The determination of the value of contrast enhancement in carotid artery plaques with multi detector computed tomography

Multi dedektör bilgisayarlı tomografi ile karotid arter plaklarında kontrastlanma miktarlarının saptanması

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Abstract

Aim: The purpose of the study is to determine the accuracy of carotid artery plaque density measurements using multi detector computed tomography (MDCT) with contrast administration to differentiate symptomatic from asymptomatic plaques.

Materials and Methods: Seventy-two patients who did not have calcified plaques were identified retrospectively among patients undergoing neck and brain MDCT due to atherosclerotic carotid artery disease diagnosis or pre-diagnosis. The plaque density measurements were made on the same axial unenhanced and contrast-enhanced sections in large window, using a circular ROI in 1-4 mm² in size. The symptom differentiation of patients was based on neurological examination and radiological findings. The measured density values were compared according to the clinical and laboratory findings and medical histories of the patients. Student t-test was used for statistical analyses.

Results: Significant differences (p<0.001) were found between the unenhanced and contrast-enhanced plaque densities, but the same density difference was not observed among symptomatic patients. A significant relationship was shown between the plaque density and localization (p<0.003). In addition, the comparison between the degree of stenosis and symptoms was statistically significant (p<0.001). There was no significant association between the plaque density and symptoms, gender, stenosis side, infarct type, hyperlipidemia, hypertension, diabetes, coronary artery disease and cigarette use.

Conclusion: An increased density with MDCT was determined depending on the contrast agent uptake in carotid plaques. However, it was not statistically significant between the symptomatic and the asymptomatic patients groups.

Keywords: Carotid plaque, plaque density, CT angiography.

Öz

Amaç: Multi dedektör bilgisayarlı tomografi (MDBT) ile karotid arter plaklarının kontrastsız ve kontrastlı görüntüleri üzerindeki dansite artışının saptanması ve bu dansite artışının semptomatik hastalardaki miktarının belirlenmesi amaçlandı.

Gereç ve Yöntem: Aterosklerotik karotid arter hastalığı tanı ya da ön tanısıyla supraaortik damarların incelenmesine yönelik MDBT tetkiki yapılmış ve kalsifik plak içermeyen 72 hasta retrospektif olarak tespit edildi. Plak dansite ölçümleri, kontrastlı ve kontrastsız olmak üzere aynı aksiyel kesitlerde, geniş pencerede, 1-4 mm² büyüklüğündeki dairesel ROI kullanılarak yapıldı. Hastaların semptom ayrımında nörolojik muayene bulguları ve radyolojik görüntüleme bulguları kullanıldı. Ölçülen dansite değerleri hastaların özgeçmiş, klinik ve laboratuvar bulguları ile karşılaştırıldı. İstatistik hesaplamaları student-t testi ile yapıldı.

Bulgular: Tüm hastaların kontrastsız ve kontrastlı plak dansiteleri arasındaki fark anlamlı (p<0.001) bulundu, fakat semptomlu hastalarda aynı dansite farkı tespit edilmedi. Plak dansitesi ile lokalizasyon arasında anlamlı (p<0.003) bir ilişki saptandı. Ayrıca stenoz derecesi ile semptom arasındaki karşılaştırma (p<0.001) anlamlı idi. Plak dansitesi ile semptom, cinsiyet, stenoz tarafı, infarkt tipi, hiper lipidemi, hipertansiyon, diabet, koroner arter hastalığı varlığı ve sigara kullanımı arasında anlamlı ilişki bulunmadı.

Sonuç: MDBT ile karotid plaklarında kontrast madde tutuluşuna bağlı dansite artışı, semptomatik ve asemptomatik hasta grupları arasında anlamlı bulunmadı.

Anahtar Sözcükler: Karotis plak, plak dansitesi, BT anjiografi.

Introduction

Throughout the world, death from ischemic stroke associated with cerebrovascular diseases is in third rank following coronary diseases and cancer (1). Nearly 800,000 people experience stroke every year, either new or recurrent. More than 15 million people suffer from stroke each year worldwide, resulting in a mortality of 5 million (2). Ischemic stroke, as well as being a frequent cause of death, is the primary reason for disability in adults. Patients with ischemic stroke comprise of more than half of the patients referred to hospital due to neurologic diseases. It is obvious that a stroke is a very important and preventable health problem in our country whose population is increasingly getting older (1).

Two types of embolism cause an ischemic stroke; cerebral embolism and cerebral thrombosis. The most important cause of an ischemic stroke (approximately one third) is an embolic stroke. The major cause of an embolic stroke is atherosclerotic plaques in the internal carotid artery (ICA). Aortic atherosclerotic plaques are common in patients with an ischemic stroke of an undetermined etiology, and in particular those with carotid, intracranial and coronary atherosclerosis, or with high intima media thickness (IMT) values. In these patients, the computed tomography angiography (CTA) of the aorta should be seriously considered (3).

In recent years, studies on vulnerable plaque imaging have increased. In the standard imaging of atherosclerotic carotid artery lesions, Ultrasonography (USG), Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) can be used. USG is unable to give morphologic details such as fibrous capsule thickness and hemorrhage which are still known as important features of plaque sensitivity even today (4,5). MRI has given the highest specificity in the establishment of plaque hemorrhage and it has shown a relatively lower sensitivity (6-10). However, new CT technologies with a multi detector can rapidly scan arteries from the arch of the aorta to the base of the skull at the arterial phase and with a higher resolution. Identifying plaque calcifications, ulcerations, and intraluminal thrombosis is possible with a CT (11-13). Furthermore, CT angiography has a high sensitivity and a high negative predictive value for carotid disease. CT angiography appears to be an excellent screening test for internal carotid artery stenosis, and the authors advocate its use for the initial imaging of patients with a suspected stroke or transient ischemic attack (TIA) (14).

Our study focuses on vulnerable plaque distinctions on CT images. The purpose of the study is to determine the accuracy of carotid artery (CA) plaque density measurements using multi detector computed tomography (MDCT) with contrast administration in order to differentiate symptomatic (vulnerable) from asymptomatic plaques.

Materials and Methods

This retrospective study was carried out by using the image archive at the radiology department of Ege University Medical School. We identified 72 patients from the archive who had had a supra-aortic neck and brain CT examination that did not include calcification and showed 50% or more ICA stenosis in their carotid bifurcation. The neck and brain MDCT angio examinations were carried out using a 128 detector CT system (Somatom Sensation; Siemens, Erlangen, Germany). The MDCT angio examination protocol included kVp: 120, mAs: 100-225, slice thickness: 0.6 mm, kernel filter: 326f medium smooth, tube rotation time: 0.3 s, pitch: 0.8, detector coverage: 128*0.6 mm, and matrix: 512*512. The examinations were performed by using scans with both an unenhanced and enhanced-contrast as a cover from the supra-aortic area to the vertex of the brain. Contrast application was performed using an automatic injector (Ulrich) and by giving intravenous (4-5 ml/s) 60 ml non-ionic contrast material, directly after 25 ml of serum physiologic.

To differentiate between symptomatic and asymptomatic patients and stenosis, clinical examination and radiologic findings were used according to the American Heart Association and American Stroke Association recommendations on carotid endarterectomy for carotid artery stenosis (Table-1,2) (24-26). The clinical findings were assessed by a neurologist with 5 years of experience. The radiological findings were determined by two interventional and neuro-radiologists with 12 years of experience by examining the CT and MRI images of the patients. According to the American Heart Association and American Stroke Association recommendations on carotid endarterectomy for carotid artery stenosis and also our findings, patients having embolic stroke/ischemic stroke or the presence and type of infarction (embolic/watershed) on the same side as the ICA plaques on the MDCT angio and MRI images, and a cured carotid endarterectomy + medical therapy were considered to be "symptomatic"; in the case of the presence of a lesion contralateral to the plaque, these patients were considered to be "asymptomatic" (Table-1,2) (24-26).

The plaque measurements were performed on images unenhanced and enhanced and contrasted by using cross-sections at the same table level. The cross-sections on which the plaque measurements were performed were magnified by 200%.

Table-1. Overview of Carotid Endarterectomy versus Medical Therapy Trial.*

Trial (year)	Stenosis (%)	Treatment	Results
Symptomatic patients			
NASCET (1991)	70–99	CEA / PTA + medical therapy	65% lower rate of ipsilateral cerebral events with CEA
ECST (1991)	70–99	CEA / PTA + medical therapy	Incidence of ipsilateral ischemic stroke 2.8 versus 16.8% with aspirin alone
VA (1991)	50–99	CEA / PTA + medical therapy	Death or stroke 7.7% with CEA versus 19.4% with medical therapy
Asymptomatic patients			
ACAS (1995)	60–99	CEA / PTA + medical therapy	Relative risk reduction of 53% with CEA
ACST (2004)	60–99	CEA / PTA + medical therapy	5-year stroke risk 6.4% with CEA versus 11.8%
VA (1993)	50–99	CEA / PTA + medical therapy	61% lower risk of TIA or stroke with CEA

*ACAS: Asymptomatic Carotid Atherosclerotic Study; ACST: Asymptomatic Carotid Surgery Trial; CEA: Carotid endarterectomy; ECST: European Carotid Surgery Trial; NASCET: North American Symptomatic Carotid Endarterectomy Trial; PTA: Percutaneous transluminal angioplasty; TIA: Transient ischemic attack; VA: The Veterans Affairs Cooperative Study Group (22,24).

Table-2. American Heart Association and American Stroke Association Recommendations on Carotid Endarterectomy for Carotid Artery Stenosis.*

Stenosis (%)	Recommendation	Level of recommendation
Symptomatic stenosis		
High grade (≥70%)	CEA / PTA mortality rate <6%	Class I level of evidence A
Moderate (≥50 and <70%)	CEA / PTA depending on patient	Class I level of evidence A
Mild (<50%)	No indications for CEA / PTA	Class I level of evidence A
Asymptomatic stenosis		
High grade (≥60%)	CEA / PTA mortality rate of <3%	Class I level of evidence A

*CEA: Carotid endarterectomy; PTA: Percutaneous transluminal angioplasty (23,24).

Table-3. Demographic Data Showing The Patients' Clinical Status.*

	Gender		Symptom		Infarct		Infarct Type		Localiz.		HL		HT		DM		CAD		Smoke	
	F	M	+	-	+	-	E	W	B	pB	+	-	+	-	+	-	+	-	+	-
n	20	52	40	32	40	32	27	13	58	14	25	47	21	51	8	64	9	63	13	59
Pre-D	32.2	36.7	37.8	33.8	36.2	33.4	39.5	33.0	38.1	28.5	34.7	36.1	35.5	35.7	30.1	36.3	32.1	36.1	32.8	36.2
Post-D	57.3	57.0	56.7	57.5	54.2	58.0	60.3	48.2	60.1	44.5	53.8	58.8	52.3	59.1	52.8	57.6	51.6	57.9	49.4	58.8
ΔD	25.1	20.2	18.8	23.6	17.9	24.6	20.7	15.2	22.0	16.0	19.1	22.7	16.8	23.3	22.7	21.3	19.5	21.7	16.6	22.5

*Localiz.: Localization; n: Number; Pre-D: Density on unenhanced image; Post-D: Density on enhanced-contrast image; ΔD: Density difference between unenhanced and enhanced-contrast images; F: Female; M: Male; E: Embolic; W: Wateshed; B: Bulbar; pB: Post-bulbar; HL: Hyperlipidemia; HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease.

All the measurements were made on the cross-sections with and without contrast in order to establish the transition densities between the plaque and arterial lumen, and the same wider window level (width=900, level=250) was used. Initially, the measurement was made on the contrast-enhanced cross-sections to both visualize the arterial lumen and to clearly establish the location of the plaque. Subsequently, the density measurements were repeated on the unenhanced image with the same localization and the same table level. Single circular ROI area with a magnitude of 1-4 mm^2 was used for the density measurements according to the status of stenosis (Figure-1,2).

The SPSS Program was used for statistical analyses. The independent-samples T test was used to compare the density rates according to clinical status and the dual comparisons were done with the paired sample T test. The results were evaluated according to their significance status. A ROC Curve analysis was conducted to explore the diagnostic value of unenhanced and enhanced images in detecting symptomatic patients.

Results

The data of these 72 patients that had at least 50 % bulbar and post-bulbar carotid stenosis are summarized in Table-3. The mean age of the patients was 67.13 years (ranging from 37 to 82 years). The mean degree of the stenosis associated with the carotid artery plaque was measured as 72.29 % (50-95).
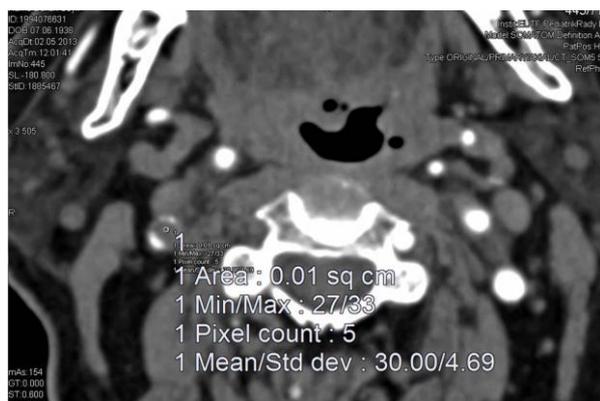
Figure-1. The ROI area on enhanced-contrast sections over the plaque located in the right carotid artery.
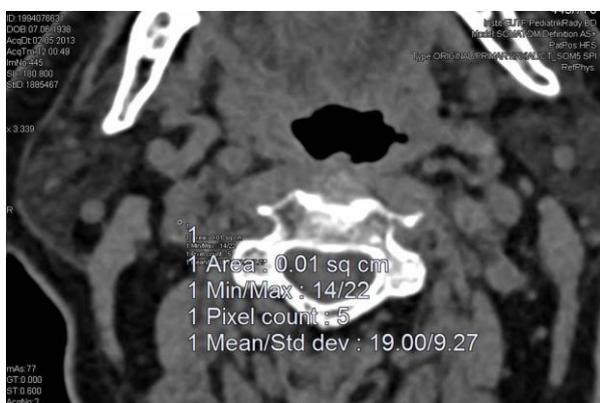

Figure-2. The ROI area on unenhanced sections over the plaque located in the right carotid artery.

Significant difference was detected in three different types of analyses. The first was the difference between the average plaque density of the unenhanced images as 35.67 (6-70) Hounsfield Unit (HU) and the average plaque density of the enhanced contrast images measured as 57.14 (17-141) HU. The mean increase in the plaque density after contrast was found to be 21.47 (0-94) HU. This increase is statistically significant (p<0.001).

The second difference was in the plaque density (Pre-D) according to plaque localization (p<0.003); the density value of plaques at post-bulbar localization being lower.

Thirdly, the degree of stenosis was significantly different according to symptomatology (p<0.001). The stenosis percentages of symptomatic patients were higher.

According to the ROC Curve analysis, the unenhanced (pre-D) and enhanced (post-D) image densities were not found to be useful for detecting symptomatic patients (Figure-3).

A statistically significant relationship was not detected between the plaque density and symptoms, gender, the site of the stenosis, the type of infarction, hyper lipidemia, hypertension, diabetes, presence of coronary artery disease or smoking status.
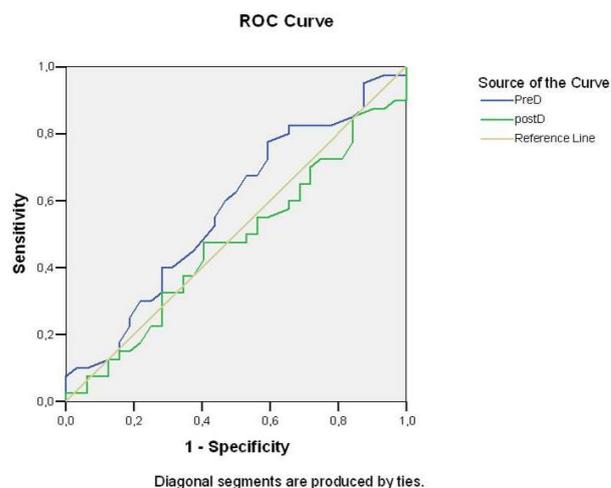

Figure-3. ROC Curve analyze of densities between on unenhanced (pre-D) and enhanced (post-D) images of symptomatic patients.

Discussion

As a result of pathological studies carried out on plaques, a classification (also approved by the American Heart Association) was developed. There are eight types of atherosclerotic lesions according to this classification. Fibrotic lesions are characterized by fibrous tissue and do not contain a lipid structure. Fibrotic and calcific plaques are more stable plaques and their probability to rupture is very low; however, they exhibit a symptom of hampering blood flow from the carotid artery (15).

The main aim in radiological imaging of a patient with atherosclerotic carotid artery disease is to detect the degree of carotid artery stenosis caused by the plaque. As the percentage of stenosis increases, the possibility of becoming symptomatic increases. The generally accepted view is that plaques that cause 70% or more stenosis should be treated (16).

De Weert et al. (17) suggested that the surface structure of the atherosclerotic plaque can be examined by an MDCT angio. Adraktas et al. (18) and Van Gils et al. (19) were able to reveal the risk factors showing temporal alterations on the plaques of the patients with carotid stenosis who were followed up with MDCT. The use of ionized radiation and the artifacts resulting from the calcifications and metallic implants limit in general the utilization of CT. Furthermore, it is not able to show the plaques' soft components such as a hemorrhage (20). A diagnostic improvement in the discrimination between soft tissues through a dual energy CT has been reported; in the future this technique could be used more frequently in carotid plaque examination (21).

In our study, a significant difference was found between the unenhanced and enhanced contrast plaque densities, the plaque densities increasing after the contrast medium administration on MDCT. The retention of the contrast material means that the plaques contain

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inflammation and neo-angiogenesis. Generally vulnerable plaques which are likely to become symptomatic contain plenty of inflammation cells and microvascular angiogenesis. In light of this information, theoretically vulnerable plaques (i.e. symptomatic plaques) are expected to retain more contrast material than stable, asymptomatic plaques. In the literature, there are only a few studies on this topic which use the same technique presented here (i.e., MDCT) with inconsistent results. Saba et al. have found statistically significant density increases in symptomatic plaques and suggested that the discrimination of "vulnerable" plaque could be made in MDCT angio examinations where unenhanced and enhanced contrast imaging is performed (22,23). On the contrary, we could not find any significant difference between the asymptomatic and symptomatic plaques in terms of density increase on the unenhanced and enhanced contrast images in MDCT. Ha et al. have found similar results with a lack of significant correlation in the averaged HU value between the pre-contrast and post-contrast early arterial phase and between the symptomatic and asymptomatic sides, in MDCT. However, they had found a statistically significant difference in the post-contrast HU values and difference of pre-contrast and post-contrast HU values between the symptomatic and asymptomatic sides (27).

Our study demonstrated that there was a statistical difference among the plaque densities between the bulbar and post-bulbar locations; the plaques at the post-bulbar location having lower density values. Lower densities imply that the plaque contains more fat and/or less micro-calcification. These characteristics are likely to belong to the "vulnerable" plaque. Besides the degree of plaque stenosis among the symptomatic patients were also found to be significantly higher in our study, which is also consistent with literature (16).

In the density measurement on MDCT cross-sections, some of the limitations of this study that we thought influenced the results negatively are given below;

1. There may be changes in the locations of unenhanced and contrast-enhanced examinations due to breathing, swallowing and other causes. This could result in an error in measuring location.

2. Beam heartening artifact affects density measurements directly. Although plaques containing calcification were not included, the effects of these artifacts could originate from other soft tissue and bony structures and could not be completely eliminated.

3. Since contrast-enhanced images were taken at the early arterial phase to prevent venous contamination for ideal MDCT angiography, intra-plaque contrast retention (density increase) might not have been sufficiently established; thus imaging at a later phase might give more correct results.

Conclusion

According to our results, contrast agent uptake due to increased density has been observed in the carotid plaque. However, the increase was not statistically significantly different between symptomatic and asymptomatic patients groups.

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