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Assessment of Carotid Intima-Media Thickness in Patients with Diabetic Retinopathy

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Abstract

Background: Diabetic retinopathy (DR) is suggested to be associated with cardiovascular disease (CVD) risk in patients with diabetes. Carotid intima-media thickness (CIMT), as a marker for atherosclerosis presence and progression, is considered useful for evaluating the risk and incidence of CVD.

Objectives: To evaluate CIMT in patients with DR who have no reported CVD to detect the association between DR and subclinical atherosclerosis.

Methods: A cross-sectional study was done on fifty Egyptian middle-aged adults diagnosed with diabetes. All participants were subjected to history, clinical examination, laboratory tests, comprehensive eye examination, electrocardiogram (ECG), echocardiography, duplex study to measure Ankle/brachial index (ABI), and CIMT.

Results: Among the fifty patients with diabetes, thirty-one subjects (62%) had retinopathy. The retinopathy group had significantly higher CIMT than the non-retinopathy group (0.92 ±0.15 mm, 0.79 ±0.12 mm) respectively, (p-value =0.002).

Conclusion: DR is associated with increased CIMT and subclinical atherosclerosis.

Keywords: Diabetic retinopathy, CIMT, subclinical atherosclerosis

1. Introduction

Cardiovascular disease (CVD) has become an important etiology of mortality in diabetic patients (1). For early diagnosis and prevention of CVD, cardiovascular risk factors should be detected and managed properly in diabetic patients. Changes in the microcirculation in diabetes are thought to be associated with atherosclerosis (2). Diabetic retinopathy (DR) was suggested to be associated with CVD risk and subclinical atherosclerosis (3).

Carotid intima-media thickness (CIMT) is a non-invasive imaging technique that can serve as a marker for cardiovascular health. It can detect subclinical atherosclerosis and predict future cardiovascular events (4).

This study was designed to assess CIMT in patients with DR who had no CVD to establish a relation between DR and subclinical atherosclerosis.

2. Subjects and Methods

2.1 Study subjects and protocol

The study included fifty adults with diabetes aged from 19 to 60 years old. Diabetes mellitus diagnosis was according to the American Diabetes Association (ADA) guidelines.

This cross-sectional study included recruited participants from the Internal Medicine Department at Kasr Al-Aini Hospital Cairo University. All participants were subjected to history, examination, and Laboratory tests including glycosylated hemoglobin (HbA1c), lipid panel, serum creatinine, albumin/creatinine(A/C) ratio, comprehensive eye examination, ECG, echocardiography, ABI, and CIMT by duplex.

The retinopathy was confirmed by an experienced ophthalmologist by ophthalmoscopy or fundus fluorescein angiography. The clinically manifest CVD was excluded by history, examination, ECG, and echocardiography, and peripheral arterial disease was excluded by measuring the ABI.

2.2 Measurements

The Doppler examination was done on all patients by the same skilled sonographer with a color-coded Doppler sonography linear transducer 5 to 10 MHz to measure CIMT and ABI.

2.2.1 Carotid intima-media thickness (CIMT)

The measurements were performed proximal to the bifurcation on the wall of the right and left common carotid arteries. The transducer was manipulated to maximize the lumen diameter longitudinally. Sonographic images of the carotid artery were obtained. The sonographer located the leading edges representing the transition zones between lumen-intima and media-adventitia, not including plaques. An average of three measurements were obtained for the right and left common carotid artery.

2.2.2 Ankle Brachial Index (ABI)

It was obtained by measuring the systolic pressure of the tibial arteries over the systolic pressure of the brachial artery (ABI < 0.9 was excluded).

2.3. Statistical analysis

Data analysis was performed using the computerized (SPSS) version 28. Means and standard deviations or medians and/or ranges were used to interpret numerical data. The student's t-test was used for group comparisons for normally distributed variables, while the Mann-Whitney test was utilized for non-normally distributed numeric variables. To measure the strength of association between the normally distributed measurements, Pearson's correlation coefficients were computed (r is the correlation coefficient & it ranges from -1 to +1), Spearman's correlation coefficients were utilized for non-normally distributed variables (r is the correlation coefficient & it ranges from -1

to +1). P-value ≤ 0.05 is considered significant. Multiple linear regression analysis was done to estimate the dependence of a quantitative variable based on its relationship to more independent variables.

3-Results

The mean age of patients was 48 (±11), 54% were females and 46% were males.

Table (1): Relation between the presence of retinopathy and CIMT

	Retinopathy		
	Yes	No	
	Mean ± SD	Mean ± SD	P value
CIMT (mm)	0.92 ±0.15	0.79 ±0.12	0.002

SD: Standard deviation, P value <0.05 is considered significant
CIMT: Carotid intima -medial thickness

Table (1) shows a significantly higher mean value of CIMT in the retinopathy group compared to the non-retinopathy group (0.92 ±0.15 mm, 0.79 ±0.12 mm) respectively, with p-value =0.003. CIMT was directly correlated to age, duration of diabetes, blood pressure, presence of retinopathy, HbA1c, total cholesterol (TC), and low-density lipoproteins (LDL) (Table 2).

Table (2): Correlation between CIMT with different parameters

Parameters	**CIMT**	
	r-value	**p-value**
Age (years)	0.498	0.001**
Duration (years)	0.448	0.001**
SBP (mmHg)	0.346	0.014*
DBP (mmHg)	0.276	0.046*
BMI (kg/m2)	0.015	0.919
Retinopathy#	0.421	0.002*
HbA1c (%)	0.792	0.001**
Creatinine (mg/dl)	-0.239	0.095
A/C ratio (mg/g)	-0.113	0.436
TC (mg/dl)	0.600	0.001**
HDL (mg/dl)	-0.117	0.417
LDL (mg/dl)	0.721	0.001**
TG (mg/dl)	0.106	0.462

Using: Pearson's correlation coefficient (r)& it ranges from -1 to +1
#Spearman's rank correlation coefficient (rs). P-value <0.05 is considered significant*
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, A/C ratio: albumin/creatinine ratio, CIMT: Carotid intima -medial thickness, TG: Triglycerides

Multiple linear regression analysis (table 3) shows that the presence of diabetic retinopathy and HbA1C as independent variables were positively and significantly correlated with CIMT.

Table (3): Multiple linear regression analysis using CIMT as the dependent variable

Parameters	Unstandardized Coefficients		Standardized Coefficients	t	p-value
	□	±*SE*	*Beta*		
(Constant)	0.138	0.109		1.264	0.213
Age (years)	0.001	0.001	0.039	0.402	0.690
Duration(years)	0.008	0.003	0.272	2.876	0.006*
SBP (mmHg)	0.001	0.001	0.082	0.701	0.487
DBP (mmHg)	0.000	0.002	0.023	0.211	0.834
BMI (kg/m2)	0.000	0.002	0.006	0.076	0.940
Retinopathy	0.076	0.024	0.247	3.224	0.002*
HbA1c (%)	0.054	0.006	0.652	8.487	0.001**
Creatinine (mg/dl)	-0.030	0.019	-0.124	-1.580	0.122

β: Regression coefficient, SE: Standard error
R square = 0.817 and Adjusted R Square = 0.782
P-value <0.05 is considered significant * indicates significant, ** indicates highly significant
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglycerides, A/C ratio: albumin/creatinine ratio

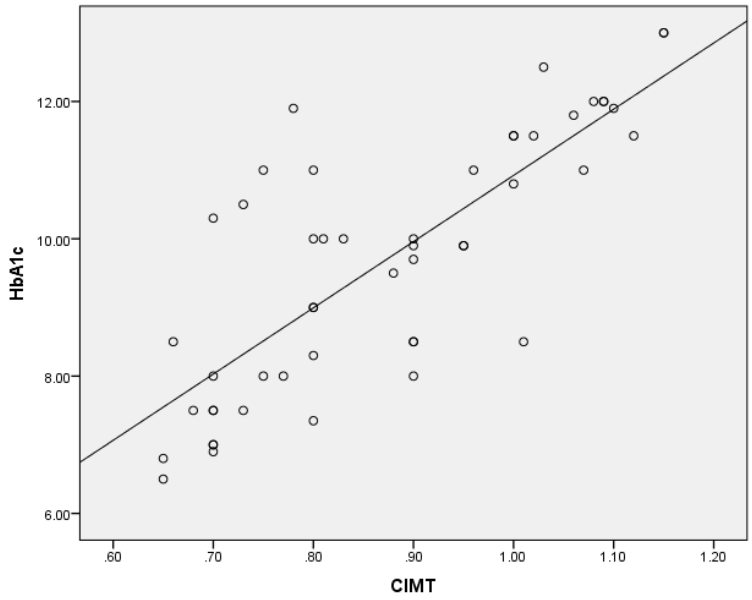

Figure (1): Scatter plot between CIMT and HbA1c

4. Discussion

Cardiovascular disease (CVD) has become an important etiology of mortality in diabetic patients (1). The changes of microcirculation in diabetes are thought to be related to atherosclerosis progression (2). Diabetic retinopathy (DR) was suggested to be associated with CVD risk (5).
Carotid intima-media thickness (CIMT) is a noninvasive and not expensive imaging technique that can serve as a marker for cardiovascular health. It can predict future cardiovascular events (4).

In this study, we found that in diabetic patients who were free of CVD, DR was significantly associated with increased CIMT and subclinical atherosclerosis. This relation was independent of other CVD risk factors such as blood pressure, age, and serum creatinine.

Supporting our study results, Gao et al. reported a strong relation between DR and CVD in the diabetic Chinese population and the risk increased with the severity of DR. After adjustment of other risk factors, proliferative diabetic retinopathy (PDR) was an independent risk marker for CVD (6).

Similarly, Tulpor et al. found that patients with retinopathy had higher CIMT than those without retinopathy (p-value: <0.0001 for each) (7).

Moreover, Momeni et al reported that the mean CIMT of patients with DR was higher than patients without DR ($P < 0.001$). CIMT is also directly related to age, duration of diabetes, systolic blood pressure, and renal functions (8).

Liu et al. in a cross-sectional study of the middle-aged and elderly diabetic Chinese population, observed that patients with DR had increased CIMT than those without DR and that DR was associated with subclinical atherosclerosis, which is consistent with our study results (2).

Moreover, Alonso et al. results documented that DR in patients with diabetes, without CVD, and with normal kidney functions, precipitated to a higher atherosclerotic risk regarding the presence and number of plaques in the carotid arteries concluding that carotid doppler examination in patients with DR may be needed for CVD risk assessment (9).

Similarly, Carbonell et al. reported that in patients with type 1 diabetes without previous CV disease or known kidney disease, the presence of DR is associated with a higher atherosclerotic risk (10).

The significant relation between DR and CIMT after adjusting other risk factors indicates the presence of other underlying mechanisms involved in this association, mostly oxidative stress and inflammation which play a major role in the pathogenesis of DR and atherosclerosis.

The limitations of the study are the relatively small number of patients. Also, the association between subclinical atherosclerosis and the severity of retinopathy should be evaluated further. Thus, detailed research in future larger studies is warranted.

Conclusion: DR is associated with subclinical atherosclerosis and is considered an additional CVD risk factor in diabetic patients through its role in increasing atherosclerosis progression. Screening for diabetic retinopathy can be a potential early marker for detecting CVD risk in diabetic patients.

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Statements and Declarations

Conflict of interest: All authors declare that there was no conflict of interest.

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Ethics approval and consent to participate**:** This study was approved by The Ethics Committee of Cairo University Kasr Al-Ainy Hospital. Written informed consent was obtained from each participant in the study.

We declare that there is no prior publication of this article.

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