Prevalence of Peripheral Arterial Disease in Diabetic Patients

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Abstract

Objective: Peripheral Arterial Disease (PAD) is a state characterized by atherosclerotic occlusive disease of lower extremities. Diabetes is the main risk factor for PAD.

Material and Methods: To assess the prevalence of PAD, a cross sectional study was performed on 352 diabetic patients who referred to Yazd diabetes research center from 2007 to 2010. Vascular assessment was done by measuring the Ankle-Brachial Index (ABI) and Toe-Brachial Index (TBI). PAD was defined when ABI was less than 0.9 in each leg or ABI was more than 1.3 and TBI less than 0.6.

Result: The mean age of diabetic patients was 56.97±10.3 and the mean of diabetes duration was 12.6±7.5 years. Fifty-two percent of these subjects were women and 48% men. ABI less than 0.9 was found in 8.5%, ABI 0.9-1.3 in 84.5%,and ABI more than 1.3 in 7%of the patients. Prevalence of PAD was 9.8%.In this study the age of diabetic patients with ABI less than 0.9 was significantly more than other groups.

Conclusion: The prevalence of PAD in type 2 diabetes is 9.8% and history of cerebrovascular disease significantly associated with PAD.

Keywords: Peripheral Arterial Disease, Diabetes, Ankle-Brachial Index, Toe-Brachial Index

Introduction

Peripheral arterial disease (PAD) is a state characterized by atherosclerotic occlusive disease of the lower extremities (1). Diabetes is the most significant risk factor for PAD (2). Peripheral arterial disease is the main cause of lower-extremity amputation, and cardiovascular and cerebrovascular events, and is seen along with an increase in mortality of more than 30% at 5 years and 50% at 10 years (4, 5).

PAD in diabetic patients also has negative effects on quality of life, resulting in long term disability and severe functional impairments (3,6). Large epidemiological studies have shown that the risk of PAD in patients with diabetes mellitus (DM) is fourfold higher compared to non-diabetic population. Because

of the fact that a large number of diabetic patients have no PAD symptom, the prevalence of undiagnosed PAD is high (7). PAD is associated with significant increase in morbidity and mortality in diabetic patients. It occurs at an earlier age in these patients, the progress is faster than non-diabetic patients, and it is diagnosed at its advanced stages. All these factors enhance the rate of limb amputation and reduce the likelihood of revascularization in DM patients with PAD (8). In this light, early diagnosis of PAD in DM patients is crucial to identify patients who need further diagnostic producers and aggressive management to prevent amputations and decrease cardiovascular morbidity and mortality.

The prevalence of PAD differs significantly depending on the population studied, definition of PAD, methods of diagnosis, age, gender and the presence of other risk factors (7). The present study was designed to identify high-risk diabetic patients with PAD and determine the contributing factors of this disorder in diabetic patients.

Material and Methods

In this cross sectional study, 352 diabetic patients who referred to Yazd Diabetes Research Center were recruited consecutively from November 2007 to July 2010. Patients with varicose veins, acute vascular diseases, collagen vascular disease and amputation due to causes other than diabetes were excluded.

From the subjects' medical records, we obtained general information including demographic information, medication type and history of medical disorders.

Informed consent was obtained from all subjects and the research had the approval of the institutional review board and ethics committee of the Yazd University of Medical Sciences and was carried out in accordance with the Declaration of Helsinki.

Vascular assessments were done according to a standard protocol, by measuring the Ankle Brachial pressure Index (ABI), Toe Brachial Index (TBI) and Toe pressure.

Doppler ultrasound (Multi/Super Duplex II) was used to measure the systolic blood pressure (SBP) on bilateral brachial, posterior tibial, dorsal pedis and toe arteries in a supine position after a 5-minutes rest. The occluding cuffs (55×12.5 cm) were applied just above the malleoli to measure ankle pressure. The first appearance of Korotkoff sounds was recorded as SBP.

The ABI for each leg was calculated by the higher SBP in the dorsal or posterior tibial arteries respectively, divided by the higher value of the two arm SBPs. The higher arm SBP was used because of the variation in arm blood pressures and the strong association between PAD and subclavian stenosis (9). If ABI was 0.9-1.3 we interpreted as normal group. PAD was defined to be present if ABI<0.9 in each leg or ABI was more than 1.3 and TBI less than 0.6.

Blood sample was obtained for measuring of Fasting Blood Sugar (FBS), 2-hour postprandial Glucose (2hPP), Hemoglobin A1c (HbA1c), Total Cholesterol (TC), Triglyceride (TG), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL),uric acid, Blood Urea Nitrogen (BUN) and creatinine.

Statistical Analysis

Statistical analyses were performed by using Statistical Package for Social Sciences (SPSS version 11.50, Chicago, IL). Chi-square test was used to compare discrete variables., Kruskal-Wallis One-Way analysis of Variance was used to compare different risk factors in diabetic patients stratified by ABI. We also used multiple regression analysis to evaluate independent risk factors of PAD. Significance was considered to be P<0.05. Results are given with their 95% CIs. Data are presented as mean ± SD.

Results

In this study the mean age of diabetic patients was 56.97±10.3 and the mean of diabetes duration was 12.6±7.5 years and 52% were women and 48% men. Among the subjects

prevalence of PAD at ABI<0.9 in each leg was 8.5% and 84.5% of the subjects had ABI 0.9-1.3 and 7% had ABI above 1.3. The mean ABI in these subjects was 1.07±0.18. If we consider the patients with ABI less than 0.9 or ABI more than 1.3 and TBI less than 0.6 as the PAD group, prevalence of PAD was 9.8%.The PAD prevalence was 7% and 5.3% for subjects with and without history of coronary heart diasese (CHD), respectively (P=0.5).

Figure 1 shows the distribution of PAD prevalence across the different age groups, with an increase in prevalence with increasing age especially in males. Subjects with PAD were older than non-PAD subjects (P=0.03), which 62.5% of diabetic patients with PAD were more than 60 years and 3.1% were less than 40 years.

Table 1 compares the possible risk factors in diabetic patients in three ABI groups. The patients with ABI less than 0.9 and more than 1.3 were older than the normal group (p=0.03). Toe brachial index in patients with ABI<0.9 was lower than the other groups (p=0.008).The other risk factors of PAD were not significantly different between ABI groups.

In our study, the level of FBS, HbA1c, TG, TC, HDL, LDL, BUN and creatinine were not significantly different among three ABI groups (P<0.05).
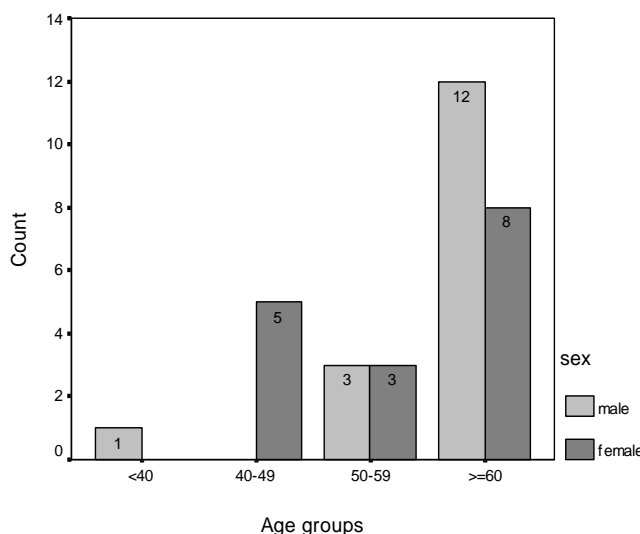

Figure 1: Frequency of PAD according to age and sex

Table 2 shows Odds Ratios (OR) of risk factors and their 95% CI for PAD groups in patients with type 2 diabetes. The patients with PAD had 3.65 folds history of stoke compared with patients without PAD which was significant (P=0.01). The other risk factors were not significant between the groups.

To evaluate the independent predictors of the PAD, Multiple Logistic Regression analysis was used to test age, sex, duration of diabetes, history of smoking, history of CHD and stroke.

Table 1- Comparison of PAD risk factors according to the ABI group in type 2 diabetic patients

Risk Factors	<0.9	0.9-1.3	>1.3	P-value
Age , (year)	60.2±11*	56.2±9.9*	60.6±11.3	0.035
Diabetes Duration (year)	13.1±7.8	12.3±7.4	13.8±7.2	0.595
BMI (kg/m^2)	27.9±2.5	27.7±4.6	29.7±3	0.744
Smoking ever/never	3/25	31/245	2/21	0.931
CHD History(%)	17.9%	18.2%	21.7%	0.912
Stroke History (%)	14.3%	5.8%	8.7%	0.221
Toe Brachial Index	0.56±0.17	0. 68±0.19	0.73±0.22***	0.008
HbA1c (%)	7.05±.6	7.7±1.8	8.4±2.2	0.239
FBS (mg/dl)	164.7±51.5	176.3±60.6	182.4±64.1	0.570
2hPP(mg/dl)	212.1±79*	259±82.3	290±91.3***	0.01
TG(mg/dl)	167.6±66	205.1±120.1	183.7±97.6	0.277
TC (mg/dl)	197.9±46.8	187.2±46	173±33.3	0.216
HDL(mean) (mg/dl)	55.8±17	51.1±16.5	49.4±16.7	0.571
LDL(mg/dl)	96.07±39.9	94.8±36.7	90.36±24.4	0.916
Creatinine (mg/dl)	1±0.2	0.9±0.2	1±0.2	0.746
BUN (mg/dl)	16.5±2.9	20.9±9.5	18.9±5.2	0.3
Uric acid (mg/dl)	7.61±6.82	6.23±8.38	5.07±1.37	0.514

*P<0.05, ABI<0.9 vs. ABI 0.9-1.3
** P<0.05, ABI 0.9-1.3 vs. ABI>1.3
*** P<0.05. ABI<0.9 vs. ABI >1.3

Table 2- Odds ratios for risk factors in PAD groups in patients with type 2 diabetes

Risk Factors	Change of Risk Factors	PAD	
		OR (95% CI)	P value
Age	<50*	---	---
	≥50	1.43(0.55-3.5)	0.3
Sex	male vs. female	1.1 (0.5-2)	0.4
	<25 kg/m^{2*}	---	---
BMI	25-29 kg/m^2	5.8(0.68-52.6)	0.08
	>=30 kg/m^2	3.57 (0.32-50)	0.29
CHD History	Yes vs. No	0.93 (0.37-2.3)	0.5
Stroke History	Yes vs. No	3.65 (1.32-10)	0.01
History of Smoking	Yes vs. No	0.75 (0.21-2.6)	0.4
	<5 years*	---	---
Diabetes Duration	5-15 years	1.78 (0.5-6.2)	0.2
	>15 years	2.2(0.62-8.3)	0.18

*Reference category

Table 3 shows positive history of stroke significantly increased the risk of PAD (OR=3.77; 95% CI:1.31-10.8).

Discussion

A number of studies have indicated an association between diabetes and an increased prevalence of PAD (10,11). PAD is usually defined by occlusive arterial disease of the lower extremities and many patients have no symptom or have atypical exertional symptoms (12). Diversity in data on PAD incidence and prevalence seen in various researches is related to non-standardized diagnostic methods (subjective difficulties, physical examination, hemodynamic measurements, etc.) (13). As a result, the recommended diagnostic test for PAD is ABI. An index of 0.9 or less diagnoses PAD and has 95% sensitivity and specificity for angiographically confirmed disease (2).

In studies using ABI as the preferred screening technique, the prevalence of PAD (defined as an ABI <0.90) in diabetic individuals varied from 20% to 30% (14-16).

A study by Colwell et al. (17) noted that 10% to 20% of type 2 diabetic patients had PAD. Li et al. (18) demonstrated the overall prevalence of PAD in diabetic patients was 16.7%. The crude prevalence of PAD in an Asian population with diabetes was 10.4% (19) and is consistent to our results which showed the prevalence of PAD in diabetic patients was 9.8%.

A large number of epidemiological and clinical studies have pointed to the relationship of cumulative PAD incidence with patient's age and diabetes duration (3,20,21). In our study, the patients with ABI less than 0.9 were older than non-PAD subjects (p=0.03), but by univariate analysis, the OR of age more than 50 years was 1.43 (95% CI: 0.3-6.82) and by logistic regression analysis, the OR was not significant.

The risk of PAD in our patients increased with

Table 3- Multivariate Logistic regression analysis of Independent risk factors for PAD in patients with diabetes.

Risk Factors	Change of Risk Factors	PAD	
		OR (95% CI)	P value
Age	<50*	---	---
	≥50	0.906(0.342-2.4)	0.843
Sex	male vs. female	1.183 (0.54-2.589)	0.675
CHD History	Yes vs. No	0.971 (0.368-2.563)	0.953
Stroke History	Yes vs. No	3.776 (1.310-10.8)	0.014
History of Smoking	Yes vs. No	0.879 (0.233-3.307)	0.848
	<5 years*	---	---
Diabetes Duration	5-15 years	0.531 (0.37-2.059)	0.360
	>15 years	0.355(0.62-1.794)	0.298

the duration of diabetes, as it was 2.2 (0.62-8.3) in patients with diabetes duration longer than 15 years, but this relationship was not significant.

In our study positive history of stroke was the main risk factor of PAD and history of stroke was 3.65 times more prevalent in the patients with PAD compared with the subjects without history of stroke. Consistent with other studies, it demonstrated that history of cerebrovascular accidents was associated with low ABI (18).

Some studies have shown that smoking is a risk factor for PAD in the general population (22,23) as well as diabetic patients (18). Nevertheless, our findings indicated that smoking history was not related to the prevalence of PAD which is similar with Tseng's study (24).

In our study we did not find a significant relationship between BMI and PAD and our results are inconsistent with the result of Li et al. (18), who showed that higher BMI was significantly associated with low ABI.

Our study had some limitations. The number of subjects in our study was not adequate and we need to study a larger population to evaluate the risk factors of PAD. Also, because of the cross sectional nature of this study, we could not infer causality between PAD and diabetes.

In conclusion, the prevalence of PAD in type 2 diabetes is 9.8% and history of cerebrovascular disease significantly associated with PAD.

Acknowledgements

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