



Carotid Plaque: Looking Beyond Stenosis - A Comparison between Duplex Sonography and CT Angiography

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Abstract

Background and Objectives: *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. 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. Ulcerated 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 US-ECD in the evaluation of carotid plaque complicated by ulceration 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 ulceration 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 ulceration. This can be ascribed, in part, to the fact that acoustic shadowing from calcification obscures ulcers, and the sonography probe may not be parallel to the axis of the vessel in the region of the ulceration. Sonography is limited by its accuracy and reproducibility, especially when the lesion is calcified. The recent development of 3D US and the use of CEUS may help improve the detection of carotid ulceration*

Keywords: *Plaque ulceration, 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 western world 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. 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)¹ and European Carotid Surgery Trial² and, the Asymptomatic Carotid Atherosclerosis Study³ but factors other than the degree of stenosis are also important in assessing whether a carotid lesion will remain clinically silent; plaques that are more prone to disruption or fracture and ulcerated plaques are associated with a higher risk of embolism and occlusion, producing ischemic neurologic events. In the NASCET study, in the group of patients who received medical therapy, 30% of patients who had a severe carotid stenosis associated with an ulcerated plaque suffered an ischemic cerebral event within 2 years, whereas only 17% of patients with severe stenosis but no ulcerated plaques had an ischemic cerebral event within 2 years¹ The presence of ulceration alone represents an important risk for neurologic symptoms⁴ and a high-grade stenosis, combined with plaque ulceration, produces an increased risk of stroke^{1,5} An accurate delineation of plaque morphology is therefore very important^{4,5}. Plaque ulceration is significantly more frequent in symptomatic patients. Plaque ulceration has been defined as “an intimal defect larger than 1000- μ m in width, exposing the necrotic core of the atheromatous plaque⁶

Conventional angiography has been considered the standard method for evaluating stenosis of the

carotid artery, but it is not sufficiently reliable for detecting plaque ulceration. Moreover, conventional angiography is also associated with an increased risk of thromboembolic events. Consequently, noninvasive techniques, such as ultrasound (US) echo color Doppler (US-ECD), and CT angiography (CTA) have been more and more frequently used to study carotid artery pathology.

The purpose of this study was to evaluate the diagnostic efficacy of multidetector row CT angiography (MDCTA) and US-ECD in the evaluation of carotid plaque complicated by ulceration with MDCT being taken as reference standard

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 ulceration

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).

Visual inspection of greyscale and Carotid US images

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 correlation criteria.

Ulcerations were classified based on location of ulcer neck and orientation⁷

Table 1: Types of Ulceration

Type 1	Ulcer that points out perpendicular to the lumen.
Type 2	Has a narrow neck and points out proximally and distally.
Type 3	Has an ulcer neck proximally and points out distally .
Type 4	Has an ulcer neck distally and points out proximally.

Observations and Results

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.

Analysis of ICA, common carotid artery and the carotid bifurcation was done in both methods and the atherosclerotic plaques were classified based on type of ulceration

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 Kock⁸.

Table 2 Interpretation of kappa coefficient and intra-class correlation coefficient.

K value	Degree of agreement
<0	poor
0 - 0.20	slight
0.21 - 0.40	fair
0.41 - 0.60	moderate
0.61 - 0.80	substantial
0.81 - 1	almost perfect

Comparative Analysis of Plaque Ulceration with CDUS and CT Angiography

The results of the duplex sonography were obtained, analysed and compared with those obtained by CTA and following inferences were made by us.

Common carotid artery

- Out of 60 CCA evaluated in our study, ulcerated plaques were seen in 14 arteries which were further subdivided various types into type-1(8), type-3(2),type-4(2) and type-5(2)
- CTA of the same vessels revealed presence of ulcerated plaques in 18 arteries of which 10 were of type- 1 morphology, 4 of type-2 morphology , 2 of type-3 and 2 of type-4 morphology.(table 3)
- For type 1 Ulcers out of total of 10 ulcerated plaques CTA was able to Identify only 6 of them (concordance rate of 60%)
- CTA was able to identify 2 vessels each having type 3 and 4 ulcerated plaques which is same as that reported on CDUS (Concordance 100%)
- For type 2 Ulcerated plaques on CDUS, out of total of 4 ulcerated plaque reported on CDUS none of them were reported as having the same morphology on CTA. 2 were found out to be normal and 2 were found out to be type 5 instead on CTA.
- In mismatch group, (table 4)(10 vessels having Ulcerated plaques) 6 plaques were underestimated by one category(60% of all non discordant scans) 2 plaques were Overestimated by one category and 2 plaques were over estimated by 2 categories (20% of non discordant scans)

CCD ulceration * CCA ulceration Crosstabulation

Table 3 Comparison of the Ulcerated plaques with CT angiography and colour Doppler US

		CCA ulceration					Total
		Normal	Type 1	Type 3	Type 4	Type 5	
CCD ulceration	Normal	40	2	0	0	0	42
	Type 1	4	6	0	0	0	10
	Type2	2	0	0	0	2	4
	Type3	0	0	2	0	0	2
	Type4	0	0	0	2	0	2
Total		46	8	2	2	2	60

		Value
Measure of Agreement	Kappa	.620
N of Valid Cases		60

Table 4 - Correlation of results of CT angiography and Doppler in grading of Ulcerated plaque in mismatch group of CCA

		Ulceration 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	40	2	0	0	0	
	Type 1	6	0	0	4	0	
	Type 2	0	0	2	2	0	
	Type 3	2	0	0	0	0	
	Type 4	2	0	0	0	0	
Type 5		0	0	0	0	0	

Overall the degree of agreement in evaluating the ulcerated plaque in CCA was good with kappa value 0.62

Internal carotid artery

- Of the total of 60 ICA CDUS evaluation of the vessels revealed 10 arteries (Out of 60 studied) as having ulcerated plaques 8 of which were of

type 1 morphology and 2 were of type 2 morphology

- CTA evaluation of the arteries 10 revealed the presence of ulcerated plaques of which 6 showed type-1 morphology, 2 show type 2 and 2 show type 3 morphology (Table 5)

ICD ulceration * ICA ulceration Crosstabulation

Table 5 Comparison of the Ulcerated plaques with CT angiography and colour Doppler US

		ICA ulceration				Total
		Normal	1	2	3	
ICD ulceration	Normal	44	2	2	2	50
	1	6	2	0	0	8
	2	0	2	0	0	2
Total		50	6	2	2	60

		Value
Measure of Agreement	Kappa	.198
N of Valid Cases		30

- Out of total of 50 arteries identified on CDUS, CTA was able to correctly identify 44 (88%) of these arteries with ulcerated plaques in remaining 6 vessels
- Of the 8 vessels showing Type 1 ulcerated plaques on CDUS only 2 were correctly identified on CTA as having ulcerated plaques with same morphology on CDUS (concordance rate of 33%).
- Only 2 vessels showing plaque with type 2 morphology was identified which could not be correlated in as the same category on CTA
- None of the type 3 plaque could be identified on CDUS whereas CTA angio showed their presence in 2 vessels
- In mismatch group (14 arteries), degree of ulceration was underestimated by one category on 8 arteries (57% of non discordant scans) ,overestimated by one category in 4 arteries (28% of all non discordant scans) and overestimated by one category in 2 arteries (14% of all non discordant scans) (table 6)

Table 6 - Correlation of results of CT angiography and Doppler in grading of Ulcerated plaque in mismatch group

		Ulceration By CT Angiography				Under-estimated by two categories
		Direct Correlation	Over-estimated by one category	Over-estimated by two categories	Under-estimated by one category	
Colour Doppler-US	Normal	44	2	4	0	0
	Type 1	2	0	0	6	0
	Type 2	0	0	0	2	0
	Type 3	2	0	0	0	0
		0	0	0	0	0

Overall the agreement for ulcerated plaques in ICA is poor with kappa value 0.20

Types of ulceration

Case 1: Type 1 Ulcerated Plaque



a



b

Images Case 1: MIP axial Images Case 1: MIP axial (a) and coronal images of a 65 year old patient (a, b) shows ulcerated plaque pointing out perpendicular to the lumen

Case 2: Type 2 Ulcerated plaque



a

b

c



d



e

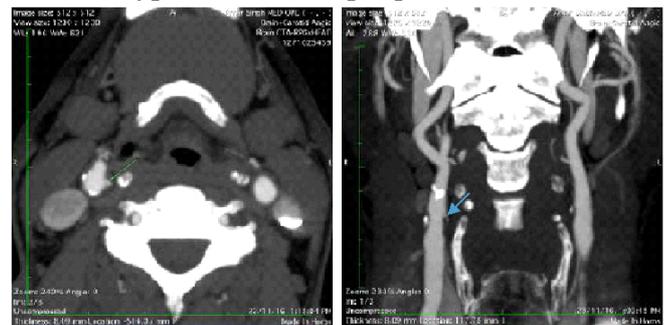
Images case 2: Axial (a), Coronal (b) Sagittal (c) MIP images and Volume reconstructed (d) images in a 75 year old male who came with stroke show an ulcerated plaque in right CCA with narrow neck that points out both proximally and distally. Axial MIP images (e) of the brain shows acute infarct rt occipital lobe

Case 3: Type 3 Ulcerated plaque



Image case 3: Coronal MIP image of a 65 year old female shows an ulcerated plaque with narrow neck that points out distally

Case 4: Type 4 Ulcerated plaque



a

b



Images case 8: Axial CTA (a) of a 63 year old male shows an ulcerated plaque in its medial wall. Coronal MIP image (b) of the same patient shows an ulcerated plaque (blue arrow) with narrow neck that points out proximally. Volume reconstructed (c) image shows the proximally project in ulcerated plaque.

Discussion

Carotid ulceration is now considered a major hallmark in determining the vulnerability of atherosclerotic plaque because it indicates a previous plaque rupture and is a strong predictor of subsequent events. Determining the presence of an ulceration is particularly important in the moderate stenosis group, because it may change the therapeutic approach. In addition, in the presence of a plaque ulceration, surgeons tend to manipulate carotid arteries with greater carefulness.

MDCTA generally has high sensitivity in detecting plaque ulceration. The identification of plaque ulceration may assist in the appropriate management of patients at risk of future ischemic events. We have reviewed the literature regarding the various radiologic techniques used to demonstrate plaque ulceration

A direct comparison of the sensitivity and specificity of different imaging modalities is difficult because the definition of plaque ulceration varies in different studies.

Pathologically, ulceration is defined as an erosion of the single cell-layer intima by microscopic examination⁽⁹⁻¹¹⁾ In some studies with CTA,^{12,13} a general definition “the extended lumen into plaque” has been used. In some of the CTA studies, a more specific definition has been described, such as the intimal defect must be larger than 1 mm in width^{14,15} or 2 mm in depth.¹⁶ Taking CTA as the reference standard for identifying and grading the ulcerated plaques and comparing them with CDUS, the degree of agreement in common carotid arteries and internal carotid arteries was given by the kappa values of 0.6 and 0.2 respectively in our study indicating poor agreement especially in internal carotid artery.

A similar study was done by Sameh Abd El Raouf et al¹⁷ in which the agreement in the ulcer identification was 88.4% but the resulting kappa value was 0.325 indicating poor agreement which correlated well with our study. In another study by Saba et al.¹⁸ in the definition of ulceration plaque, the observed agreements were 88.4% but the kappa value was only 0.325 which can be compared to our study. Similarly, in the definition of the type of plaque, the observed agreements were 77.2% and the kappa value was 0.657 which is again comparable to our study. Agreement observed in the evaluation of plaque morphology was 78.3% with a kappa value of 0.513 which is less when compared to our study. However, in contrast to our study, Reitera et al.¹⁹ demonstrated sensitivity of CDUS for detection of plaque ulceration 100% and specificity 93%. Likewise a study done by Detelina Valchkova Lukanova et al²⁰ 2015 showed the sensitivity of ultrasound, multi-detector computed tomography and magnetic resonance imaging is 94%, 83% and 100%, and the specificity is 93%, 73% and 89% for detection of unstable carotid plaque.

The study of various literature revealed that ultrasound has a relatively low sensitivity (60%) for the detection of ulcers, while the surface roughness is more accurately depicted (sensitivity 97%, specificity 81%)^{18,21,22}

Ajduk et al.²³ published direct comparison of MDCT and CDS for detecting plaque haemorrhage, demonstrating a high diagnostic reliability of the first over the second method (sensitivity 100% against 78.2% and specificity 70.4% against 59.2%. However, no such case was reported in our patients.

Moreover, CTA is far superior to US-ECD in detecting ulcerations we demonstrated that ulcerations are much more common in fatty versus calcified plaques and confirmed the results of Walker et al.²⁴

The relationship between plaque morphology and clinical behavior in the carotid circulation has been incompletely studied, but it has been demonstrated that cerebral infarcts are more frequent in patients with a lipid core than in patients without a lipid core and calcified carotid artery atherosclerotic plaques are less symptomatic than those that are noncalcified.⁸ Calcium likely confers stability to the plaque, resulting in protection against biomechanical stress and subsequent complications as ulcerations. We thus concluded that CDUS is inferior w.r.t CTA to assess plaque morphology and especially in identification of ulceration as. This can be ascribed, in part, to the fact that acoustic shadowing from calcification obscures ulcers, and the sonography probe may not be parallel to the axis of the vessel in the region of the ulceration. Sonography is limited by its accuracy and reproducibility, especially when the lesion is calcified. The recent development of 3D US and the use of CEUS may help improve the detection of carotid ulceration.

However, ionization must be considered when using CTA. Optimization of the scanning protocol and the use of new reconstruction techniques can help reduce the radiation dose. The application of dual-source CTA may also help to improve the sensitivity and accuracy in detecting ulceration within calcified plaques.

Conclusion

Because of its relative insensitivity in detecting some plaque characteristics of risk and relative insensitivity in stenosis quantification, it would be unwise to rely solely on the US-ECD exam alone. It would be appropriate to undertake a CTA exam in those patients who are candidates for carotid endarterectomy or any other intervention.

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