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DIAGNOSTIC VALUE OF MAGNETIC RESONANCE IMAGING IN EVALUATING CAROTID ARTERY ATHEROSCLEROTIC PLAQUE MORPHOLOGY

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Abstract: Magnetic Resonance Imaging has the ability to describe vessel wall thickness, plaque structure, distinguish fibrotic, fatty, calcific or hemorrhagic plaque contents with excellent soft tissue contrast. Our aim in this study is to determine symptomatic and asymptomatic carotid plaque morphology and imaging properties. We tried to understand whether plaque components in images match with histopathological sections. MRI was performed in 37 patients known to have carotid stenosis and endarterectomy decision has been taken. 24 patients were symptomatic and 13 were asymptomatic for carotid disease. A surface coil used in MRI; 5 cm of carotid segment was imaged with the carotid bifurcation in the middle. Necrotic core, fibrous cap, hemorrhage, calcification and intraluminal thrombus were determined in MR images. After surgery, the specimens were evaluated by a pathologist who was blind to the radiological findings. All plaque contents (necrotic core, hemorrhage, calcification and fibrous cap) can be imaged and separated from each-other with MRI. Necrotic core was detected in 87.9% of patients on MR images. No significant difference was found between symptomatic and asymptomatic cases in terms of the rate and dimensions of necrotic core on MRI. The presence of calcification did not show a significant difference between symptomatic and asymptomatic cases. The sensitivity of MRI in detecting in-plaque hemorrhage was calculated as 82.3% and specificity as 68.75%. The calculated rates were interpreted as MRI is significant in distinguishing cases without bleeding. Fibrous cap was more preserved in asymptomatic patients. The structure of the atheroma plaque can be imaged and distinguished from each other with MRI. The statistical results did not show the expected performance mainly due to the small number of asymptomatic cases, which was the main limitation of the study.

Keywords: Carotid plaque, Plaque morphology, Vulnerable plaque, Magnetic resonance imaging

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1. Introduction

Stroke causes about 15 million death annually and is the 3rd most common cause of death after heart diseases and cancer (Kolodgie et al., 2007; Caliste et al., 2020; URL1). Ischemic stroke accounts for the largest reason followed by intracerebral hemorrhage and subarachnoid hemorrhage. The most common source of embolism in transient ischemic attacks and embolic stroke is the atherosclerotic disease of the carotid bifurcation (Thom et al., 2006; Rosamond et al., 2007). Developing radiologic diagnostic methods detect increasing number of carotid plaques in both symptomatic and asymptomatic people. The presence of asymptomatic plaques brings some questions in mind: What is the risk of the carotid plaque of an asymptomatic person? What is the risk of the plaque at the asymptomatic carotid side of a symptomatic one? Why a person with bilateral carotid plaque often has one sided neurologic symptom while the genetic and environmental conditions are the same for both right and left carotid artery? Questions induced scientists to investigate the morphology of the atherosclerotic plaques.

Postmortem studies of sudden death cases with coronary artery disease and histopathology studies of endarterectomy specimens confirms that the inner structure of the atherosclerotic plaque is also an important risk for stroke along with the degree of stenosis (Saam et al., 2006b).

Plaque morphologic features and composition which gave rise to the concept of ‘‘vulnerable plaque’’ have been suggested as a complement to the degree of luminal narrowing. Several morphologic features such as thin fibrous cap, large necrotic core, surface ulceration, hemorrhage and the extent of inflammatory activity within the carotid plaque have been reported as related to increased risk for stroke (Gronholdt et al., 2001; Kerwin et al., 2007). The detection of unstable plaque is important for preventing future stroke. Therefore noninvasive in vivo imaging of carotid atherosclerotic plaques holds considerable promise for clinical decision and treatment. Color or power Doppler ultrasound has been used to characterize carotid atherosclerotic lesion, is reproducible, easy and noninvasive but has its own limitations like dependency to operator, plaque position and low soft tissue contrast. Digital subtraction angiography (DSA) is a method to show vascular lumen and fails to show plaque morphology.

High-resolution magnetic resonance imaging (MRI) allows direct investigation of the vessel wall and is the most promising imaging method to visualize the carotid atherosclerotic plaque. MRI has excellent soft tissue contrast resolution and is able to characterize plaque components such as fibrous cap, lipid, hemorrhage, calcification and inflammatory activity. Beyond its ability to detect the degree of luminal stenosis, it can also catch out the features of instability and gives chance to determine asymptomatic patients with high risk of stroke. MRI is non-invasive and does not cause radiation exposure. It is also highly reproducible to follow-up the plaque progression.

We aimed to investigate the correlation of MRI and histopathological features between the symptomatic and asymptomatic plaques.

2. Material and Methods

2.1. Study Population

We examined 37 cases of carotid stenosis with endarterectomy decision at Dokuz Eylül University Medical Faculty. 27 patients were men (%73) and the median age was 65.8 (ages range 48 to 85). 24 patients were symptomatic while 13 patients were asymptomatic. Inclusion criteria for the symptomatic group included temporary visual loss, a transient ischemic attack or a stroke related to the diseased carotid artery within 6 months. The severity of carotid artery stenosis had been evaluated by DSA, magnetic resonance angiography (MRA) or computed tomography angiography (CTA), with the North American Symptomatic Trial Collaborators (NASCET) criteria. After the radiologic studies, all patients underwent carotid endarterectomy (CEA) for the treatment of the atherosclerotic carotid artery stenosis in our hospital. With respect to common risk factors for stroke, all patients were screened for hypertension, diabetes mellitus, hypercholesterolemia, coronary heart disease and smoking.

2.2. MRI Imaging

Patients were imaged at 1.5 T Philips Intera Achieva MRI system equipped with a surface coil (Philips Sense Flex Medium IPX4) within the week before surgery. The carotid bifurcation was centered and 5 cm segment of the artery was imaged. Axial T1, T2, proton weighted (PD) images were performed for black blood; 3D TOF MRA for bright blood. Data collected from electrocardiogram gated images. Black blood double inversion recovery technique with T1 and pre-saturation pulses with T2 and PD images were used to reduce luminal signal. MR imaging parameters are summarized in Table 1.

Table1. MR imaging parameters

Parameters	T1	T2	PD	3D TOF MRA
TR	1091 (RR)	2182 (2RR)	2182 (RR)	25
TE	18	40	15	4
FOV	120	120	120	120
Slice thickness	3	3	3	2
Gap	0.5	0.5	0.5	-1
TSE factor	9	5	5	
NSA	2	2	2	2
Matrix	208	208	208	208
Matrix reconstruction	800	800	800	800
Flip Angle (FA)	90	90	90	18
Fat Suppression	SPIR	SPIR	SPIR	Water select
Black-blood inversion delay (msec)	398.7	-	-	-
Mean study time (seconds)	04:50	02:48	02:48	02:30

Plaque tissue components such as lipid-rich necrotic core (NC), hemorrhage, calcification, luminal thrombus and fibrous cap (FC) were identified by using previously published MR imaging criteria (reference?). All signal intensities were compared with the sternocleidomastoid (SCM) muscle at a point adjacent to the carotid arteries. All NC dimensions measured at two plans. The FCs were categorized as thinner and thicker than 0.5 mm.

All patients have been questioned for any known allergic reaction especially for contrast agents. Following the unenhanced MRI series, 10ml gadopentetate dimeglumine (Magnevist ®, Bayer Healthcare Pharmaceuticals Inc., Whippany, New Jersey) injected via the antecubital vein 2 ml per second speed. Contrast enhanced T1 weighted series performed with the same imaging parameters as the non-enhanced series (TR, TE, matrix, FOV, FA). Two patients were excluded from the study because of poor image quality. MR images of two cases were excluded from the study due to severe motion artifacts. Totally 4 patient excluded from the study? 33 of the patients underwent endarterectomy.

2.3. Plaque Excision and Histopathologic Examination

After the surgery, plaque components were examined at histology sections. While excising the specimen careful attention was paid to not to harm the atheroma plaque. After fixation specimens added to paraffin, were sliced into pieces first 2 mm and then 4 microns.

At the first level hematoxylin-eosin (HE) dying, immune dying CD 68 (CD 68-Ab-4, Neomarkers®, New Hampshire, USA) 1/50 dilution and Aktin (Smooth Muscle Ab-1, Neomarkers®, New Hampshire, USA) 1/200 dilution have been used by the pathologist. CD 68 dyed the macrophage cells and actin the smooth muscle cells. The collagen fibers have been also dyed with Masson trichrome for histochemical analysis.

All specimens were examined by a pathologist who is blind to the symptoms and radiologic imaging results of the patients, according to the criteria in Table 2.

Table 2. Histopathologic examination criteria

1. Necrotic core:	a. Presence b. Size c. Position: concentric/ eccentric
2.Fibrous cap	a. Thickness b. Inflammatory cell infiltration (macrophage, lymphocyte) c. Smooth muscle cell density (decreased, medium, high) d. Preserved or ruptured e. fissures f. thrombus adjacent to the cap g. calcification
3. Lumen	a. thrombus b. a site where the endothelium is shed (erosion)
4. Ulceration	
5. Bleeding into the plaque (into the necrotic core or other area)	
6. Vaso -vasorum	
7. Calcification, calcified nodules	
8. Evidence of healed old plaque rupture	

2.4. Evaluation of Images and Matching with Histopathology Findings

Five different sets of MR images were obtained with different parameters at all levels displayed. The pathology preparations were re-evaluated under the light microscope and simultaneously brought side by side with the MR images and the compatibility of the radiologically detected lesions with the histopathologic appearance was investigated. While matching, criteria such as the distance to the main carotid artery bifurcation, morphological features such as lumen and wall shape, and the presence of large areas of calcification that can be easily detected were taken as basis.

Atheroma plaque tissue contents were defined according to MR imaging criteria previously published in the literature (Yuan et al., 2001; Chu et al., 2004; Saam et al., 2005). Signal intensity (SI) measurements were made by manually inserting Region of Interest (ROI) into the plaque contents that could be distinguished. SI was measured with ROI from an area of the SCM muscle on the same side that is closest to the carotid arteries and at approximately the same depth from the skin surface. The ratio and standard deviation values of the SI, in-plaque hemorrhage and the NC were calculated with the SCM muscle SI measurements at the same level.

2.5. Evaluation of plaque content with MRI

2.5.1. Fibrous cap (FC)

The FC was evaluated in three separate categories as thick, thin and torn. Based on the study of Hatsukami TS et al. (2000), those thicker than 0.25 mm were considered as "thick fibrous cap" and those thinner than 0.25 mm as "thin fibrous cap". According to the same study, fibrous caps which have preserved their integrity and are thick would be seen as a smooth, continuous, thick hypointense band adjacent to the lumen on 3D TOF images. Based on the studies in the literature, it was assumed that there might be moderate-to-high degree of contrast enhancement in contrast-enhanced MRI in the fibrous cap (Yuan et al., 2001; Wasserman et al., 2002). FC thickness was measured as the distance between two imaginary lines drawn perpendicular to the lumen and NC on black blood images. (Figure 1 and Figure 2).

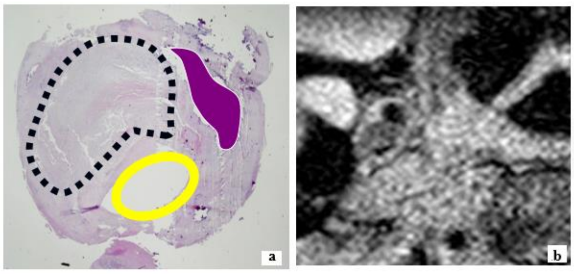

Figure 1. 58-year-old male, asymptomatic, almost complete stenosis in right ICA. In comparison with the a) histopathology preparation, the necrotic core, lumen and the fibrous cap located between the two are seen in the b) T1-weighted image. HE dye … necrotic core, - lumen, - calcification (on MR figure the structures need to be marked to understand the image).

2.5.2. Calcification

Calcification areas within the plaque would be seen as hypointense in all sequences. It was accepted that calcification areas adjacent to the luminal surface could not be separated from the lumen clearly in black-blood sequences but could be seen more clearly in 3D TOF images because the lumen was bright.

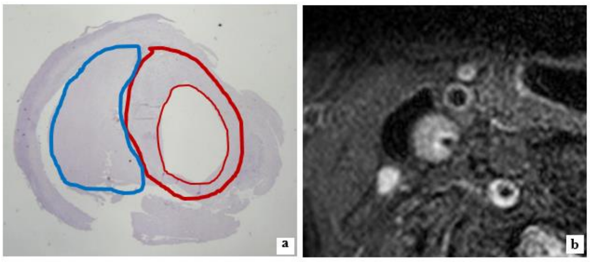

Figure 2. 63-year-old male, asymptomatic, almost complete stenosis in right ICA. In comparison with the histopathology preparation (a), the necrotic core, lumen and the fibrous cap located between the two are seen in the T2-weighted image (b) HE dye - Necrotic core, - fibrous cap (on MR figure the structures need to be marked to understand the image).

2.5.3. Hemorrhage

Defined signal changes were searched while investigating the bleeding signal, but lesions were not grouped according to bleeding time.

2.5.4. Necrotic core (NC)

According to the studies of Saam et al. (2006b), NC rich in fat has iso-hyperintense in TOF and non-contrast T1-weighted sequences and variable signal intensity in PD and T2-weighted sequences. NC does not or mildly enhance in contrast agent admitted T1-weighted images. It appears to be hypointense compared to the more strongly enhanced surrounding tissues. In all cases with NC, surface area was calculated in the largest section.

3. Results

24 (64.9%) of 37 patients had neurological symptoms, 13 patients (35.1%) were asymptomatic. In the symptomatic group, 2 patients (5.4%) had temporary visual loss in the last 6 months, 1 patient slurred speech (2.7%), 12 patients (32.4%) loss of sensation or motor function concerning the ipsilateral carotid artery territory, 3 patients (8.1%) syncope and 5 patients (13.5%) transient ischemic attack (TIA) (Figure 3 and Figure 4).

The carotid artery stenosis degrees measured with Doppler ultrasound before the operation in the study group are shown in Table 3.

Risk factors for cerebrovascular disease included hypertension in 29 patients (78.4%), diabetes mellitus in 11 patients (29.7%), hyperlipidemia in 24 patients (64.9%), coronary artery disease in 11 patients (29.7%), and smoking history in 19 patients (51.4%).

After MR imaging, 4 patients were excluded from the study, 2 with pulsation and motion artifacts and 2 patients were found unsuitable for surgery due to chronic lung disease. The data of the remaining 33 patients were evaluated.

3.1. Necrotic Core (NC)

Necrotic core was detected in all of the 33 specimens and in 29 (87.9%) of MR images 20 (90.9%) of 22 symptomatic cases were found to have NC, and 2 (18.1%) of 11 asymptomatic cases did not have NC. In the Fischer exact test, p = 0.586, there was no significant difference between symptomatic and asymptomatic patients in terms of the rate of NC on MRI.

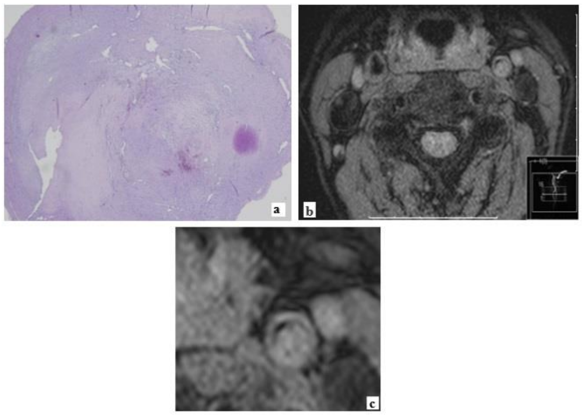

Figure 3. 52-year-old female, transient ischemic attack, left ICA occluded. In comparison with the histopathology preparation, a thrombus is observed in the necrotic core in the PD image. a) Thrombus in histopathology preparation b) Thrombus in the necrotic core in the PD image c) Thrombus in the necrotic core in the PD image (on MR figure the structures need to be marked to understand the image).

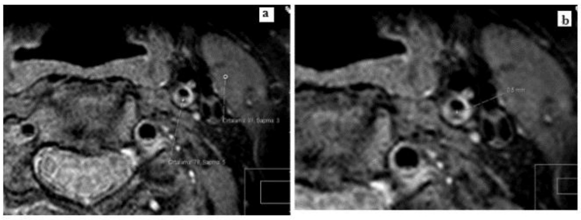

Figure 4. 56-year-old male, right hemiparesis, left ICA stenosis. View of the necrotic core on the left ICA a) Signal measurement from necrotic core and SCM muscle in PD image b) Measurement of fibrous cap thickness in PD image (on MR figure the structures need to be marked to understand the image).

Table 3. Carotid stenosis of study group according to NASCET criteria

	Asymptomatic	Symptomatic	Total
50-75%	1 (2.7%)	3 (8.1%)	4 (10.8%)
75-90%	2 (5.4%)	5 (13.5%)	7 (18.9%)
90-99%	6 (16.2%)	6 (16.2%)	12 (32.4%)
Near-occlusion	4 (10.8%)	8 (21.6%)	12 (32.4%)
Occlusion	1 (2.7%)	1 (2.7%)	2 (5.4%)
Total	14 (37.8%)	23 (62.2%)	37 (100%)

NC areas measured in MRI and pathology specimens were compared. Mean NC size for MRI was calculated as 9.17±8.92 mm² and for pathology as 11.06±10.68 mm².

The p value in the Wilcoxon ordinal signs test was 0.184 and the result shows no statistical difference MRI and histopathology.

The median values of NC areas measured in patients with and without symptoms were evaluated. Since the number of symptomatic and asymptomatic cases did not provide parametric conditions, Mann Whitney-U test was used for statistical analysis. U=103.5, z=-0.670, and P=0.51. As a result of the analysis, no significant difference was found between the patients with and without symptoms in terms of NC dimensions. In the MR images, necrotic core was more detectable in T2-weighted sequence. The ratio of NC signal intensity to SCM muscle signal is nearly 1 in PD, T1 and 3D TOF images, while the average ratio in T2-weighted images is 1.56±0.67 and higher than other sequences.

3.2. Hemorrhage

MRI hemorrhage signal changes were best seen in T1 and T2-weighted images. In-plaque hemorrhage was detected in 16 (48.5%) of 33 patients in histologic examination, while it was detected in 14 patients (45.2%) on MRI. The sensitivity of MRI was 82.3%, specificity was 68.75%, positive predictive value was 78.5%, and negative predictive value was 70.5%. The calculated rates were statistically interpreted that MRI can be used instead of histopathology and has a significant selectivity in distinguishing cases without bleeding (Figure 5).

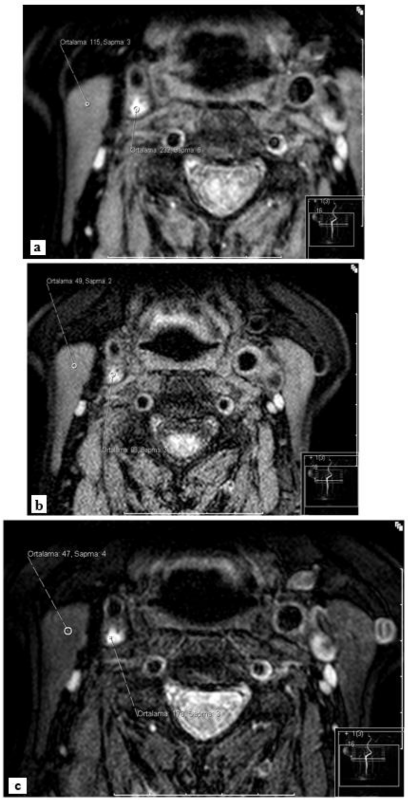

Figure 5. 69-year-old female, transient ischemic attack, near-occlusion in right ICA. Hyperintense hemorrhage in PD, T1 and T2 in the right ICA a) Hyperintense hemorrhage in PD b) Hyperintense hemorrhage in T1W c) Hyperintense hemorrhage in T2W.

In histopathological examination, 7 (63.6%) of 11 asymptomatic cases did not have hemorrhage within the atheroma plaque, while 12 (54.5%) of 22 symptomatic cases had in-plaque hemorrhage. Pearson's chi-square test was P=0.325, which indicates that there is no significant difference between symptomatic and asymptomatic patients in terms of in-plaque hemorrhage in pathology examinations.

On MR images, hemorrhage was detected in 10 (45.4%) of 22 symptomatic cases, while 7 (63.7%) of 11 asymptomatic cases did not have hemorrhage. In the Fischer exact test, P=0.719, no significant difference was found between patients with and without symptoms in terms of the rate of hemorrhage on MRI.

The ratio of hemorrhage signal to SCM muscle signal was close to 1 in PD and 3D TOF images, but in all other sequences the hemorrhage signal was higher than the muscle signal. The average signal ratio in T1-weighted images is 1.63±0.22, and in T2-weighted images it is 3.25±1.19, which is higher than other sequences.

3.3. Calcification

30 of 33 patients were found to have calcification in both histopathology MR images. The sensitivity and selectivity of MRI is 100% and the statistical result was interpreted as MRI can be used instead of pathology in defining the presence of calcification (Figure 6).

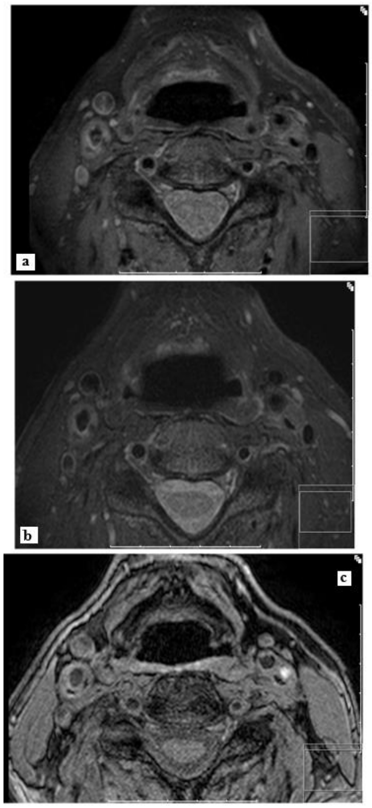

Figure 6. 85-year-old male, transient ischemic attack, 75-90% stenosis in right ICA. Hypointense calcification in PD, T2 and TOF MRA in the right ICA a) Hypointense calcification in PD b) Hypointense calcification in T2W c) Hypointense calcification in TOF angiography (on MR figure the structures need to be marked to understand the image).

3.4. Macrophage and lymphocyte Cell Infiltration, Density of Smooth Muscle Cells, Fibrous Cap Thickness and Integrity

These were evaluated histopathological in all cases (35 cases) that were operated. Macrophage and lymphocyte cell infiltration was found to be high in 13 (59.1%) of 22 symptomatic cases and in two (15.4%) of 13 cases without symptoms. In statistical analysis, the P value was 0.012, indicating that macrophage and lymphocyte infiltration was significantly higher in symptomatic cases compared to asymptomatic ones.

The number of smooth muscle cells decreased in 68.2% of symptomatic cases. The rate of large amount of smooth muscle cells in asymptomatic cases was calculated as 69.2%. The P value in statistical analysis is 0.032, which indicates that the amount of smooth muscle cells is significantly higher in asymptomatic cases compared to symptomatic ones.

3.5. Fibrous Cap

In histopathological examination, thickness and integrity of the fibrous cap could be evaluated in 28 of the 35 operated patients. Fibrous cap thickness was measured more than 0.25 mm in 91.6% of the asymptomatic cases. In 56.2% of the symptomatic patients, there was a FC thicker than 0.25 mm. The P value was calculated as 0.088 in Fisher's exact test. There was no significant difference in FC thickness between patients with and without symptoms. The fibrous cap integrity was preserved in 81.3% of symptomatic cases and 81.8% of asymptomatic cases. The P value was calculated as 1.000, and there was no significant difference between the symptomatic and asymptomatic cases in terms of the integrity of the fibrous cap.

In MR images, FC thickness was 0.5 mm in 12 cases, less than 0.5 mm in 8 cases (mean 0.65 mm), and thinner than 0.5 mm in 6 cases, it was thought to be thinner than 0.5 mm in 3 cases but its continuity was not observed (ruptured cap?) And fibrous cap could not be seen in 4 cases.

Histopathological examination was based on 0.25 mm. According to this: FC was thicker than 0.25 mm in 19 cases, 0.25 mm in 6 cases, less than 0.25 mm in 2 cases, and in 6 cases FC could not be seen. 3 of the cases that could not be seen in pathology were lesions defined as ruptured fibrous cap on MRI. As a result, fibrous cap was not seen in 4 cases in MRI and in 6 cases in pathology.

There is no result about the ulceration, vaso vasorum, evidence of healed old plaque ruptured?

4. Discussion

Studies on the pathophysiology of stroke shows that the degree of stenosis in the carotid artery has a poor correlation with symptomatic occlusion and revealed the definition of "vulnerable plaque structure", which is prone to rupture and bleeding and increases the risk of thromboembolism or occlusion. According to histopathological studies, atherosclerosis progression is sporadic and depends on the fissure or rupture of the atheroma plaque. The presence of large acellular necrotic core and bleeding, separated from the lumen by a thin fibrous cap in an unstable rupture-prone plaque structure (Falk, 1992; Bassiouny et al., 1997).

Since carotid angiography does not provide information about plaque morphology other than ulceration on the luminal surface, non-invasive imaging techniques are needed to show the carotid artery wall. MRI seems to be an ideal imaging method with its high soft tissue resolution and multiplanar imaging. It provides the opportunity to examine all vascular beds such as the aorta, coronary arteries and carotid arteries.

In our study, all MR examinations were performed on a 1.5 T system. Recently, ex-vivo studies have been carried out on 3T and above systems to provide higher spatial resolution and signal to noise ratio (SNR).

The multi-channel phased array coil used in the study has been shown highly effective in carotid artery imaging and provide a significant increase in SNR (Hayes et al., 1996; Fayad, 2002). The superficial location of the carotid arteries provides a very suitable ground for obtaining data simultaneously from each channel of the multi-phase array spiral (Roemer et al., 1990). There are two general approaches to image vascular structures with MRI: Bright-blood imaging and black-blood imaging. Bright blood appearance is typically seen in gradient echo sequences (GRE) used in MRA. The bright blood technique is insufficient to directly evaluate the internal structure of the atheroma plaque due to the high signal coming from stationary tissues. In addition, saturation formed in blood protons due to the dephasing effect of the flow may cause an overestimation of the degree of stenosis (Jackson et al., 1998; Townsend et al., 2003).

Black blood techniques based on the principle of eliminating the signal from the flowing blood provide a wide range of use in examining the vascular wall structures and allow to define the luminal surface. Black blood imaging is based on two basic techniques: in-flow saturation (22) (Edelman et al., 1990) and double inversion recovery (DIR) (23). (Edelman et al., 1990).The DIR technique is very successful in removing the blood signal and has a low dependence on blood flow velocity (Simonetti et al., 1996).

In our study, 3D TOF MRA technique was applied in bright blood imaging, and other sequences (T1, T2, PD) were obtained by black blood technique. Due to its time-consuming nature, the DIR technique was used only in T1-weighted images. The signal of intravascular blood was deleted in PD and T2-weighted images with cardiac trigger and pre-saturation bands.

In our study MRI has a high sensitivity in detecting NC correct positive cases. In the study, no significant difference was found between symptomatic and asymptomatic cases in terms of the rate of NC on MRI.

Takaya et al. (2006), performed control MRI after 38.2 months of follow-up to154 patients. They found evidence of thinning of the fibrous cap, bleeding in the plaque and increase in NC diameters in patients with symptoms.

According to this research, each 10 mm^2 enlargement of NC increases the clinical symptom risk 1.6 times compared to the normal population, while the presence of intraplaque hemorrhage and thinning of the fibrous cap increases this risk 2.6 times. Despite that some authors did not find any significant difference between the size and presence of NC and calcification in symptomatic and asymptomatic plaques (Saam et al., 2006a) in bilateral carotid plaques with neurological symptoms in the single carotid artery territory.

Since the number of cases in our study did not match the parametric conditions, we used the Mann Whitney-U test to evaluate any relationship between necrotic core size and being symptomatic. As a result of the test, there was no significant difference in terms of NC area. This result is consistent with the results of some studies in the literature. It was thought that the low number of cases in our study might have affected the statistical results.

When evaluating MR images, the necrotic core was more pronounced in T2-weighted sequence compared to the others. The ratio of necrotic core signal intensity to SCM muscle signal is close to one in proton density, T1 and 3D TOF images, while the average ratio in T2-weighted images is 1.56±0.67 and higher than other sequences.

According to the studies published by Jianming et al. (2005), the fat-rich necrotic core has iso-hyperintense signal compared to the muscle in TOF and non-contrast T1-weighted sequences, and variable signal intensity in PD and T2-weighted sequences. They do not or slightly enhance in post-contrast T1-weighted images and appeared to be hypointense compared to the more strongly enhanced surrounding tissues. Yuan et al., also measured the ratio of fat-rich necrotic core signal intensity to SCM muscle significantly lower than the fibrous cap (Yuan et al., 2001).

Since 30 of 33 patients were found to have calcification in both histopathological examination and MRI, the presence of calcification did not show a significant difference between symptomatic and asymptomatic cases. As mentioned in previous studies, calcification was observed in the atheroma plaque as well as in other tissues, with low signal intensity and sharp margins. 3D TOF MRA sequence which uses gradient echo sequence demonstrated calcification the best.

In our study MRI had a high sensitivity in detecting the presence of in-plaque hemorrhage and this information is in accordance with the literature. The lack of a significant relationship between in-plaque bleeding and symptomatology may be due to the small numbers of cases. There are many studies in the literature showing that MRI has high sensitivity and specificity in defining bleeding within the atheroma plaque (Kampschulte et al., 2004; Kerwin et al., 2007). Classification according to the location and age of hemorrhage with more cases may be more meaningful to explain the relationship between the presence and absence of symptoms.

The study with the largest case series of symptomatic carotid plaques in the literature was conducted by Redgrave et al. with of 526 symptomatic cases. According to this research, rupture of the FC, large NC and dense macrophage infiltration play an important role in plaque instability. They showed that macrophage infiltration is a stimulus for FC rupture (Redgrave et al., 2006). In their retrospective study published by Yuan et al. (2002). Rupture of the fibrous cap in developed atheroma plaques was closely related with symptoms. In a study comparing the ipsilateral and contralateral carotid arteries with stroke in symptomatic patients, intraplaque hemorrhage and FC rupture were found at a higher rate in the ipsilateral atheroma plaque (Yamada et al., 2007).

In our study, as a result of histopathology examinations, the amount of smooth muscle cells was significantly higher in asymptomatic cases compared to symptomatic cases, and macrophage and lymphocyte infiltration was found to be significantly higher in symptomatic cases. 91.6% of the asymptomatic cases and 56.2% of the symptomatic cases had a FC thicker than 0.25 mm. Although the rates indicate that the thickness and integrity of the FC is more preserved in asymptomatic patients, statistically there was no difference between symptomatic and asymptomatic cases in terms of fibrous cap thickness and integrity. Although MR findings alone can distinguish between symptomatic and asymptomatic plaques, it did not show the performance we expected statistically. The statistical results were mainly due to the small number of asymptomatic cases, which was the main limitation of the study.

Author Contributions

All authors have equal contribution and all authors read and approved the final manuscript.

Conflict of Interest

The authors declared that there is no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval/Informed Consent

The Dokuz Eylul University Clinical Research Ethics Committee granted approval for this study (approval number 206/2008 and date 26.05.2008), and all patients provided written informed consent to participate in all procedures associated with the study.

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