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Original Research Article

Prevalence and Severity of Coronary Artery Disease in Patients with Symptomatic Lower Limb Peripheral Arterial Disease

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Abstract

Introduction: The presence of combined lower extremity peripheral arterial disease (PAD) and coronary artery disease (CAD) is associated with nearly doubled all-cause mortality. However diagnosis of CAD in PAD patients remains difficult because of absence of symptoms due to reduced physical activity. Data regarding the coexistence of CAD in lower limb PAD patients are scarce. So, the aim of this study was to assess prevalence and severity of coronary artery disease in patients with symptomatic lower limb PAD.

Methods: From December 2012 to February 2015, all consecutive patients with PAD undergoing invasive peripheral and coronary angiography were included. Patients with the history of percutaneous or surgical interventions for lower limb PAD or for coronary arteries, recent (≤ 3 months) acute limb ischemia or acute myocardial infarction were excluded. Significant CAD was defined as ≥50% diameter stenosis in atleast one major epicardial coronary artery. Severity of CAD was assessed by Gensini score.

Results: Total 151 patients were included. Mean age was 57.26±9.74 years. The overall prevalence of CAD was 74.83%. Among CAD patients, 46.4% were asymptomatic and majority of patients were having multivessel involvement (77.87%). Diabetes and dyslipidemia were significantly associated with a higher prevalence of CAD ($p < 0.001$ for both). Though not statistically significant, multivessel CAD was more prevalent in patients with aortoiliac iliac disease in comparison to patients with non-aortoiliac disease. The prevalence of multivessel CAD was significantly high in extensive PAD (≥3 lesions irrespective of site) in comparison to limited PAD. ($p=0.02$) Severity of CAD assessed Gensini score doesn't show significant correlation with pattern or severity of PAD.

Conclusion: Overall, there is high prevalence of CAD in patients with symptomatic lower limb PAD. About 50% of CAD are asymptomatic. Diabetes mellitus and dyslipidemia are the independent risk factor for development of CAD. PAD patients are more prone for multivessel CAD.

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Key words: coronary artery disease; Lower Limb; Peripheral Arterial Disease

Introduction

Peripheral arterial disease (PAD) of the lower limb is the occlusive disease of arteries distal to the aortic bifurcation.[1] The prevalence of PAD in the lower limbs in general population >55 years of age is in between 10% to 25% and it increases with age.[2] PAD is frequently associated with atherosclerotic involvement of others vascular beds such as coronary artery. Compare to general population, the incidence of new coronary events is increased in PAD patients. [3,4,5,6]

The prevalence of coronary artery disease (CAD) in patients with PAD is varying widely from 46% to 71%, depending upon the variability in definition used to diagnose CAD. [7,8] The presence of CAD in patients with PAD is the important determinant of mortality and long term prognosis.[3,9,10]The presence of combined lower extremity PAD and CAD is associated with nearly doubled all-cause mortality compared with either disease alone.[11] Also, the peri-operative and long-term prognosis after non-cardio vascular surgery is predominantly determined by the presence and severity of underlying CAD.[12]Peri-operative cardiac events were significantly increased from 3 to 8.5% in patients with concomitant CAD undergoing vascular surgery in the CASS registry.[13] Cardiac death (particularly fatal MI) accounted for ~40% of 30-day all-cause mortality. [12]

Although it is well recognized that the incidence of CAD is high in patients with PAD with its associated increased overall mortality and morbidity, the diagnosis of CAD in PAD patients remain difficult because majority of the patients do not have cardiac symptoms due to reduced daily physical activity. Currently there are also no definitive evidences to support the need for screening tests to detect asymptomatic CAD in patients with lower extremity PAD.[14]

Previous studies showed widely variable results regarding the prevalence and severity of CAD with the site and severity of lower limb PAD. Still the data are insufficient to conclude it and to apply it in day to day clinical practice to diagnose the CAD at its earliest stage and thus to prevent the adverse consequences related to the coexistence of CAD in lower limb PAD patients.

So, the aim of this study was to assess the prevalence and severity of CAD in patients with symptomatic lower limb PAD.

Methods

All consecutive symptomatic lower limb PAD patients undergoing invasive peripheral and coronary angiography after taking written consent. Patients with the pahistory of percutaneous or surgical interventions for lower limb PAD or for coronary arteries, recent (≤ 3 months) acute limb ischemia or acute myocardial infarction were excluded. Significant PAD was defined as ≥50% diameter stenosis in at least one of the lower limb major vessel. Significant CAD was defined as ≥50% diameter stenosis in at least one major epicardial coronary artery. Severity of CAD was assessed by Gensini score. Statistical analysis was performed with SPSS software (version 18). Qualitative variables expressed as numbers and percentages were compared by the Pearson's Chi-square test with P value of less than 0.05 was considered significant. The present study was approved by an institutional research and ethics committee.

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Results

Out of 158 patients screened, 151 patients were included in the present study. Of the 7 patientsexcluded,3 had coronary revascularisation, 2 had lower limb revascularisation and 1 had acute lower limb ischemia. In one patient, coronary angiography could not be performed.Mean age was 57.26±9.74 years. 94% (n=142) of patients were males. (Table 1)Isolated femoro-popliteal disease was the predominant form of PAD present in 47.68% (n=72). Isolated aortoiliac, isolated in frapopliteal and multiple level PAD were present in 12.58% (n=19), 5.29% (n=8) and 34.44% (n=52) respectively. (Table 2)The overall prevalence of CAD was 74.83% (n=113) among the PAD patients. (Table 3) Among the CAD patients, 46.4% (n=70) were symptomatic (p <0.001). (Figure 1)Also, among all CAD cases, majority of patients were having multivessel coronary artery involvement (77.87%, n=88) while single vessel involvement was present in only 22.1% (n=25). Normal coronaries or non-significant CAD was present in 25.1% (n=38). Diabetes and dyslipidemia were significantly associated with a higher prevalence of CAD (p <0.001 for both). (Figure 2) CAD was present in 79.2% (n=19) of patients with aortoiliac disease (n=24) in comparison to 78.8% (n=63) in non-aortoiliac disease (n=80) and 66% (n=31) in patients with both segments involvement (p=.24). Multivessel CAD was present in 62.5% (n=15) of patients with aortoiliac disease in comparison to 56.3% (n=45) in non-aortoiliac disease and 59.6% (n=28) in patients with both segments involved (p= .842).Interestingly, multivessel CAD was present in 75.8% (n=25) of patients with extensive PAD (≥3 lesions irrespective of site) in comparison to 53.4% (n= 63) in limited PAD group. (p=0.02) (Table 4)

Gensini score of < 32 was present in 54.2% (n=13) of patients with aortoiliac disease in comparison to 46.3% (n=37) in non-aortoiliac disease and 42.6% (n=20) in patients with both segments involved. Gensini score of 32-57 was present in 8.3% (n=2) of patients with aortoiliac disease in comparison to 16.3% (n=33) in non-aortoiliac disease and 14.9% (n=7) in patients with both segments involved. Gensini score of ≥58 was present in 37.5% (n=9) of patients with aortoiliac disease in comparison to 37.5% (n=30) in non-aortoiliac disease and 42.6% (n=20) in patients with both segments involved (p= .831).

Table 1: Baseline characteristics

Characters	Prevalence, n (%)
Age (years) (Mean: 57.26±9.74)	
<40	33 (21.9)
40-49	50 (33.1)
50-59	55 (36.4)
≥60	13 (8.6)
Sex (males)	142 (94)
Hypertension	70 (46.3)
Diabetes Mellitus	69 (45.7)
Dyslipidemia	66 (43.7)
Smoking	133 (88)
BMI (Kg/m^2) (Mean: 26.69±1.89)	
< 25	22 (14.6)
25-29	113 (74.8)
≥30	16 (10.6)

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Fontaine's Class	
I	1 (7)
IIA	31 (20.5)
IIB	81 (53.6)
III	14 (9.3)
IV	24 (15.9)
Rutherford's Grade	
I	113 (74.8)
II	37 (24.5)
III	1 (7)
Rutherford's category	
1	10 (6.6)
2	32 (21.2)
3	70 (46.4)
4	16 (10.6)
5	23 (15.2)

Table 2. Distribution & severity of PAD

PAD (Vessel involved)	Prevalence, n (%)
Aorta (Infrarenal)	8 (5.3)
Aorto-iliac	
Unilateral	43 (28.5)
Bilateral	29 (19.2)
None	79 (52.3)
Femoral-popliteal	
Unilateral	63 (41.7)
Bilateral	53 (35)
None	35 (23.2)
Infrapopliteal	
Present	62 (41.1)
Absent	89 (58.9)
Lesion location	
Proximal	24 (15.9)
Distal	80 (53.0)
Both	47 (31.1)
Limited v/s Extensive PAD	
Limited	118 (78.1)
Extensive	33 (21.9)
TASC II class (Highest class)	
A	44 (29.1)
B	38 (25.2)
C	43 (28.5)
D	26 (17.2)

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Table 3: Prevalence and pattern of coronary artery disease

Characters	Prevalence, n (%)
Clinical CAD	70 (46.4)
CAD on invasive coronary angiography	113 (74.8)
Vessel involvement	
SVD	25 (16.6)
SVD+LMCA	02 (1.3)
DVD	41 (27.2)
DVD+LMCA	04 (2.6)
TVD	37 (24.5)
TVD+LMCA	04 (2.6)
LMCA	10 (6.6)

SVD: single vessel disease, DVD: double vessel disease, TVD: triple vessel disease, LMCA: left main coronary artery disease

Table 4: Correlation of No or single v/s multivessel coronaries involvement with pattern and extensiveness of PAD

PAD (Vessel involved)	Number of coronaries involved, n (%)		p value
	No vessel or SVD	≥2 (MULTIVESSEL)	
Proximal v/s Distal			
Proximal involvement (Aorto-iliac)	9 (37.5)	15 (62.5)	
Distal vessels involvement (Non aorto-iliac)	35(43.8)	45 (56.3)	0.842
Both	19 (40.4)	28 (59.6)	
Limited v/s Extensive PAD			
Limited	55 (46.6)	63 (53.4)	0.02
Extensive	8 (24.2)	25 (75.8)	

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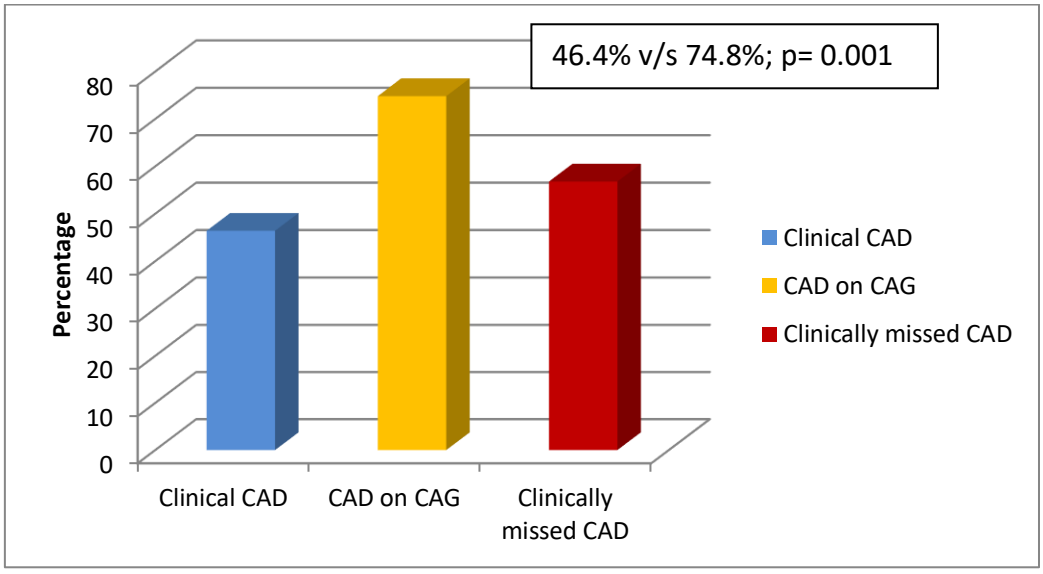

Figure 1: Variations in CAD diagnosis with mode of diagnosis in PAD

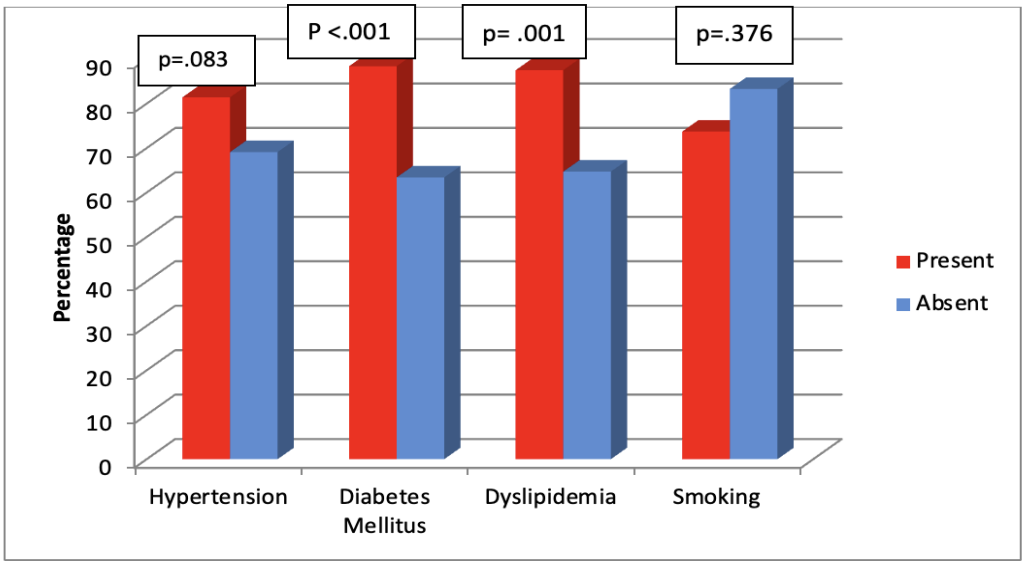

Figure 2: Baseline predictors of CAD in PAD patients (values in %age)

Discussion

Because of the common etiopathogenesis and almost similar underlying risk factors including age, sex, diabetes mellitus, hypertension, dyslipidemia, obesity and smoking, which are responsible for atherosclerosis, the association of peripheral arterial disease and coronary artery disease is a common occurrence.

In the present study which included 151 patients of symptomatic lower limb peripheral vascular disease, mean age of presentation was 57.26±9.74 years, predominantly affecting males which constituted 94% of total study group.

Previous data on prevalence of CAD in patients with PAD showed highly variable results varying from 14% to 90%.[7, 8,15,16,17]This wide variability in prevalence might be due to the variation in definitions used to define CAD (≥50% or ≥70% diameter stenosis), diagnostic

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modality (invasive CAG or computed tomography coronary angiography) and territory of PAD (lower extremity, carotid artery, abdominal aorta or renal artery). In the present study significant CAD was present in 74.8% (n=113). Beatrice A. et al. in his review of cross-sectional data for co-prevalence CAD in PAD found that CAD was present in 19% to 47% of PAD patients in studies using clinical history plus ECG; in 62% to 63% using stress tests (modified stress ECG or dipyridamole-stress thallium); and in 90% of subjects when coronary angiography was used.[18] Similarly, in present study, clinically detectable CAD (on basis of history and ECG) was present in only 46.4% (n=70) of the study population in comparison to invasive coronary angiography in which significant CAD was present in 74.8% (n=113) of the patients with a p value of <0.001. In patients with no clinical evidence of CAD, 56.79% (n=46) of patients were found to have significant CAD on invasive coronary angiography. Hence, it indicates a large number of the patients were having silent coronary artery disease, probably because of limitation of physical activity in PAD patients.

Nearly 95% of patients were having significant CAD on invasive coronary angiography in the patients who had clinically detectable CAD indicating that once there are clinical evidences of coronary ischemia, the diagnosis of significant CAD is almost confirmed. The similar finding was also observed by Daniel F. Phillips et al. in 203 patients of peripheral vascular disease including 71 patients of aortoiliac disease proposed for peripheral vascular reconstructive surgery.[19]

Among the CAD patients, majority (77.87%, n=88) of patients were having multivessel disease. The prevalence of TVD, DVD and SVD was 41.59% (n=47), 36.28 (n=41) and 22.1% (n=25) respectively. Sukhija et al. studied 200 consecutive patients admitted for symptomatic lower limb arterial disease and reported a higher prevalence of 3-vessel or 4-vessel CAD in patients with PAD compared without PAD.[7] Importantly, Ishihara et al in his study of severity of coronary artery disease affects the prognosis of patients with peripheral artery disease found that the severity of CAD affected the prognosis of patients with lower extremity PAD.[20] Hence early detection of CAD in this group of the patients might be critical for improving the prognosis in PAD patients.

Among baseline risk factors, diabetes and dyslipidemia were significantly associated with higher prevalence of significant CAD in symptomatic lower limb peripheral vascular disease patients with a p value of <.001 and .001 respectively indicating that the presence of diabetes and/or dyslipidemia are associated independently with higher incidence of concomitant CAD and PAD. Yilmaz et al also reported that age, metabolic syndrome and diabetes were independent predictors of severe CAD in PAD patients.[21] Another study demonstrated that hypertension and diabetes could predict the presence of CAD and multi-vessel CAD in PAD patients.[22] Sung Woo Cho et al also showed that diabetes significantly increases the risk of CAD in patients with PAD and the odds ratio of having multi-vessel CAD was 2.5 (1.1-5.9, p = 0.037) in multivariate regression analysis.[23] Taken together, previous publications and our data indicate that diabetes and dyslipidemia are the only common factors to predict CAD in patients with lower extremity PAD. Therefore, screening of CAD should be strongly considered in PAD patients with diabetes and dyslipidemia.

Prevalence of significant CAD was not significantly different in patients with aortoiliac disease in comparison to non-aortoiliac or combination of both (79.2% v/s 78.2% v/s 66%; p= 0.240). These results are similar to the study done by M vikas et al. which showed CAD were present

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in 54% of Abdominal-iliac, 54% in femoro-popliteal, 70% distal PAD & 75% multiple level, but with the lower prevalence than the present study.[24]

Multivessel coronary artery involvement was present in 62.5% (n=15) of patients with aortoiliac disease in comparison to 56.3% (n=45) in non-aortoiliac disease and 59.6% (n=28) in patients with both segments involved (p= .842) indicating though the prevalence of multivessel CAD was not statistically significantly different in patients with aortoiliac disease in comparison to non-aortoiliac or combination of both, there was a trend of increased prevalence of multivessel CAD in proximal PAD (aortoiliac disease) in comparison to non-aortoiliac PAD. Sung Woo Cho et al studied 107 patients of lower extremity PAD and showed that multivessel CAD involvement was significantly higher in comparison to normal or single vessel disease in patients with proximal PAD (defined as having stenosis located in aortic-iliac and femoral-popliteal arteries) (95% v/s 75%; p= 0.003), but not in distal PAD (defined as having stenosis located in below knee arteries) (4% v/s 0%; p= 0.590).[23] Another study by M Vikas et al. studied 224 patients of lower limb PAD and found that prevalence of triple vessel disease was 66.4% in abdominoiliac disease, 24.4% in femoral-popliteal disease and 14.6% in distal disease.[24] It showed that more proximal is the PAD, greater the prevalence of triple vessel disease. The present study also showed similar trend, with few differences which might be due to inconsistency among definition of CAD (≥ 50% or ≥ 70% luminal narrowing) and PAD (aortoiliac v/s non aortoiliac disease or proximal v/s distal disease).

Multivessel coronary artery involvement was found to be significantly higher in patients with extensive PAD in comparison to the patients with limited PAD (75.8% v/s 53.4%, p=0.02). It indicates that more extensive is the PAD involving the multiple segments together, more likely the patient should have multivessel coronary artery disease. Sung Woo Cho et al studied 107 patients of lower extremity PAD and showed that multivessel CAD involvement was significantly higher in comparison to normal or single vessel disease in patients with combined proximal and distal disease vessel involvement (21% v/s 5%; p= 0.003).[23] Another study by Rigatelli G in 112 patients showed that aortoiliac disease is associated frequently with multivessel CAD.[25]

Gensini's score is a well validated score for the evaluation of severity of coronary artery disease. Gensini's score for the patients was <32, 32-57 and ≥58 in 46.3% (n=70), 14.6% (n=22) and 39% (n=59) respectively. The present study did not show a significant correlation between severity of coronary artery disease as assessed by Gensini score and the site (aortoiliac/non-aortoiliac) or severity (as quantified by ABI, Fontaine's class, Rutherford's grade/category, TASC class, or extensive/limited) of peripheral artery disease.

There are few limitations of present study: 1) Small sample size, 2) Present study included the patients presented to outpatient department of a tertiary care hospital. Hence there are chances of patient's selection vias. 3) Female patients are underrepresented in thepresent study.

Conclusion

Overall, there is high prevalence of CAD in patients with symptomatic lower limb PAD (74.8%). About 57% CAD patients were asymptomatic. Diabetes mellitus and dyslipidemia are the independent risk factor for development of CAD. PAD patients are more prone for multivessel CAD specifically the patients with extensive PAD. Hence this study strengthen the need for coronary angiography in all cases of symptomatic lower limb PAD to detect CAD at earliest, particularly in patients with diabetes and dyslipidemia.

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What is Already Known?

Prevalence of CAD, particularly multivessel is high in lower limb peripheral arterial disease with associated nearly doubled all-cause mortality. There is also increase prevalence of asymptomatic CAD but data are scare to predict the CAD in this group of patients.

What this Study Adds:

There is high prevalence of CAD in patients with symptomatic lower limb PAD. About 50% of CAD are asymptomatic. Diabetes mellitus and dyslipidemia are the independent risk factor for development of CAD. PAD patients are more prone for multivessel CAD specifically the patients with extensive PAD. Hence this study strengthen the need for coronary angiography in all cases of symptomatic lower limb PAD to detect CAD at earliest, particularly in patients with diabetes and dyslipidemia.

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