Abdominal Aortic Diameter and the Risk for Asymptomatic Peripheral Arterial Disease in Patients with Type 2 Diabetes

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Abstract

Peripheral arterial disease (PAD) is common among older people because it often results from atherosclerosis, which becomes more common with age. The disease is particularly common among people who have diabetes. Little information is available on the relation between abdominal aortic diameter and PAD in elderly patients with diabetes. This article studies the relationships between abdominal aortic diameter, PAD, and the cardiovascular risk factors in asymptomatic elderly patients suffering from type 2 diabetes mellitus. A case–control study was conducted on 90 participants aged 60 years and older divided into 60 cases (30 males and 30 females) and 30 age-matched healthy controls (15 males and 15 females). The relationships between the size of the abdominal aorta and ankle–brachial index (ABI), plasma cholesterol, triglycerides (TG), and high-sensitivity C-reactive protein were examined. Approximately, 15% of patients with diabetes had asymptomatic PAD. The patients with diabetes with PAD were of older age (70.4 ± 3.6 vs. 63.4 ± 3.9 years; $p = 0.000$), had larger abdominal aortic diameter (22.4 ± 3.08 vs. 18.7 ± 2 mm; $p = 0.000$), and higher CRP levels (8.3 ± 1.1 vs. 5.8 ± 2.2 mg/L; $p = 0.002$), while other variables revealed no significant difference. Abdominal aortic diameter correlated well with ABI measured by Doppler method in diabetic patients ($r = -0.471$, $p = 0.000$). Older age and larger abdominal aorta are independent risk factors for asymptomatic PAD in the elderly with type 2 diabetes mellitus.

Keywords

- ▶ peripheral arterial disease
- ▶ abdominal aortic diameter
- ▶ diabetes mellitus
- ▶ ankle–brachial index
- ▶ C-reactive protein

Atherosclerosis is a life-threatening progressive process affecting all vessels including coronary artery disease, cerebrovascular disease, and peripheral arterial disease (PAD). When atherosclerotic disease develops in one vessel, it should be approached as a generalized process with possible affection of other vessels.¹

It is well known that diabetes increases the risk of atherosclerotic disease in all vascular beds.² The risk of PAD is twofold to fourfold higher among patients with diabetes

when compared with general population.^{3,4} PAD in patients with diabetes has poorer prognosis with higher risk of lower extremity amputation compared with the persons without diabetes.⁵

PAD is not only a predictor of lower limb ischemia. It is a strong predictor of cardiovascular morbidity and mortality in patients with diabetes. The rates of cardiovascular and cerebrovascular events are higher in the patients with diabetes suffering from PAD compared with those without PAD.⁶ The

risk of development of PAD among persons with diabetes is higher with advanced age, longer duration of diabetes, and presence of peripheral neuropathy.⁶

The severity of diabetes increases the incidence of PAD. The distribution of vascular lesions is altered in patients with diabetes.² The patients with diabetes more commonly have infrapopliteal arterial occlusive disease and vascular calcification than nondiabetic cohorts.⁵

Atherosclerotic process may manifest differently at different vascular beds because of altered pathophysiology and morphology. Both occlusive vascular disease and abdominal aortic aneurysm are atherosclerotic process.⁷ The aortic vessels are prone to arterial dilation than to occlusion primarily which is a part of generalized vascular aging.⁸ The Rotterdam Study revealed that elderly patients had a larger distal abdominal aortic diameter.⁹

Patients with PAD are at high risk for the development of an abdominal aortic aneurysm.^{10,11} The aim of this study is to determine the relationship between abdominal aortic diameter and ABI in asymptomatic elderly patients suffering from type 2 diabetes mellitus.

Patients and Methods

Study Population

A total of 90 elderly (≥ 60 years) attending the outpatient clinic at Ain Shams University Hospital, Cairo, Egypt. In total, 60 subjects had type 2 diabetes mellitus (30 males and 30 females) and 30 healthy subjects (15 males and 15 females) were recruited in the study. Diabetes mellitus was defined according to the American Diabetes Association criteria (fasting plasma glucose ≥ 126 mg/dL (minimum of 8 hour 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 or cerebrovascular disease were excluded. We also excluded cases with ABI > 1.3 . Subjects were categorized in as current smokers, former smokers, or those who had never smoked.

Anthropometric Data

Weight and height were measured without shoes. The body mass index (BMI) was calculated as body weight (kg)/height² (m²).

Laboratory Assessment

Serum level total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels were measured by enzymatic hydrolysis and oxidation of a fasting sample using Stanbio cholesterol colorimetric detection kit (Boerne, Texas, United States), CRP was measured using enzyme-linked immunosorbant assay using DiaMed EuroGen diagnostic Kit (Brussels, Belgium).

Radiological Assessment

A Hewlett-Packard Sonos 2,500 and a 2.7/3.5-MHz transducer were used by a single radiologist for ultrasound

evaluations of the distal abdominal aorta just above the aortic bifurcation. The maximum diameter of the aorta was measured from one edge to the other. A maximum anteroposterior or transverse diameter ≥ 3 cm was considered a diagnostic criterion for abdominal aortic aneurysm.¹²

A diagnosis of PAD was made based on an ankle-brachial index (ABI) of less than 0.90 on either leg.

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, Cairo, Egypt.

Statistical Methods

The collected data were coded, tabulated, revised, and statistically analyzed using SPSS program (version 16, IBM SPSS software Inc.). 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 chi-square test. Correlation between two quantitative variables was done using Pearson correlation coefficient. Spearman correlation coefficient was used for nonparametric correlations. Statistical difference was accepted when $p < 0.05$. Linear regression analysis was performed to identify which variables were independently associated with abdominal aortic diameter. Regression parameters and correlation coefficient *r* were estimated. ANOVA statistics were used to assess the significance of the regression and accepted for $p < 0.05$.

Results

Although not reaching statistical significance, percentage of PAD was higher in the case group. In the study nine (15%) persons with diabetes had a measured ABI < 0.9 (seven males and two females) while only two males (6.7%) of the control group had a measured ABI < 0.9 . General characteristics of the study population are presented in ►Table 1.

Among cases with diabetes mellitus, 33 (55%) had aortic diameter less than 20 mm, 25 (41.7%) had aortic diameter between 20 and 29 mm, while only 2 (3.3%) had aortic diameter above 30 mm both considered small aneurysms. Among controls, 25 (83.3%) had aortic diameter less than 20 mm, 5 (16.7%) had aortic diameter between 20 and 29 mm, while none had aortic diameter above 30 mm ($\chi^2 = 7.241$, $p = 0.027$).

The patients with diabetes had larger abdominal aortic diameter than control subjects (19.4 ± 2.6 vs. 16.9 ± 1.6 mm; $p = 0.000$) (►Table 1). Among cases, the mean abdominal aortic diameter for males was 20.7 ± 2.4 mm and females was 18.0 ± 1.9 mm ($p = 0.000$). In the control group, the mean abdominal aortic diameter for males was 17.5 ± 1.4 mm and for females was 16.3 ± 1.7 mm ($p = 0.04$) (see ►Table 4).

Table 1 Comparison between the two groups as regard the studied variables

Characteristics	Cases (n = 60)	Controls (n = 30)	p value
Age (y), mean $\pm$ SD	64.4 $\pm$ 4.6	64 $\pm$ 5.2	0.70
BMI (kg/m ²), mean $\pm$ SD	28.4 $\pm$ 4.7	25.3 $\pm$ 3.8	0.002 ^a
FBS (mg/dL), mean $\pm$ SD	157.5 $\pm$ 39.7	89.7 $\pm$ 13.5	0.000 ^a
2hPP (mg/dL), mean $\pm$ SD	250.5 $\pm$ 57.6	143.6 $\pm$ 23.4	0.000 ^a
hs-CRP (mg/L), mean $\pm$ SD	6.3 $\pm$ 2.3	4.2 $\pm$ 2.3	0.000 ^a
TC (mg/dL), mean $\pm$ SD	209.2 $\pm$ 20	192.3 $\pm$ 44.7	0.01 ^a
TG (mg/dL), mean $\pm$ SD	120.8 $\pm$ 23.5	112.4 $\pm$ 17.6	0.08
HDL (mg/dL), mean $\pm$ SD	37.7 $\pm$ 5.7	45.5 $\pm$ 11.6	0.000 ^a
LDL (mg/dL), mean $\pm$ SD	166.7 $\pm$ 16.4	123.7 $\pm$ 20.8	0.000 ^a
Abdominal aortic diameter (mm), mean $\pm$ SD	19.4 $\pm$ 2.6	16.9 $\pm$ 1.6	0.000 ^a
ABI, mean $\pm$ SD	0.91 $\pm$ 0.13	0.94 $\pm$ 0.09	0.34
PAD, n (%)	9 (15)	2 (6.7)	0.25
Current smokers, n (%)	17 (28)	10 (30)	0.4

Abbreviations: ABI, ankle brachial index; BMI, body mass index; FBS, fasting blood sugar; HDL, high-density lipoprotein; hs-CRP, high sensitivity C-reactive protein; LDL, low-density lipoprotein; PAD, peripheral arterial disease; SD, standard deviation; TC, total cholesterol; TG, triglycerides; 2hPP, 2 hours postprandial.

^aStatistically significant.

The patients with PAD among cases had higher age, high sensitivity C-reactive protein (hs-CRP), and abdominal aortic diameter compared with those without PAD ($p < 0.05$). There was no statistical significant difference between patients with and without PAD as regards BMI, fasting blood sugar, 2 hours postprandial, duration of diabetes, TC, TG, HDL, and LDL ($p > 0.05$) (**►Table 2**). Among controls, there is no significant difference between those with and without PAD as regards all the studied variables ($p > 0.05$) (**►Table 2**).

Abdominal aortic diameter correlated well with ABI in the case group ($r = -0.471$, $p = 0.000$) (**►Table 3**). This correlation tended to be stronger in men ($r = -0.532$, $p = 0.002$) compared with women ($r = -0.307$, $p = 0.099$) (**►Table 4**). The difference between the sexes was seen in the absence of any significant difference in ABI (ABI mean $\pm$ SD was 0.89 ± 0.15 in males, 0.94 ± 0.1 in females, $p = 0.19$) (**►Table 4**). The ABI negatively correlated to age ($r = -0.456$, $p = 0.000$), and hs-CRP ($r = -0.317$, $p = 0.014$) (**►Table 3**).

Table 2 Characteristics of patients with PAD

Characteristics	Diabetic group		p	Nondiabetic group		p
	PAD			PAD		
	Yes	No		Yes	No	
Age (y), mean ± SD	70.4 ± 3.6	63.4 ± 3.9	0.000 ^a	66.0 ± 8.5	63.85 ± 5.1	0.58
BMI (kg/m ²), mean ± SD	30.2 ± 2.3	28.1 ± 4.9	0.2	25.2 ± 1.5	25.3 ± 3.9	0.96
FBS (mg/dL), mean ± SD	179.4 ± 48.8	153.6 ± 37.2	0.07	99 ± 15.5	89 ± 13.3	0.32
2hPP (mg/dL), mean ± SD	240.7 ± 73.7	252.2 ± 55.1	0.58	137 ± 49.4	144 ± 22.1	0.68
DM duration (y), mean ± SD	11.3 ± 4.6	9.27 ± 6.7	0.38	–	–	–
hs-CRP (mg/L), mean ± SD	8.3 ± 1.11	5.8 ± 2.24	0.002 ^a	5.5 ± 3.53	4.07 ± 2.3	0.41
TC (mg/dL), mean ± SD	212.2 ± 19.4	208.6 ± 20.3	0.62	195 ± 7.1	192.1 ± 46.3	0.93
TG (mg/dL), mean ± SD	123.2 ± 21.8	120.4 ± 23.9	0.74	120 ± 0.0	111.9 ± 18.2	0.54
HDL (mg/dL), mean ± SD	38.4 ± 5.5	37.7 ± 5.8	0.70	42.5 ± 3.5	45.7 ± 12.0	0.72
LDL (mg/dL), mean ± SD	163.9 ± 19.7	167.2 ± 15.9	0.58	117.5 ± 10.6	124.2 ± 21.4	0.67
AAD (mm), mean ± SD	22.4 ± 3.1	18.7 ± 2	0.000 ^a	19 ± 1.4	16.8 ± 1.6	0.06

Abbreviations: AAD, abdominal aortic diameter; BMI, body mass index; FBS, fasting blood sugar; HDL, high-density lipoprotein; hs-CRP, high sensitivity C-reactive protein; PAD, peripheral arterial disease; LDL, low-density lipoprotein; SD, standard deviation; TC, total cholesterol; TG, triglycerides; 2hPP, 2 hours postprandial.

^aStatistically significant.

Table 3 The correlation between abdominal aortic diameter, ABI, and the risk factors in diabetics

Cardiovascular risk factors in diabetic patients	ABI in diabetic patients		AAD in diabetic patients	
	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value
Age	−0.456	0.000 ^a	0.351	0.006 ^{**}
FBS	−0.140	0.286	0.034	0.798
2-h PP	0.077	0.557	−0.14	0.284
Diabetes duration	−0.050	0.704	−0.037	0.781
hs-CRP	−0.317	0.014 ^a	0.054	0.681
Total cholesterol	−0.007	0.956	0.0	0.997
Triglyceride	0.002	0.987	−0.254	0.05 ^b
LDL	−0.038	0.773	0.005	0.97
HDL	0.003	0.982	0.163	0.213
BMI	−0.193	0.140	0.027	0.838
Current smoking ^c	−0.272	0.03 ^b		
Sex ^c	−0.120	0.36		

Abbreviations: AAD, abdominal aortic diameter; ABI, ankle brachial index; BMI, body mass index; FBS, fasting blood sugar; HDL, high-density lipoprotein; hs-CRP, high sensitivity C-reactive protein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides; 2hPP, 2 hours postprandial.

Note: Correlation between ABI, AAD; $r = -0.471$.

^a p value = 0.000.

^bStatistically significant.

^cSpearman correlation coefficient used.

^{**}Highly significant.

Using multiple regression analysis revealed that hs-CRP, abdominal aortic diameter, were independent predictors PAD after adjustment of other coronary risk factors such as sex, age, presence of diabetes, TC, and TG (► **Table 5**).

Discussion

The presence of atherosclerotic disease in one vessel should be considered as a marker for atherosclerotic process in the other vascular regions.¹³ Results from previous studies reported a negative association between diabetes and AAA.¹⁴ In contrast, patients with PAD are at high-risk for the development of AAA.¹¹

The purpose of this study was to study the relationship between abdominal aortic diameter and the risk of asymptomatic PAD among elderly patients.

In this study, only 15% of the patients suffering from diabetes mellitus had PAD. According to Elhadd et al, the prevalence of PAD among diabetics older than 40 years of age was 20%.¹⁵ The prevalence of PAD was 29% in patients with diabetes > 50 years of age.¹⁶ The less prevalence in this study is due to excluding symptomatic and previously diagnosed patient with PAD and the exclusion of patients with apparent cardiovascular or cerebrovascular comorbidity from this study.

Different previous studies suggested that diabetes reduces the risk of abdominal aortic aneurysm,¹⁷ and reduces aneurysmal expansion rate.¹⁸ Le et al demonstrated that glycaemia decreased the infrarenal aortic diameter even in nondiabetic.¹⁹ Surprisingly, we found that the mean abdominal aortic diameter in diabetics was 19.4 ± 2.6 mm while in nondiabetics the mean abdominal aortic diameter was

16.9 ± 1.6 mm. This can be explained by higher BMI in cases 28.4 ± 4.7 versus 25.3 ± 3.8 kg/m² ($p = 0.002$). Allison et al found that BMI is significantly correlated with increasing aortic diameter independent of the other cardiovascular disease risk factors.²⁰ Additional studies are needed to explore the relation between diabetes and abdominal aortic diameter in the elderly patients.

Our study showed that the patients with PAD among cases had a higher mean of age when compared with patients without PAD (70.4 vs. 63.4) ($p < 0.01$). This agrees with all studies that related advanced age to increased risk of developing PAD.^{3,21,22} Selvin and Erlinger³ found 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. Al-Delaimy et al²³ found a strong positive association between the duration of diabetes and the risk of occurrence of the PAD. The duration of diabetes in our study was higher in the patients with PAD than in patients without PAD (11.3 vs. 9.27) but with $p > 0.05$. This nonsignificant relationship may be due to delayed diagnosis of diabetes in the sample studied due to lack of routine screening for diabetes among them.

This study showed that patients in the case group with PAD had larger abdominal aorta than those without PAD. ABI negatively correlated with abdominal aortic diameter in diabetic subjects ($r = -0.471$, $p = 0.000$). This agrees with Rajkumar et al²⁴ who found that abdominal aortic diameter correlated with calf:brachial systolic ratio measured by doppler over the posterior tibial artery ($r = -0.28$, $p = 0.04$).

C-reactive protein as an inflammatory marker-related atherosclerosis, including PAD even in the subclinical phase.²⁵ In diabetes, many inflammatory and metabolic changes such

Table 4 The gender difference of studied variables

Characteristics	Cases		<i>p</i>	Controls		<i>p</i>
	Male	Female		Male	Female	
Age, mean ± SD	65.2 ± 4.90	63.63 ± 4.26	0.19	65.46 ± 5.59	62.53 ± 4.47	0.12
BMI, mean ± SD	27.95 ± 4.49	28.89 ± 4.96	0.44	24.33 ± 3.07	26.23 ± 4.35	0.18
FBS, mean ± SD	162.60 ± 40.29	152.46 ± 39.2	0.32	91.20 ± 9.8	88.20 ± 16.55	0.55
2hPP, mean ± SD	235.6 ± 58.89	265.4 ± 53.33	0.04 ^a	142.7 ± 25.5	144.4 ± 21.86	0.85
hs-CRP, mean ± SD	5.79 ± 2.21	6.73 ± 2.25	0.03 ^a	4.09 ± 2.37	4.24 ± 2.39	0.86
TC, mean ± SD	212.0 ± 20.36	206.3 ± 19.6	0.27	195.33 ± 46.5	189.33 ± 44.2	0.72
TG, mean ± SD	115.37 ± 18.19	126.37 ± 26.95	0.07	114.2 ± 14.32	110.67 ± 20.8	0.59
HDL, mean ± SD	38.46 ± 4.98	37.10 ± 6.31	0.36	47.73 ± 13.5	43.2 ± 9.28	0.29
LDL, mean ± SD	167.17 ± 14.49	166.23 ± 18.35	0.83	125.13 ± 16.77	122.4 ± 24.7	0.72
AAD, mean ± SD	20.73 ± 2.44	18.0 ± 1.85	0.00 ^a	17.53 ± 1.35	16.33 ± 1.71	0.04 ^a
ABI, mean ± SD	0.89 ± 0.15	0.94 ± 0.1	0.19	0.91 ± 0.11	0.97 ± 0.05	0.09
PAD, <i>n</i> (%)	7 (23.3)	2 (6.7)	0.07	2 (6.7)	0 (0)	0.24
Current smoking, <i>n</i> (%)	17 (56.6)	0 (0)	0.00	10 (66.7)	0 (0)	0.00 ^a
Correlation		ABI in diabetic males			ABI in diabetic females	
		<i>r</i>	<i>p</i> value		<i>r</i>	<i>p</i> value
Age		−0.0529	0.003 ^a		−0.296	0.113
hs-CRP		−0.578	0.001 ^a		−0.075	0.694
Abdominal aortic diameter		−0.532	0.002 ^a		−0.307	0.099

Abbreviations: ABI, ankle brachial index; BMI, body mass index; FBS, fasting blood sugar; HDL, high density lipoprotein; hs-CRP, high sensitivity C-reactive protein; LDL, low density lipoprotein; TC, total cholesterol; TG, triglycerides; 2hPP, 2 hours postprandial.

^aStatistically significant.

as hyperglycemia, adipokines, modified lipoproteins, and free fatty acids enhance CRP production by endothelial cells.²⁶

The results of the previous studies proved that CRP level is an independent predictor of diabetes.²⁷ This study revealed that cases had significant higher hs-CRP (6.26 ± 2.26 vs. 4.17 ± 2.34 mg/L, $p = 0.000$). In this study, we found that hs-CRP had a highly significant relationship with PAD in the case group. The patient in case group with PAD had mean CRP

8.3 mg/L whereas those without PAD had mean CRP 5.8 mg/L ($p < 0.01$).

Those with diabetes and an elevated CRP had the greatest likelihood of the development of PAD (odds ratio, 8.57; 95% confidence interval, 2.16–34.02; $p = 0.001$).²⁸

In this study, the prevalence of PAD was 23.3% in males and 6.7% in females. Yet, this is of no statistical significance ($p > 0.05$) due to small sample size (seven cases of PAD

Table 5 Multiple regression for different variable predictors of PAD

Variable	Standardized β coefficients	SE	<i>p</i> value	95% Confidence interval	
				Lower	Upper
Sex	1.693	1.327	0.2	0.014	2.479
Diabetes	3.411	1.889	0.071	0.748	1.228
Age	0.164	0.102	0.108	0.965	1.438
TC	0.000	0.019	0.963	0.963	1.037
TG	0.039	0.025	0.11	0.991	1.092
CRP	0.793	0.352	0.024	1.11	4.403
AAD	0.991	0.411	0.016	1.202	6.031
Constant	−4.259	1.368	0.002		

Abbreviations: AAD, abdominal aortic diameter; CRP, C-reactive protein; PAD, peripheral arterial disease; TC, total cholesterol; TG, triglycerides.

found in males and only two cases of PAD found in females). The females were nonsmokers while 56.6% of males were current smokers. All seven males with PAD were current smokers.

Hypercholesterolemia is a well-known risk factor for PAD.⁹ There was, however, no significant difference in the lipid profile between those with and without PAD in our study. This finding could be related to the elevated cholesterol in all subjects having type 2 diabetes mellitus those with and without PAD.

Conclusion

So, after studying the relationships between abdominal aortic diameter, PAD and the cardiovascular risk factors in asymptomatic elderly patients suffering from type 2 diabetes mellitus, we concluded that even without symptoms, PAD is common in elderly with type 2 diabetes mellitus. It should be considered as a part of generalized vascular affection. The hs-CRP, abdominal and aortic diameter, were independent predictors PAD.

Study Limitations

Our study has some limitations. Importantly, this was a small single site observational study. Data regarding HgbA1C level is lacking in our study.

Author Contributions

Moatasem S. Amer helped with the study design, analysis, interpretation of data, and revised the manuscript. Omar H. Omar, Randa A. Reda, and Tomader T. Abdel Rahman helped with the acquisition and analysis of data. Doha Rasheedy also helped with the acquisition and analysis of data and drafted the article. All the authors gave final approval of the version to be published.

Note

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Conflict of Interests

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