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Original Research Article

A study to assess frequency of peripheral arterial disease in patients presenting with acute coronary syndrome

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ABSTRACT

Background: To determine the frequency of peripheral arterial disease (PAD) in patients presenting with acute coronary syndrome (ACS) and association of PAD with different risk factors of coronary artery disease (CAD) and to look for in hospital outcome of ACS patients with or without PAD.
Methods: This cross-sectional observation study was undertaken in the department of cardiology, IPGME&R Hospital, Kolkata from June 2015 to August 2016 to recruit 199 consecutive patients admitted with ACS and were evaluated with detailed clinical history, physical examination, ABI (Ankle Brachial Index) measurement, echocardiography and appropriate blood investigations.
Results: Among 199 total ACS patients, STEMI was the predominant mode of presentation (71.86%) and majorities were male. PAD was seen in 26 patients and mean age was 56.68±8.84 years. Factors independently related with PAD in acute coronary syndromes are hypertension (OR- 1.49; 95% CI: 0.615-3.232), diabetes (OR- 2.55;95% CI : 0.9762-6.6665), smoking (OR-2.55; 95% CI: 1.055-6.19), past history of CVA (OR-11.15;95% CI: 1.77-70.32), LV systolic dysfunction (OR-1.388; 95% CI:0.607-3.1742). 2 and 13 patients died within 7 days of admission among 26 ACS-PAD group (7.69%) and 173 ACS-non-PAD group (7.5%) respectively and most of them had STEMI.
Conclusions: Significant numbers of ACS patients are having PAD and older age, male sex, diabetes, hypertension, smoking and LV systolic dysfunction were found to be independent predictors for PAD in ACS patients. Early in hospital mortality was seem to be dependent on clinical presentation, not on presence or absence of PAD.

Keywords: Acute coronary syndrome, Peripheral arterial disease

INTRODUCTION

Coronary artery disease (CAD) is leading cause of morbidity mortality worldwide and is also on the rise in the developing world.[1,2] The rate of Acute Coronary Syndrome (ACS) rises sharply in both men and women with increasing age.[3] ST-elevation myocardial infarction, non-ST-elevation myocardial infarction or Unstable Angina are the different modes of presentation of acute coronary syndrome (ACS). It is well established that a significant proportion of patients suffering from CAD also have underlying peripheral arterial disease (PAD). PAD refers to atherosclerotic and thromboembolic processes that affect the aorta, its visceral arterial branches and arteries of the extremities and it represents an independent risk for cardiovascular morbidity and mortality.[4,5] Approximately 30% of patients with CAD may have PAD as the only clinical manifestation of cardiovascular disease.[6] Traditional risk factors for PAD are similar to those that lead to atherosclerosis in the carotid, coronary and other vascular beds. For epidemiological purposes, the most useful noninvasive

test to screen for PAD is the ankle brachial index (ABI) measured by a hand-held Doppler probe which is the ratio between systolic BP in the ankle and systolic BP in the arm.[7] The lower the ABI, the higher the prevalence of 3 or 4 vessel CAD and the lower the prevalence of 1 vessel CAD.[8] The normal value of the ABI ranges from 0.9 to 1.3. PAD is defined as an ABI of less than 0.9. Several studies have shown worse prognosis in acute coronary syndrome (ACS) when PAD present in both selected and unselected western population admitted with ACS.[9-12] However, the prevalence and the impact of PAD in patients with acute coronary syndrome in the South-Eastern countries are limited. The rationale of our study, therefore, was to look for PAD in patients presenting with ACS so that these patients are treated even more aggressively in order to achieve a significant morbidity and mortality reduction.

METHODS

This cross-sectional observation study was undertaken in the department of cardiology, IPGMER Hospital, Kolkata. Approval was taken from the institutional ethics committee before starting the study. We recruited 199 consecutive patients age>18 years admitted in cardiology department of our hospital with ACS from June 2015 to August 2016. Patients diagnosed with ACS were enrolled after applying exclusion criteria (advanced kidney disease with GFR <15 ml or patients on dialysis, chronic debilitating condition like neoplastic diseases and pregnancy). After taking detailed history, general and systemic examination was done. ABI (Ankle Brachial Index) was measured with hand held dopplar machine. Echocardiography was done with GE machine with 5 maga hartz probe. Blood investigations were sent and appropriate treatment was started. All data were collected, saved in master chart and evaluated at the end of the study.

Statistical analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 20.0.1 and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. Univariate analysis was performed by logistic regression method for calculation of risk factors. Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

RESULTS

Among 199 total ACS patients, 143 presented with STEMI (71.86%), 42 presented with NSTEMI (21.10%), 14 presented with UA (7.03%). In our ACS patients, all were male predominant (67.84%) (P-value <0.0001) (as shown in table 1). PAD was seen in 26 patients among total 199 ACS admission (13.06%). Among all 26 ACS-PAD group, 19 patients were male (73%) (P-value 0.00086) and 7 patients were female (27%). Mean age in our ACS patients was 56.68±8.84 years.

Among total 199 ACS patients, 118 were diagnosed as diabetic (59.3%) (P-value 0.0002) and 20 patients had PAD among them (16.9%) and among 81 non-diabetic patients, 6 patients had PAD (7%). Out of 26 ACS-PAD group, 20 patients were diabetic (76.9%) (p-value 0.0001). 122 patients were hypertensive (64.3%) (P-value <0.0001) and 18 had ABI <0.9 among them (14.75%) and among 77 non-hypertensive patients, 8 had reduced ABI (<0.9) (10.39%). Among 26 ACS-PAD group, 18 patients were hypertensive (69.23%) (P-value 0.0056). Among all ACS patients, 54 had eGFR<60 ml/min/1.73m^2 (27.14%) and 18 patients had PAD among them. Among total 26 ACS-PAD group, 18 patients had eGFR<60ml/min/1.73m^2 (69.23%) (P-value-0.0056).

All of our female patients were non-smokers. Among 135 male patients 99 were smoker (73.33%) and PAD was present in 18 patients (13.33%). 36 male patients were non-smoker and PAD was detected in only one patient (2.8%). Among 26 PAD-ACS group 18 were smoker (69.23%) (P-value 0.0056).

History of CVA was present in 5 patients and among them 3 patients had ABI<0.9 (60%). 23 had ABI<0.9 among 194 patients without any past history of CVA (11.85%). Out of 26 ACS-PAD group, 3 patients had history of CVA (11.54%) and among 173 ACS-non-PAD group only 2 patients had history of CVA (1.16%).

Out of total 143 STEMI patients, 88 had EF<50% (61.54%) while among 42 NSTEMI patients, 5 had EF<50% (12%) and all of the 14 unstable angina patients had preserved LV systolic function (EF> 50%). So, our study shows most of the NSTEMI and Unstable Angina patients had good LV systolic function (P-value <0.0001) and majority of STEMI patients had poor LV systolic function (P-value 0.0001). Most of them had anterior wall myocardial infarction and 14 among them had PAD (15%). Out of 26 ACS-PAD group, 14 patients had LVEF <50% (53.86%) (P-value 0.5823) and among 173 ACS-non-PAD group 79 had LVEF<50% (45.66%) (P-value 0.1074). Thus, significant association of LVEF

with PAD was not established. 2 patients were died within 7 days of admission among 26 ACS-PAD group (7.69%) and both of them had STEMI. Whereas 13 patients were died among 173 ACS without PAD group (7.5%), 10 patients among them had STEMI. Thus, early in hospital mortality was seem to be dependent on clinical presentation of patients, not on presence or absence of PAD.

Table 1: Age and gender wise distribution of all ACS patients with or without PAD with distribution of risk factors and their in-hospital mortality.

		STEMI-143				NSTEMI-42				UA-14				Total		
		M-99		F-44		M-27		F-15		M-9		F-5		199		
		PAD+ (13)	PAD- (86)	PAD+ (5)	PAD- (39)	PAD+ (5)	PAD- (22)	PAD+ (2)	PAD- (13)	PAD+ (1)	PAD- (8)	PAD+ (0)	PAD- (5)	PAD+ (26)	PAD- (173)	
Age (years)	<50	2	23	0	9	1	7	0	4	0	2	0	2	3	47	50
	50-60	4	32	2	15	2	7	1	4	0	3	0	2	9	63	72
	>60	7	31	3	15	2	8	1	5	1	3	0	1	14	63	77
DM+		9	49	4	22	4	13	2	6	1	4	0	4	20	98	118
DM-		4	37	1	17	1	9	0	7	0	4	0	1	6	75	81
HTN+		8	54	4	25	3	14	2	5	1	3	0	3	18	104	122
HTN-		5	32	1	14	2	8	0	8	0	5	0	2	8	69	77
eGFR≥60		4	74	1	26	2	18	1	8	0	8	0	3	8	137	145
eGFR<60		9	12	4	13	3	4	1	5	1	0	0	2	18	36	54
Smoking+		12	64	0	0	5	12	0	0	1	5	0	0	18	81	99
Smoking-		1	22	5	39	0	10	2	13	0	3	0	5	8	92	100
CVA+		1	1	1	1	1	0	0	0	0	0	0	0	3	2	5
CVA-		12	85	4	38	4	22	2	13	1	8	0	5	23	171	194
LVEF>50%		4	37	2	12	3	20	2	12	1	8	0	5	12	94	106
LVEF<50%		9	49	3	27	2	2	0	1	0	0	0	0	14	79	93
7days in hospital mortality		1	7	1	3	0	2	0	1	0	0	0	0	2	13	15

Table 2: Correlation of different risk factors with PAD.

Risk factors		PAD		95% Confidence Interval		
		Positive	Negative	Odds Ratio	Lower	Upper
HTN	YES	18	104	1.4928	0.6150	3.6232
	NO	8	69			
DM	YES	20	98	2.5510	0.9762	6.6665
	NO	6	75			
Smoking	YES	18	81	2.5556	1.0550	6.1906
	NO	8	92			
CVA	YES	3	2	11.1522	1.7686	70.3198
	NO	23	171			
LVEF	Abnormal	14	79	1.3882	0.6071	3.1742
	Normal	12	94			

Factors independently related with PAD in acute coronary syndromes are hypertension (OR- 1.49; 95% CI: 0.615-3.232), diabetes mellitus (OR- 2.55; 95% CI: 0.9762-6.6665), smoking (OR-2.55; 95% CI: 1.055-6.19), past history of CVA (OR-11.15; 95% CI: 1.77-70.32), poor LV systolic function (OR-1.388; 95% CI: 0.607-3.1742) (as shown in table in Table 2).

DISCUSSION

In our study, ACS patients were male predominant (P-value <0.0001). The skewed gender distribution males (67.84%) versus females (32.16%) of the study population can be attributed to the gender bias and atypical presentation in females, which was also a feature in interheart study (overall male 76%) and its South Asian cohort (overall male 85%) and study from Jayadeva institute by Sharma R et al (male 79.5%).[13,14]

STEMI constitutes major portion of ACS in our institution (71.86%) which differ from western data. Western data in NRMI registry from 1990 to 2006 shows, the proportion of NSTEMI increased from 14.2% to 59.1% (P < 0.0001), whereas the proportion of STEMI

decreased.[15] But, Indian data in CREATE registry, of the 20,468 patients who were given a definite diagnosis, 12,405 (60.6%) had STEMI and Sharma R et al showed most patients had STEMI 995 (63.7%) followed by UA 390 (25%) and NSTEMI 177 (11.3%).[16]

Prevalence of PAD in ACS patients in this study (13.06%) was lower than western study but was more than the middle Eastern countries and male prevalence of PAD is established which is consistent with previous studies. In PLASMICA registry, 1410 ACS patients (71.4% male) were included. PAD determined by ABI was documented in 561 patients (39.8%).[17] In Morrilas P et al study, of total 1054 ACS patients clinical PAD was present in 150 patients (14.2%) and 298 cases of subclinical PAD were detected (28.3%).[12] Benjamin D. K. Leong et al, showed 24.5% of ACS patients had PAD (25.3% of male and 20.0% of female).[18]

Mean age of presentation was 56.68±8.84 years (56 years for male and 58 years for female) which was comparable to other studies done in India, that is, CREATE registry (56±13 years), R. Sharma et. al (54.71±19.90) and Jose and Gupta study (57±12 years) but lower than the western population as in COURAGE trial 62±5 years conducted in USA, study by Hochman et al.[20] (69 years), and Chang et al (73 years).[21] Peripheral arterial disease occurrence increases with age. Most studies have shown a linear relation between age and PAD. The Rotterdam Study showed a prevalence of 7.6% in age group of 55-59 years, which increased to 59.6% in age >85 years.[22] Newman et al. have shown a prevalence of 26% in a population aged ≥ 60 year.[23] In our study, 6%, 12.5% and 18% patients were detected to have PAD in above three age groups respectively (<50 years, 50-60 years and >60 years).

59.3% patients were diabetic in this study (P-value 0.0002) which was higher than CREATE registry where 30.4% patients had diabetes and Sharma R et al. study where 37% patients were diabetic among all ACS patients. 64.3% patients were hypertensive (P-value <0.0001) in this present study. In CREATE registry 37.7% and Sharma R et al study 40.2% patients were hypertensive among all ACS patients. Among total 118 diabetic patients, 20 patients had PAD (16.9%) and among 81 non-diabetic patients, 6 patients had PAD (7%). Out of 26 ACS-PAD group, 20 patients were diabetic (76.9%) (p-value 0.0001). Out of 122 hypertensive patients, 18 had ABI<0.9 (14.75%) and among 77 non-hypertensive patients, 8 had reduced ABI (<0.9) (10.39%). Among 26 ACS-PAD group, 18 patients were hypertensive (69.23%) (P-value 0.0056). The Framingham data documented a 2·5-fold increase in the risk of PAD in men with hypertension and a 3·9-fold increase in women with hypertension.[24] However, Reunanen et al, showed that hypertension was not significantly related to PAD.[25] Out of the total 199 patients, 54 had eGFR<60ml/min/1.73m^2 (27.14%) and 18 patients had PAD among them. Among total 26 ACS-PAD group, 18 patients had eGFR<60ml/min/1.73m2 (69.23%) (P-value-0.0056). Present study shows most of the NSTEMI and Unstable Angina patients had good LV systolic function (P-value <0.0001) and majority of STEMI patients had poor LV systolic function (P-value 0.0001). Most of them had anterior wall myocardial infarction and 14 among them had PAD (15%). All of our female patients were non-smokers. Among 135 male patients 99 were smoker (73.33%) and PAD was present in 18 patients (13.33%). Among 26 PAD-ACS group 18 were smoker (69.23%) (P-value 0.0056) and among 173 ACS-non-PAD group 81 were smoker (46.82%). In CREATE registry, 8242 (40.2%) were smokers. In R. Sharma et. al ACS study, smoking was most prevalent risk factor seen in 770/1562 (49.30%) patients. Active smoking was noticed only in male, that is, 770 (62%) of total male (1242) patients and women were rather tobacco chewers. Studies like Framingham Study, Cardiovascular Health Study, and Edinburgh Artery Study showed that amongst smokers PAD was 2–5 times higher. History of CVA was present in 5 patients and among them 3 patients had ABI<0.9 (60%). Out of 26 ACS-PAD group, 3 patients had history of CVA (11.54%).

In PLASMISA registry [17], factors independently related to PAD were age (OR: 1.04; 95% CI: 1.03-1.06; p < 0.001), smoking (OR: 1.88; 95% CI: 1.41-2.49; p < 0.0001), diabetes (OR: 1.30; 95% CI: 1.02-1.65; p < 0.05), previous cardiac disease (OR: 1.54; 95% CI: 1.22–1.95; p < 0.001) and previous cerebrovascular disease (OR: 1.90; 95% CI: 1.28-2.80; p < 0.001). In Hassan A. Al-Thani et al, PAD patients were also more likely to have diabetes mellitus (69% versus 40%, P <0.001), hypertension (77% versus 50%, P <0.001), dyslipidemia (66% versus 31%, P = 0.001), previous history of CAD (79% versus 45%, P <0.001), prior coronary revascularization (35% versus 15%, P <0.001), chronic lung disease (17.5% versus 5%) and renal failure (45% versus 17%, P = 0.001).[19] So, our study was consistent with most of the previous studies as far as the independent risk factors of PAD are concerned.

In Hassan A. Al-Thani et. al. PAD was associated with higher rate of heart failure in comparison to non-PAD patients. After adjustment, PAD was associated with high mortality in STEMI (adjusted OR 2.6; 95% CI 1.23-5.65, P = 0.01). In our study, early in hospital mortality was seem to be dependent on clinical presentation of patients, not on presence or absence of PAD in our observation.

CONCLUSION

Patients with acute coronary syndrome present either as ST-elevation myocardial infarction, non-ST-elevation myocardial infarction or unstable angina. Most of the patients are male in our study and STEMI was the predominant mode of presentation which is consistent with other Indian data but inconsistent with recent western trends. CAD and PAD share the common

pathogenesis of atherosclerosis and therefore, they share similar risk factors profile and these two conditions commonly occur together. 13.06% of total ACS patients had PAD in this study which was bit lower than western data. Older age group, male sex, diabetes, hypertension, impaired renal status and smoking were found to be independent predictors for PAD among patients with ACS in our study. But, 7 days in-hospital mortality didn't differ significantly between PAD and non-PAD groups in ACS patients in contrast to other studies where in hospital mortality was higher in ACS-PAD group. The number of study participants was small which may be responsible for the lower incidence of PAD. In our study 61% patients were less than 60 years age whereas most of the previous studies included older age group. This could be another explanation for our result. The study was conducted in one centre and the results cannot be generalized. However, given the high prevalence of PAD among ACS patients with majority of them asymptomatic, PAD should be actively sorted for in patients with ACS by health care provide.

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