International Journal of Advanced Biotechnology and Research (IJBR)
ISSN 0976-2612, Online ISSN 2278–599X,
Vol-8, Issue-4, 2017, pp1504-1509
http://www.bipublication.com

Research Article

Diagnostic value of carotid artery intima media thickness in patient with type 2 diabetes and its correlation with HbA1c levels

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ABSTRACT

Purpose: The aim of this study was to assess the role of carotid ultrasonography and measuring the IMT and its correlation with HbA1c to observe the CVD risks in T2DM patients.

Patients and Methods: In this observational study, 205 T2DM patients were consecutively included. Hemoglobin A1C (HbA1c) levels were measured by high pressure liquid chromatography with a thermo system. Carotid arteries ultrasonography was performed with an Aloka SSD 5500 apparatus with a 7.5MHz transducer. Measurements involved a primary transverse and longitudinal scanning of the common carotid artery, bifurcation, and internal carotid. CIMT was measured in the supine position with a slight neck extension.

Results: On comparing duration of diabetes with CIMT no statistically significant difference was existed between two study groups (P = 0.425), whilethe differences ofcratinine, HbA1c and urine albumin were statistically significant (P = 0.020, P=0.041, P=0.016, respectively). There was no correlation between age (r=0.19, P=0.792), and duration of diabetes (r=0.125, P=0.081) with CIMT. Furthermore, there was no remarkable association between weight and CIMT (r= 0.12, P=0.881) and between FBS and CIMT (r= 0.062, P=0.405). There was also negative non-significant correlation between HbA1c% and CIMT (r= -0.127, P=0.127).

Conclusion: The atherosclerosis complications in diabetes are the most prevalent and challenging issue in this era of diabetic management today. Assessment of cIMT by ultrasound is a safe and inexpensive way of determining atherosclerosis. Thus the predictive worth of the ultrasound as a safe and noninvasive examination may alert the experts of the related field early enough to intervene, to prevent major cardiovascular complications.

Keywords: Diabetes, HbA1c, intima-media thickness, ultrasound

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most common types of chronic diseases, which encountered for about 90% of the diabetic patients. T2DM is associated with a high risk of cardiovascular diseases (CVD), including coronary artery disease (CAD) with chest pain (angina), heart attack, stroke, atherosclerosis and hypertension[1].T2DM along with obesity, insulin resistance have a pro-inflammatory profile of circulating adipokines and cytokines, which may contribute to the development of cardiovascular disease[2].In T2DM, close-fitting glycaemic control decreases the risk of diabetic complications, but it remains tentative whether

variability of glycaemia and its correlates such as glycatedhaemoglobin (HbA1c) influences outcomes. Several studies reported that long-term glycaemic variability expressed by HbA1c could predict the development of cardiovascular complications[3]. Atherosclerosis is the major risk factor of CVD, is enhanced in T2DM.Atherosclerosis-induced vascular complications are the major cause of morbidity and mortality in T2DM patients.The carotid artery intima media thickness (CIMT) can be measured by ultrasonography, which provides a high degree of accuracy estimate of the arterial wall thickness. This imaging method is relatively safe, noninvasive and inexpensive method of assessing sub-clinical atherosclerosis. Uncontrolled and late diagnosed vascular atherosclerosis such as carotid artery may lead to accelerating the risk of cardiovascular complications and their mortality in T2DM patients. Thus the aim of this study was to assess the role of carotid ultrasonography and measuring the IMT and its correlation with HbA1c to observe the CVD risks in T2DM patients.

Patients and Methods:

Study design and population: In this observational study, 205 T2DM patients were consecutively included. The study was approved by Ahvaz Jundishapur University of Medical Sciences Ethical Committee and all participants signed the unformed consent prior to enrollment.

Inclusion criteria: Patients with diabetes, body mass index (BMI) more than 25 Kg/m^2, age between 30 to 50 years, history of diabetes from 5 to 15 years, systolic blood pressure less than 140 mmHg and diastolic blood pressure less than 90 mmHg, triglyceride less than 200 mg/dL, HDl more than 40 mg/dL in males and more than 50 mg/dL in females, no history of smoking were included.

Exclusion criteria:patients with history of CVD, smoking, hypertension, age more than 50-year or less than 30-year, diabetes more than 15-year or less than 5-year, history of radiation therapy and chemotherapy were excluded.

Data collection: Information includingage, sex, weight, height, history of smoking, and hypertension were collected. Body-mass index (BMI) was calculated as body weight divided by the square of the height. Laboratory test, including Fasting blood glucose, serum creatinine, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and triglyceride levels were recorded. Glucose, creatinine, and lipid profile were determined using standard methods. Hemoglobin A1c (HbA1c) levels were measured by high pressure liquid chromatography with a thermo system. The urine albumin then were calculated and patients were divided into three groups, including normal (<30mg), microalbuminuria (30-150 and 150-300), and macroalbuminuria (>300 mg).

Carotid Ultrasonography: Carotid arteries ultrasonography was performed with an Aloka SSD 5500 apparatus with a 7.5MHz transducer. Measurements involved a primary transverse and longitudinal scanning of the commoncarotid artery, bifurcation, and internal carotid. CIMT was measured in the supine position with a slight neck extension. The CIMT was measured on the far wall at 1 cm from bifurcation of the common carotid artery as the distance between the lumen-intima interface and the media-adventitia interface. At least three measurements were performed on both sides, and the average measurement was taken as the CIMT. All measurements were made at a plaque-free site.

Statistical analysis: All statistical calculations were done by SPSS 19.0 (SPSS for Windows, version 17.0, Inc., Chicago, IL, USA). Categorical variables were expressed as number and percentage, while continuous variables were expressed as mean ±standard deviation (SD). Chi-square (χ^2) test was used to compare categorical variables; hencecontinuous variables were compared with Student *t*-test. Correlation analysis was performed using Pearson or Spearman tests. Levels of statistical significance were set at a *P*value <0.05.

RESULTS

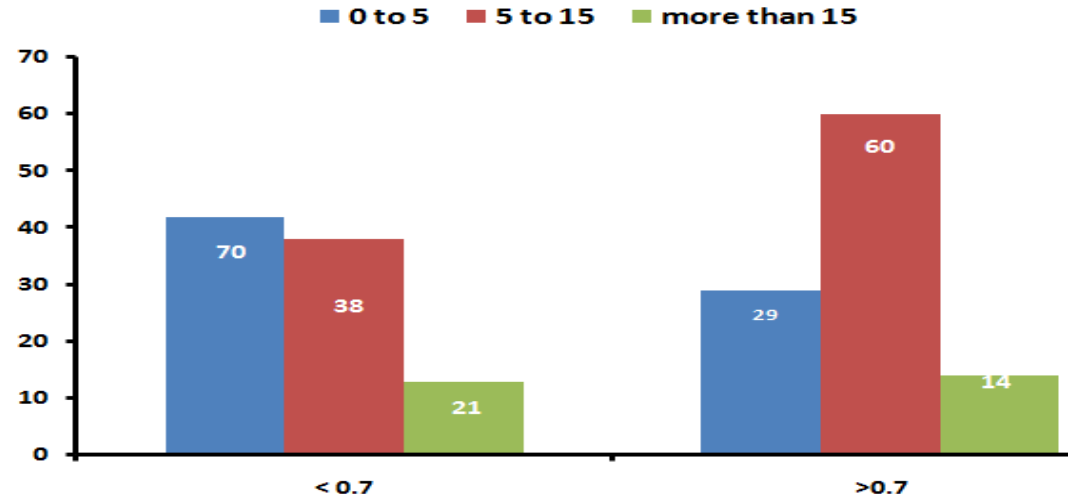
A total of 205 patients were studied of which 120 (58.5%) were females. The mean values of the various parameters expressedbetween the groups with a CIMT less than and more than 0.7mmwere calculated (Table1). On comparing duration of diabetes with CIMT no statistically significant difference was existed between two study groups (P = 0.425). Besides comparing cratinine, HbA1c and urine albumin between two groups there were statistically significant differences (P = 0.020, P=0.041, P=0.016, respectively). While the rest variables showed no statistically significant differences (Table 1). Overall mean of the CIMT was around 0.7mm, while the mean CIMT in female patients was relatively smaller than males (0.66mm vs. 0.69mm). There was no correlation between age and CIMT (r=0.19, P=0.792). There was non-significant correlation between duration of diabetes and CIMT (r=0.125, P=0.081). It was also noticed that as albuminuria was significantly correlated with CIMT (r=420, P=0.000).Furthermore, there was no remarkable association between weight and CIMT (r= 0.12, P=0.881) and between FBS and CIMT (r= 0.062, P=0.405). There was also negative non-significant correlation between HbA1c% and CIMT (r= -0.127, P=0.127).

Table 1: Means of variables compared between the groups

Variable	CIMT<0.7mm N= 99	CIMT≥0.7mm N = 106	P-values
Age (year)	55.57(10.06)	57.30 (5.55)	0.226
Weight (Kg)	75.30 (13.2)	73.98 (11.4)	0.546
Diabetes duration	8.43 (6.73)	8.87 (5.42)	0.425
FBS	163.14 (61.2)	155.91 (72.2)	0.223
TG	179.37 (125.8)	173.11 (74.6)	0.080
Cholesterol	183.41 (58.11)	164.89 (33.41)	0.493
LDL	101.30 (43.12)	105.12 (34.28)	0.566
HDL	45.76 (9.55)	47.32 (9.57)	0.727
Cr	**0.83 (0.24)**	**1.06 (0.33)**	**0.020**
HBA1c%	**7.58 (2.02)**	**7.38 (11.4)**	**0.041**
Urine ALB	**36.66 (62.09)**	**104.89 (101.83)**	**0.016**
GFR	106.23 (35.13)	103.24 (41.37)	0.496

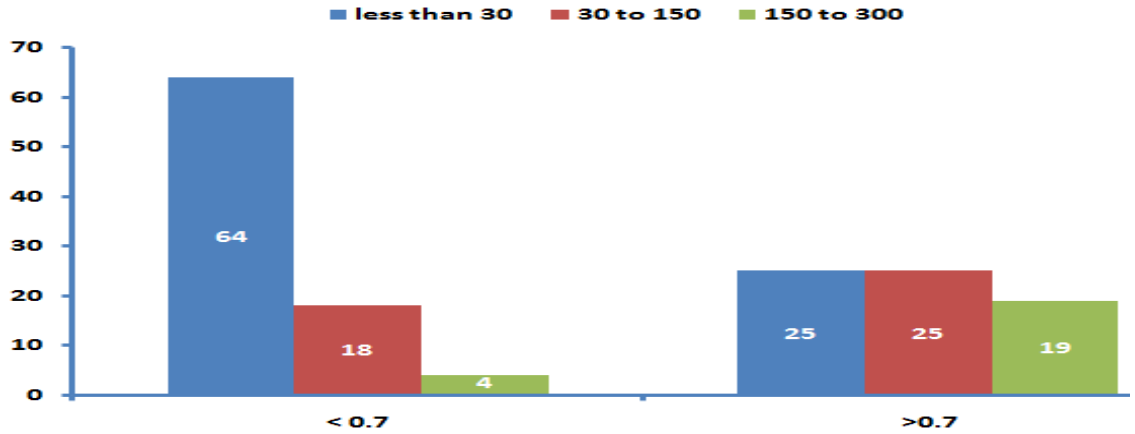
Among those with diabetes duration of more than 15 years, only 38.5% had increased CIMT, hence in the group with duration of 5 to 15 years, 56.6% had increased CIMT (P= 0.451, Figure 1).

Figure 1: Association of duration of diabetes with CIMT



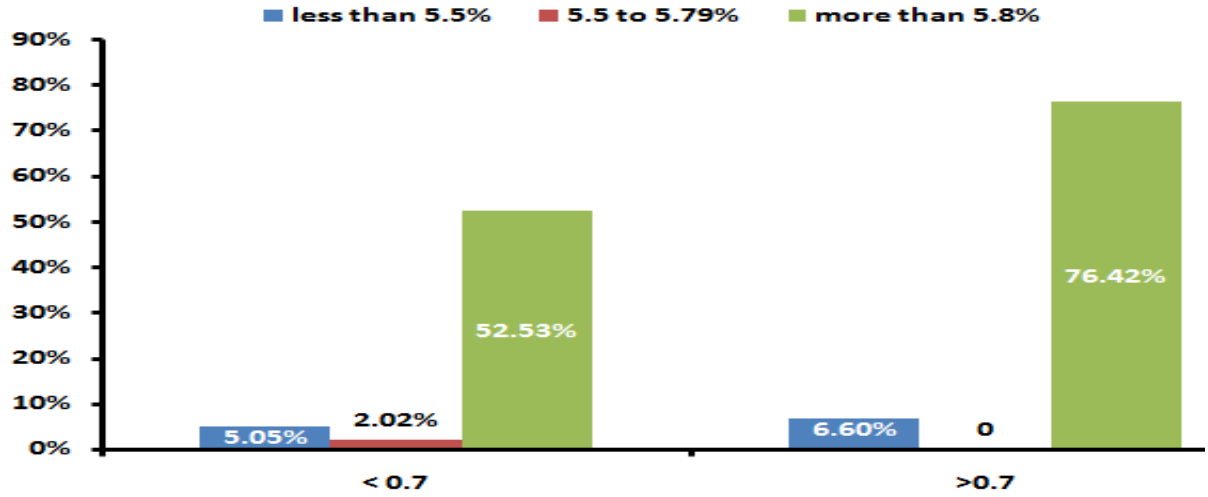
Comparing the microalbuminuria between two groups considering the CIMT cutoff (0.7mm), significant difference was exist (22.2% vs. 41.5%, P<0.001, Figure 2).

Figure 2: Association of albuminuria with CIMT



Comparing variousHbA1c% values with CIMT, showed that increased CIMT (>0.7mm) was significantly more prevalent in patients with HbA1C> 5.8% (Figure 3, 76.43 vs. 52.53%, P=0.006).

Figure3: Association of various values of HbA1c% with CIMT



The factors which were significant in uni-variate analysis were considered for multivariate analysis by multiple linear regression models. Among the various variables the maximum significance was obtained with weight, duration of diabetes, HDL and Cr with values of 0.012, 0.029, 0.021 and 0.036, respectively (Table 2).

Table 2: Multivariate Analysis of the variables of interest

Variables	Wilk's Lambda value	F-test	P-value
Duration of diabetes	**0.510**	**4.859**	**0.029**
Weight	**0.627**	**5.569**	**0.012**
FBS	0.812	2.201	0.138
HbA_{1c}	0.755	3.083	0.069
LDL	0.991	0.089	0.915
HDL	**0.666**	**4.761**	**0.021**
Cr	**0.706**	**3.963**	**0.036**
Cholesterol	0.980	0.190	0.829
TG	0.975	0.242	0.787

DISCUSSION

Measuring CIMT by invasive techniques such as ultrasonography could help in the diagnosis of cardiovascular complications like arteriosclerosis in the early clinical phases, and may help in the detection of non-symptomatic cardiovascular diseases as well. Thus,an associationoran increaseinthe CIMTincrease the risk of

cardiovascular complications such asarteriosclerosis also has a great importance. The averageCIMTinthis studywasapproximately0.7mm; hence0.9mmhas been reportedin other studies. Besides, the mean CIMin women was less than expected than men due to the supportive role of female hormones, and the male is more pronetoarteriosclerosis [4]. In our study, the mean CIMT was also lower in female patients than in male patients.

Inthis study there was no significant relationship between age and CIMT. In two studies, Drouth *et al.*[5] and Gayathri *et al.* [6]also reported noassociation betweenage andCIMT. But Robin andcolleagues reported age as independentpredictor thatpositivelycorrelated with CIMT.Inthis study, we found that theduration ofdiabetes was not significantlycorrelated withthe CIMT. Whereas Gayathri*et al.*[6]observed increased CIMT with increasing duration of diabetes.

Our findings indicated that there is no significant correlation between the weight and CIMT, in which Gayathri*et al.* [6]study confirmed these findings and also showed no significant relationship between body mass index and the CIMT. While De Michele *et al.* [7] demonstrated independent association between general and central obesity increased body mass index with increasing CIMT.

The present study showed a significant correlation between FBS and CIMT. Similarly Mita *et al.* [8] observed thatlevel of glycemic control was associated with CIMT. Slyper*et al.* [9] showed that CIMT was increased in the obese adolescents compared with the normal-weight-matched controls

The present study showed thatHbA1c levels had a significant inverse correlation with the CIMT. Haring *et al.*[10] studied the association between HbA1c and the mean CIMT among 1,798 individuals without diabetes. They reported a positive correlation between HbA1c and the mean CIMT, so this may explain the association between high HbA1c levels and the increased risk of cardiovascular diseases and mortality. Larsen *et al.*[11] considered CIMT as a validated surrogate marker of early atherosclerosis. They assessed the association between CIMT and HbA1c in over 18-year old patients with diabetes, and reported that these patients have earlier and more advanced development of atherosclerosis compared with age- and sex-matched controls.

Bayir*et al.*studied50 patients with diabetes were compared with45healthy controls. They showed a significantly higher cIMT was found in the patients with diabetes when compared with control group. So diabetes is associated with higher cIMT, especially in a pediatric population, but cIMT was not affected by mean HbA1c level and median HbA1c level [12].

Verdoia*et al.* [13] evaluated the relationship between HbA1c and cIMT in the patients without diabetes mellitus, and reported that HbA1c was significantly associated with cIMT.

Larsen *et al.* [11] elucidated the association of cIMT with long-term mean HbA1c and preclinical coronary atherosclerosis using ultrasonography in In 39 individuals over 18 years with diabetes. They suggested an important role of HbA1c in the development of atherosclerosis, especially in women with diabetes, and cIMT reflects preclinical coronary atherosclerosis.

CONCLUSION

The atherosclerosis complications in diabetes are the most prevalent and challenging issue in this era of diabetic management today. Assessment of cIMT by ultrasound is a safe and inexpensive way of determining atherosclerosis. Thus the predictive worth of the ultrasound as a safe and noninvasive examination may alert the experts of the related field early enough to intervene, to prevent major cardiovascular complications.

Moreover A healthy lifestyle and good glycemic control can cover the way for significantly reducing such unpleasant events.This may make a huge change in the diabetes-related cardiovascular complications, which may eventually lead to healthy lives.

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