

Evaluation of Ankle-Brachial Pressure Index and Carotid Intima Media Thickness by Doppler Ultrasound in type two Diabetics.

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Summary:

Background: Atherosclerosis causes thickening of the artery walls. The intima-media thickness (IMT) of the common carotid artery (CCA) is widely used as an early indicator of the development of coronary artery disease, atherosclerosis, and independently cardiovascular disease (CVD). Diabetes increased the risk of cardiovascular disease, also accelerates the common IMT progression. The Sonographic measurement of carotid intima-media thickness is used as a valid simple and noninvasive method for the assessment of atherosclerosis disease.

Also the ankle brachial index (ABI) is considered as a strong predictor for future cardiovascular events, and a golden standard for the diagnosis of peripheral arterial disease (PAD).

Objectives: To estimate the validity of carotid IMT plus the ankle brachial index as a marker of atherosclerosis in diabetic patients.

Materials and methods: This study involved (101) patients with type 2 Diabetes Mellitus, (37) with hypertension and (64) without hypertension. (46) normal volunteers represent the (Control group). The three groups were subjected to the routine laboratory tests including: fasting blood sugar, lipid profile. Measurements of blood pressure, BMI, waist circumference were taken, ECG, carotid intima media thickness and ABI by using Doppler ultrasound machine.

Results: Statistical significant differences are found for the mean of the carotid intima media thickness, lipid profile, and systolic blood pressure for both arms and legs in type 2 D M patients with and without hypertension, and normal subjects. The diabetic patient's data revealed an increase in the carotid IMT more than the non diabetic subjects. Furthermore no significant differences were found to exist in ABI results among the diabetic and normal groups.

Conclusion: The external examination by Doppler ultrasound of the carotid intima media thickness can be used to predict the occurrence of artery atherosclerosis, while ABI is less validated in this study with the selected type 2 diabetes mellitus patients without any cardiovascular disease.

Key words: Diabetes, Common carotid artery, intima media thickness, atherosclerosis, ankle brachial index.

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Introduction:

Patients with type 2 diabetes mellitus (2DM) are at high risk for developing atherosclerosis, cardiovascular and peripheral arterial diseases (1). Eight percent (8%) of diabetics would have peripheral arterial disease at the time of diagnosis of diabetes, which increase to (45%) by 20 years of duration of the disease (2). Atherosclerosis is a disease in which plaque builds up inside the arteries leading to ischemic heart disease (IHD), and peripheral vascular diseases (PVD)(3). It is a slowly progressive disease with multiple contributing factors such as diabetes mellitus, fatty diet, hypercholesterolemia, hypertension, advancing age, obesity, family history of premature coronary heart disease (CHD), and smoking (4). Many researchers believe atherosclerosis begins with an injury

to the innermost layer of the artery "endothelium". Although atherosclerotic and stenosis process occurs at the same time in the most arteries but the assessment of carotid atherosclerosis by the ultrasonography measurement of common carotid intima media thickness (CIMT) took over as surrogate measure of clinical atherosclerosis (5), and more contentiously to trace the progression of atherosclerosis. The use of ultrasound measurements as a non-invasive tool to track changes in arteries and then as indicator for further risk of clinical cardiovascular outcomes has increased since 1990 (6).

the ratio of the ankle to brachial systolic blood pressure (ankle-brachial index "ABI") was evaluated as an indication of atherosclerosis, and the severity of peripheral arterial disease (7). The ABI is the most simple and inexpensive test for the diagnosis of PAD, although the method sensitively is poor

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for the assessment of vascular risk. In most epidemiological studies, the ABI which measured by Doppler ultrasound, represents a good diagnostic standard. The present study has two main objectives, firstly: to analyze the relationship between the ankle brachial index (ABI), and the carotid intima media thickness (IMT) in type 2 diabetes mellitus with and without history of an atherosclerosis in those patients.

Materials and methods:

This study was conducted at the National Diabetes Center of AL-Mustansiriah University (Baghdad-Iraq) for the period between October 2011 and April 2012. This work involved (101) patients with type 2 diabetes Mellitus (2 DM) and (46) normal volunteers (Control group). The Patient group was subdivided in to two groups:

Group (1): Includes thirty seven type 2 diabetes patients with history of hypertension. Age range between 43-70 years (male 6, female 31).

Group (2): Contains sixty four patients with type 2 diabetes with no history of hypertension and again with no manifestation of ischemic heart disease, cerebrovascular disease and peripheral vascular disease. Age range between 32-70 years (male 22, female 42).

Group (3): Consists forty six apparently normal subjects considered as a control group. Age range between 36-68 years (male 12, female 34).

Full medical history and examination including FPG, Lipid profile, DM duration, the weight and height. Waist and Body mass index (BMI) were also measured. Blood pressure was monitored by sphygmomanometer on the day of diagnosis. Patients were considered as hypertensive when systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg according to the criterion of Joint National Committee 7 (JNC7), based on the average of 2 readings, and also on the pressure reported by the patient, with a known history of hypertension.

All groups were subjected to a routine laboratory tests including fasting blood sugar, lipid profile, lipoprotein using Spectrophotometer "Cecil CE 72000-France".

Exclusion criterion: Age < 30, Patient with ischemic heart disease, peripheral vascular disease, stroke, antilipid drug > 6 months.

The scanning protocol involved studying the right and left CIMT. All ultrasound scanning, through the whole study, were performed by the same radiologist, and ultrasound equipment. Ultrasound machine (FUKUDA DENSHI of Japanese production "UF- 750 XT" with a 6-9 MHz linear probe "FUT-L D386-9A") was used to evaluate intima media thickness (IMT) of the common carotid arteries, and ankle-brachial arteries. After the patient had rested for at least 5 min in the supine position with the neck in slight hyperextension. The ultrasound probe was placed medial to the sternocleidomastoid muscle, and the common carotid artery was identified. Longitudinal

projections at different angles were utilized to detect the maximal Carotid Intimal Media Thickness. IMT was assessed in both sides of neck. Ankle Brachial Pressure index (ABPI) or (ABI): Is the ratio of the systolic blood pressure in ankle (Pleg) to the systolic blood pressure in the brachial (Parm) arteries (8).

Firstly: blood pressure was checked manually {including systolic (SBP) and diastolic (DBP) blood pressure} for both upper and lower limbs respectively. Secondly: the blood pressures checked again by Doppler ultrasound device according to the following steps. The blood pressure cuff was inflated until the blood flow signal on the ultrasound monitor disappears. Then the cuff deflates gradually till the signal re-appear. The pressure reading on the sphygmomanometer monitor at this moment indicating the systolic blood pressure (SBP) at the examined limb. The same maneuver was done for both upper and lower limbs. In this work the ABI was calculated using the higher systolic blood pressure measured in the left (LT) or right (RT) tibial artery (Pleg) divided by higher systolic blood pressure reading in the left or right brachial artery (Parm). Data were analyzed using Statistical packages for social sciences-version 17 (SPSS -17). Statistical analyses for significance of differences for the quantitative data were done employing ANOVA test.

Results:

The mean \pm standered deviation of the clinical, and the Sonographic data plus the blood samples results of patients groups (1), (2), and control group (3) in the present study are summarized in table (1). The P value for each parameter listed in table (1) is obtained according to the ANOVA analyses among the three groups. The probability (P value) of ≤ 0.05 is considered significant. Table (1) revealed that there are no significant differences in height, weight between the groups.

The Body mass index for the type 2 DM patients with history of hypertension (group 1) (30.51 ± 4.903 Kg/m²), and patients without history of hypertension (group 2) (30.22 ± 5.587 Kg/m²) show a slight increase in comparison with the control (group 3) (28.19 ± 4.13 Kg/m²), but the differences are not significant. In contrast the waist circumferences (WC), results demonstrate a high significant difference ($P < 0.000$) in the mean values for patient groups (104.84 ± 9.71 and 103.42 ± 18.269 cm) relative to the control group (93.22 ± 9.35 cm). In addition there are differences in systolic blood pressure (SBP), measured at the upper arm, among the diabetic patients groups (154.59 ± 21.028 , 140.22 ± 24.712 mmHg) and control (117.07 ± 17.593 mmHg), but not in the diastolic blood pressure.

Table (1): The mean and slandered deviation for the clinical and ultrasonographic parameters of the three groups, with the P value.

Examined parameters	Normal Value	Group 1 Mean ± SD (2 DM with hypertension)	Group 2 Mean ± SD (2 DM with no hypertension)	Group 3 Mean ± SD (Normal subjects)	P value
Age (years)		56.68±6.312	54.54±8.561	47.63±8.255	N.S
Duration of DM (years)		6.38±5.063	5.88±5.341	NO	N.S
Height (cm)		159.38±7.959	161.288±9.528	162.4±6.861	
Weight (Kg)		78.581±12.099	78.745±14.642	76.11±14.44	
BMI (Kg/m ²)		30.51±4.903	30.22±5.587	28.19±4.134	N.S
WC (cm)	80-95	104±0.714	103.42±18.269	93.22±9.357	0.000
BP S (mm Hg)	90-140	154.59±21.028	140.22±24.712	117.07±17.593	0.000
BP D (mm Hg)	60-90	85.41±12.822	79.53±9.989	81.85±9.508	0.030
B.urea (mg/dL)		30.92±6.094	30.50±6.726	29.41±7.968	N.S
Creatinine(mg/dL)	0.6-1.3	0.72±0.185	0.70±0.178	0.52±0.225	0.000
FPG (mg/dL)	80-110	166.38±44.349	190.97±62.196	99.50±8.966	0.000
CH.(mg/dL)	≤200	193.70±69.839	184.17±62.456	154.41±34.305	0.004
TG (mg/dL)	≤130	157.27±94.078	154.61±93.517	101.09±23.695	0.001
LDL (mg/dL)	≤100	119.68±66.224	111.61±56.821	89.57±29.865	0.024
VLDL (mg/dL)	≤40	30.43±15.928	31.06±20.329	20.39±4.814	0.001
HDL.(mg/dL)	≥50	46.73±7.777	45.98±8.082	48.48±6.966	N.S
IMT RT (mm)	≤ 0.8	0.84±0.092	0.84±0.123	0.71±0.102	0.000
IMT LT(mm)	≤ 0.8	0.881±0.145	0.82±0.119	0.72±0.097	0.000
P.leg RT (mm Hg)		180±23.333	160.86±29.190	148.91±17.15	0.000
P.leg LT (mm Hg)		176.49±24.292	161.56±24.974	151.30±15.86	0.000
P.arm RT (mm Hg)		154.86±22.063	139.53±17.721	125.43±12.420	0.000
P.arm LT (mm Hg)		154.46±24.489	138.78±17.884	123.70±12.712	0.000
ABI		1.18±0.133	1.18±0.175	1.20±0.092	N.S

N.S: No significant

Fasting Plasma Glucose (FPG) shows a high significant difference ($P < 0.000$) for patients with history of hypertension (166.38 ± 44.349 mg/dL), without hypertension (190.97 ± 62.196 mg/dL) as compared to control (99.50 ± 8.966 mg/dL). The creatinine, also indicates a high significant difference ($P < 0.000$) showing an increase in the mean values for the patient groups (1) & (2), (0.72 ± 0.185 mg/dL) (0.70 ± 0.178 mg/dL), which are higher than the control (0.52 ± 0.225 mg/dL), table

(1). No statistical significant difference is found between the three groups regarding the mean of blood urea (B.urea). Analysis of lipid profile demonstrate a significant rise in the mean value of cholesterol in patients with hypertension (193.70 ± 69.839 mg/dL), and without hypertension (184.17 ± 62.456 mg/dL) compared to control (154.41 ± 34.305 mg/dL), ($P \leq 0.004$). There are no high differences in mean of TG and LDL within patient groups. But the TG and LDL are

significant higher in patient groups (1) and (2) than control group result. The mean value of HDL in patient groups are (46.73±45.98 mg/dL), and (45.98±8.082 mg/dL) which is less than value of the control (48.48±6.966 mg/dL), table (1).

The diabetic patient results for both groups reveal atherosclerosis in the common carotid arteries (CCA) more than the non-diabetic subjects. Where the mean of the intima media thickness of the left CCA (0.88 ± 0.145, 0.82 ± 0.119, 0.72 ± 0.097mm), and the right side (0.84 ± 0.092, 0.84 ± 0.123, 0.71 ± 0.102 mm) respectively, table (1). Results also indicate that there is a significant difference (P<0.000) between the mean of the IMT for the left side (0.88±0.145 mm) compared to the right side (0.84±0.092 mm) in hypertensive patients, where results in non hypertensive patients is almost similar.

The mean of the ABI results, for three groups, indicate no significant differences between them, table (1). In spite of the actual parameters, (the left and the right Ankle and Brachial systolic blood pressures which are used in the ABI calculations) demonstrate a significant differences between these groups.

Discussion:

People with type 2 diabetes mellitus have a greater incidence of cardiovascular disease, cerebrovascular disease, and renal disease than general population. Hypertension, duration of diabetes, hyperglycemia, and dyslipidemia has been identified as significant risk factors raising the carotid IMT.

The present study demonstrates a statistically significant increase in the mean of carotid IMT in patients with type 2 diabetes mellitus compared to control subjects, table (1). Such finding is in agreement with Amer et al (9) and Marcos et al (10).

The results also indicate that the left side of carotid IMT in hypertensive patients with type 2 DM is higher than right side. Foerch et al (11) had also reported a significant difference between the left and right common carotid artery intima-media thickness in untreated hypertensive patients. Rosfors et al study (5), support an earlier observation of such changes in the IMT, suggesting faster development of carotid atherosclerosis on the left than on the right side. This raises the possibility that atherosclerotic lesions develop earlier on the left side, perhaps because of the different in blood pressure or may be due to the gross anatomy of the left and the right CCA, where the left CCA originating directly from the aortic arch (12). Furthermore, Casiglia et al (13) indicated that hypertensive patients have a greater carotid IMT than normal subjects. Since hypertensive patients whom were free from any other important medical disease having high circulation levels of pro inflammatory cytokines (14). Cytokines may cause inflammation, and then further damage to the endothelium layer which may elevate blood pressure (15). Bots et al (16) reported that, the IMT of type 2 diabetic patients with coronary artery disease (CAD) was significantly greater than that of diabetic patients without CAD. The most typical lipoprotein pattern in diabetes, which

is also known as diabetic dyslipidemia consists of moderate elevation in cholesterol (CH), triglyceride levels (TG), low density lipoprotein (LDL) and low level of a high density lipoprotein (HDL) particles. This lipoprotein pattern is associated with insulin resistance, and presented even before the onset of diabetes. Patients with type 2 DM are particularly prone to dyslipidemia which accelerate carotid IMT and atherosclerosis compared to general population (17). Scoppola et al (18) conclude that the lower the degree of blood glucose control, the higher is the whole body cholesterol production. The increase of LDL and decrease of HDL cholesterol levels is an important contributor to accelerated atherosclerosis in diabetes mellitus and insulin-resistant conditions, which may leads to hypertension (19). Mooradian (20) reported a high triglyceride and low HDL cholesterol levels generally associated with increased cardiovascular risk. In the present study the mean of the BMI is almost the same for the three groups. Even though Fontains et al (21) postulate that, obesity probably acts as a diabetogenic factor, through increasing resistance to the action of insulin, in those genetically predisposed to develop type 2 DM. they also indicated obesity is associated with an increased risk of type 2 DM, hypertension, and cardiovascular disease. But Guagnano et al (22) indicated that the BMI seems to have no significant relationship to hypertensive risk, even among subjects with severe obesity (BMI >40), and the risk of hypertension was weakly statistically significant with BMI ranging between 25-29.9. Diabetes and duration of diabetes is positively associated with the severity of macro- and micro-vascular complications, both of which contribute to the development of renal and/or atherosclerotic hypertension (23).

Even though the mean of the blood urea and serum creatinine for the three groups are within the normal range, but still the creatinine in groups (1), and (2) are higher than the control, table (1)

Huda et al (24); and Shahid et al (25) found, the groups of diabetes mellitus with hypertension patients demonstrated a significant increase in creatinine compared to the control subject. Their results are in agreement with our observation.

It has been indicated that the ABI is a sensitive method for diagnosis of Peripheral Arterial Disease (PAD) (7, 26). Diabetes is the most powerful risk factor for PAD, among many other factors like: age, duration of diabetes, and the presence of neuropathy (27). From the ABI data, for the three groups table (1), it can be concluded that the ABI play no role among the patients of type 2 diabetes, without PAD, and control. But there are significant differences among the systolic blood pressure of arms and legs in these groups. So the systolic blood pressures of the ankle or brachial may be considered an appropriate tool for the initial screening of arterial stenosis and lower extremity circulation instead of ABI. Doobay et al (7) indicated that ABI ≤ 0.9 is the mean parameter for PAD diagnosis. Potier et al (28) in selected diabetic patients at high risk of PAD, show

that the ABI between 0.9 and 1.3 or greater than 1.3 can be explained by the high risk of arterial calcification in such patients, leading to overestimating ankle arterial pressure.

Conclusion:

Although included low mean age in control group than patient groups this may cause slight differences in common CIMT results. But still it can be concluded that:- The type 2 diabetes mellitus patients have high carotid IMT than the normal subjects.

Furthermore, among diabetic patients the carotid IMT is lower in diabetic patients than in diabetic patients with hypertension. Also the IMT at left side is higher than the right side. The ABI is less prospective parameter than common CIMT, and other classic risk factors such as blood pressure as a non invasive marker of arteriosclerosis.

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