Prevalence of Peripheral arterial disease (PAD) in Patients of Chronic Obstructive Pulmonary Disease (COPD) attending Tripura Medical College and Dr. BRAM Teaching Hospital

Dulal Chakraborty[1], Avik Chakraborty[2], Nirmalya Saha[3], Sannibesh Das[4]

ABSTRACT

Introduction: Peripheral arterial disease (PAD) in patients of Chronic Obstructive Pulmonary Disease (COPD) is on increase specially in developing countries. So the aim of this study was to determine the prevalence of peripheral arterial disease (PAD) and the associated risk factors for patients with COPD.

Material and Methods: This prospective cross-sectional study enrolled 115 COPD patients (mean age: 68.02 years). Demographic data, lung function and cardiovascular risk factors were recorded. The ankle-brachial index (ABI) was used to detect PAD (ABI<0.90).

Results: Among the enrolled 115 COPD patients, the prevalence of PAD was 29.57%. The prevalence of PAD in younger (<65 years) were 2 (1.74%) and among older (>65 years) were 32 (27.83%). Hypertension was found to be the most common cardiovascular comorbidity (n= 66, 57.39%), followed by diabetes mellitus (n =32, 27.83%), and hyperlipidemia (n= 29, 25.22%). There was no significant difference in lung function (forced vital capacity and forced expiratory volume in one second) between the two groups. Hyperlipidemia was found to be the strongest independent factor for PAD (odds ratio (OR): 19.38), followed by old age (OR: 7.143), and hypertension (OR: 4.15).

Conclusion: The prevalence of PAD among COPD patients in TMC and Dr. BRAM Hospital is 29.57%.In our study the associated cardiovascular risk factors were Hyperlipidemia, increased age, hypertension and smoking. No association was found between COPD GOLD stage and PAD.

Keywords: ABI: Ankle - Brachial index. FEV1: Forced expiratory volume in 1 second. FVC: Forced vital capacity. GOLD: Global initiative for chronic obstructive lung disease. DM: Diabetes mellitus.

INTRODUCTION

Peripheral arterial disease (PAD) also known as peripheral vascular disease (PVD) is narrowing of the arteries other than those that supply the heart and brain. When narrowing occurs in the heart and the brain it is called coronary artery disease and cerebrovascular disease respectively. PAD most commonly affects the lower limbs, but other arteries may get involved. Classical symptom is leg pain on walking which is known as intermittent claudication that resolves with rest,[1] other symptom like skin ulcer, cold skin, bluish skin, poor nail and hair growth may occur in the affected limb. Possible complications are infection or tissue death which may need amputation; stroke, or coronary artery disease. Approximately 50% of cases of PAD are asymptomatic.[1] Cigarette smoking is the main risk factor and other risk factors include hypertension, diabetes, and hyperlipidemia.[2] Atherosclerosis and arterial spasm could be the underlying mechanism of PAD which can be diagnosed by duplex ultrasonography and angiography. Angiography is more accurate for diagnostic and therapeutic purposes.[3]

In 2010 worldwide approximately 202 million people had PAD. It affects about 5.3% of people between 45 - 50 years and 18.6% of 85 - 90 years in developed world. It affects 4.6% of 45 - 50 years and 15% of 85 – 90 years. PAD is equally common among men and women in the developed world while women are more commonly affected in the developing world.[2]

Chronic obstructive pulmonary disease (COPD) is leading cause of morbidity and mortality worldwide, with prevalence rates between 5% and 13%.[4-6] COPD is projected to represent the third leading cause of death in middle –income countries by 2030.[7] Smoking is the major cause of COPD, as smoking induced inflammation causes vascular endothelial damage via oxidative stress.[8] Peripheral arterial disease (PAD) and its risk factors are common to other atherosclerotic diseases including cardiovascular diseases.[9] PAD is an atherosclerotic process that effects non coronary arteries and often refers to occlusion of the arteries of the lower limbs.[10,11]

Chronic obstructive pulmonary disease (COPD) has been defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as a disease state characterized by airflow limitation that is not fully reversible.[12]

Aim and objective of the research were to the find out the prevalence of PAD in patients of COPD attending TMC and Dr. BRAM Teaching Hospital, to find out other comorbidities associated in patients of COPD and CAD and to evaluate the association of lung function (FEV1 and FVC) and GOLD staging in patients with PAD.

MATERIAL AND METHODS

This cross sectional study was done over a period of six months at TMC and Dr. B. R. Ambedkar Teaching Hospital. A total of 115 diagnosed and treated patients with COPD were included in the study.

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Inclusion criteria

1. Male/Female subjects aged 40-80 years.
2. Baseline post bronchodilator FEV1 of ≥80% predicted and FEV1/FVC of < 0.7 without reversibility of <15% according to GOLD criteria.
3. Ability to comply with the requirements of the protocol and be available for study visits.
4. Willing to participate in the study.

Exclusion criteria

1. Subjects aged < 40 and >80 years.
2. Except COPD other pulmonary diseases such as Bronchial asthma, asthma- COPD overlap, Interstitial lung disease, bronchiectasis, cystic fibrosis, lung tumor, pulmonary TB, Pneumonia, pneumoconiosis etc.
3. Any acute peripheral artery diseases i.e. thromboembolic peripheral artery disease.

Patient aged between 40-80 years attending medicine OPD/ IPD with history suggestive of COPD were screened by spirometry for diagnosis of COPD as per GOLD criteria of COPD. Detailed history of risk factors of development of COPD was taken along with the detailed history of risk factors of development of Peripheral artery diseases. Detailed examination with special emphasis on peripheral pulse, respiratory and cardiovascular system was done. Patients fulfilling the inclusion and exclusion criteriawere taken up for the study.

Spirometry was done in all patients including pre and post bronchodilator after 200 mcg of salbutamol inhalation by Metered Dose inhaler (MDI). Study population will be categorized according to GOLD criteria of COPD. According to GOLD criteria:[13]

Stage I COPD Patient denotes Mild cases with Spirometry findings FEV1/FVC <0.7 and FEV1 ≥80% predicted.

Stage II COPD Patient denotes Moderate cases with Spirometry findings FEV1/FVC <0.7 and FEV1 ≥50% but <80% predicted.

Stage III COPD Patient denotes Severe cases with Spirometry findings FEV1/FVC <0.7 and FEV1 ≥30% but <50% predicted.

Stage IV COPD Patient denotes Very severe cases with Spirometry findings FEV1/FVC <0.7 and FEV1 <30% predicted.

Diagnosed cases of COPD shall be subjected to detailed history and physical examination pertaining to PAD. All subjects shall undergo peripheral artery Doppler with hand held vascular Doppler (VD-320) and Ankle brachial index (ABI) will be calculated. Clinically PAD will be classified according to classification introduced by Robert B. Rutherford in 1986 and revised in 1997.[14-15]

Grade 0, Category 0 = No symptoms.
Grade I, Category 1 = Mild claudication.
Grade I, Category 2= Moderate claudication.
Grade I, Category 3= Severe claudication.
Grade II, Category 4= Rest pain.
Grade III, Category 5= Minor tissue loss; Ischemic ulceration not exceeding ulcer of the digits of the foot.
Grade IV, Category 6= Major tissue loss; severe ischemic ulcers or frank gangrene.

When the blood pressure readings in the ankles are lower than that in the arms, blockages in the arteries which provide blood from the heart to the ankle are suspected. PAD was confirmed by ABI using hand held vascular Doppler. Normal range of ABI is 1.00 to 1.40.The patient was diagnosed of having PAD when the ABI is ≤ 0.90. ABI values in between 0.91 to 0.99 were considered ''borderline'' and values more than 1.40 indicate non compressible arteries. PAD was graded as mild to moderate if the ABI was between 0.41 and 0.90, and an ABI less than 0.40 was suggestive of severe PAD. These relative categories have prognostic value.[16]

Calculation of sample size

$n = 4 p q / L^2$

Where p = Prevalence = 7 % (Prevalence as per the study, "Prevalence of COPD in India: a systematic review")[17]

q = (100-p) =93%

L = Allowable error (absolute) = 5%

By the formula $n = 4 p q/L^2$

Calculated sample size =104. Extra 10% sample added to compensate any incomplete data

So, final sample size = 115.

STATISTICAL ANALYSIS

All relevant data so collected was entered in the master chart and analyzed using IBM SPSS Statistics 20. Descriptive statistics was used to infer results.

RESULTS

Of the 115 participants, male were 112 (97.39%). Age >65 years were 88 (76.52%) and <65 years were 27 (23.48%). Mean age was 68.02.Thirty four (29.57%) were diagnosed to have PAD, among those 28 (24.35%) were asymptomatic PAD and 6 (5.22%) were symptomatic PAD. The prevalence of PAD in younger (<65 years) were 2 (1.74%) and among older (>65 years) were 32 (27.83%).

The most common cardiovascular comorbidity was hypertension (n= 66, 57.39%), followed by diabetes mellitus (n =32, 27.83%), and hyperlipidemia (n= 29, 25.22%). All the patients included in the study had history of smoking (at least 10 pack years), including current (n= 98, 85.22%) and former (n= 17, 14.78%) smokers. The mean pack-years of smoking were 44.324. Sixteen patients (13.91%) had a significant reversibility of short acting bronchodilators. There was no patient with severe respiratory failure in our study. Twenty two patients (19.13%) were overweight, 8 (6.96%) were obese. PAD seen in different stages of COPD stage I –IV were 3%, 35%, 50%, 12% respectively.

DISCUSSION

This was a cross-sectional study to investigate the prevalence of PAD among COPD patients in TMC and Dr. BRAM Teaching Hospital, Tripura. We used an ABI<0.9 for the diagnosis of PAD.

Among the enrolled 115 COPD patients, the prevalence of PAD was 29.57%. The prevalence of PAD in younger (<65 years) were 2 (1.74%) and among older (>65 years) were 32 (27.83%).

Hypertension was found to be the most common

cardiovascular comorbidity (n = 66, 57.39%), followed by diabetes mellitus (n =32, 27.83%), and hyperlipidemia (n= 29, 25.22%). Age, hyperlipidemia, and hypertension were the associated factors in the elderly COPD patients. No significant difference in lung function (FEV1 and FVC % predicted) test and GOLD stage between the COPD patients with and without PAD was found in our study. Hyperlipidemia was found to be the strongest independent risk factor for PAD in the patients with COPD.

Few studies investigated the prevalence of PAD in patients with COPD (Table 3). The first study regarding the prevalence of PAD in patients with COPD was in France, which enrolled 151 moderate to severe COPD patients and found that the prevalence of low ABI (<0.9) was 81.4%.[18] This is very high compared to studies from Israel and Spain which reported the prevalence of low ABI to be approximately 30% to 40%.[19,20] As shown in Table 3, the prevalence of hyperlipidemia in two of the studies was about 68%, which is almost 2 times higher than in our study (25.22%). The strongest independent factor for the development of PAD in the current study was hyperlipidemia, and this may explain the prevalence rate. The prevalence rates of hypertension,

	All (n = 115)	PAD (-) n = 81	PAD (+) n= 34
Age (years)	68.02	66.954	70.56
Gender: male	112(97.39%)	78(96.3%)	34(100%)
Height (cm)	157.48	158.55	154.94
BW (kg)	57.42	57.52	57.18
BMI	23	22.66	23.8
Normal	85(73.91%)	58(71.6%)	27(79.41%)
Overweight	22(19.13%)	17(20.99%)	5(14.71%)
Obese	8(6.96%)	6(7.41%)	2(5.88%)
Smoker	115(100%)	81(100%)	34(100%)
Pack-years	44.34	42.47	48.8
Current	98(85.22%)	70(86.42%)	28(82.35%)
Former	17(14.78%)	11(13.58%)	6(17.65%)
DM	32(27.83%)	20(24.69%)	12(35.29%)
Hypertension	66(57.39%)	39(48.15%)	27(79.41%)
Hyperlipidemia	29(25.22%)	7(8.64%)	22(64.70%)
ABI	1.05	1.13	0.86
Lung function			
Pre-bronchodilator			
FEV1 (L)	1.16	1.21	1.04
FVC (L)	1.96	2.02	1.82
FEV1/FVC (%)	56.8	56.9	55.5
Post-bronchodilator			
FEV1 (L)	1.28	1.28	1.16
FEV1 (pred %)	51.2	51.1	51.8
FEV1/FVC (%)	56.9	57.15	56.3
GOLD stage			
I	8(6.96%)	7(8.64%)	1(2.94%)
II	54(46.96%)	42(51.85%)	12(35.29%)
III	38(33.04%)	21(25.93%)	17(50%)
IV	15(13.04%)	11(13.58%)	4(11.76%)

Table-1: Demographic data of the COPD patients with and without PAD.

	GOLD Stage I	GOLD Stage II	GOLD Stage III	GOLD Stage IV
Participants (n)	8	54	38	15
Age (years)	60.6	77.82	69.4	72.03
Pre-bronchodilator				
FEV1 (%predicted)	87.8	62.5	40.5	24.3
FEV1/FVC	67.3	61.9	53.3	43.5
Post-bronchodilator				
FEV1 (L)	2.05	1.54	1.03	0.69
FEV1/FVC	67.0	62.1	53.7	43.4
PAD	1(12.5%)	12(22.22%)	17(44.74%)	4(26.67%)
Diabetes	2(25%)	14(25.93%)	10(26.32%)	6(40%)
Hypertension	3(37.5%)	38(70.37%)	16(42.11%)	9(60%)
Hyperlipidemia	0	15(27.78%)	9(23.68%)	5(33.33%)

Table-2: Lung function, age and co-morbidities between each COPD grade.

Study	Prevalence (%)	Diagnostic method	Enrolled subjects	Lung function	Hyperlipidemia	Diabetes	Hyper tension	Others
Castagna O et al.[18]	81.4	ABI<0.9	151 moderate-to-severe COPD patients, mean age: 6763.1 years	FEV1: 37 % FEV1/FVC: 47 %	68.1%	25.6%	74.8%	BMI: 22.9
Blum A et al.[19]	31	ABI<0.9	87 COPD patients, mean age: 69.8611.8 years	FEV1: 34%, with PAD FEV1:45 %, without PAD	Unavailable	43 %	72.4%	BMI: 29.3
Pecci R et al.[20]	36.8	ABI<0.9	9 246 COPD patients, mean age: 70.2611 years; men: 79%	FEV1: 46 %, with PAD FEV1:52 %, without PAD	68%	27.2%	57.3%	Obesity: 33%
Lin MS et al.[21]	8	ABI<0.9	427 COPD patients, mean age: 70.069 years; men: 97.7%	FEV1: 51 % FVC: 62 %	13.3%	18.3%	48.5%	BMI: 23
Our study	34	ABI<0.9	115 COPD patients, mean age: 68.02 years; men: 97.39%	FEV1: 51.2 % FEV1/FVC: 56.8 %	25.22%	27.83%	57.39%	**BMI: 23**

Table-3: Prevalence and risk factors for PAD in the COPD patients by ethnicity.

diabetes and obesity documented in our study were much lower than in previous reports. Previous studies have shown that decreased pulmonary function is independently associated with

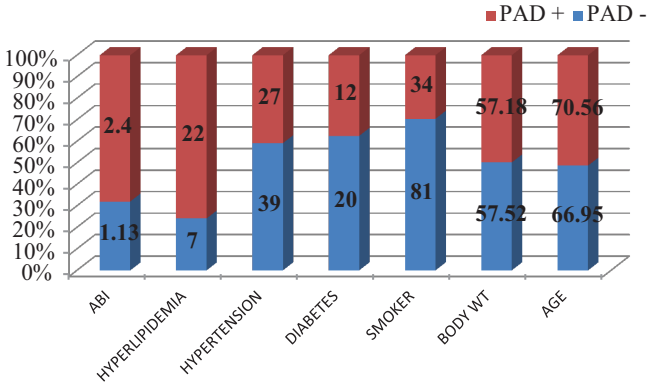

Figure-1: Demographic data and PAD.

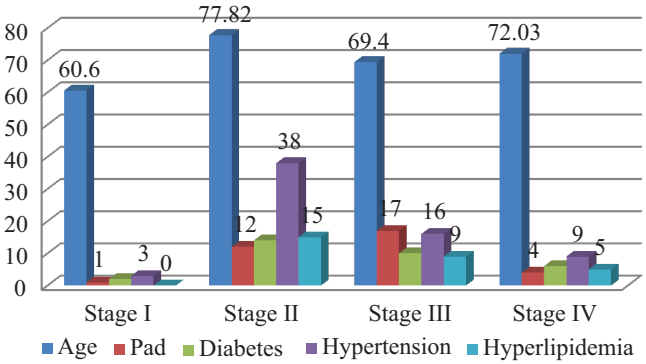

Figure-2: Comorbidities in stages of COPD.

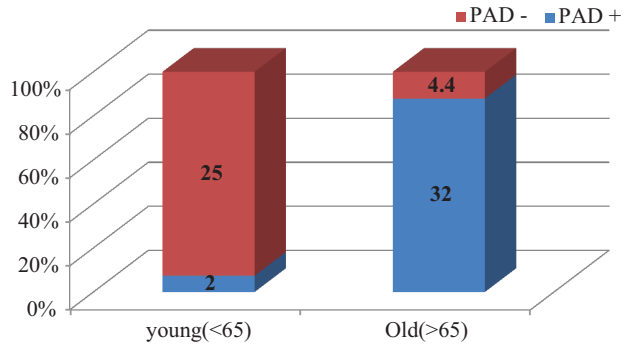

Figure-3: Age distribution of PAD.

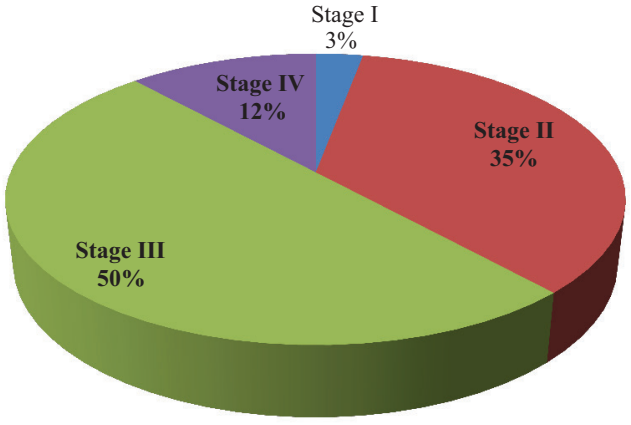

Figure-4: PAD in different stages of COPD.

subclinical atherosclerosis, arterial stiffness and coronary heart diseases.[27-31] Only few studies have investigated the relationship between ABI of less than 0.9 and lung function. Diminished lung function were documented in patients with PAD in two studies.[19-20] In the study from Spain, COPD severity was found to be positively associated with ABI<0.9, however, they did not consider cardiovascular factors such as diabetes, hyperlipidemia, and hypertension as co-variables for multivariate regression analysis.[18] No association between lung function and low ABI (<0.9) could be detected in our study, in either the younger or elderly COPD patients. Smoking might be the cause of the higher prevalence rate of PAD among COPD patients than in the general population in our study. Smoking is the most important modifiable risk factor for the development of PAD.[27] However, it is very difficult to stop smoking before they become ill, and it could be the reason why the prevalence of current smokers (67% vs. 45%) was higher among younger than elderly patients in our study. High BMI is associated with the development of PAD.[28-31] However, patients with COPD tend to be underweight and cachexic. The mechanism underlying this phenomenon involves systemic inflammation and impaired muscle oxidation.[32-34] In our study, only 6.96% of all enrolled COPD patients were obese, which is much lower than our previous data for the general population (overweight: 31.9% and obese: 11.2%).[35] Hence, COPD related cachexia might be a protective effect against the development of PAD. Limitation to this study is that the most of the enrolled patients were male (97.39%), thus, it is unknown whether the results can be applied to women.

CONCLUSION

The prevalence of PAD was 29.57% in COPD patients (1.74% in the younger patients and 27.83% in the elderly patients). Hyperlipidemia was the strongest independent factor associated with PAD, followed by old age and hypertension. Lung function was not associated with PAD in the patients with COPD.

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