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CAROTID PLAQUE MORPHOLOGY: A COMPARISON BETWEEN DUPLEX SONOGRAPHY AND CT ANGIOGRAPHY

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ABSTRACT

Background and objectives: Cerebrovascular disease incidence is increasing in present day scenario with more and more people being affected by stroke. Stenosis degree is considered the leading parameter in the choice of therapeutic options but factors other than the degree of stenosis are also important in assessing whether a carotid lesion will remain clinically silent. Thus additional assessment of plaque morphologic parameters is necessary in order to better define the most correct therapeutic treatment . Some of these plaques are associated with a higher risk of embolism and occlusion, producing ischemic neurologic events..

The purpose of this study was to evaluate the diagnostic efficacy of multidetector row CT angiography (MDCTA) and Ultrasound in the evaluation of morphology of carotid plaque with MDCT being taken as reference standard

Methods: Total of 30 patients with symptoms pertaining to cerebrovascular disease were selected over a period of one year and plaque morphology was evaluated and compared by both Doppler ultrasound and CT angiography.

Results: We concluded that CDUS is inferior w.r.t CTA to assess plaque morphology and especially in identification of echogenic/mixed plaques For thrombosed, mixed/calcified plaques the co relation among the two modalities was excellent.This can be ascribed, due less resolution of usg with brightness of echogenic plaque being confused for calcification.

Conclusion: We recommend the use of CDUS as a first line screening examination in a patient of cerebrovascular disease. However, because of its relative insensitivity in some important plaque risk determinants for example plaque ulceration and presence of echogenic plaques we recommend the use of a second more definitive screening examination like CTA prior to any intervention being undertaken (in cases of significant stenosis) in order to produce a detailed and reproducible plaque characterisation and assessment of the degree of stenosis.

KEYWORDS : Carotid plaque,Calcified plaque carotid vascular disease, cerebrovascular disease, Doppler ultrasound , CT angiography

INTRODUCTION

Cerebrovascular disease with stroke in particular is one of the most important causes of death and the greatest cause of disability all over the world[1] and also in India. Lesions of the extra-cranial carotid arteries, particularly the internal carotid artery near the bifurcation, are implicated in majority of cases of cerebrovascular disorders and are the major single etiological factor for stroke as opposed to intracranial occlusive diseases and cardio embolisation[2]. This location is readily amenable to examination by sonography as well as surgical intervention.

Stenosis degree is considered the leading parameter in the choice of therapeutic options as evidenced by the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[3] and European Carotid Surgery Trial[4] and, the Asymptomatic Carotid Atherosclerosis Study[5] but factors other than the degree of stenosis are also important in assessing whether a carotid lesion will remain clinically silent. It is possible that even a low-grade stenosis in the carotid arteries can lead to the development of cerebrovascular events. Recent work emphasises the need for assessing additional plaque morphologic parameters in order to better define the most correct therapeutic treatment[6,7,8] , most important ones being : plaque ulceration and type of plaque (Fatty, Calcified or mixed)[9,10,11,12] Hence, it is important to look beyond the degree of stenosis[13]. The concept of "vulnerable plaque[10]" has now been postulated for carotid arteries which was traditionally postulated for coronary arteries[5]. "Vulnerable Plaque" is an atherosclerotic-plaque that contains a large necrotic lipid core covered by a thin or disrupted fibrous cap having a high tendency to rupture potentially resulting in embolisation or thrombosis.

The selection of initial imaging study for evaluation of carotid vascular disease remains controversial. Carotid duplex ultrasonography, Computed Tomography Angiography (CTA) or Magnetic Resonance Angiography (MRA) are the most commonly used imaging modalities for evaluation of carotid vascular disease.

Potential and results of MDCT in evaluation of carotid plaques has been well documented in various studies[14-19] , with the advantage of being fast and having a high temporal and spatial resolution. This technique is considered by many authors as a reference standard in diagnosing the pathology of carotid artery like grading of internal carotid artery stenosis and occlusion, convincingly showing the distal flow in apparent totally occluded vessel, diagnosing tandem lesions and studying intracranial circulation in the shortest time. The limitations include ionising radiation dose and ballooning artefacts of heavy circulation.

Carotid duplex sonography (CDUS) is a non-invasive means by which to estimate the degree of cervical carotid stenosis and is often the initial screening method of choice for carotid pathology prior to evaluation by MDCT owing to its low cost, high accuracy easy availability, absence of ionising radiation and lack of contrast nephrotoxicity. However it is often operator dependent and is sometimes not accurate in defining

the extremely narrowed lumen group separate from total occlusion and can even miss the tandem plaques. To employ US-ECD as the unique diagnostic test for the patients' selection for carotid endarterectomy has been widely discussed[20] because it has been reported that with the only US-ECD use, errors can occur and performances may vary across institutions[21].

In low-income and middle income countries like India, cerebrovascular diseases are steadily increasing, largely being driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors. The poor are now becoming increasingly affected by stroke, because of both changing population exposures to risk factors and most tragically, non-affordability for the high cost of stroke care.

The purpose of this study was to assess the agreement between US-ECD and MDCTA in the quantification and evaluation of morphology of carotid plaques.

MATERIAL AND METHODS

This was a prospective observational study for a period of one year from Jan 2016- jan 2017. Consisting of total of 30 patients or the patients with symptoms pertaining to cerebrovascular disease . Duplex sonography and CTA were done

First complete clinical history and family history of patient was taken . After explaining the procedure and its benefits and obtaining the informed consent from the patient, colour doppler ultrasonography and gray scale sonography of extra cranial carotid arteries was done.

CT angiography of the carotid artery was done for the patients coming back with recommendation of CT angiography by the clinician. Alternatively, duplex sonography was also done on all the patients coming initially for CT angiography of the carotid vessels. The data so obtained was analysed and the findings of gray scale ultrasonography and Doppler ultrasonography parameters with CT angiographic findings was compared for plaque morphology Scans were obtained along the entire course of cervical carotid artery from the supra-clavicular notch cephalad to the angle of mandible.
After transverse imaging, longitudinal scans of the carotid artery were obtained (coronal and sagittal).

A. Vessel wall thickness - Thickening of Intimo medial complex greater than 0.8mm was considered to be abnormal. However due to non-reproducibility on CTA was not included in the the correlation criteria.
B. Plaque characterisation - Plaque texture was classified as being hypo echoic(lipid) , echogenic (mixed) or calcified or thrombosed. (Table 1)

Table 1: Showing plaque morphology

ULTRASOUND TYPES OF PLAQUE MORPHOLOGY	
TYPE 1	Predominantly echo lucent ,with a thin echogenic cap.
TYPE 2	Substantially echo lucent with small areas of echogenecity(>50% sonolucent)
TYPE 3	Predominantly echogenic with small areas of echolucency(<50% sonolucent)
TYPE 4	Uniformly echogenic

Based on the density, carotid plaques were classified into three different groups on Ct[22] :

Table 2 : Caractérisation of plaques on CTA

Type	Characterisation	Ct value
Type 1	Fatty(soft) plaques	<50 HU
Type 2	Mixed(intermediate) plaque	50 - 119 HU
Type 3	Calcified plaque	>120

Window level and window centre were set at 700 HU and 200 HU, respectively, for optimum visualisation of the vascular structures.

OBSERVATIONS AND RESULTS

We conducted the present study on 30 patients with symptoms pertaining to cerebrovascular disease who were referred to the department of Radio-diagnosis for imaging work up. Total of 180 arteries (60 CCA+ 60 ICA+ 60 ECA) were analysed in the course of study comprising of extra-cranial vessels on both sides of neck. The arteries were examined on transverse and longitudinal sections with and without colour doppler. Morphological analysis of ICA, common carotid artery and the carotid bifurcation was done in both methods and the atherosclerotic plaques were classified into calcified, cholesterol or mixed.

All statistical analysis was done in SPSS 21. The interpretation of the kappa coefficient and ICC was done according to the one proposed by Landis and Kock[23].

Complete clinical history followed by routine investigations was done. The results of the duplex sonography were obtained, analysed and compared with those obtained by CTA and following inferences were made by us.

A. Common Carotid artery

Morphologic assessment of plaques was done by both CDUS and CTA. The type of plaque was identified on CDUS and correlated with corresponding category on CTA. In our study, we found out that 44 common carotid arteries were diseased with presence of plaques. Following inferences were made:

- Of the total of 16 arteries identified as normal on CDUS all were perfectly co related on CDUS thus having concordance rate of 100%
- In cases of vessels with plaque showing mixed echogenicity out of the total of 14 vessels which showed mixed echogenicity plaques on CDUS , only 4 were perfectly co related for this respective category on CTA showing the concordance rate of 28% only with 2 arteries being reported as normal and 8 as calcified on CTA
- All the 14 calcified plaques showed perfect concordance on both CTA and CDUS with concordance rate of 100%
- Similarly all the thrombosed arteries on CDUS were well correlated by CTA as having thrombosis with concordance rate of 100%
- Out of 12 arteries showing simultaneous presence of both mixed and calcified plaques on CDUS 10 of the vessels were perfectly co related on CTA with correlation coefficient of 83%
- In the mismatched group (12 arteries) (table 3) ,out of the total 10 arteries showing Moderate stenosis on CDUS, 2 were found out to be normal , 8 found out as having calcified plaques on CTA which could be partially attributed to difficulty in differentiating highly echogenic plaques from calcified plaques on CDUS .
- The Morphology of plaque was one category higher in 10 arteries (83 % of non discordant scans) and one category lower in 2 arteries (17% of non discordant scans)
- Also 2 arteries showing which were not clearly visible on CDUS due to inadequate patient positioning and suspected to have both calcified and mixed plaques were found out to be thrombosed.
- Overall the degree of agreement between CDUS and CTA in Evaluating the morphology of plaque in common carotid arteries was Substantial with kappa value of 0.74

Table 3 - Correlation of results of CT angiography and Doppler in grading of Plaque Morphology in mismatch group

		Morphology By CT AngiographyMorphology By CT Angiography				
		Direct Correlation	Over-estimated by one category	Over-estimated by two categories	Under-estimated by one category	Over-estimated by two categories
Colour Doppler -US	Mixed	4	8	0	2	0
	Thrombosed	4	0		0	0
	M+C	10	2	0	0	0
Total occlusion		10	0	0	0	0

B.Internal Carotid artery

Similarly CDUS we found out that 42 Internal carotid arteries were diseased with presence of plaques. On further subdividing the diseased arteries based on the type of plaque present , we found out that 2 had fatty plaques, 10 had mixed echogenic plaques 10 had calcified plaques , 14 internal carotid arteries had presence of both calcified as well as mixed plaques and 6 arteries were thrombosed

CTA of the same vessels revealed that 2 arteries had the presence of lipomatous plaque 6 arteries had presence of mixed plaque 12 had calcified plaques 12 had both calcified as well as mixed plaques and 10 arteries were thrombosed.

- Out of total 18 arteries which were normal on CDUS , only 14 were found to be normal on CTA having concordance rate of 78%
- 2 arteries which were labelled as having fatty plaque were found to have calcified plaque on CTA.
- For echogenic plaques the concordance was again found to be low (40%) with CTA detecting only 4 out of 10 arteries as having echogenic plaques .
- All the thrombosed and calcified plaques on CDUS were also found on CTA indicating perfect agreement
- In the mismatch group (table 4) , out of total 8 arteries 6 were overestimated by 2 categories(75% of non discordant scans) and 2 were over estimated by one category(25% of non discordant scans)(table 24)
- Measure of Agreement in cases of Morphology of plaques in ICA was also substantial with Kappa value of 0.75

Table 4 - Correlation of results of CT angiography and Doppler in grading of Plaque Morphology in mismatch group

		Morphology By CT Angiography				
		Direct Correlation	Over-estimated by one category	Over-estimated by two categories	Under-estimated by one category	Under-estimated by two categories
Colour Doppler -US	Normal	14	2	2	0	0
	Lipid	0	0	2	0	0
	Mixed	4	0	2	0	0
	Clacified	10	0	0	0	0
	Thrombosed	10	0	0	0	0
Total occlusion		10	0	0	0	0

C.Total(CCA+ICA)

On comparing the correlation between the degree of stenosis in both ICA and CCA we found that:

- Out of total of 34 normal arteries on CDUS, 30 were identified on CTA with concordance rate of 88%.
- Out of total of 24 mixed echogenic plaques only 8 were identified on CTA (concordance rate of 33%)
- All of the calcified and thrombosed plaques on CDUS were correctly identified on CTA (concordance of 100%)
- In plaques with mixed and calcified aetiology, out of 24 plaques identified on CDUS 22 were correctly identified on CTA thus showing a concordance of 92%(table 5)

Table 7 - Comparison of the Morphology of plaques with CT angiography and colour Doppler US.

		CCA+ICA_morphology						Total
		0	Lipid	Mixed(M)	Calcified ©	thrombosis	M+C	
CCD+ICD_morpholo gy	0	30	2	2	0	0	0	34
	Lipid	0	0	0	2	0	0	2
	Mixed(M)	6	0	8	8	2	0	24
	Calcified(C)	0	0	0	24	0	0	24
	Thrombosed	0	0	0	0	12	0	12
	M+C	0	0	0	0	2	22	24
Total		36	2	10	34	16	22	120

		Value
Measure of Agreement	Kappa	.747
N of Valid Cases		120

- The agreement in assessing the plaque morphology was substantial with kappa value of 0.7

DISCUSSION

Atherosclerotic narrowing at the carotid bifurcation[100] is often the inciting factor for ischemic cerebrovascular events and thus improved methods of diagnosis, treatment and prevention of these diseases would result in a significant improvement in quality of life and decrease in healthcare costs[101].Angiography provides detailed information of the location and extent of the lesions and serves as roadmap for the surgeon or interventional radiologist. But catheter angiography is also associated with an increased risk of thromboembolic events and a marked financial cost besides being an invasive procedure associated with patient discomfort. In the present scenario of rapid medical advances particularly in the field of intervention radiology, non-invasive laboratory has come to occupy an important place in the evaluation of patients with carotid vascular disease..

Even low-grade stenosis can result in a cerebrovascular event, so it is important to look beyond the lumen stenosis to plaque morphology as well[26]. Doppler ultrasound is widely used clinically to measure lumen stenosis in carotid arteries and also to measure or identify atherosclerotic plaque site, size of the fibrous cap, wall thickness, and plaque composition or ulceration. Ultrasound has been used to differentiate stable from unstable plaques. But overall , the results for identifying unstable plaques have been largely unsuccessful[27]. Also, this technique suffers from inter-observer and intra-observer variability determined by several parameters[28] (e.g. sonographer's experience and type of sonographic scanner).

Nowadays MDCTA sensitivity in the evaluation of stenosis degree is compared with angiography but with less risks and in particular, MDCTA reaches excellent sensitivity for stenosis between 70% and 99%. The purpose of our study was grading and comparison of degree of stenosis, plaque morphology and composition between the CDUS and CTA. Keeping with the present trend of opting for non-invasive diagnostic modalities, we have attempted to study, evaluate and

correlate the findings of Doppler scanning, with MDCT Angiography with MDCT angiography being the reference standard.

The results of CDUS scans and CTA were analysed and compared for plaque morphology, in common carotid artery including carotid bifurcation, internal carotid and external carotid arteries. Measurement of only the luminal stenosis may give incomplete information about the plaque burden. The diseased adventitial boundary can compensate for a large carotid plaque by outward expansion of the vessel wall. Atheromas initially form eccentrically with compensatory dilatation of the lumen such that there is no luminal stenosis. Once atheroma occupies roughly 40% of the area circumscribed by the internal elastic lamina (IEL), luminal encroachment begins. This phenomenon of vessel remodelling was first described by **Glagov et al**[29]. In addition, luminograms give no information regarding the plaque "vulnerability"

Ultrasound can provide local diameter and wall thickness measurements as well as flow characteristics, including waveforms, gradient, and peak velocities. However, it is operator dependent and has limited field of view. **Gronholdt et al**[30] in their study found out that patients with echo-lucent plaques on CDUS are at increased risk of CVA as compared to those with echo-rich plaques. **Biasi GM et al**[31] in their study revealed that high echolucency increases the risk of stroke. Subsequently, **Reiter and colleagues**[32] showed no such relationship between plaque echo-lucency and stroke risk with carotid angioplasty and stenting (CAS). CTA images also give information regarding the plaque composition and surface irregularities[33].

In a recently published study, plaque relative lipid volume (using attenuation of <60 HU) was associated with the presence of ulceration[34]. There is a positive association between fatty plaque type and symptoms and between >70% stenosis and symptoms and an inverse association between calcified plaques and symptoms[35].

In our study, we found out that for the evaluation of calcified plaques and thrombosed plaques on CDUS almost perfect agreement exits with CTA identifying nearly all the calcified and thrombosed plaques in our patients however when the plaque is echogenic on CDUS and shows mixed density on CTA considerable difference arises between the CDUS and CTA findings with concordance rate of only 33%. In cases of simultaneous presence of mixed and calcified plaques in our study the concordance obtained was 92%.

No patient with vulnerable plaque was seen in our study

Out of the 24 echogenic plaques identified in our study, CTA was able to identify only 8 of these plaques with concordance of just 33% which is significantly lower when we compare our study to the similar study by **Sameh Abd El Raouf et al**[36] in which CDUS showed soft atheromatous plaques in 33 carotid arteries, and from them only 28 were confirmed by CTA with a concordance rate of 84.8%. The concordance rate in cases where colour doppler US showed mixed atheromatous plaques was 93.3% (14/15) which is approximately the same as in our study , and in cases when colour doppler US showed calcified atheromatous plaques, it was 66.7% (6/9) which is less when compared with our study. In another study by Vit A **et al**[37] , 3 out of 35 plaques on CT-angiography were determining total carotid occlusion; all three of them were also shown on colour-doppler sonography which corresponds well with findings of our study ; 12 of 35 plaques were responsible for a degree of stenosis over 60% on CT-angiography and 11 of them (91.6%) were correctly shown on colour doppler sonography. 19 out of 35 plaques were determining a degree of stenosis less than 60% on CT-angiography and 11 of them (89.5%) were correctly shown on colour-doppler sonography. The positive and negative predictive values were 92.3% and 95%, respectively, in detecting the plaques responsible for a degree of stenosis greater than 60%.

M Das et al[38] in their study found out that The sensitivity of dual source CT for the detection of calcification was 100% (standard deviation (SD) 0%, confidence interval (CI): 99–100), which is same as compared to our study. While the sensitivity for the detection of mixed plaques was 89% (SD 12%, CI: 79–98), it was 85% (SD 10%, CI: 76–92) for the detection of low-density fatty plaques. The mean degree of agreement was k=0.81 which is slightly more nevertheless comparable to our study in which the kappa value of 0.75 was observed indicating an overall good correlation.

However, poor correlation was seen in identifying echogenic plaques many of which were erroneously labelled as calcified plaques. This could be due to decreased resolution of the older generation of USG machine used with brightness of echogenic plaque being confused for calcification. For mixed, calcified and thrombosed plaques the degree of co relation was excellent.

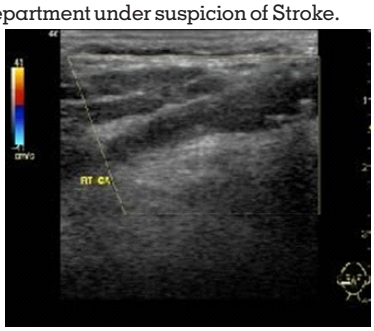
Hence we conclude that CDUS can be used as an initial screening tool for assessing the plaque composition with CTA being reserved for confirmation of the findings of CDUS.

CONCLUSION:

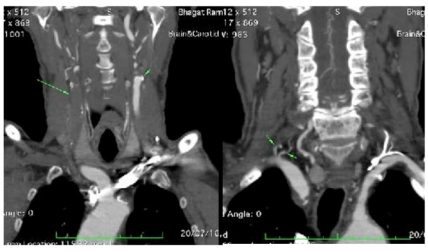
Owing to good correlation in defining grade of stenosis and plaque composition along with ease of use and cost effectiveness we recommend the use of CDUS as a first line screening examination in a patient of cerebrovascular disease. However, because of its relative insensitivity in some important plaque risk determinants for example plaque ulceration and presence of echogenic plaques we recommend the use of a second more definitive screening examination like CTA prior to any intervention being undertaken (in cases of significant stenosis) in order to produce a detailed and reproducible plaque characterisation and assessment of the degree of stenosis.

Illustrated Cases

- **Case 1 showing Total Occlusion:** A 70 year old male came to our department under suspicion of Stroke.

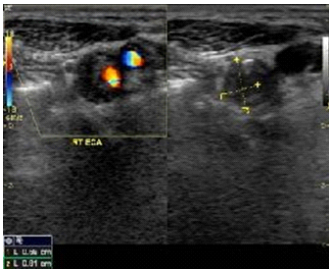


Images Case 1: Oblique coronal colour doppler images show presence of an echogenic thrombus with foci of calcification casting posterior acoustic shadowing in right CCA and ICA showing no colour flow on doppler suggestive of total occlusion .

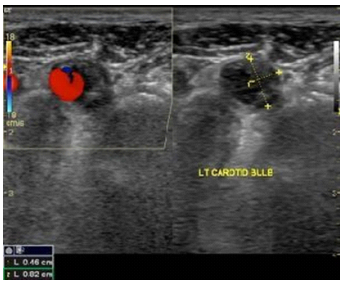


Images Case 1 CTA coronal MIP image(a) of the same patient shows a large thrombotic plaque with peripheral calcification (Green arrows) completely occluding its lumen of right CCA and ICA as seen on CTA along with collateral vessels arising from rt.subclavian artery(green arrows b).

Case 2 Showing Severe Stenosis: A 78 year old hypertensive and diabetic male came to our department under suspicion of stroke.



(a)

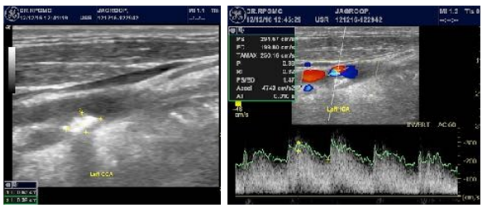


(b)

Images Case 2: Axial gray scale and colour doppler image (a) of right carotid artery show the presence of an echogenic plaque at right proximal ICA just distal to its origin measuring approx 0.8 by 0.6 cm causing severe stenosis. Echogenic plaque is also seen along the origin of right ECA causing its narrowing. Axial (gray scale and doppler image(b) of left carotid artery shows presence of an echogenic plaque measuring 0.8 by 0.5 cm arising from left carotid bulb extending to left proximal ICA causing severe stenosis of its lumen .

Images Case 2: Coronal MIP images of the same patient show soft plaques in Proximal ICA's with foci of internal calcifications causing severe luminal narrowing.**Case 3 Showing Moderate stenosis:** A 60 year old hypertensive male came to our department with complaints of Transient loss of vision right eye.

(a) (b)



(c) (d)

Images Case 3 : Coronal oblique gray scale and corresponding colour doppler pulse waveform images (a and b) of right ICA shows an echogenic plaque with foci of calcification measuring 0.7 by 0.2 cms (a) at right proximal ICA showing PSV of 134 cm/s (b) suggestive of mild stenosis. Oblique coronal gray scale and colour doppler pulse waveform images (c and d) of left ICA shows a calcified plaque at left proximal ICA measuring 0.6 by 0.4 cm (c) causing severe stenosis of left ICA with PSV of 294 cm/s (d).

Images Case 3: Coronal MIP images of the same patient shows a soft plaque (green arrow) in right proximal ICA (a) causing its moderate stenosis and a calcified plaque (green arrow) in left proximal ICA (b) causing its severe stenosis

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