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Original Research Article

An observational study of incidence and severity of coronary artery disease in peripheral artery disease patients in South India

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ABSTRACT

Background: There are many studies that have evaluated peripheral artery disease (PAD) using ankle brachial index. However, there is very little epidemiological data on angiographically diagnosed PAD and its association with definite coronary artery disease (CAD) in Indians. The aim of this study is to evaluate the relationship between PAD and CAD in South Indian patients.
Methods: This was an observational, descriptive, single-arm, single-centre, retrospective clinical study. The study included 111 patients with known PAD who were admitted to a tertiary care hospital in South India. Patients with PAD by history, clinical examination, and those who underwent peripheral as well as coronary angiography were included in the study. Student t test, chi-square/fisher exact test have been used to find the significance of study parameters.
Results: Out of total 111 patients with PAD included in the study, 98 patients were male. 61.1% of patients had co-existing significant CAD and significant PAD. Diabetes was a strong predictor of CAD (p=0.003) and smoking was strongly related to PAD (p=0.028). Elderly patients were associated with occurrence of significant CAD as well as PAD.
Conclusions: It can be concluded that there is a definite and significant correlation between PAD and CAD. The elderly population and those at increased risk for atherosclerotic vascular disease have higher liability of PAD; however, PAD is the condition that is mostly under diagnosed and under treated. The awareness about the co-existence of CAD and PAD, and implementation of co-diagnosis in general clinical practice has been poor.

Keywords: Coronary artery disease, Peripheral artery disease, India

INTRODUCTION

Peripheral arterial disease (PAD) is generally defined as partial or complete obstruction of one or more peripheral arteries due to atherosclerosis. PAD involving the arteries of lower limbs is one of the major causes of morbidity and mortality especially affecting the elderly population.[1,2] The prevalence of PAD is higher in patients with diabetes, smoking, hypertension, and hyperlipidemia.

The PAD has been reported to be symptomatic or asymptomatic. The symptomatic disease attenuates functional capacity and quality of life, and the asymptomatic disease is also equally essential as it may increase risk of future ambulation, lower extremity ulcers or need for vascular surgery or amputation. Nevertheless, asymptomatic as well as symptomatic PAD are the strong independent predictors of coronary artery disease (CAD) events and mortality. Several studies have shown that patients with PAD are at escalated risk of CAD.[3]

Moreover, literature states that almost 50% of the patients with PAD have simultaneous CAD.[4]

However, the prevalence of CAD in patients with PAD has been ranged widely (14% to 90%) in the results of various studies, which reveals the variances in sensitivity of the applied techniques.[5] Additionally, CAD was present in 19% to 47% patients with PAD in studies using clinical history plus ECG; while, the prevalence was demonstrated to be 62% to 63% using stress tests (modified stress ECG or dipyridamole-stress thallium) and 90% when angiography was applied. Unfortunately, there is very little epidemiological data on PAD and its association with CAD in Indians. The aim of this study was to detect the co-existence of CAD and PAD through invasive angiography and to evaluate its severity in PAD patients as well as to assess the relationship between CAD and PAD in South Indian patients.

METHODS

Study design and population

This is an observational, descriptive, single-arm, single-centre, retrospective clinical study which included 111 patients with known PAD who were admitted to a tertiary care hospital in India between January, 2010 and January, 2015. Patients with PAD by history or clinical examination and those who underwent peripheral as well as coronary angiography were included in the study. Patients with acute coronary syndrome, sepsis, acute kidney injury and chronic renal failure were excluded from the study. The study was approved by the institutional ethics committee. The ethics committee registration number is: ECR/747/Inst/KA/2015 and the approval no. is: VEIC/2016/APP/154. As a routine practice at our institute, at the time of any procedure, a written informed consent for use of properly anonymised clinical data is obtained from each and every patient, irrespective of study to be performed in future. The study was conducted in compliance with declaration of Helsinki.

Data collection

Data was collected in a pretested proforma meeting the objectives of the study. For patients with PAD- history, risk factors for PAD, anthropometric data, reports of basic blood investigations, coronary and peripheral angiography was noted from the medical records.

Out of the major cardiovascular risk factors, the presence of family history of diabetes in first-degree relatives, hypertension (systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg in at least two distinct readings), diabetes [fasting blood glucose ≥7.0 mmol/l (126 mg/dl)], BMI distribution and kidney function test (urea and creatinine), smoking, tobacco and alcohol habits were recorded.[6,7] Definite CAD was defined as per the the ACC/AHA guidelines as ≥50% stenosis in left main or ≥70% stenosis non-left main arteries. The severity scoring of PAD was done on clinical basis by Fontaine classification and angiographically by Bollinger classification.

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD and results on categorical measurements are presented in frequency and percentages. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Significance is assessed at 5% confidence level. All the data were analysed using the statistical package for social sciences (SPSS Inc; Chicago, IL, USA) program, version 20.

RESULTS

Out of total 111 patients with PAD included in the study, 98 patients were male. Diabetes, hypertension, smoking and alcohol consumption was concomitant in 35 (31.5%), 45 (40.5%), 51 (45.9%), and 17 (15.3%) patients, respectively. Serum creatinine was >1.1 mg/dl in 19.4% patients. Baseline demographics of patients have been detailed in Table 1. It was observed that 63 (56.8%) patients had significant CAD and 18 patients had significant disease in other vessels (renal/carotid) (Figure 1).

Upon analysis, it was observed that occurrence of diabetes was significantly different between patients with insignificant and significant CAD (16.7% vs. 42.9%; p=0.003). Smoking was observed to be noteworthy factor for patients with significant PAD (p=0.028) (Table 2).

Table 1: Baseline demographics of patients.

Characteristics	Patients (n=111)
Age (mean±SD, years)	52.68±11.84
BMI (mean±SD, kg/m2)	20.349±3.98
Urea (mean±SD, mg/dl)	23.7±8.45
Creatinine (mean±SD, mg/dl)	1.65±7.8
SBP (mean±SD, mmHg)	130±22.03
DBP (mean±SD, mmHg)	81.53±11.54

Continued.

Characteristics	Patients (n=111)
Age group (in years)	**N (%)**
<30	5 (4.5)
30-40	11 (9.9)
41-50	30 (27)
51-60	39 (35.1)
61-70	23 (20.7)
>70	3 (2.7)
Gender	
Male	98 (88.3)
Female	13 (11.7)
Risk factors	
Diabetes mellitus	35 (31.5)
Hypertension	45 (40.5)
Smoking	51 (45.9)
Alcohol	17 (15.3)
Tobacco	2 (1.8)
SBP (mm Hg)	
<120	31 (27.9)
120-140	59 (53.2)
>140	21 (18.9)
DBP (mm Hg)	
<80	35 (31.5)
80-100	73 (65.8)
>100	3 (2.7)
BMI	
<18.5	25 (29.8)
18.5-25.0	51 (60.7)
25.01-30	5 (6.0)
>30	3 (3.6)
Urea (mg/dl),	
<20	36 (36.7)
20-40	60 (61.2)
>40	2 (2)
Serum creatinine (mg/dl)	
<1.1	79 (80.6)
>1.1	19 (19.4)

BMI - body mass index; SBP -systolic blood pressure; DBP: diastolic blood pressure.

Table 2: Clinical conditions in relation to CAD and PAD findings.

Variables	Insignificant (n=48)	Significant (n=63)	Total	P value
	N (%)	N (%)		
CAD				
Family history	0 (0.0)	1 (1.1)	1	1.000
Diabetes mellitus	8 (16.7)	27 (42.9)	0.003*	0.003*
Hypertension	17 (35.4)	28 (44.4)	0.337	0.296
Smoking	23 (47.9)	28 (44.4)	0.716	0.499
Alcohol	8 (16.7)	9 (14.3)	0.73	0.700
Tobacco	1 (2.1)	1 (1.6)	1	1.000
PAD	**Insignificant (n=16)**	**Significant (n=95)**		
Family history	1 (6.3)	0 (0.0)	0.144	0.087
Diabetes mellitus	6 (37.5)	29 (30.5)	0.579	0.391
Hypertension	6 (37.5)	39 (41.1)	0.789	0.652
Smoking	3 (18.8)	48 (50.5)	0.028*	0.024*
Alcohol	1 (6.3)	16 (16.8)	0.458	0.181
Tobacco	1 (6.3)	1 (1.1)	0.269	0.166

Chi-square test/fisher exact test.

Table 3: Clinical conditions in relation to CAD and PAD findings.

CAD	Insignificant (n=48)	Significant (n=63)	P value
Age (mean±SD, years)	45.65±12.16	58.05±8.31	<0.001*
SBP (mean±SD, mm Hg)	128.75±20.17	130.95±23.47	0.604
DBP (mean±SD, mm Hg)	82.29±11.16	80.95±11.88	0.547
BMI (mean±SD, Kg/m^2)	20.3966±4.26	20.4112±3.76	0.987
Urea (mean±SD, mg/dl)	21.24±7.1	25.61±8.97	0.01*
Serum Creatinine (mean±SD, mg/dl)	2.616±11.77	0.8984±0.26	0.281
PAD	**Insignificant (n=16)**	**Significant (n=95)**	
Age (mean±SD, years)	44.44±13.51	54.07±11.02	0.002*
SBP (mean±SD, mm Hg)	135±31.2	129.16±20.19	0.479
DBP (mean±SD, mm Hg)	87.5±12.91	80.53±11.05	0.025*
BMI (mean±SD, Kg/m^2)	22.1767±6.34	20.1086±3.43	0.291
Urea (mean±SD, mg/dl)	21.26±7.71	24.1±8.54	0.245
Serum Creatinine (mean±SD, mg/dl)	6.3429±20.63	0.8702±0.25	0.339
Other vessels	**Insignificant (n=93)**	**Significant (n=18)**	
Age (mean±SD, years)	51.74±12.06	57.56±9.52	0.056
SBP (mean±SD, mm Hg)	129.68±21.44	131.67±25.5	0.728
DBP (mean±SD, mm Hg)	82.37±11.55	77.22±10.74	0.083
BMI (mean±SD, Kg/m^2)	20.6762±4.11	18.9177±2.97	0.145
Urea (mean±SD, mg/dl)	22.93±8.33	27.11±8.38	0.057
Serum creatinine (mean±SD, mg/dl)	1.8129±8.63	0.9372±0.31	0.669

Student t test, SBP – Systolic blood pressure; DBP – Diastolic blood pressure; BMI – Body mass index.

Table 4: Association of CAD and PAD.

Characteristics (n=111)	PAD		P value
	Insignificant (n=16) N (%)	Significant (n=95) N (%)	
CAD			
Insignificant	11 (68.8)	37 (38.9)	0.026*
Significant	5 (31.2)	58 (61.1)	
Other vessels			
Insignificant	16 (100)	77 (81.1)	0.069
Significant	0 (0.0)	18 (18.9)	

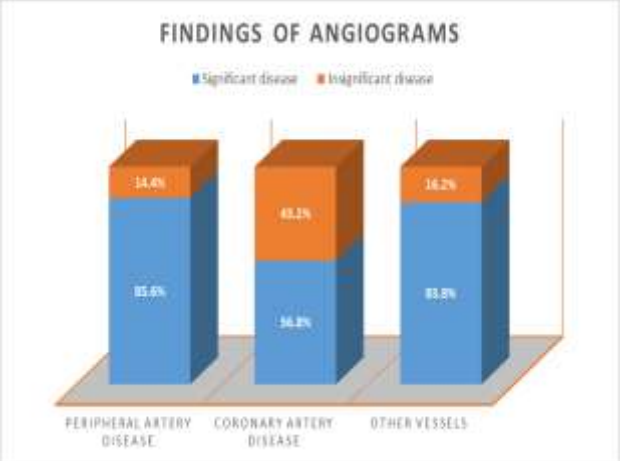

Figure 1: Significant findings of coronary and peripheral angiography.

Moreover, higher age (p<0.001) was predictor of significant CAD. Higher age (p=0.002) and lower diastolic blood pressure (p=0.025) were associated with significant PAD (Table 3). Table 4 depicts that the significant CAD and PAD were observed to be associated statistically (p=0.026).

DISCUSSION

The PAD is defined as partial or complete obstruction of one or more peripheral arteries due to atherosclerosis. However, almost 90% of the patients present with occlusion in the legs.[8] The extension of atherosclerotic plaque in extremities as well as in the coronary tree turns a matter of double jeopardy. Both CAD and PAD are carried through common pathogenesis and risk factors. Majorly affecting risk factors are smoking, dyslipidemia, hypertension, and diabetes mellitus.[9] Though both the co-morbidities share similar risk factors and pathogenesis,

the exact association between them is still unclear. Different hypotheses are postulated to explicate the link between occurrence of PAD and coronary events. These include: highly extensive atherosclerotic burden, escalated inflammatory burden, worsened endothelial function, and reduced physical activity.[10]

Our study included a total of 111 patients who presented to our institute with PAD, of whom 88.3% were males. While a study on prevalence of PAD in Kerala, interestingly observed higher prevalence of PAD in females (56.8%) than males.[11] Moreover, the Rotterdam study also reported female predominance in PAD prevalence. Whereas, many other studies have observed greater PAD prevalence in men or equal in both the genders.[12,13] Various recent studies have stated a linear relation between age and PAD.[13,14] Moreover, in a previous study that included geriatric patients, reported that CAD was existent in more than two-thirds of the PAD patients.[15] So is the case in our study too, older patients presented with significant PAD (p=0.002) and CAD (p<0.001).

Smoking has been a strong predictor of occurrence of significant PAD (p=0.028). Previous studies, namely Framingham study, cardiovascular health study, and Edinburgh artery Study have reported that in smokers there has been 2–5 times higher prevalence of PAD, than non-smokers.[13,16] In the present study, though all traditional factors not being statistically differentiating the patients with significant PAD, yet hypertension, smoking, age and alcohol intake were higher in patients with significant PAD than in insignificant PAD. Likewise, diabetes, age, hypertension and smoking were higher in patients with significant CAD than in those with insignificant CAD. Recent studies have documented that patients having both PAD and CAD are older in age and have been associated with a higher number of cardiovascular risk factors than the patients with involvement of any one of these morbid conditions.[15] Parallely, in this study also older age was associated with increased incidence of CAD and PAD; moreover, reduced diastolic blood pressure was also associated with increased incidence of PAD.

In our study, 61.1% of patients had co-existing significant CAD and significant PAD. In a study by Taimur SD et al on the total population of 77 patients with PAD that were diagnosed using angiography, 35 patients (45.45%) had coexisting CAD.[17] Likewise, the occurrence of CAD in PAD-positive cases was 46.88% while in PAD-negative cases was 20% in a study by Sarangi S et al.[18] Moreover, in a study by Duran NE et al, 72% of patients with PAD had concomitant CAD. Presence of hypertension, diabetes, and increased total cholesterol, triglyceride, and low density lipoprotein cholesterol values were associated with significant CAD in that study.[19] Her K et al also documented that patients with PAD undergoing coronary angiography revealed CAD in 69.5% of patients.[20] Another study by Hur DJ et al reported that 55% of patients with PAD had at least one epicardial coronary artery with ≥70% diameter narrowing.[21] Thus, the results of this study pose to be parallel with the previous studies. Moreover, the studies have also reported that patients with PAD have a greater co-existence of asymptomatic CAD. In addition, the co-existence of PAD and CAD accompanies extensive vessel involvement (i.e., multivessel disease) in such patients, than in CAD patients without PAD.[15] Table 5 indicates comparative results of different studies denoting extent of co-existence of PAD and CAD.[17, 18, 22-25]

Table 5: Comparative results of different studies denoting extent of co-existence of PAD and CAD.

Study/ Author	Total number of patients (N)	Significant PAD (N)	Insignificant PAD (N)	Significant CAD (N)	Co-existent significant CAD and PAD (%)
Present study	111	95	16	63	61.1
Sarangi et al[18]	182	32	150	45	46.88
Rahman et al[22]	250	250	0	125	50
Agarwal et al[23]	146	21	125	41	52.38
Goud et al[24]	100	17	83	-	76.19
Taimur et al[17]	77	68	9	55	71.4
Krishnan et al[25]	1148	299	849	-	33.34

Co-existence of PAD and CAD has been reported to be a strong independent predictor of short as well as long term adverse outcomes.[15] Nearly doubled all-cause mortality (4.6% per year) has been observed in comparison to existence of either disease alone.[26] One year rate of events of cardiac death, MI, stroke, or hospitalization for atherothrombotic events in the patients with coexistence was reported to be 23.1% (whereas 13-17% in either disease alone) in the REACH registry.[27] Nowadays, medication along with revascularization has been the most preferred current treatment approach which aims towards salvaging the affected limbs in cases of PAD, and prevention of future cardiovascular events. Nevertheless, the patients have been allied with poor prognosis. The prognosis can be improved by close

monitoring of patients, lifestyle modifications, control of cardiovascular risk factors (e.g., smoking, diabetes mellitus, hypertension) with use of optimal medical therapy and use of antithrombotics to prevent further blood clot formation.[28]

The present study bears some limitations. It was a retrospective study, sample size was small, and no long-term follow-up was taken for assessing future events.

CONCLUSION

In view of the results, it can be concluded that there is a definite and significant correlation between PAD and CAD. The elderly population and those at increased risk in atherosclerotic vascular disease have higher liability of PAD; however, PAD is that condition that is mostly under diagnosed and under treated. The awareness about the co-existence of CAD and PAD, and implementation of co-diagnosis in general clinical practice has been poor.

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