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B-Mode ultrasound assessment of intima-media thickness of common carotid, internal carotid, brachial, femoral arteries and abdominal aorta in patients with cardiovascular risk factor

Kardiyovasküler risk faktörü olan hastalarda ana karotid, internal karotid, brakiyal, femoral arterler ve abdominal aorta intima-media kalınlığının B-Mod ultrasonografi ile değerlendirilmesi

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Abstract
Aim: The aim of the present study was to assess the association between common carotid intima-media thickness (IMT) and vascular IMT values measured from different anatomic regions.
Methods: We prospectively included 256 patients. The IMT values of the common carotid and internal carotid, brachial and femoral artery and abdominal aorta were measured by B-mode ultrasound (CC-IMT, IC-IMT, B-IMT, F-IMT and A-IMT). Patients were divided into two groups as increased and normal CC-IMT.
Results: Increased CC-IMT was detected in 55 of 256 patients (21.5%). All IMT variables showed a positive correlation with CC-IMT. Femoral IMT was independently associated with increased CC-IMT. In regression model, each 0.1 mm increase in F-IMT increased the risk of increased CC-IMT by 70.2%. When F-IMT value 1.1 mm was accepted as a cut-off value for the prediction of increased CC-IMT, sensitivity and specificity were 96.4% and 90%, respectively. In ROC curve analyses, the area under curve was calculated as 0.936.
Conclusions: Another vascular IMT location presenting increased CC-IMT best is F-IMT. The limit value for increased F-IMT >1.1mm may be used in practice. The CC-IMT measurement is closely and positively associated with all other vascular IMT measurements.
Keywords: Intima-media thickness, Common carotid artery, Femoral artery

Öz
Amaç: Bu çalışmada, farklı anatomik bölgelerden ölçülen intima-media kalınlığı (IMT) ile ana karotid IMT arasındaki ilişkiyi değerlendirmeyi amaçladık.
Yöntemler: 256 hasta prospektif olarak incelendi. B-mod ultrasound ile ana karotid, internal karotid, brakiyal ve femoral arter ile abdominal aort IMT değerleri ölçüldü (CC-IMT, IC-IMT, B-IMT, F-IMT ve A-IMT). Hastalar normal ve artmış CC- IMT değerlerine göre iki gruba ayrıldı.
Bulgular: 256 hastanın 55'inde (%21,5) artmış CC-IMT tespit edildi. Tüm IMT değerleri CC-IMT ile pozitif olarak korelasyon göstermekteydi. Femoral IMT bağımsız olarak artmış CC-IMT ile ilişkiliydi. Regresyon analizine göre F-IMT'deki her 0,1 mm'lik artış, artmış CC-IMT riskini % 70,2 artırmaktaydı. F-IMT cut-off değeri 1,1 mm olarak kabul edildiğinde artmış CC-IMT varlığını %96,4 duyarlılık ve %90 özgüllük ile tespit etmekteydi. ROC eğri analizinde, eğri altında kalan alan değeri 0,936 olarak ölçüldü.
Sonuç: Artmış CC-IMT'i en iyi belirleyen diğer IMT bölgesi F-IMT olduğu bulundu. Klinik pratikte F-IMT sınır değeri olarak >1,1 mm kullanılabilir. CC-IMT ölçümü tüm diğer vasküler IMT ölçümü ile yakın ve pozitif olarak ilişkilidir.
Anahtar kelimeler: İntima-media kalınlığı, Ana karotid arter, Femoral arter

Introduction

The intima-media thickness (IMT) of the common carotid artery was found increased in the patients with hypertension (HT), diabetes mellitus (DM), stroke, myocardial infarction and coronary artery disease (CAD); therefore it is recommended as a routine examination [1-6]. The studies that examine the presence of subclinical target organ damage by another vascular IMT except common carotid IMT (CC-IMT) are limited [7-12]. The most important reasons for using CC-IMT when compared with other vascular IMT, the localization of the carotid artery on the neck is superficial, easy to view and it can be examined in high resolution regardless of probe frequencies.

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There are limited numbers of studies comparing IMT values in different regions in the literature. Such limited number of studies reported that increase of IMT is similar in all vascular system and all vascular IMT values are positively associated with each other [7, 13]. The aim of the present study was to determine the association between vascular IMT value measured from different anatomic regions and CC-IMT as well as the IMT location which would detect the increased CC-IMT best.

Materials and methods

We prospectively included 256 patients (mean age: 53.7±9.8 years, male/female: 88/168) with at least one cardiovascular risk factor, including HT, dyslipidemia, DM and smoking. Patients were categorized into two main groups: patient with increased CC-IMT (>0.9 mm) or normal CC-IMT (≤0.9 mm). Patients with secondary or malignant HT, congestive heart failure, cerebrovascular disease, severe heart valve disease, inflammatory disorders, hematologic disorders, cancer and pregnancy were excluded from the study. The Local Ethics Committee approved the study protocol, and each participant provided written informed consent. After assessment of detailed medical history and a complete physical examination, the baseline characteristics of patients including age, sex, HT, current smoking status, family history of CAD, hyperlipidemia, presence of CAD and stroke, body mass index (BMI) were recorded for all patients.

Left and right CC-IMT and internal carotid IMT (IC-IMT), brachial artery IMT (B-IMT), common femoral artery IMT (F-IMT) and abdominal aorta IMT (A-IMT) were examined with a high-resolution ultrasound (USG) Doppler system (Philips EPİQ 7), equipped with a 5-12 MHz high-resolution convex and linear transducer (Philips Health Care, Bothell, WA, USA). Ultrasound scanner setting was made to be useful for every patient for all B-mode USG examination (gain [55–75 dB]; penetration depth [2.5–8cm]). All arteries were studied in both longitudinal and transversal sections. All arteries were scanned longitudinally to visualize the IMT in the posterior or far wall of artery. All measurements were made on frozen images. Two images of the best quality were chosen for analysis in each study subject. The IMT is defined as the distance from the front edge of the first echogenic line to the anterior margin of the second line. The first line represents the intima-lumen interface and the second line represents the collagen-containing top layer of the adventitia. Vascular IMT was measured using ultrasonic calipers in case by 2 independent and blinded observers. All IMT values were calculated as averages of six measurements.

Subjects were examined at supine position. Patients' head were turned 45° from the site being scanned for carotid artery. Carotid IMT was measured from the far wall of the right and left carotid artery within 10 mm proximal (for common) and after (for internal) to bifurcation on two-dimensional ultrasound images (Figure 1a). Brachial artery was assessed and B-IMT was obtained level of the antecubital fossa and 1-2 cm proximal from bifurcation (Figure 1b). Common femoral artery was assessed and F-IMT was obtained 1-2 cm proximal from the bifurcation (Figure 1c). Abdominal A-IMT was examined midway between the origins of the celiac truncus (tripod) and iliac arteries (Figure 1d). Increased IMT was accepted for A-IMT, CC-IMT, IC-IMT, F-IMT and B-IMT as higher than 2.99 mm, 0.90 mm, 0.90 mm, 1.3 mm and 0.35 mm, respectively [1-2,14-15].

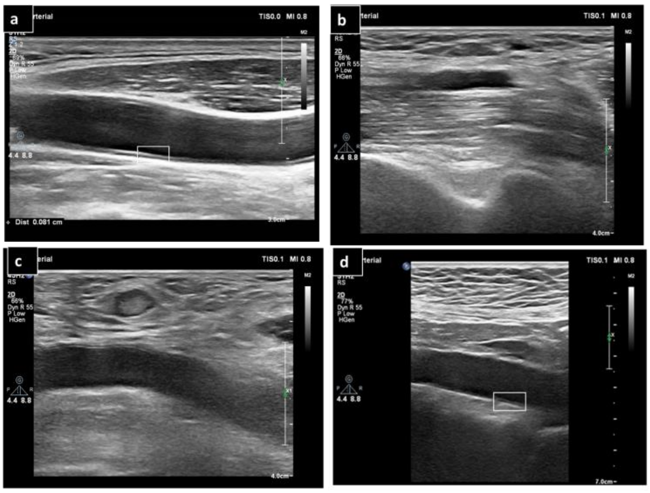

Figure 1: IMT measurements with B-mode ultrasound from different vascular regions a) CC-IMT b) B-IMT c) F-IMT d) A-IMT

Statistical analysis

All analyses were performed through SPSS 20.0 statistical software package (SPSS for Windows 20.0, Chicago, IL, USA). Continuous parameters in the group data were specified as mean ± standard deviation. Categorical parameters were presented in numbers and percentage. Continuous parameters that showed normal distribution were compared using the t test, whereas the Mann-Whitney U test used for non-normally distributed samples. Chi-Square test was used for comparison of categorical variables. Multivariate, stepwise forward conditional logistic regression analysis was used to determine the independent predictors of increased CC-IMT. As results of such analysis, increase or decrease of the significant variables were presented by Odds Ratio according to the unit increase. All significant parameters in the univariate analysis were selected in the multivariate model. A receiver operator characteristic (ROC) curve analysis was carried out to identify the optimal cut-off point of F-IMT to detect increased CC-IMT. The value of the area under the curve was calculated as a measure of the accuracy of the test. The statistical significance level was accepted as $p<0.05$.

Results

We detected the CC-IMT increased in 55 patients (21.5%). Patients were categorized into two main groups: patient with increased CC-IMT or normal CC-IMT. Comparison of the baseline clinical and demographics were shown in Table 1. Besides the age, BMI and presence of CAD, there was not any statistically significant difference in clinical and demographics parameters ($p>0.05$). Advanced age and presence of CAD was higher in patients with increased CC-IMT group. CC-IMT group had to smaller BMI than normal group (Table 1). Patients with increased CC-IMT presented a significantly higher IC-IMT, A-IMT, F-IMT and B-IMT (Table 2). All IMT variables showed a positive correlation with CC-IMT as determined by B-mode USG (Table 3).

Table 1: Baseline characteristics

	Increased CC-IMT n=55	Normal CC-IMT n=201	p
Age (year)	55.6±10.9	53.1±9.4	0.033
Gender (female)	33	135	0.175
Heart rate (beat/min)	79.2±12.1	78.5±10.8	0.804
Systolic blood pressure (mmHg)	84.5±15.9	82.6±15.3	0.712
Diastolic blood pressure (mmHg)	137.1±9.3	136.7±9.1	0.082
Body mass index (kg/m^2)	27.5±2.8	28.4±2.6	0.002
Hypertension, n (%)	82 (74.5%)	271 (67.4%)	0.093
Smoking, n (%)	22 (14.5%)	84 (20.9%)	0.808
Diabetes mellitus, n (%)	20 (18.2%)	70 (17.4%)	0.888
Hypercholesterolemia, n (%)	24 (21.8%)	70 (17.4%)	0.330
Family history, n (%)	36 (32.7%)	140 (34.8%)	0.855
Coronary artery disease, n (%)	12 (10.9%)	18 (4.5%)	0.019
Cerebrovascular disease (n, %)	4 (3.6%)	8 (2%)	0.684

CC-IMT: Common carotid intima-media thickness

Table 2: Vascular ultrasound finding in patients with increased CC-IMT and normal CC-IMT

	Increased CC-IMT n=55	Normal CC-IMT n=201	p
Internal carotid IMT (mm)	0.95±0.10	0.72±0.16	<0.001
Abdominal aortic IMT (mm)	2.53±0.37	1.25±0.64	<0.001
Femoral IMT (mm)	1.25±0.20	0.78±0.22	<0.001
Brachial IMT (mm)	0.43±0.10	0.38±0.08	<0.001
Increased internal carotid IMT (n, %)	42 (38.2%)	82 (20.4%)	<0.001
Increased abdominal aortic IMT (n, %)	54 (49.1%)	56 (13.9)	<0.001
Increased femoral IMT (n, %)	42 (38.2%)	40 (10%)	<0.001
Increased brachial IMT (n, %)	42 (%38.2)	102 (25.4%)	<0.001

CC-IMT: Common carotid intima-media thickness

Table 3: Correlation analysis of B-mode ultrasound variables in relation to the variables in CC-IMT

	p value	Coefficient of Correlation
Internal carotid IMT (mm)	<0.001	0.693
Abdominal aortic IMT (mm)	<0.001	0.544
Femoral IMT (mm)	<0.001	0.437
Brachial IMT (mm)	<0.001	0.282

IMT: Intima-media thickness

Multivariate linear regression analysis showed that IC-IMT and A-IMT most important variables in predicting CC-IMT (β level 0.562, $p<0.001$ and β level 0.280, $p=0.017$, respectively). The only independent predictor of increased CC-IMT was the F-IMT ($p<0.001$). Logistic regression analysis showed that every 0.1 mm increase in F-IMT caused a 70.2% increase in the risk of increased CC-IMT (Table 4). Receiver operating characteristic (ROC) curve analysis also showed that when F-IMT value 1.1 mm was accepted as a cut-off value for the prediction of increased CC-IMT, sensitivity and specificity were 96.4% and 90%, respectively. The area under ROC was calculated as 0.936 (0.915–0.956), which indicates good discriminatory power.

Table 4: Independent risk factors for occurrence of increased CC-IMT

	Odds Ratio	95% Confidence Interval	p
Femoral IMT (0.1 mm)	1.702	1.506 – 1.894	<0.001

IMT: Intima-media thickness

Discussion

The most important outcome of the present study was to detect a close, positive association between CC-IMT and all other vascular IMT measurements. An independent relation exists between CC-IMT and F-IMT values. Furthermore, the F-IMT ≥1.1 mm independently detects increased CC-IMT.

The increase in CC-IMT is closely associated with subclinical organ damage and atherosclerosis; and it is recommended as a routine examination [1]. The CC-IMT detected by B-mode USG is known as a feasible and repeatable evaluation in the patients with HT [2]. CC-IMT is closely associated with presence and severity of CAD; and stroke and myocardial infarction [3-6].The most important causes of CC-IMT as target IMT include superficial location on the neck, easy imaging and easy access because of open location of such area and number of CC-IMT data in the literature. However, some studies were conducted with IMT in other anatomic regions [2, 9,16,17].

There are studies focusing on subclinical target organ damage through examination of abdominal A-IMT in HT patients [11,12]. However, since evaluation of A-IMT is more difficult than CC-IMT and there is not any device enabling sufficient tissue penetration, it is not a routine test for monitoring of the patients with HT. Measurement of A-IMT was considered as a better parameter to detect subclinical target organ damage during early stages of CV diseases, especially in pediatric and adolescent children group. Only a limited number of studies reported availability of descending thoracic A-IMT measurement through transesophageal echocardiography (TEE) [2,9,10]. Belhassen et al. [2] reported that the increase of descending A-IMT (≥ 3 mm) detected by TEE determined presence of CAD independently. In a recent study including middle-aged patients group diagnosed with sporadic idiopathic hypoparathyroidism found a close association between A-IMT and CC-IMT. In addition to the close correlation detected in the previous studies, we also found a close and independent association between CC-IMT and A-IMT in regression analysis.

A close association exists between the atherosclerosis detected in the brachial artery by autopsy and atherosclerosis of coronary and carotid arteries [18]. In a study conducted on the individuals with CV risk factor, a close association was found between CC-IMT and B-IMT [15]. In the aforesaid study, the patents with risk factor for CV disease could be detected when limit value for B-IMT is taken as 0.28 mm [15]. Another study assessing the B-IMT reported average B-IMT of the patients with CV mortality as 0.37 mm [19]. However, several studies conducted showed a poor association between B-IMT and CC-IMT [20,21]. A close association was detected between B-IMT and CC-IMT in the present study; however, such association was poorer than the association between CC-IMT and F-IMT as well as A-IMT.

It was shown that the increase in F-IMT is a determinant for increased vascular hypertrophy [16] and associated with early atherosclerosis formation and increased CC-IMT [13,17]. CC-IMT is related to peripheral artery disease as well as other vascular diseases such as atherosclerosis. Kirhmajer MV et al. [22] reported in their study that a close association exists between F-IMT and severity of CAD; and F-IMT may be used as a novel determinant for CV risk factor such as CC-IMT. Another study conducted demonstrated that formation of atherosclerotic plaque is more in common femoral artery when compared with carotid artery; and F-IMT is thicker than CC-IMT [23]. Similarly, we detected that thickness of F-IMT is more than CC-IMT in the patients with CV risk factors. As a result of our study, use of F-IMT measurement was considered as a determinant to indicate subclinical target involvement such as CC-IMT.

The studies conducted reported the normal F-IMT thickness as 0.562±0.074 mm for males and 0.543±0.063 mm for females [24]. However, as much as we searched, there is not any limit value for increased F-IMT. Although the average F-IMT value was found in the patients with CAD was found 1.3 mm, this does not reflect increased F-IMT [14]. Similar to the aforesaid study, the F-IMT value in the patients with increased CC-IMT was found 1.25±0.20 mm. Furthermore, in addition, the limit value of F-IMT was found 1.1mm for prediction of increased CC-IMT in ROC analysis.

There are limited numbers of studies in the literature comparing the IMT values in at least 4 different regions mentioned above. Furthermore, there is not any study measuring CC-IMT, IC-IMT, B-IMT, F-IMT and A-IMT simultaneously with vascular ultrasound in adult patients. Only a study conducted on middle aged patient group with congenital adrenal hyperplasia measured IMT of 4 different vascular regions including common carotid, carotid bulbus, femoral and abdominal aorta. In such study, IMT increase was detected in all vascular system of the patients with congenital adrenal hyperplasia [7]. Neiva Neto et al. [13] reported in their study that A-IMT values of the carotid, vertebral, femoral and abdominal arteries are positively and significantly associated with each other and detection the IMT increase in any of these arteries would be sufficient. A recent and similar study evaluated the association between internal, external and common carotid arteries, vertebral artery and femoral artery and abdominal aorta IMT [13]. A positive association was found between all vascular IMT measurements in such study conducted with fewer patients [13]. Results of the present study are consistent with previous studies and all vascular IMT levels are associated with each other.

Although there are data for IMT measurement from vascular regions other than CC-IMT, the studies conducted for CC-IMT are wider and multi-centered; and increase of CC-IMT was included in the guidelines. However, the actual objective of our study was to detect the vascular IMT region which is closest to CC-IMT. The most ideal measurement for IMT increase in peripheral vascular system should continue to be carotid IMT. However, inclusion of vascular IMT values into the ultrasound report during upper limb Doppler and abdominal USG scans may be useful for the clinician. It was concluded that the patients with F-IMT of ≥1.1 mm should be specified.

There are same limitations in our study. In a study measuring CC-IMT and F-IMT in the patients with CAD showed higher values and a close association between both IMT value and severity of CAD [14]. However, presence and severity of CAD was not assessed in the present study. CAD was detected more in the patients with increased CC-IMT; however severity of CAD was not examined. It was shown that the treatments used for atherosclerosis, in particular, regress IMT [25]. However, we did not review the effect of medical treatments on IMT in the present study. Our study is not a follow-up study and therefore no disease control CC-IMT and other IMT assessments have been performed [26]. Automatic measurement especially removes operator dependence and is more useful for repetitive measurements. However, our high-resolution device did not have this software program so we could not make this evaluation.

In conclusions, as a result of the present study and review of the previous studies, it was concluded that evaluation of vascular IMT which is a determinant for initiation of atherosclerosis as well as subclinical target organ damage should be performed on carotid and femoral arteries. The limit value for CC-IMT is used as >0.9 mm according to the guidelines whereas it may be >1.1 mm for F-IMT according to the result of the present study.

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