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Relation Between Cardiovascular Disease Risk Factors and Common Carotid Artery Intima Media Thickness

Kardiyovasküler Hastalık Risk Faktörleri ve Karotis Arter Intima Media Kalınlığı Arasındaki İlişki

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ABSTRACT

AIM: *To determine the effects of age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, history of coronary artery disease and cerebrovascular disease on carotid intima media thickness.*

METHODS: *Patients (N=222) undergoing Color Doppler Ultrasound examination of the extra cranial carotid arteries for any reason in a four-month-period were prospectively investigated. Posterior wall intima media thickness on 1-1.5 cm distal part of both common carotid arteries was measured three times for each patient. The mean values of measurements of right and left common carotid arteries, the presence of atherosclerotic plaque and vessel stenosis ≥ 15% were recorded. The effects of age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, and cerebrovascular disease on common carotid arteries intima media thickness and the relationship between common carotid arteries intima media thickness and plaque existence were investigated.*

RESULTS: *Age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease and cerebrovascular disease individually increased the common carotid arteries intima media thickness according to univariate analysis. All of the parameters but diabetes mellitus were defined as risk factors by using regression analysis. Hypertension followed by hyperlipidemia, coronary artery disease and cerebrovascular disease had more power.*

CONCLUSION: *Intima media thickness of common carotid arteries is affected by un-modifiable factors such as age and sex and by modifiable factors such as smoking, hypertension, hyperlipidemia, coronary artery disease and cerebrovascular disease.*

Key words: *cardiovascular diseases; carotid intima-media thickness; demography; Doppler; echocardiography; risk*

ÖZET

AMAÇ: *Yaş, cinsiyet, arteriyel hipertansiyon öyküsü, diabetes mellitus, hiperlipidemi, koroner arter ve serebrovasküler hastalık öyküsü ve sigara kullanımının karotis intima media kalınlığı üzerine etkisini belirlemektir.*

YÖNTEM: *Herhangi bir nedenden dolayı kliniğimizde, dört aylık periyotta ekstrakranial karotis arterlere yönelik Renkli Doppler Ultrasonografi incelemesi yapılan olgular (N=222) prospektif olarak değerlendirildi. Her olgunun karotis intima media kalınlığı, her iki ana karotis arterin yaklaşık 1-1,5 cm'lik distal bölümünden, yalnızca posterior duvardan, üçer kez ölçüldü. Sağ ve sol ana karotis arterden ölçülen değerlerin ortalaması alınıp kaydedildi. Aterosklerotik plak varlığı kaydedildi. Çap ölçümüne göre ≥ % 15 darlığı olan olgular seçildi. Yaş, cinsiyet, hipertansiyon, diyabet, hiperlipidemi, kardiyovasküler hastalık öyküsü ve sigara kullanımının ana karotis arterin intima media kalınlığı üzerine etkisi ve plak varlığı ile karotis karotis intima media kalınlığı arasındaki ilişki araştırıldı.*

BULGULAR: *Yaş, cinsiyet, sigara, koroner arter ve serebrovasküler hastalık öyküsü, hiperlipidemi, hipertansiyon ve diabetes mellitus, univariate analizde ana karotis arterin intima media kalınlığı üzerine tek başlarına etkili risk faktörleri oldukları saptandı. Yapılan regresyon analizi sonucunda diabetes mellitus dışındaki tüm parametrelerin ana karotis arterin intima media kalınlığı üzerine anlamlı etkisi olduğu görüldü. En önemli etkinin hipertansiyondan kaynaklandığı bunu, hiperlipidemi, koroner arter ve serebrovasküler hastalık öyküsü değişkenlerinin takip ettiği saptandı. Plak ve darlık saptanan olguların ana karotis arterin intima media kalınlığı ölçümlerinin, saptanmayanlara göre istatistiksel olarak anlamlı düzeyde yüksek olduğu görüldü.*

SONUÇ: *Ana karotis arterin intima media kalınlığı; yaş ve cinsiyet gibi değiştirilemeyen risk faktörlerinin yanı sıra, sigara kullanımı, hipertansiyon, hiperlipidemi, koroner arter ve serebrovasküler hastalık gibi değiştirilebilen risk faktörlerinden etkilenir.*

Anahtar kelimeler: *kardiyovasküler hastalıklar; karotis intima-media kalınlığı; demografi; Doppler; ekokardiyografi; risk*

Introduction

Atherosclerosis is with fatty deposits called atheromatous plaques located on the internal walls of great and moderate arteries. Approximately half of people in the United States of America and in Europe die of diseases related with atherosclerosis[1].

Increased carotid intima media thickness (IMT) is the earliest morphological sign of atherosclerosis and these

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early changes can be easily detected by B-Mode ultrasonography[2,3]. It is stated that there was a relation between myocardial infarction (MI), stroke and coronary artery disease (CAD) related deaths and carotid IMT[4]. The relation between carotid IMT and traditional cardiovascular risk factors such as age, gender, hypertension (HT), diabetes mellitus (DM), hyperlipidemia and smoking in addition to CAD and cerebrovascular disease (CVD) was studied previously[5-19]. However, results of these studies are conflicting.

The present study aimed to determine whether the risk factors such as age, gender, HT, DM, hyperlipidemia, CAD, CVD and active smoking influence carotid IMT.

Methods

The patients undergoing extra cranial carotid artery Color Doppler Ultrasound (CDUS) for various reasons in Lütfü Kırdar Training and Research Hospital Radiology Clinic between May 2012 and August 2012, and between April 2013 and May 2013 were included. All included patients were voluntary to participate and the data were prospectively evaluated. The study was approved by the local ethics committee.

In order to identify the risk factors, the patients were questioned. Age, active smoking habit and history of HT, DM, hyperlipidemia, CAD and CVD were recorded. Exclusion criteria included smokers for less than five years, daily cigarette consumption of less than a half pack, and retrospective smokers quitted.

Patients received antihypertensive therapy or were diagnosed with HT but did not receive any therapy were defined as HT patients. Insulin or oral anti-diabetic drug use or a diagnosis of DM managed with diet therapy was defined as DM. Cholesterol level over 200 mg / dl[1] was considered as hyperlipidemia. History of MI, coronary bypass, angina pectoris and use of drugs for CAD were defined as CAD patients. History of stroke and/or transient ischemic attack (TIA) was considered as CVD. The cases that failed to give adequate anamnesis and the cases that underwent endarterectomy of carotid arteries or that had carotid stent were excluded. A total of 222 cases participated.

Ultrasound (US) examination was performed by an experienced radiologist while the patients were in supine position with the head in mild extension and approximately 20° contralateral cervical rotation. Standard US devices (Logic 9, General Electric Company, USA) and 10 MHz linear transducer were used during examinations.

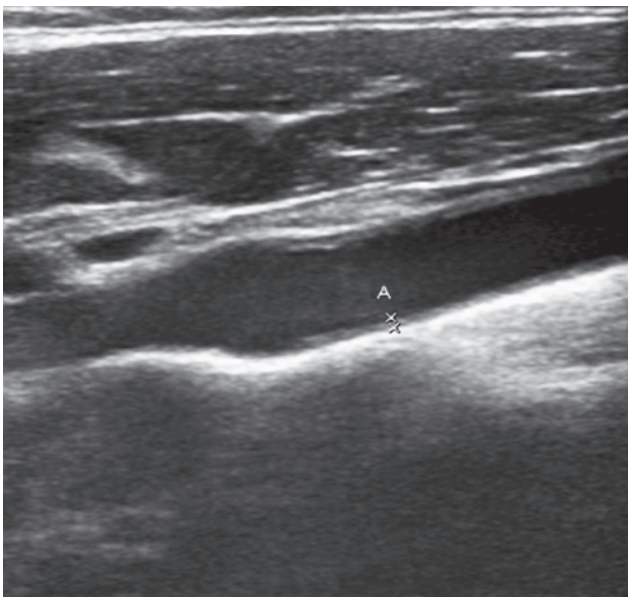

Figure 1. Intima-media thicknesses were measured from the posterior wall at the 1-1.5 cm distal part of Common Carotid Artery.

Common carotid artery (CCA), internal carotid arteries (ICA) and external carotid arteries (ECA) of all cases were evaluated in longitudinal and transverse axes by grey scale, CDUS and Power Doppler Ultrasound (PDUS) techniques. In each case, only posterior wall IMT on the 1-1.5 cm distal part of both CCAs was measured three times (Figure 1). The characteristic echogenicities of lumen-intima media and media-adventitia were used for measuring IMT. The values measured from the right and left CCA were separately recorded and their arithmetical mean was calculated. Segments with atherosclerotic plaque were omitted during measurements. An IMT value of 1.5 mm or higher was considered as plaque[20]. Carotid plaque thickness was evaluated on transverse images (short axis), because it was accepted to demonstrate plaque thickness most correctly[21]. IMT value of 1.5 mm or more on transverse axis was diagnosed and recorded as plaque. The amount of stenosis in the stenotic area was specified proportionally. For this purpose, the NASCET (North American Symptomatic Carotid Endarterectomy Trail) method recommending was used (proportioning narrowest diameter in longitudinal plane to the normal arterial diameter in the distal part)[22]. The cases with a stenosis of ≥15% of the diameter were recorded. Effect of age, gender, HT, DM, hyperlipidemia, CAD, CVD and active smoking on CCA IMT, as well as relation between presence of a plaque and carotid IMT, were investigated.

NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) programs were used for statistical analyses. While evaluating study data, in addition to the descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum), for evaluation of quantitative data Student t Test was used as well for paired group comparison of the parameters that showed normal distribution. Relation between the parameters was analyzed by Pearson's correlation analysis. Multivariate Stepwise Linear Regression Analysis was performed to determine the effect of demographic characteristics and risk factors on CCA IMT. The level of significance was evaluated at the levels of $p<0.01$ and $p<0.05$.

Table 1. *Common carotid artery intima media thickness of 222 patients and the distribution of the risk factors*

	Mean±SD	Min-Max
CCA IMT	0.83±0.21	0.30-1.40
	N	%
Plaque	118	53.2
Stenosis	45	20.3
Smoking	69	31.1
CAD	18	8.1
Hyperlipidemia	71	32.0
HT	111	50.0
DM	40	18.0
CVD	25	11.3

CCA: Common carotid artery, IMT: Intima media thickness, CAD: Coronary artery disease, HT: Hypertension, DM: Diabetes Mellitus, CVD: Cerebrovasculary disease.

Results

A total of 222 cases, 152 (68.5%) females and 70 (31.5%) males, participated in the study. The ages of the patients ranged between 15 and 83 years with a mean of 54.31±13.22 years. The reason for being referred to our clinic was vertigo in 149 (67.1%), headache in 22 (9.9%), paresthesia in the upper extremity in 15 (6.7%), tinnitus in 4 (1.8%), syncope in 4 (1.8%), new-onset stroke in 6 (2.7%), and TIA in 2 (0.9%) of the cases. The remaining 20 (9.0%) cases had been referred to our clinic for a regular control visit.

The CCA IMT values of the cases ranged between 0.30 mm and 1.40 mm with a mean of 0.83±0.21 mm. Plaque and stenosis were detected in 53.2% (n=118) and 20.3% (n=45) of the cases, respectively.

The prevalence of smokers was 31.1% (n=69); whereas, 8.1% (n=18) of the cases had CAD, 32.0% (n=71) had hyperlipidemia, 50% (n=111) had HT, 18.0% (n=40) had DM, and 11.3% (n=25) had CVD. Distribution of CCA IMT and the risk factors is demonstrated in Table 1.

Univariate analysis revealed that age, gender, smoking, CAD, hyperlipidemia, HT, DM and CVD were individual risk factors and independently effected CCA IMT. Regression analysis demonstrated that all parameters except DM had significant effect on CCA IMT. It was determined that HT was the most effective factor followed by hyperlipidemia, CVD and CAD. Whilst the effects of CAD and smoking were found to be significant at the level of $p<0.05$, age, male gender, hyperlipidemia, CVD and HT were found to be effective at the level of $p<0.01$. Relation of demographic characteristics and risk factors with CCA IMT is demonstrated in Table 2. The mean CCA IMT increased with

Table 2. *Relation between some demographic characteristics and common carotid artery intima media thickness*

	Extra-Standard coefficients		95.0% Confidence Interval for B	
Model	B	p value	Lower limit	Upper limit
(constant)	0.264	0.001	0.175	0.353
Age	0.007	0.001	0.005	0.008
Gender	0.060	0.004	0.020	0.100
Hyperlipidemia	0.123	0.001	0.086	0.160
Smoking	0.049	0.016	0.009	0.089
CVD	0.082	0.004	0.027	0.136
CAD	-0.068	0.039	-0.132	-0.003
HT	0.137	0.001	0.097	0.177
DM	0.028	0.258	0.026	0.135

CVD: Cerebro vasculary disease, CAD: Coronary artery disease, HT: Hypertension, DM: Diabetes Mellitus,

age (0.007; 95% CI: 0.005-0.008). CCA IMT values were significantly higher in the cases with plaque and/or stenosis ($p<0.01$).

Discussion

Atherosclerosis is a diffuse disease involving various parts of the arterial system[23]. Epidemiological studies indicate many factors contributing to the development and progression of atherosclerosis. In addition to unchangeable risk factors such as genetic susceptibility, local arterial and hemodynamic factors and gender, modifiable risk factors such as HT, hypercholesterolemia, smoking, glucose intolerance, obesity and sedentary life style as well contribute to the development of atherosclerosis[21]. Increased carotid IMT is the earliest morphological sign of atherosclerosis[2]. Typically, atherosclerosis most commonly evolves on posterolateral wall of the bulb and then spreads all around[24].

Histological studies revealed that media and adventitia thicknesses on ultrasound images are quite close to their real thicknesses[25]. Whilst internal hyperechogenic line represents the lumen-intima interface, external hyper-echogenic line represents the media-adventitia interface and the distance between two lines indicates IMT. Thickness increases with age[26]. In addition to the change with age, IMT also increases with earlier plaque formation; therefore, IMT measurement is used as the sign of cardiovascular risk in many clinical settings[27] and the carotid IMT is a strong predictor of cardiovascular events such as MI and stroke. In addition, increased carotid IMT is associated with HT, hyperlipidemia and cardiovascular diseases[28,29]. There are studies suggesting that individuals under risk for atherosclerotic diseases can be determined by measuring carotid IMT in young people and children[30].

Age is among unchangeable factors that contribute to the development and progression of atherosclerosis[21] and the positive correlation between age and carotid atherosclerosis is increasingly being emphasized[6-8]. Consistent with the literature, the present study demonstrated that IMT increased with age.

Atherosclerosis is several times more prevalent in young and middle-aged males versus females. It is suggested that male sex hormones are atherosclerogenic or female sex hormones are protective[1]. The facts that CAD is less prevalent among premenopausal females, symptoms appear meanly 10 years earlier in females versus males and the risk of disease increases with menopausal state confirm this hypothesis[21,31]. As was determined in the present study, the literature comprises the studies that reveal positive correlation between male gender and carotid IMT[7,10,11]. However, there are studies suggesting that gender has no effect on carotid IMT. Ertan et al. stated that gender does not influence carotid IMT and they attributed this to the female participants' being in the postmenopausal state[9].

Smoking is a modifiable risk factor[21,32]. In recent years, combating smoking has become one of the main goals of public health units in the USA and United Kingdom[33]. In the present study, we as well found significant relation between carotid IMT and active smoking. Besides, there are studies in the literature stating that smoking does not influence carotid IMT[7,19]. In their study, Oren et al. stated that smoking does not influence carotid IMT and they related with their sample characteristics consisting of young participants aged 27-30 years[19].

HT is defined as one of the well-known atherosclerotic risk factors[21]. Prospective studies demonstrated that high blood pressure was associated with increased risk of atherosclerotic cardiovascular disease[34,35]. Regression analysis performed in the present study revealed that HT had the most important effect on carotid IMT, as reported previously[7,12,13,36]. However, some studies suggested that HT did not increase carotid IMT[14]. Fabris et al. propounded that HT influenced intracranial arteries rather than extra-cranial arteries[37].

In the present study, we found that carotid IMT was statistically significantly higher in patients with histories of CVD and CAD. Consistent with our study, relation between carotid IMT and hyperlipidemia, CVD and CAD was documented previously[4-6,8,38].

In addition to the researchers in the literature stating that DM increases carotid IMT, there are also researchers reporting no relation[7,15,16,39,40]. In the present study, univariate analyses demonstrated that DM is among the risk factors effective on carotid IMT; whereas, regression analysis revealed no significant effect of DM on carotid IMT. We think this outcome emerges from the fact that substantial proportion of DM participants in the present study consists of individuals with good glycemic control. Studies have put forward that good glycemic control decreased complications of DM. It was emphasized that an increase in HbA1C by 1% provided 14% decrease in MI and 37% decrease in DM-related microvascular complications[41].

Various previous studies have mentioned about the relation between the presence and severity of plaque in carotid arteries and IMT[7,42]. In our study, the carotid IMT was significantly higher in the cases with plaque detected in the extra cranial ICA and CCA. Moreover, we observed that carotid IMT was statistically higher in the cases with a 15% or higher stenosis.

In conclusion, un-modifiable risk factors such as age and gender, as well as modifiable risk factors such as active smoking, HT, hyperlipidemia, CVD and CAD, increase carotid IMT.

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