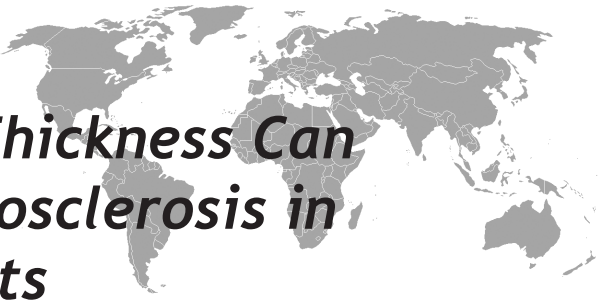

Carotid Intima-Media Thickness Can Predict Coronary Atherosclerosis in Diabetic Elderly Patients

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Eur J Gen Med 2010;7(3):245-249

Received: 07.08.2009

Accepted: 15.12.2009

ABSTRACT

Aim: *To evaluate the relationship between coronary risk and carotid vessels as revealed by duplex study in diabetic elderly patients.*

Method: *Case control study was designed. Participants were recruited from Geriatric department Ain Shams University Hospital, Cairo-Egypt. The cases were subdivided into two groups (group 1: diabetic with coronary artery diseases (CAD), group 2: diabetic without CAD). The diabetic group (cases) included 60 patients (25 males and 35 females). The control group included 30 elderly subjects matched for age and sex. All groups were subjected to: comprehensive geriatric assessment, laboratory measurements including: fasting blood sugar, lipid profile, lipoprotein (a), and carotid duplex for measurement of the intima-media thickness and the degree of stenosis.*

Result: *On analysis of the collected data, diabetic patients did have atherosclerosis in the carotid arteries more than the non diabetic subjects, and among the diabetic patients group, it was revealed that those who had CAD, had their carotid arteries more atherosclerotic than the others without CAD. Multinomial logistic regression done showed significant independent association between the presence of thickened carotid intima-media and coronary artery disease among diabetic patients (p=0.042, OR 1.71(0.52-5.6)*

Conclusion: *Thickened carotid intima-media can predict risk to have coronary artery disease among elderly diabetic patients.*

Key words: *Carotid intima-media thickness, coronary atherosclerosis, diabetes*

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Karotis İntima Media Kalınlığı Yaşlı Diyabetik Hastalarda Koroner Atherosklerozu Öngörebilir

Amaç: *Yaşlı diyabetik hastalarda doppler ultrason ile değerlendirilen karotid arterler ile koroner risk arasındaki ilişkilerin değerlendirilmesi.*
Metod: *Çalışma vaka-kontrol şeklinde dizayn edildi. Katılımcılar Ain Shams Universitesi Kahire, Mısır Hastanesinden çalışmaya alındılar. Vakalar iki alt gruba ayrıldılar (Grup 1: Koroner arter hastalığı (KAH) olan diyabetikler, Grup 2: KAH olmayan diyabetikler). Diyabetik grupta 60 hasta mevcuttu (25 erkek, 35 kadın). Kontrol grubu olarak yaş ve cinsiyet açısından eş, 30 yaşlı kişi çalışmaya dahil edildi. Tüm gruplarda kapsamlı geriatrik değerlendirme, açlık kan şekeri, lipid profili, lipoprotein a' yıda içeren laboratuvar incelemeleri yapıldı ve carotis doppler ultrasonu ile intima media kalınlığı ve stenoz derecesi değerlendirildi.*
Bulgular: *Toplanmış verilerin analizinde diyabetik hastalarde diyabetik olmayanlara göre daha atherosklerotik olduğu, Diyabetik grupta KAH olan grupta KAH olmayanlara göre karotis arterlerinin daha aterosklerotik olduğu gözlemlendi. Multinominal logistic regresyon analizinde diyabetik hastalarda karotid arter intima media kalınlığı ile koroner arter hastalığı arasında bağımsız bir ilişki olduğu tespit edildi (p=0.042, OR 1.71 (0.52-5.6)).*
Sonuç: *Kalınlaşmış carotis intima media yaşlı diabetik hastalarda KAH'a sahip olma riskini öngörebilmektedir.*
Anahtar kelimeler: *Karotis intima media kalınlığı, koroner ateroskleroz, diyabet*

INTRODUCTION

Diabetes greatly increases the risk of CVD (heart disease and stroke). From two-thirds to three-quarters of people with diabetes die of some form of heart or blood vessel disease. Diabetes is associated with a more atherosclerosis- prone carotid arteries, compared with general population (1). Type-2 diabetes mellitus is associated with a 2- to 4-fold increase in the risk of coronary artery disease (CAD). Multiple metabolic disturbances may promote atherogenesis and predispose the patient to CAD. These include reduced concentrations of HDL cholesterol; increased small, dense LDL; and insulin resistance. Individuals with a higher proportion oft abdominal fat have a greater risk of developing CHD, type II diabetes and CVD-related morbidity and mortality than those with a lower proportion. Increased carotid IMT is relatively simple, inexpensive, and reproducible noninvasive marker of global atherosclerotic disease. Measurement of IMT may be used as a marker of the total burden of atherosclerosis present in the individual, and it may serve as a graded marker for future risk of clinical cardiovascular and cerebrovascular outcomes (2). This study aimed to evaluate the relationship between coronary risk and carotid vessels in diabetic elderly patients.

MATERIALS AND METHODS

Participant selection criteria

A case control study was conducted to evaluate the relationship between coronary risk and carotid atherosclerosis as revealed by duplex study in diabetic elderly patients.

The subjects of this study were recruited from Geriatric Department Ain Shams University Hospitals and were subdivided into: Group (1): Thirty elderly diabetic patients with coronary heart disease, diagnosed by coronary catheter. Group (2): Thirty elderly diabetic patients, and with no manifested ischemic heart disease, and group (3): Thirty elderly non-diabetic subjects with no manifested ischemic heart disease matched for age (±5 years) and sex with each group of the cases. Ischemic heart disease was excluded in group 2 and 3 by lack of symptoms, and absence of ischemic changes in ECG and echocardiography. Diagnosis of diabetes was considered according to fasting plasma glucose level ≥126 mg/dl (3) or when the patient is known to have DM on treatment. Diabetes was excluded among controls by fasting plasma glucose level <110 mg/dl and 2 hours postprandial plasma glucose level <140 mg/dl (3).

Tools of Assessment

All groups were subjected to: Comprehensive geriatric assessment including: Full medical history and examination: Including the calculation of weight and height and waist hip ratio. Hypertension was diagnosed when systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg based on the average of 2 readings (4) or presence of known history of hypertension on treatment. Laboratory Investigation were done including: Fasting blood sugar, and Lipid profile including: TG, Cholesterol, LDL, HDL, lipoprotein a. Lp(a). The diagnosis and classification of dyslipidemia was based on the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults Guidelines (5).

***Table 1**. Comparison between cases and controls as regards BMI, WHR, lipid profile and IMT*

	Group 1	Group 2	Group 3	f	p
BMI	27.67±10.45	28.99±5.03	24.87±5.65	2.39	0.097
WHR	0.93±0.22	0.97±0.21	0.88±0.11	1.48	0.233
Cholesterol	190.07±62.76	182.30±58.81	153.83±59.19	3.01	0.055
HDL	55.97±27.44	72.88±36.41	57.07±25.81	2.94	0.058
LDL	95.70±47.50	87.27±59.17	82.27±50.93	2.39	0.097
TG	124.43±70.77	98.70±48.92	75.20±42.13	5.95	0.004
Lpa	40.40±23.29	44.18±26.81	40.32±28.08	0.21	0.808
IMT	1.61±0.55	1.39±0.43	0.93±0.25	19.90	0.000

p value <0.05 is statistically significant.
BMI=body mass index, WHR= waist/hip ratio, HDL=high density lipoprotein, LDL=low density lipoprotein, TG= triglyceride, Lpa=lipoprotein a, IMT= intima media thickness.

Radiological investigations: Carotid duplex was done to measure the intimal medial thickness of the carotid arteries and the degree of stenosis. Carotid ultrasonography was done using B-mode ultrasound device LOGIC 500 of GE Medical Systems. Sonography and reading were done by trained and certified sonographers and ultrasound readers with regular quality control at the radiology department. They were not aware of the aim of the study. Scanning protocol involved studying the right and left common carotid arteries (CCAs) in all subjects. Patients were examined in the supine position, and each carotid wall and segment was interrogated independently from continuous angles to identify the thickest intima-media site. Intima-media thickness (IMT) was defined as the distance from the leading edge of the lumen-intima interface to the leading edge of the media-adventitia interface of near and far walls. Observations led to estimate that, on average, a healthy person reaches an IMT of 0.78mm at the age of 76 years (6). But in many studies, the maximum thickness of the intima-media complex of healthy elderly was 1.0mm and IMT ≥1mm represents a risk of myocardial infarction and/or cerebrovascular disease (7). Therefore, we defined thickened IMT as when the axial thickness of the intima-media complex was ≥1.0 mm. The maximum percent stenosis was assessed and the patient was considered to have hemodynamically significant stenosis if its degree was ≥70% (8,9).

Statistical methods

Data collected was revised, coded, tabulated and introduced to PC for statistical analysis. All data manipulation and analysis were performed using the 11th version of SPSS (Statistical Package for Social Sciences). Qualitative data was presented in form of frequency tables (number and percentage). Quantitative data was presented in form of mean ± standard deviation and range. Pearson chi-squared was used with correction to test association between qualitative variables. ANOVA test was also used to compare groups with quantitative continuous variables. Multinomial logistic regression analysis was done to determine the independent association of different factors. All the included variables were made qualitative variables. P value was always set as significant at 0.05.

RESULTS

The sample of this study included 90 patients; 37 males and 53 females with age ranging from 60 to 78 (mean age 67.2). The diabetic group (cases) included 60 patients (25 males and 35 females) and the remaining 30 were the non diabetic group (controls). The cases were subdivided into two groups (group 1: diabetic with CAD. group 2: diabetic without CAD). Cases and controls were matched for age and sex. Coronary risk factors including smoking and family history, were asked about during history taking. Body mass index (BMI) and waist hip ratio (WHR) were measured and the levels of blood lipids were measured in the serum of both cases and controls sharing in this study. Carotid atherosclerosis was assessed by measuring the carotid intima-media wall thickness and the degree of stenosis if present using high-resolution mode B ultrasound. No statistical significant difference was found between the 3 groups as regards mean BMI, WHR, cholesterol, HDL, LDL, Lpa (Table 1), whereas statistical significant difference (p <0.05) was found as

Table 2. *Comparison between the 3 groups as regards available coronary risk factors*

	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)	X^2	p
FH	19(63.3)	5(16.7)	2(6.7)	26.72	0.000
Smoking					
Non-smoker	21(70)	22(73.3)	16(53.3)	13.71	0.008
Ex-smoker	4(13.3)	5(16.7)	14(46.7)		
Smoker	5(16.7)				
HTN	26(86.7)	23(76.7)	0(0)	54.38	0.000
IMT	24(80)	21(70)	8(26.7)	19.92	0.000
Stenosis	16(53.3)	14(46.7)	4(13.3)	11.72	0.003
Obesity	24(80)	16(53.3)	8(26.7)	17.14	0.000
Hypercholesterolemia	14(46.7)	9(30)	5(16.7)	6.32	0.042
Low HDL	10(33.3)	3(10)	7(23.3)	4.76	0.093
High LDL	3(10)	3(10)	2(6.7)	0.27	0.872
Hypertriglyceridemia	9(30)	7(23.3)	1(3.3)	7.54	0.023
High Lpa	21(70)	20(66.7)	19(63.3)	0.30	0.861

p value <0.05 is statistically significant.
Hypercholesterolemia=cholesterol>200mg/dl, hypertriglyceridemia=triglyceride>150mg/dl, highLDL=LDL>130mg/dl, lowHDL=HDL<40mg/dl.

regards triglyceride serum level, and the mean carotid intima-media thickness (Table 1). Using chi-square test, statistical significant difference ($p < 0.05$) was found between groups as regards family history of IHD, smoking, hypertension, and hypercholesterolaemia(Table 2). Carotid duplex study showed 53.3% of group 1 having stenosis compared to 46.7% and 13.3% of group 2 and 3 respectively with statistical significant difference ($p<0.05$) (Table2). 80% of group1 were having thickened carotid intima-media compared to 70% and 26.7% of group 2 and 3 respectively with statistical significant difference ($p<0.05$) (Table2). Multinomial logistic regression was done showing significant independent association between the presence of thickened carotid intima-media and coronary artery disease among diabetic patients ($p=0.042$, OR 1.71(0.52-5.6)

DISCUSSION

The hypothesis of this study was that the carotid arteries are more atherosclerotic in diabetic patients than in non diabetic subjects, and also they are more atherosclerotic in diabetic patients with CAD than in diabetic patients who do not have manifest CAD. In the pathogenesis of atherosclerosis, IMT was regarded as a later development than arterial stiffness (10). Stensland-Bugge et al. stated that ultrasound measurement of carotid artery intima-media thickness (IMT) is regarded as a valid index of atherosclerosis (11). On analysis of the collected data, diabetic patients did have atherosclerosis in the carotid arteries more than the non diabetic subjects, and among the diabetic patients group, it was revealed that those who had CAD, had their carotid arteries more atherosclerotic than the others without CAD. Elderly diabetic patients having thickened carotid intima-media have 1.71 folds more risk to have coronary artery disease than those without thickened carotid intima-media.

Haffner et al. found diabetic subjects with CAD to have the greatest intima-media wall thickness, whereas non-diabetic subjects without CAD had the least atherosclerosis. Subjects with diabetes but without CAD had slightly greater intima-media wall thickness than non-diabetic subjects with CAD, although these differences were not statistically significant. Thus, diabetic subjects even without CAD had extensive atherosclerosis in the carotid artery (12). Inclusion of other risk factors, which could also affect carotid intima-media thickness, apart from diabetes, e.g. dyslipidaemia, hypertension and smoking, in both cases and controls might be one of the limitations of our study. Yet, still diabetes mellitus is associated with a more atherosclerosis prone carotid arteries. Bonora et al, study revealed that type II diabetes and, to a lesser extent, impaired glucose tolerance are statistically significant risk predictors of 5-year changes in carotid atherosclerosis (13).

Lekakis et al, conducted a study to examine the association between carotid IMT and the extent and severity of CAD as well as the effects of traditional vascular risk

factors on the atherosclerotic changes in the carotid artery. Their results revealed that the carotid IMT was increased significantly with an increase in CAD extent. Using multiple stepwise regression analysis, the following parameters were found to be independent predictors of CAD extent: male gender (p<0.0001), common carotid artery IMT (p = 0.015), age (p=0.02), diabetes mellitus (p=0.035), and carotid artery bulb IMT (p=0.04). They concluded that carotid bulb was independent predictor of CAD extent (14).

Hansa et al also conducted a study to determine whether carotid intima-media wall thickness was associated with CAD and cardiovascular risk factors in the Indian population. On multivariate logistic regression analysis, carotid IMT was the only factor found to be an independent predictor of coronary artery disease. There was a significant association between risk factor count and the average and maximum IMT values in the combined study population. Those results indicated that raised values of average and maximum carotid IMT were significantly associated with the presence of CAD and this association was independent of the presence of other conventional cardiovascular risk factors (15). So to conclude, IMT is more among diabetics and has significant independent association with the risk of coronary artery disease, so carotid intima-media is a mirror for the coronary vasculature and can be used as a predictor of ongoing carotid atherosclerosis.

Diabetics are prone to CAD and with the associated diabetic-neuropathy, they are at risk of having silent ischemic heart disease, so they need screening tools for early detection. Relatively small sample size is a limitation of the current study, so the use of carotid duplex study as a screening among diabetics for CAD risk needs further larger studies.

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