Original Research Article

Imaging Characteristics of Carotid Plaques by Doppler Ultrasonography and Magnetic Resonance Imaging in Ischemic Stroke: A Comparative Analysis

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Abstract

Background: Carotid plaques contribute a significant cause of stroke and transient ischemic attacks together with long term disability worldwide. About 20-30% of cerebral infarction has been correlated with carotid atherosclerotic plaque and artery stenosis. The characterization of carotid artery plaque presents an opportunity to quantify patients with risk of cerebrovascular events and may be used to improve the therapeutic decision-making process such as carotid endarterectomy or angioplasty or stent placement. This study attempted to evaluate the imaging characteristics of carotid plaques using ultrasonography with Magnetic Resonance Imaging correlation and predict the risk of plaque rupture based on plaque enhancement characteristics as a surrogate marker.

Materials and methods: Aim of the study was to evaluate and compare morphological characteristics of carotid plaques with Doppler ultrasonography and MRI and to predict plaque

enhancement characteristics on MRI as a potential surrogate marker for plaque rupture leading to recurrent strokes. The present study evaluated 113 patients (65 males and 48 females) with stroke and transient ischemic attacks with ultrasound documented carotid plaques. These cases underwent Doppler evaluation of the carotid plaques and contrast enhanced MRI on the same day. The plaque morphology was evaluated both in the longitudinal as well as the transverse axis, and the stenosis was calculated based on the pulsed- wave Doppler evaluation of blood flow velocity as well as the area and diameter of the stenosis together with the signal and enhancement characteristics of the carotid plaques on MRI. The carotid artery at the region of maximal intimal thickness was evaluated for maximal area stenosis and diameter stenosis. The area stenosis was calculated as percentage stenosis in axial sections at the site of maximal thickness of the plaque.

Results: The maximum incidence of carotid plaques was noted in the 61-80 years age group. The incidence was maximal at 71-80 years of age. Out of the 113 lesions, 65 (57.5%) were in men and 48 (42.4%) were in women. 44(38.9%) lesions were in patients who presented with TIA, while 69 (61.06%) presented with Ischemic stroke. 67 (59.29%) lesions were found on the left side and 46 (40.7%) on the right side. 67(59.3 %) lesions were found in the carotid bulb. The intimal thickness ranged from 1.1 mm to 5.6 mm with a mean of 2.97 mm. The range of stenosis was from 0% to 100%. Heterogeneous plaques were associated with symptomatic lesions in 76.2 % and homogeneous plaques were seen in 23.8%. The incidence of plaque calcification was inversely proportional to symptomatic plaques. Only 47.2 % of patients showed concordance between US and MRI with regard to homogeneity of the plaque. T2 weighted MR imaging of exvivo atherosclerotic plaques aided in the detection and evaluation of fibrous caps. 39 (34.1%) patients were given a gadolinium-based contrast agents, out of which 19 (48.7 %) did not show enhancement and 20 (51.2%) showed enhancement of the carotid plaque tissue. Doppler showed abnormalities in 29 patients (61.7%), whereas in MRA it is 18 patients (38.2 %), p value = < 0.004* in cases with less than 50% stenosis (n=47). In cases with 50-69% stenosis (n=29), doppler showed abnormalities in 19 patients (65.5%) whereas in MRA it was (34.4 %); P value was 0.431, The difference was not found to be statistically significant. While as in cases with 70-90% stenosis (n=37), MRA showed abnormalities in 25 patients (67.5%) whereas Doppler showed it in 12 (32.4%); P value was 0.017. Calcification was seen in 22 patients which appeared as hypointense focus on T1, T2, and TOF images. The heterogeneous lesions were better visualized on ultrasound compared to MRI.

Conclusion: Ultrasound is a more sensitive modality than MRI for plaque size < 1.5 mm and a better tool in assessing the plaque characteristics when the area of stenosis is less than 50%. Hence, ultrasound is better as a screening tool. The homogenous lesions on ultrasound appeared homogenous on MRI with the plaque content of fat. The heterogeneous plaque on ultrasound, however, did not correlate with MRI. Enhancement of carotid plaque tissue, which implies vascular wall inflammation, is a marker of vulnerable plaque. MRA has a better discriminatory power compared with duplex ultrasonography in detecting 70-90% stenosis.

Key words

Ultrasound, Magnetic Resonance Imaging, Plaque, Stenosis, Doppler.

Introduction

Importance of the subject of the study

The study has a very important potential role in determining the plaque enhancement on MRI as a surrogate marker for plaque rupture with future ischemic insults which lead to long term mortality and morbidity together with comparison of accuracy of Doppler versus MRI in predicting the vulnerable plaque.

Ischemic Stroke is one of the leading causes of death and a major cause of long term disability worldwide [1-4]. About 20 -30% of cerebral infarction has been correlated with carotid atherosclerotic plaque and artery stenosis [5, 6]. Multiple non- invasive imaging modalities are currently being used to image, and classify carotid atherosclerotic plaque such as MR imaging [7-10], CT [7, 11, 12, 13], and sonography [14, 15, 16] in an effort to provide clinically relevant predictive metrics for use in patient risk stratification and to define appropriate treatment options. The characterization of carotid artery plaque presents an opportunity to quantify patients' the risk of cerebrovascular events and may be used to improve the therapeutic decision-making process such as carotid endarterectomy or angioplasty or stent placement [14, 15, 16]. The major risk factors for stroke are hypertension, smoking, diabetes mellitus, atrial fibrillation and hyperlipidemia [17].

Hypertension is a major risk factor for all stroke subtypes, infarction as well as haemorrhage. Hypertension is the most prevalent and powerful modifiable risk factor.

There are several possible mechanisms for the relation of smoking to the risk of ischemic stroke. First, smoking is associated with increased fibrinogen concentrations, increased platelet aggregability, increased hematocrit, reduced fibrinolytic activity, and reduced blood flow in brain due to vasoconstriction, which may contribute to accelerated thrombus formation.

Diabetic patients suffering from stroke have a higher incidence of carotid artery atherosclerotic lesions than diabetes without stroke [18]. By provoking anaerobic metabolism, Lactic acidosis and free radical production, hyperglycaemia may exert direct membrane lipid peroxidation and cell lysis in metabolically challenged tissues. Insulin resistance is a known risk factor for the onset of stroke, acting through a number of intermediate vascular disease risk factors i.e. thrombophilia, endothelial dysfunction, and inflammation. A poor lipid profile has been clearly established as a risk factor for stroke. Studies have confirmed the independent associations of lipids with atherosclerotic disease. Hypertriglyceridemia is commonly found in patients with ischemic cerebrovascular disease. Vascular diseases including stroke increases with advancing age [19].

Genetic susceptibility to hypertension may account for a significant proportion of the heritability of ischemic stroke [20]. Atherosclerosis is a type of arteriosclerosis derived from the Greek words "Atheros" meaning "gruel" and "sclerosis" meaning "hardening" and is characterized by intimal lesions called atheromas that protrude into vascular lumina. It is synonymous with atheroma and atheromatous plaque [21].

Materials and methods

The study was conducted in the Department of Radiodiagnosis and Imaging, Sher-I-Kashmir Institute of Medical Science, Srinagar from June 2018 to June 2021with patients referred from the Department of Neurology and Department of Emergency Medicine, Sher-e-Kashmir Institute of Medical Science, Srinagar. It was a prospective hospital-based cohort study. No randomization was done. A total of 113 lesions from cases of stroke and TIA who were admitted in our hospital were taken. All patients were informed about the study and their informed consent was taken. All patients underwent Doppler ultrasonography of carotid and MRI of carotid on the same day.

The study evaluated the characterization of carotid plaque morphology with MRI and Doppler ultrasonography. Correlation of plaque morphological features on Doppler ultrasonography and MRI with ischemic stroke/ TIA with plaque enhancement on contrasts enhanced MRI and Color Doppler served as a surrogate marker for plaque rupture.

Ultrasound carotid duplex scanning was performed with a LOGIC P5, with standard pre-sets. Linear phased array probes (7 and 12 MHz) with standard pre-setting were used to assess carotid plaques. The same machine pre-sets were maintained for all patients. The plaque morphology was evaluated both in the longitudinal as well as in the transverse axes, and the stenosis was calculated based on the pulsed-wave Doppler evaluation of blood flow velocities as well as the area and diameter of the stenosis.

MR studies were performed using 1.5 T scanner (Magneton Symphony Quantum Gradient: Siemens Medical System, Germany). The MR scan was centred on the carotid bifurcation on the side of the stenosis to assure proper matching between the contrast weighted imaging series of each patient. The patients were positioned on a vacuum pillow to avoid head – neck region movements during the MRI scan to ensure proper alignment between the images acquired in the three contrast – weighted imaging of each patient. Sequences used were 3D time of flight (TOF), T1-Weighted spin echo sequence (T1W), T2-Weighted spin echo sequence, Proton Density T2-Weighted spin echo sequence, T1-Weighted Fat-Sat Post-contrast sequence, and 3D-time of Flight sequence.

All statistical analysis was done by using SPSS software. All the categorical variables were shown in the form of frequency and percentage. Moreover, continuous variables were analyzed by proper statistical test. All variables were discussed at a 5% level of significance.

Results and Discussion

The age of the subjects detected to have carotid artery plaque in this study ranged from 37 years to 85 years with a mean of 62.8 $\pm$ 9.34 years (Mean $\pm$ SD) (**Figure – 1**). The maximum incidence was noted in the 61-70 years age group (48.9%). Out of the 113 lesions, 65 (57.5%) were in men and 48 (42.4%) were in women. Smoking greater than 5 years was associated with 40(35.3%) lesions and was not associated with the rest 73 (64.6%) lesions. Smoking was associated in 48.8% of the lesions in our study.

Of the 113 lesions, 67 lesions (59.29%) of the lesions were associated with diabetes mellitus for at least 5 years. 73 lesions (64.6 %) were associated with hypertension.44 (38.9%) lesions were seen in patients who presented with TIA, while 69 (61.06%) lesions in patients with Ischemic stroke. 67 (59.29%) were found on the left side and 46 (40.7%) on the right side. 67 (59.3 %) lesions were found in the carotid bulb. The distribution of carotid plaques with respect to location and age is depicted in **Table – 1** and **Table - 2**, respectively. The intimal thickness ranged from 1.1 mm to 5.6 mm with a mean of 2.97 mm. The carotid artery at the region of maximal intimal thickness was evaluated for maximal area stenosis and diameter stenosis. The area stenosis was calculated as percentage stenosis in axial sections at the site of maximal thickness of the plaque. The range of stenosis was from 0% to 100%. The atherosclerotic plaques can become symptomatic irrespective of the degree of stenosis. However, their incidence of stroke in high degree of stenosis (90%) or above is associated with a lesser degree of symptoms and a lesser risk of stroke/TIA. Out of the 113 lesions, heterogeneous plaques were associated with symptomatic lesions in 76.2% and homogeneous plaques were seen in 23.8%. The heterogeneous plaque was associated with a statistically greater incidence of plaque hemorrhage and ulceration, pathologic features that correlated with a greater incidence of transient ischemic attack or stroke. Calcification in the carotid plaque was visualized in 39 (34.5%) lesions. The incidence was also inversely proportional to symptomatic plaques. Of the 34 lesions that were homogenous on ultrasound, 27 were also homogenous on MRI and were composed of lipids (**Figure – 2, 3**). The remainder 7 lesions appeared heterogeneous on MRI and were composed of lipid and intracellular methemoglobin.

Figure – 1: Age distribution of study participants.

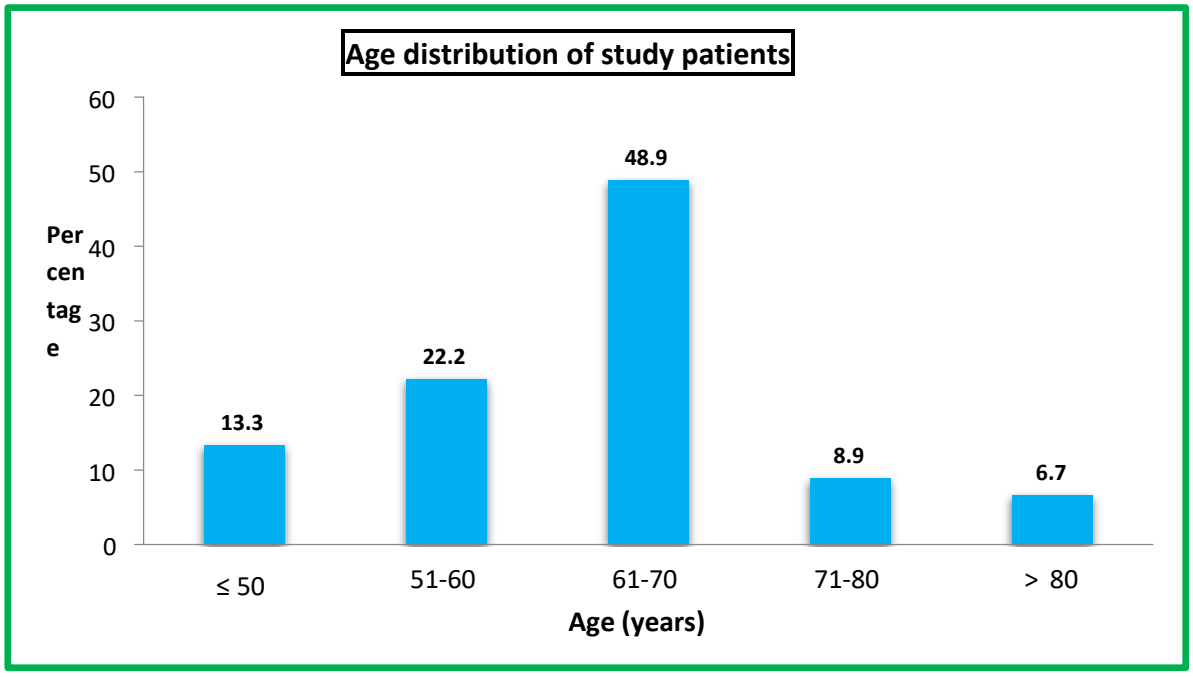


Table - 1: Location of carotid plaques in study patients.

Location of plaque	Number	Percentage
CCA	12	10.6
ICA	24	21.2
ECA	0	0.0
Carotid bulb	67	59.3
ICA and carotid bulb	10	8.8
Total	113	100

Table - 2: Distribution of carotid plaque by age.

Age (Years)	Number	Percentage
≤ 50	14	12.3
51-60	21	18.5
61-70	59	52.2
71-80	11	9.7
> 80	8	7.0
Total	113	100
Mean ± SD = 62.8 ± 9.34		

Of the 42 plaques that were heterogeneous on ultrasound, only 18 were heterogenous on MRI. The rest of the 24 plaques appeared homogeneous on MRI and showed the presence of lipid only. There were 24 plaques that were homogenous both on ultrasound and MRI. There were 18 plaques which appeared heterogeneous on both ultrasound and MRI. Thus, only 42.85 % of patients showed concordance between US and MRI in regard to homogeneity of the plaque. More lesions appeared heterogeneous on ultrasound, however the content of these plaques and the stage of blood within the plaque as intracellular methaemoglobin could be analyed only on MRI. The incidence of heterogeneous plaque on MRI was 15.92 %. The heterogeneous

plaques contained blood products and lipids. All heterogeneous plaques on MRI, in our study, showed lipid and intracellular methaemoglobin as the cause of heterogeneity, which corroborates with the study by Yuan et al. [22] where they had analyzed the plaque morphology of 18 patients with heterogeneous plaques, 87 % had lipid and blood products within.

Figure – 2: Morphological characteristics of plaque on MRI.

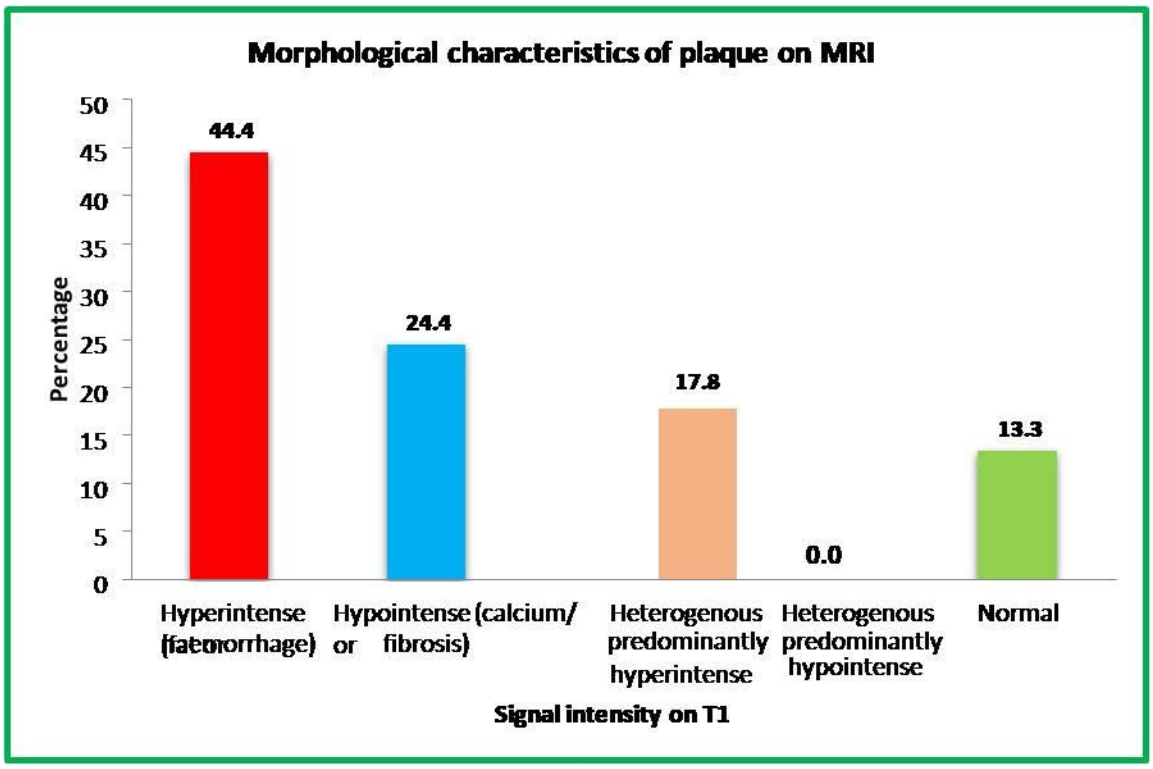


Table - 3: Morphological characteristics of plaque on MRI.

Signal intensity on T1	Number	Percentage
Hyperintense (fat or haemorrhage)	49	43.3
Hypointense(calcium or fibrosis)	24	21.2
Heterogenouspredominantly hyperintense	21	18.5
Heterogenous predominantly hypointense	0	0.0
Normal	19	16.8
Total	113	100

Table - 4: Comparison of stenosis on Doppler USG and MRI.

Stenosis	Doppler		MRI		P-value
	No.	Percentage	No.	Percentage	
Normal	0	0.0	56	49.5	-
≤ 15%	54	47.7	11	9.7	<0.001*
16-49%	33	29.2	17	15.0	0.004*
50-69%	17	15.0	9	7.9	0.431
70-79%	9	7.96	22	19.4	0.017*
Total	113	100	113	100	-

*Statistically Significant Difference (P-value<0.05)

Figure – 3: Comparative analysis of carotid plaque on USG and MRI.

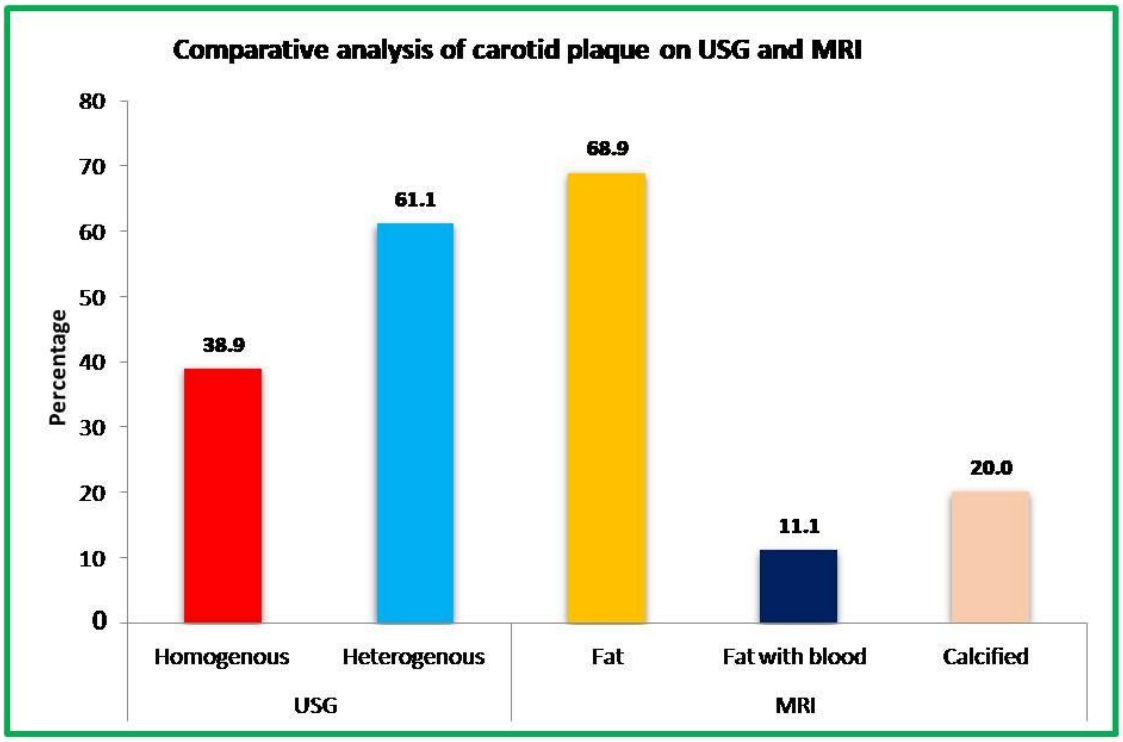
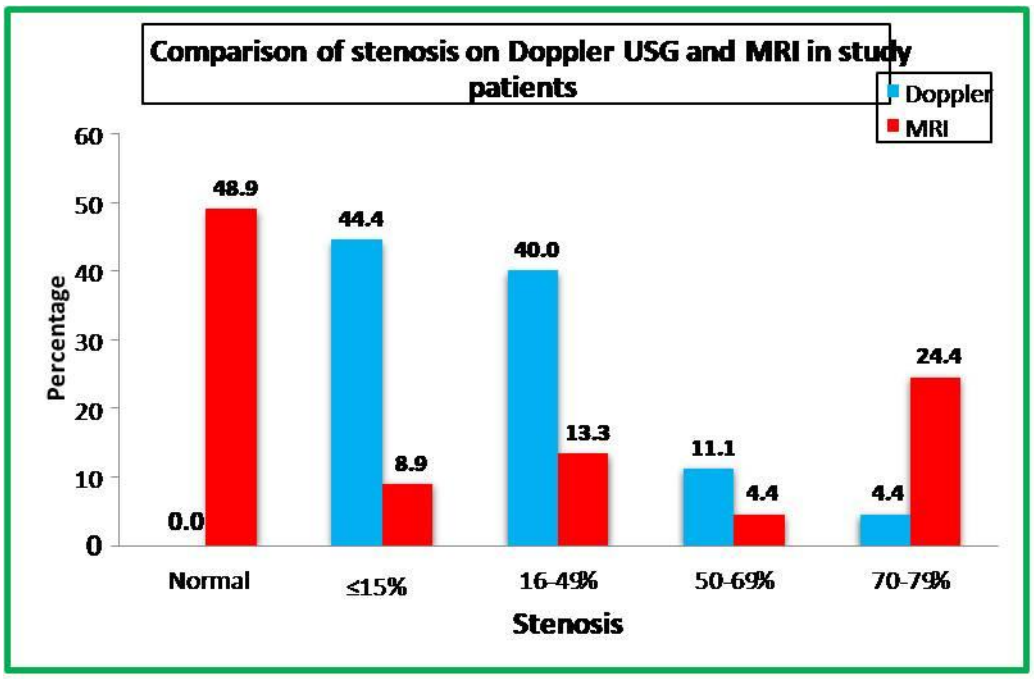


Figure – 4: Comparison of stenosis on Doppler USG and MRI in study patients.



39 (34.5%) plaques showed calcification in the carotid artery, which shows concordance with the study by Yuan et al. [22] where they had identified calcification as a hypointense focus on TOF, T1, T2 weighted images. In our study, we were not able to identify the fibrous cap or its rupture in any of the lesions either on US or MRI. Contrary to our findings, a study done by Winn et al., has demonstrated that T2 weighted MR imaging of ex-vivo atherosclerotic plaques aided in the detection and evaluation of fibrous caps. They detected fibrous caps / rupture with a

specificity of 90% and 98%, respectively. However, this had a very low sensitivity of 37% and 12%, respectively, for the detection of fibrous cap and rupture, respectively [23].

39 (34.1%) patients were given a gadolinium-based contrast agent, out of which 19 (48.7 %) did not show enhancement and 20 (51.2%) showed enhancement of the carotid plaque tissue. This corroborates with the study of Levy AP et al. [27] done in 2006 who suggested that plaque neo- vasculature may play an important role in the pathogenesis of intraplaque hemorrhage. As neo-vasculature and increased endothelial permeability are both associated with plaque inflammation, gadolinium enhancement of the vessel wall has been hypothesized to be a marker of vascular wall inflammation. To probe this hypothesis further using quantitative analyses, Kerwin, et al. [28] used dynamic contrast-enhanced MRI to measure the rate of uptake of gadolinium-based contrast, characterized by the transfer constant K^{trans}, and compared these measurements to histological measurements of plaque composition and inflammation and concluded that carotid MRI is a histologically validated tool that can identify the key features that are believed to characterize the vulnerable plaque, including fibrous cap status, plaque composition, neo vasculature and vascular wall inflammation [24].

Plaques with degree of stenosis on Doppler and MRI

A total of 113 lesions from the symptomatic individuals were evaluated with ultrasound and MRI. We had analyzed the morphological pattern of the plaque with ultrasound and MRI and the findings were further correlated. Morphological characteristics of carotid plaques are depicted in **Table - 3**. Doppler showed abnormalities in 29 patients (61.7%) whereas in MRA it was 18 patients (38.2 %) p value = < 0.004*. This corroborates with the study of Erickson, et al. (1989) [25] who analyzed 49 patients with various Doppler velocity parameters for carotid artery stenosis and correlated with angiography. They found that B-mode measurement of diameter stenosis is most accurate at less than 40% diameter stenosis [25].

In cases with 70-90% stenosis, MRA showed abnormalities in 25 patients (67.5%), whereas in the Doppler it was 12 (32.4%). P value is 0.017*. The difference was found to be statistically significant. Comparison of stenosis with Doppler and MRI is depicted in **Table – 4, Figure - 4**. This corroborates with the study of Paul J. Nederkoorn, et al. [26] who found that MRA has better discriminatory power compared with duplex ultrasonography in detecting 70-99% stenosis [26].

Fibrous cap was not visualized in any of the 113 cases, both on T2 weighted images as well as in the base images of the 3D TOF. Calcification was seen in 39 (34.5%) patients during our study which appeared as a hypointense focus on T1, T2, and TOF images.

The heterogeneous lesions were better visualized on ultrasound compared to MRI. However, the content of these plaques such as intracellular meth-hemoglobin and lipid was analyzed only on MRI.

Conclusion

We conclude that MRA has a better discriminatory power compared with duplex ultrasonography in detecting 70-90% stenosis and B mode measurement of diameter stenosis is most accurate at less than 40% diameter stenosis. Ultrasound was found to be more sensitive than MRI for plaque size < 1.5 mm. Ultrasound is a better modality in assessing the plaque characteristics when the area of stenosis was less than 50%. Hence, ultrasound is better as a screening tool. Symptomatic individuals had a high degree of correlation with heterogeneous plaques on ultrasound. The homogenous lesions on ultrasound appeared homogenous on MRI with the plaque content as fat. All heterogeneous lesions on MRI contained intra-plaque blood with intracellular methaemoglobin and lipids.

The heterogeneous plaque on ultrasound, however, did not correlate with MRI. Fibrous cap was not visualized although a thinner slice with a smaller FOV could have helped in analyzing the fibrous cap. Although MRI gives objectivity to the characterization of the plaque, ultrasound was found to be more sensitive for plaque disease <50% area stenosis. Enhancement of carotid plaque tissue which implies vascular wall inflammation which is a marker of vulnerable plaque.

Statement of Ethics

Proper written and informed consent was taken from every subject involved, for publication of data in any medical journal for research purposes.

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