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Research Article

MRI and Carotid Duplex assessment of vulnerable carotid atheromatous plaques in acute ischemic stroke patients

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Abstract

Background: Stroke is a global health problem that leads to disability. In 2005, stroke was responsible for 5.7 million (16.6%) deaths, and 87% of these deaths occurred in low-income and middle-income countries. Two-thirds of strokes are ischemic in origin and 50% of these are associated with severe internal carotid artery disease. The underlying predominant cause of carotid artery disease is atherothrombosis. **Method:** 20 patients with acute ischemic stroke were enrolled in this study. They were diagnosed clinically and radiologically by MRI brain, then referred to us to be assessed by carotid Duplex and carotid MRI. **Results:** All patients had carotid atheromatous plaques that show more than one criteria of the following, lipid-rich necrotic core of the atheromatous plaque (90%), surface ulceration of the plaque (90%), thrombus on top (80%), hemorrhage in plaque (75%), only 35% had more than 90% stenosis of the carotid lumen by plaques. MRI assessment for carotid atheromatous plaques at acute ischemic stroke patients, it was evident that the right carotid arteries (CCA, ICA) were more affected 14 (70%), most of the atheromatous plaques had thin fibrous cap with lipid rich core 18 (90%), ulcerated surface18 (90%), calcification15 (75%), thrombus on top 16 (80%) as well as hemorrhage within the plaque 15 (75%) with statistically significant P-value (0.01, 0.0001, 0.0001, 0.04, 0.001,0.04) respectively. Most atheromatous plaques 10 (50%) caused about 70-90% luminal stenosis with statistically non-significant difference P-value 0.4. **Conclusion:** Carotid duplex and MRI had complementary role in assessment of carotid atheromatous plaques in stroke patients.

Keywords: Stroke, Atheromatous Plaque, Carotid Duplex, MRI, Vulnerable plaques

Introduction

Stroke is clinically defined as the syndrome of rabidly developing symptoms and signs of focal or global loss of cerebral function with no apparent cause other than of vascular origin. It is the third cause of death after coronary artery disease and all types of cancers. [1, 2].

Stroke is a global health problem and is a leading cause of adult disability. Of 35 million deaths attributable to chronic non-communicable diseases that occurred worldwide in 2005, stroke was responsible for 5.7 million (16.6%) deaths, and 87% of these deaths occurred in low-income and middle-income counties. [3, 4]

Two-thirds of strokes are ischemic in origin and 50% of these are associated with severe internal carotid artery disease, the underlying, predominant cause of carotid artery disease is atherothrombosis. [5, 6]

Vulnerable atheromatous plaques: It is a must to look beyond the lumen and the degree of stenosis and to identify those imaging characters of vulnerable carotid plaques that are best suited for stroke risk prediction including lipid rich necrotic core with thin fibrous cap, surface irregularity and ulceration, intra plaque hemorrhage, and to lesser extent calcification. All that would lead to thrombus

formation on top, then thrombus embolus formation .Finally stroke occurs. [7]

Criteria of vulnerable atheromatous plaque:

- Plaque ulceration: it means intimal defect more than 1 mm in width exposing the necrotic core of atheromatous plaque leading to activation of thrombosis cascade with formation of thrombus on top of ulcerating surface with more narrowing of lumen and increase possibility of detachment of the thrombus and embolization to reach cerebral arteries and completely occluding them. [8]
- Thinned fibrous cap: it is a layer of fibrous connective tissue that cover the lipid core of the atheromatous plaque, it increases risk of rupture of and increase risk of ischemic stroke.[9-11]
- Large lipid rich necrotic core: it increases risk of rupture of and increase risk of ischemic stroke.[9-11]
- Presence of intra plaque hemorrhage :-as a result of neovascularity or plaque rupture itself.[12]

Carotid Duplex study: is still the basic examination modality in carotid artery assessment as it is simple, cheap, easy to be applied, non-invasive and rapid. It measures the intima-media thickness as well as the heterogeneity or homogeneity of the atheromatous plaque, in addition to degree of luminal stenosis, blood flow parameters. [13]

MR imaging: it now provides accurate method of detection of the plaque components and intra plaque hemorrhage. This is very important as the effects of atheromatous plaques nowadays depend on the criteria of the vulnerable atheromatous plaques rather than degree of stenosis. [14-15]

Aim of the work

The aim of this study was to assess the criteria of vulnerable atheromatous plaques at stroke patients using carotid duplex and carotid MRI.

Patients and Method

Twenty patients (15 males and 5 females) who fulfilled Clinical and radiological diagnostic criteria for diagnosis of acute ischemic stroke were included in the study, who were referred to radiology department after being diagnosed - at neurology department - clinically and by brain imaging (MRI). Age ranged 40 up to 70 years old. Patients with recent history of stroke (within the last 2 weeks), with diagnosis of acute anterior circulation arterial cerebral ischemic event, based on both clinical assessment and cerebral imaging findings were included in the study. Patients with embolic causes of stroke, hemorrhagic cerebral stroke, posterior circulation ischemic stroke and patients with absolute contra indication to MRI assessment were excluded from the study. Informed consent was taken from all participants in the study or 1st degree relatives. The study was approved by the ethics committee of the Faculty of Medicine.

All patients were diagnosed clinically and radiologically by MRI brain to be acute ischemic stroke, then were subjected to carotid Duplex and carotid MRI

A. Carotid Duplex study for the cervical carotid arteries: using color Duplex machine, using high end Ultrasound machine and linear probe of high frequency 7- 9 MH to assess cervical carotid arteries.

B. MRI (Magnetic resonance imaging) for the cervical carotid arteries: using MRI machine, 1.5 Tesla system using cervical coil. Sequences (T1WI, T2WI, PDW and TOF).

Statistical analysis:

Data entry and analysis was done using SPSS version 21, graphics by Microsoft excel. Data presented as frequency distribution Z test, Chi square test and fisher exact test were used to detect the statistical significance. P-value of less than 0.05 considered as a cutoff significance

Results

Twenty acute ischemic stroke patients were included in this study (5 females and 15 males) with age group from 40 up to 70-year-old. Ischemic groups15 male stroke occurred more at elderly patients (61-70) year-old, with male predominance (75%) at all ages, as shown in **table (1).**

By carotid duplex assessment for cervical carotid artery, all 20 patients of the study had carotid atheromatous plaques, right carotid arteries (CCA, ICA) were more affected in 14 patients (70%), most of the atheromatous plaques were hypoechoic in 12 patients (60%),

and they had irregular surface in 15 patients (75%) with statistically significant difference (P-value 0.01, 0.03, 0.04) respectively.

Most atheromatous plaques in 9(45%) of the studied patients caused about 70-90% luminal stenosis, most plaques had calcification in 13(65%) and thrombus on top in 12(60%) of patients with statistically non-significant difference (P-value 0.3, 0.2, 0.2) respectively, as shown in table (2).

Table (3) shows: MRI assessment for carotid atheromatous plaques at acute ischemic stroke patients, right carotid arteries (CCA,ICA) were more commonly affected in 14 (70%) patients, most of the atheromatous plaques had thin

fibrous cap with lipid rich core in 18(90%) patients, ulcerated surface in 18(90%), calcification in 15 (75%), thrombus on top in16 (80%) and hemorrhage within the plaque in15 (75%) with statistically significant difference (P-value 0.01, 0.0001, 0.0001, 0.04, 0.001, 0.04) respectively. Most atheromatous plaques in 10(50%) patients caused about 70-90% luminal stenosis with statistically non-significant difference (P-value 0.4).

All acute ischemic stroke 20 patients had one or more characters of the vulnerable carotid atheromatous plaques. The most common characters noted were rich lipid necrotic core of plaque in 18 (90%) and surface ulceration in 18(90%) patients, followed by thrombosis on top of plaques, calcification of plaque, hemorrhage within plaque in (16(80%), 15 (75%) and 15 (75%) patients) respectively, as shown in fig. (1).

Table (1): Demographic distribution within Acute ischemic stroke patients

Age group(years)	Total number No=20 (100%)	Female No= 5 (25%)	Male No= 15(75%)
40-50	1(5%)	0(0%)	1(5%)
51-60	7(35%)	2(10%)	5(25%)
61-70	12(60%)	3(15%)	9(45%)

Table (2): Carotid Duplex assessment of atheromatous plaques within CCA and cervical ICA at ischemic stroke patients (N=20)

	Number of patients
Site	
Right carotid arteries	14(70%)
Left carotid arteries	6(30%)
P-value	0.01*
Stenosis	
Less than 70%	4(20%)
70% - 90%	9(45%)
More than 90%	7(35%)
P-value	0,3
Echogenicity of plaque	
Hyperechoic	3(15%)
Isoechoic	5(25%)
Hypoechoic	12(60%)
P-value	0.03*
Surface of plaque	
Irregular	15(75%)
Smooth	5(25%)
P-value	0.04*
Thrombus on top	
Present	12(60%)
Absent	8(40%)
P-value	0.2

P-value significant if less than 0.05

Table (3): Carotid MRI assessment of atheromatous plaques within CCA and cervical ICA at ischemic stroke patients (N=20)

Atheromatous plaque characters	Number of patients
Site	
Right carotid arteries	14(70%)
Left carotid arteries	6(30%)
P-value	0.01*
Stenosis	
Less than 70%	3(15%)
70% - 90%	10(50%)
More than 90%	7(35%)
P-value	0.4
Composition of plaque	
Thin fibrous cap, rich lipid core	18(90%)
Thick fibrous cap, poor lipid core	2(10%)
P-value	0.0001*
Surface ulceration of the plaque	
Present	18(90%)
Absent	2(10%)
P-value	0.0001*
Thrombus on top of plaque	
Present	16(80%)
Absent	4(20%)
P-value	0.0001*
Calcification	
Present	15(75%)
Absent	5(25%)
P-value	0.04*
Hemorrhage in plaque	
Present	15(75%)
Absent	5(25%)
P-value	0.04*

P-value significant if less than 0.05

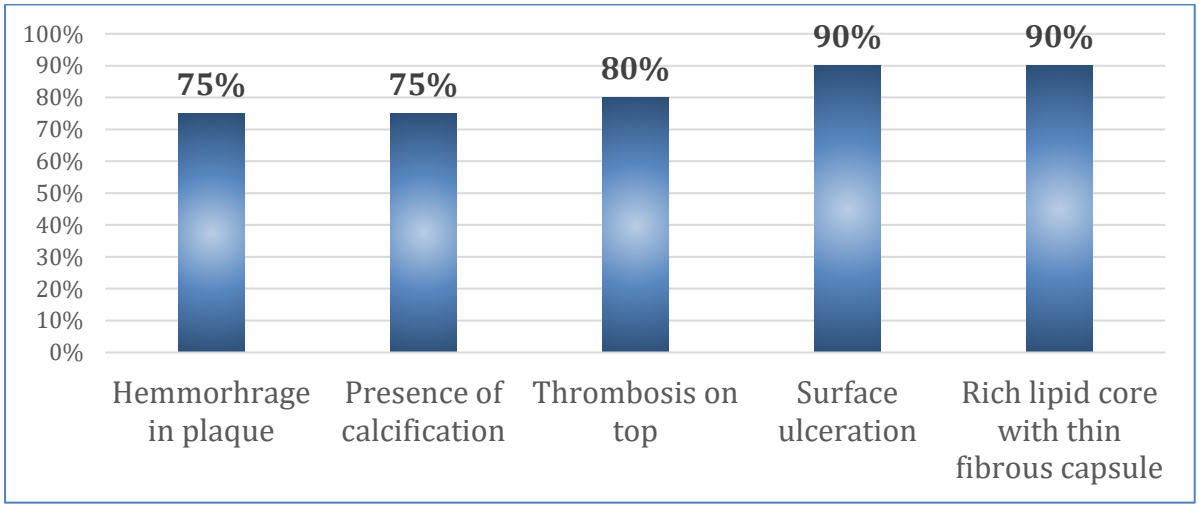


Figure (1): criteria of vulnerable carotid atheromatous plaques at acute ischemic stroke patients by carotid MRI (N=20)

Case

Case No.1

History:- 60 year-old male.
Clinical presentation:- Right sided lower limb weakness
Proved brain MRI findings:- Diagnosed as left parietal non hemorrhagic infarction
Carotid duplex:-

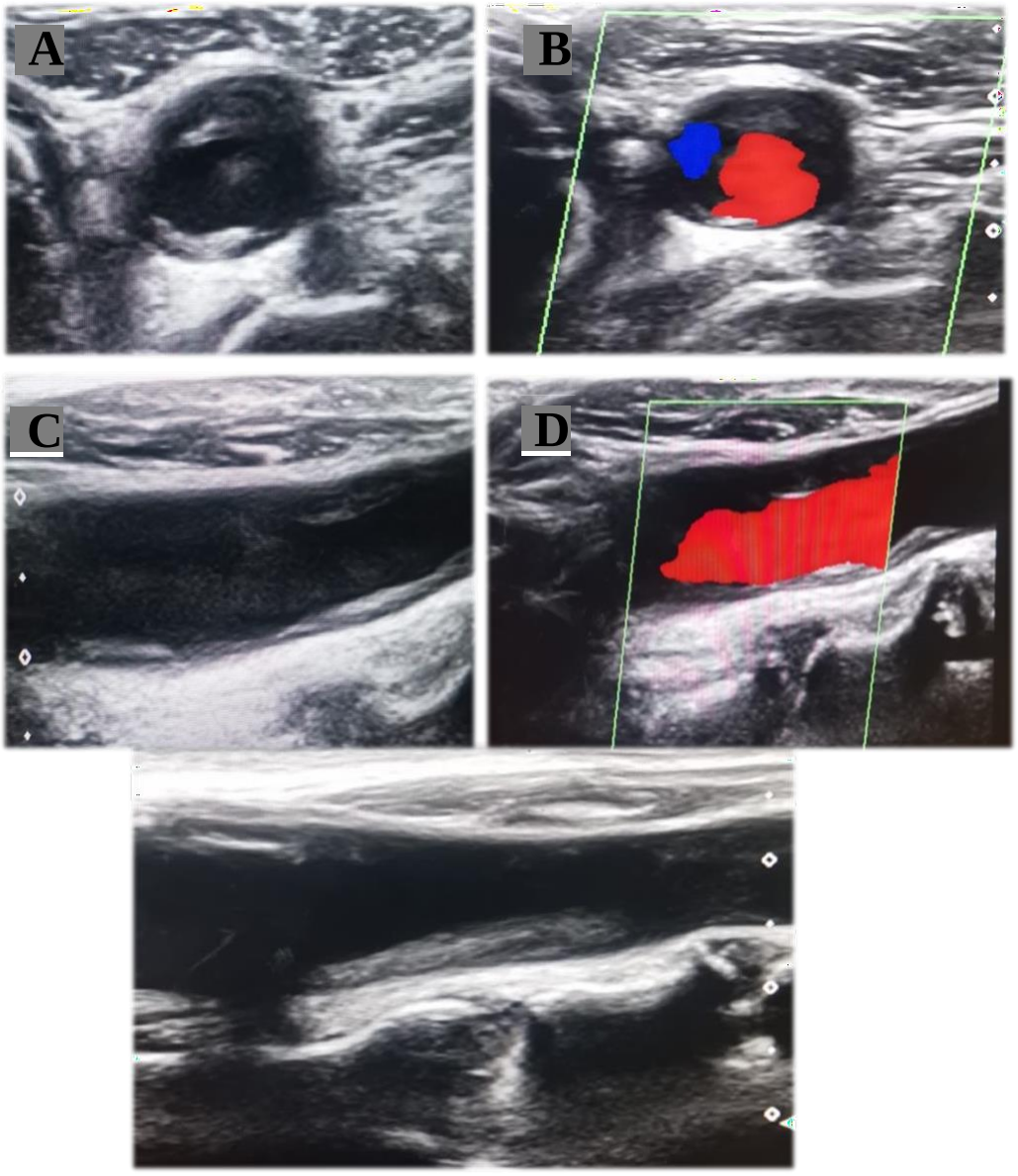
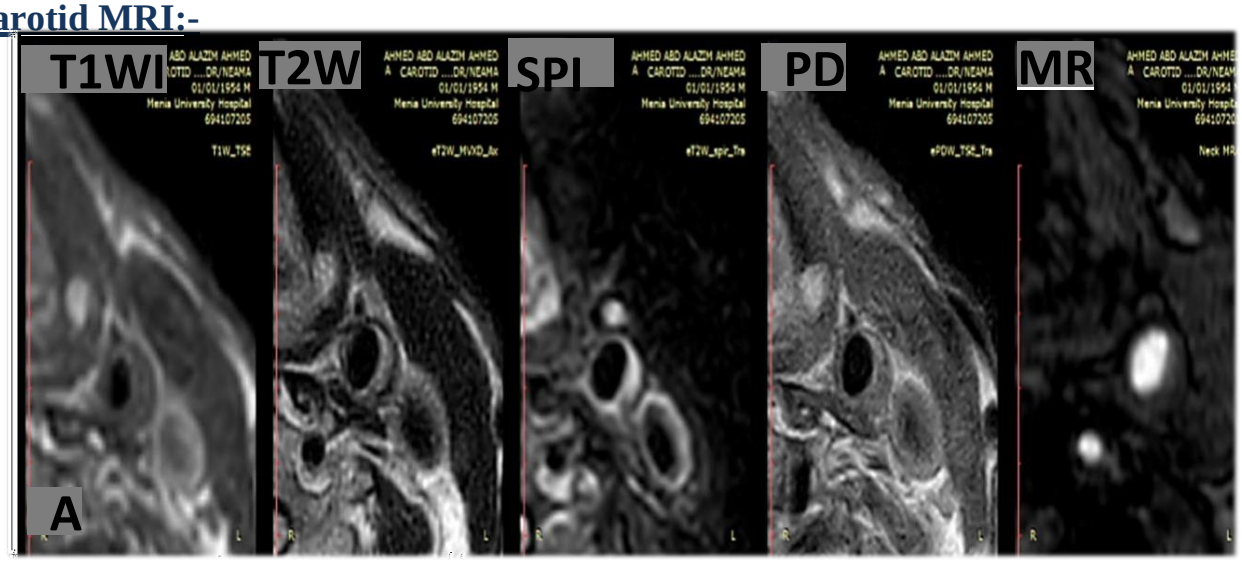


Figure 1
A, B: Transverse -section ultrasound /Doppler images of the left CCA ,
C,D: longitudinal –section ultrasound/Doppler images of left CCA
A hypo to iso echoic athermanous plaque with smooth surface exerting less than 70% stenosis of thelumen
E: longitudinal –section ultrasound image showing a hyper echoic atheromatous plaque at distal leftCCA.

Carotid MRI:-



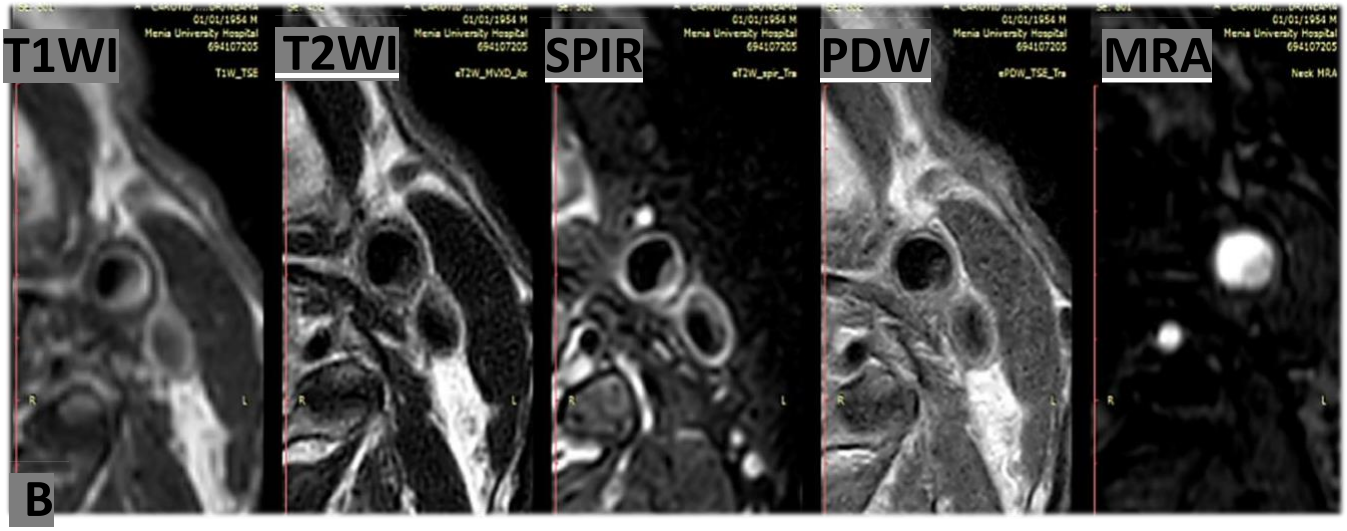


Figure 2

A: T1WI,T2WI and MRA axial images showing an atheromatous plaque within the left CCA with smooth surface and less than 70% occlusion of its lumen ,PDW axial image showing thinned fibrouscap

B:- A thrombus is noted at the distal left CCA that appear hyper intense at T1WI axial image , iso tohyper intense at T2WI axial image , At PDW axial image, it shows an interruption of the underlyingendothelium.

Radiological diagnosis:-

- **Vulnerable atheromatous plaque at left CCA with thinned fibrous cap that is seen interrupted at its distal portion with thrombus on top (about 2-3 weeks age) hyper intense at T1, iso to slight high signal at T2**

- MRI has converse role in detection of thrombus on distal margin of plaque (above endothelium lining) , not another plaque as considered by carotid Duplex

Case no.2

History:- 68 year-old male.
Clinical presentation:- Dysarthria for 15 minutes
Proved brain MRI findings:- left temporal non hemorrhagic infarction
carotid duplex:-

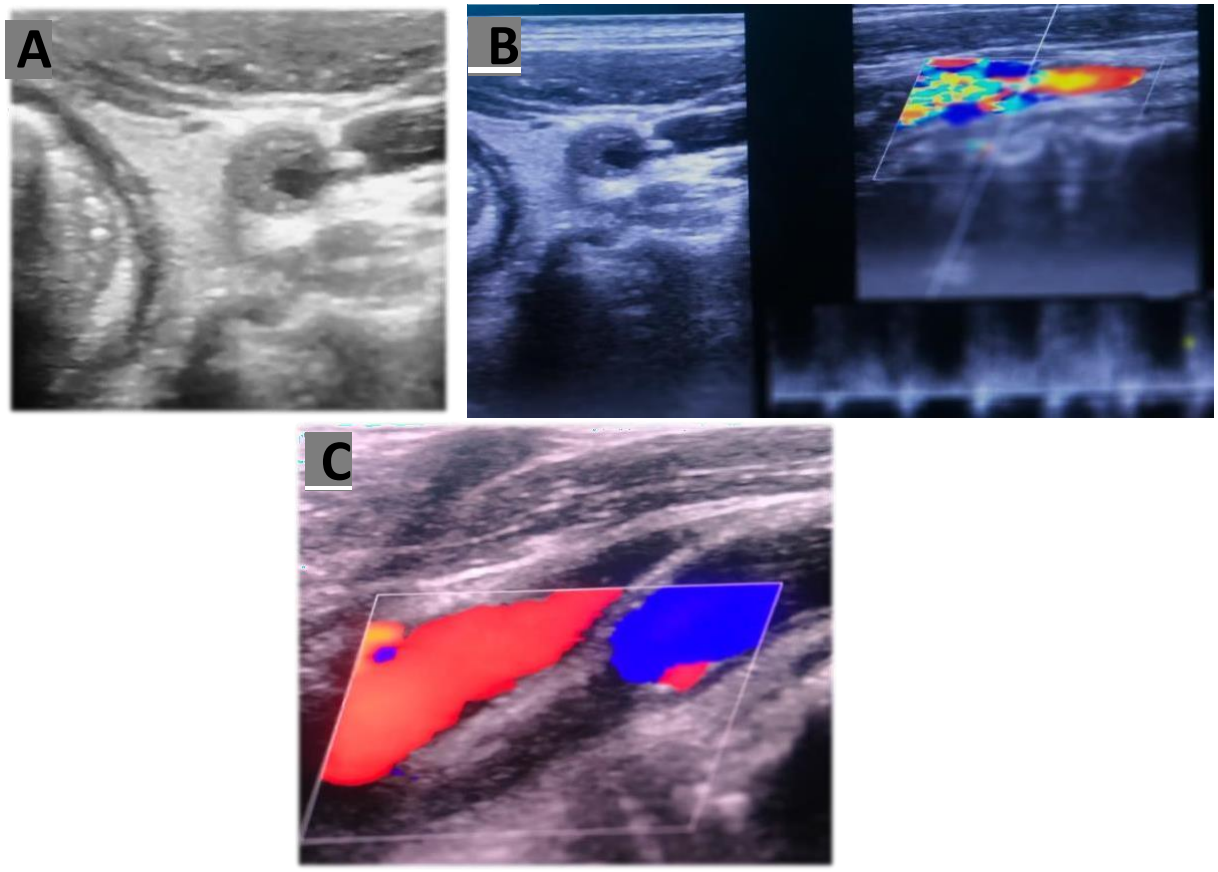


Figure 1

- **A,B** transverse section ultrasound/Doppler images of left CCA showing a hypo echoic atheromatous plaque seen at the left CCA with smooth surface .B, the plaque has more than 70% stenosis with high PSV about 250 cm/sec .
- **C** Longitudinal section ultrasound /Doppler images of cervical portion of right ICA that is seen completely occluded (same or relatively reduced caliber) by hypo to iso echoic thrombus…..**Chronicocclusion.**

Carotid MRI:-

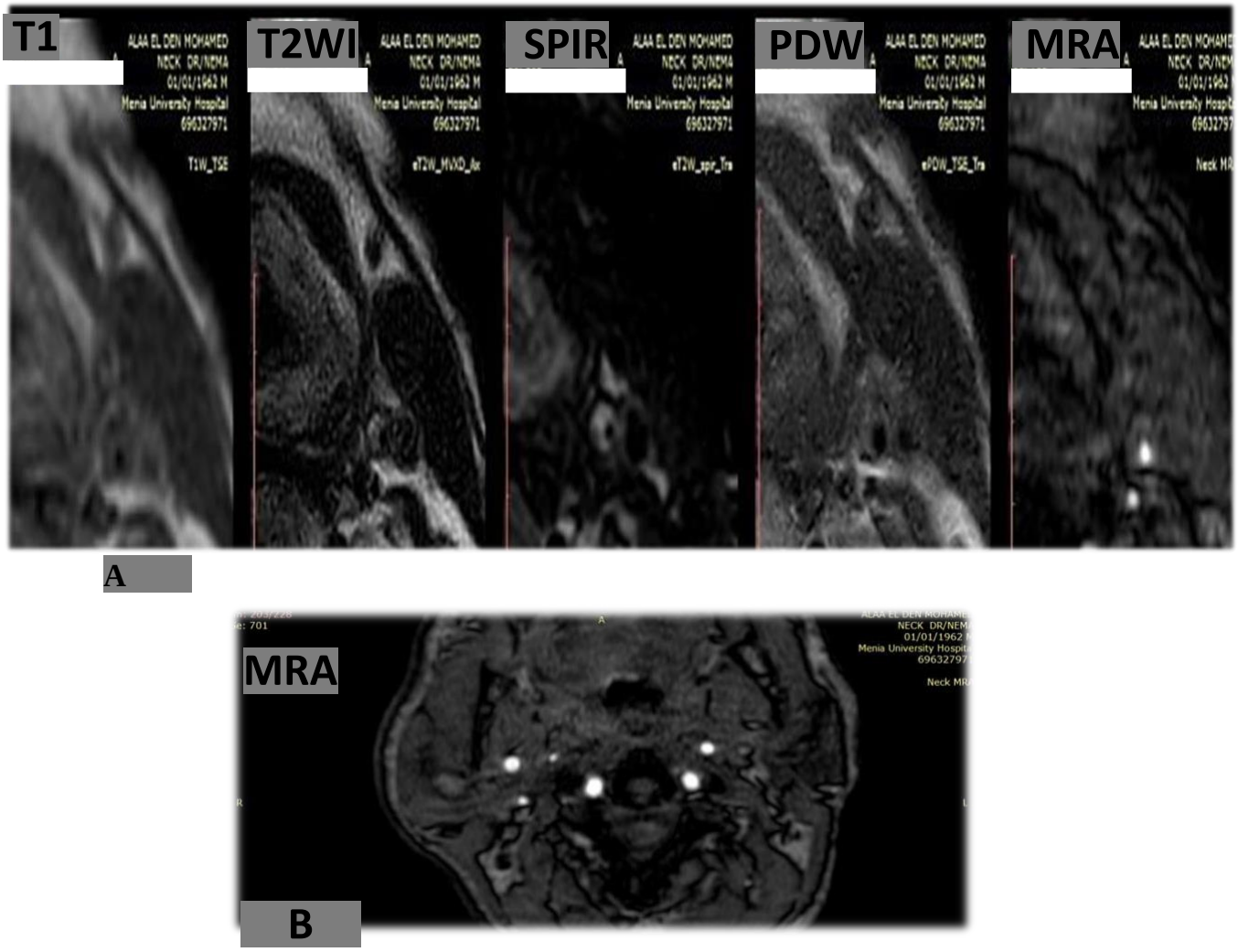


Figure 2

- **A**, An atheromatous plaque is noted at the left CCA with smooth surface that shows intra plaque hemorrhage attaining high signal at T1WI,SPIR axial images and T2 axial image denoting recent intra plaque hemorrhage (1 week age).
- **A**, Mixed calcification of plaque is noted (deep and superficial) , superficial calcification appears only at MRA .
- **B**: Near totally occluded right cervical ICA detected at MRA axial image as chronic thrombus
- (more than 6 weeks) appears with low signal intensity cannot be detected by other conventional MRI sequences . Prominent right ECA and ascending cervical artery at the right side due to chronic near complete occlusion of right ICA

- **Radiological diagnosis:-**
- Vulnerable atheromatous plaque at left CCA with intra plaque hemorrhage (recent about 1 week age) hyper intense at T1 and T2 SPIR as well as mixed calcifications
- MRI has additional role in detection of intra plaque hemorrhage and mixed calcification
- MRI has converse role in detection of tiny flow within the apparently totally occluded right ICA by carotid duplex.

Discussion

In this study, acute ischemic stroke in 20 patients had higher incidence with increase age, (61-70 years old) were 12 patients (60%), this was in agreement with the study done by Olivia van et al., 2005[16] and Díaz-Guzmán et al., 2008.[17] who revealed, age-specific prevalence rates of CVD, stroke and transient ischemic attacks increased exponentially with advancing age.

Regarding carotid MRI characteristics of atheromatous plaque, 18(90%) of stroke patients showed rich lipid necrotic core of their carotid atheromatous plaques with significant p-value =0.0001. This matched with the findings of Kevin DeMarco et al., 2014 [18] study of 97 consecutive patients with 50%–99% stenosis referred for carotid plaque MRI, there were significant associations between recent ipsilateral carotid stroke and the presence of a LRNC (lipid rich necrotic core) as well as the presence of a thin or ruptured FC (fibrous cap), with no correlation between carotid artery stenosis and symptoms.

Eighteen (90%) of stroke patients showed surface ulceration of their carotid atheromatous plaques with significant p-value =0.0001. This matched with Tobias Saam, 2007[19] who reported that one of the vulnerable plaques to had fibrous cap rupture and surface ulceration, confirmed that histological findings after using 3D TOF MRA demonstrating high level of agreement (89%) between MRA and histological findings. Also, in agreement with Alistair C. Lindsay et al., 2012[20], who clarified those carotid plaques seen in 22 of 41patients (54%) in the symptomatic group with neurological manifestation versus 8 of 40(20%) in the asymptomatic group (p-value 0.05). They were caused by surface rupture (24% vs. 5%; p-value 0.03).

Fifteen (75%) of stroke patients in our study, showed intra plaque hemorrhage of their carotid atheromatous plaques with significant p-value =0.04. This matched with Alistair C. Lindsay et al., 2012[20] who reported that carotid plaques were seen in 22 of 41 patients (54%) in the symptomatic group versus 8 of 40(20%) in the asymptomatic group (p-value 0.05). They were caused by intra plaque hemorrhage (34% vs. 18%; p-value 0.08). Also, Kevin DeMarco et al., 2014[18] noted that during a mean follow-up of 38 months in 154 patients with asymptomatic moderate carotid artery stenosis, 12 carotid cerebro-vascular events occurred. Both the presence and size of IPH (intra plaque hemorrhage) correlated with a new ipsilateral carotid stroke or TIA.

In this study, 16(80%) of stroke patients showed thrombus on top of their carotid atheromatous plaques with significant p-value =0.0001. This matched with Luigi et al., 2004[21] who showed a thrombotically active carotid plaque associated with high inflammatory infiltrate was observed in 71 (74.0%) of 96 patients with ipsilateral major stroke (and in all 32 plaques from patients operated within 2 months of symptom onset).

In this study, there is no significant difference (p-value=0.9) between patients with stenosis more than 70% at carotid duplex 16 (53%) and carotid MRI 17(56%), this matched with the findings of Paul J. et al., 2003[22] that gathered sixty-three publications on duplex, MRA, or both and were included in the analysis, yielding the test results of 64 different patient series on DUS(Duplex ultrasound) and 21 on MRA. For the diagnosis of 70% to 99% versus _70% stenosis, MRA had a pooled sensitivity of 95% (95% CI, 92 to 97) and a pooled specificity of 90% (95% CI, 86 to 93). These numbers were86% (95% CI, 84 to 89) and 87% (95% CI, 84 to 90) for DUS, respectively. For recognizing occlusion, MRA yielded a sensitivity of 98% (95% CI, 94 to 100) and a specificity of 100% (95% CI, 99 to 100), and DUS had a sensitivity of 96% (95% CI, 94 to 98) and a specificity of 100% (95% CI, 99 to 100).

Regarding carotid duplex ultrasound (DUS) in our study, atheromatous plaques were classified by DUS into three categories, hypoechoic 18(60%), isoechoic 8(27%) and hyperechoic 4(13%), but there are different studies with conflict to the accurate assessment of plaque echogenicity. This could be explained by David A. Russell et al., 2007[23] who reported that change in plaque echoegnicity occurred over months from incidence of CVI (cerebrovascular insult), whether Patricia et al., 2012[24] showed that changes in echogenicity occurred over week. Xiaowei et al., 2016[25] showed that echoge-nicity depended on its

compostion, for example hemmorrage and high fibrous content apperead hyperechoic.

Carotid Duplex had exclusive role as it was dynamic imaging technique so it could detect free floating thrombus as clarified by CSABA CSOBAY et al., 2011[26]

Conclusion

It was evident that stroke patients have more than one criteria for vulnerable atheromatous plaques that increased incidence of stroke. Ultrasound is not considered the best technique for detection of an irregular plaque surface or ulcerations because of acoustic shadowing of calcified components. MRI has exclusive role in detection of lipid core, fibrous cap of atheromatous plaques, so carotid duplex and MRI had complementary role in assessment of carotid atheromatous plaques in stroke patients.

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