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A Study on the Role of Grayscale and Colour Doppler Ultrasonography of Extracranial Carotid Arteries In Patients of Ischaemic Stroke

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ABSTRACT

Stroke is the third most common cause of death worldwide. There is a close relationship between ischemic cerebral vascular accidents and carotid artery stenosis due to various causes. Imaging of the extra cranial portion of the carotid arteries plays a important role in diagnosing various carotid artery diseases including atherosclerosis, which in turn can predict atherosclerosis of the entire vascular system of the body. Atherosclerosis of intracranial arteries is a well-recognized cause of ischemic stroke in Asians, and extracranial carotid artery disease is more often seen in western countries. Due to its wide availability, USG can be used as an important diagnostic tool for proper evaluation of patients of cerebrovascular accident in emergency setting. This paper aims to discuss the results of our hospital based cross sectional study on the various morphological and physiological changes taking place in the extracranial portion of carotid arteries as an underlying pathological process in patients presenting with signs and symptoms of cerebrovascular insufficiency. Increased IMT, presence of plaque, and evaluation of plaque characteristics such as types, surface, sites, morphology, etc. can be useful to estimate the predictable risk for a cerebrovascular event in the future. Echolucency of plaque, intraplaque hemorrhage, and plaque ulceration are plaque morphologies, that have been found to be associated with increased risk of Ischaemic stroke. In addition to that, doppler velocity parameters of the stenotic segments can provide information about the resultant changes in the hemodynamics.

Keywords: Atherosclerosis, Ischemic Stroke, Cerebrovascular Insufficiency, Grayscale and Colour Doppler Ultrasonography, Doppler Velocity.

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INTRODUCTION

Stroke, being one of the leading causes of death and debility worldwide, can result in catastrophic events and various degrees of neurological impairment[1]. Severe and slowly progressive stenosis caused by atherosclerotic disease involving the extra cranial carotid arteries is implicated in 20-30% of stroke[2]. About 80% of the stroke cases are thromboembolic in origin, carotid atheromatous plaques being the source of embolus[3]. When there is cerebrovascular insufficiency lasting for several seconds, the neurons lack glycogen and there is manifestation of neurological deficits. If this cessation of blood flow persists for more than a minute, there is resultant infarction or death of brain tissue occurs. Thus, Transient Ischemic Attack (TIA) is a transient episode of neurological dysfunction caused by focal brain ischemia without acute infarction. There is increased risk of ischemic stroke after an episode of TIA, ranging from 10% to 15% in the initial 3 months, with maximum risk in the next 48 hours[4]. Therefore, urgent diagnosis and timely intervention are crucial. Atherosclerosis of intracranial arteries is a well-recognized cause of ischemic stroke in Asians, and extracranial carotid artery disease is more often seen in western countries[5]. It is the third most common cause of death and has a frequency of 200 in every 100,00 deaths[6].

North American Symptomatic Carotid Endarterectomy Trial (NASCET) was an extensive study conducted on 2885 patients on this domain, where randomization of the patients was done to medical treatment and endarterectomy and subsequently followed up for a mean duration of 5 years with the help of assessment by Duplex Ultrasonography and angiography techniques[7]. The risk of stroke in 2 years in patients with symptomatic severe stenosis was 26%. Along with severe symptomatic stenosis, when there was also association of TIA, hemispheric TIA, recurrent TIA and ulcerated plaque was seen, the resultant risk being 18.6%, 43.5%, 41.2% and 73.2% respectively. T. Ohara et.al. in their study concluded that eccentric stenotic carotid vessels with stenosis more than 70% were found to be independent risk factors for stroke[8]. Ratnakar Sahoo et al. found significantly increased intima media thickness in acute ischemic stroke patients of all the age group of patients on comparison to the control group[9]. According to Topakian R. et al[10] and Huibers A. et al[11], plaque echolucency had close association and better predictability of the risk of Ischaemic stroke in patients with asymptomatic carotid stenosis. Duplex ultrasonography showed sensitivity of 86% and specificity of 87% (for degree of carotid stenosis 70% to 99%), which is lower than that of MR angiography[12]. However, in detecting occlusion of carotid artery, the sensitivity and specificity were almost similar (98% and 100% respectively. The focal plaques superimposed with carotid intima media thickening occur in high risk group for vascular events[13]. Although there is

established association of carotid intima media thickening with the risk of future cardiovascular events, changes of carotid intima media thickness can occur with time also due to various other reasons. Some plaque features like resultant severe degree of stenosis and intraplaque hemorrhage were found to have independent predictability of risk of future cerebrovascular events[14]. The annual risk rates of ipsilateral cardiovascular events in patients with symptomatic carotid stenosis having intraplaque hemorrhage are 9.0%, 18.1% and 29.3% in <50% stenosis, 50% to 69% stenosis and 70% to 99% stenosis respectively, which was higher than those without any intraplaque hemorrhage.

The objective of this paper is to study the morphological and physiological changes that take place in the extracranial portion of carotid arteries in patients of cerebrovascular insufficiency. For that purpose, a hospital based cross sectional study has been carried out and various grayscale and colour doppler findings in extracranial portion of carotid arteries are studied, which occur as an underlying pathological process in such patients presenting with signs and symptoms of cerebrovascular insufficiency. Increased IMT, presence of plaque, and evaluation of plaque characteristics such as types, surface, sites, morphology, etc. can be useful to estimate the predictable risk for a cerebrovascular event in the future. Echolucency of plaque, intraplaque hemorrhage, and plaque ulceration are plaque morphologies, that have been found to be associated with increased risk of Ischaemic stroke. In addition to that, doppler velocity parameters of the stenotic segments may provide significant information about the resultant changes in the hemodynamics. Based on these observation, early detection of plaque and evaluation of plaque characteristics will help in initiating timely diagnosis and subsequent management.

MATERIALS AND METHOD

Hospital based cross sectional study on 100 number of patients presenting with ischaemic cerebrovascular accident, such as transient ischaemic attack, ischaemic Stroke, etc., was conducted with due approval of the Institutional ethical committee, Gauhati Medical College and Hospital during the period from 1st of August, 2018 to 31st of July, 2019 for a duration of twelve months. Grayscale and Colour Doppler study of carotid artery was done on SAMSUNG RS80A ultrasound machine using high frequency 3-12 MHz advanced piezoelectric crystal design linear array transducer.

Inclusion Criteria:

Patients with symptoms of cerebrovascular insufficiency (Ischemic stroke and Transient ischemic attack) such as

- Episodes of transient neurological dysfunction
- Sudden weakness or numbness

- Hemiparesis
- Focal neurological deficit
- Sudden episode of loss of consciousness
- Altered sensorium
- Slurring of speech
- Diminution of vision

Exclusion Criteria:

Cases of hemorrhagic stroke, posterior circulation stroke/vertebro-basilar territory Infarct, neoplasm and other causes of stroke, patients with pre-existing cardiac and epileptic disorders and previous history of head trauma were excluded from our study.

RESULTS AND DISCUSSION:

- We obtained that males (81%) were more commonly affected by Ischaemic stroke and most of the patients belonged to the age group above 50 years. Only a smaller number of the patients were female (19%), all of which were above 50 years of age. In our study group, among the other prevalent risk factors hypertension and dyslipidemia were found out to be the most common association, followed by smoking, diabetes and obesity.
- Non-enhanced CT was used as the mainstay of initial imaging in acute cerebrovascular accidents as it is widely available, fast and does not require administration of intravenous contrast material. It helps in excluding parenchymal hemorrhage, which is one of the exclusion criterias. NCCT brain can help in diagnosis of acute infarct by the earliest CT detectable signs of it (hyper dense vessel sign, insular ribbon signs and obscuration of the lentiform nucleus due to loss of gray white matter differentiation)[15].
- The disadvantage of NCCT brain is its detection rate is dependent on certain factors e.g. territory of infarct, experience of the radiologist and duration of time of scan from onset of stroke. Depending on the blood supply of the brain tissue by end artery or collateral circulation, the cytotoxic oedema takes time to set in. Approximately 60-70% of the Middle cerebral artery infarcts are detected in the first 6 hours, however obscuration of the lentiform nucleus on CT images can be seen within 2 hours with acute ischemia of the lenticulostriate territory[16].
- CT perfusion study can help in differentiation of the ischaemic core and the adjacent penumbra and thus plays crucial role in selection of candidates for reperfusion therapy. Early signs of crossed cerebellar diaschisis is seen in CT perfusion studies. CT angiography is capable of detecting thrombus within the involved vessels after going through volumetric helical acquisition and post processing to construct multiplanar

reformatted and maximum intensity projection images[17].

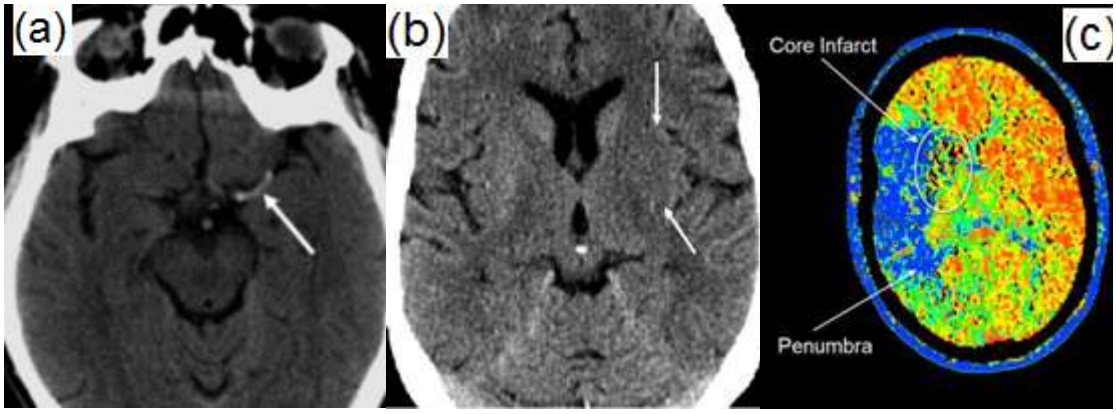

Figure 1: (a) Axial NCCT Brain image showing hyperdense left MCA (proximal segment), (b) Hypoattenuation and obscuration of the left lentiform nucleus in acute ischemia in the lenticulostriate distribution (c) CT perfusion study showing infarct core and salvageable penumbra.

MRI Brain has more sensitivity and specificity than NCCT brain in detecting acute cerebral ischemia early within initial hours after its onset. In early hyperacute stages, diffusion weighted MRI images show increased DWI signal and reduced ADC values within the core of the infarcted brain tissue. Even though the involved brain parenchyma may appear normal in other sequences of MRI, but MR angiography may demonstrate changes in the cerebral blood flow in the affected vessel and SWI can detect thromboembolism. In Late hyperacute stage, FLAIR and then T2 hyperintensity noted in the infarcted tissue after 6 hours even tends to increase. Similarly, after around 16 hours, T1 hypointensity sets in the involved area[18,19]. During the acute stage within the initial week, the ischemic brain tissue shows high signals in DWI and low ADC values, which by its end starts showing higher ADC value. The pseudonormalisation on ADC map takes place in the subacute stage at around 10 to 15 days, but signal intensity remains high on T2-weighted images, and it may be slightly high on diffusion weighted images[20]**.** Cortical laminar necrosis and T2 hyperintensity persists in the chronic stage. Although, persistence of cortical contrast enhancement for around 2 to 4 months is considered normal, but beyond 12 weeks parenchymal enhancement should always warrant exclusion of underlying lesions.

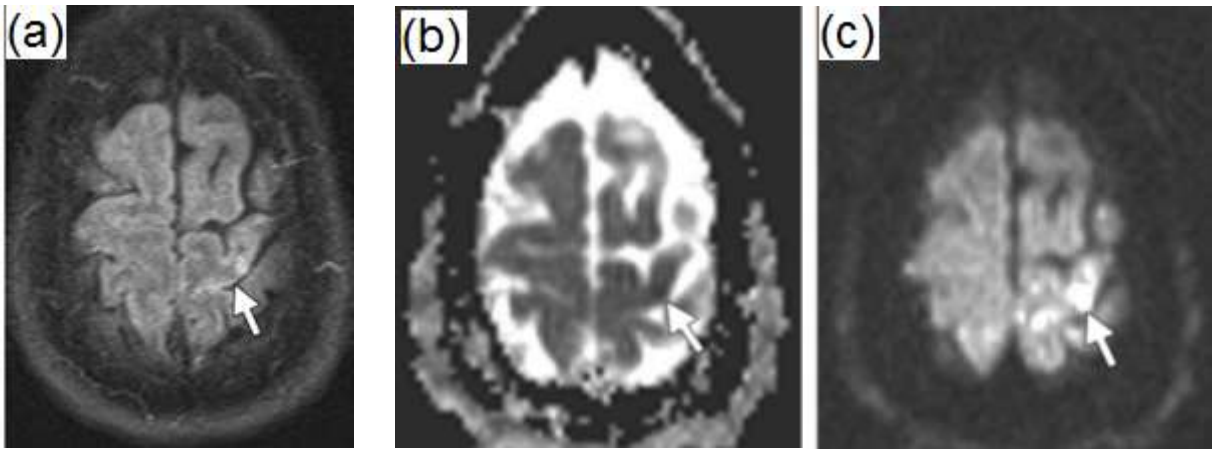

Figure 2: In late hyperacute stroke, (a) FLAIR and T2WI showing hyperintensity in the left motor cortex with other scattered subcortical hyperintense areas on the right side; (b), (c) ADC map and DW MR images showing an area of restricted diffusion in the left motor.

With the help of these radiological imaging studies, out of the 100 patients of cerebrovascular insufficiency in our study, 76 were diagnosed with cerebral infarcts by CT brain and MRI studies of which 29 patients had acute, 32 had subacute and 15 chronic infarcts. There were 6 cases of infarct, who were also diagnosed with hemorrhagic transformation. In the remaining 24 patients, who presented with transient focal neurological deficit in the form of transient paresis, slurring of speech or loss of consciousness, the initial evaluation with normal NCCT brain and/or MRI were diagnosed as transient ischaemic attack. Since patients with infarct of posterior cerebral circulation were one of the exclusion criteria of for selecting our study group, the 76 patients included in our study had infarct in middle cerebral artery only or both in middle and anterior cerebral artery territory.

In all these patients, duplex sonography was done, which combines high resolution images with Doppler spectral analysis, to evaluate the extra cranial potion of the entire carotid artery system was evaluated in our study including mainly common carotid artery, internal and external carotid arteries.

The evaluated parameters are

- Intima-media thickness
- Plaque characterization e.g. (Presence, location and characterization e.g. number, size, surface, types, morphology)
- Doppler parameters e.g. Peak systolic velocity (PSV), End diastolic velocity (EDV), Systolic Velocity ratio known as cardinal Doppler parameters.

Intima Media Thickness (IMT)

For assessment of the intima media thickness, Gray-scale image in longitudinal scan of the carotid artery is obtained with vessel walls parallel to the probe surface. The upper and lower hyperechoic parallel lines that are noted along the artery wall represents the interface between

the blood and intima and that between the tunica media and adventitia layer respectively. The media is represented by the intervening echo void area and the intima media thickness by the distance between the two hyperechoic lines. The Intima-media thickness less than 0.8 mm is taken to be normal in healthy individuals[21]. The sensitivity and specificity of carotid ultrasonography to detect stroke by using only intima media thickening are 87% and 71% respectively.

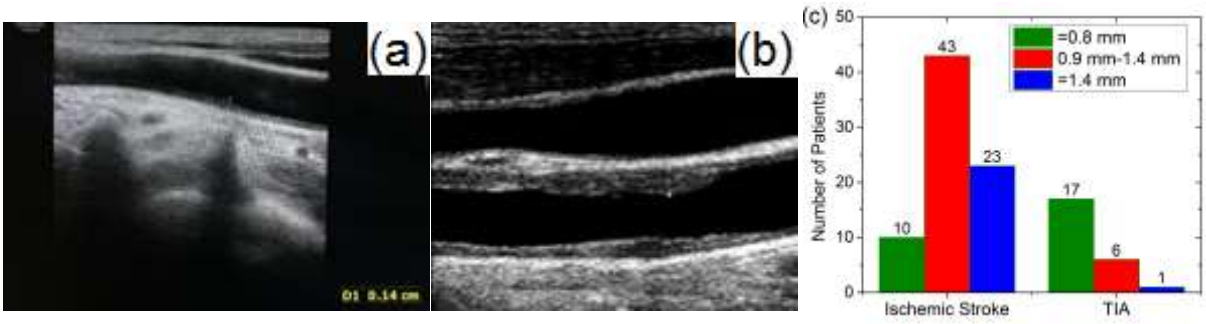

Figure 3: (a) Doppler US image showing increased intima media thickness of the carotid vessels, (b) Increased IMT measurement in left CCA[22], and (c) Distribution of intima media thickening grading in stroke and TIA cases.

Plaque characterization

In our study, total 106 number of atheromatous plaques were found in 66 patients. 70% of the infarct cases and 54% of the TIA patients are detected with atheromatous plaques. The data on distribution of these plaques showed that majority occurred in the carotid bulb/ Bifurcation. Plaque morphology characterization can be done as homogeneous or heterogeneous with the latter being a collective term for hyperechoic, isoechoic and hypoechoic plaques.

Figure 4: Plaque Morphology on Grayscale carotid ultrasonography[22].

Based on plaque morphology, 106 plaques of our study were classified from type I to type IV[23]

Type 1- Predominantly echolucent, with a thin echogenic cap.

Type 2- Substantially echolucent with small areas of echogenicity (>50% sonolucent).

Type 3- Predominantly echogenic with small areas of echolucency (<50% sonolucent).

Type 4- Uniformly echogenic.

Figure 5: (a) Type I echolucent plaque in carotid bulb, (b) Type III echogenic plaque, and (c) Type IV plaque with calcification along with background changes of thickened IMT.

Patients with infarcts had predominantly echo lucent plaques (Type I & II), together accounting for 66% of plaques. Those with TIA had predominantly hyperechoic and calcified plaques (Stable plaques Type III & IV), accounting for 61% of plaques.

Plaque can be characterized based on some secondary changes like intraplaque hemorrhage and calcification. Intraplaque hemorrhage can be a potential precursor of plaque ulceration[24].

In proportion to the degree of luminal stenosis caused by atheromatous plaques and thickened intima media, there are changes in the flow velocity in the stenotic segment and its pre and post stenotic segments with resultant hemodynamic instability in some instances.

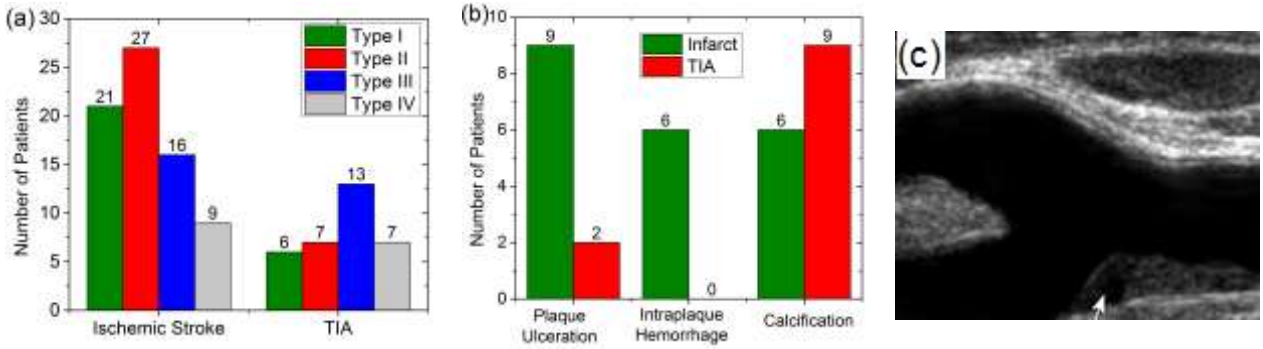

Figure 6: (a) Distribution of types of atheromatous plaque in cerebrovascular insufficiency, (b) Distribution of plaque changes among ischemic stroke patients, and (c) Gray-scale US image showing plaque containing hypoechoic area, possibly suggestive of hemorrhage[22].

Peak systolic velocity

At the level of stenotic segment of the artery, the peak systolic velocity is affected depending on the stenotic segment length (longer stenosis causes lower velocity) and some physiological factors that differ in different patients.

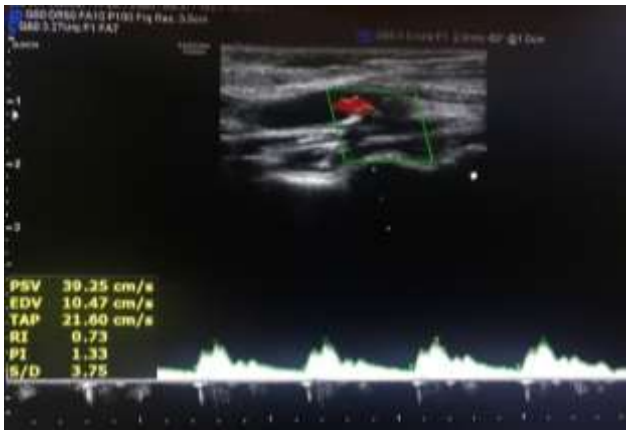

Figure 7: US image showing calcified plaque in the proximal ICA with a type 4 plaque, but with no sign of turbulence and normal PSV.

End Diastolic velocity

It is very useful in assessing high grade stenosis of the arterial lumen. The end diastolic velocity remains within normal range until the luminal stenosis of the artery is less than 50% due to not much significant pressure gradient along the stenotic segment in the diastole. However, when stenosis progresses more than 50%, due to the established pressure gradient across the stenosis during diastole, EDV also increase depending on the severity of stenosis and pressure gradient.

Systolic velocity ratio

It is the ratio of PSV in the stenotic Internal Carotid Artery to PSV in the ipsilateral Common Carotid Artery. Its advantage is that it does not have errors due to other physiological factors among different patients and due to collateralization. The primary parameters to evaluate are ICA PSV and the presence of plaque. However, if the primary parameters are inconclusive to characterize the degree of grading, the importance of the additional parameters come into play. The resultant diameter stenosis caused by plaques were estimated ultrasonographically. In patients detected with multiple plaques, the larger plaque causing greater diameter stenosis was taken into consideration during statistical analysis. The important features of severe ICA or CCA stenosis detected on carotid ultrasonography as follows[25].

- PSV greater than 230 cm/sec
- Atheromatous plaque causing luminal stenosis of ≥50%
- Color aliasing despite a high color velocity scale setting (≥100 cm/sec)
- Spectral broadening
- Post stenosis turbulence
- Color bruit artifact in the adjacent area of the stenotic artery
- End-diastolic velocity of greater than 100 cm/sec
- ICA/CCA PSV ratio ≥ 4.0
- High-pitch sound at PW Doppler imaging

The doppler and grayscale findings of the total 66 patients detected with atheromatous plaque were analyzed and their resultant stenosis was graded using the NASCET criteria.

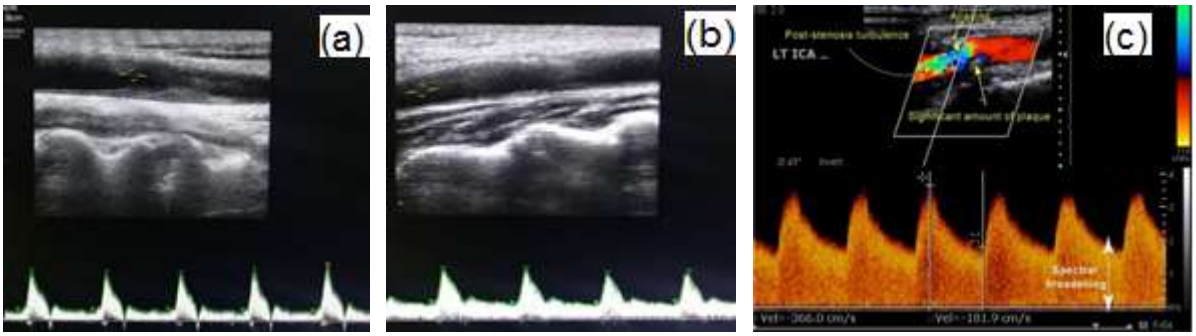

Figure 8: (a), (b) Doppler US finding of (a) CCA with an atheromatous plaque causing increased PSV, (b) increased PSV with spectral broadening in the post stenotic segment of CCA, (c) Duplex US image showing severe stenosis (70% to near occlusion) of the ICA.

Table 1: The NASCET criteria for quantification of the degree of stenosis[26].

Degree of stenosis	Findings
No Stenosis	Normal wave form
<15 % Stenosis	Deceleration spectral broadening with a peak systolic velocity (PSV) of<125 cm/s
16-49 % Stenosis	Pan-systolic spectral broadening with a peak systolic velocity (PSV) of <125 cm/s
50-69 % Stenosis	• Pan-systolic spectral broadening with a peak systolic velocity (PSV) of 125 cm/s *and* • End diastolic velocity (EDV) < 110 cm/s *or* • ICA/CCA PSV ratio > 2 but < 4
70-79 % Stenosis	• Pan-systolic spectral broadening with PSV> 270 cm/s *or* • EDV > 110 cm/s *or* • ICA/CCA PSV ratio > 4
80-99% Stenosis	EDV > 140 cm/s
Complete Occlusion	No flow; terminal thump

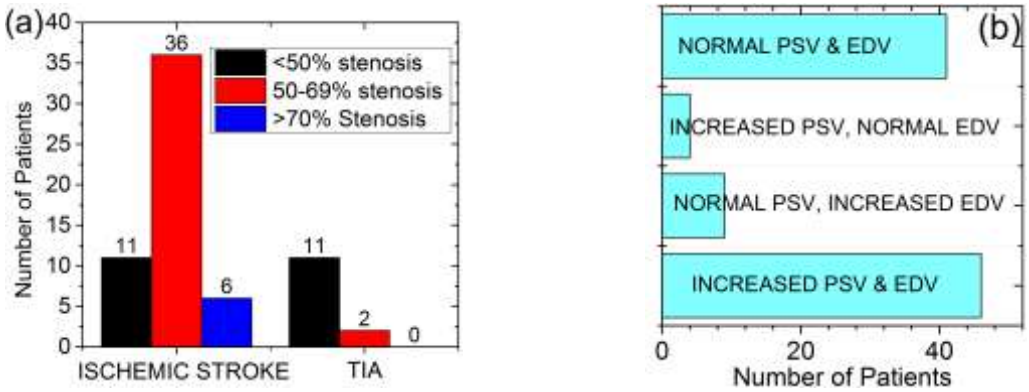

Figure 9: Distribution of (a) different grading of carotid artery stenosis among stroke and TIA patients, and (b) Doppler velocity parameter changes among patients of cerebrovascular insufficiency.

- Transient ischemic attack cases were less commonly encountered (24%) during our study. It may be due to the transient neurological deficit caused by TIA; for which most of the cases do not report to tertiary care set up after the initial episode. Proper awareness and surveillance for cerebrovascular accidents are of utmost importance for proper timely diagnosis and intervention for such vulnerable population.
- In cases of acute cerebrovascular insufficiency, Carotid artery doppler US being a bedside diagnostic modality, is a much convenient diagnostic modality to detect, localize as well as to quantify the stenotic segment of the supplying artery[27]. B mode helps in measuring the IMT and also evaluation of the plaque morphology. An elevated intima media thickening can be considered as a surrogate marker of atherosclerosis and thus it is of significance to differentiate the type of ischemic stroke[28]. Increased intima media thickness more than 0.8 mm may represent the earliest changes of atherosclerotic disease[29]. In our study, majority (73%) of the patients of ischaemic stroke had increased intima media thickness, this resonated well with the previous studies carried out by Ratnakar Sahoo et al[9], Stefan et al[30] and A. Einstein et al[7] etc.
- The sensitivity and specificity to detect the risk of stroke by using only intima media thickening is found to be 87% and 71% respectively in our study. The study conducted by Malik Rajesh et. Al obtained a sensitivity of 84% of carotid doppler in stroke[31]. This slight differences in the statistical values were mainly due to the variation in composition and size of the sample size of the different studies. Our study mainly constituted of patients, all of which presented with signs and symptoms of cerebrovascular insufficiency and later on, were diagnosed either as ischemic stroke or transient ischemic attack. On the other hand, many of the previous studies were constituted by people, all of which not necessarily had any cerebrovascular insufficiency.
- 54% of the patients presenting with cerebrovascular insufficiency had abnormal doppler velocity parameters (PSV and EDV) whereas 66% had plaque. This finding is similar to the finding of Grant. et al.[32] that found 90% sensitivity of Peak Systolic Velocity to detect carotid stenosis. However, in spite of the presence of plaque and thickened intima media, many cases did not show signs of turbulence or hemodynamically significant stenosis. Sanjeev Sehrawat et al concluded PSV to be the best parameter to quantify stenosis due to its proportionate relationship with it[33].
- Echogenic plaque with fibrous cap and calcification i.e. Type III and Type IV plaques were the commonly encountered plaque in patients presenting with Transient ischemic attack (61%) (56% in study by Malik Rajesh et. Al). Majority (66%) of the plaques seen

in ischaemic stroke patients are of echolucent Type I and Type II morphology. Topakian et al in their study concluded echolucent plaques to be more closely related with ipsilateral cerebrovascular accidents[10]. Majority of such ulcerated plaques (82%) belonged to patients presenting with stroke. This finding corroborates with the finding of Ulf Scheminke and Tillian Motsch et al[34]. These ulcerated carotid plaque surfaces act as sources of intracranial emboli causing stroke. Recent study conducted by Andreas Schindler et al also revealed intraplaque hemorrhage to be an independent risk factor for future cerebrovascular events[14].

CONCLUSION:

From our study, we can conclude that each facet of carotid ultrasonography examination is valuable in diagnosing the presence and extent of the disease. Grayscale and Colour doppler examination of the extracranial carotid artery is a noninvasive diagnostic technique for evaluation of the causes of cerebrovascular insufficiency with the help of plaque morphology and estimation of the degree of stenosis of the extracranial carotid artery system. The grayscale findings like increased intima media thickness of the carotid arterial system, presence of plaque, their number, site, morphology and type help detecting those with increased risk of stroke. Increased IMT of carotid arteries is a surrogate marker for of early atherosclerotic process in the whole arterial complex, not only the cerebrovascular system[35]. Similarly, doppler velocity parameters of the stenotic segments give us information about the resultant changes in the hemodynamics. Hence, timely detection of those at risk can also help in causing a significant reduction of the burden of such events. Standardization of the technical parameters, scanning techniques, analysis and interpretation of the results of doppler parameters can give us more accurate results. It has role in screening of the cases at risk of ischemic stroke and also helps in determining the line of treatment for the patients.

REFERENCES

1. Carroll, B. A. "Carotid sonography." *Radiology* 178, no. 2 (1991): 303-313.
2. Walker, Michael D., John R. Marler, Murray Goldstein, Patricia A. Grady, James F. Toole, William H. Baker, John E. Castaldo et al. "Endarterectomy for asymptomatic carotid artery stenosis." *Jama* 273, no. 18 (1995): 1421-1428.
3. Fontenelle, Larry J., Steven C. Simper, and Travis L. Hanson. "Carotid duplex scan versus angiography in evaluation of carotid artery disease." *The American surgeon* 60, no. 11 (1994): 864-868.
4. Easton, J. Donald, Jeffrey L. Saver, Gregory W. Albers, Mark J. Alberts, Seemant Chaturvedi, Edward Feldmann, Thomas S. Hatsukami et al. "Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the

American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease: the American Academy of Neurology affirms the value of this statement as an educational tool for neurologists." *Stroke* 40, no. 6 (2009): 2276-2293.

5. Lee, Y., and S. Yeh. "Correlation of common carotid artery intima media thickness, intracranial arterial stenosis and post-stroke cognitive impairment." *Acta Neurologica Taiwanica* 16, no. 4 (2007): 207.
6. Bronner, Leslie L., Daniel S. Kanter, and JoAnn E. Manson. "Primary prevention of stroke." *New England Journal of Medicine* 333, no. 21 (1995): 1392-1400.
7. Ferguson, Gary G., Michael Eliasziw, Hugh WK Barr, G. Patrick Clagett, Robert W. Barnes, M. Christopher Wallace, D. Wayne Taylor et al. "The North American symptomatic carotid endarterectomy trial: surgical results in 1415 patients." *Stroke*30, no. 9 (1999): 1751-1758.
8. Ohara, T., K. Toyoda, R. Otsubo, K. Nagatsuka, Y. Kubota, M. Yasaka, H. Naritomi, and K. Minematsu. "Eccentric stenosis of the carotid artery associated with ipsilateral cerebrovascular events." *American Journal of Neuroradiology* 29, no. 6 (2008): 1200-1203.
9. Sahoo, Ratnakar, M. Vamshi Krishna, D. K. S. Subrahmaniyan, T. K. Dutta, and S. Elangovan. "Common carotid intima-media thickness in acute ischemic stroke: A case control study." *Neurology India* 57, no. 5 (2009): 627.
10. Topakian, R., A. King, S. U. Kwon, A. Schaafsma, M. Shipley, H. S. Markus, and ACES Investigators. "Ultrasonic plaque echolucency and emboli signals predict stroke in asymptomatic carotid stenosis." *Neurology* 77, no. 8 (2011): 751-758.
11. Huibers, A., G. J. de Borst, R. Bulbulia, H. Pan, and A. Halliday. "Plaque echolucency and the risk of ischaemic stroke in patients with asymptomatic carotid stenosis within the first Asymptomatic Carotid Surgery Trial (ACST-1)." *European Journal of Vascular and Endovascular Surgery* 51, no. 5 (2016): 616-621.
12. Nederkoorn, Paul J., Yolanda van der Graaf, and MG Myriam Hunink. "Duplex ultrasound and magnetic resonance angiography compared with digital subtraction angiography in carotid artery stenosis: a systematic review." *Stroke* 34, no. 5 (2003): 1324-1331.
13. Lorenz, Matthias W., Joseph F. Polak, Maryam Kavousi, Ellisiv B. Mathiesen, Henry Völzke, Tomi-Pekka Tuomainen, Dirk Sander et al. "Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT

collaborative project): a meta-analysis of individual participant data." *The Lancet* 379, no. 9831 (2012): 2053-2062.

14. Schindler, Andreas, Regina Schinner, Nishaf Altaf, Akram A. Hosseini, Richard J. Simpson, Lorena Esposito-Bauer, Navneet Singh et al. "Prediction of Stroke Risk by Detection of Hemorrhage in Carotid Plaques: Meta-Analysis of Individual Patient Data." *JACC: Cardiovascular Imaging* (2019): 3059.
15. Tomandl, Bernd F., Ernst Klotz, Rene Handschu, Brigitte Stemper, Frank Reinhardt, Walter J. Huk, K. E. Eberhardt, and Suzanne Fateh-Moghadam. "Comprehensive imaging of ischemic stroke with multisection CT." *Radiographics* 23, no. 3 (2003): 565-592.
16. Tomura, N., K. Uemura, A. Inugami, H. Fujita, S. Higano, and F. Shishido. "Early CT finding in cerebral infarction: obscuration of the lentiform nucleus." *Radiology* 168, no. 2 (1988): 463-467.
17. Katz, David A., Michael P. Marks, Sandy A. Napel, Paige M. Bracci, and Sarah L. Roberts. "Circle of Willis: evaluation with spiral CT angiography, MR angiography, and conventional angiography." *Radiology* 195, no. 2 (1995): 445-449.
18. Provenzale, James M., Reza Jahan, Thomas P. Naidich, and Allan J. Fox. "Assessment of the patient with hyperacute stroke: imaging and therapy." *Radiology* 229, no. 2 (2003): 347-359.
19. Elster, Allen D., and Dixon M. Moody. "Early cerebral infarction: gadopentetate dimeglumine enhancement." *Radiology* 177, no. 3 (1990): 627-632.
20. Copen, William A., Lee H. Schwamm, R. Gilberto González, Ona Wu, Carla B. Harmath, Pamela W. Schaefer, Walter J. Koroshetz, and A. Gregory Sorensen. "Ischemic stroke: effects of etiology and patient age on the time course of the core apparent diffusion coefficient." *Radiology* 221, no. 1 (2001): 27-34.
21. Jadhav, Uday M., and N. N. Kadam. "Carotid intima-media thickness as an independent predictor of coronary artery disease." *Indian heart journal* 53, no. 4 (2001): 458-462.
22. Tahmasebpour, Hamid R., Anne R. Buckley, Peter L. Cooperberg, and Cathy H. Fix. "Sonographic examination of the carotid arteries." *Radiographics* 25, no. 6 (2005): 1561-1575.
23. Rumack, Carol M., Stephanie R. Wilson, J. William, and Deborah Levine. "Diagnostic ultrasound 4th edition." (2011): 953.
24. Carotid Artery Stenosis:Gray-Scale and Doppler US Diagnosis—Society of Radiologists in Ultrasound Consensus Conference1.Edward G. Grant, MD Carol B. Benson, MD .Gregory L. Moneta, MD.Andrei V. Alexandrov, MD, RVT .J. Dennis Baker, MD. Et al Radiology 2003; 229:340–346.

25. Tahmasebpour, Hamid R., Anne R. Buckley, Peter L. Cooperberg, and Cathy H. Fix. "Sonographic examination of the carotid arteries." *Radiographics* 25, no. 6 (2005): 1561-1575.
26. Zwiebel, William J., and John S. Pellerito. *Introduction to vascular ultrasonography*. Philadelphia, PA, USA: Elsevier Saunders, 2005.
27. Jogestrand, T., M. Lindqvist, J. Nowak, and Swedish Quality Board for Carotid Surgery. "Diagnostic performance of duplex ultrasonography in the detection of high grade internal carotid artery stenosis." *European journal of vascular and endovascular surgery* 23, no. 6 (2002): 510-518.
28. Cupini, L_M, P. Pasqualetti, M. Diomedi, F. Vernieri, M. Silvestrini, B. Rizzato, F. Ferrante, and G. Bernardi. "Carotid artery intima-media thickness and lacunar versus nonlacunar infarcts." *Stroke* 33, no. 3 (2002): 689-694.
29. Bogousslavsky, Julien, Guy Van Melle, and Franco Regli. "The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke." *Stroke* 19, no. 9 (1988): 1083-1092.
30. Rosfors, Stefan, Staffan Hallerstam, Kerstin Jensen-Urstad, Maria Zetterling, and Christian Carlström. "Relationship between intima-media thickness in the common carotid artery and atherosclerosis in the carotid bifurcation." *Stroke* 29, no. 7 (1998): 1378-1382.
31. Rajesh, Malik, and R. Tiwari. "Carotid Doppler Evaluation of Transient Ischemic Attack and Stroke Patients and its correlation with the CT scan head: A prospective study." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* 7 (2013): 20-25.
32. Grant, Edward G., André J. Duerinckx, Suzie M. El Saden, Michelle L. Melany, Gasser M. Hathout, Peter T. Zimmerman, Alan K. Marumoto, Stanley N. Cohen, and J. Dennis Baker. "Ability to use duplex US to quantify internal carotid arterial stenoses: fact or fiction?" *Radiology* 214, no. 1 (2000): 247-252.
33. Sehrawat, Sanjeev, Sarabjit Singh Thind, Vikram Singh, Rajesh Kuber, Satish Naware, and Harshawardhan Shrotri. "Colour Doppler evaluation of extracranial carotid artery in patients presenting with features of cerebrovascular disease: A clinical and radiological correlation." *Medical Journal of Dr. DY Patil University* 5, no. 2 (2012): 137.
34. Schminke, Ulf, Lillian Motsch, Lutz Hilker, and Christof Kessler. "Three-dimensional ultrasound observation of carotid artery plaque ulceration." *Stroke* 31, no. 7 (2000): 1651-1655.
35. Poli, Andrea, Elena Tremoli, Alessandra Colombo, Marina Sirtori, Paolo Pignoli, and Rodolfo Paoletti. "Ultrasonographic measurement of the common carotid artery wall

thickness in hypercholesterolemic patients A new model for the quantitation and follow-up of preclinical atherosclerosis in living human subjects." *Atherosclerosis* 70, no. 3 (1988): 253-261.