Original Research Article

Role of colour doppler in the evaluation of carotid artery disease in patients of stroke

S Althaf Ali[1], R Prabhakara Rao[2*]

[1]Associate Professor, [2]Assistant Professor, Department of Radio Diagnosis, Deccan College of Medical Sciences, Hyderabad, INDIA.
Email:althafalis123@gmail.com

Abstract

Objective: To study the role of carotid doppler in evaluation of carotid arteries for stenosis, Characterization of plaque, distribution and risk factors between Non-Lacunar and Lacunar subtypes in patients with stroke. **Design:** A prospective cross sectional study by single operator using Doppler ultrasound for plaque characterization and to obtain flow velocity wave forms in Carotid vessels. **Duration:** September 2016 to November 2017. **Setting:** Department of Radio-diagnosis in association with Department of Medicine, Deccan College of Medical Sciences, Hyderabad. **Participants:** Seventy patients with positive CT findings of ischemic stroke admitted in DCMS. **Methods:** Pearson's chi square-correlation estimation with Y ates correction, Odds ratio, unpaired 't' test were used for the data tabulated from the flow velocity waveforms. **Results:** Non-Lacunar stroke patients were associated with male sex, smoking, alcohol, high mean age, higher Carotid IMT(1.1mm), more echolucent plaques(76%) and Carotid artery stenosis(82.5%) compared to Lacunar stroke. In our study diabetes and hypertension did not show any significant difference in association between Lacunar and Non-Lacunar stroke. **Conclusion:** Presence of risk factors for atherosclerosis, increased IMT and echolucent plaques on carotid Doppler study are at a higher risk for future stroke and must be followed up for progression of atherosclerosis.
Key Words: Carotid Artery Disease, Colour Doppler, Atherosclerosis, Stroke.

***Address for Correspondence:**
Dr.R. Prabhakara Rao, Assistant Professor, Department of Radio Diagnosis, Deccan College of Medical Sciences, Hyderabad, INDIA.
Email:althafalis123@gmail.com
Received Date: 03/09/2018 Revised Date: 14/10/2018 Accepted Date: 01/11/2018
DOI:https://doi.org/10.26611/1013831

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 04 December 2018

INTRODUCTION

Stroke is one of the leading causes of death worldwide. One third of cases are fatal, and survivors usually have prolonged or irreversible disabilities. Four out of five ischemic events are caused by atherosclerotic diseases, with most changes affecting the Carotid bifurcation. This necessiates the evaluation of extra cranial Carotid artery system[1]. Stroke is a heterogenous disease and consideration needs to be directed to manage different stroke subtypes differently. At present, there is no recommendation to differentiate among subtypes of anterior circulation infarcts. However, evidence is mounting that demonstrates a difference in patho-physiology of Lacunar and non-Lacunar (large artery) infarcts[2]. Lacunar infarcts mostly do not arise from large artery atheromatous disease or by cardio-embolic phenomena, and there is a negative predictive value for severe Carotid stenosis in Lacunar strokes[3]. However, the arterial pathology remains poorly understood. Much of our current understanding is based upon studies of Fisher *et al* in the 1960s and 1970s[4]. Progress since then has been limited, but there is growing evidence to suggest that the Lacunar arteriopathy may differ from the athero-thrombo-embolic processes that lead to non-Lacunar stroke[5-7]. Epidemiological studies have identified several risk factors for ischemic stroke, including hypertension, smoking, diabetes mellitus, alcohol intake and total serum cholesterol levels[8]. Several studies have showed an association between increased Carotid IMT and stroke in elderly and middle aged subjects[9-12]. The initial manifestation is the increase in vascular Intima-Media Thickness (IMT), whose progression leads to plaque formation and narrowing of vascular lumen[13]. For stroke prevention, identification of Carotid plaque and

How to cite this article:S Althaf Ali, R Prabhakara Rao. Role of colour doppler in the evaluation of carotid artery disease in patients of stroke. *MedPulse – International Journal of Radiology.* December 2018; 8(3): 44-51. http://www.medpulse.in/Radio%20Diagnosis/

quantification of stenosis is primarily important. Plaque characterization in the form of its composition and morphology along with lumen stenosis are better in predicting future event of stroke. Ultrasound of Carotid is the most common imaging study performed for diagnosis of carotid Artery Disease. Ultrasound studies have shown that Carotid stenosis ≥ 70% increases the incidence of future stroke, whereas the risk is limited when stenosis is ≤ 60%[13]. At present Doppler study is the main non-invasive imaging technique, widely available with sensitivity approaching that of angiography[14]. Doppler imaging has dramatically changed the diagnostic evaluation of suspected Carotid disease. Doppler sonography provides a rapid, non-invasive, relatively inexpensive and accurate means of diagnosing Carotid stenosis[15]. It is established that denuded or ulcerated Carotid plaque surfaces are common sources of cerebral emboli that cause stroke or other neurological events, emphasizing the need for plaque charecterization[16]. The purpose of this study is to highlight the role of various risk factors among the subtypes of ischemic stroke, to study the Carotid plaque characteristics to help predict future stroke events and also to quantify the degree of Carotid stenosis to help in better management of stroke patients. As the Carotid stenosis develops, the PSV first becomes elevated, therefore, PSV is a principal measure of stenosis severity. EDV lags behind relatively as stenosis severity progresses but rises rapidly as the stenosis becomes severe, thus EDV is a good marker for high grade stenosis. ICA to CCA ratio of PSV is important as it compensates for abnormally high and low flow states[17]. Hence we have chosen PSV, EDV and ICA to CCA ratio of PSV as Doppler indices for estimation of carotid stenosis in our study.

MATERIALS AND METHODS

The present study was conducted at Deccan College of Medical Sciences (DCMS),Hyderabad, in the Department of Radio-diagnosis in association with the Department of Medicine during the period September 2016 to November 2017.

Study Population: Patients with positive CT scan findings of Ischemic stroke admitted in Owaisi Hospital and Research Center (OHRC),Hyderabad, Telangana.

Inclusion Criteria

1. Symptomatic patients with positive CT scan findings of Ischemic stroke.
2. Patients with recent (<2 weeks duration) episode of stroke.

Exclusion Criteria

1. Patients with posterior circulation stroke and vertebral steal.
2. Patients with Hemorrhagic stroke.
3. Patients with carotid anomalies and tortuous course.
4. Patients with carotid dissection.
5. Patients who underwent carotid Endarterectomy or stenting.
6. Patients with symptoms of Central Retinal Vein or Artery disease.

Duration of Study: Between September 2016 and November 2017, for a period of 15 months.

Examination Method: Patients are explained about the atraumatic and non-invasive nature of the procedure. A brief history is taken and physical examination is carried out. Patients are subjected to Ultrasonographic and Doppler examination.

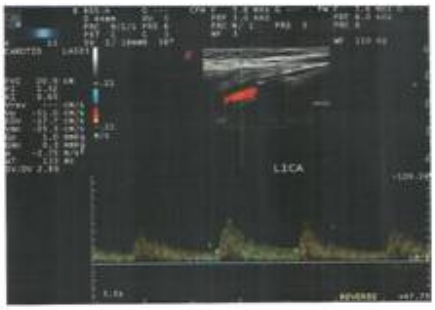
Doppler US Technique: The US machines used are Philips HD15 with a 7.5MHz linear probe. The acoustic power in the Doppler mode is limited to that recommended by the current U.S. Food and Drug Administration guidelines for Doppler scanning. The Doppler US study is performed with patient lying down in supine or semi-supine position with the head slightly hyper-extended and rotated 45Degree away from the side being examined. The extent, location, and characteristics of atherosclerotic plaque in the common carotid artery (CCA) and internal carotid artery (ICA) and Intima-Media Thickness in CCA is documented with gray-scale imagining. The point of measurement was taken 1 cm proximal to the carotid bulb at the site of maximal thickness (96). After gray-scale imaging, Color Doppler imaging is performed to detect areas of abnormal blood flow that require Doppler spectral analysis. Pulsed wave (PW) Doppler spectral analysis is then performed, and the velocity of blood flow in the mid-CCA and proximal ICA as well as at the diseased areas is measured and recorded in a standardized format. The entire data is tabulated and the risk factors like age, sex, history of smoking, alcohol, diabetes, and hypertension are correlated with USG and Doppler parameters to find out the relationship between the clinical findings, morphological and radiological changes in Carotid vessels and various risk factors.

Statistical Methods: Pearson's chi square-correlation estimation with Yates correction, Odds ratio, unpaired 't' test were used for the data tabulated from the flow velocity waveforms.

Ethical Issues: Informed oral consent was taken from patients. The study was cleared by the approved ethical committee of the Institution. The rights and welfare of human subjects on whom the study was conducted were adequately protected.

OBSERVATIONS AND RESULTS

Left CCA shows increased IMT (1.9mm)

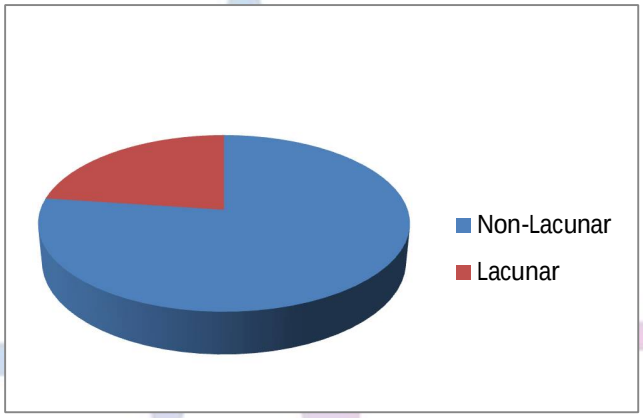


Filling of Spectral window left ICA; PSV normal.

Figure 1: Left CCA shows increased IMT (1.9 mm); **Figure 2:** Filling of spectral window left ICA: PSV normal.

Case Distribution of Non-Lacunar and Lacunar Stroke: A total of 70 cases were included in this study based on the inclusion criteria. Of these cases fifty four cases (54) had non-Lacunar stroke and sixteen cases (16) had Lacunar stoke

Figure 3: Case distribution of non-lacunar and lacunar stroke



Age Distribution of Non-Lacunar And Lacunar Stroke: In our study mean age of patients with non-Lacunar stoke was 61.69 years and those with Lacunar stroke was 51.75 years as depicted in chart 2. We used Un-Paired test for calculation of mean age.

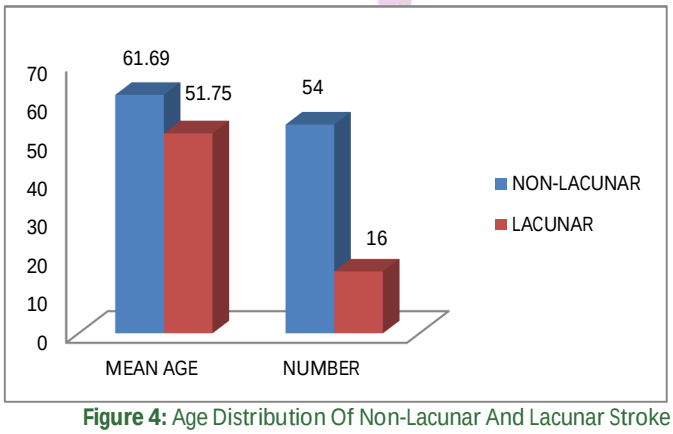


Figure 4: Age Distribution Of Non-Lacunar And Lacunar Stroke

In present study, 'P' value is <0.0001 (value less than 0.05 is significant), suggesting the difference in mean age between non-Lacunar and Lacunar stroke is significant.

Sex Distribution in Ischemic Stroke Subtypes

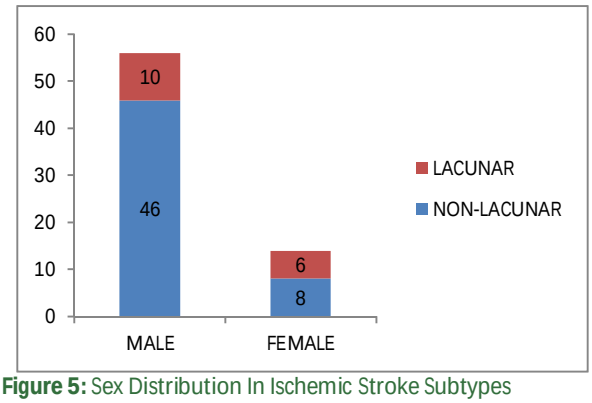


Figure 5: Sex Distribution In Ischemic Stroke Subtypes

In preset study number of male patients presenting with Non Lacunar stroke were forty six(46) and number of female patients were eight (8), in the Lacunar Stroke Ten (10) were Male, Six (6) were Female. The incidence of non-Lacunar stroke was significantly higher in males compared to Lacunar stroke with 'P' value of 0.04 this difference is considered to be statistically significant and overall stroke was also higher in males than females.

IMT DISTRIBUATION IN STROKE SUBTYPES

Table 1: IMT Distribuation In Stroke Subtypes

Stroke Subtype	IMT Increased	IMT Normal	Total
Non-Lacunar	48	6	54
Lacunar	6	10	16

Table 1 shows that out of the 70 cases in our study, 48 cases (89%) with non-Lacunar stoke showed increased IMT and only 6 cases (37%) with Lacunar stroke showed increased IMT.

Relationship of Diabetes and Stroke Subtypes

Table 2: Relationship Of Diabetes And Stroke Subtypes

Stroke Subtype	Diabetes Present	Diabetes Absent	Total
Non Lacunar	47	7	54
Lacunar	11	5	16

In present study, as shown in table 2, diabetes was present in 87 % (47 cases out of 54) of cases with non-Lacunar stroke and in 69% (11 cases out of 16) of cases with Lacunar stroke. The present study shows that diabetes is slightly higher in non-Lacunar than Lacunar ischemic strokes. However, the p value (0.08) and chi-square value are (2.90) suggesting there is a trend of non-Lacunar stroke in diabetics although the difference is not statistically significant.

Relationship of Hypertension and Stroke Subtypes

Table 3: Relationship Of Hypertension And Stroke Subtypes

Stroke Subtypes	Hypertensive	Non-Hypertensive	Total
Non-Lacunar	44	10	54
Lacunar	13	3	16

In present study, as shown in table 3, hypertension was present in 81% (44 cases out of 54) of cases with non-Lacunar stroke and in 81% (13 cases out of 16) of cases with Lacunar stroke.The present study shows that hypertension is equally common in the non-Lacunar and Lacunar ischemic strokes with non-significant 'P' value of 0.983 and Odds ratio of 1.01 with 95% confidence limits of 0.24 and 4.42.

Relationship of Smoking and Stroke Subtypes

Table 4: Relationship of Smoking and stroke subtypes

Smoking	Smokers	Non-Smokers
Non-Lacunar	41	13
Lacunar	8	8

Table 4 depicts that 76% (41 cases out of 54) of cases with non-Lacunar stroke were smokers, whereas only 50% (8 cases out of 16) of cases with Lacunar stroke were smokers. The present study shows that smoking is slightly more

common in the non Lacunar and Lacunar ischemic strokes with p value (0.047) and chi-square value (3.95) showing borderline significance.

Relationship of Alcohol and Stroke Subtypes

Table 5: Relationship Of Alcohol And Stroke Subtypes

Stroke Subtype	Alcoholic	Non-Alcoholic
Non-Lacunar	38	16
Lacunar	7	9

Table 5 depicts that 70% (38 cases out of 54) of cases with non-Lacunar stroke were alcoholic, whereas only 44% (7 cases out of 16) of cases with Lacunar stroke were alcoholic.The present study shows that alcohol is more commonly associated with non Lacunar and Lacunar strokes. The p value (0.005) and chi-square test value (3.81) showing borderline significance.

Plaque Site Distribution

Table 6: Plaque Distribution In Ischemic Stroke Subtypes

Plaque Location	Absent	ICA	Bifurcation	CCA	Diffuse
Non Lacunar	19	17	46	8	18
Lacunar	11	2	13	2	4

In our study, majority of the plaques were distributed around the carotid bifurcation as shown in table 6. Overall plaque distribution in cases of ischemic stroke:

Table 7: Overall Plaque Distribution In Ischemic Stroke Cases

Plaque	Absent	ICA	Bifurcation	CCA	Diffuse
Number	30	19	59	10	22
Percentage	21.4%	13.6%	42%	7%	16%

Table 8: Plaque Characteristics In Ischemic Stroke Cases

Plaque Characteristics	Absent	Echolucent	Hyperechoic	Calcified	Total
Non Lacunar	19	42	23	24	108
Lacunar	11	13	06	02	32

In present study, as shown in table 8, majority of the echolucent plaques were present in patients with non-Lacunar stroke (76%) than in Lacunar stroke (24%). In present study plaques were present in 82% of patients with non-Lacunar stroke (89 out of 108 Carotid arteries), whereas only 34% of patients with Lacunar stroke showed presence of plaque (11 out of 32 Carotids).

Ulcerated Plaque at Bifurcation of Left Carotid Artery

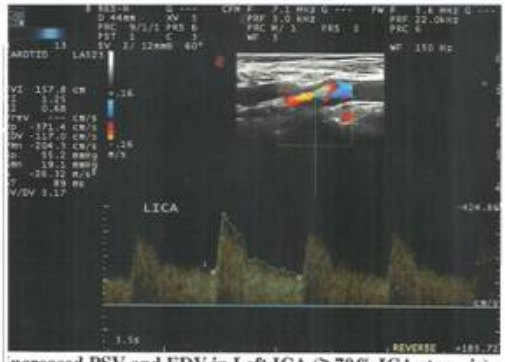
Figure 12:

Percentage of Carotid Stenosis in Patients With Stroke

Table 9: Percentage of carotid stenosis in patients with stroke

Percentage Stenosis	Plaque Absent	<50%	50-69%	>70	Near Occlusion 95%	Occlusion 100%
Percent Of Cases	20.70%	61.40%	5.70%	5%	2.20%	5%

In present study, as shown in table 9, 20.7% cases had no plaque in the Carotid arteries and the remaining which showed plaques, 61.4% cases had only mild Carotid artery stenosis(<50%).



ncreased PSV and EDV in Left ICA.(≥ 70% ICA stenosis).

Figure 14:

Table 10: Distribution Of Carotid Stenosis In Stroke Subtypes

Stroke Subtype	No Stenosis Of Carotid Arteries	Carotid Stenosis Present >50% Stenosis
Non Lacunar	19(17.5%)	89(82.5%)
Lacunar	10(32%)	22(68%)

In present study, as shown in table 10, 82.5% of cases with non-Lacunar stroke showed presence of carotid artery disease, while 17.5% showed a normal carotid Doppler study. There were only 68% of cases with Lacunar stroke which showed presence of carotid artery disease, while 32% showed a normal carotid Doppler study. The 'P' value in our study was 0.15 and the chi-square value was 2.03. The odds ratio in our study was 2.1 with 95% confidence interval of 0.86 and 5.2. The difference was not statistically significant; However, it did show a trend between carotid artery disease and non-Lacunar stroke.

Table 11: Plaque Surface In Stroke Subtypes

Plaque Surface	Plaque Absent	Smooth	Irregular	Ulcerated
Non Lacunar	30	53	38	1
Lacunar	1	6	10	1
Total	**31**	**59**	**48**	**2**

In present study, 59 patients had smooth plaque, 38 had irregular plaques and 2 patients had uncerated plaques.

DISCUSSION

Stroke is third leading cause of mortality worldwide. Carotid Intima-Media Thickness is a marker of atherosclerosis and is also a predictor for ischemic stroke (96). In most of the ischemic strokes the underlying pathophysiology is atherosclerosis. We compared risk factors for non-Lacunar versus Lacunar ischemic stroke like age, sex, and carotid Intima-Media Thickness, history of diabetes, hypertension, alcohol intake and smoking. Only patients with positive CT scan findings of Ischemic stroke were included in the study and they were classified into non-Lacunar and Lacunar. Lacunar infarction was defined in which CT findings were suggestive of infarction due to occlusion of single perforating artery, that is a subcortical, sharply marginated hypodense lesion with a diameter <2 cm. A non-Lacunar infarct was defined as a case in which CT findings were suggestive of infarction involving the cortex or showed a large (diameter >2 cm) subcortical lesion. We also studied plaque characterization, plaque morphology, plaque surface and percentage of carotid stenosis. Plaques were characterized into Hypoechoic, Echogenic and Calcified. Degree of ICA Stenosis Diameter was calculated as by Consensus Panel Table of Ultrasound and Doppler Criteria. Plaque morphology was classified as either homogenous or heterogenous. Homogenous plaques were defined as those producing uniform echo patterns. Plaques with focal areas of increased echogenicity are prognostically the same as homogenous plaques and are therefore, frequently classified as such. The surface of homogenous plaque is always smooth. Heterogenous plaques were defined as those having a complex echo pattern and contain at least one focal sonolucent area. The intimal surface may be either smooth or irregular.

Age Distribution: In our study mean age of patients with Non-Lacunar stroke was 62 years and those with Lacunar stroke was 52 years. In our study, P value is <0.0001 suggesting significant statistical difference between the mean age of the two.

Sex Incidence in Stroke: In our study 54 patients had non-Lacunar stroke was significantly higher in males

compared to Lacunar stroke. Carotid Intima-Media Thickness (IMT) is a marker of atherosclerosis and is also a predictor for ischemic stroke. We determined the frequency of IMT in patients with acute ischemic stroke. Our study shows mean carotid IMT of 1.11mm in patients with non-Lacunar stroke and 0.87mm in patients with Lacunar stroke to be. In our study, 'P' value is 0.00008 and 'Pearson chi-square' test value is 18.48 which are highly significant. Carotid IMT is a strong predictor of future vascular events. For an absolute carotid IMT difference of 0.1 mm, the future risk of stroke increases by 13% to 18%.

Diabetes and Stroke: In present study diabetes was present in 87% (47 cases out of 54) of cases with non-Lacunar stroke and in 69% (11 cases out of 16) of cases with Lacunar stroke. The present study shows that diabetes is slightly higher in non-Lacunar than Lacunar ischemic strokes. However, the 'P' value (0.08) and 'chi-square test' value are (2.90), suggesting there is a trend of non-Lacunar stroke in diabetics although the difference is not statistically significant.

Hypertension and Stroke: In present study hypertension was present in 81% (44 cases out of 54) of cases with non-Lacunar stroke and in 81% (13 cases out of 16) of cases with Lacunar stroke. The present study shows that hypertension is equally common in the non-Lacunar and Lacunar ischemic strokes with non-significant p value of 0.983 and Odds ratio of 1.01 with 95% confidence limits of 0.24 and 4.42).

Smoking and Stroke: 76% (41 cases out of 54) of cases with non-Lacunar stroke were smokers, whereas only 50% (8 cases out of 16) of cases with Lacunar stroke were smokers. The present study shows that smoking is slightly more common in the non-Lacunar and Lacunar ischemic strokes with p value (0.047) and chi-square value (3.95) showing borderline significance. Our study shows Odds ratio of 1.5 with 95% Confidence interval of 0.9 to 2.5.

Alcohol And Stroke: The present study shows that alcohol consumption is slightly more common in the non-Lacunar than Lacunar ischemic strokes with p value (0.05) and chi-square value (3.81) showing borderline significance. Our study shows Odds ratio of 1.60 with 95% confidence interval of 0.9 to 2.5.

PLAQUE DISTRIBUTION IN STROKE PATIENTS: In our study, majority of the plaques were distributed around the carotid bifurcation.

PLAQUE CHARACTERISTICS IN STORKE PATIENTS: In present study plaques were present in 82% of patients with non-Lacunar stoke (89 out of 108 carotid arteries), whereas only 34% of patients with Lacunar stoke showed presence of plaque (11 out of 32 carotids). In present study majority of the echolucent plaques were present in patients with non-Lacunar stroke (76%) than in Lacunar stoke (24%).

Percentage of Plaques In Various Degrees Of Carotid Stenosis: In present study 20.7% cases had no plaque in the carotid arteries and the remaining which showed plaques, 61.4% cases had only mild carotid artery stenosis (<50%). In our study we found that number of normal carotid arteries was higher in patients with Lacunar stroke whereas number of carotid arteries with stenosis was more in non-Lacunar stroke (RR 1.1, 95% confidence interval 0.9 to 1.5).

CONCLUSIONS

1. Number of normal carotid arteries was higher in patients with Lacunar stroke whereas number of carotid arteries with stenosis was more in non-Lacunar Stroke further supporting that Lacunar Strokes may have a Non-Atherosclerotic pathogenesis.
2. Mean age of patients with non-Lacunar stroke was higher than patients with Lacunar stroke.
3. Incidence of non-Lacunar stroke was significantly higher in males compared to Lacunar stroke.
4. Hypertension and diabetes appear equally common in Lacunar and non-Lacunar ischemic stroke whereas, Smoking and alcohol are slightly more common in the non-Lacunar and Lacunar ischemic strokes. Thus, are associated with increased risk of non-Lacunar stroke.
5. Echolucent plaques were more commonly seen in patients of non-Lacunar stroke.
6. The present study highlights the importance of Doppler Sonography in the evaluation of plaque characteristics in predicting future stroke.
7. The study by assessing the plaque morphology and percentage stenosis of carotid arteries also gives a guide for further lifestyle modification.
8. Doppler Sonography provides rapid, non-invasive relatively inexpensive and accurate means of diagnosing carotid artery stenosis.

Carotid IMT was higher in non-Lacunar stroke patients than in patients with Lacunar stroke. This supports the hypothesis that non Lacunar stroke have atherosclerotic pathology and Lacunar stroke have non-atherosclerotic pathogenesis. Thus, patients with non-Lacunar stroke and increased IMT are at a higher risk for future stroke events and must be followed up with Doppler for progression of atherosclerosis, while patients with Lacunar stroke and normal IMT may not be followed up with Doppler.

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Source of Support: None Declared
Conflict of Interest: None Declared