization and rapid progression, Intraplaque hemorrhages are associated with frank ulceration and rapid progression to result in severe luminal narrowing. This therefore means that subcritical carotid stenotic lesions play a role in pathogenesis of stroke.(Nezu & Hosomi, 2020). Calcification in plaques occurs in regions of necrosis and hemorrhage, generating strong distal acoustic shadows and reflections (Tegos et al., 2000).

5.2.3 Internal Carotid Artery stenosis amongst patients with ischemic stroke

Carotid ultrasound is a reliable diagnostic tool that has an important role in the diagnosis and grading of ICA stenosis (Lorenzová, 2016). Society of Radiologists in Ultrasound Consensus Conference data was used to classify stenosis. This criteria was first developed by Carpenter before being extended and standardized by The Society of Radiologists in Ultrasound (E. G. Grant et al., 2003). The ICA PSV and the ICA/CCA PSV ratio were mainly used for the classification as they are considered to be accurate and the best in assessing stenosis and predicting significant stenosis as the ratio compensates for instrument and patient variability (Fernandes et al., 2016; Zwiebel, 2000).

The side with greatest degree of stenosis was taken to represent the magnitude of stenosis in that patient while the presence of plaque was used to differentiate between individuals without stenosis and those with mild stenosis as the percent stenosis cut-off point for the two is similar (<50%). Among the 71 patients, 43 (60.6%) did not have stenosis, 20 (28.2%) had mild stenosis (<50%), 5 (7.0%) moderate stenosis (50-69%), 2 (2.8%) had severe stenosis (70-89%) while one (1.4%) had critical stenosis (Near occlusion). This compared with the study in KNH where the proportion with significant stenosis was 1.6% and moderate stenosis was 3.9% (Mwazo, 2007). A similar study done in Egypt also found a relatively low proportion of patients with significant stenosis at 9.3% for both moderate and severe stenosis.(El Hady, Mohammad, Elkhatib, & Khalil, 2019)

In contrast, a study in Nepal in 2020 found a higher proportion, 34% of patients with stenosis > 50% , among these, 18% had moderate , 8.9% had severe stenosis, 2.5% had near total occlusion, and 3.8% had complete occlusion(Yadav et al., 2020).

A similar study in Nepal in 2019 also found a relatively high percentage, 34% of patients with stenosis >50% , and 2% had complete occlusion. (Pathak, Gautam, & Pathak, 2019)

In Punjab India, a study involving 50 ischemic stroke patients reported that 20 (40.0%) had mild stenosis (<50%) stenosis, 7 (14.0%) moderate (50-69%) stenosis and 3 (6.0%) severe stenosis (≥70%). In South India, 12 (24.0%) of the 50 patients assessed had significant stenosis of > 60% (Fernandes et al., 2016). In another study in India, 38% of the 50 ischemic stroke patients evaluated had stenosis of more than 50% (Haq et al., 2017), which was higher that the proportion found in this study.

Notably, the proportions of significant stenosis were low in our study and the studies done in KNH and Egypt, compared to the studies in India and Nepal. This could be attributed to the difference in lifestyle e.g higher numbers of participants with history of chronic smoking, racial and geographical differences.

However, the result of most of these studies need to be interpreted with caution due to the small sample sizes involved and the differences in classification of stenosis observed.

Management of patients with ICA stenosis depends on the degree. According to North American Symptomatic Carotid Endarterectomy Trial (NASCET), medical therapy is recommended for patients with less than 50% stenosis with symptoms while for those with 50-69% stenosis, medical therapy and follow up after every 6 months is recommended in order to detect the cases which might necessitate surgical intervention (Filis et al., 2002). Patients with moderate stenosis can also be able to benefit from surgery as was shown by a trial conducted by NASCET (Barnett et al., 1998). Symptomatic patients with stenosis of 70% and above and near occlusion can benefit more from Carotid endarterectomy (Rothwell et al., 2003).

5.2.4 Factors associated with internal carotid artery stenosis

Hypertension, smoking and diabetes mellitus are significant known cardiovascular risk factors associated with ischemic stroke and atheromatous plaque formation. (Fernandes et al., 2016; Haq et al., 2017)

There was a statistically significant relation of diabetes, hypertension and smoking with ICA stenosis, p.values of 0.01, 0.025 and 0.032 respectively.

This compared well with a study in Egypt which found significant relation of diabetes, hypertension and smoking with ICA stenosis , with p.values of 0.02, 0.038 and 0.02 respectively.(El Hady et al., 2019)

In contrast, a study in Iran in 2018 found no relationship between DM, HTN and smoking, with ICA stenosis, and found p.values of 0.14, 0.44, and 0.50 respectively.(Mosarrezaii, 2018)

This difference could be due to a larger size of study population in (149) with a wider age range of study participants (18-103). It was also noted that about 24% of the study participants in the Iranian study had a history of ischemic heart disease and myocardial infarction.

Most of the patients had hypertension, as was the case in KNH where 74.6% of the 126 participants had hypertension comorbidity. The proportion of those with diabetes in this study (35.2%) was nearly similar to that reported in the study by Mwanzo at KNH (30.2%) (Mwazo, 2007).

In this study, 35.2% of the patients had diabetes mellitus of which only one had severe stenosis. This proportion was higher than that reported in South India (16%) (Fernandes et al., 2016). However, a study carried out by Lindsberg and Roine reported that two-third of the included ischemic stroke patients had diabetes mellitus of which three had severe stenosis (Lindsberg & Roine, 2004).

Only 8.5% were smokers. This proportion was lower than 28.6% reported in the study done at KNH (Mwazo, 2007). Chronic cigarette smoking is strongly associated with severe extracranial carotid atherosclerosis (O'donnell et al., 2010). A high correlation has also been reported between stenosis and smoking (Garg et al., 2016).

Garg et al carried-out color Doppler evaluation of extracranial carotid artery and found the percentage of stenosis to increase with age and was more prevalent in male than female. Among the total 1043 cases under study, 33.9% (354) patients had stenosis. Those with significant stenosis (> 50%) were 17.8% (63) with the majority, 82.20% (291) having mild stenosis. severe stenosis (>70%) was shown in seven males (3.4%) and in one female (0.6%). The prevalence of severe stenosis was shown to be low with mild stenosis being high (Garg et al., 2016), as was the case in this study.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

ICA was the most common site for plaque formation, with homogenous plaques being the most common. The proportion of patients with significant ICA stenosis was low, with a majority of the patients having no ICA stenosis or mild stenosis. Having Diabetes, hypertension and a smoking history was significantly associated with internal carotid artery stenosis, a likely indicator of the proven link between the two as shown in literature with hypertension, DM and smoking being known traditional modifiable ischemic stroke risk factor.

Color Doppler sonography and grey scale imaging can be used to successfully grade stenosis and provide a detailed description of plaque which are key in ischemic stroke intervention.

6.2 Recommendation

Routine screening of symptomatic patients above 50 years with a history of diabetes, hypertension and smoking is recommended.

There is need for well-designed case control studies to determine the risk factors associated with stenosis in patients with ischemic stroke.

REFERENCES

Alrubaye, A. M. K., Ali-Hussaini, H., Hassan al-timimi, H., & Al-Saadi, W. I. (2017). Value of carotid Doppler ultrasound and brain CT scan in ischemic stroke. *Al-Qadisiyah Medical Journal*, *13*(24), 72-81.

Baidya, O. P. (2015). Acute ischemic stroke in young adults-a hospital based study in North India. *Steroids*, *6*, 12.

Barnett, H. J., Taylor, D. W., Eliasziw, M., Fox, A. J., Ferguson, G. G., Haynes, R. B., ... & Spence, J. D. (1998). Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *New England Journal of Medicine*, *339*(20), 1415-1425.

Bongartz, G. (1996). The Carotid and Vertebral Arteries *Magnetic Resonance Angiography* (pp. 153-171): Springer.

Budoff, M. J., & Shinbane, J. S. (2016). *Cardiac CT imaging: diagnosis of cardiovascular disease*: Springer.

Calanchini, P. R., Swanson, P. D., Gotshall, R. A., Haerer, A. F., Poskanzer, D. C., Price, T. R., . . . Futty, D. E. (1977). Cooperative study of hospital frequency and character of transient ischemic attacks: IV. The reliability of diagnosis. *JAMA*, *238*(19), 2029-2033.

Carroll, B. (1991). Carotid sonography. *Radiology*, *178*(2), 303-313.

Chamarthi, M., Lava Kumar, B., Nirusha, R., Pravallika, I., & Kejriwal, G. (2017). Color Doppler Evaluation of Carotid Arteries in Stroke Patients: A Study Conducted in A rural Tertiary Care Medical College Hospital in South india. *atherosclerosis, 3*, 4.

Chung, C.-P. (2017). Types of stroke and their differential diagnosis *Primer on Cerebrovascular Diseases* (pp. 372-376): Elsevier.

Coutinho, J. M., Derkatch, S., Potvin, A. R., Tomlinson, G., Kiehl, T. R., Silver, F. L., & Mandell, D. M. (2016). Nonstenotic carotid plaque on CT angiography in patients with cryptogenic stroke. *Neurology*, *87*(7), 665-672.

Dabilgou, A. A., Dravé, A., Kyelem, J. M. A., Koanda, H., Napon, C., & Kaboré, J. (2019). Extracranial Carotid Atherosclerosis and Acute Ischemic Stroke in a Tertiary Hospital in Burkina Faso. *World Journal of Neuroscience, 9*(02), 39.

Di Carlo, A., Lamassa, M., Baldereschi, M., Pracucci, G., Basile, A. M., Wolfe, C. D., . . . Inzitari, D. (2003). Sex differences in the clinical presentation, resource use, and 3-month outcome of acute stroke in Europe: data from a multicenter multinational hospital-based registry. *Stroke, 34*(5), 1114-1119.

Dublin, A. B., & Al-Dhahir, M. A. (2019). Anatomy, Head and Neck, Temporal Region *StatPearls [Internet]*: StatPearls Publishing.

Duffy, P. (1993). Carotid colour Doppler. *Australasian radiology, 37*(2), 166-170.

El Hady, A., Mohammad, H. S., Elkhatib, T. H., & Khalil, G. A. (2019). Assessment of Extracranial Carotid Arteries in Acute Ischemic Stroke: Correlation with Risk Factors. *International Journal, 7*(1), 1-6.

Elhfnawy, A. M., Volkmann, J., Schliesser, M., & Fluri, F. (2019). Symptomatic vs. asymptomatic 20–40% internal carotid artery stenosis: Does the plaque size matter? *Frontiers in neurology, 10,* 960.

Erickson, S. J., Mewissen, M. W., Foley, W. D., Lawson, T., Middleton, W., Quiroz, F., . . . Lipchik, E. (1989). Stenosis of the internal carotid artery: assessment using color Doppler imaging compared with angiography. *American Journal of Roentgenology, 152*(6), 1299-1305.

Eyding, J., Geier, B., & Staub, D. (2011). Current strategies and possible perspectives of ultrasonic risk stratification of ischemic stroke in internal carotid artery disease. *Ultraschall in der Medizin-European Journal of Ultrasound, 32*(03), 267-273.

Feigin, V. L., Krishnamurthi, R. V., Parmar, P., Norrving, B., Mensah, G. A., Bennett, D. A., . . . Truelsen, T. (2015). Update on the global burden of ischemic and hemorrhagic stroke in 1990-2013: the GBD 2013 study. *Neuroepidemiology, 45*(3), 161-176.

Fernandes, M., Keerthiraj, B., Mahale, A. R., Kumar, A., & Dudekula, A. (2016). Evaluation of carotid arteries in stroke patients using color Doppler sonography: A prospective study conducted in a tertiary care hospital in South India. *International Journal of Applied and Basic Medical Research, 6*(1), 38.

Filis, K. A., Arko, F. R., Johnson, B. L., Pipinos, I. I., Harris, E. J., Olcott IV, C., & Zarins, C. K. (2002). Duplex ultrasound criteria for defining the severity of carotid stenosis. *Annals of vascular surgery, 16*(4), 413-421.

Flaherty, M. L., Kissela, B., Khoury, J. C., Alwell, K., Moomaw, C. J., Woo, D., ... & Kleindorfer, D. (2013). Carotid artery stenosis as a cause of stroke. *Neuroepidemiology, 40*(1), 36-41.

Garg, S., Kashikar, S. V., & Phatak, S. (2016). Colour Doppler evaluation of extracranial carotid arteries: A Clinical and radiological correlation. *Journal of Clinical and Diagnostic Research: JCDR, 10*(1), TC06.

Gargano, J. W., Wehner, S., & Reeves, M. J. (2009). Do presenting symptoms explain sex differences in emergency department delays among patients with acute stroke? *Stroke, 40*(4), 1114-1120.

Genkel, V. V., Kuznetsova, A. S., Sumerkina, V. S., Salashenko, A. O., & Shaposhnik, I. I. (2019). The prognostic value of various carotid ultrasound parameters in patients at high and very high cardiovascular risk. *International journal of cardiology, 292*, 225-229.

Grant, E. G., Benson, C. B., Moneta, G. L., Alexandrov, A. V., Baker, J. D., Bluth, E. I., . . . Hertzberg, B. S. (2003). Carotid artery stenosis: grayscale and Doppler ultrasound diagnosis—Society of Radiologists in Ultrasound consensus conference. *Ultrasound quarterly, 19*(4), 190-198.

Grant, E. G., Tessler, F. N., Hoang, J. K., Langer, J. E., Beland, M. D., Berland, L. L., . . . Hamper, U. M. (2015). Thyroid ultrasound reporting lexicon: white paper of the ACR thyroid imaging, reporting and data system (TIRADS) committee. *Journal of the American college of radiology, 12*(12), 1272-1279.

Grant, E., Duerinckx, A., El Saden, S., Melany, M., Hathout, G., Zimmerman, P., . . . Baker, J. (1999). Doppler sonographic parameters for detection of carotid stenosis: Is there an optimum method for their selection?. *American journal of roentgenology, 172*(4), 1123-1129.

Haq, S., Mathur, M., Singh, J., Kaur, N., Sibia, R. S., & Badhan, R. (2017). Colour Doppler Evaluation of Extracranial Carotid Artery in Patients Presenting with Acute Ischemic Stroke and Correlation with Various Risk Factors. *Journal of clinical and diagnostic research: JCDR, 11*(3), TC01.

Ho, V., & Reddy, G. P. (2010). *Cardiovascular Imaging E-Book*: Elsevier Health Sciences.

Hunink, M., Polak, J., Barlan, M. M., & O'leary, D. (1993). Detection and quantification of carotid artery stenosis: efficacy of various Doppler velocity parameters. *AJR. American journal of roentgenology, 160*(3), 619-625.

Iemolo, F., Martiniuk, A., Steinman, D. A., & Spence, J. D. (2004). Sex differences in carotid plaque and stenosis. *Stroke, 35*(2), 477-481.

Israel, G. D. (1992). Determining sample size.

Johnson, M. B., Wilkinson, I. D., Wattam, J., Venables, G. S., & Griffiths, P. D. (2000). Comparison of Doppler ultrasound, magnetic resonance angiographic techniques and catheter angiography in evaluation of carotid stenosis. *Clinical radiology, 55*(12), 912-920.

Jowi, J., & Mativo, P. (2008). Pathological sub-types, risk factors and outcome of stroke at the Nairobi Hospital, Kenya. *East African medical journal, 85*(12).

Kapral, M. K., Fang, J., Hill, M. D., Silver, F., Richards, J., Jaigobin, C., & Cheung, A. M. (2005). Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke, 36*(4), 809-814.

Kumar, P., Sharma, R., Misra, S., Kumar, A., Nath, M., Nair, P., . . . Prasad, K. (2020). CIMT as a risk factor for stroke subtype: A systematic review. *European Journal of Clinical Investigation, 50*(11), e13348.

Lindsberg, P. J., & Roine, R. O. (2004). Hyperglycemia in acute stroke. *Stroke, 35*(2), 363-364.

Lorenzová, A. (2016). Carotid ultrasound in primary and secondary prevention of stroke. *Cor et Vasa, 58*(2), e273-e278.

Middleton, W., Foley, W. D., & Lawson, T. L. (1988). Color-flow Doppler imaging of carotid artery abnormalities. *American Journal of Roentgenology, 150*(2), 419-425.

Moneta, G. L., Edwards, J. M., Chitwood, R. W., Taylor Jr, L. M., Lee, R. W., Cummings, C. A., & Porter, J. M. (1993). Correlation of North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiographic definition of 70% to 99% internal carotid artery stenosis with duplex scanning. *Journal of vascular surgery, 17*(1), 152-159.

Mosarrezaii, A. (2018). Investigating the Frequency of Symptomatic Extracranial Artery Stenosis in Patients with Ischemic Stroke Admitted to Imam Khomeini Hospital of Urmia in 2011–2012 and Its Relationship with Cardiovascular Risk Factors. *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm, 12*(02).

Murray, C. S., Nahar, T., Kalashyan, H., Becher, H., & Nanda, N. C. (2018). Ultrasound assessment of carotid arteries: Current concepts, methodologies, diagnostic criteria, and technological advancements. *Echocardiography, 35*(12), 2079-2091.

Mwazo, M. K. (2007). *Prevalence Of Carotid Artery Stenosis And It's Risk Factors In Patients With Ischaemic Stroke As Seen In Kenyatta National Hospital* (Doctoral dissertation, University of Nairobi).

Nedelmann, M., Stolz, E., Gerriets, T., Baumgartner, R. W., Malferrari, G., Seidel, G., & Kaps, M. (2009). Consensus recommendations for transcranial color-coded duplex sonography for the assessment of intracranial arteries in clinical trials on acute stroke. *Stroke, 40*(10), 3238-3244.

Nezu, T., & Hosomi, N. (2020). Usefulness of carotid ultrasonography for risk stratification of cerebral and cardiovascular disease. *Journal of Atherosclerosis and Thrombosis*, RV17044.

O'donnell, M. J., Xavier, D., Liu, L., Zhang, H., Chin, S. L., Rao-Melacini, P., . . . McQueen, M. J. (2010). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *The Lancet, 376*(9735), 112-123.

Ogeng'o, J. A., & Olabu, B. O. (2010). Cortical stroke in Kenya. *International Journal of Stroke, 5*(6), 517-518.

O'Leary, D. H., Polak, J. F., Kronmal, R. A., Kittner, S. J., Bond, M. G., Wolfson Jr, S. K., . . . Savage, P. J. (1992). Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. *Stroke, 23*(12), 1752-1760.

Osawa, K., Trejo, M. E. P., Nakanishi, R., McClelland, R. L., Blaha, M. J., Blankstein, R., . . . Budoff, M. J. (2020). Coronary artery calcium and carotid artery intima-media thickness for the prediction of stroke and benefit from statins. *European Journal of Preventive Cardiology, 25*(18), 1980-1987.

Pathak, M. R., Gautam, M., & Pathak, Y. R. (2019). Evaluation of Extracranial Carotid Arteries in Ischemic Stroke Patients Using Color Doppler Sonography and Correlation with Various Risk Factors. *Journal of Nobel Medical College, 8*(2), 10-14.

Polak, J. F., & Pellerito, J. (2012). Normal findings and technical aspects of carotid sonography. *Introduction to Vascular Ultrasonography 6th Ed. Philadelphia: Saunders/Elsevier*, 136-146.

Polak, J. F., Shemanski, L., O'Leary, D. H., Lefkowitz, D., Price, T. R., Savage, P. J., . . . Reid, C. (1998). Hypoechoic plaque at US of the carotid artery: an independent risk factor for incident stroke in adults aged 65 years or older. Cardiovascular Health Study. *Radiology, 208*(3), 649-654.

Poznyak, A., Grechko, A. V., Poggio, P., Myasoedova, V. A., Alfieri, V., & Orekhov, A. N. (2020). The Diabetes Mellitus–Atherosclerosis Connection: The Role of Lipid and Glucose Metabolism and Chronic Inflammation. *International Journal of Molecular Sciences*, *21*(5), 1835. MDPI AG. Retrieved from

Prestige Primary Care of Texas. (2020). Carotid Doppler Ultrasound. Retrieved from Https://www.prestigeprimarycaretexas.com/carotid-doppler-ultrasound.html

Rothwell, P., Eliasziw, M., Gutnikov, S., Fox, A., Taylor, D., Mayberg, M., . . . Collaboration, C. E. T. (2003). Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *The Lancet, 361*(9352), 107-116.

Rothwell, P., Villagra, R., Gibson, R., Donders, R., & Warlow, C. (2000). Evidence of a chronic systemic cause of instability of atherosclerotic plaques. *The Lancet, 355*(9197), 19-24.

Sabeti, S., Schillinger, M., Mlekusch, W., Willfort, A., Haumer, M., Nachtmann, T., . . . Minar, E. (2004). Quantification of internal carotid artery stenosis with duplex US: comparative analysis of different flow velocity criteria. *Radiology, 232*(2), 431-439.

Scoutt, L., Kirsch, J., & Hamper, U. (2010). Ultrasound Evaluation of the Carotid Arteries. .

Sethi, S., Solanki, R., & Gupta, H. (2005). Color and duplex doppler imaging evaluation of extracranial carotid artery in patients presenting with transient ischaemic attack and stroke: a clinical and radiological correlation. *Indian Journal of Radiology and Imaging, 15*(1), 91.

Setia, M. S. (2016). Methodology series module 5: Sampling strategies. *Indian journal of dermatology, 61*(5), 505.

Simpson, C. R., Wilson, C., Hannaford, P. C., & Williams, D. (2005). Evidence for age and sex differences in the secondary prevention of stroke in Scottish primary care. *Stroke, 36*(8), 1771-1775.

Skotsimara, G., Antonopoulos, A. S., Oikonomou, E., Siasos, G., Ioakeimidis, N., Tsalamandris, S., ... & Tousoulis, D. (2019). Cardiovascular effects of electronic cigarettes: a systematic review and meta-analysis. *European journal of preventive cardiology*, *26*(11), 1219-1228.

Spencer, M. P., & Reid, J. M. (1979). Quantitation of carotid stenosis with continuous-wave (CW) Doppler ultrasound. *Stroke, 10*(3), 326-330.

Tegos, T. J., Sabetai, M. M., Nicolaides, A. N., Pare, G., Elatrozy, T. S., Dhanjil, S., & Griffin, M. (2000). Comparability of the ultrasonic tissue characteristics of carotid plaques. *Journal of ultrasound in medicine, 19*(6), 399-407.

Tell, G. S., Polak, J. F., Ward, B. J., Kittner, S. J., Savage, P. J., & Robbins, J. (1994). Relation of smoking with carotid artery wall thickness and stenosis in older adults. The Cardiovascular Health Study. The Cardiovascular Health Study (CHS) Collaborative Research Group. *Circulation*, *90*(6), 2905-2908.

Timsit, S., Sacco, R. L., Mohr, J., Foulkes, M., Tatemichi, T., Wolf, P., . . . Hier, D. (1992). Early clinical differentiation of cerebral infarction from severe atherosclerotic stenosis and cardioembolism. *Stroke, 23*(4), 486-491.

Touboul, P.-J., Hennerici, M., Meairs, S., Adams, H., Amarenco, P., Desvarieux, M., . . . Kownator, S. (2004). Mannheim intima-media thickness consensus. *Cerebrovascular diseases*, *18*(4), 346-349.

WHO. (2012). *Global Health Estimates.* . Retrieved from Geneva: http://www.who.int/healthinfo/global_burden_disease/en/

WHO. (2014). *Global Status Report on noncommunicable diseases*. Retrieved from Geneva: https://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854_eng.pdf

Yadav, A. K., Dev, B., Taparia, S., Yadav, N., Upadhyaya, B. B., Kumar, P., . . . Rajbanshi, L. K. (2020). Role of Color Doppler Ultrasonography in Evaluation of Extracranial Carotid Artery in Stroke Patients: A Prospective Study. *Birat Journal of Health Sciences*, *5*(2), 1091-1098.

Zwiebel, W. (2000). Vascular disorders of the liver. *Introduction to vascular ultrasonography. 4th ed. Philadelphia, PA: WB Saunders*, 443-445.

APPENDICES

Appendix I: Consent Form

English Version

Investigator: My name is Dr. Onwong'a Mercyline Kerubo, I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a postgraduate degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which is to study patterns of Carotid Doppler findings and associated factors among adult patients with ischemic stroke at Moi Teaching and Referral Hospital Eldoret.

Purpose: This study will seek to describe the pattern of carotid artery Doppler findings and associated factors among adult patients with ischemic stroke at MTRH

Procedure: Patients who have ischemic stroke on CT and whom consent has been obtained will be enrolled in the study. They will be transferred to the ultrasound room where the carotid arteries will be assessed by both grey scale and color Doppler. The data gathered from the color Doppler examination will be entered in a structured data entry form. Patients with stenotic lesions will be referred to physicians and or vascular surgeons for evaluation and further management.

Confidentiality: The data gathered will be stored safely under lock and key in the office of the principal investigator and will only be accessed by her and the 2 supervisors.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants attributable to this study.

Rights to Refuse: Participation in this study is voluntary, there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional

Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Patient/legal Guardian: ……………… Investigator: …………………...

Date............................

Appendix II: Kiswahili Version

Mpelelezi: jina langu ni Daktari Onwong'a Mercyline Kerubo. Mimi ni daktari aliyehitimu na kusajiliwa na bodi ya Kenya ya Madaktari na Madaktari wa meno. Mimi sasa natafuta shahada ya uzamili katika Radiology na Imaging katika Chuo Kikuu cha Moi. Ningependa kukuhusisha katika utafiti wangu ambao ni wa kuchunguza jinsi mishipa ya shingo inavyoonekana kwa kutumia chombo cha ultrasound kwa wagonjwa walio na kiharusi katika hospitali ya mafundisho na ya rufaa ya moi.

Kusudi: Utafiti huu utajaribu kuonyesha jinsi mishipa ya shingo inayopeleka damu kwenye ubongo, inavyoonekana kwenye ultrasound na kuonyesha iwapo mishipa hii ina kasoro yoyote inayoweza kuchangia mgonjwa apate shida ya kiharusi.

Utaratibu: wagonjwa watakaopatikana kuwa na ugonjwa wa kiharusi kupitia chombo cha CT scan na waliotoa kibali kuhusika katika utafiti huu watapelekwa kwenye chumba cha ultrasound. Chombo cha ultrasound kitatumiwa kuchuguza mishipa ya shingo ili kujua iwapo ina kasoro yoyote, na majibu yatakayopatikana yataandikwa kwa njia ya ripoti. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa katika nyumba ya mpelelezi mkuu katika kipindi cha utafiti.

Faida: Kutakuwa hakuna faida moja kwa moja ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa nahaki nakupewa ubora sawa na wale ambao hawatofanyiwa utafiti huo.

Hatari: Hakuna hatari ya kutarajia kwa washiriki inatokana na utafiti huu.
Usiri: habari zote zilizopatikana katika utafiti huu wa kutibiwa zitawekwa kwa usiri mkubwa na wala haitatolewa kwa mtu yeyote asiye husika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni hiari yako, kuna uhuru wa kukataa kuchukua sehemu au kutoka wakati wowote. Utafiti huu umeidhinishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha kufundisha cha Moi na Hospitali kuu ya Rufaa.

Weka sahihi au kufanya alama kama unakubali kushiriki katika utafiti

Mgonjwa / Mlezi: .... Mpelelezi: ....

Tarehe: ....

Appendix III: data collection sheet.

1. DEMOGRAPHIC DATA

Date		
Serial number		
Age / DOB		
Gender	Male	
	Female	

2. DIAGNOSIS

C.T Diagnosis (Specify the territory of infarct.)	

3.RELEVANT HISTORY

	YES	**NO**
Smoking history		

4. CO-MORBIDITIES

	YES	**NO**
Presence of Hypertension.		
Presence of Diabetes.		

5. RESULTS

	Right	Left
CCA IMT (cm)		

SITE OF PLAQUES (tick appropriately)	Right	Left
CCA		
ICA		
Carotid bulb		
ECA		

PLAQUE CHARACTERISTICS (tick appropriately)	Right	Left
Homogeneous		
Non- homogeneous		
Ulcerated		
Calcified		
Intra-plaques hemorrhages.		

	Right	Left
ICA PSV (cm/sec)		
ICA/CCA PSV Ratio.		
ICA EDV (cm/sec)		

Degree of stenosis(%)	Right	Left
<50%		
50-69%		
70-89%		
Near occlusion.		

APPENDIX III: CAROTID ULTRASOUND PROTOCOL

Patient preparation

- Inform the patient about the procedure
- Seek consent
- Maintain confidentiality and privacy

Equipment required

Pre-warmed coupling gel

7-10 MHz linear transducer.

Positioning

- Patient wears hospital gown
- Patient lies supine on the examination couch.
- Neck exposure was enhanced by tilting and rotating the head away from the side being examined, and ipsilateral shoulder being dropped as far as possible
- The examiner was seated at the right side of the patient.

Imaging procedure

The examination was conducted using either of the two Minday M7 ultrasound machines in the radiology department.

Patient lies supine neck is exposed and paper towel used to protect patient's clothes.

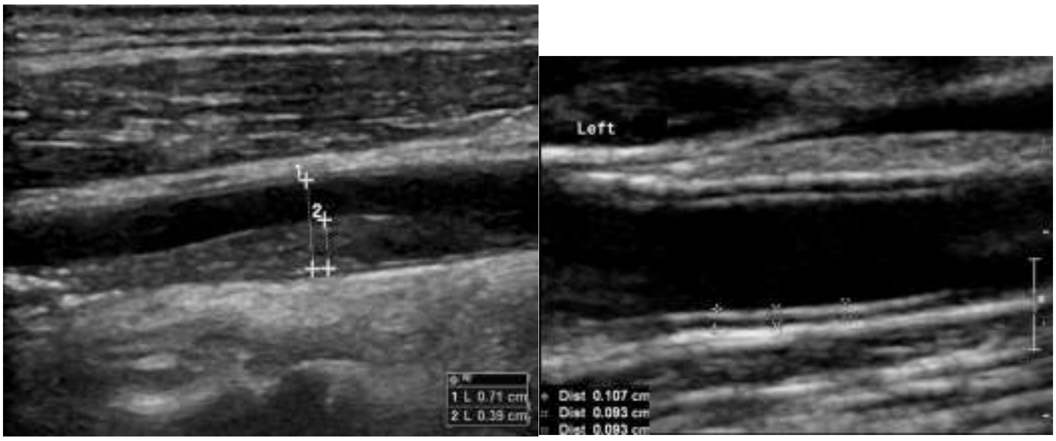
Pre-warmed coupling gel is applied to the 7-10 MHz linear transducer and carotid ultrasound conducted.

The posterolateral and far posterolateral transducer positions were used to examine the carotid arteries in long axis (longitudinal). Short axis (transverse) views of the carotid arteries were obtained from an anterior, lateral or posterolateral approach

Doppler ultrasonography is done (angle <60 degrees) and various parameters of CCA, ICA and ECA assessed.

Gray scale carotid ultrasound

- Longitudinal and transverse views.
- The ICA normally runs lateral or posterolateral to the ECA in its first part, and the extra-cranial ICA does not give off any branches.
- Carotid intima media thickness (CIMT) is determined: inner high-reflective line represents the luminal-intima interface and the outer high-reflective line represents the media-adventitia interface, with the distance between the two lines being a measure of the thickness of the intima and media combined.
- Presence or absence of plaque, location of plaque and plaque characteristics such as heterogeneous (mixed) or homogenous (uniform) echogenicity, calcification, any ulceration, or intra-plaque hemorrhage are evaluated

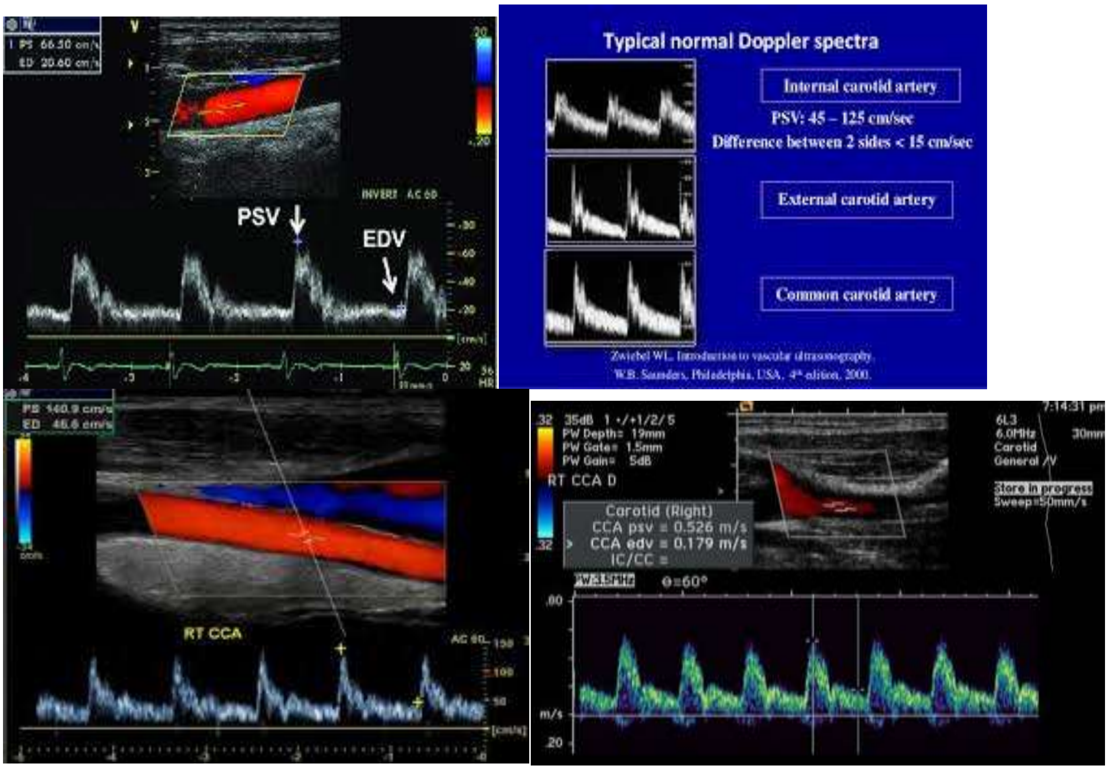


Carotid Doppler ultrasound.

- PSV and EDV of CCA, ICA and ECA are evaluated.
- CCA PSV and EDV are measured in the distal CCA approximately 1 cm proximal to the bulb.
- ICA PSV and EDV are measured just distal to the bulb to avoid the complex hemodynamics within the bulb.
- At sites of stenosis, the cursor is moved through the stenosis to obtain the maximum velocity.
- The spectral Doppler waveform of the ICA is low resistance with a high diastolic component in comparison to the ECA, which is of high resistance

with a low diastolic component. The waveform of the CCA is usually of low resistance but may appear as a hybrid of those of the ICA and ECA.

- The society of radiologists in ultrasound (SRU) consensus criteria of 2004 in the United States used to determine the degree of stenosis of the internal carotid artery.
- The SRU criteria involves estimating the percentage of stenosis using ICA PSV, ICA/CCA PSV ratios, and degree of stenosis at most stenotic portion



Appendix IV: IREC Approval

MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2018/114
Approval Number: 0003087

6th September, 2018

Dr. Mercyline Kerubo Onwong'a,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
06 SEP 2018
APPROVED
P.O. Box 4606-30100 ELDORET

Dear Dr. Onwong'a

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Evaluation of Carotid Arteries using Doppler Ultrasound among Patients with Ischemic Stroke at Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3087*** on 6th September, 2018. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 5th September, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	-	SOM
	Principal	-	CHS	Dean	-	SON	Dean	-	SOD

Appendix V: Hospital Approval

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

14th September, 2018

Dr. Mercyline Kerubo Onwong'a,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Evaluation of Carotid Arteries using Doppler Ultrasound among Patients with Ischemic Stroke at Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

14 SEP 2018

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - DCEO, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM

All correspondence should be addressed to the Chief Executive Officer
Visit our Website: www.mtrh.go.ke
TO BE THE LEADING MULTI-SPECIALTY HOSPITAL FOR HEALTHCARE, TRAINING AND RESEARCH IN AFRICA