Thickened Common Femoral Artery Intima Media Thickness: a Surrogate Marker for Subclinical Peripheral Arterial Disease in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Thickening of arterial wall is an early indicator of atherosclerosis which is mostly a poly vascular disease. Thickened carotid intima media thickness is now well accepted as a surrogate marker for cardiovascular, cerebrovascular, and peripheral vascular affection. Some data exists regarding the relationship between intima media thickness of the common femoral artery as a predictor of different vascular beds atherosclerosis.

.**Aim:** To evaluate the ability of common femoral artery intima media thickness to predict subclinical peripheral arterial disease in elderly patients with type 2 diabetes mellitus.

Methods: 60 elderly subjects with type 2 diabetes were examined for the presence of asymptomatic PAD. All were assessed by measuring Common Femoral Artery Intima Media Thickness CFA IMT, ankle brachial index (ABI).

Results: The patients with reduced ABI (N=9) had greater CFA-IMT than those without (N=51). The correlation between CFA-IMT and ABI was highly significant. CFA IMT≥ 8.5 mm had an area under the curve of 0.962 (95% CI; 0.917- 1.007, p = 0.000*) for predicting subclinical PAD in patients with type 2 diabetes.

Conclusions: This data suggests that thickened CFA IMT is a significant predictor of asymptomatic PAD in patients with type 2 diabetes

Keywords: Diabetes mellitus Thickened common femoral artery intima media thickness - PAD- elderly

Background

Peripheral arterial disease (PAD) is a major problem in diabetic population because of higher incidence. [1] And poorer prognosis compared to those without diabetes. [2] PAD is a strong predictor of atherosclerotic changes in other vascular beds. The incidence of cardiovascular and cerebrovascular events is higher in the diabetic patients suffering from PAD compared to those without PAD. [3] PAD in the most of diabetic patient is asymptomatic and the pain perception is altered by the presence of peripheral neuropathy making the true prevalence of PAD among diabetics difficult to determine. [4]

Previous arteriography based studies have demonstrated that diabetes is characterized by infrapopliteal arterial occlusive disease and vascular calcification. The only above knee affected artery was profunda femoris artery. [2]

A reliable diagnosis of PAD can be made using the ankle-brachial index (ABI). This is a simple, non-invasive and reasonably accurate screening recommended in all diabetic individuals >50 years of age. However, ABI measurement has its drawbacks because medial calcification of the tibial arteries making them non-compressible, resulting in unusually

high ABI values (>1.40). [3]

The intima-media thickness is the best method for early detection of atherosclerosis even before plaque is developed. Moreover, the measurement of the intima-media thickness is independent of the blood pressure. [5] Previous studies reported the association between femoral IMT and ABI in hypertensive high risk group. [6] In another study the CFA IMT was higher in those with PAD compared to the control group. [7]

The aim of the present study is to investigate whether intima–media thickness of the common femoral artery is predictive of silent PAD in patients with type 2 diabetes mellitus.

Methods

Study population

60 elderly (≥ 60 years) diabetic subjects (30 males and 30 females) attending the outpatient clinic at Ain Shams University Hospital, Cairo, Egypt were recruited for the study. Diabetes mellitus was defined according to the American Diabetes Association criteria (fasting plasma glucose glucose ≥126 mg/dl (minimum of 8 h fasting), a random or postload serum glucose level glucose ≥200 mg/dl after an oral glucose tolerance test, or use of hypoglycemic medication. Subjects with hypertension, history or symptoms suggestive of PAD, ischemic heart disease (IHD) or cerebrovascular disease were excluded. We also excluded cases with suspected medial calcification with ABI >1.3.

Vascular assessment:

A diagnosis of peripheral arterial disease (PAD) was made based on an ankle–brachial index (ABI) of less than 0.90 measured with a sphygmomanometer cuff and a handheld 8-MHz Doppler probe. CFA IMT was measured on both legs using Hitachi, EUB-565A, B mode-Doppler with color imaging then values averaged. Measuring the double line pattern which corresponds to the lumen–intima and the media–adventitia measurements were conducted in plaque-free portions of the CFA the maximal IMT of the vessel was determined by the observer. The Pulse-Volume Recordings and Continuous-Wave Doppler Ultrasound of lower extremity arteries were performed for common femoral artery, superficial femoral artery, popliteal artery, posterior tibial, peroneal and anterior tibial arteries.

Ethical considerations

Informed consent was taken from every elder participating in this study. The study methodology was reviewed and approved by the Research Review Board of the Geriatrics and Gerontology Department, Faculty of medicine, Ain Shams University.

Statistical methods:

The collected data were coded, tabulated, revised and statistical analyzed using SPSS program (version 16).

Quantitative variables were presented in the form of means and standard deviation. Qualitative variables were presented in form of frequency tables (number and percent).The comparison between quantitative variables was done using t-test. Comparison between qualitative variables was done using Pearson's Chi square test. Correlation between two quantitative variables was done using Pearson's correlation co-efficient. Spearsman's correlation coefficient was used for non- parametric correlations. Statistical difference was accepted when $P < 0.05$. ROC analysis was performed to test the predictive power of the CFA IMT.

Results

Of the 60 subjects enrolled in the study 9 (15%) had a measured ABI <0.9 (7 males, 2 females) while 51(85%) had a measured ABI >0.9. General characteristics of the study population are presented in Table 1

In this study the mean CFA IMT for males was 8.1±1.6mm and females, 6.7±1.7mm (p=0.002).

Table 1: **Characteristics of the studied population**

	Cases (n=60)
Age y	64.4±4.6
BMI kg/m^2	28.4±4.7
FBS mg/dl	157.5±39.7
2hPP mg/dl	250.5±57.6
CFA IMT mm	7.6±1.7
ABI	0.91±0.13
PAD n (%)	9 (15%)
Current smokers, n (%)	17(28%)

BMI: body mass index; FBS: fasting blood sugar; 2hPP: 2 hours postprandial, CFA IMT: common femoral artery intima media thickness; ABI: ankle brachial index. *Statistically significant.

Diabetic patients with PAD had higher age, and CFA IMT compared to those without PAD (P<0.05).There was no statistical significant difference between patients with and without PAD as regards FBS, 2hPP, duration of diabetes (p>0.05) (table 2).

Table 2: Characteristics of Patients with PAD:

|	**PAD**		**P**
	Yes	No	
Age (y)	70.4± 3.6	63.4± 3.9	0.000*
FBS (md/dl)	179.4± 48.8	153.6± 37.2	0.073
2hPP (md/dl)	240.7± 73.7	252.2± 55.1	0.584
DM duration (y)	11.3±4.6	9.27±6.7	0.38
CFA IMT mm	10.1± 1.05	6.9± 1.4	0.000*
ABI	0.633± 0.05	0.96± 0.05	0.000*

FBS: fasting blood sugar; 2hPP: 2 hours postprandial, CFA IMT: common femoral artery intima media thickness ABI: ankle brachial index. *Statistically significant.

Table 3: Correlation of CFA IMT with studied variables in diabetic patients:

	CFA IMT in diabetic	
	r	P value
Age	0.43	0.001*
ABI	-0.625	0.000*
Male gender #	0.336	0.009*
smoking	0.429	0.001*

CFA IMT ≥ 8.5 mm was 100% sensitive, 88.2% specific, with an area under the curve of 0.962 (95% CI; 0.917- 1.007, p = 0.000*) for predicting subclinical PAD. (Figure 1)

Figure 1: ROC curve for predicting PAD in patients with type 2 diabetes mellitus
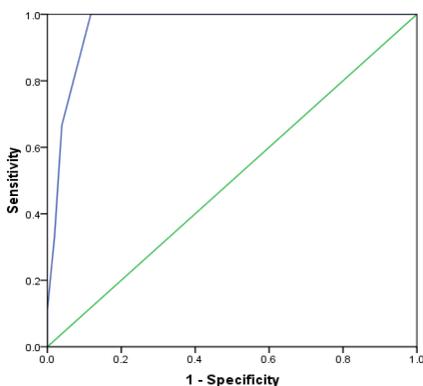
Discussion

Many previous studies addressed the association between diabetes and peripheral arterial disease. Most of them have been based on the occurrence of symptomatic disease. [8, 9] In this study only 15% of the patients suffering from diabetes mellitus had PAD. This was lower than previous studies [8, 9] due to exclusion of symptomatic cases and cases with cardiovascular or cerebrovascular diseases.

Our study showed that the patients with PAD had a higher mean of age when compared to patients without PAD (70.4 vs. 63.4) (p value<0.01). This agrees with Selvin and Erlinger, [10] who showed that that the prevalence of PAD is increased in older age. It was 4.3% in those older than 40 years and 14.5% among individuals aged 70 years.

Owing to the lack of routine screening for diabetes in the Egyptian elderly, the duration of diabetes in those with PAD was non significantly higher than those without PAD (11.3 vs. 9.27) but (p value was>0.05). While many studies reported increased carotid wall IMT in patients with PAD there is few data regarding the relationship between the femoral IMT and PAD. [6] Previous studies found that patients with diabetes exhibited infra- popliteal vascular affection [2] whether PAD has an effect of on IMT of femoral arteries in patients with DM is not known.

The ultra-sonographic measurement of the IMT is the most accurate method of assessing early atherosclerosis because it is not affected by lumen diameter. Moreover, the early atherosclerotic lesions progresses without luminal reduction due to simultaneous dilation. [11]

In the present study, we demonstrated that the IMT of the common femoral artery was significantly higher in patients with silent PAD than in those without PAD among patients with type 2 diabetes mellitus.

Age, male gender and smoking are related to the IMT in the common femoral artery (r= 0.43, p=0.001) (r=0.336, p=0.009) (r= 0.429, p=0.001) respectively. Joensuu et al. in their previous study reported that both the carotid and femoral IMTs increased significantly with age and the IMT was greater in men. [12] The AXA study [13] also reported significant relationships between the carotid and femoral IMTs with age and smoking. Cigarette smoking alone increased the IMT of both the carotid and femoral arteries in the study of van den Berkmortel et al. 1994 who demonstrated that the carotid (P=0.02) and femoral (P<0.0001) IMTs were significantly larger in smokers than nonsmokers matched for age and gender. [14]

In the current study CFA IMT correlated well with ABI measured by Doppler method in diabetic patients (r=--0.664, p=0.000), and those with PAD had thicker CFA IMT compared to those without PAD (10.1 vs.6.9 mm p=0.000)

This data was elicited among hypertensive subjects. Suurkula et al. 1996 who compared high cardiovascular risk to low risk group in hypertensive population. Subjects with high cardiovascular risk had a lower ABI and thicker CFA IMT compared to the low risk group (P<0.0001, 0.0009 respectively). [6.] In this study ABI correlated with CFA IMT. CFA IMT had a good AUC in ROC analysis for predicting subclinical peripheral arterial disease.

The limitations in interpreting the present results are: First, it is a cross-sectional study design, Second, data provided is preliminary because the number of cases with PAD is small (n=9).These points need to be addressed in the future studies applied to a larger sample size.

Conclusion:

Increased common femoral artery intima-media thickness is a strong predictor of subclinical peripheral

arterial disease in patients with type 2 diabetes mellitus. The common femoral artery intima-media thickness which is not dependent on the arterial blood pressure can be used as screening tool for PAD in patients with type 2 diabetes, especially those with medial calcification causing false high ABI.

Disclosure:

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

References

1. Gregg EW, Sorlie P, Paulose-Ram R, Gu Q, Eberhardt MS, Wolz M, Burt V, Curtin L, Engelgau M, Geiss L, the 1999–2000 National Health and Nutrition Examination Survey: Prevalence of lower-extremity disease in the U.S. adult population $\geq$40 years of age with and without diabetes: 1999–2000 National Health and Nutrition Examination Survey. Diabetes Care, 2004; 27: 1591–1597

2. Jude EB, Oyibo SO, Chalmers N, Boulton AJ. Peripheral arterial disease in diabetic and nondiabetic patientsa comparison of severity and outcome. Diabetes Care. 2001; 24:1433-1437.

3. American Diabetes Association Peripheral arterial disease in people with diabetes Diabetes Care, 2003; 26: 3333-3341

4. Dhaliwal G, Mukherjee D. Peripheral arterial disease: Epidemiology, natural history, diagnosis and treatment. Int J Angiol; 2007:16(2): 38-44

5. Cheng KS, Mikhailidi DP, Hamilton G, Alexander M. Seifalian AM. A review of the carotid and femoral intima-media thickness as an indicator of the presence of peripheral vascular disease andcardiovascular risk factors. Cardiovascular Research; 2002: 54:528 –538.

6. Suurkula M, Fagerberg B, Wendelhag I, Agewall S, Wikstrand J. on behalf of the Risk Intervention Study (RIS) Group. Atherosclerotic Disease in the Femoral Artery in Hypertensive Patients at High Cardiovascular Risk. The Value of Ultrasonographic Assessment of Intima-Media Thickness and Plaque Occurrence. Arterioscler Thromb Vasc Biol. 1996; 16: 971–977.

7. Etherington MS, Layne AJ, Mohler ER, Davis JT, Fairman RM, Woo EY et al. Femoral Intima Media Thickness As A Marker For Peripheral Arterial Disease. AAS and SUS Abstracts for the Eighth Annual Academic Surgical Congress. Journal of surgical research. 2013;179(2)

8. Elhadd, T, Robb R., Jung R., Stonebridge P, Belch J. Pilot study of prevalence of asymptomatic peripheral arterial occlusive disease in patients with diabetes attending a hospital clinic. Practical Diabetes Int. 1999; 16:163–166.

9. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA. 2001; 286:1317–1324.

10. Selvin E and Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999–2000.Circulation, 2004; 110: 738–743.

11. Sodhi HS, Shrestha SK, Rauniyar R, and Rawat B. Prevalence of peripheral arterial disease by ankle-brachial index and its correlation with carotid intimal thickness and coronary risk factors in Nepalese population over the age of forty years. Kathmandu University Medical Journal .2007: 5(1): 12-15.

12. Joensuu T, Salonen R, Winblad I, Korpela H, Salonen JT. Determinants of femoral and carotid artery atherosclerosis. J Intern Med. 1994;236:79-84

13. Gariepy J, Salomon J, Denarie N, Laskri F, Megnien JL, Levenson J, and Simon A. Sex and topographic differences in associations between large-artery wall thickness and coronary risk profile in a French working cohort: the AXA Study. Arterioscler Thromb Vasc Biol .1998; 18: 584-590.

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