"STUDY OF PREVALENCE AND SEVERITY OF ATHEROSCLEROTIC DISEASE IN EXTRA CRANIAL CAROTID ARTERIES AMONG TYPE 2 DIABETES MELLITUS PATIENTS USING COLOR DOPPLER SONOGRAPHY- A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

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ABSTRACT

INTRODUCTION

Atherosclerosis is a chronic inflammatory disease that progresses gradually for several decades before symptoms and complications appear and by this time, the disease would have had irreversible histopathological changes.

Diabetes mellitus is one of the major risk factors for developing cerebrovascular, coronary artery and peripheral arterial diseases. Higher incidence of stroke and myocardial infarction occurs at younger ages in diabetic patients as compared to non-diabetic patients.

Hence, there is a need to detect the atherosclerotic changes by the accurate screening techniques at the beginning of the disease process.

Accuracy, patient ease, reduced radiation risk has made carotid Doppler ultrasonography as a preliminary investigation in assessing extracranial carotid vessels because its accuracy is well established.[2]

Digital Subtraction Angiography (DSA) is considered the gold standard investigation in detecting atherosclerotic plaques. However, the invasiveness of the procedure and associated risk of permanent neurological complications is a necessity for alternate less invasive investigations.

This study was done to assess the prevalence and severity of atherosclerosis in extracranial carotid arteries in diabetic patients using carotid Doppler ultrasonography with an aim to identify the deformity early, which will reduce the morbidity and mortality in the patients.

OBJECTIVES OF THE STUDY:

- Find out the age, gender distribution, prevalence of atherosclerosis among type 2 diabetes mellitus cases.
- To evaluate the utility of the peak systolic velocity ratio of ICA / CCA in assessing carotid artery stenosis.

MATERIALS AND METHODS

This is a cross sectional study carried out on 65 patients who were known cases of type 2 diabetes mellitus over a period of 1 year duration at KLE's Dr. Prabhakar Kore Hospital & MRC, Belagavi. The study participants underwent carotid Doppler ultrasonography.

The current study was a hospital based cross sectional study, conducted in the Department of Radiodiagnosis at the KLE's Dr.PRABHAKAR KORE Hospital & MRC, BELAGAVI. Patients diagnosed with type 2 diabetes mellitus who were referred to Department of Radiodiagnosis at the KLE's Dr.PRABHAKAR KORE Hospital & MRC, BELAGAVI for carotid Doppler ultrasonography between January 2019 & December 2019 were considered for the study.

The study included 65 patients who satisfied the inclusion criteria. All the patients underwent carotid artery ultrasonography on GE VOLUSON 8 machine (GE Healthcare, USA) fitted with a linear array transducer of 7.5-12 MHz high frequency. The findings of the Doppler ultrasound were assessed and analyzed.

Descriptive analysis was carried out for the quantitative data. Data was represented using appropriate diagrams like bar diagram and charts.

RESULTS

- Out of 65 patients in the study, the mean age was 60.29±10.19 yrs. The number of male patients affected were higher as compared to the females. Most of the patients were from the age group of 60-69 yrs 27 cases (41.5%).
- 13 cases (20%) were normal, 5 (7.7%) had increased IMT without evidence of plaques, 47 cases (72.31%) had atherosclerotic plaques making the prevalence of atherosclerosis in the study as 80%.
- Left internal carotid artery at its origin was the most common site of involvement of atherosclerosis followed by right proximal internal carotid artery at its origin and right carotid bulb. Left proximal ECA was the least involved site in the study.
- Heteroechoic plaque with specks of calcifications was the most common type of plaque.
- Out of 34 CCA's involved, maximum number of CCA's had <50% stenosis, i.e 25 CCA's (73.5%).
- Total of 55 carotid bulb's were involved in 38 cases, maximum number of carotid bulb's had <50% stenosis.
- 20 external carotid arteries were involved in 16 cases; maximum number of ECA's had <50% involvement.
- 62 internal carotid arteries were involved in 41 cases; 48 ICA's had <69% stenosis whereas 4 ICA's had near total occlusion.
- None of the arteries in the study had total occlusion.
- PSV of ICA/CCA was calculated in all the cases having plaques in internal carotid artery, and it was found that all cases which had < 50% stenosis had ICA/CCA ratio < 2, 50-69 % stenosis had ICA/CCA ratio in the range of 2-4, >70 %

stenosis has ICA/CCA ratio >4 ; however in 3 cases the ratio didn't correlate to the range as specified by the criteria in our study, thus indicating that PSV (ICA/CCA) ratio can be used as an additional parameter in assessing stenosis of ICA.

INTERPRETATION AND CONCLUSION

- Non-invasive, cost effective, no risks of radiation are the factors which make Color Doppler ultrasonography as the safest and first line investigation for evaluation of extracranial carotid vessels.
- This study establishes evidence that prevalence of atherosclerosis is high in patients suffering from type 2 diabetes mellitus. 80% was the prevalence in this study.
- This study indicates that prevalence of atherosclerosis is more common in men and the maximum number of cases were from the age group of 60-69 years.
- Detailed evaluation of atherosclerosis like site and nature of plaque and percentage stenosis in extracranial carotid arteries was assessed.
- (ICA/CCA) PSV ratio was an additional parameter analysed in this study in assessing the percentage stenosis of ICA and it proved to be an useful parameter.

KEYWORDS

Carotid Doppler ultrasonography of carotid arteries (US), atherosclerosis in diabetics.

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INTRODUCTION

Atherosclerosis is a method of gradual thickening and hardening of the walls of medium sized and large sized arteries as an effect of fat sediment on their inner lining. In diabetes mellitus patients its occurrence is high.

One of the major risk factors of developing cerebrovascular, coronary artery and peripheral arterial diseases is diabetes mellitus. Higher incidence of stroke and myocardial infarction occurs at younger ages in diabetic patients as compared to non-diabetic patients. This threat is three times more in diabetic patients than non-diabetic individuals.[3, 5]

According to an investigation report published by the health and family welfare ministry (Indian council of medical research-India diabetes) in October 2019, there are 7.2 crore (11.8%) adults suffering from diabetes in India. Glycemic status is associated with all degrees of carotid atherosclerosis, from early signs such as increased IMT to progressive atherosclerosis, which is evidenced by the presence of carotid stenosis.[4]

Atherosclerosis is primarily a chronic inflammatory disease that goes on in stillness for several decades before symptoms and thrombotic complications appear and by this point of time, the disease would have had unrepairable histopathological changes.

Therefore, there is a need to detect the atherosclerotic changes by the screening techniques at the beginning of the disease process.

Carotid Doppler ultrasonography has become a foundation in assessing extracranial carotid vessels because its accuracy is well established when compared to carotid angiography.[2]

Advantages of ultrasonography imaging are patient ease, reduced radiation risk and accuracy. CTA (computed tomography angiography) is high-priced, invasive and contrast related adverse effects accord to significant morbidity.[2]

In addition to estimating the severity of stenosis, ultrasonography can help in identifying and characterizing plaque and plaques which have high risk of embolization. The so-called “echolucent” or “predominantly echolucent” plaques are those which correspond to type 1 and type 2 in the GRAY WEALE classification & are erratic plaques that will become symptomatic, regardless of whether they are associated with stenosis or not. These plaques need additional attention during ultrasound of the carotid artery. [6]

This study will allow us to know the allocation by age, gender distribution, prevalence and strength (degree of stenosis) of atherosclerosis in type 2 diabetes mellitus cases, as well as identify the deformity early, which will narrow morbidity and mortality in the public in general.

AIM:

To study the prevalence and severity of atherosclerotic disease in extra cranial carotid arteries among type 2 diabetes mellitus patients using carotid Doppler ultrasonography.

OBJECTIVES:

- Find out the age, gender distribution, prevalence of atherosclerosis among type 2 diabetes mellitus cases.
- To evaluate the utility of the peak systolic velocity ratio of ICA / CCA in assessing carotid artery stenosis.

REVIEW OF LITERATURE

ANATOMY:

"Major blood vessels that supply arterial blood supply to the brain are the two internal carotid and two vertebral arteries

The central nervous system gets most of its blood supply from three major blood vessels that originate from the superior mediastinum. Superior mediastinum is the starting point for the three branches of arch of aorta such as brachiocelaphic trunk, left subclavian and left common carotid arteries. The innominate arteries are about 4 to 5 centimeters above the posterior right side of the neck. The innominate arteries further branch into right subclavian and right common carotid at the right sterno-clavicular junction. The left common carotid from the aortic arch descends towards the left right sterno-clavicular junction. They further distribute as internal and external carotid arteries at the top edge of thyroid cartilage.

INTERNAL CAROTID ARTERIES (ICA):

Much of anterior circulation of blood for the cerebrum is from the internal carotid arteries (ICA's). The internal carotid arteries can be relatively straight in their cervical section or tortuously curved as they pass through the base of the skull. The ICA in the neck do not have any branches. While they continue intracranially, ICA produces branches such as caroticotympanic and meningo-pituitary branches in the petrous bone and meningo-pituitary branches. The ICA also gives rise to ophthalmic arteries and posterior communicating arteries, which is the juncture for posterior cerebral arteries. The cerebral arteries are further divided into middle and anterior

arteries by cephalad ICA. The cephalad ICA gives rise to choroidal arteries (posterior and anterior).

EXTERNAL CAROTID ARTERIES (ECA):

External carotid arteries do not usually supply blood to the brain but in ICA or vertebral artery occlusion, some of its branches act as important collateral pathways. The ECA branches are ascending pharyngeal, the upper thyroid, lingual, maxillary, occipital, facial, posterior auricular, maxillary and the superficial temporal arteries. ECA plays a vital role in collateral circulation. It also communicates with opthalmic arteries, occipital and vertebral arteries which interconnects muscular branches.

VERTEBRAL ARTERY:

Vertebral arteries that originate from subclavian arteries contribute more for posterior circulation of blood to the brain. They form the major arteries of the neck region and is found in foramina transversarium region of the upper part of cervical vertebrae coursing towards subarachnoid space, which is situated beside medulla oblongata. They further move anteriorly to join basilar artery. The basilar artery gives rise to four branches before branching into posterior cerebral arteries. The four branches are responsible for the supply of pons and medulla to upper and lower parts of cerebellum.

Circle of Willis:

The circle of Wills is an arterial circle that acts as a junction for internal carotid and vertebral arteries in the lower part of the brain. It is responsible for intracranial collateral circulation and aneurysm formation. It has hexagonal arrangement of arteries that constitute posterior, anterior and middle arteries bonded together by

communicating arteries. The circle acts as collateral pathways during carotid vertebro-basilar system occlusion.

Anomalies:

1. Extra- cranial Circulation:
   - A close connotation or sharing of the origin of innomiate artery with common left carotid artery is most frequent.
   - Abnormal left vertebral artery origin on the aortic arch between common carotid left and subclavian arteries.
   - Hardly right subclavian artery on aortic arch may have aberrant origin."[64]

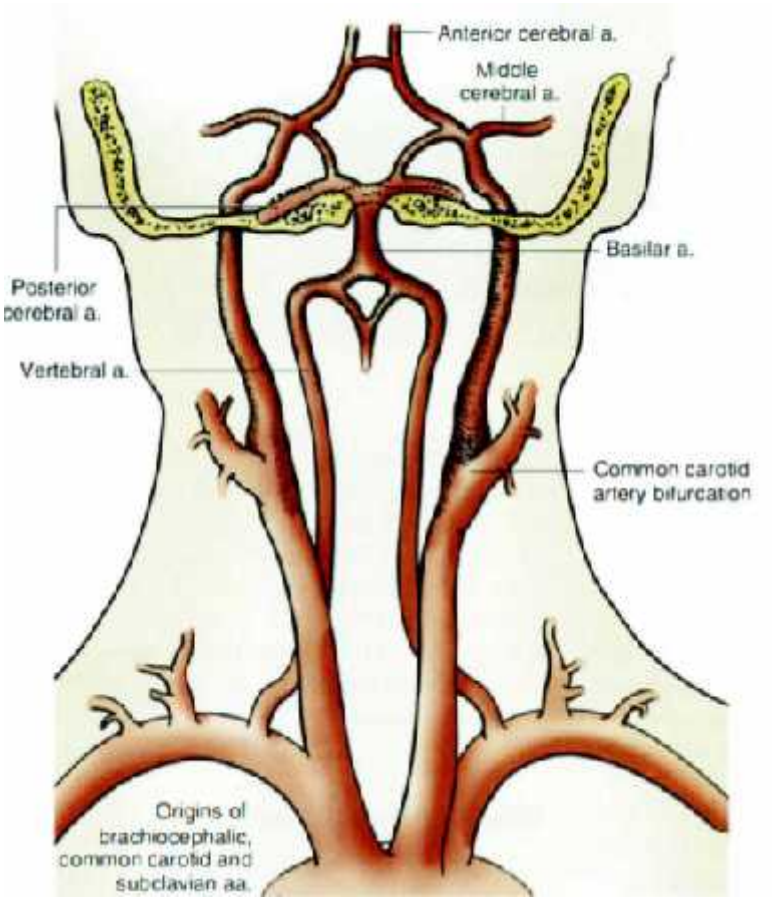


Fig 1: Diagrammatic illustration of the carotid vascular anatomy

Microscopic anatomy of the carotid artery wall:

Arteries are categorized as follows according to their size and function:

(i) Arteries that are large and has high elasticity

(ii) Moderate sized muscular arteries

(iii)Small sized arteries and blood vessels

The artery wall consists of three strata as follows:

(i) Tunica intima: Is the artery's innermost strata lined by flat endothelial cells.

(ii) Tunica media: Is the middle stratum of the arterial wall. It is composed of smooth muscles, collagen and elastin that are accountable for the enlargement of the arteries during systole and diastole recoil.

(iii) Tunica adventitia: This layer is made of connective tissue (collagen and elastin) which anchors arteries to the adjacent structures.

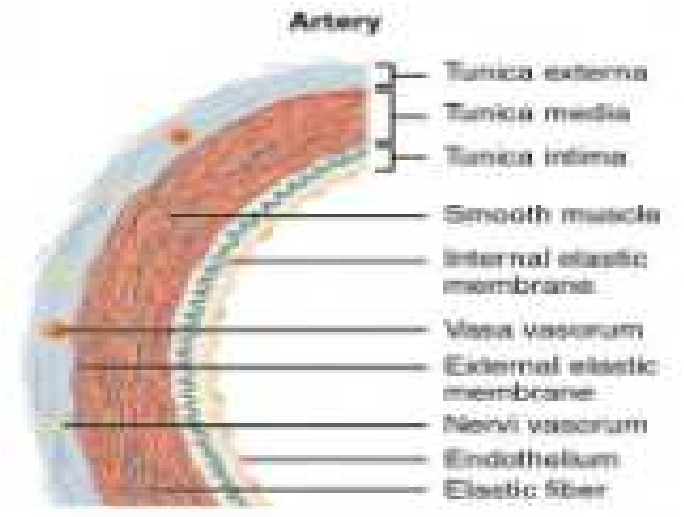


Fig 2: Diagrammatic illustration of different layers of the arterial wall

Atherosclerosis is an arterial wall disease, which occurs in the major conduit arteries at susceptible sites. It is caused by lipid accumulation, oxidation, and alteration, which eventually induces chronic irritation or swelling, causing stenosis or thrombosis.[7]

The term atherosclerosis comes from the Greek word "athero" which means wax or gruel. It refers to necrotic core region at the base of the plaque. The word “sclerosis” also comes from the greek word “skleros” which means hard or stiffening and it refers to the fibrous cap of plaque.

Risk factors:

- High Blood Pressure (Hypertension)
- Diabetes mellitus
- Abnormal levels of cholesterol in the blood
- Tobacco consumption
- Obesity
- Unhealthy lifestyle , lack of exercise and imbalanced diet
- Ageing

Three major vascular areas which tend to have clinical signs of atherosclerosis. They are (i) carotid extra-cranial vasculature; (ii) coronary arteries; and (iii) peripheral arteries; Clinical pathology of atherosclerosis is exacerbated by diabetes mellitus.[11]

EPIDEMIOLOGY:

Diabetes prevalence varies according to the region of distribution. According to the National Diabetes and Diabetic Retinopathy Survey (ICMR-INDIAB Study) report published by the Ministry of Health and Family Welfare in 2019, India has higher rates of diabetes when compared to western countries. Also, the prevalence of DM in India remained at 11.8% since four years (2015-2019).

Males and females had almost equal diabetes prevalence (12 percent) to females (11.7 percent). In the year 2019, people who were already known to have diabetes represented 67.3 percentage of participants, while 32.7 precentage were new diabetics. People of age group 70-79 years were observed to have high prevalence for diabetes, which was around 13.2%. The urban region had prevalence range of diabetics from 10.9 percent to 14.2 percent.

The prevalence of global diabetes estimated to be 9.3 per cent (463 million people) in 2019.

Many studies conducted across the globe have shown substantial prevalence of atherosclerosis in people with diabetes.

Although women are comparatively safe against atherosclerotic complications compared to men, DM negates the benefits of female sex.[11]

Pathophysiology:

Chronic hyperglycemia, dyslipidemia and insulin resistance are the major abnormal metabolic states that accompany diabetes causing arterial dysfunction i.e. atherosclerosis.

DM alters multiple cell functions at various levels, which are discussed below.

Endothelial cell dysfunction:

Vascular endothelium dysfunction is a hallmark of the majority of conditions associated with both diabetes and atherosclerosis, and may lead to cardiovascular diseases (CVD).

Single strata of endothelial cells lining the innermost surface of the vessels synthesizes vital bioactive substances including prostaglandins, nitric oxide, angiotensin II and endothelin which regulate the function and structure of the blood vessels.

Nitric oxide (NO) is primarily responsible for suppression of platelet trigger, inflammation, and reduction of leukocyte adhesion.

Diabetes blocks the production of NO that impairs the endothelium dependent vasodilation (nitric oxide-mediated). Diabetes blocks the activation of endothelial nitric oxide synthase (eNOS) which causes increase in production of reactive oxygen radicals in the vascular smooth muscle cells and the endothelium.

Insulin resistance is also a prime factor that causes excessive production of free fatty acids in the adipose tissue. This excessive production of fatty acids activates protein kinase C that produces excessive reactive oxygen.

Hence, due to increased levels of peroxynitrite and decrease in NO levels can further cause improper production of vasodilators. In addition to it, DM causes increased production of many vasoconstrictors, mainly Endothelin-1 which is responsible for activation of Endothelin-A receptors that causes vasoconstriction.

T-cell lymphocytes pass into the tunica intima and takes part in atherogenesis. During atherogenesis, T-cells help in modulating the formation of lesions by secreting cytokines. Early atherogenesis is symbolized by localized accretion of foam cells, leading to development of fatty streaks. Hyperglycemia through reduced NO production and increased oxidative stress and receptor activation for advanced glycation end products causes increased activation of transcription factors such as nuclear factor kb and activator protein. Gene expressions that encode many mediators of atherogenesis, that transfer lymphocytes and monocytes into the vessel wall and pro-inflammatory mediators found in atheroma, including IL-1 and tumor necrosis, are controlled by these two factors. Lipid abnormalities found in DM triggers the increase in cell adhesion molecule and cytokine expression. DM also triggers plaque instability and clinical sequela in addition to atherogenesis.

Diabetes interferes with the collagen breakdown process and reduces the stability in fibrous cap of plaque leading to plaque rupture and thrombosis.

Diabetes and vascular smooth muscle dysfunction:

Vascular smooth muscle cells are sources of collagen that fortify the atheroma, making it more averse to crack and cause thrombosis. Progressed atherosclerotic injuries in diabetic patients have less vascular smooth muscle cells and furthermore oxidized glycated low density lipoprotein which provokes apoptosis of muscle cells of the vessels.

Impaired platelet function:

Diabetes abnormalities causes increased activation of platelet and simultaneously reduce the production of endogenous inhibitors of platelet activity.

This results in abnormal regulation of intra-platelet calcium bringing about platelet shape change, production, conglomeration and thromboxane formation. These conditions clarify that increased thrombotic events are the possible characteristics of diabetes.

Abnormal coagulation:

Diabetes not only potentiates platelet function but also causes increases blood coagulability, making atherosclerotic plaque eruption more probable, which will result in thrombotic blocking.

DM increases the expression of coagulation factors, and reduces endogenous anticoagulants like antithrombin III and protein C. In this manner in DM, an expanded tendency towards coagulation, combined with debilitated fibrinolysis favours thrombus formation.

In an investigation directed by Eggen DA, Solberg LA concluded that all the cases develop fibrous plaques irrespective of the risk group, which dynamically extend to cover 20%-46% of the coronary vessel surface. In high risk class, fibrous plaques are seen at a younger age (17 yrs to 23 yrs) and generally grow more quickly (0.8% versus 0.5% of surface every year).[14]

Previous pathological studies of sudden coronary death have demonstrated evidence of plaque rupture associated with thrombosis in 73% of cases. Of the remaining cases, 8% consist of plaque fissure with intra-plaque fibrin deposition and hemorrhage, while 19% show no evidence of thrombi.[15] Consequently, recent reviews have agreed plaque rupture as the critical event leading to coronary artery thrombosis and death.[16]

Vascular calcification (Vc) is an extreme, irreversible patho-phenotype exceptionally common in patients with atherosclerosis, DM and chronic kidney disease. DM patients have high probability to increase Vc with loss of flexibility of smooth muscle cells and elastic tissue. The osteogenic indicators for instance soluble phosphatase, runt and osteocalcin related transcription factor in vascular cells are elevated leading to mineralization.[13]

It is widely accepted that high-density lipoprotein (HDL) glycation in DM may be the reason for HDL impairment, which reduces its atheroprotective effects. It is also proved that glycated end products could promote Vc.[17]

La Sala L et al in a study in 2019 after considering evidences which showed hyperglycemia and atherogenic factors share common mechanisms, they suggested a hypothesis between diabetes and atherosclerosis that both of them originate from same ancestors. 'Nuclear factor kB' is the main controller, which apparently triggers hyperglycemia-induced consequences on the endothelial function, or in the gene expression of selected microRNAs which are the factors associated with atherosclerosis.[9]

Complications due to atherosclerosis:

Cardiovascular disease (CVD) is the leading complication of type 2 DM and approximately one half of patients with type 2 DM will die of a cardiovascular cause. Angina, myocardial infarction, stroke, peripheral artery disease, and congestive heart failure are all common among patients with type 2 diabetes. The prevalence estimate of stroke among patients with type 2 diabetes range from 4 to 12% in clinic-based populations and between 4 and 5% in population-based studies. The incidence of

stroke in patients with type 2 DM can be more than three times the risk for the general population and seems to be more marked for men than for women.[10]

In a study conducted by Bollipo JP, Rao PB in the year 2018, which included 100 stroke patients, 51% were males and 49% were females. 59% of the patients were above 61 years of age, 24% of them were between 51-60 years and 12% were between 41-50 years. 82% of the patients had the presence of atherosclerotic plaque while 18% had increased intima-media thickness without the plaque. Among the patients with atherosclerotic plaque, 63.4% had diabetes suggesting that Color Doppler assessment of extra cranial carotid arteries could be used in predicting CVA in patients with carotid atheromatous disease.[38]

A study by Palomäki H, Kaste M, Raininko R, Salonen O, Juvela S, Sarna S showed the presence of atherosclerotic plaques in 61% of the patients who had transient ischemic attack or minor stroke suggesting its significant prevalence.[39]

Diagnostic modalities:

Diagnostic modalities used in the evaluation of extra-cranial carotid vasculature:

1. Intra-arterial contrast angiography
2. Carotid duplex USG
3. Computed tomographic angiography
4. MRI angiography

Intra-arterial contrast angiography: Intra-arterial digital subtraction angiography (DSA) is considered as the gold standard for detection of carotid stenosis.

Atherosclerotic vascular disease in angiography shows vessel irregularity, tortuosity and narrowing of the vessel lumen as well as frank occlusion.

Advantages:

i. Allows study of entire carotid system

ii. Plaque morphology, collateral circulation can also be assessed more accurately.

Disadvantages:

i. Invasive, expensive and risk of neurological complications.

Computed tomographic angiography (CTA):

CT angiography is known to be an excellent aid to detect carotid artery occlusion and grading stenosis depending upon the percentage of occlusion.

MRI angiography (MRA):

Different techniques for MRI angiography include Time of flight MRA (TOF-MRA), black blood MR angiography (BBMRA) and MR angiography for phase contrast (PC MRA).

3D-TOF-MRA is the mostly preferred MRA for assessing intracranial steno-occlusive disorder in ischemic stroke, mostly as an adjunct to MR DWI. The poor flow from in-plane de-phasing or moderate flow, leads to incorrect prediction or outcomes by increasing the severity of stenosis or a false prediction of a vascular obstruction, 3D-TOF-MRA has proven to be highly insensitive.

In spite of the fact that T1 spin-echo sequence can precisely distinguish sub-acute hemorrhage or thrombi, it has major limitations in the detection of vessel thrombosis.

The high contrast and high spatial resolution of 3D (BBMRA) helps in recognizing the extra luminal vessel from the intraluminal black blood, permitting improved diagnosis of intravascular thromboembolic obstructions.[40]

Advantages:

- Assessment of Circle of Willis, distal ICA and the vertebral-basilar vessels is done.

Disadvantages:

- More expensive, time consuming and less easily available.
- Difficult in critically ill patients or patients who are unable to lie supine or have a pacemaker and those who have undergone recent implant surgery.

Lv P, Lin J, Guo D, Liu H, Tang X, Fu C, Hu J conducted a study to determine the efficacy of CTA, BBMRA and TOF MRA in detecting carotid stenosis by using DSA as a reference standard. This study included 30 cases with carotid artery stenosis. CTA showed a high sensitivity of 100% and specificity of 97% whereas BBMRA showed sensitivity of 100% and specificity of 95% , MRA showed sensitivity of 79% and specificity of 95%.CTA and black blood MRA recognized plaque surface abnormality more often than with TOF MRA. This research proved black blood MRA as an effective imaging method in assessment of carotid artery stenosis.[19]

An study conducted by Binaghi S, Maeder P, Uské A, Meuwly JY, Devuyst G, Meuli RA in 2001, to assess the role of CTA and MRA in the measurement of atherosclerotic stenosis of carotid blood vessel bifurcation as compared to digital

substraction angiography (DSA) and Doppler sonography (DS). Study included 25 DSA confirmed cases of carotid artery stenosis, who underwent CTA and MRA and DS. 97 percent of MRA measures were similar to DSA. 96% of CTA measures were proportionate to DSA. 77% stenosis were accuaretly identified by DS, overestimation of stenosis was seen in 21% of cases and underestrimation seen in 2%. This study proved CTA and MRA as highly sensitive imagining modalities in measuring the level of carotid stenosis.[20]

Doppler ultrasonography:

This is a non-invasive, safe and inexpensive technique. Direct examination of the extracranial carotid can be achieved using high definition gray scale ultrasound and doppler spectral analysis and color flow doppler sonogrpahy. Ultrasonic examination allows to detect carotid stenosis with high accuracy.[41]

As an adjuvant, transcranial doppler USG can be used to examine intracerebral vessels through the orbits.

In 1881 Piercce and Jacques discovered piezoelectric effect. D.Howry, J. Wild and G.Luduing demonstrated independently that when ultrasound waves generated by piezoelectric crystal transducer were transmitted into the body, ultrasound waves of different acoustic impedence would be returned to the transducer.

The use of Doppler ultrasound for the assessment of extra cranial carotid vasculature was first reported by Miyazaki and Kato et al in 1965.

Barber et al 1974: proposed the use of ultrasound for the investigation of carotid bifurcation disease.[21]

D.Eugene strandness JR 1977: showed that the addition of the colour to the duplex scanning system would serve as road map.

B MODE- B stands for brightness modulation display. The display system will keep a record of all the dots so that as the transducer is scanned across the patient. All the echoes that are produced from the interface will be displayed and recorded in the position from which they were produced. B mode yields a 2-D picture of the area covered by the transducer. The picture actually represents a slice of the patient, the thickness of the slice will be equal to the width of the ultrasound beam.

Doppler physics:

Australian physicist Johann Christian Doppler was the first to describe Doppler effect in 1842.

Principle: The Doppler principle states that when energy is reflected from a moving boundary, the frequency of the reflected energy varies in relation to the velocity of the moving boundary. The difference between receiving and transmitting frequencies gives the Doppler shift frequency.

The Doppler effect can be described as a change or variation in the frequency of the detected wave while the source or the indicator is moving. In clinical ultrasonography, a Doppler shift happens when reflectors moves relatively with the transducer.

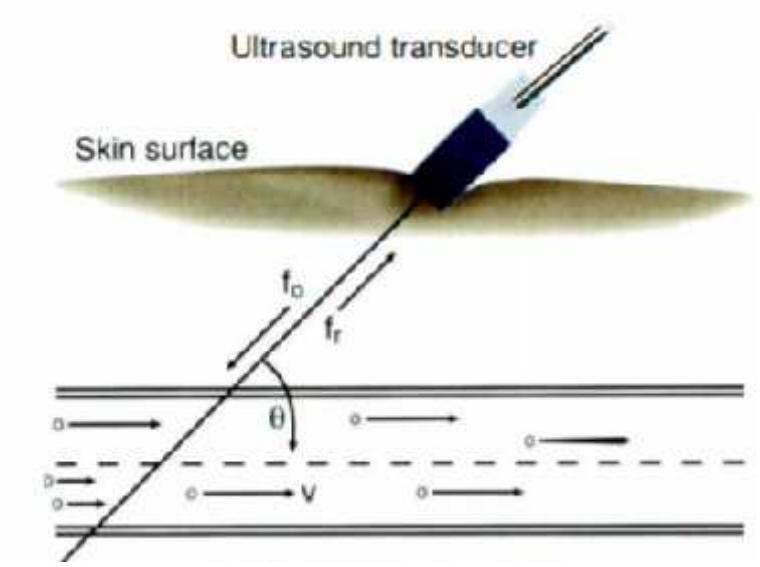


Fig 3: Digramatic illustration of the equation of Doppler study

$$\Delta F = (F_R - F_T) \frac{2F_T \cdot V \cdot \cos\Phi}{C} \quad \text{or} \quad V = \frac{\Delta F \cdot C}{2F_T \cdot \cos\Phi}$$

ΔF represents Doppler shift/variance frequency

θ is angle formed between flow direction and the ultrasound beam's axis.

F_T is transmitted frequency

F_R is received frequency

V is blood flow velocity

C is speed of sound in tissue

Blood flow velocity is calculated by the above-mentioned equation. Doppler signals detected are strongly influenced by Doppler angle θ. If the Doppler angle

becomes 90^o there is no Doppler shift. Velocities that are measured using this formula are accurate if the angle is maintained below 60^o

INSTRUMENTATION (DOPPLER MODES):

- Continuous wave Doppler (CW)
- Pulsed wave Doppler (PW)
- Color flow mapping (CF)
- Duplex sonography
- Power Mode Doppler

CONTINUOUS WAVE DOPPLER (CW):

Satomura was the first to develop a CW Doppler device. The transducer contains two piezoelectric elements-one emits ultrasound continuously and the other receives the back-scattered signals. The advantage of this equipment is that it is relatively inexpensive and portable. The disadvantage is that the signals are obtained from all moving structures in the line of the Doppler beam.

PULSED WAVE DOPPLER (PW):

Pulsed wave Doppler offers a major advantage over the CW Doppler because of the formers ability to obtain flow velocity information from a specific target vessel.

Pulse repetition frequency (PRF) should be at least double the Doppler signal's frequency.

Methods to eliminate aliasing:

- PRF has to be increased and kept at Nyquist limit in order to obtain maximum Doppler frequency and thereby reducing aliasing.
- Spectral baseline parameters can be adjusted such that the overall spectral display flow is in one direction.

DUPLEX SONOGRAPHY:

Duplex ultrasound instruments are B-mode scanner with integrated Doppler abilities. Anatomical structures are best outlined by high-resolution B-mode scanner whereas the Doppler analysis provides the information about the flow and movement patterns.

Barberl in 1974, pioneered duplex sonography which displays the real time image simultaneously with pulsed wave Doppler waveforms.

POWER MODE DOPPLER:

Power mode Doppler is an alternative way to assess the quality of the Doppler signal detected at different areas or targets. As compared to pulse wave Doppler imaging:

Advantages:

1. Energy mode is more sensitive to low-and feeble flow states than that colour velocity.
2. Aliasing is not a cause of any problem in energy display mode.

3. This method provides a continuous display of flow which helps to monitor most of the scan regions that are usually difficult to scan.

Disadvantages:

Information on velocity of reflector and the direction of flow corresponding to transducer is not displayed.

PROCESSING OF DOPPLER SIGNALS:

These signals are then processed in two different ways.

- Zero-crossing detection
- Doppler spectrum analysis.

Fast Fourier Transformation does the analysis of the various frequencies and their plotting against time. The spectral analysis takes the form of a graph with frequency on the vertical axis and time on horizontal axis.

Spectral analysis:

Spectral analysis is an approach to isolate a complicated signal to their corresponding frequency ranges, so the overall contribution of every frequency to its original signal can be identified. The overall power of Doppler signals relies upon the measure of blood that generated that signal, hence the brightness of every frequency range shows velocity and quantity of the flow relating to its Doppler frequency.

No evidence of any significant biological effects on patients from exposure to the present day diagnostic ultrasound instruments as issued by American institute of ultrasound in medicine.

INTERPRETATION:

A comprehensive sonographic examination is essential and valuable in final determination of the presence and extent of disease.

Linear array high frequency (7.5-12 mHz) transducer is used for the evaluation of extra cranial carotid vessels.

Sonograhic anatomy of the carotid artery walls:

- High-resolution ultrasonography is used to visualize boundaries of the different layers of the normal carotid artery wall. On longitudinal view, both the near and far walls appear as two parallel bright lines separated by hypoechoic space.

- The first echo on the far wall arises from the lumen intima interface while the second brighter echo arises from the media-adventitia interface. The inner margin of the echogenic adventitia is defined by the relatively anechoic media. Combined intima-media thickness is the distance from the first bright line along the far wall to the second bright line.

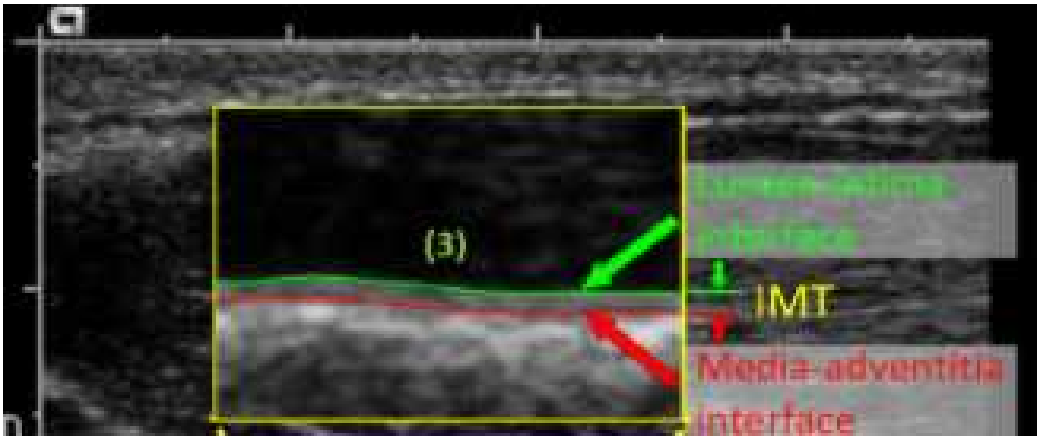


Fig 4: Shows different layers of normal carotid artery wall

Table 1: Shows features for identification of ECA & ICA.

Distinct Features	Carotid arteries	
	External artery	**Internal artery**
Size/Magnitude	Usually small in size	Usually large in size
Branching	Yes	No
Orientation/Location	Anteriorly	Posteriorly
Doppler features	Shows a flow pattern with high resistance	Shows a flow pattern with less resistance
Temporal Tapping	Show Wave like deflections	Show deflections

Normal spectral waveform pattern:

In normal arteries, the flow is laminar. Carotid bifurcation is a common site where flow disturbance occurs, where a swirl is established in the bulbous portion of common carotid artery (CCA). It has been observed that atherosclerotic plaques originate mainly in bulbous portion of CCA i.e in the region of flow reversal.

Waveforms in the CCA have a broad systolic peak and a moderate level of flow during diastole. Velocities exceeding 100 cm/sec are uncommon.

The waveforms of ICA have broad systolic peaks and a high level of flow all through diastole. Normal PSV in the ICA ranges from 54 to 88 cm/sec in grown-ups and an ICA speed surpassing 100 cm/sec ought to be seen as anomalous. ECA has sharp systolic peaks and moderately less flow during diastole. Normal PSV in ECA is 77 cm/sec (mean) and above 115 cm/sec is considered abnormal.

Intima-Media Thickness (IMT):

The IMT is checked in the upper common carotid artery. Thickening of the intima-media complex ≥0.08 cms is considered as abnormal and is the earliest change of atherosclerosis according to a study by POLAK in 1993.[59]

Riyazuddeen M et al conducted a cross-sectional study in 2019 on 59 type 2 diabetes mellitus patients at PIMS Puducherry and found significant positive correlation with carotid IMT (CIMT) and concluded that CIMT is established indicator of atherosclerosis, hence it can be used to estimate cardiovascular risk and to advise preventive measures.[8]

Plaque Characterization :

"Atherosclerotic plaque is an echogenic material encroaching on the arterial lumen and produces signal void."[25]

Plaques are detected by B-mode ultrasonography, value ≥1.2 mm (lumen to adventitia) indicates presence of plaque.

Extent , location, surface contour and inhomogeneity's of the plaques need to be noted as they are the cause of embolic stroke and are the most common cause for TIA as proven by MERITT et al in 1992.[43]

Plaque echotexture is stratified as homogenous or heterogeneous.

Homogenous plaque have a uniform echo pattern and a smooth surface. The uniform acoustic texture corresponds pathologically to dense fibrous connective tissue.

Heterogeneous plaque has a more complex echo pattern and contains at least one or more focal echolucent areas . Calcification is one of the causes of heterogeneity. A Swiss cheese plaque appearance with multiple sonolucent areas is characteristic of intra plaque haemorrhage.

Heterogeneous plaques were also associated with an incidence of cerebrovascular symptoms (TIA/stroke) that was higher than in homogeneous plaques for all grades of stenosis.[42]

Whereas calcified plaque is the one that produces posterior acoustic shadowing and is commonly found in asymptomatic individuals.

A focal depression or the break in the plaque surface and eddies of colour within the plaque is the criteria for ulcerated plaque.[22]

Patients with heterogeneous plaque are more prone to develop hemispheric neurologic symptoms, including transient ischemia and stroke than those having homogeneous plaques.[23,24]

Few studies have classified plaques into four major categories:[42]

Type 1 – Echolucent

Type 2- Echolucent with echogenic areas

Type 3- Echogenic with small echolucent areas

Type 4- Echogenic

Type 1 and 2 plaques are commonly found in patients presenting with CNS symptoms and also frequently associated with ulceration and intraplaque

haemorrhage whereas type 3 and 4 plaques were mainly seen in asymptomatic individuals.

Main limitation of ultrasonographic characterization of plaque morphology is reproducibility.

Ultrasonography is usually a technologist dependent study with machine to machine variation.

Evaluation of Stenosis: Grey scale, colour flow and power mode Doppler images better demonstrate and quantify low grade stenosis but high grade occlusive disease is better quantified by Doppler spectral analysis.

Blood flow velocities (peak systolic velocity, end diastolic velocity) are obtained and spectral analysis was performed at and distal to site of stenosis.

In a study conducted by ERICKSON. S. J in 1989 found that the degree of stenosis (percentage of reduction in diameter) determined by COLOR DOPPLER and DSA was in agreement in 59 (71 %) of 83 longitudinal Color Doppler flow imaging (CDFI) measurements and 54 (65%) of 83 transverse CDFI measurements concluding that Measurements of the diameter reduction are to be made longitudinal plane as it better correlates with angiographic method of calculating diameter stenosis.[25]

Blackshear WM et al conducted an retrospective study wherein they compared the angiography with Doppler findings and observed that there is difference in velocity ratios (ICA/CCA) between normal, low-level, and high level stenosis and it appears to be far better parameter than absolute velocity. The experimental outcomes showed that all patients having high level stenosis (having more than 60% diameter reduction) and all normal vessels were correctly identified. Classification accuracy

was 61% where stenosis was in the range of 10% -55%, Also 10 % of the vessels having definite plaque were missed out.[26]

A study conducted by Staikov IN et al to determine optimal Duplex sonographic criteria in diagnosing severe carotid stenosis and to correlate the findings with European carotid surgery trial (ECST) and North American symptomatic carotid endarterectomy trial (NASCET), optimal values for PSV and EDV for diagnosing severe stenosis (PSV >220 cms/sec and >80 cm/sec respectively) were well within range published by other authors for NASCET method of angiographic grading and the values were also similar to those for diagnosing stenosis ≥ 80% or greater, graded with ECST method.[27]

Recognizing that duplex criteria from different centres differ for the threshold levels of angiographic stenosis determined by NASCET, a panel of authorities from a variety of medical specialties assembled to review the carotid ultrasound literature. This group, which convened in 2002, focused on previously untreated atherosclerotic stenosis of the proximal ICA. The panel developed a consensus regarding the key components of the carotid ultrasound examination and reasonable criteria for stratification of ICA stenosis.[31]

The consensus committee recommended that all carotid examinations be performed with gray-scale imaging, Color Doppler, and spectral Doppler. The examination should be performed by a credentialed vascular technologist in accordance with the standards of one of the accrediting bodies. Doppler waveforms should be measured with an insonation angle as close to 60^{o} possible but not exceeding 60^{o} and the sample volumes should be placed within the area of maximal stenosis.

Based on extensive discussions and review of numerous studies the consensus panel recommended stratifying the degree of ICA stenosis, based on Doppler and imaging results, into the following strata. [28,29,30,32]

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% diameter reduction	<2.0	<40
50-69	125-230	≥50% diameter reduction	2.0-4.0	40-100
>70	≥230	≥50% diameter reduction	>4.0	>100
Near occlusion	High, low, undetectable	Visible	variable	variable
Total occlusion	undetectable	Visible, no lumen	Not applicable	Not applicable

Table 2: Ultrasound and Doppler criteria for diagnosis of ICA stenosis

If the peak systolic velocity (PSV) is less than 120 cms/sec, the evaluation of stenosis is to be done primarily by Color flow imaging.

Dampened waveform with markedly decreased EDV of ipsilateral CCA when compared to the contralateral CCA, early diastolic flow reversal on colour flow imaging in the segment proximal to occlusion and thrombus completely filling lumen of ICA are signs of ICA occlusion as concluded by ERICKSON.S.J. et al in 1988.[25]

Studies show that ultrasound technique is highly effective to identify the presence of abnormalities, because it is able to detect both morphological and hemodynamical changes. Duplex ultrasound has replaced arteriography as the first choice technique for preoperative assessment of carotid arteries.[34]

Vit A et al conducted a comparative study to observe the diagnostic efficiency of CT-angiography and Color-Doppler ultrasonography to investigate whether percutaneous transluminal angioplasty or endarterectomy is to be done for treating extra cranial stenosis of the internal carotid artery. The true-positive and false-negative values were observed as 92.3% and 95% respectively while identifying the plaques causing significant stenosis using Doppler ultrasonography. The study reported that Color-Doppler ultrasonography can be used as a preliminary investigation for diagnosing carotid atherosclerosis and can also be used to characterize plaques as to identify which type needs to be treated using endarterectomy or with percutaneous trans luminal angioplasty.[35]

In a study conducted by Logason K, Karacagil S, Hårdemark HG, Boström A, Hellberg A, Ljungman C found no significant differences in perioperative results in patients undergoing carotid stenosis surgery even if conventional angiography wasn't done preoperatively. Hence concluded that carotid endarterectomy can safely be performed without preoperative angiography in cases with conclusive duplex scan findings.[37]

A study done by Sun B et al in MRI diagnosed carotid atherosclerotic lesions to study the relationship between HbA1c levels, plaque morphological and compositional qualities and acute cerebral infarction (ACI) seriousness in hypertensive individuals. 80 hypertensive patients reported with acute stroke were segregated into high and low HbA1c gatherings, carotid plaque attributes and ACI

volume in the region where blood is supplied by the internal carotid artery (ICA) was evaluated. Presence of plaque was around 63.8% on the symptomatic side and 38.7% on asymptomatic side. Plaque burden was more in high HbA1c class as compared to the low HbA1c class. High HbA1c was an independent risk indicator for the occurrence of plaque. This investigation proposed that a raised HbA1c may have adversary effects on the carotid plaque demonstrating that observing the HbA1c levels and features of carotid atherosclerotic plaque in good management of stroke patients.[44]

In an research done by Sun B et al which was intended to discover the relationship between carotid plaque features and acute cerebral infarct (ACI) lesions in T2DM patients using MRI. This investigation was done on 140 Patients who exhibited acute cerebrovascular disorder in interior carotid artery territory of which 68 individuals had DM. Results proved that Type 2 DM patients had bigger plaque burden , bigger lipid-rich necrotic core (LRNC) in contrast to non-diabetic patients. Also infarct size in the internal carotid artery region of Type 2 DM patients was bigger with ipsilateral carotid LRNC plaque than those in non-Type 2 DM patients which demonstrates a noteworthy relationship between plaque attributes and acute cerebral infarction.[45]

Das et al in 2011 led an investigation which included 80 instances of acute ischemic strokes and 40 controls .To understand the relationship of plaque, pulsatility index (PI) and IMT, resistivity index (RI) in both diabetic and non-diabetic subjects are highly useful. It was reported that the mean estimations of IMT, PI, RI were reasonably higher in diabetics when contrasted with controls The overall count of plaques in diabetic patients when contrasted with controls were highly significant and the average plaque region was 46 square mm for diabetics and 20 square mm for

controls. This examination additionally recommended that plaque type, RI, IMT and PI are significant parameters for prediction of acute ischemic stroke along with its subtypes. They can be utilized as non-invasive method for predicting and preventing ischemic stroke in patients having hypertension and DM.[18]

Levantino P, Polizzi G, Evola S, Leone G, Evola G, Novo G, Novo S in 2019 analysed the association between carotid and coronary atherosclerosis in terms of the severity of the disease. This study included 478 patients who underwent carotid Doppler ultrasound and coronary angiography. The severity of coronary artery disease was analysed by SYNTAX scoring. 68.2% of the examined population showed atherosclerosis in both carotid and coronary arteries. The absence of carotid atherosclerosis was predominantly associated with angiographically normal coronary arteries in 37.6% and the highest rate described was related to a three vessel coronary artery disease (CAD) (41.6%). Hence proving a strong correlation between carotid atherosclerosis and CAD in terms of severity.[47]

Treatment:

Separation among symptomatic and asymptomatic patients with carotid stenosis is fundamental for an appropriate management.

Symptoms: Ipsilateral vision loss, unresponsiveness of contralateral upper/lower limb, the face, slurring of speech and aphasia.

Symptoms of repeated dizziness, general subjective weakness, syncope or close-syncope episodes, foggy vision or transient positive visual phenomenal are viewed as asymptomatic even during the presence of high-severity carotid artery stenosis.

It is essential to reduce the risk of frequent occurrence of early cerebrovascular events in prioritized patients with symptomatic carotid artery stenosis. The probability of ipsilateral stroke is usually high during first 3 months and even more probable in the 1st month of having an episode of TIA. Immediate treatment can help in reducing the risk by 80% .[48]

This study proposed a scoring system and is mainly used to predict short-term risks for ipsilateral stroke after occurrence of TIA.

ABCD SCORING SYSTEM FACTOR	SCORE
Patients age	1
Blood pressure(BP)	I
Clinical features: Unilateral weakness Speech impairment	2 1
Duration of TIA: ≥60 min 10-59 min	2 1
DM	1

Table 3: ABCD system of scoring

There is a risk probability of 1.2 % for stroke within 7 days in individuals who had a TIA and ABCD score of 0-3. When score is between 4-5 and 5-6 according to this system, the risk probabilities for stroke within 7 days are 5.9 % and 11.7 % respectively.[49]

Patients with Symptomatic carotid artery stenosis:

Medical treatment:

Includes antihypertensive medication and gradual reduction in BP is advised. It also includes use of statin medication, used for reduction of the cholesterol value below 70mg/dl (low-density lipo-protein).

Aspirin is used as an antiplatelet.

Surgical treatment:

Two types of surgeries for patients with symptomatic carotid artery stenosis are:

- Carotid angioplasty and stenting (CAS)
- Carotid endarterectomy (CEA)

Risk of ipsilateral stroke is much higher in the first few weeks after an episode of TIA. So treatment should be performed immediately.

For invasive treatment, Carotid endarterectomy is standard criterion. Carotid endarterectomy is suitable for symptomatic carotid artery patients who exhibit high percentile of stenosis around 70% to 99%. It is also advisable for symptomatic patients having stenosis around 50% to 69%, if there exists no symptoms for ischemic stroke.

Debakey was the first person to perform thromboendarterectomy in 1953.

North American Symptomatic Carotid Endarterectomy Trial(NASCET) and European Carotid Endarterectomy Trial (ECET) demonstrated that in patients with 60%-70% Internal carotid artery stenosis, whether symptomatic or asymptomatic long term benefits of endarterectomy were significantly greater than the medical treatment.

The trials showed that endarterectomy was effective at or above these levels of stenosis.[33]

Stenting and Carotid angioplasty are proposed as an alternative to CEA. Advantages of CAS: Patient under mild sedation, requires no incision, carries no risk of cranial nerve palsy, and has fewer cardiovascular complications.

CEA has been shown to be safer, effective option in preventing ipsilateral stroke with less chances of restenosis. Recent research suggests CEA to be done in the first 2 weeks after TIA or minor stroke.[54]

A meta-analysis done in 2008 has reported that the probability of recurrence of stroke within a month is more in CAS than that of CEA groups. However CAS has shown good long term results (2-3 years) to prevent ipsilateral strokes. It has been reported that the occurrence of ipsilateral strokes does not differ in both CAS and CEA in the long run.[50,51,52]

Recurrence of strokes after carotid revascularization can be prevented by proper treatment of cardio-vascular disorders and timely initiation of antiplatelet.

Major risks to be considered for intervention are individuals who exhibit:

1. Severe cardio-pulmonary diseases.
2. If large sized infarct with haemorrhagic transformation.

Patient with asymptomatic Carotid Artery Stenosis:

Intensive medical treatment may be the most appropriate therapeutic option for maximum number of patients.

Antihypertensives, antiplatelets and statins are the medications advised.

Lifestyle modification such as smoking cessation, weight reduction and exercises are also an important part of the treatment.

In asymptomatic carotid artery stenosis, surgery is advised only for few patients in light of the marginal benefit from revascularization.

METHODOLOGY

Materials and methods:

Study Design: This was a cross sectional study.

Study site: This study was conducted in the Department Of Radio Diagnosis at Jawaharlal Nehru Medical College, Belagavi, Karnataka.

Study population: Information would be gathered from patients with type 2 diabetes mellitus referred to the Department of Radiodiagnosis for carotid Doppler ultrasonography at KLE's Dr. Prabhakar Kore Hospital & Medical Research Centre, Belagavi.

7.2 Method of collection of data:

Inclusion criteria:

- Patients with type 2 diabetes mellitus of both genders who are referred to department of Radiodiagnosis at KLE's Dr. Prabhakar Kore Hospital & Medical Research Centre, Belagavi for carotid Doppler ultrasonography.
- As stated by the WHO, the diagnosis measure for diabetes mellitus has been defined as fasting plasma glucose level of ≥126 mg/ml and plasma glucose level of ≥200 mg/dl at 2 hrs post glucose tolerance test or random plasma glucose level of ≥200 mg/dl and HBA1c ≥6.5%.

Exclusion criteria:

- Patients diagnosed with type I diabetes mellitus.
- Patients diagnosed with hypertension or with history of smoking which are also risk factors for atherosclerosis.
- Patients who underwent surgical / interventional treatment of carotid arteries for atherosclerotic disease.
- Patients diagnosed with gestational diabetes mellitus.

Sample size:

Based on predominance the minimum sample size equation is

$$n = \frac{Z\alpha 2\ P(1-P)}{d^2}$$

Where P is the percentage of predominance and d is the percentage likely difference in the predominance.

Zα correlates with the level of importance. For 5 % level of importance $z_\alpha = 1.96$. With P = 73 % and d = 15 % of P, the above equation gives the value of **65.**

Statistical Analysis:

In the present cross sectional analysis, the mean and standard deviation will be determined for the continuous quantitative variables. For comparative purposes, if the data is separated into two groups with respect to such qualitative characteristics, such as gender or some other qualitative characteristics, the continuous variables will be compared using appropriate methods, such as ANOVA, correlation , regression, etc., that will be used as needed.

Discrete variables will be represented by median. Suitable graphs will be used to depict the comparison.

Median will be interpreted by discrete variables. Effective graphs will be used to represent the comparison.

It will convey the categorical data in terms of prices, ratios and percentages. The relation between the result, clinical and demographic characteristics will be evaluated using either the Chi-square or the exact Fisher test.

The value of p less than 5% (0.05) will be considered important for all the tests.

Study Duration: 1st January 2019 till 31st December 2019.

Ethical considerations: This research was accepted by institutional human ethics committee. All research participants received informed written consent and only those participants willing to sign the informed consent were included in the research. Before obtaining consent the participants were clarified the risks and benefits involved in the research and the voluntary nature of participation. Confidentiality of the participants in this research was preserved.

METHODOLOGY: An informed written consent was received from all the subjects. A pre-structured proforma was used to gather clinical data.

A comprehensive history, related risk factors (smoking, hypertension, hyperlipidemia, obesity) and laboratory (random blood sugar) investigations was taken.

The above study population will be subjected to carotid artery Doppler ultrasonography on GE VOLUSON machine (GE Healthcare, USA) fitted with a linear array transducer of 7.5-12 MHz high frequency.

EXAMINATION TECHNIQUE:

Ultrasound examination of the carotid artery is performed with patient lying supine and head turned away from the side being examined and neck extended slightly.

A sonographic analysis of the grey scale starts with transverse projection. The vessels were imaged as completely as possible, with caudal angulation of the transducer in the supraclavicular region and cephalic angulation at the level of the mandible.

Transverse screening:

- Starts at the clavicle and shift cephalad.
- Identification of the CCA, carotid bifurcation and both its main branches.
- Localization of the plaques and areas of stenosis in the CCA and its branches ECA and ICA. Surface and type of plaque were documented.
- Calculation of residual lumen area and percentage diameter pruning.

Longitudinal screening:

Lateral transducer view:

- Begins just above the clavicle and move cephalad, all the vessels are identified.
- Localization of the plaques and areas of stenosis in the CCA, ECA or ICA.

Postero-lateral transducer view:

- This is done in order to locate the ICA as far cephalad as possible.
- Extent and characteristic of plaque was noted.
- Peak systolic and End diastolic velocities were measured of CCA, ICA and ECA.

Data collection tools: Recorded all the necessary parameters in a structured research proforma.

The data gathered was analyzed and presented where possible in the form of tables, graphs, figures and diagrams.

RESULTS

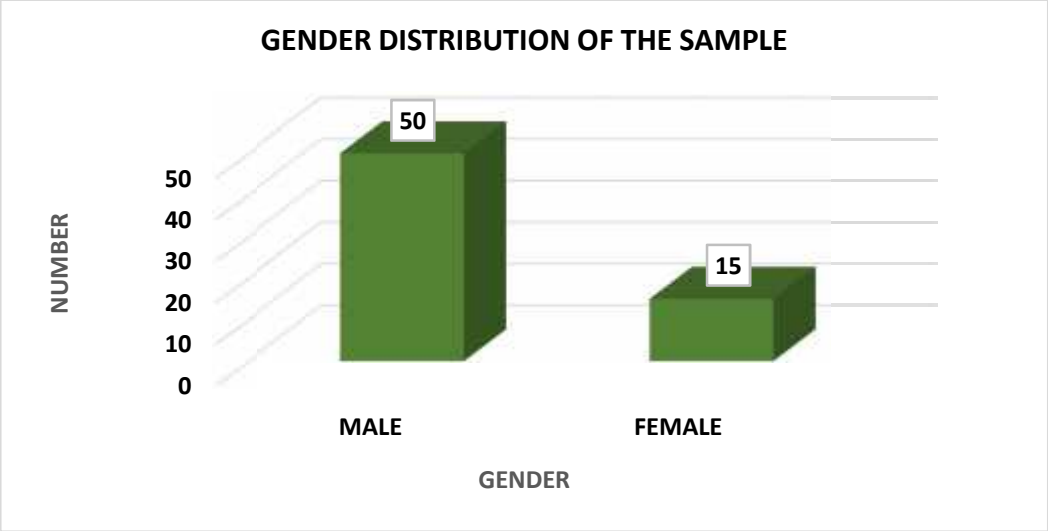
Study population:

65 diabetic patients who were referred for carotid Doppler ultrasonography were prospectively evaluated in this study.

Table 4: Descriptive inspection of gender among the study group (N =65)

GENDER	FREQUENCY	PERCENTAGE
MALE	50	76.92
FEMALE	15	23.08
TOTAL	65	100.00

Graph 1: Gender distribution among study group

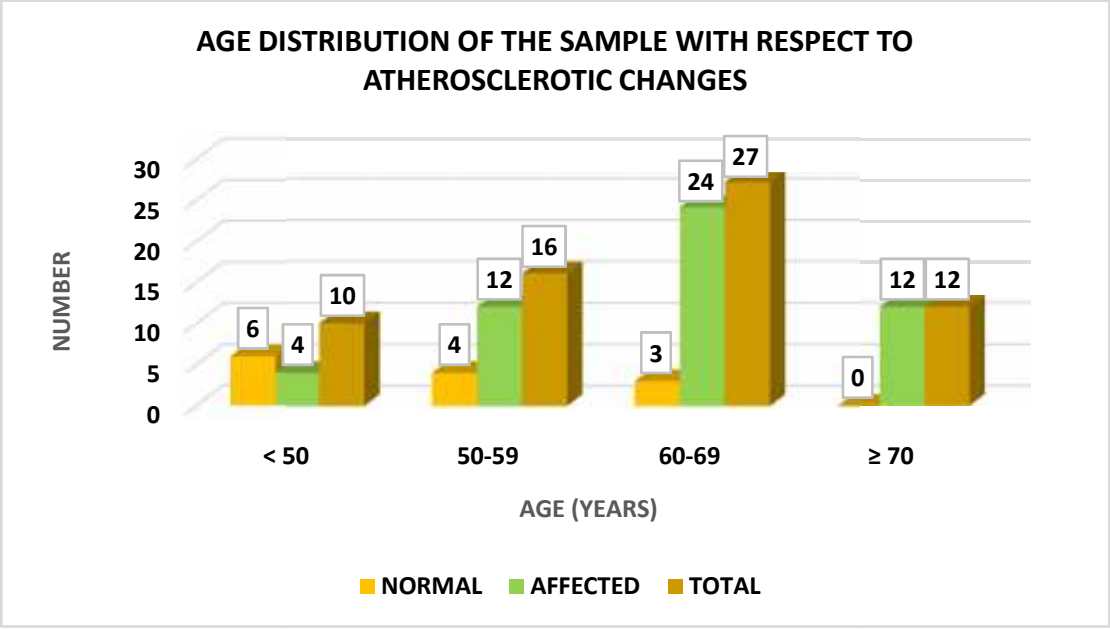


In the current study number of male patients were more (76.9%) as compared to the female patients (23.08%).

Table 5: Descriptive inspection of age distribution among the studypopulation (N=65)

			NORMAL		AFFECTED	
AGE (YEARS)	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE	FREQUENCY	PERCENTAGE
< **50**	10	15.38	6	46.15	4	7.69
50-59	16	24.62	4	30.77	12	23.08
60-69	27	41.54	3	23.08	24	46.15
≥ **70**	12	18.46	0	0.00	12	23.08
TOTAL	65	100.00	13	100.00	52	100.00

Graph 2: Age distribution among study population



The current study included maximum number of its patients from the age group of 60-69 yrs (41.5%) trailed by age group of 50-59 yrs (24.62%). Mean age was 60.29yrs.

Utmost number of normal carotid Doppler studies were found in patients in the age group of <50yrs (46%) followed by age group of 50-59 yrs (30.7%).

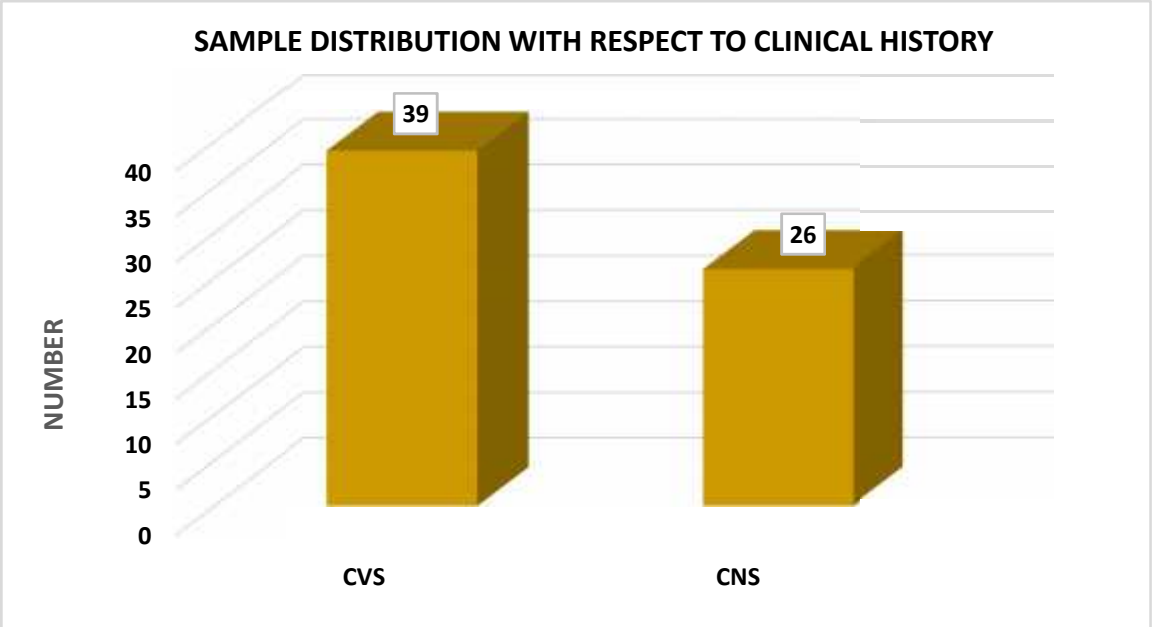
Maximum number of patients affected were in the age group of 60-69 yrs (46.15%). Least number of patients to be affected were in the age group of < 50 yrs (7.7%).

All 12 patients above the age of 70 yrs were affected.

Table 6: Descriptive inspection of distribution with respect to clinical history in study population (N=65)

CLINICAL HISTORY	NO.OF CASES	PERCENTAGE
DM with CVS	39	60.00
DM with CNS	26	40.00
TOTAL	65	100.00

Graph 3: Distribution with respect to clinical history(N=65)

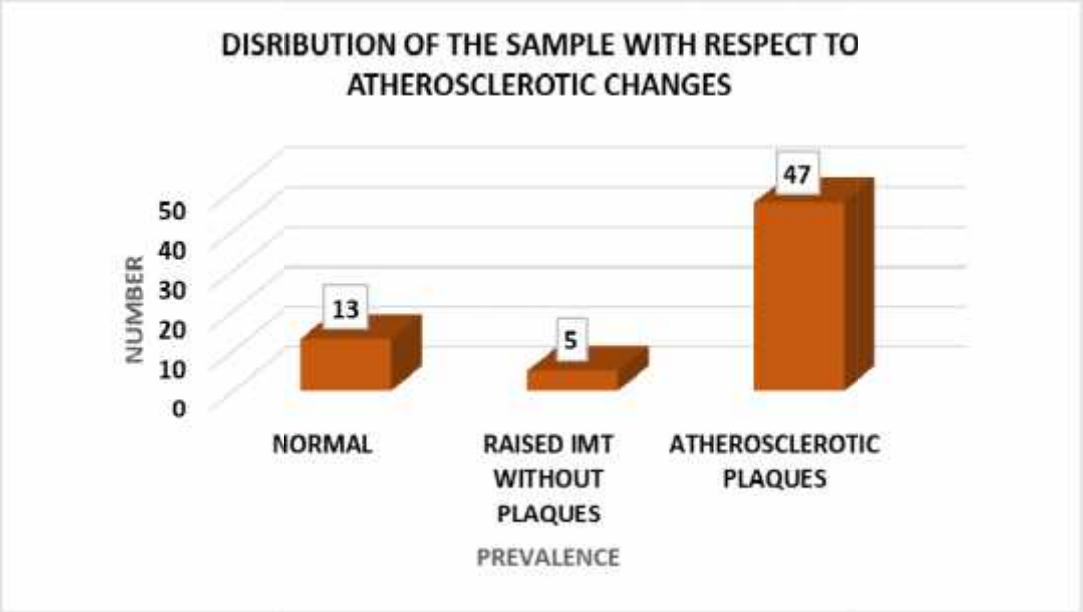


In the current research more number of patients presented with history relating to cardiovascular system (60%) and the rest of the patients had history relating to central nervous system (40%).

Table 7: Descriptive analysis of distribution in terms of prevalence of atherosclerosis (N=65).

PREVALENCE	NO.OF CASES	PERCENTAGE
NORMAL	13	20.00
RAISED IMT WITHOUT PLAQUES	5	7.69
ATHEROSCLEROTIC PLAQUES	47	72.31
TOTAL	65	100.00

Graph 4: Distribution with respect to prevalence of atherosclerosis(N=65).

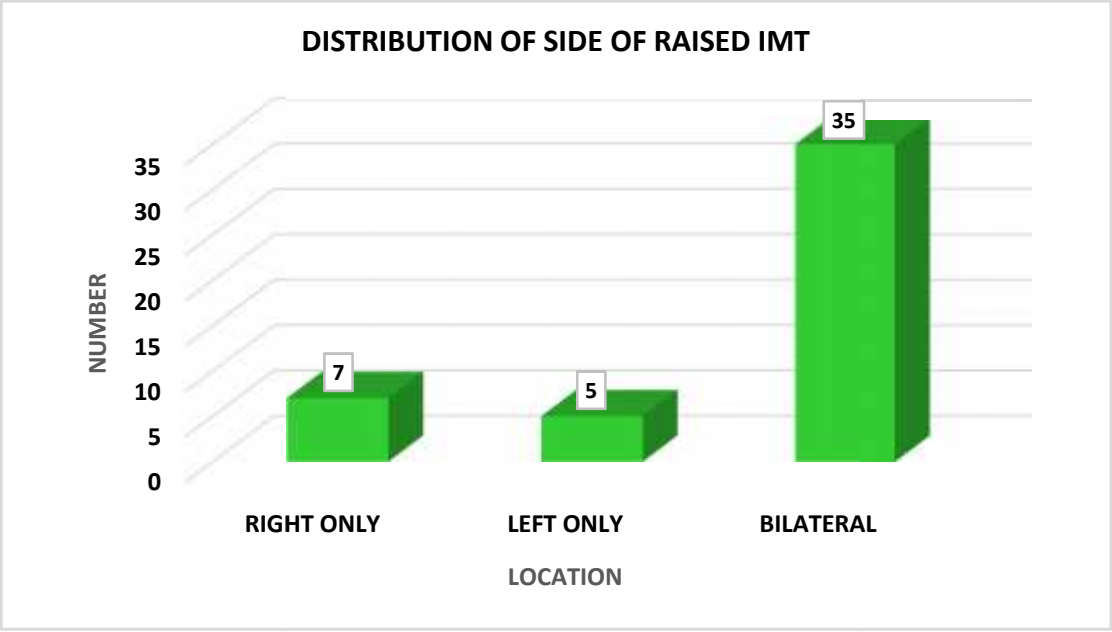


In the current research with sample size of 65 there were 13 cases who didn't have any atherosclerotic changes (20.0%), 5 cases (7.7 %) had raised IMT with no proof of atherosclerotic plaques,47 cases (72.31%) had atherosclerotic plaques.

Table 8: Descriptive analysis of distribution in terms of side of raised IMT

SIDE OF RAISED IMT	NO.OF CASES	PERCENTAGE
RIGHT ONLY	7	14.89
LEFT ONLY	5	10.64
BILATERAL	35	74.47
TOTAL	47	100.00

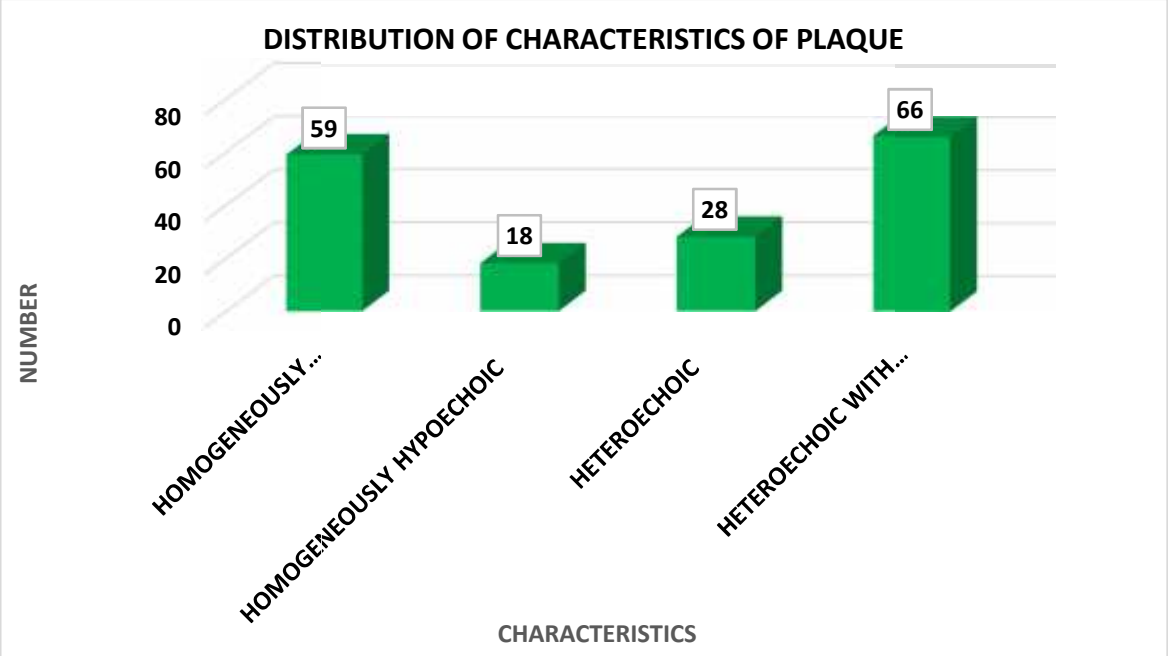
Graph 5: Distribution with respect to side of raised IMT



7 cases (14.9%) had increased IMT only on right side, 5 cases (10.6%) had increased IMT only on left side, whereas 35 cases (74.4%) had increased IMT on both sides.

Table 9: Distribution with respect to type of plaques

CHARACTERISTICS OF PLAQUE	NUMBER	PERCENTAGE
HOMOGENEOUSLY HYPERECHOIC	59	34.50
HOMOGENEOUSLY HYPOECHOIC	18	10.53
HETEROECHOIC	28	16.37
HETEROECHOIC WITH CALCIFICATION	66	38.60
TOTAL	171	100.00



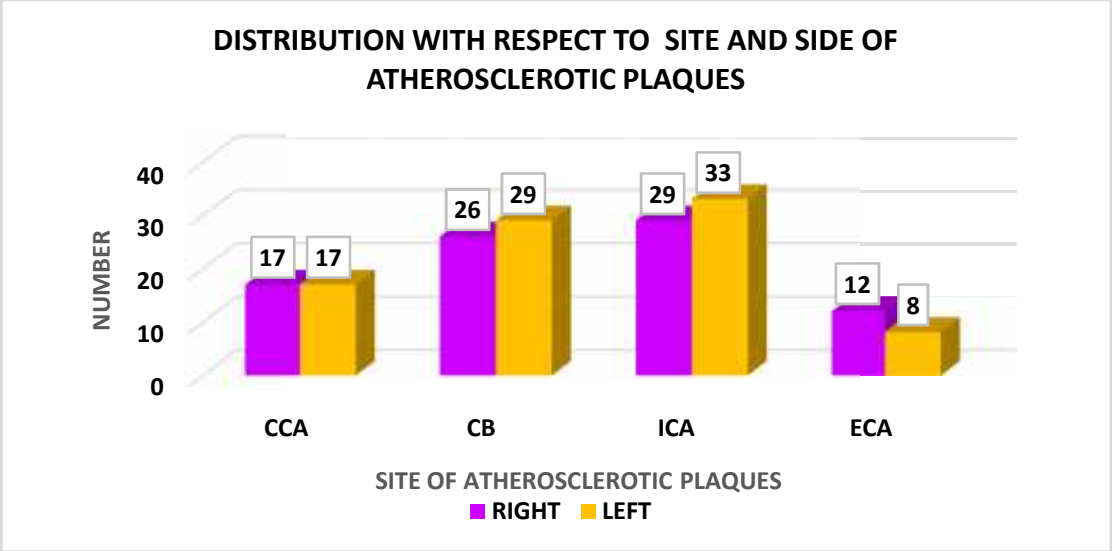
Graph 6: Graphical representation of type of plaques in the study group

Heteroechoic plaque with specks of calcification was the most common type of plaque found in this study (38.60%), the least common type of plaque being homogenously hypoechoic plaque (10.53%).

Table 10: Distribution with respect to side and site of association of plaques

SITE OF ATHEROSCLEROTIC PLAQUES	RIGHT SIDE	PERCENTAGE	LEFT SIDE	PERCENTAGE	TOTAL	PERCENTAGE
CCA	17	20.24	17	19.54	34	19.88
CB	26	30.95	29	33.33	55	32.16
PROXIMAL ICA	29	34.52	33	37.93	62	36.26
PROXIMAL ECA	12	14.29	8	9.20	20	11.70
TOTAL	84	100.00	87	100.00	171	100.00

Graph 7: Graphical representation showing side and site of association of plaques



In the current study group, the most common site of involvement of the plaque was in the left proximal ICA [at its origin] (33 cases) trailed by right proximal ICA [at its origin] (29 cases) and the left carotid bulb (29 cases). The least influenced site being left proximal ECA (8 cases).

Table 11: Distribution with respect to side of involvement CCA

SIDE OF INVOLVEMENT OF CCA	NO.OF CASES	PERCENTAGE
RIGHT ONLY	9	34.62
LEFT ONLY	9	34.62
BILATERAL	8	30.77
TOTAL	26	100.00

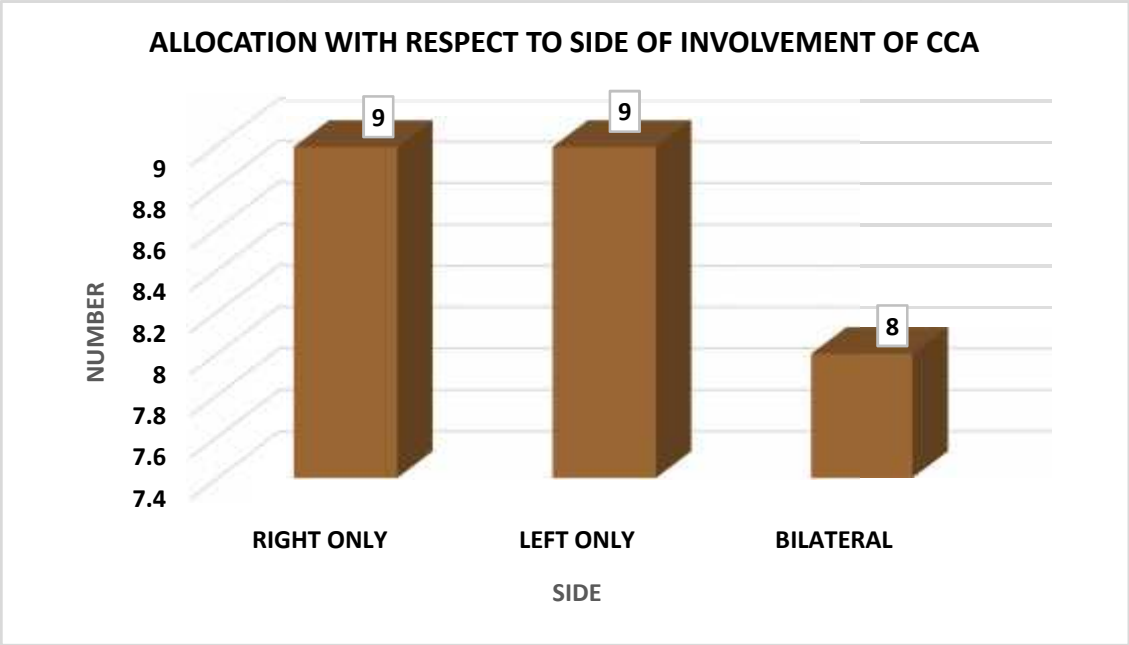
Table 12: Distribution with respect to side of involvement and percentage stenosis of CCA

	RIGHT SIDE		LEFT SIDE		TOTAL	
%STENOSIS OF CCA	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
< **50**	12	70.59	13	76.47	25	73.53
50-69	4	23.53	4	23.53	8	23.53
70-80	1	5.88	0	0.00	1	2.94
NT OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL	17	100.00	17	100.00	34	100.00

34 CCA's in 26 patients are indicating atherosclerotic changes in the current study. In 9 cases CCA is involved distinctly on right side, 9 cases show involvement of only left CCA and 8 cases show bilateral involvement. 25 (73.5%) of the involved CCA's show stenosis of < 50%, 8 (23.5%) CCA's show stenosis of 50-69% and 1 (2.9%) CCA revealing stenosis of 70-80%.

No evidence of near total and total occlusion in any of the common carotid arteries noted in any of the cases on both sides.

Graph 8: Graphical representation of side of involvement of CCAin the study group



Graph 9: Graphical representation of percentage stenosis of CCA in the study group

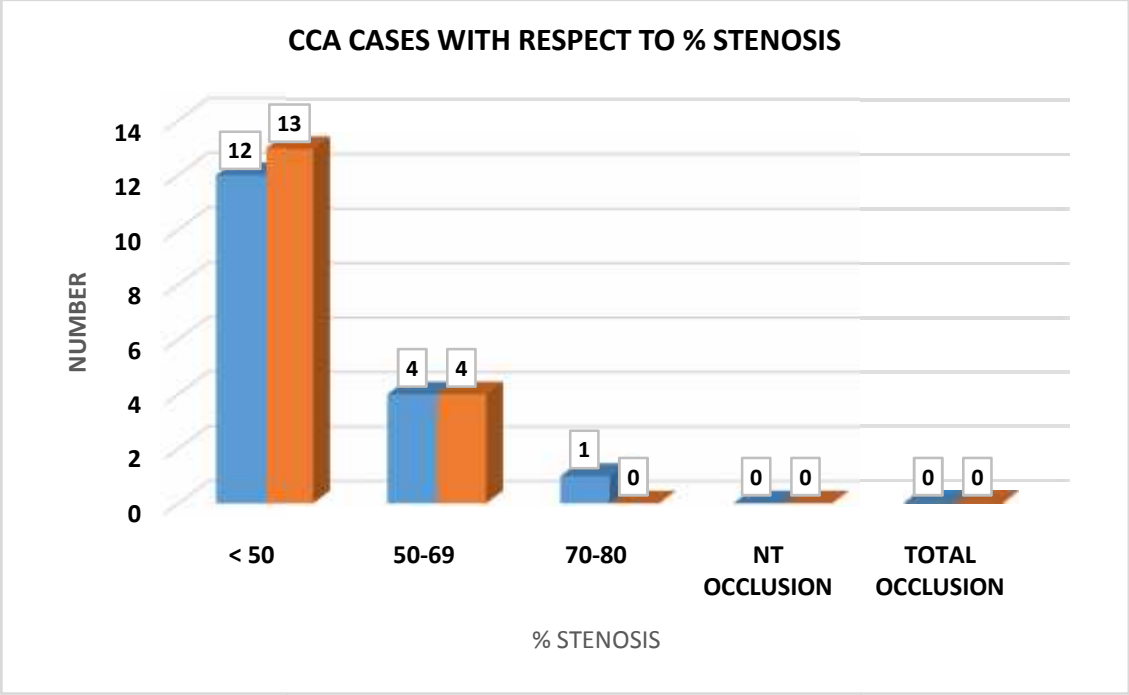


Table 13: Distribution with respect to side of involvement of CB

SIDE OF INVOLVEMENT OF CB	NUMBER	PERCENTAGE
RIGHT ONLY	9	23.68
LEFT ONLY	12	31.58
BILATERAL	17	44.74
TOTAL	38	100.00

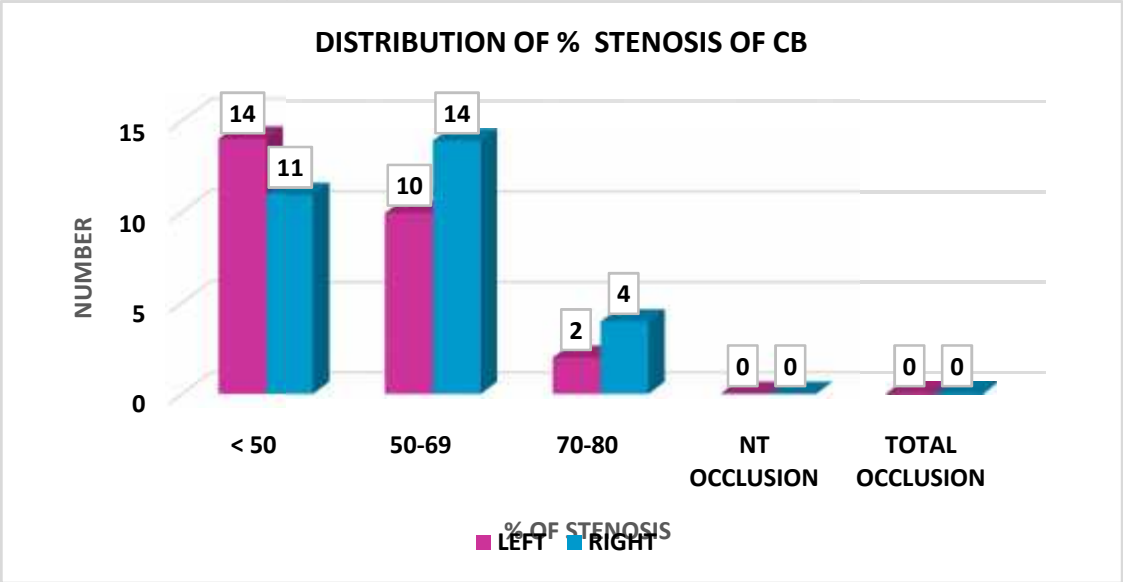
Table 14: Distribution with respect to side of involvement and percentage stenosis of CB

	RIGHT		LEFT		TOTAL	
% OF STENOSIS OF CB	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
< 50	14	53.85	11	37.93	25	45.45
50-69	10	38.46	14	48.28	24	43.64
70-80	2	7.69	4	13.79	6	10.91
NT OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL	26	100.00	29	100.00	55	100.00

55 CB's in 38 patients are indicating atherosclerotic changes in the current study. In 9 cases CB is involved distinctly on right side, 12 cases show involvement of only left CB and 17 cases show bilateral involvement. 25 (45.45%) of the involved CB's show stenosis of < 50%, 24 (43.6%) CB's showed stenosis of 50-69% and 6 (10.9 %) CB's indicating stenosis of 70-80%.

No case indicated any proof of near total and total occlusion of the carotid bulbs in any case on both sides.

Graph 10: Graphical representation of percentage stenosis of CB in the study group



Graph 11: Graphical representation of side of involvement CBin the study group

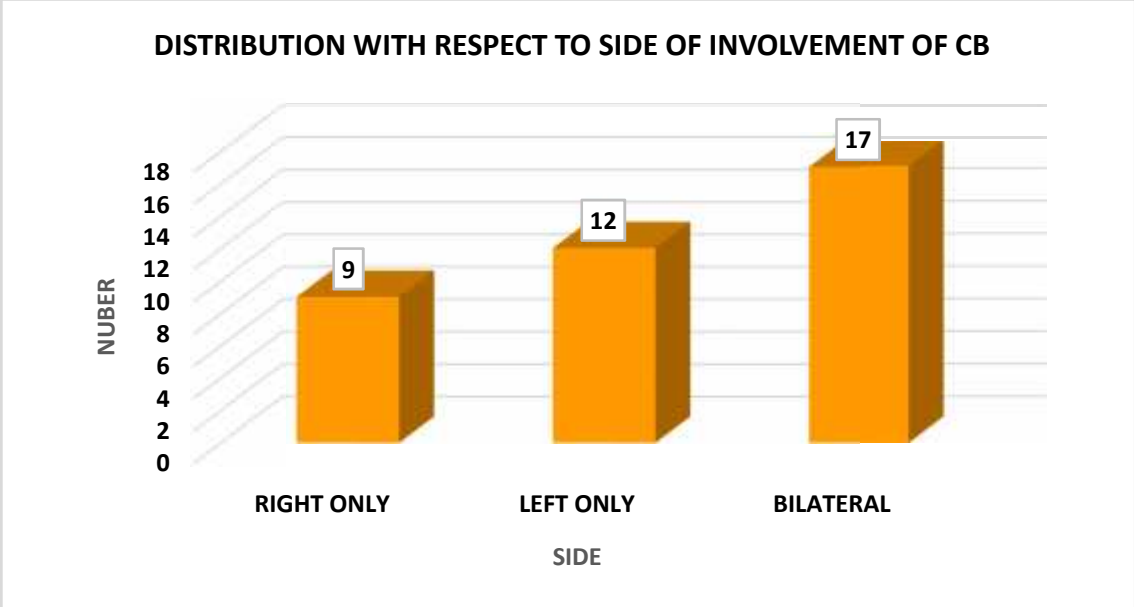


Table 15: Distribution with respect to side of involvement ECA

SIDE OF INVOLVEMENT OF ECA	NUMBER	PERCENTAGE
RIGHT ONLY	**8**	50.00
LEFT ONLY	**4**	25.00
BILATERAL	**4**	25.00
TOTAL	**16**	100.00

Table 16: Distribution with respect to side of involvement and percentage stenosis of ECA

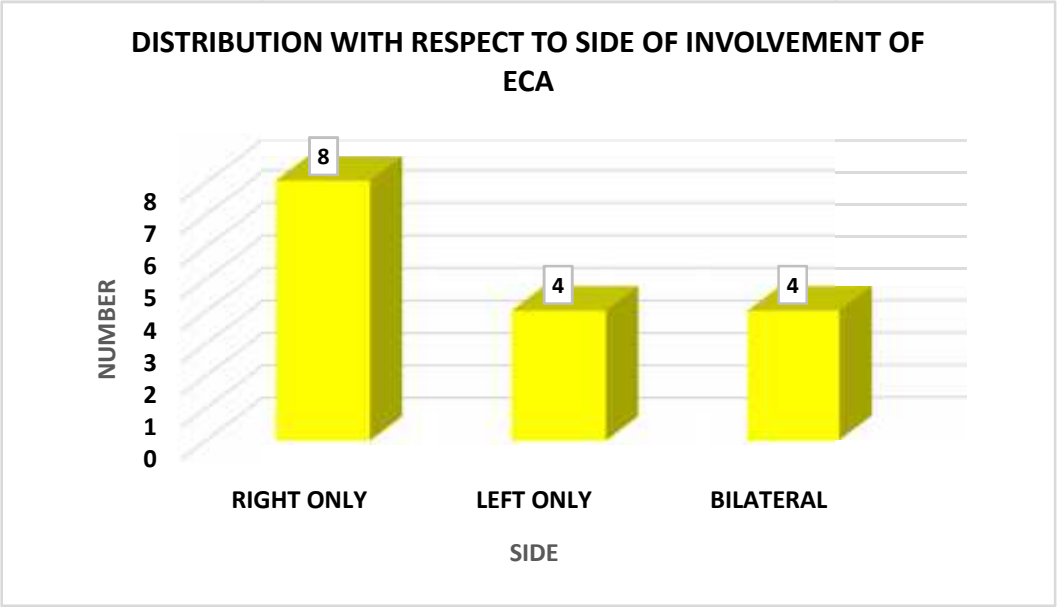
	RIGHT SIDE		LEFT SIDE		TOTAL	
% OF STENOSIS OF ECA	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
< **50**	9	75.00	2	25.00	11	55.00
50-69	2	16.67	6	75.00	8	40.00
70-80	1	8.33	0	0.00	1	5.00
NT OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL	12	100.00	8	100.00	20	100.00

In the present study 20 ECA's in 16 patients are showing atherosclerotic changes. In 8 cases ECA is involved only on right side, 4 cases show involvement of only left ECA and 4 cases showed bilateral involvement. 11 (55%) of the involved ECA's showed stenosis of < 50%, 8 (40.0%) showed stenosis of 50-69% and 1 (5%) showed stenosis of 70-80%.

No proof of near total and total occlusion in any of the external carotid arteries noted on both sides.

Graph 12: Graphical representation of side of involvement ECAin the study

group



Graph 13: Graphical representation of percentage stenosis of ECA in the study group

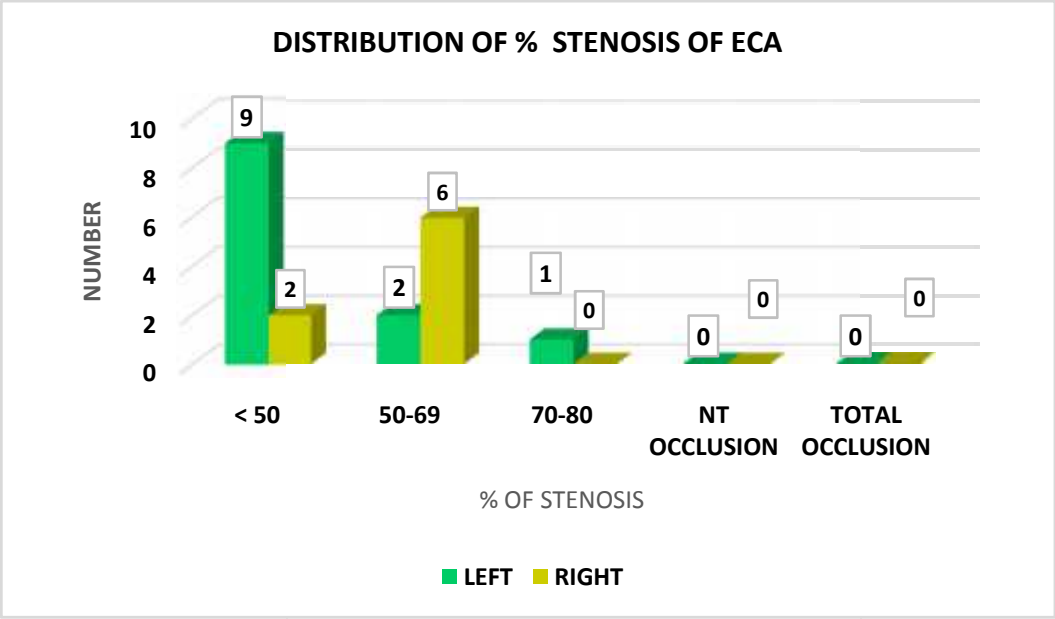


Table 17: Distribution with respect to side of involvement ICA

SIDE OF INVOLVEMENT OF ICA	NUMBER	PERCENTAGE
RIGHT ONLY	**8**	19.51
LEFT ONLY	**12**	29.27
BILATERAL	**21**	51.22
TOTAL	**41**	100.00

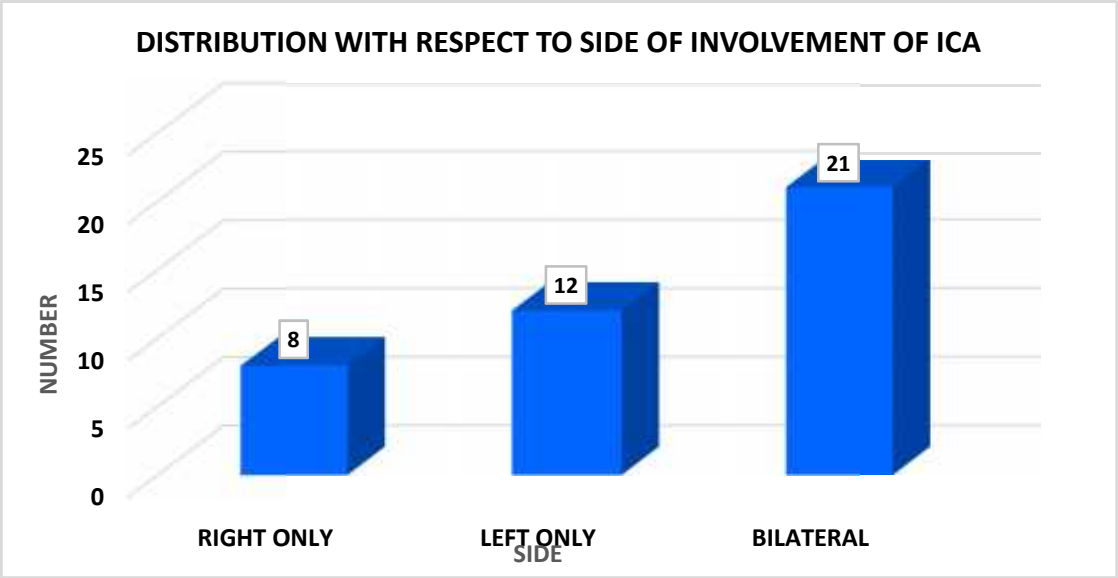
Table 18: Distribution with respect to side of involvement and percentage stenosis of ICA

	RIGHT		LEFT		TOTAL	
% OF STENOSIS OF ICA	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
< 50	11	37.93	13	39.39	24	38.71
50-69	12	41.38	12	36.36	24	38.71
70-80	4	13.79	6	18.18	10	16.13
NT OCCLUSION	2	6.90	2	6.06	4	6.45
TOTAL OCCLUSION	0	0.00	0	0.00	0	0.00
TOTAL	29	100.00	33	100.00	62	100.00

In the present study 62ICA's in 41 patients are showing atherosclerotic changes. In 8 cases ICA is involved only on right side, 12 cases show involvement of only left ICA and 21 cases show bilateral involvement. 24 (38.7%) of the involved ICA's show stenosis of < 50%, 24 (38.7%) ICA's show stenosis of 50-69%, 10 (16.1%) ICA's showing stenosis of 70-80% and 4 (6.4%) ICA's showing near total occlusion.

No evidence of total occlusion in any of the internal carotid arteries notedin any case.

Graph 14: Graphical representation of side of involvement ICAin the study group



Graph 15: Graphical representation of distribution ofpercentage stenosis of ICA in the study group

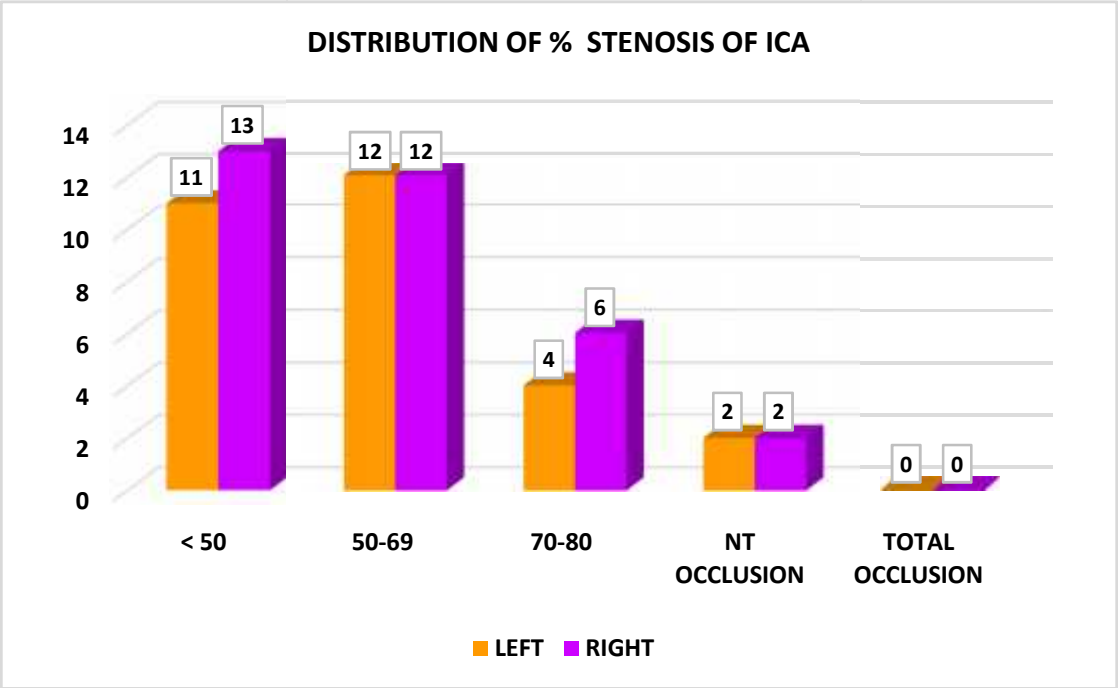


Table 19: Distribution with respect to stenosis of ICA and PSV ratio of (ICA/CCA) on right side

% STENOSIS	CRIETERIA PSV (ICA/CCA)	NUMBER OF CASES	NUMBER OF CASES THAT FOLLOWED THE CRIETERIA
< 50	< 2	11	11
50 - 69	2 – 4	12	12
70 – 80	>4	4	3
NT occlusion	variable	2	-
Total occlusion	variable	0	-

All the arteries which had stenosis of ≤50% and 50-69% followed the criteria. One artery which had stenosis of 70-80% range dint follow the criteria. Range of PSV ratio (ICA/CCA) in vessels having near total stenosis was found to be variable.

Table 20: Distribution with respect to stenosis of ICA and PSV ratioof (ICA/CCA) on left side

% STENOSIS	CRIETERIA PSV (ICA/CCA)	NUMBER OF CASES	NUMBER OF CASES THAT FOLLOWED THE CRIETERIA
< 50	< 2	13	13
50 - 69	2 – 4	13	12
70 – 80	>4	6	5
NT occlusion	variable	2	-
Total occlusion	variable	0	-

All the arteries which had stenosis of ≤50% followed the criteria. One artery which had stenosis of 50-69% and one artery having stenosis of 70-80% range dint follow the criteria. Range of PSV ratio (ICA/CCA) in vessels having near total stenosis were variable.

DISCUSSION

Diabetes mellitus is an independent risk factor for atherosclerosis. Color Doppler ultrasonography is a non-invasive and cost effective imaging modality which plays an important role in assessing the severity of atherosclerotic disease in extracranial carotid vessels of type 2 DM patients.

Age & Sex distribution:

Current study, which included 65 individuals number of male patients were more, 50 cases (76.9%) as compared to the female patients who were 15 (23.08%).

Maximum number of cases in this study were from the age group of 60-69 yrs, 27 cases (41.5%) followed by age group of 50-59 yrs which had 16 cases (24.62%).

31 yrs was the minimum age of the patient in our study and the maximum age was 80 yrs. Mean age being 60.29 yrs.

Maximum number of patients with normal carotid Doppler studies were found in the age group of <50yrs (6 cases) followed by age group of 50-59 yrs (4 cases).

24 cases (46.15%) who had atherosclerotic changes belonged to the age group of 60-69 yrs, All the patients who belonged to the age group of > 70 yrs had atherosclerotic changes making this age group as the most vulnerable age for atherosclerosis.

Men were more affected as compared to women.

The findings of our study were consistent with the findings in a study conducted by Palomäki H et al which was done to know the potential risk factors for atherosclerosis, they proved that atherosclerosis was more common in age group of more than 60 yrs and more common in men.[55]

In a study conducted by Sehrawat S, 61-70 yrs group had the maximum number of patients with significant stenosis (>50% stenosis).[66]

Paivansolo M et al also in their study proved that males were more commonly affected as compared to females and established the ratio as 2:1.[63]

Iemolo F, Martiniuk A, Steinman DA, Spence JD in their study concluded that men had more plaque area as compared to women.[56]

Symptomatology:

In our study, 39 patients (60%) had symptoms pertaining to CVS whereas 26 (40%) patients had CNS symptoms. Among patient presenting with CNS symptoms, the most common presentation was stroke.

A study conducted by Lindsberg PJ and Roine RO found that two-third of the patients who presented with ischemic stroke had hyperglycemia on admission.[65]

Prevalence of atherosclerosis:

In this study out of 65 patients, 13 patients (20%) had no changes of atherosclerosis in their carotid vessels, whereas 5 patients (7.7%) had raised IMT without evidence of any atherosclerotic plaques.

Total of 47 patients (72%) in our study had atherosclerotic changes in the form of atherosclerotic plaques.

Considering raised IMT as an early change of atherosclerosis, 52 out of 65 cases in our study had atherosclerotic changes, making the prevalence in the given diabetic study population as 80%.

The possible cause for prevalence being so high was because of the study population, which included only symptomatic cases.

Findings in this study were similar to a study conducted by Bollipo JP, Rao PB in which they found presence of atherosclerotic plaques in 82% of symptomatic cases and 18% of the cases had raised IMT without the presence of atherosclerotic plaques.[38]

Raised IMT:

POLAK in his study concluded that IMT of ≥ 8 mm should be considered as raised and as an earliest indicator of atherosclerosis.[59]

In our study we found that 47 cases had raised IMT, 7 cases (14.9%) had raised IMT on right side, 5 cases (10.6%) had raised IMT on left side, whereas 35 cases (74.4%) had raised IMT on both sides.

Wagenknecht LE et al in their study established positive correlation between diabetes with increased CCA IMT and also concluded diabetes as an independent risk factor in atherosclerosis.[62]

Type of plaque and site of involvement:

In this study, classification of the plaque characteristics was in accordance to J.F.Polak as:

- Homogenously hypoechoic
- Homogenously hyperechoic
- Heteroechoic with calcification.
- Heteroechoic

J.F.Polak summarized plaque echogenicity in the following manner. Hyperechoic signals are the ones which are comparable to the signals detected from the fascial layers ; isoechoic signals are comparable to neck muscles and hypoechoic signals is similar to that of blood.[59]

Most common type of plaque in our study was found to be heteroechoic plaque with specks of calcification (38.60%), the least common type of plaque being homogenously hypoechoic plaque (10.53%).

This was contrary to a study done by Sehrawat S et al, in their study majority type of plaque was hypoechogenic plaques in 45% of the cases, calcified plaque comprised 23% and 25% were hyperechogenic plaques.[66]

AbuRahman AF et al in their study concluded that heterogeneous plaques were more commonly associated with symptoms for all grades of stenosis and also found that heterogeneous plaque was more commonly associated with higher grade of stenosis and more cerebrovascular symptoms.[57]

According to a study conducted by Zwiebel J, it was found that carotid bifurcation was most common site of involvement of atherosclerotic plaque, next common site being origin of carotid arteries.[58]

In present study, the most common site of involvement of the plaque was in the left proximal ICA at its origin (33 cases), followed by right proximal ICA (29 cases) and the left carotid bulb (29 cases). The least affected site was the left proximal ECA (8 cases).

Sehrawat S et al in their study observed that the most common site for atherosclerotic plaque was the proximal ICA and the least involved site was the proximal ECA.[66]

4 cases had single type of plaque whereas 43 cases had multiple types of plaques (>1 type of plaque).

Involvement of Common carotid artery:

130 CCA'S (65x2) were evaluated in this study in which we found that CCA had atherosclerotic plaques in 26 cases. A total of 34 CCA's in 26 patients were involved. CCA was involved only on right side in 9 cases, 9 cases showed involvement of only left CCA and 8 cases showed involvement of bilateral CCA's.

Most of the common carotid arteries had stenosis of <50% which was seen in 25 CCA's (73.5%), whereas 8 CCA's (23.5%) showed stenosis of 50-69% and 1 (2.9%) CCA showed stenosis of 70-80%.

Near total and total occlusion was not found in any of the cases.

Involvement of carotid bulb:

In our study we found that carotid bulb had atherosclerotic plaques in 38 patients.

Among 55 carotid bulb which were involved, most of the cases had bilateral involvement (17 cases) and most of the individuals had involvement of left CB (29 cases). 25 CB's (45.45%) had stenosis of < 50%, 24 CB's (43.6%) had stenosis of 50-69% and 6 CB's (10.9 %) had stenosis of 70-80%.

Total occlusion of carotid bulb was not found in any of the cases.

Most of the plaques which were found in the carotid bulbs were seen to extend into the external and internal carotid arteries.

Involvement of external carotid artery:

In the present study 20 ECA's in 16 patients are showing atherosclerotic changes. Most commonly right ECA was involved (12 cases) whereas 4 cases showed bilateral involvement. Most of the ECA's had stenosis of < 50% (11 ECA's) whereas 8 (40.0%) had stenosis of 50-69% and 1 ECA (2.9%) had stenosis of 70-80%.

Involvement of internal carotid artery:

41 patients had atherosclerotic plaques in the proximal ICA. In total of 62 ICAs involved, most common side affected was on the left side (33 cases). Most common site was the left proximal ICA at its origin. 24 (38.7%) of the total number of involved ICA's showed stenosis of < 50%, 24 ICA's (38.7%) showed stenosis of 50-69%, 10 ICA's (16.1%) showed stenosis of 70-80% whereas 4 ICA's (6.4%) showed near total occlusion.

Total occlusion was not found in any of the cases.

These findings were consistent with the findings in the study conducted by Bollipo JP where they found that majority of the symptomatic patients who had atherosclerotic plaques had stenosis of <50%, followed by stenosis of 50-70%. None of the patients had total occlusion of the proximal internal carotid arteries.[38]

In all the ICA who had stenosis due to atherosclerotic plaques, the peak systolic velocity was elevated and was in the range of <125 cms/sec for arteries having stenosis of less than 50%, 125-230 cms/sec for arteries having stenosis of 50-69%, >230 cms/sec for arteries having stenosis of 70-80%. PSV of variable range was found in arteries having near total occlusion.

End diastolic velocity (EDV) was also elevated in cases of ICA stenosis, EDV was < 40 cm/sec in cases having stenosis of <50%, EDV was in the range of 40-100 in cases having stenosis of 50-69%, whereas same like PSV, EDV was also variable in cases of near total occlusion.

This is similar to the study of Grant et al in which they found PSV >140 cm/sec in cases where the stenosis of >70%. They also found that, as the grade of stenosis increased, mean PSV also increased. They found a specificity of 90.6% and concluded that Doppler ultrasound is excellent method to diagnose stenosis.[31]

PSV RATIO OF (ICA/CCA):

Only peak systolic velocities cannot be used as a parameter to assess stenosis due to physiological variability. A ratio compensates for person to person physiological variability and also for instrument variability. PSV ratio can be considered best for assessing stenosis

which was proved by Zwiebel William J.[61]

Peak systolic velocities of all the involved ICA'S and PSV of CCA of the ipsilateral side was noted. Ratio was calculated.

According to consensus panel table of ultrasound and Doppler criteria for diagnosis of internal carotid artery stenosis, the criteria was set to this study and we found that.

On right side all the ICA's which had stenosis of 50% and 50-69% had ratio of <2 and 2-4 respectively. In one case ICA which had stenosis of 70-80% range had ratio <4 which dint follow the criteria.

On left side all the ICA's which had stenosis of ≤50% followed the criteria. One artery which had stenosis of 50-69% had a ratio of 1.6 and one artery having stenosis of 70-80% had ratio of 1.8 which was not according to the criteria.

The range of ratio of PSV (ICA/CCA) in vessels which had near total stenosis was found to be variable which ranged from 2.2 to 5.0.

The findings were similar to Bollipo JP and Rao PB study which concluded that in all the cases where ICA was involved, the arteries followed the PSV, EDV and ratio of PSV (ICA/CCA) range criteria similar to our study.[38]

Erickson SJ et al in their study found that grading of stenosis with only peak systolic velocity underestimated the degree of stenosis and velocity ratio increased the sensitivity of degree of stenosis estimation.[25]

Thus, this study proves that PSV ratio can be a good indicator to grade the stenosis and can be used as an additional parameter in diagnosis of stenosis of ICA.

LIMITATIONS.

Examination technique and criteria for grade of stenosis are major limitations when it comes to carotid artery evaluation by duplex sonography.

In cases where the vessel is tortuous, imaging becomes difficult. Calcified plaques obscure the area of stenosis because of its properties (interference with sound transmission).

Carotid blood flow is altered in certain disease conditions like low cardiac output cases and proximal stenosis cases where there is less blood flow in the carotid arteries which leads to underestimation of values. Aortic insufficiency is another condition wherein the characteristic features of ICA and ECA waveforms change.

CONCLUSION

- Non-invasive, cost effective, no risks of radiation are the factors which make Color Doppler ultrasonography as the safest and first line investigation for evaluation of extracranial carotid vessels.
- This study establishes evidence that prevalence of atherosclerosis is high in patients suffering from type 2 diabetes mellitus. 80% was the prevalence in this study.
- This study indicates that prevalence of atherosclerosis is more common in men and was more common above 60 yrs of age.
- Detailed evaluation of atherosclerotic changes like site and nature of plaque and percentage stenosis in extracranial carotid arteries was assessed.
- (ICA/CCA) PSV ratio was an additional parameter analysed in this study in assessing the percentage stenosis of ICA and it proved to be a useful parameter.

SUMMARY

- Atherosclerosis is one of the most common pathology affecting the carotid arteries and diabetes being one of the commonest risk factor. This study was aimed to assess the prevalence and severity of atherosclerosis in extracranial carotid arteries among diabetics.
- The study was a hospital based cross sectional study, conducted from January 2019 – December 2019 in patients referred to radiology department of KLE'S Dr Prabhakar Kore Hospital Belagavi for carotid Doppler ultrasonography.
- 65 diabetic cases were included in this study, who underwent carotid Doppler ultrasonography, 26 had symptoms pertaining to CNS and 39 had symptoms pertaining to CVS.
- It was found that males were affected more as compared to females.
- Maximum numbers of cases were in the age group of 60 to 69 yrs and all the cases above the age group of 70 yrs had atherosclerotic changes.
- 13 cases were normal, 5 had increased IMT without evidence of plaques, 47 cases had atherosclerotic plaques. The prevalence of atherosclerosis in given study group was found to be 80%.
- The most common site of involvement of atherosclerosis was left internal carotid artery at its origin followed by right proximal internal carotid artery at its origin and right carotid bulb.
- Most common type of plaque was heteroechoic plaque with specks of calcifications.
- 34 common carotid arteries were involved in 26 cases, it was found that maximum number of common carotid arteries had <50% stenosis, i.e 25 CCA's (73.5%).

- 55 carotid bulb's were involved in 38 cases, maximum number of carotid bulb's had <50% stenosis and 24 carotid bulbs had 50-69% stenosis.
- 20 external carotid arteries were involved in 16 cases; 11 external carotid arteries had <50% involvement. In this study left proximal ECA was the least involved.
- 62 internal carotid arteries were involved in 41 cases; 24 internal carotid arteries had < 50% stenosis; 24 had 50-69% stenosis whereas 4 ICA's had near total occlusion.
- None of the arteries had total occlusion.
- PSV ratio of ICA/CCA was calculated in all the cases having plaques in internal carotid artery and it was found that all cases which had < 50% stenosis had ICA/CCA ratio < 2, 50-69 % stenosis had ICA/CCA ratio in the range of 2-4, >70 % stenosis has ICA/CCA ratio >4 ; however in 3 cases the ratio didn't correlate to the range as specified by the criteria in our study, thus indicating that PSV (ICA/CCA) ratio can be used as an additional parameter in assessing stenosis of ICA.

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ANNEXURE I –

INFORMED CONSENT

TITLE OF THE STUDY: "STUDY OF PREVALENCE AND SEVERITY OF ATHEROSCLEROTIC DISEASE IN EXTRA CRANIAL CAROTID ARTERIES AMONG TYPE 2 DIABETES MELLITUS PATIENTS USING COLOR DOPPLER SONOGRAPHY."A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

PRINCIPAL INVESTIGATOR: REG.NO. BS0118003

INTRODUCTION AND PURPOSE:

Diabetes mellitus is one of the main risk factors of cerebrovascular disease, coronary artery disease and peripheral arterial disease. Comparing non-diabetic and diabetic patients, the latter ones have a higher incidence of stroke and myocardial infarction which tends to occur at younger ages, the risk is three times compared to the non-diabetic individual. Thus there is a need for detection of the atherosclerotic changes by the screening methods early in the disease process.

Color Doppler ultrasonography of extracranialcarotid arteries will help in early diagnosis of atherosclerotic disease in type 2 diabetes mellitus patients, and hence allow for a better and early treatment plan.

PROCEDURE:

I request you to kindly participate in the study titled **"STUDY OF PREVALENCE AND SEVERITY OF ATHEROSCLEROTIC DISEASE IN EXTRA CRANIAL CAROTID ARTERIES AMONG TYPE 2 DIABETES MELLITUS PATIENTS USING COLOR DOPPLER SONOGRAPHY." A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY**at Dr. Prabhakar Kore charitable hospital

and Medical Research Centre, Belagavi" is being conducted by **REG.NO. BS0118003**, post graduate in Radiodiagnosis at J. N. Medical College,Belagavi.Under the guidance of Dr._____Professor, Dept. of Radiodiagnosis, J. N. Medical College, KAHER,Belagavi.

We request you to participate in this study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you will be required to answer to the best of your knowledge. U will also be clinically examined as per the protocol drawn.

If you agree to participate in the study please furnish the details pertaining to the study.

BENEFITS:

- Results will help in early diagnosis of atherosclerotic disease in type 2 diabetes mellitus patients, and hence allow for a better and early treatment plan.
- Noninvasive, cost effective modality.

COMPLICATIONS:

- No risk to the patient has been documented from Color Doppler ultrasonography conducted earlier.

ALTERNATIVES:

If patient is not willing to take part in the study, his / her treatment or any other further investigations the patient wants to undergo, in future, in KLE will not be affected by his / her decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. The patient may choose not to take part in this study, or if the patient decides to take part, he / she can later change his/ her decision and withdraw from the study. The patient's decision will not change the present or future health care or other services that the patient would receive.

COSTS:

NIL (The study is to be conducted on the participants with T2DM who are advised Color Doppler ultrasonography as an investigation by the referring consultant and the participants will bear the charges for it).

PAYMENT FOR PARTICIPATION: No incentive will be paid to me for participating in this study.

COMPENSATION:

In the event that I become injured as a result of taking part in this study, treatment whatever available at KLE charitable hospital, Belagavi, will be offered to me. No reimbursement, compensation or free medical care is given.

CONFIDENTIALITY:

All information collected about me during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify me in this research record. Information from this study may be published but my identity will be confidential in any publication.

QUESTION:

If any enquiries in the future or in case of research related injury illness, you may contact following person.

REG.NO. BS0118003	**DR_____**	**DR. ROOPA M BELLAD**
Post-Graduate, Department of Radio-Diagnosis. J.N.Medical College, Belagavi	Guide , Professor, Department of Radio-Diagnosis J.N.Medical College, Belagavi	Chairman, College Ethical Dissertation and Research Committee J.N. Medical College Institutional Ethical Committee for Human Subjects Research
Ph._____, Ext. 1163	Ph. No. _____, Ext. 1163	Ph. No: 0831-2473777, Ext. 1529

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. I understand that I am participating in the study, which includes Color Doppler sonography of the extracranial carotid vessels
2. I confirm that I have read and understood the information in the patient information sheet. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.
3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.
4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.
5. I understand that there is no significant risk involved in the test that would be done in this study.
6. No guarantee or assurance has been given by anyone as to the results that may be obtained.
7. My signature on this form signifies that I have willingly decided to participate after understanding the above information.

Participant's Name/legally authorizedrepresentative:……

Signature/ Left Thumbimpression :……....

Name and signature of witness:……..

Date:……..

Place:……..……

ANNEXURE II -ETHICAL CLEARANCE LETTER

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed-to-be-University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http/www.jnmc.edu
E-Mail : doms@jnmc.edu
Phone: (+91-(0)831 Office : 2472550
Principal: 2471701
Fax No. -91 (0831) – 2470750

Ref: MDC/DOME/16 Date: 24/11/2018

REG.NO. BS0118003

Dr. Onkar Shivakumar Patil,
PG student in Radio-Diagnosis,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"STUDY OF PREVALENCE AND SEVERITY OF ATHEROSCLEROTIC DISEASE IN EXTRA CRANIAL CAROTID ARTERIES AMONG TYPE 2 DIABETES MELLITUS PATIENTS USING COLOR DOPPLER SONOGRAPHY. ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE III-PROFORMA

PROFORMA FOR DATA COLLECTION

1. PATIENT DATA:

IPD/OPD NO		DATE	
PATIENT NAME		DATE OF ADMISSION	
AGE		SEX	

2. HISTORY :

SYMPTOMS	
DIZZINESS	PRESENT / ABSENT
EPISODIC HEADACHE	PRESENT / ABSENT
EMOTIONAL IMBALANCE	PRESENT / ABSENT
DYSPNEA	PRESENT / ABSENT
CHEST PAIN	PRESENT / ABSENT
PALPITATION	PRESENT / ABSENT
POLYURIA	PRESENT / ABSENT

3. PERSONAL HISTORY:

SMOKING	PRESENT / ABSENT
ALCOHOLISM	PRESENT / ABSENT
OCCUPATION	

4.PHYSICAL AND LABORATORY EXAMINATION:

HEIGHT	...m
WEIGHT	…Kgs
BMI	……
PULSE	……
RANDOM BLOOD SUGAR	……

5. SYSTEMIC EXAMINATION:

CVS-ARRYTHMIAS/MURMURS	PRESENT / ABSENT
CNS-FOCAL NEUROLOGICAL DEFICITS	PRESENT / ABSENT
PA BRUIT/ABDOMINAL MASS	PRESENT / ABSENT

6. DUPLEX SONOGRAPHY OF EXTRA CRANIAL CAROTID ARTERIES

GREY SCALE:

ORIGN, COURSE AND BIFURCATION SITE	NORMAL/ABNORMAL

INTIMA MEDIA TICKNESS (IMT):

ARTERY	R (cm)	L (cm)
CCA		

PLAQUE TYPE AND % STENOSIS:

NON FLOW LIMITING (%stenosis)	Plaque type and site	FLOW LIMITING (%stenosis)	Plaque type and site
<50%		50-69%	
		70-80%	
		NEAR TOTAL OCCLUSION	
		TOTAL OCCLUSION	

INDICES:

ARTERY	PSV (cm/sec)		EDV(cm/sec)	
	R	L	R	L
ICA				
CCA				
ECA				
PSV (ICA/CCA)				

ANNEXURE IV: FIGURES

Fig 5: GE VOLUSON USG machine used for the study

Fig 6: High frequency linear array transducer used for the study

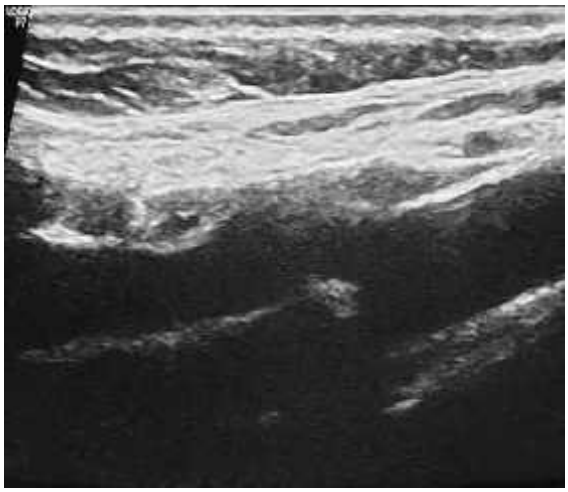

Fig 7: USG image showing normal anatomy of common carotid artery and its bifurcation into internal and external carotid arteries

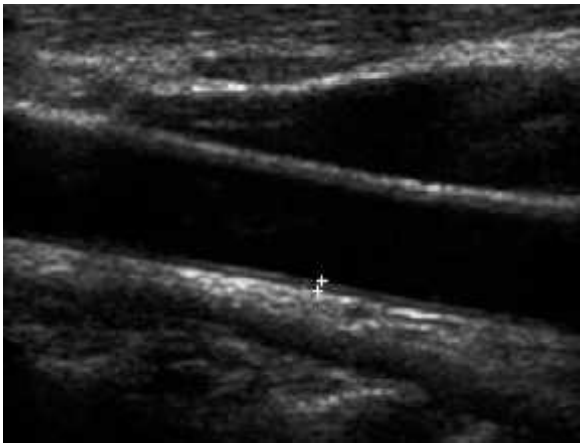

Fig 8: B mode USG image showing intima media thickness measurement

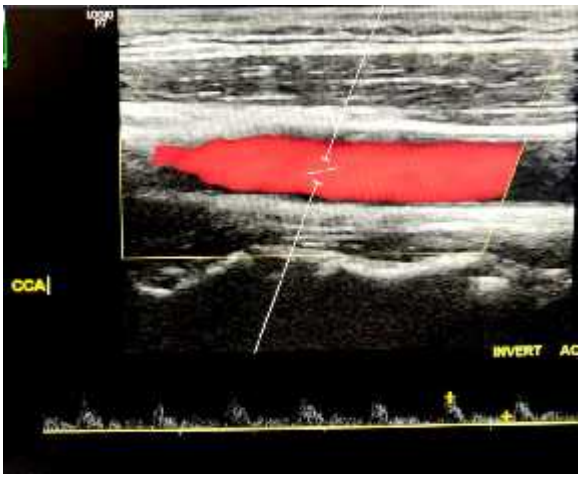

Fig 9: Normal common carotid artery Doppler waveform

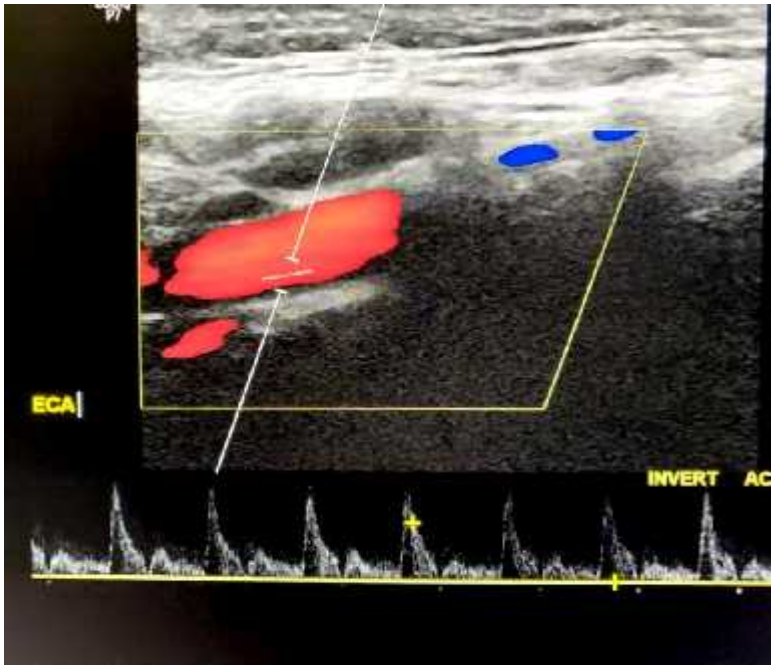

Fig 10: Normal external carotid artery Doppler waveform

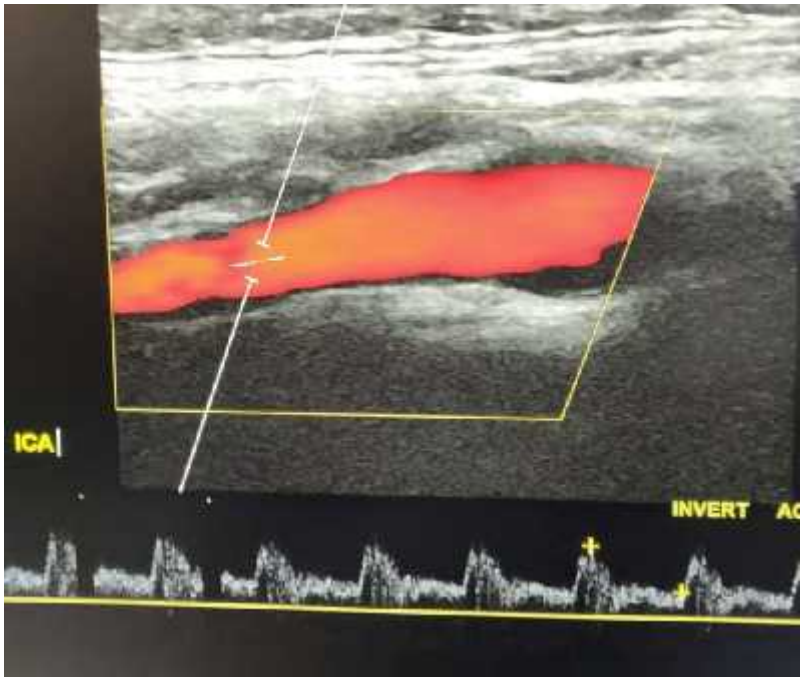

Fig 11: Normal internal carotid artery Doppler waveform

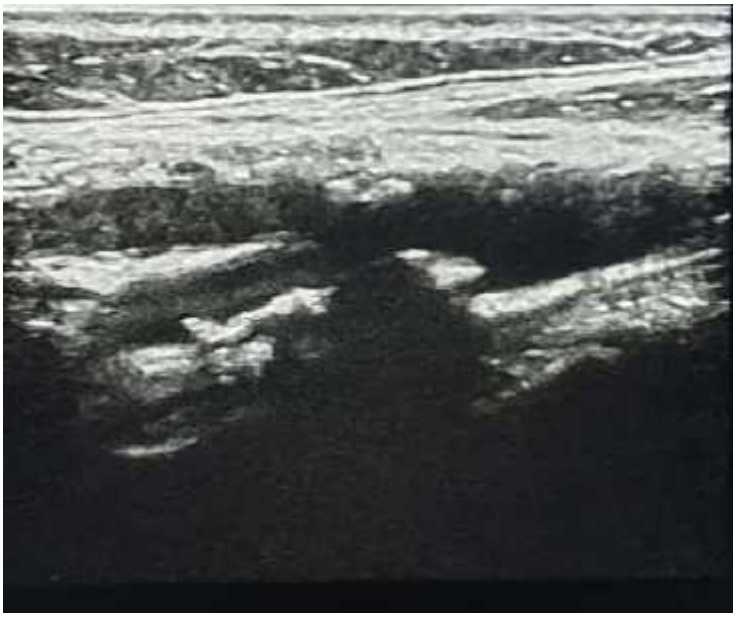

Fig 12: B mode USG image showing calcified plaque in the region of carotid artery bifurcation extending into proximal internal carotid artery resulting in approximately 70% diameter reduction

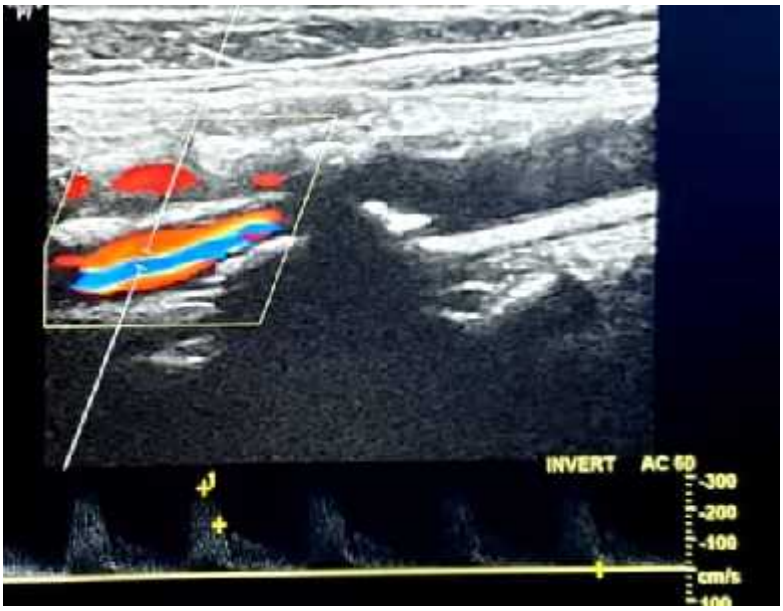

Fig 13: Color Doppler indicates significant narrowing of ICA, spectral waveform pattern indicates raised PSV with spectral broadening

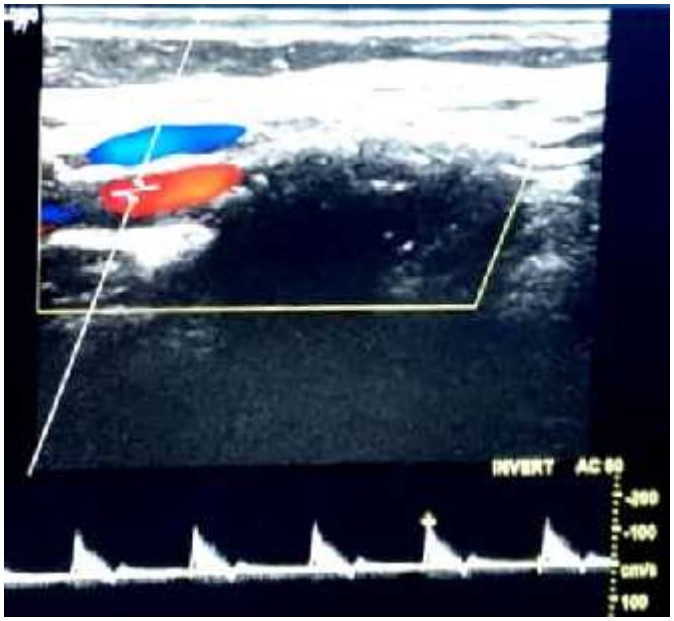

Fig 14: Color Doppler indicates >50% narrowing of ECA, spectral waveform pattern indicates raised PSV with spectral broadening

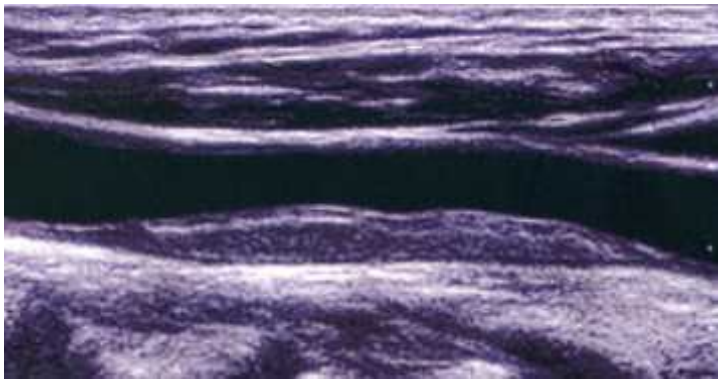

Fig 15: B mode USG shows eccentric plaque in the common carotid artery

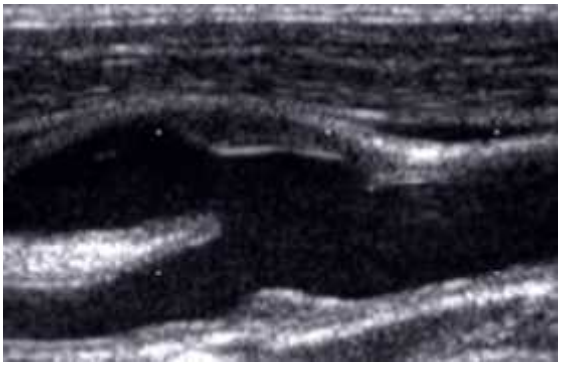

Fig 16: B mode USG showing eccentric plaque in the region of common carotid artery bifurcationextending into proximal ECA and ICA

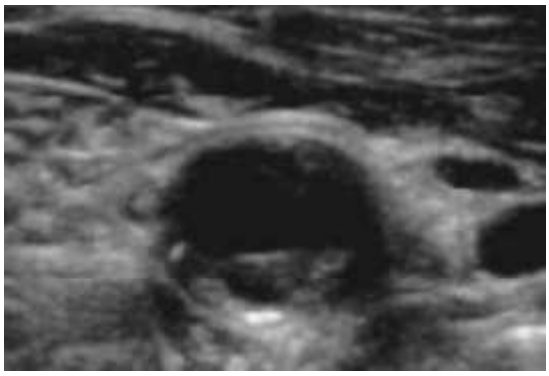

Fig 17: USG image (transverse view) showing eccentric plaque in the common carotid artery

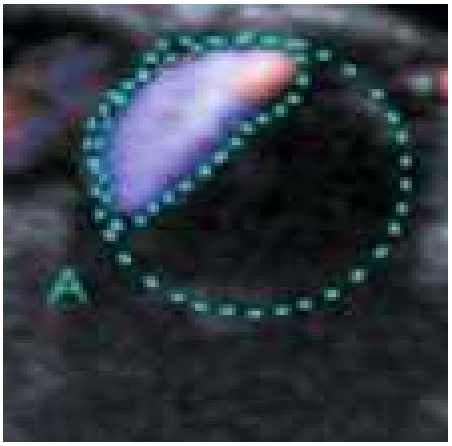

Fig 18: Image illustrating measurement of carotid artery stenosis

ANNEXURE V: KEY TO MASTERCHART

CAD	**Coronary artery disease**
R	**Right**
L	**Left**
HH	**Homogenously hyperechoic**
HE	**Heteroechoic**
HEC	**Heteroechoic with specks of calcification**
HYP	**Hypoechoic**
PL	**Plaque**
E	**Eccentric**
P	**Proximal segment**
M	**Mid segment**
D	**Distal segment**
%S	**Percentage stenosis**
C	**Concentric**
NT	**Near total**
B/L	**Bilateral**
loc	**Loss of consciousness**
CCA	**Common carotid artery**

CB	**Carotid bulb**
ICA	**Internal carotid artery**
ECA	**External carotid artery**
IMT	**Intima media thickness**
cm	**Centimeter**
sec	**Second**
PSV	**Peak systolic velocity**
EDV	**End diastolic velocity**
RHD	**Rheumatic heart disease**
V	**Velocities**
TIA	**Transient ischemic attack**
IWMI	**Inferior wall myocardial infarction**
SA	**Stable angina**
DCM	**Dilated cardiomyopathy**
S.NO	**Serial number**
AWMI	**Anterior wall myocardial infarction**
UA	**Unstable angina**

S.NO	USG NUMBER	AGE(yrs)	SEX	CLINICAL HISTORY	IMT(cm)		CCA						ICA						CB		PL echotexture	Ratio of PSV (ICA/CCA)	ECA					
					RIGHT	LEFT	RIGHT			LEFT			RIGHT			LEFT			RIGHT	LEFT			RIGHT			LEFT		
							PL,%S	V(cm/sec)		PL,%S	V(cm/sec)		PL,%S	V(cm/sec)		PL,%S	V(cm/sec)		PL,%S	PL,%S			PL,%S	V(cm/sec)		PL,%S	V(cm/sec)	
								PSV	EDV		PSV	EDV		PSV	EDV		PSV	EDV						PSV	EDV		PSV	EDV
1	3978	76	M	CAD	0.09	0.1	-	50.1	16	-	44.8	13.6	-	51.3	24	-	74.5	26.6	-	-	-	B/L- <2	-	47.4	11.7	-	52.6	15
2	4000	47	M	loc,slurring	0.07	0.07	-	66.5	10	-	55.9	15.1	-	62	12.1	-	60.1	12	-	-	-	B/L- <2	-	55.5	9.8	-	50.5	14.5
3	4075	60	F	IWMI	0.09	0.07	-	50.5	16.8	-	57.6	16.8	E,P,35%	60	25	-	80	29.3	E,35%	E,<30%	HEC	B/L- <2	-	54.1	10	-	70	12
4	4094	42	F	SA	0.07	0.06	-	89.5	22.2	-	90	29.3	-	68.3	23.9	-	73.3	22.2	-	-	-	B/L- <2	-	78	11.5	-	70	11.5
5	4141	60	M	IWMI	0.1	0.1	-	80.7	22.2	-	70.5	25.1	-	66.5	25.7	E,P,78%	255.5	108.6	-	-	L-HH	R-<2,L-3.8	-	73.6	27.5	-	78.6	10.5
6	4145	65	M	DCM	0.07	0.07		68.3	15.1	E,M,40%	65.8	16.8	-	73.6	20.4	E,P,65%	136.5	40	E,<30%	E,40%	B/L-HEC	R-<2,L-2.1	-	70.5	15.1	-	64.7	16.8
7	4664	72	M	L hemiplegia	0.1	0.1	-	60.1	14.9	-	54.5	10.1	E,P,65%	155.5	47.5	E,<30%	65.9	18.2	-	-	R-HEC,L-HH	R-2.6,L-<2	-	68.9	15.2	-	70.5	11
8	4881	58	M	loc,slurring	0.09	0.1	-	54.6	9.8	-	64.9	18	-	46.7	13.4	-	43.1	15.3	-	E,<30%	L-HEC	B/L- <2	-	53.3	11.5	-	55.8	11.9
9	4883	59	M	UA	0.09	0.09	-	64.5	18.2	-	56.4	10.2	E,P,66%	170.2	45.3	-	70.8	18.5	E,66%	E,<30%	R-HEC;L-HH	R-2.6,L-<2	-	70.8	15.5	-	60.1	14.5
10	4930	66	M	L hemiparesis	0.09	0.1	E,D 50%	62	11.6	E,D,45%	63.8	21.8	-	88.5	23.7	-	85.5	11	E,50%	E,45%	R-HEC,L-HH	B/L- <2	E,50%	100.5	13.6	-	80.2	8.2
11	5110	66	M	SA	0.1	0.1	-	45.5	10.5	-	56.2	6.1	E,P,75%	255.5	123.5	C,NT	280	170.8	E,70%	E,80%	B/L-HEC	R-5;L-5	-	85.6	6.1	-	78.5	4.3
12	5116	60	F	CAD	0.1	0.09	-	75.1	15.1	-	80.4	16.8	-	66.5	23.9	-	61.2	22.2	-	-	-	B/L- <2	-	68.3	20.4	-	59.4	20.4
13	10596	55	M	CAD	0.1	0.12	-	39.1	7.2	-	53.9	14.9	-	82.5	22.7	E,P,60%	180.2	51	-	E,60%	L-HEC	R-<2,L-3.3	-	56.5	12.5	-	65.9	14.9
14	10787	51	M	AWMI	0.11	0.1	-	36.7	9	-	48.8	12.5	-	35.5	26.3	E,P,45%	70.2	23.7	-	E,45%	L-HE	B/L- <2	-	57.4	20.2	-	34	15
15	10869	65	F	CAD	0.09	0.06	-	95.5	25	-	66.4	13.3	-	78	25.2	E,P,75%	119.8	75.2	-	-	L-HH	R-<2,L-1.8	-	45	8	E,P,50%	180	85.5
16	10891	65	M	CAD	0.09	0.12	E,P 35%	75.5	11.6	-	38.5	10.5	E,P,35%	60.5	27.3	E,P,65%	128.5	42.3	E,<30%	-	R-HH,L-HEC	L-3.3,R-<2	E,<30%	52.5	8	-	41.2	7.8
17	11315	52	M	R hemiparesis	0.12	0.11	E,D,40%	60.8	10.7	-	65.6	25.7	E,P,55%	129	41	E,P,40%	119	39.5	E,55%	E,40%	R-HH,L-HY	R-2.2,L-<2	-	100	10	E,40%	102.2	27.5
18	11393	63	F	UA	0.09	0.07	-	52.4	13.8	-	42.9	13.5	E,P,30%	70.8	26.3	C,P,60%	126.8	42.8	E,<30%	C,55%	R-HH;L-HEC	L-2.9,R-<2	-	89.8	14.2	-	72.5	11
19	11424	54	M	SA	0.07	0.07	-	50	10	-	75.3	23.4	-	42.4	10.5	-	40	20	-	-	-	B/L- <2	-	35.8	9.4	-	47.7	10.6
20	11450	52	M	TIA	0.06	0.05	-	48.1	13.5	-	66.6	16.4	-	36	15.7	-	50.3	23.3	-	-	-	B/L- <2	-	44.1	10.9	-	63.6	9.2
21	11471	65	M	loc,slurring	0.1	0.1	-	52.3	11.5	-	70	15.1	E,P,40%	83.5	15.2	E,P,40%	94.5	16.8	E,40%		B/L-HEC	B/L- <2	-	75.2	12.8	-	62.9	10.8
22	11626	70	F	DCM	0.07	0.1	-	54.1	9.8	-	56.5	16	-	41.8	11.3	-	64.6	25.7	-	-	-	B/L- <2	-	45.2	9.8	-	65.5	20.8
23	12675	48	M	L hemiparesis	0.11	0.07	-	45.5	9.5	-	53.5	14.8	E,P,60%	175.5	46.5	E,<30%	82.5	22.7	E,60%	-	B/L-HYP	R-3.8,L-<2	-	56.5	12.3	-	65.9	14.9
24	12835	61	M	R hemiparesis	0.09	0.1	-	50.5	14	E,D,40%	60	22.3	-	45.4	14.2	E,P,62%	95.5	50	-	E,60%	B/L-HYP	R-<2,L-1.6	E,<30%	70.4	10.5	-	41.8	16.7
25	12835	64	M	R hemiparesis	0.09	0.12	-	60.5	18.5	E,M,50%	80.5	25.5	E,P,30%	65.5	25.5	C,P,60%	161	40	-	C,55%	R-HH;L-HEC	R-<2,L-2.1	-	55.5	8.5	-	66.5	9
26	12906	72	M	TIA	0.1	0.1	-	75.5	20.5	C,D,40%	95.5	40.5	-	60.5	24.7	C,75%	235.5	105	-	C,65%	L-HH	R-<2,L-4.1	-	70.5	8.5	-	85.5	10
27	12914	65	F	R hemiplegia	0.12	0.1	E,P,30%	68.5	14.2	-	58.5	16.5	C,P,55%	145.5	48.5	E,P,30%	68.5	20	C,40%	-	B/L-HH	R-2.1,L-<2	E,<30%	48.5	15.5	-	60.5	18.6
28	12918	50	M	L hemiplegia	0.12	0.1	E,P,40%	55	18	E,P,30%	80.5	28.5	C,P,72%	I92.8	100	E,P,30%	68.5	24.2	-	-	B/L-HY	R-3.5,L-<2	E,35%	80.5	14.5	-	58.2	16.5
29	12954	42	M	R hemiparesis	0.1	0.09	E,P,40%	69.5	25.5	-	55	19	C,P,60%	140	55	-	55	25.5	C,55%	-	R-HE	R-2.1,L-2	-	65.5	10	-	70.5	20.2
30	13003	76	M	R hemiparesis	0.07	0.09	-	60.5	10.2	E,M,30%	65.5	20.2	-	45.4	14.2	E,P,64%	140.2	41.5	-	E,60%	R-HH;L-HY	R-<2,L-2.1	-	50.5	10.2	-	65.3	10.8

32	13111	80	M	TIA	0.1	0.09	E,P,30%	66.5	10.5	E,P,40%	80.5	20.5	E,P,55%	135.5	42.5	-	80.5	25.2	E,50%	-	B/L-HE	R-2.1,L-<2	-	59.7	8.5	-	55.6	9.5
33	13125	72	M	loc,slurring	0.1	0.12	-	55	15.8	-	65.2	18.5	E,P,60%	168	50.5	-	80.5	20	-	-	R-HH	R-3.0,L-<2	-	47.4	11.7	-	56.5	20.5
34	13132	62	M	L hemiparesis	0.1	0.12	E,P,30%	60.5	24.5	E,M,40%	70.5	28.5	E,P,75%	280	125	E,P,30%	80.5	30.5	-	-	B/L-HY	R-4.2,L-<2	E,40%	85.5	15.5	-	55.6	9
35	13197	55	M	R hemiplegia	0.09	0.07	E,P,30%	55.5	12.5	-	45.5	12.5	-	45.5	20.5	C,P,78%	290.5	120	-	E,72%	B/L-HY	R-<2,L-6.0	-	48.5	10.5	-	60.5	9
36	13245	69	F	SA	0.09	0.08	E,D,35%	65.2	18.6	-	50.8	18	-	57.5	19	-	60.2	19.5	-	-	R-HE	B/L-<2	-	59.2	14.2	-	61.2	10.5
37	13719	58	M	TIA	0.09	0.1	E,D,50%	50.5	15.5	-	38.5	14.2	C,P,80%	240	110.5	-	78	25.2	E,40%	-	B/L-HH	R-4.8,L-<2	E,30%	75.2	25.5	-	55.2	10.2
38	13901	56	F	R hemiparesis	0.12	0.11	-	55.5	25	-	60.5	24.5	E,P,30%	75.5	22.5	C,P,80%	300	140.2	-	C,75%	B/L-HH	L-5,R-<2	-	48	12.2	E,50%	86.5	18.5
39	22522	45	M	CAD	0.07	0.075	E,D,58%	90.2	25	E,D,45%	75.2	18.5	-	45.4	14.2	-	51.8	23.1	E,45%	-	B/L-HH	B/L- <2	-	60.2	15.2	-	41.8	16.8
40	22938	41	M	AWMI	0.07	0.07	-	56.4	12.2	-	48.8	13.1	-	80	18.4	-	52.7	15.5	-	-	-	B/L- <2	-	78	16.5	-	76.2	19.2
41	23079	52	M	IWMI	0.09	0.07	C,D,50%	78.6	23.5	C,D,55%	70.2	18.8	C,P,50%	103.5	16.2	C,P,50%	43.5	15.4	E,50%	E,50%	B/L-HH	B/L- <2	-	76.5	11.2	-	80.5	7.5
42	23107	72	M	CAD	0.12	0.1	C,70%	55.8	5.8	C,60%	80.2	14.2	C,P,NT	I80.5	32.5	-	105.8	57.8	C,70%	C,60%	B/L-HEC	R-3.2,L<2	-	63.5	5.5	-	115	25.8
43	23162	60	M	TIA	0.06	0.06	-	45	10.3	-	70.4	14.1	-	45.7	14.9	-	54.6	17.1	-	-	-	B/L- <2	-	66.2	12.1	-	67.8	19.2
44	23255	55	F	L hemiparesis	0.1	0.07	-	47.6	13	-	40.2	13.2	-	45.7	15.5	-	49.3	18.2	-	-	-	B/L- <2	-	66.4	8.5	-	45.8	9.5
45	23265	65	M	CAD	0.1	0.1	-	35	11.5	-	80	11.2	E,P,40%	75	12.2	-	90	16.8	E,40%	E,30%	R-HE;L-HH	B/L- <2	E,P,20%	40	12.5	E,P,20%	65	15.2
46	23272	66	M	UA	0.12	0.12	-	60.5	20.5	C,D,40%	100.7	46.7	C,P,68%	128.6	55	C,P,40%	106.5	38.5	C,68%	C,40%	B/L-HE	R-2.2,L-<2	-	57.6	10.7	-	66.3	10.8
47	23431	60	M	SA	0.07	0.05	-	40.2	10.5	-	54.6	14.9	-	29.8	12	-	31.4	13.8	-	-	-	B/L- <2	-	31.4	15	-	60	15
48	23468	65	F	CAD	0.06	0.07	-	54.6	10	-	43.5	12.7	-		12.7	-	30.3	14.9	-	-	-	B/L- <2	-	38	9.4	-	41.3	11.2
49	23470	59	M	AWMI	0.07	0.06	-	40.3	10.4	-	32	7.2	-	31.3	7	-	43.3	9	-	-	-	B/L- <2	-	40	8.8	-	72.4	13.5
50	23519	65	M	DCM	0.07	0.08	E,M,35%	64.1	16.5	-	44.6	8.8	E,P,35%	83	17.2	E,P,35%	70.5	18	-	E,<30%	R-HH;L-HEC	B/L- <2	-	90	17	-	63.2	17.8
51	23635	55	M	L hemiplegia	0.1	0.2	C,45%	30	8.8	-	64.5	21.5	NT	I40.8	20.5	E,P,65%	134.5	70	E,45%	E,60%	HE	R-2.2;L-2	-	28	9	E,60%	60	10
52	23641	61	F	loc,slurring	0.07	0.08	-	57.2	14.2	-	74.3	14.2	-	82.9	16.1	E,P,30%	84.5	16.1	-	E,<30%	B/L-HEC	B/L- <2	-	59.2	7.5	-	74.3	7.5
53	23936	31	M	RHD	0.07	0.07	-	49	12.7	-	45.7	12.7	-	44.6	17.1	-	73.3	30.3	-	-	-	B/L- <2	-	40.2	7.2	-	38	11.6
54	23953	75	M	CAD	0.1	0.12	E,D,40%	70	20.2	C,D,40-50%	75	21	-	64.5	31.4	-	80	26.3	-	-	R-HEC,L-HEC	B/L- <2	-	54.6	8.5	-	75.5	9
55	23957	50	F	CAD	0.07	0.06	-	52	16.8	-	67.4	16.8	-	36.6	20	-	55.3	24.5	-	-	-	B/L- <2	-	35	20	-	33.3	21.5
56	23989	72	M	IWMI	0.08	0.1	-	45	13	-	48	13.5	-	65	14	-	67	13.8	-	-	-	B/L- <2	-	59.2	13.5	-	60	13
57	24164	67	M	IWMI	0.11	0.12	-	35.5	19	E,P,40%	110	22	-	88.5	15	E,P,30%	90	25	E,30%	-	R-HH;L-HE	B/L- <2	-	45.2	20	-	38.5	18.5
58	24188	74	M	CAD	0.1	0.1	-	48.8	9.5	-	44.2	19.8	E,P,40%	116	19.1	E,P,55%	128.1	41	E,40%	E,50%	B/L-HH	L-2.1,R-<2	E,40%	105.5	18.4	E,55%	148	16.5
59	24194	67	M	CAD	0.12	0.12	-	53.5	10.5	E,D,60%	60.5	11	C,P,30%	70.6	20	NT	200	35.8	C,65%	C,70%	B/L-HEC	R-<2;L-3.3	C,25%	100	15	-	42.4	14.7
60	24212	55	F	RHD	0.07	0.07	-	80.4	20	-	82.5	22.7	-	60	15	-	69.1	14	-	-	-	B/L- <2	-	58	16.5	-	39.6	18.8
61	24295	35	F	AWMI	0.07	0.07	-	61.5	27	-	78.8	31.3	-	90.4	35	-	88.5	24	-	-	-	B/L- <2	-	78.5	16.2	-	75.5	18.3
62	24318	67	M	CAD	0.11	0.09	-	66.7	6.1	-	78.7	15.4	E,P,52%	128.5	41.8	E,P,30%	73.5	13	-	-	B/L-HEC	R-2.1,L-<2	-	59.7	12.2	-	68.3	11.2
63	24400	73	M	UA	0.1	0.1	-	52.4	12.7	-	80.7	6.5	C,P,55%	128.5	48.5	C,P,55%	165.5	45.9	C,52%	C,55%	B/L-HH	B/L-2.3	C,P,70%	200	21.3	C,P,52%	175.7	38.5
64	24422	65	M	AWMI	0.1	0.1	-	85	18.2	-	83.3	16.8	-	70.1	21.6	-	75.5	24.6	E,<30%	C,60%	B/L-HEC	B/L- <2	E,58%	130	12.1	C, 65%	165	16.8
65	24540	62	M	CAD	0.1	0.1	-	46.8	13.8	-	60.8	25.8	-	86.5	30.5	C.P.75%	2I2.4	110.5	E,<30%	E,50%	B/L-HEC	R-<2,L-3.5	-	80.4	13	-	54.5	8.1