Original Article

Association between Peripheral Arterial Disease and Coronary Artery Disease among Tobacco User Diabetic Patients

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Abstract:

Background: Peripheral arterial disease (PAD) is a marker of increased risk for cardiovascular events and of poorer prognosis in patients with coronary artery disease (CAD). The prevalence of unknown PAD amongst patients with ACS varies between studies according to the mode of diagnosis.

Aims: To evaluate the prevalence of peripheral arterial disease (PAD) in diabetic ACS patients with or without tobacco user by using ankle brachial index (ABI).We also assess the probable predictors of PAD among these patients.

Methodology: This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh starting from 1st January 2016 to 30th April 2016 over a period of four months. A total of 60 patients were studied. They were grouped on the basis of their smoking habit. Diabetic patients with ACS and tobacco user (smoke and smoke less) in group I and without tobacco user in group II.

Results: The mean age of the studied patients was 56.63 ± 8.95 years, range from 25-90 years. 73.30% was male and 26.70% was female. Twenty three patients of tobacco user in group-I (n=30) had peripheral artery disease and ten patients of group-II (n=30) had peripheral artery disease. It was statistically significant (p=0.003).

Conclusion: There is correlation between peripheral arterial disease and coronary artery disease. Diagnosis and supervision of patients with PAD is important for preventing the local progression of the disease and effective secondary prevention of future coronary and cerebrovascular events.

Key Words: Peripheral artery disease; Acute coronary syndrome; Coronary artery disease; Tobacco.

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Introduction:

Peripheral arterial disease is considered to be a set of chronic or acute syndromes, generally derived from the presence of occlusive arterial disease, which cause inadequate blood flow to the limbs. On most occasions, the underlying disease process is arteriosclerotic in nature , mainly affecting the blood supply to the lower limbs. From the physiologic point of view, ischemia of the lower limbs can be classified as functional or critical. Functional ischemia occurs when the blood flow is normal at rest but insufficient during exercise, presenting clinically as intermittent claudication. Critical ischemia is produced when the reduction in blood flow results in a perfusion deficit at rest and is defined by the presence of pain at rest or trophic lesions in the legs. In this situation, precise diagnosis is fundamental, as there exist a clear risk of loss of the limb if adequate blood flow is not reestablished, either by surgery or by endovascular therapy.

PAD is a common disorder but because it is not directly life-threatening, it has not received the same degree of attention or research as coronary heart disease. But PAD

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may be a precursor of coronary heart disease since people with narrowed peripheral arteries are also more likely to have a narrowing of the coronary arteries. PAD mostly occurs in the elderly. In the United Kingdom around 1 in 5 men and 1 in 8 women aged 50-75 years have PAD[1]. PAD affects 8 to 10 million individuals in the United States[2,3] and is associated with reduced functional capacity[4-6] and increased risk for cardiovascular morbidity and mortality[7,8]. About half of all people with PAD have no obvious symptoms and the first indication of peripheral arterial disease may be a coronary artery disease or cerebrovascular accident[1]. Approximately one third of patients diagnosed with PAD will die within five years and about one half die within ten years, primarily due to a coronary artery disease or cerebrovascular accident[1].

Peripheral arterial disease (PAD) is one of the macrovascular complications of type 2 diabetes mellitus. Distribution of atheroma is widespread but patchy. Peripherally it effect femoro-popliteal segment, distal aorta and iliac arteries and lower leg arteries with a tendency to spare the profunda femoris beyond its origin of distal popliteal artery[9]. As global patterns in tobacco use changes, the burden of death can be expected to shift dramatically from the developed world to less wealthy countries. It has been estimated that over the next two decades, 70% of tobacco deaths will be in developing countries[10]. About 80% of the world's smokers now live in low and middle income countries, at least in part due to a lack of adequate tobacco controls[11]. In Bangladesh 43.3% of adults (41.3 million) currently use tobacco in smoking or smokeless form. Among them 26.4% of men, 28% of women and 27.2% overall (25.9 million adults) currently use smokeless tobacco[12] in different form like jorda, gul, hooka etc.

The most effective treatment for PAD is to stop tobacco use. This single measure reduces the risk of disease progression amongst patients with peripheral arterial disease and dramatically reduces the need for limb amputation and the risk of premature death.

Methodology:

Study population and design

This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka for a period of 4 months starting from January, 2016 to April, 2016. A total of 60 ACS patients who were diabetic with and without tobacco user followed up during hospital period. Patients were categorized into two groups on the basis of tobacco use. Group I (diabetic ACS with tobacco user) had 30 patients and Group II (diabetic ACS without tobacco user) had 30 patients.

Diagnostic criteria

Cardiovascular risk factors

Subjects were defined as having hypertension if they were taking an anti-hypertensive agent, had been clinically diagnosed with hypertension (HTN), or had either a systolic blood pressure (SBP) ≥140 mm Hg or a diastolic blood pressure (DBP) ≥90 mm Hg. Subjects were defined to have dyslipidaemia if they met one of the following requirements: diagnosis of hyper-cholesterolemia or a medication history of hyper-cholesterolemia or Total Cholesterol >200 mg/dL or LDL-C >130 mg/dL. The following body mass index (BMI) categories were recognized: normal (18.5≤BMI<24.9), overweight (25≤BMI<30) and obese (BMI≥30). A patient who had smoked within a year prior to the study was defined as a smoker.

Ankle Brachial Index

The ankle-brachial pressure index (ABPI) or ankle-brachial index (ABI) is the ratio of the blood pressure at the ankle to the blood pressure in the upper arm (brachium). Compared to the arm, lower blood pressure in the leg is an indication of blocked arteries due to peripheral artery disease (PAD). The ABPI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure in the arm[13].

$$ABPI_{Leg} = \frac{P_{Leg}}{P_{Arm}}$$

Where P_{Leg} is the systolic blood pressure of dorsalis pedis or posterior tibial arteries

And P_{Arm} is the highest of the left and right arm brachial systolic blood pressure

The ABPI test is a popular tool for the non-invasive assessment of PVD. Studies have shown the sensitivity of ABPI is 90% with a corresponding 98% specificity for detecting hemodynamically significant (Serious) stenosis >50% in major leg arteries, defined by angiogram[14]. ABPI value of under 0.50,is considered as severe arterial disease[15].

Statistical analysis

The age and gender differences and hypertension, diabetes, dyslipidaemia, smoking habit, family history of IHD,CKD, peripheral artery and coronary artery profile were statistically analyzed to find if they influenced in any way the incidence of standard deviation (SD). Data were entered in computer using SPSS for windows version 16.0 (SPSS Inc., Chicago, IL). Results were cross-

tabulated to find out the relationships between the variables. Statistical analysis was performed using χ^2-square for test of association and Fisher's exact test as appropriate. A p-value of less than 0.05 was considered significant in all statistical analysis.

Result:

Mean age of group I patients were 55.57±9.601 years and mean age of group II patients were 55.47±8.224 years. No significant difference was observed between the two groups (0.428). Among the group I highest number of patients (73.3%) were in age group 46-65 years followed by 25-45 years (16.7%). Among the patients of group II, highest number of patients (80%) in age group 46-65 years followed by age group of 66-75 years (16.5%). 93.33 % patients of group I was male and 6.67 percent was female where as in group- II 73.30 percent was male and 26.70 percent was female was observe.No statistically significant difference was observed the sex distribution of two groups (p=0.531) (Table-I).

Table-I

Age & Sex distribution of the group-I & II study population (n=30x2)

Age & Sex distribution	Group-I (n=30)	Group-II (n=30)	p-value
Age			
25-45 years	5(16.7)	1(3.3)	
46-65 years	22(73.3)	24(80.0)	
66-75 years	2(6.7)	5(16.5)	
76-90years	1(3.3)	0(0.0)	
Mean age	55.57±9.601	55.47±8.224	0.428 NS
Sex			
Male	28 (93.3)	22(73.3)	0.531 NS
Female	2(6.7)	8(26.7)	

NS=Non significant

Twenty three (76.7%) patients of group-I and twenty four (80%) patients of group-II had hypertension. There was no statistically significant difference in hypertension between the two groups (p=0.120).Twenty five (83.3%) patients of group-I and twenty four (80%) patients of group-II had dyslipidaemia. There was no statistically significant difference in dyslipidemia between the groups (p=0.254).Nineteen (63.3%) patients of group-I and twenty five (83.3%) patients of group-II had positive family history of IHD. There was statistically significant difference in positive family history between the groups (p=0.003).No statistically significant difference were observed between two groups of patients (p>0.05) regarding the risk factors like obesity (Table-II).

Table-II

Risk Factors of the study population

Risk Factors	Group-I (n=30) diabetic with tobacco user n(%)	Group-II (n=30) diabetic without tobacco user n(%)	p-value
Hypertension			
Present	23 (76.7)	24 (80)	0.120 NS
Absent	7(23.3)	6(20)	
Dyslipidaemia			
Present	25(83.3)	24 (80)	0.254 NS
Absent	5 (16.7)	6 (20)	
Family History			
Present	19(63.3)	25(83.3)	*0.003 S
Absent	11(36.7)	5(16.7)	
BMI (Obesity)			
Obese(30-34.9kg/m²)	5(16.7)	1(3.3)	0.093 NS
Overweight(25-29.9kg/m²)	12(40.0)	18 (60)	
Normal(18.5-24.9kg/m²)	13(43.3)	11(36.7)	

S= Significant ; NS=Not significant, *p value reached from χ^2 test, p value significant d"0.05

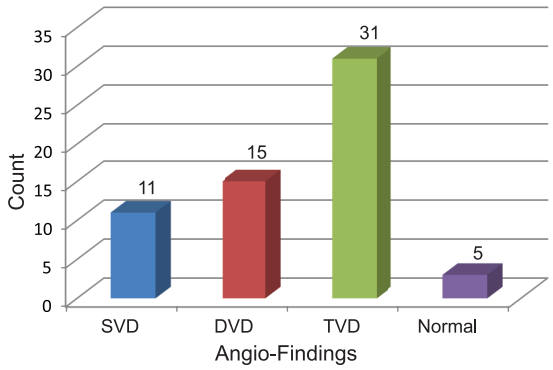

Fig.-1: *Coronary Angiogram findings of the study population (n=60).*

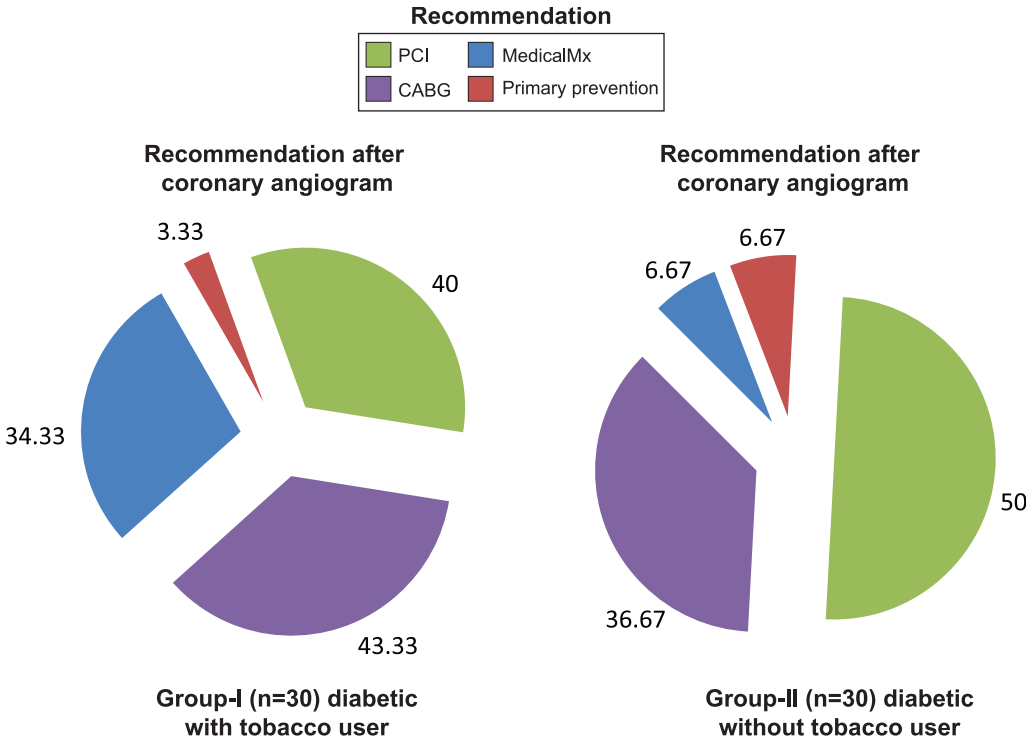

Fig.-2: *Recommendation after coronary angiogram*

Coronary angiogram findings of the study population revealed 31patients had triple vessel disease(TVD),15 patients had double vessel disease(DVD), 11 patients had single vessel disease(SVD) and rest of the patients had normal epicardial coronary arteies.(Fig:1)

After coronary angiogram 40% patients was recommended for PCI in group I and 50% patients was recommended for PCI in group II. 43.33% patients of group I was recommended for CABG and 36.7% patients of group II was recommended for CABG.13.34% patients of group I was recommended for medical management and 6.66% patients of group II was recommended for medical management. Rest of the patients of group I (3.3%) and group II (6.67%) were advised for primary prevention (Fig.-2).

80% patients of group I and 46.7% patients of group II had mild form of ABI value. 3.3% of group II patients had severe form of ABI value. There was no statistical significant difference between the two group of patients (p=0.053) (Table-III).

Table-III

The distribution of ankle brachial index values of both lower limbs and their relation to severity of peripheral artery disease.

Severity (ABI value)	Group-I (n=30) diabetic with tobacco user n(%)	Group-II (n=30) diabetic without tobacco user n(%)	p-value
Mild(0.80-0.89)	24(80%)	14(46.7%)	0.053 NS
Moderate(0.50-0.79)	0	0	
Severe(>0.50)	0	1(3.3%)	
Normal	6(20%)	15(50%)	

Over three quarters (76.7%) of group I patients developed PVD as compared to 33.3% of group II. The risk of developing PVD in diabetic smokers was observed to be more than 6 fold (95% CI: 2.109-20.479) higher than that in non diabetic tobacco user.(Table-4).

Twenty three patients of tobacco user group (n=30) had peripheral artery disease and ten patients of tobacco non user group (n=30) had peripheral artery disease which was statistically significant (p=0.003)(Table-5).

Table-IV

Association between Peripheral arterial disease and DM with or without tobacco user

PAD	DM with or without tobacco user		Odds Ratio	95% CI for OR	p- value	Fisher's Exact Test
	DM with tobacco user (Group I)	DM without tobacco user (Group II)				
Yes	23 (76.7%)	10 (33.3%)	6.571	2.109-20.479	0.001 S	0.002
No	7 (23.3%)	20 (66.7%)				

S= Significant, p value reach from χ^2 test, p value significant d"0.05
OR= Odds Ratio, CI=Confidence interval

Table-V

Association between tobacco use and peripheral artery disease

Tobacco Habit	PAD		p- value
	yes	no	
Smoking habit	18	6	*0.003 S
Smokeless tobacco	5	1	
Nonsmoker or without tobacco user	10	20	

S= Significant ; NS=Non significant
*p value reach from X^2 test, p value significant d"0.05

Thirty three (55%) patients had peripheral artery disease in study population (n=60) and fifty seven patients had coronary artery disease. Out of thirty three patients who had diagnosed PVD, thirty two patients had coronary artery disease which was not statistically significant (p=0.424)(Table-6).

Table-VI

Association between coronary artery disease and peripheral artery disease

	PVD	p value	Fisher's Exact Test	OR	95% CI for OR	
CAD	Yes	No	0.424 NS	0.583	2.560	0.219-29.869
Yes	32	25				
No	1	2				

S= Significant, p value reach from χ^2 test, p value significant $\leq$0.05
OR= Odds Ratio, CI=Confidence interval

Discussion:

The presence of peripheral arterial disease (PAD), even in the absence of overt coronary artery disease (CAD), confers the same relative risk of death from a cardiovascular cause as in patients with a previous cardiovascular event. The mean age of studied patients was 56.63±8.95 years. The commonest age group of study patients was 45-65 years in both groups (48.9% and 53.3 % in group I and group II respectively). Mean age difference was not statistically significant (p=0. 428). Nearly similar pattern of age distribution was reported by Sarangi S, et al.[16] in their study in India. This observation was being consistent with the findings of different studies done in different countries[17-19].

Out of sixty patients twenty three patients of tobacco user group I (n=30) and ten patients of tobacco non user group II (n=30) had peripheral artery disease which is statistically significant (p=0.003) between the two groups of patients. Univariate regression analysis of Gulf RACE 2009 revealed diabetes, family history of ischemic heart disease and tobacco use were independent variable for PAD(p=0.001). DM with tobacco user group showed strong association with PAD & adjusted odds ratio(OR) was 6.571 (CI 2.109-20.491). Out of 33(55%) patients who had PVD, coronary artery disease was found in 32 patients and it was statistically significant (p=.018). 80% male and 15% female had coronary artery disease, which was statistically insignificant. 51.3% male and 0.0332% female had peripheral artery disease which was statistically significant (p=0.018) and OR=6.526 (95%CI for OR 1.252-34.029) Sarangi S, et al.[16] and Al Thani, HA, et al.[20] was found statistically significant.

Various epidemiologic studies have shown that up to 50% of patients with PAD also have symptoms of cerebrovascular or heart disease[21]. In the PARTNERS study[22] of all the patients who were screened for vascular disease, only 13% had isolated PAD with no other manifestation of cardiovascular disease. Thirty two percent of the patients also had either coronary disease or cerebrovascular disease, and 24% had involvement in all 3 territories. The main cause of death in patients with PAD is ischemic heart disease (up to 50% of deaths in patients with PAD). Inversely, the prevalence of PAD in patients diagnosed with coronary disease reaches 30% [21]. The mortality in this group of patients is 2.5 times

greater than that of the group with no clinical symptoms of PAD.

In overall ACS and STEMI, patients with PAD developed worse in-hospital outcomes in terms of greater rate of death, heart failure, recurrent ischemia, stroke, and major bleeding when compared to their non-PAD counterparts. There was only one death in group who presented as STEMI and death due to ventricular septal rupture. Two patients of both groups was suffered acute left ventricular failure. Two patients of group I had diabetic foot ulcer due to peripheral artery disease. Significant difference was found in Al Thani HA, et al.[20].

Conclusion

Prevalence of PAD in ACS Bangladeshi population is low in comparison to western population.Certain traditional risk factors are independent predictors for PAD necessitates aggressive preventive measures. Screening with ABI would allow the identification of a subgroup of CAD patients at particularly high risk and who could benefit from an aggressive medical treatment strategy. Detection of PAD in ACS patients might be a useful simple bedside tool for early detection of the risk stratification.

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