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Role of Colour Doppler Ultrasonography of Extracranial Carotid Vessels in Ischaemic Stroke

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Abstract
Stroke is classically characterized as a neurological deficit attributed to a vascular cause causing an acute focal injury of the central nervous system (CNS). Stroke is one the leading causes of disability, dementia and death worldwide. The aim of our study is to evaluate carotid arteries of stroke patients with colour doppler ultrasonography and comparison of the results of study with available literature.
Material and Methods: This prospective study was approved by the Institutional ethics board and was carried out on 80 patients who presented with complaints of cerebrovascular accident to the Department of Radiodiagnosis at Kamineni Institute of Medical Sciences between June 2019 to February 2020. Written informed consent was obtained from the patients and their family members. Following a detail history and physical examination, a CT scan of the head was performed on a Toshiba Asterion 16-slice CT Imager. Patients then underwent Colour Doppler ultrasonography of bilateral extracranial vessels and all the findings were documented. Patients with hemorrhagic stroke, established carotid artery stenosis, vertebrobasilar insufficiency and those with multiple complicated carotid artery plaques were excluded.
Results: 80 patients were included in the study with 61-70 years being the most commonly affected age group. Many of the patients had varying degrees of atherosclerotic and non-atherosclerotic carotid disease. 70% of the patients showed unilateral carotid plaque disease whilst 30% accounting to bilateral disease. A total of 83 plaques were evaluated for location, morphology and degree of stenosis with the most common location of the plaque was at carotid bulb in ~47% followed by 31% in CCA, 20% in ICA and 1.2% in ECA. Based on morphology, plaques were divided into 5 types. Of these Type I and Type II were the most predominant accounting to 30% and 26.5% respectively. Majority of the patients had a stenosis of <50% and severe stenosis was seen in only 15% of the patients.
Conclusion: Carotid Duplex Ultrasonography still remains the first line modality of choice in evaluation of carotids despite availability of other investigations like MR or CT conventional angiography. In addition to identifying the presence of the carotid artery disease and assessing the degree of stenosis, it very useful in localization of the plaque and determining it's extent and morphological features.

Keywords: carotid artery stenosis, carotid doppler, ischemic stroke, peak systolic velocity in ICA

Introduction
Stroke (Cerebrovascular accident) is the second most common cause of death and third most common cause of disability worldwide. "The cumulative incidence of stroke ranged from 105 to 152/100,000 persons per year, and the crude prevalence of stroke ranged from 44.29 to 559/100,000 persons in different parts of the country during the past decade. These values were higher than those of high-income countries. [1] In India, the pooled data incorporating all the studies reveal that ischemic stroke occurs in 68-80% and hemorrhagic stroke in 20-32%. Ischemic stroke comprises large vessel (41%), lacunar (18%), cardioembolic (10%), other determined (10%), and undetermined (20%) subtypes. The extracranial carotid disease is the etiological factor in 25-26% and intracranial carotid disease in 30% of ischemic stroke cases [2]. The most common pathologic process involving the extracranial carotid artery is carotid stenosis and by extension, carotid occlusion. Though conventional angiography is the gold standard investigation of choice, color Doppler sonography remains the desirable modality as it is noninvasive, lack of radiation exposure, ease of the investigation and accuracy. Apart from the detecting the carotid stenosis and grading severity of the disease it is also helpful in both identification and characterization of the atheromatous plaques.

Though the main goal is to detect extracranial carotid artery stenosis, various other diseases are also identified such as carotid body tumors, Takayasu's arteritis etc using carotid Doppler ultrasonography. Thus, colour Doppler ultrasonography has become an important tool in the evaluation of the extracranial carotid disease.

Aims and Objectives

1. Assessment of the morphological changes occurring in the extracranial portion of the carotid artery in patients presenting with stroke and transient ischemic attacks.
2. Evaluation of the spectral pattern of the carotids in patients with significant hemodynamic carotid artery stenosis.
3. Calculation of peak systolic velocity and end diastolic velocity of internal carotid arteries and the ratio of ICA/CCA in the assessment of carotid artery stenosis.
4. Comparison of the results of present study with the previous studies in the available literature.

Materials and Methods

The present study approved by the Institutional ethics committee was included 80 patients who presented to Department of Radiodiagnosis at Kamineni Institute of Medical Sciences between July 2019 to February 2020 with the complaints of cerebrovascular accidents such as hemiparesis, hemiplegia, hemispheric or retinal transient ischemic attacks, altered sensorium, aphasia, sudden loss of consciousness, slurring of speech etc. Patients who had hemorrhagic stroke, established carotid artery stenosis, vertebrobasilar insufficiency and people with multiple complicated plaques in a carotid artery were excluded. Informed consent was obtained from patients and their concerned family members.

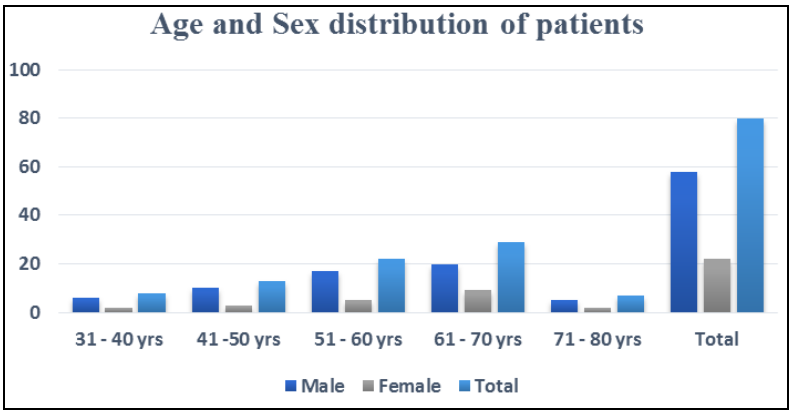
Following a thorough history and clinical physical examination, a Computed Tomography (CT) scan of the brain was performed on a Toshiba Asterion 16-slice CT imager. The findings on the CT scan recorded were side of the infarct, vascular territory and cortical or subcortical.

Patients then underwent Colour Doppler ultrasonography of bilateral extracranial vessels using Philips HD 15 and Philips Clearvue 650 with a 4 – 12 MHz linear array transducer with optimal Doppler settings. The Doppler images and spectral waveforms were obtained with an angle of insonation of 60^{O} with appropriate angle adjustments. Colour Doppler, grayscale and spectral imaging was done for all the examined arteries.

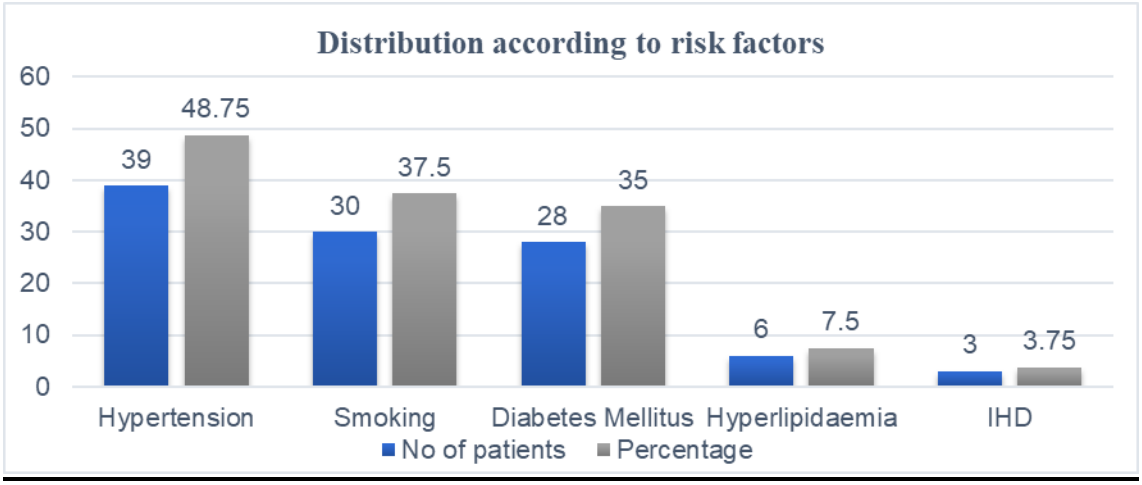
Data collection

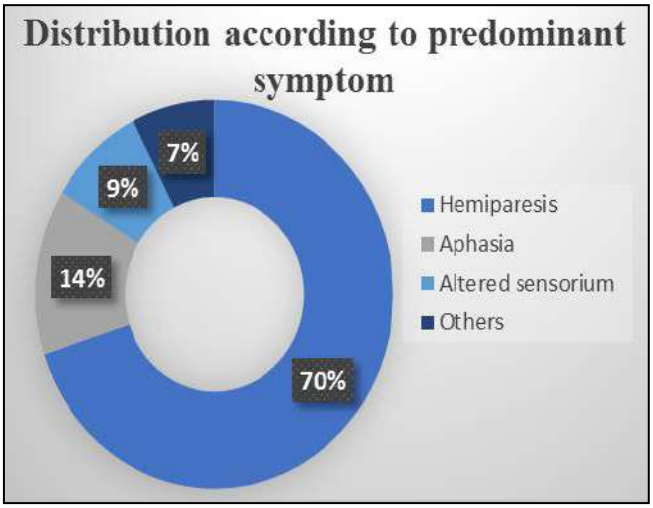
The data gathered from the colour Doppler ultrasonography included: Peak systolic velocity (PSV) of common carotid artery (CCA) and Internal carotid artery (ICA), ratio of PSV of ICA and CCA, end diastolic velocity (EDV) of ICA, morphology of the plaque was accurately assessed for location, extent, texture, thickness, luminal narrowing and severity [3]. (Bluth El) as well as detection and grading of the stenosis, analysis of the spectral patterns of CCA, ICA and external carotid artery (ECA), carotid Intimal media thickness (CIMT).

Observations and Results

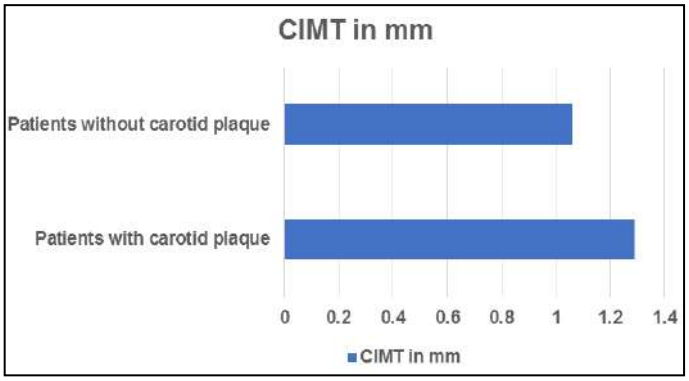


Graph 1& 2: Bar diagram showing Age and Sex distribution of patients and risk factors based distribution





Graph 3: Pie diagram showing distribution of patients according to the predominant presenting symptom



Graph 4: Bar diagram demonstrating CIMT

Table 1: Carotid intima media thickness

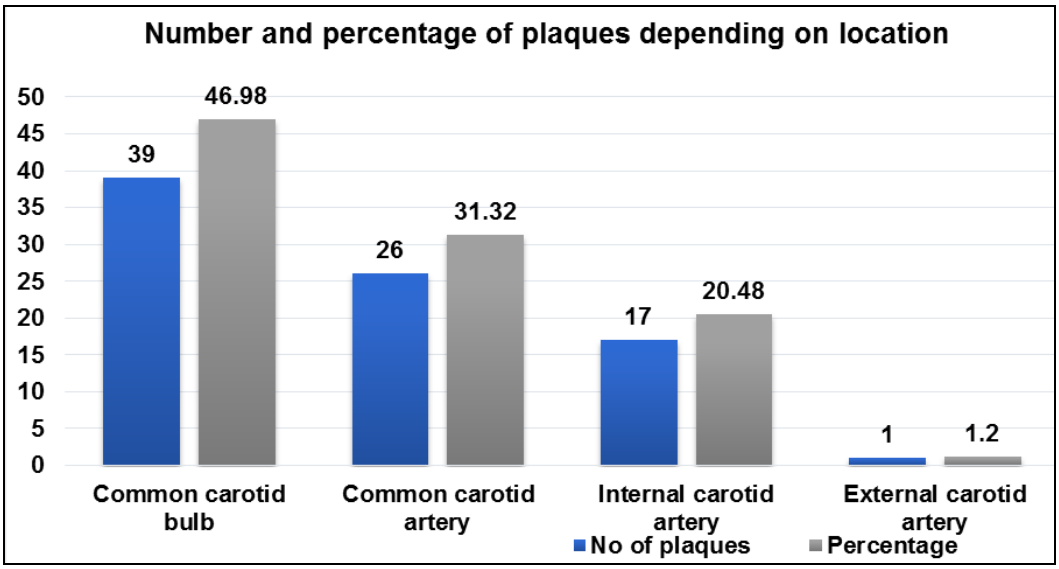
Carotid intima media thickness	
Patients with carotid plaque	1.29+0.50 mm
Patients without carotid plaque	1.06+0.11 mm

Table 2: Presence of plaque

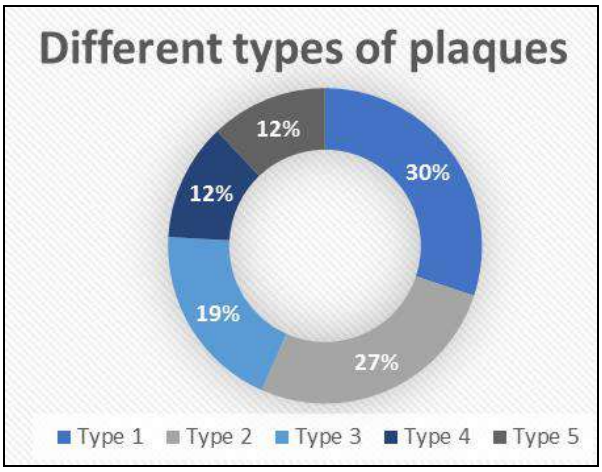
Plaque	No. of patients	Percentage
Patients with plaque	64	80.00%
Patients without plaque	16	20.00%

Table 3: Distribution of plaques

Distribution of plaques	No. of patients	Percentage
Unilateral	45	70%
Bilateral	19	30%
Total	64	100%



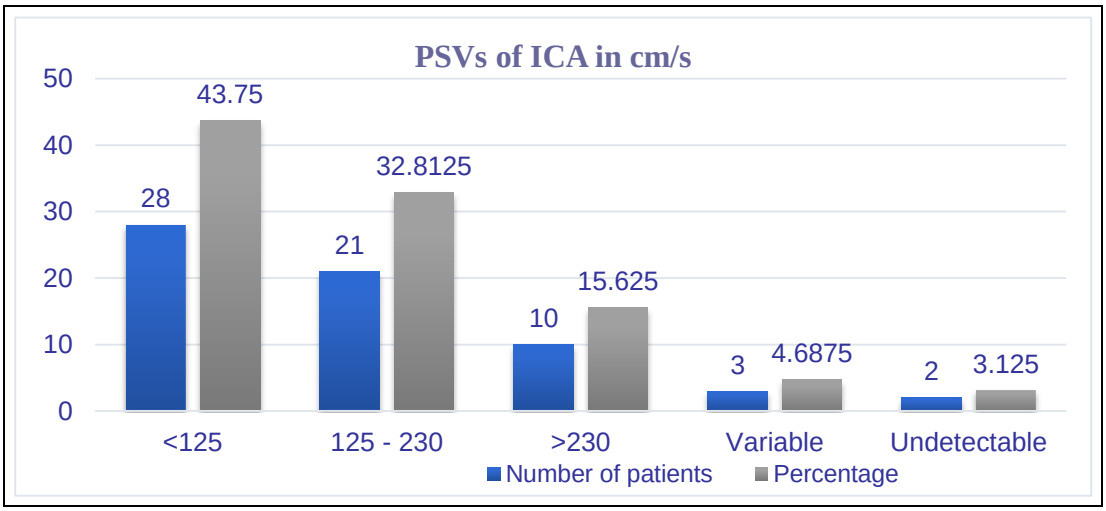
Graph 5: Bar diagram demonstrating the location of plaques



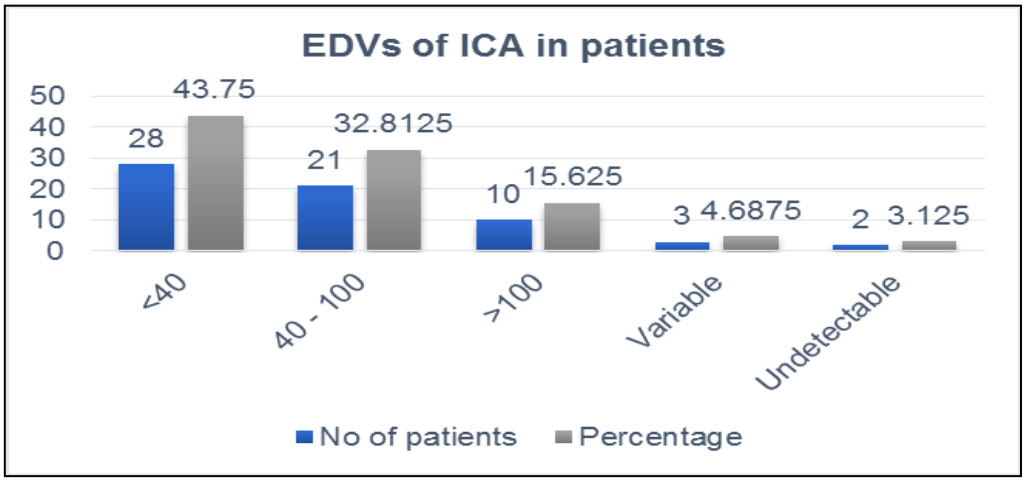
Graph 6: Characterization of different types of plaques in patients as per International Classification[3]

Table 4: Surface texture of the plaque

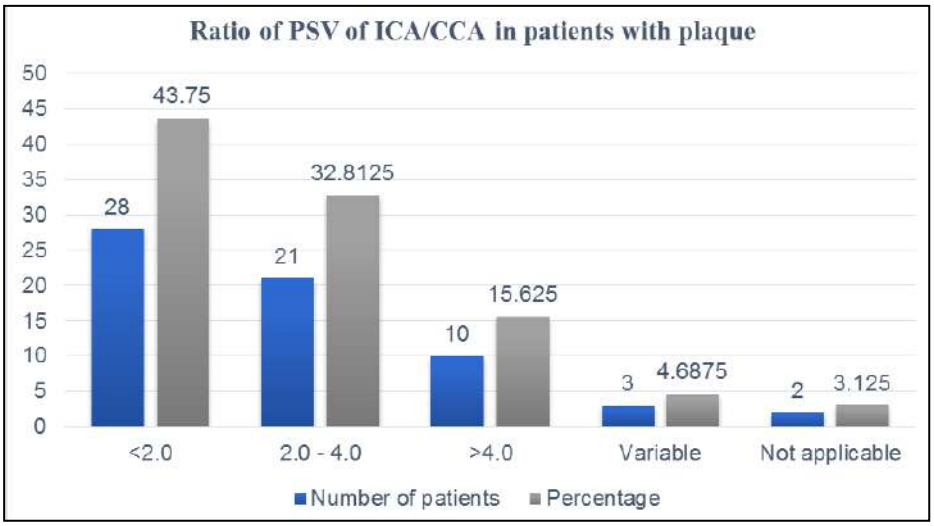
Surface texture of the plaque	Number of plaques	Percentage
Smooth	43	52%
Irregular	27	32%
Ulcerated	13	16%
Total	83	100.00%



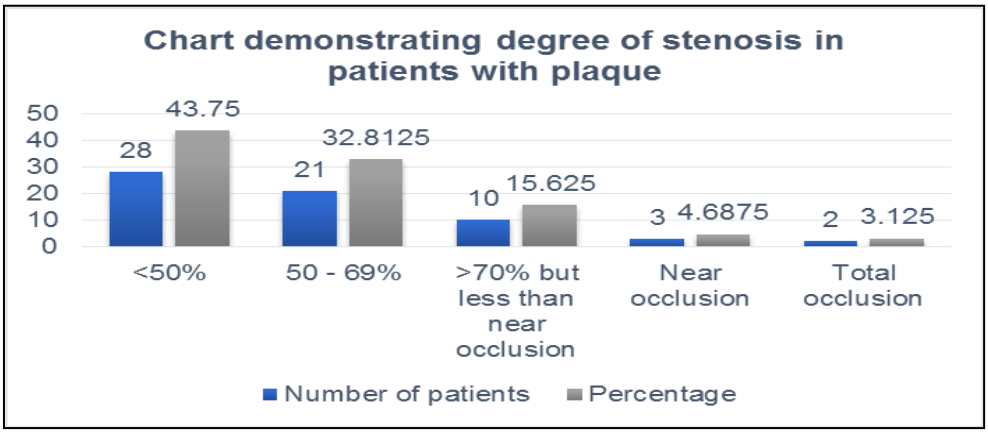
Graph 7: Peak systolic velocities of ICA in patients with plaques



Graph 8: End diastolic velocities of ICA in patients with plaque



Graph 9: Ratio of PSV of ICA/CCA in patients with plaque



Graph 10: Degree of stenosis in patients with plaque

Table 5: Colour Doppler flow pattern analysis

Colour Doppler flow pattern	Number of patients	Percentage
Aliasing	18	28%
Turbulence	31	49%
Reversal of flow	13	20%
No colour Doppler signal	2	3%
Total	64	100.00%

Representative images of cases

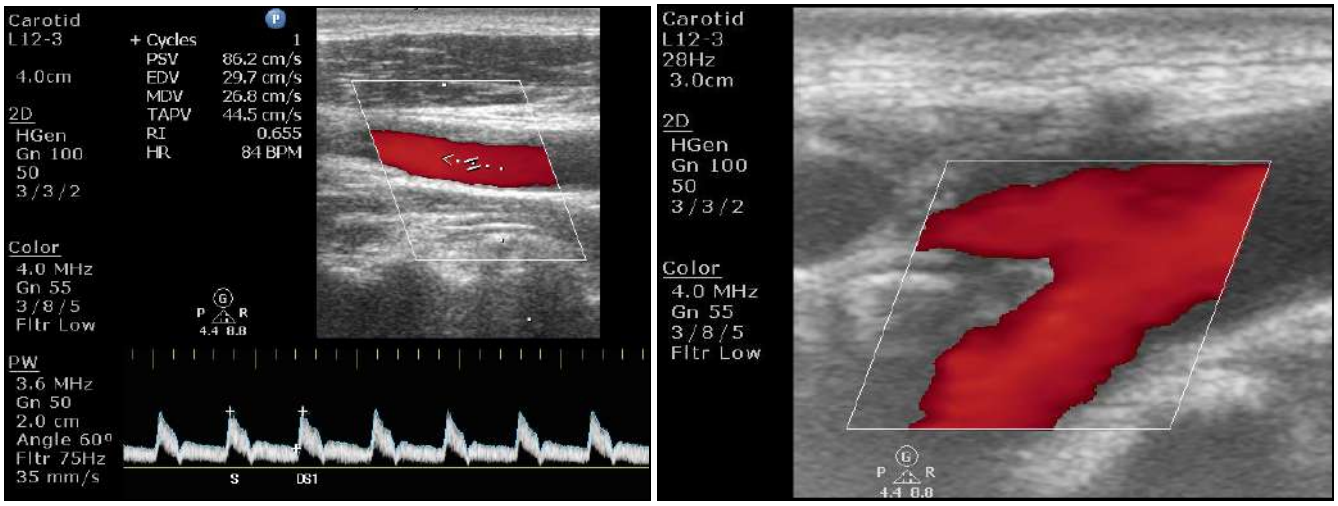


Fig 1, 2 & 3: Case 1: Normal waveform and CIMT in a patient with no carotid plaque

Fig 4, 5, 6: Case 2 - Patient with complete occlusion of ICA with echogenic content in ICA, increased CIMT and intraplaque sonolucency

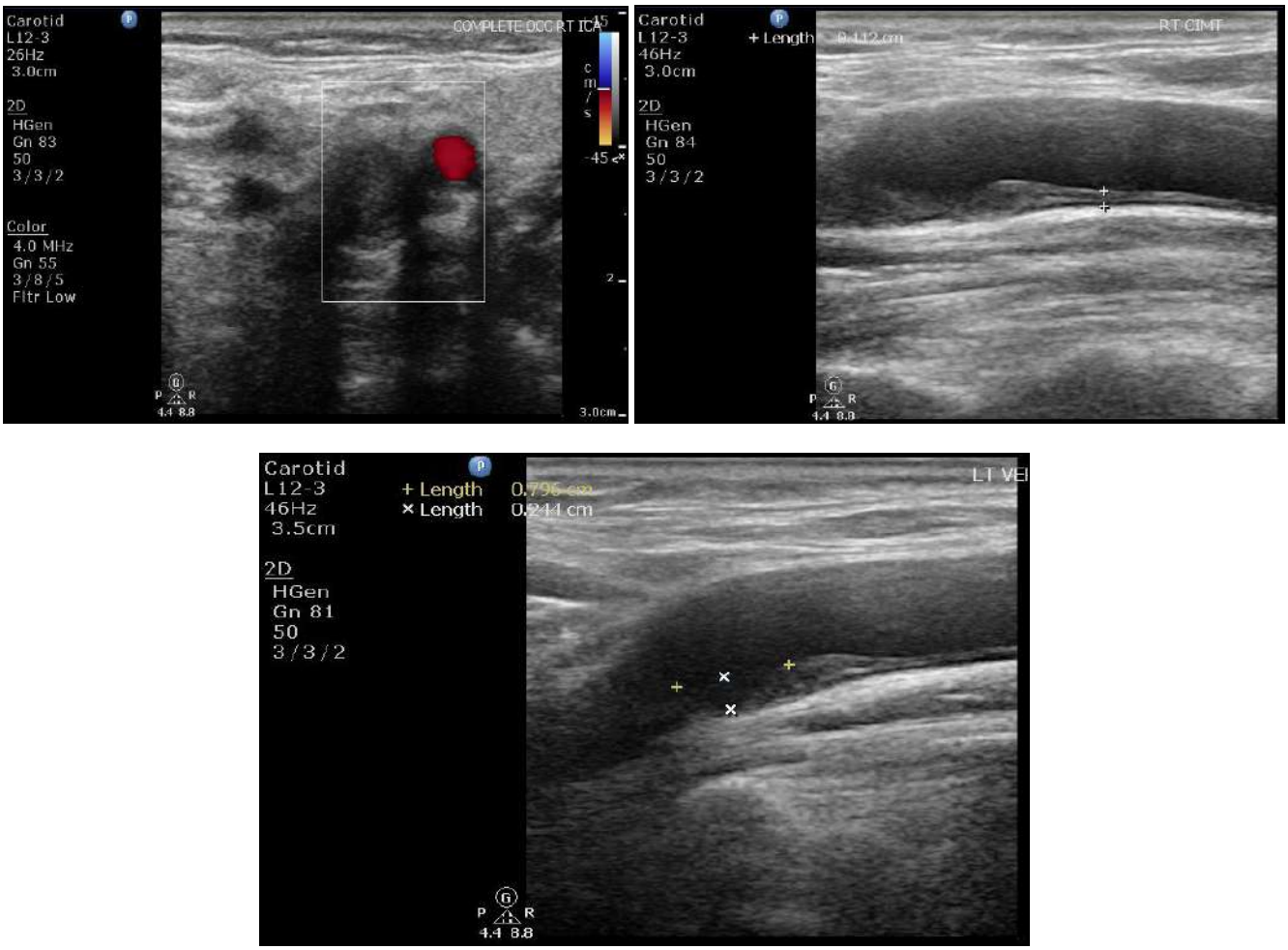
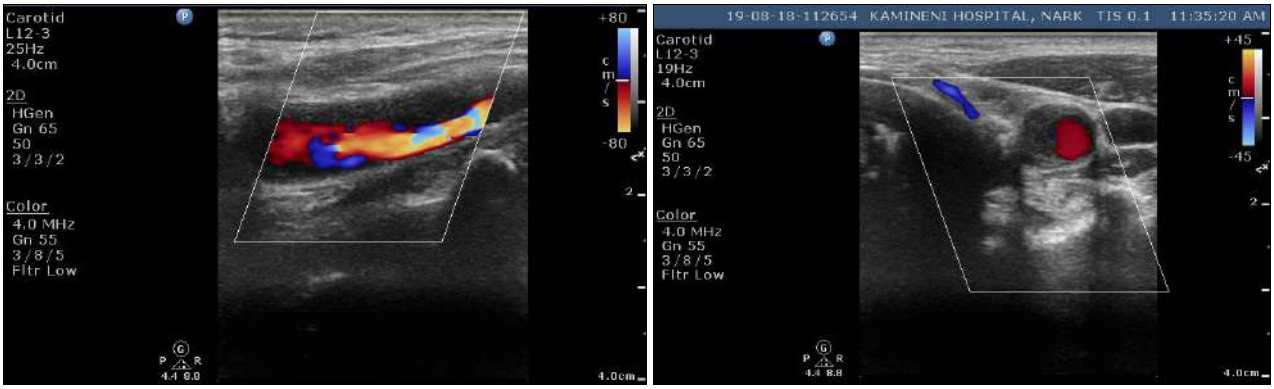


Fig 7 and 8: Case 3 - Patient with carotid plaque causing moderate stenosis with aliasing



Discussion

A stroke is defined clinically as "an abrupt onset of neurological deficit attributable to a focal vascular cause." [4] The definition of stroke is clinical, the most important supporting investigation is radiological. The major causes of ischemic stroke are divided into 2 major categories, i.e. Thrombotic and Embolic. Thrombotic causes are further divided into small vessel (lacunar stroke), large vessel thrombosis and dehydration.

In the present study, the evaluation of extracranial carotid disease is done which falls under the category of large vessel cause of ischemic stroke. The large trials which were done in this field earlier were the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [5], European Carotid Surgery Trial (ECST) [6], Asymptomatic Carotid Artery Trial (ACAS) [7] and Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) [8]. All the trials have demonstrated that patients with significant stenosis (>70%) in the carotid vasculature benefit from the endarterectomy unlike patients with less stenosis (<30%).

Prior to the introduction of the duplex sonography, the primary imaging modality was angiography which was invasive, expensive and included injection of contrast material into the patients carrying considerable risks. With the advent of the duplex sonography of the carotid vasculature, tremendous gains have been made in the field starting from detecting flows and velocities to the morphological assessment of the vessels and plaques.

Ischemic stroke - Demographics & Risk factors

The most common age group affected in the present study is

61-70 years comprising of 29 patients out of 80, accounting to 36.25% (Graph 1). According to Marjolein de Weerd *et al.* [9], in both men and women there is increase in the prevalence of moderate carotid stenosis with increasing age. The present study is also in accordance with Noor ul hadi *et al.* [10], Bollipo JP [11] *et al.*, SK Sethi *et al.* [12], and Fernandes *et al.* [13], all of which showed the most common age group to be involved being 61 – 70 years.

Table 6: Comparison of present study based on sex distribution with previous studies

	Present study (n = 80)	SK Sethi *et al.* (n = 63) 2005 [12]	Noor Ul Hadi (n = 100) 2009 [10]	Laith Ahmed *et al.* (n= 62) 2011 [14]
Males	54 (67.5%)	29 (46.04%)	70 (70.0%)	42 (67.7%)
Females	26 (32.5%)	34 (53.96%)	30 (30.0%)	20 (32.3%)

The present study correlates well with Noor Ul Hadi *et al.* [10], Laith Ahmed *et al.* [14] and Pavansalo M *et al.* [15], with male population being predominantly affected, but there is a difference from the SK Sethi *et al.* [12] in which the female population being more commonly affected than males. (Graph 1, Table 6). The present study showed 39 patients with carotid plaque having hypertension which accounts to 48.75% as a major risk factor (Graph 2) and it also shows a positive correlation of smoking to the carotid artery disease. Of the total patients, 30 patients had a history of current and smoking for a period of greater than 10 years, which accounts to 37.5%.

Table 7: Comparison of present study based on hypertension

	Present study	SK Sethi *et al.* 2005 [12]	Noor Ul Hadi *et al.* 2009 [10]	Laith Ahmed *et al.* 2011 [14]	Haq S. *et al.* [16] 2017
Percentage	48.75%	55.5%	59%	45%	64%

Table 8: Comparison of present study with available literature based on smoking

	Present study	Laith Ahmed *et al.* 2011 [14]	Malik R *et al.* 2013 [17]	Fernandez *et al.* 2016 [13]
Percentage	37.5%	58%	32%	40%

In the study done by Laith Ahmed *et al.* [14], the percentage of smokers was more. The present study correlates with Fernandez *et al.* [13] and Malik R *et al.* [17] (table 8). According to Muller HR *et al.* [18], smokers were affected by carotid stenosis more than nonsmokers.

Diabetes mellitus (DM) is one of the major risk factors for atherosclerosis of vessels, especially when combined with smoking which is said to accelerate the process of atherosclerosis. In the present study, 28 patients had diabetes mellitus which accounts for 35.0% (graph 2) and correlated with Laith Ahmed *et al.* [14] and Malik R *et al.* [17]. (Table 9)

Table 9: Comparison of the present study with available literature based on Diabetes mellitus

	Present study	Laith Ahmed *et al.* 2011 [14]	Malik R *et al.* 2013 [17]	Fernandez *et al.* 2016 [13]
Percentage	35.0%	32.3%	30.0%	16.0%

Ischemic stroke symptomatology

Majority of the patients in the present study presented with the symptoms of hemiparesis. 56 out of 80 patients presented with hemiparesis accounting to 70%. (Graph 3)

Table 10: Comparison of present study with available literature based on the symptomatology

	Present study	Malik R *et al.* 2013 [17]	Bollipo *et al.* 2018 [11]
Hemiparesis	70%	76.0%	63.0%
Aphasia	13.75%	18.0%	15.0%

Ischemic stroke - Duplex Sonography of extra cranial carotid arteries

Carotid intima media thickness (CIMT): CIMT not only includes early atherosclerosis but also non atherosclerotic changes like intimal fibro cellular hypertrophy or intimal hyperplasia [19]. The mean CIMT in the ischemic stroke patients without carotid plaque in the present study was 1.06+0.11mm and in patients with carotid plaque was 1.29+0.50mm. (Table 1, Graph 4)

CIMT sees a marked increase in thickness after the age of 40 years in men and 50 years in women [20]. According to the ESC/ESH hypertension guidelines given in 2013, CIMT>0.9mm indicates asymptomatic organ damage. So mean CIMT of 0.9mm is taken as the threshold value in the present study [21]. The mean CIMT in the present study correlated with the studies done by Cupini LM *et al.* [22] and Pruissen *et al.* [23] (table 11). The maximum CIMT was found to be as high as 1.5mm in a patient with carotid plaque.

Table 11: Comparison of the present study with available literature based on CIMT

	Present study	Cupini LM *et al.* 2002 [22]	Pruissen DM *et al.* 2007 [23]
CIMT in mm	1.06+0.11mm	1.04+0.25mm	1.08+0.38mm

Plaque characteristics

In the present study, 64 out of 80 patients showed carotid plaques accounting to 80%. (Table 2). Bollipo JP *et al.* [11] study showed 82% of the patients had atherosclerotic plaque disease. The present study correlated to the Noor Ul Hadi *et*

al. [10] as most of the plaques were unilateral in both studies (Table 12).

Table 12: Comparison of the present study with available literature based on the distribution of plaques

Distribution of the plaque	Present study	Noor Ul Hadi *et al.* 2009 [10]
Unilateral	45 (70.0%)	41 (73%)
Bilateral	19 (30.0%)	15 (27%)

Majority of the plaques were unilateral in 70% of patients consistent with Noor Ul Hadi *et al.* study (Table 3, Table 12) In the present study, the plaque was seen in decreasing frequency in CCA bulb, CCA, ICA and ECA respectively. Out of all the plaques, 39 of them were in the CCA bulb, 26 in CCA, 17 in ICA and 1 in ECA accounting to ~47%, ~31%, ~20.5% and 1.2% respectively (graph 5). All portions of the carotid artery are not affected uniformly by the atherosclerotic plaque. Majority of the plaque burden was seen in carotid bulb.

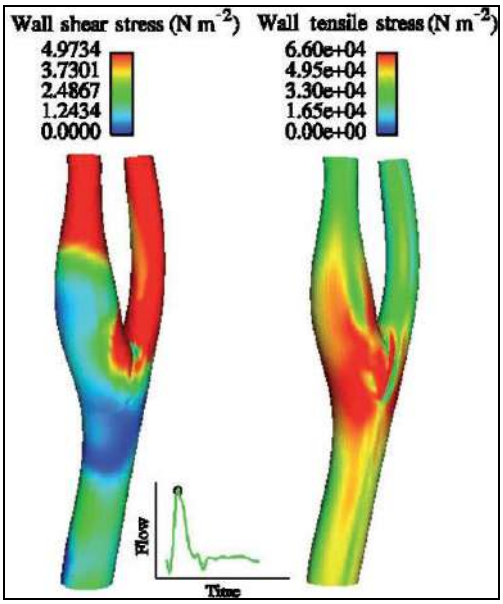


Fig 9: Showing wall shear and tensile stresses in a caroid bifurcation [24].

Table 13: Comparison of the present study with available literature based on location of the carotid plaques

Plaque location	Present study	SK Sethi *et al.* 2005 [12]	Noor Ul Hadi *et al.* 2009 [10]
Carotid bulb	39 (47%)	18 (50%)	19 (23%)
CCA	26 (31%)	11 (30.5%)	24 (43%)
ICA	17 (20.5%)	7 (19.5%)	13 (23%)

The present study correlated with the study done SK Sethi *et al.* [12] where the carotid bulb was the most common site to be affected by atherosclerotic plaque but differed from the study done by Noor Ul Hadi *et al.* [10] in which plaques were most commonly observed in CCA (table 13)

In the present study most of the plaques were smooth in surface (table 4) which is in accordance with the study done by Samrin Haq *et al.* [16]. Laith Ahmed *et al.* [14] showed that plaques with predominance of smooth plaque surface, ulceration being the least common correlating with the present study. Many of the studies previously done for evaluation of plaque surface have failed to address the issue of quantitative aspects. Also, the sensitivity of ultrasonography is as low as 33% in detection of plaque ulcerations [25].

In the present study, the international system of classification[3] of the carotid plaque is used dividing the plaques into 5 types which showed a predominance of Type I and Type II plaques unlike Malik R *et al.* [17] which showed Type II as the most common type (graph 6)

Both the studies are in accordance with the study done by Steffen *et al.* [26] where there is a predominance of Type I and Type II plaques in symptomatic patients.

Table 14: Comparison of the present study with available literature based on the type of carotid plaque

Type	Present study (n=83)	Malik R *et al.* 2013 [17] (n=64)
I	25 (30%)	16 (25%)
II	22 (27%)	20 (31.2%)
III	16 (19%)	12 (18.7%)
IV	10 (12%)	8 (12.5%)
V	10 (12%)	8 (12.5%)

Ischemic stroke and Colour Doppler parameters in Carotid Stenosis

The present study evaluated various carotid pathologies with the help of colour Doppler parameters like colour filling, pulsed wave Doppler mode giving information about PSVs and EDVs off CCA, ICA and ECA. All the appropriate parameters were evaluated according to the criteria laid down by SRU consensus conference [27] for the assessment of Carotid artery stenosis in 2003.

Peak systolic velocity of ICA

Spencer's curve" demonstrated the relationship between the degree of stenosis and velocity [28]. In a study done by Masatoshi Koga *et al.* [29], PSV>200cm/s was found to be the most reliable in prediction of stenosis of >70%. According to Moneta *et al.* [30], when the PSV > 230 cm/s is taken as the threshold to detect 70-99% stenosis. In the present study, 28 patients had PSVs of <125 cm/s, 21 patients had PSVs between 125-230 cm/s, 10 patients showed PSVs > 230 cm/s, variable PSVs in 3 patients and lastly no PSV was detectable in 2 patients. (graph 7)

Ratio of PSV of ICA/CCA

ICA/CCA PSV ratio is especially useful in conditions where there is decreased cardiac output. In the present study, 28 patients showed a ratio of <2.0, 21 patients between 2.0 – 4.0,10 patients had a ratio of >4.0 and the ratio was not measurable in 5 patients. A ratio of >4.0 implied there was hemodynamically significant stenosis. (Graph 9)

According to a study done by Moneta *et al.* [30], an ICA/CCA PSV ratio of >4.0 is an accurate predictor of stenosis of ICA between 70 – 99% with a sensitivity of 91%, specificity of 87%, PPV of 76% and NPV of 96%. The overall accuracy of this ratio in Moneta *et al.* study [30] was 88%. Similar opinion was given in a study by Fernandez *et al.* [13], that PSV ratio can be considered best for assessing carotid stenosis.

End Diastolic Velocity of ICA

According to many studies, EDV of ICA is a better adjunct parameter than the ICCA/CCA PSV ratio. Faught *et al.* [31] opined that a combination of PSV and EDV of ICA is a better predictor of carotid stenosis than PSV alone. Braun RM *et al.* [32] concluded that there is no significant

difference statistically between the correlations of all three parameters with angiography. In the present study, EDV < 40 cm/s was seen in 28 patients, 40 – 100 cm/s in 21, >100 cm/s in 10, variable velocities in 3 and no EDV could be measured in 2 patients (Graph 8)

Degree of stenosis in patients with atherosclerotic plaque
With the Doppler parameters mentioned above, the stenosis was measured according to the SRU consensus criteria [27] into 5 categories. 28 patients with <50% stenosis, 21 with 50-69% stenosis, 10 with >70% but less than near occlusion, 3 with near total occlusion and 2 showed complete occlusion. Majority of the patients showed <50% stenosis. 2 patients showed Complete carotid occlusion fulfilling the criteria laid down by Erickson SJ *et al.* [33] 3 patients in the present study were found to have near total occlusion. (Graph 10)

Table 15: Comparison of present study with available literature based on the degree of stenosis

Degree of stenosis	Present study	Noor Ul Hadi *et al.* [10]	Laith Ahmed *et al.* [14]	Bollipo JP *et al.* [11]
No stenosis	16 (20.0%)	44 (44.0%)	32 (51.6%)	18 (18%)
Mild stenosis (<50%)	28 (35%)	36 (36%)	18 (29%)	37 (45%)
Moderate stenosis (50 – 69%)	21 (~26%)	15 (15)	8 (~13%)	30 (36.6%)
Severe stenosis (>70%)	15 (~19%)	5 (5%)	4 (~6.4%)	15 (18.3%)

The present study correlated with the Bollipo JP *et al.* [11] where the predominant patients were the ones with mild stenosis. In the studies done by Laith Ahmed *et al.* [14] and Noor Ul Hadi *et al.* [10] majority of the patients belonged to the category of <50% stenosis (Table 15)
AbuRahma *et al.* [34] did a critical appraisal of the established criteria for the quantification of carotid stenosis by SRU consensus[27]. After the NASCET study [5] the degree of occlusion on angiography to be hemodynamically significant was proposed to be >70% and all the Doppler and grayscale parameters were established to classify 5 degrees of occlusion. Of those 5, > 70%, near total occlusion and total occlusion have same treatment and the patients would benefit from carotid endarterectomy. In the present study, least number of patients presented with significant stenosis.

Colour Doppler flow analysis: In the present study, patients with carotid stenosis showed an alteration in the colour Doppler signals. Aliasing and turbulence were the most common alterations. (Table 5) Changes in the degrees of stenosis causes a change in the colour Doppler flow pattern according to Steinke *et al.* [35].

Conclusion
Of the multitude of available diagnostic investigations like MR angiography, CT angiography and conventional angiography, Carotid Doppler ultrasonography is still the first line modality used in the examination of carotids as it is easily available, inexpensive, noninvasive, accurate and reliably reproducible. In addition to the presence of the carotid artery disease, it is very useful in localization of the plaques, the extent and morphology of the plaque. It is extremely useful in determining the morphological nature of the plaque which has significance because certain types of plaque are associated with increased stroke recurrence. The surface of the plaque and CIMT are also easily assessed which carry a diagnostic significance. The velocities measured with pulsed wave Doppler are useful in assessing the degree of stenosis.
Although the use of colour Doppler sonography has been extensively studied in the present study, the use of contrast enhanced ultrasound has gained considerable interest due to its ability to see for the vascularity of the atherosclerotic plaque and this area should also be further explored.MR angiography can also be used in cases where there is heavy acoustic shadowing causing obscuration of long segments of the artery or in cases where there is ambiguity in diagnosing near total or total occlusion.
Recent advances in this field which are open to exploration include using high-frame rate vector imaging which can add useful information to the conventional colour Doppler flow imaging, contrast enhanced ultrasound, typing of CCA occlusions etc.
In conclusion, a thorough examination of the carotid arteries using Doppler ultrasonography in the hands of an experienced radiologist can yield a treasure trove of information which will be helpful not only to the treating clinician but also to the welfare of the patient.

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