Original Research Article

Acute Coronary Syndrome in Patients of Chronic Obstructive Pulmonary Disease and Its Relationship with Brachial Artery Flow Mediated Dilatation

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Abstract

Background: Both Chronic obstructive pulmonary disease (COPD) and Coronary artery disease (CAD) are closely related etiologically as well as pathophysiologically. Prevalence of both the diseases is rising to a great extent and have become one of the major causes of mortality and morbidity worldwide. **Objectives:**Present study was carried out in order to study prevalence of CAD among patients of COPD and identify high risk patients via BAFMD (Brachial artery flow mediated dilatation).**Materials and Methods:**Present cross sectional study was conducted in Medicine Department of a tertiary care hospital over a duration of one year on randomly selected cases of COPD, using pre-designed validated questionnaire. All cases underwent spirometry; cardiac evaluation via electrocardiography and echocardiography; and BAFMD was studied via Doppler USG.**Result:**The prevalence of CAD in COPD patients was found to be 24%. The prevalence of CAD correlated well with the severity of COPD i.e. 25% in GOLD staging III/IV as compared to 2.5% in GOLD staging I/II. Also, BAFMD was severely impaired in patients who had evidence of CAD. Mean value of BAFMD was significantly low in patients who had CAD as compared to those without CAD (5.37± 2.36% vs 9.20± 2.50%). **Conclusion:**We recommend the screening of patients of COPD via BAFMD and Echocardiography, for identifying high risk patients and early detection of cardiac involvement giving time for proper preventive and treatment measures for better outcomes.

Keywords: Chronic obstructive pulmonary disease (COPD), Coronary artery disease (CAD), Brachial artery flow mediated dilatation (BAFMD), LV Dysfunction

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitations that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases[1].COPD is the third most leading cause of death worldwide and affects >10 million people in the United States of America[2]. Among patients of COPD, cardiovascular events are responsible for majority of deaths accounting for 30% of all deaths[3]. However, population-based studies have suggested that regardless of smoking status, age or sex, a COPD diagnosis increases the risk of cardiovascular morbidity and mortality by approximately two to four fold[4].The prevalence of COPD amongst AMI (acute myocardial infarction) populations ranges from 7% to 30%, which is possibly even an underestimation due to underdiagnoses of COPD in general[5]. In UK registry of 1 million patients (among those, 29,870 had COPD), prevalence of acute myocardial infarction was found to be 3.5 times higher in patients with COPD[5].In summary, COPD patients appear to face a greater risk of dying from or being diagnosed with CVD. Cardiovascular function, therefore, must be evaluated as soon as possible before cardiac dysfunction becomes clinically overt. Coexistence of both the diseases is very common and has diagnostic, therapeutic as well as prognostic implications.No longer 'just a disease of the lungs', COPD has recently been described as the pulmonary component of systemic endothelial dysfunction in which a range of 'inflamm ageing' processes simultaneously affect multiple organs giving rise to a state of multimorbidity. Many researchers have already assessed the association among COPD, CVD and increased serum concentrations of inflammatory markers[5-7]. Endothelial dysfunction, characterized by a reduced bioavailability of endothelium- derived NO, is an important step in the progression of atherosclerosis. Endothelial function can be assessed noninvasively and invasively.Noninvasively endothelial function can be assessed in the forearm circulation by brachial artery flow mediated dilatation (BAFMD) ultrasonographically. Typically the change in vessel diameter detected by these invasive and noninvasive approaches is more than 10%. In individuals with frank atherosclerosis or risk factors for atherosclerosis (especially Hypertension, diabetes mellitus, COPD), such studies can detect endothelial dysfunction as defined by a smaller change in diameter[8,9].Hence, in this study, BAFMD is also included as an indicator for endothelial dysfunction as endothelial dysfunction is an early phenomenon in atherosclerosis and often precedes structural changes and clinical manifestations. This non-invasive tool can be used as an early marker for determining increased cardiovascular risk and plan further prevention of CAD and its complications.

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With the above background, the present research work was conducted in order to recognize the patients at higher risk of CAD via Echocardiography and BAFMD and early detection of cardiac involvement to permit time for proper intervention before the patient develop decompensated cardiac disease or other complications.

Material and Methods

Present study was a descriptive cross-sectional study for a duration of one year (Jul 2019 to June 2020) conducted on randomly selected cases of COPD, who attended Department of Medicine in Gajraraja Medical College and Jayarogya Group of Hospitals. A total of 100 cases of COPD were enrolled in the study.

Inclusion criteria- All confirmed and stable cases of COPD (including known cases as well as newly diagnosed cases) of age > 40 years

Exclusion criteria- Patients with age<40 yrs; acute exacerbation of COPD; known cases of IHD, Hypertension and Diabetes Mellitus; and patients who refused to give informed written consent were excluded from the study.

A predesigned validated questionnaire was prepared based on the review of literature, and was used for the data collection from the study participants. Study protocol was approved by the ethical and scientific committee of the institution. All the participants were informed about the study procedure and written consent was obtained. All the subjects in the study group underwent detailed history, thorough clinical examination and investigations as listed in the proforma. Patients were classified as per severity of COPD (GOLD staging) via spirometry. Cardiac evaluation of all patients was done by 2D-echocardiography with HR Echo Doppler machine with multifrequency linear probe. CAD was diagnosed on the basis of findings accumulated via ECG and ECHO. After cardiac evaluation, patients were subjected to BAFMD calculation using HR Doppler- USG machine with linear array transducer.

The brachial artery was identified above the elbow at 5 cm proximal to the transient bifurcation by using a high quality ultrasound system. Baseline brachial artery diameter and flow velocity were recorded. After baseline imaging, the artery is then occluded completely using a sphygnomanometer cuff, tied around the right arm and inflated to at least 50 mm Hg above systolic blood pressure (SBP), for 5 minutes. After the cuff was deflated, brachial artery diameter is recorded again after 1 min of cuff deflation.

The relative change in mean arterial diameter was calculated as:

% Dilation = [Maximum diameter – Baseline diameter] × 100 / Baseline diameter

Data management and analysis was done using Microsoft Excel. The frequency distribution and graphs were generated for the data. Statistical analysis was done by using IBM-SPSS version 20 software. The results were tested at 5% level of significance and a p-value of less than 0.05 was considered significant.

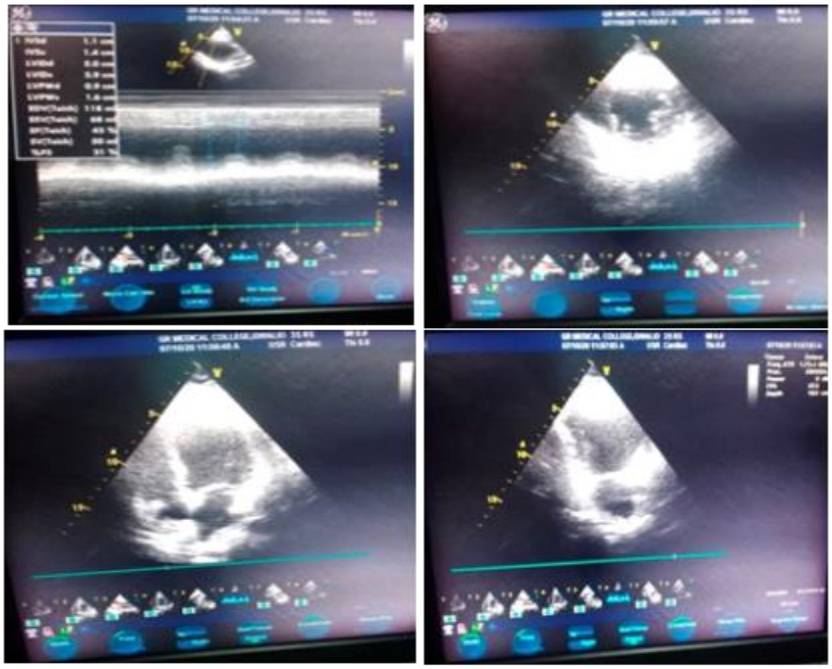

Fig 1: Echocardiographic images of ischemic heart disease – Hypokinetic LAD territory, LVEF=40%

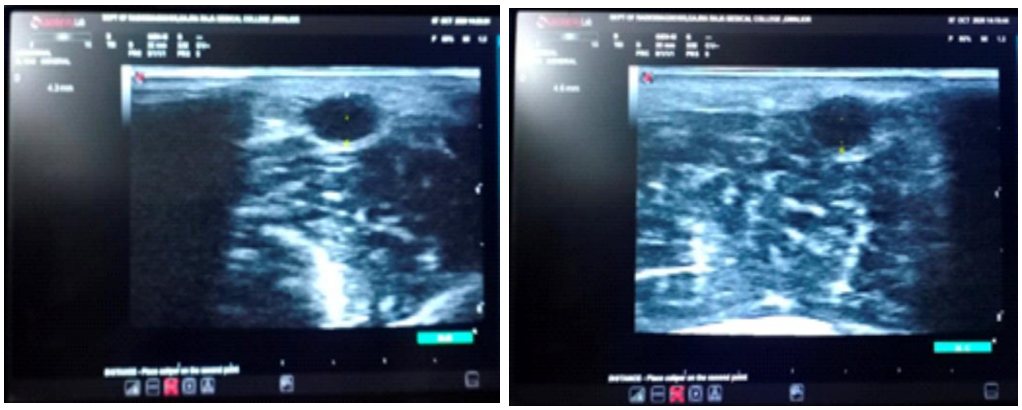

Fig 2: Brachial artery diameter a) before applying sphygnomanometer cuff i.e. Baseline diameter; and b) after cuff release i.e. brachial artery dilatation

Observations and Results

The mean age of the studied population was 61.18 ± 9.59 years and ranged from 45-86 years. Males accounted for 80%, with a male to female ratio of 4:1. The mean duration of COPD in our study population was 9.21± 6.04 years. Out of 100 patients, 12% belonged to GOLD staging I, 28% were in GOLD staging II, 33% in GOLD staging III and 27% in GOLD staging IV.

ECG was found to be normal in 36 patients while 42 patients had normal echocardiography. Most common ECG abnormality was P-pulmonale (31%) and most common ECHO abnormality was Diastotic dysfunction (43%). Echocardiographic evidence of CAD like RWMA and reduced LVEF were present in 24 patients. The mean value of BAFMD was 8.28± 2.96%. Out of studied 100 COPD patients, only 24 had normal BAFMD (i.e. >10%) while 76 had reduced BAFMD.

Table 1:Parameters of study population (n=100)

		Percentage
Age (yrs)	41-50	20
	51-60	29
	61-70	37
	>70	14
Gender	Male	80
	Female	20
Duration	< 5	28
	5-10	41
	>15	31
GOLD staging	I	12
	II	28
	III	33
	IV	27
Evidence of CAD	Present	24
	Absent	76
BAFMD	>10 (normal)	24
	7.5-10	43
	< 7.5	33
LVEF	Preserved	82
	Reduced	18

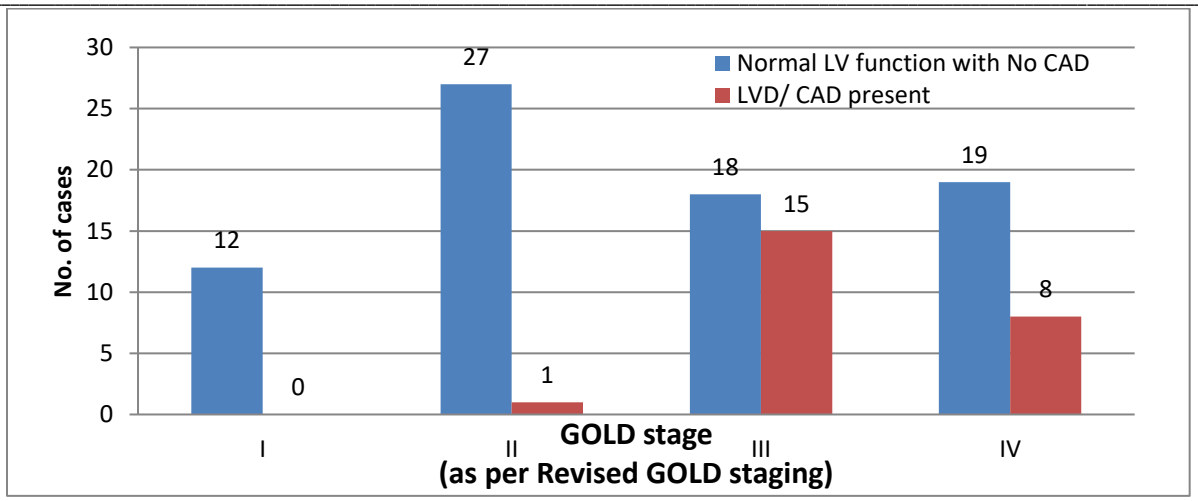

Fig 3: Correlation of CAD/LVD with the severity of COPD (by Gold staging)

Table 2: BAFMD in COPD

		Total	Mean Value (%)	>10%	<10%	P-value
Duration	<5	28	9.86 ± 2.07	13	15	0.0431
	5-10	41	7.94 ± 3.13	7	34	
	>15	31	7.40 ± 2.85	4	27	
Severity	I	12	10.56 ± 1.55	5 (41.6)	7 (58.4)	0.015975
	II	28	9.70 ± 2.57	11 (39.3)	17 (60.7)	
	III	33	7.5 ± 2.59	6 (18.2)	27 (81.8)	
	IV	27	6.55 ± 2.64	2 (7.4)	25 (92.6)	

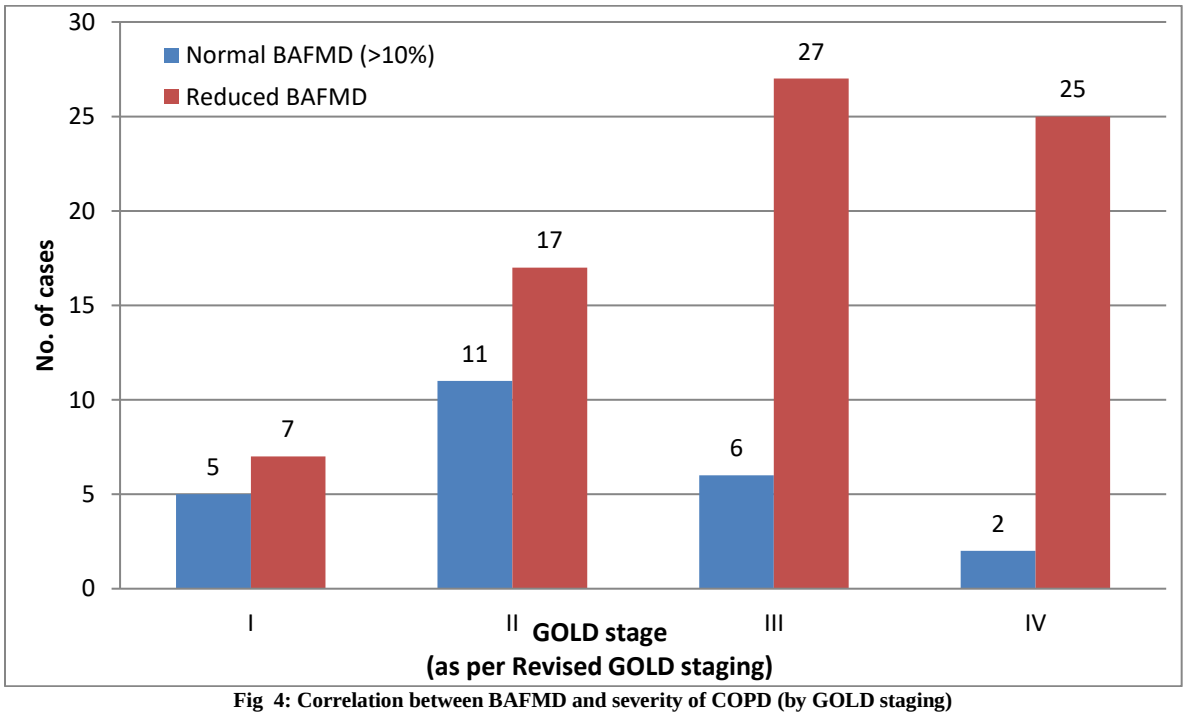

Fig 4: Correlation between BAFMD and severity of COPD (by GOLD staging)

Table 3: Correlation between CAD and BAFMD

	Total no. of patients	Mean BAFMD (%)	Normal BAFMD (>10%)	Reduced BAFMD (7.5-10%)	Reduced BAFMD (<7.5%)
No evidence of CAD	76	9.20 ± 2.50	23 (30%)	40 (52.6%)	13 (17.2%)
CAD present	24	5.37 ± 2.36	1 (4.2%)	3 (12.5%)	20 (83.3%)
Total	100		24	43	33
Chi-square test	36.251				
p-value	<0.0001				

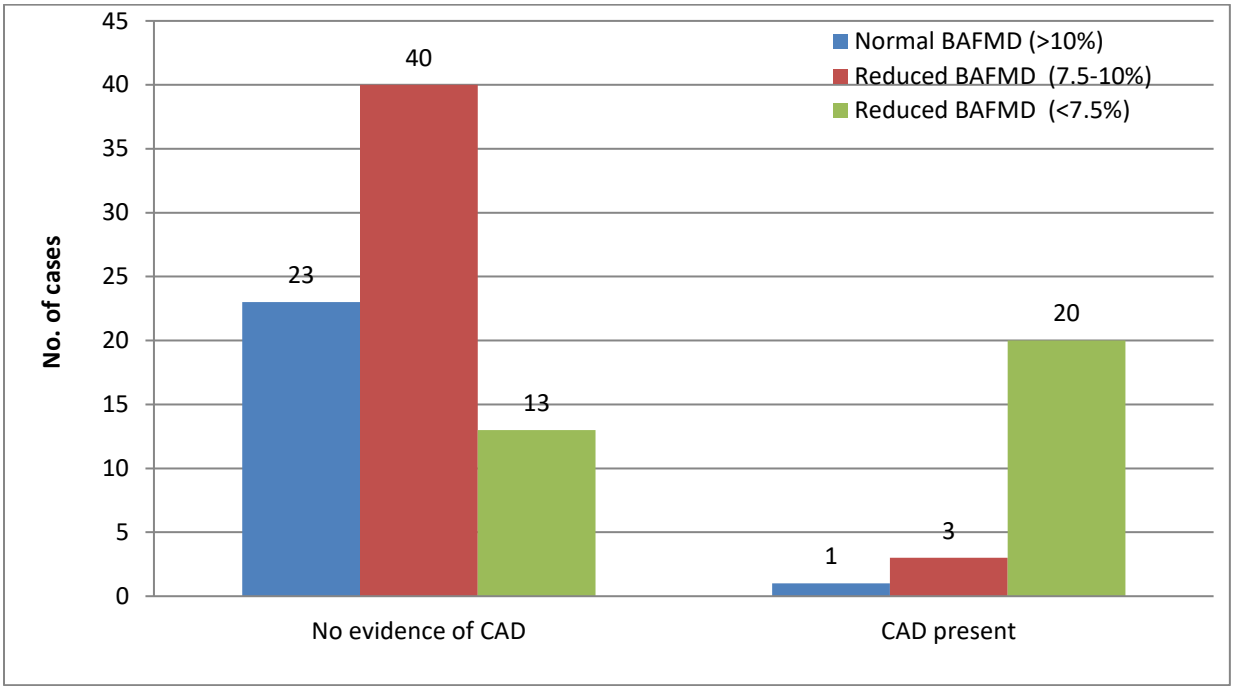

Fig 5:Correlation between CAD and BAFMD

Table 4: Association between CAD/ LVD and BAFMD and their distribution according to GOLD staging of COPD

GOLD stage(as per Revised GOLD staging)	Total no. of patients	LVD/ CAD		Reduced BAFMD<10%	
		n	Percentage(%)	n	Percentage(%)
Stage I	12	0	0	7	58.4
Stage II	28	1	3.57	17	60.7
Stage III	33	15	45.45	27	81.8
Stage IV	27	8	29.63	25	92.6
Total	100	24	24	76	76
Chi square test	16.7139			10.328	
p-value	<0.001			0.015975	

Discussion

According to a systematic review from major studies in India, the prevalence of COPD seems to range between 6.5% and 7.7% in rural and upto 9.9% in urban India.[10] Among the patients of COPD, cardiovascular diseases are a major cause of concern due to high risk of mortality and morbidity. Many studies have shown that patients with COPD are at two to three times greater risk for cardiovascular mortality accounting for 50% of total deaths[11].In the present study, we found that the prevalence of CAD in COPD was 24% (significantly higher than the general population). Also, RWMA was found to be significantly higher in severe cases of COPD i.e. GOLD staging III/IV as compared to mild-moderate cases i.e. GOLD staging I/II (25% vs 2.5%). Poor LV systolic function (reduced LVEF) was found to be significantly higher in severe cases of COPD i.e. GOLD staging III/IV as compared to mild-moderate cases i.e. GOLD staging I/II (28.33% vs 2.5%).The prevalence of CAD correlated well with the duration of COPD i.e. 0% in patients with <5 years duration, 29.27% in 6-10 years and as high as 38.71% in patients with duration >10 years (Chi-square=10.7579, p=0.0046). This shows that the risk for CAD/ACS increases significantly as the duration of COPD increases.In our study it was also found that the prevalence of CAD correlated well with the severity of COPD- 0% in GOLD staging I, 3.57% in GOLD staging II, 45.45% in GOLD staging III and 29.63% in GOLD staging IV (Chi-square = 16.7139, p<0.001). This shows that the risk for CAD/ACS increases significantly with the increasing severity of COPD. The slight dip in the prevalence of CAD from 45.45% in GOLD III to 29.63% in GOLD IV may be due to increased mortality of concomitant CAD in very severe cases of COPD, which causes under detection of such cases.

Similar findings were observed in the following studies-

In the study done by Harishchandra et al[12], prevalence of CAD was found to be 22.3% (comparable to 24% in our study). He also found that the prevalence of CAD/ACS increases significantly with the severity of COPD i.e. 0% in GOLD staging I, 21.4% in GOLD staging II, 35.7% in GOLD staging III and 54.5% in GOLD staging IV. Donaldson et al[13] showed that the risk of acute vascular events appear to be particularly high during exacerbation of COPD. After analyzing data from 25,857 COPD patients over a 2-year period, the risk of MI was found to increase by 2.3 times, higher during 1-5 days after exacerbation. Brekke et al[14]observed that 27.7% of patients who were hospitalized because of COPD showed ECG changes suggestive of MI/ACS. Jeremy et al[15] studied the cardiac disease in patients of COPD and found out that the prevalence of CAD was 33.6%, which was significantly higher as compared to matched cohort without COPD.

The mean value of BAFMD was 8.28± 2.96%. Out of studied 100 COPD patients, only 24 had normal BAFMD (i.e. >10%), while out of remaining 76- 43 had BAFMD between 7.5-10% and 33 had BAFMD <7.5%.In our study, it was found that the value of BAFMD decreases significantly as the duration of COPD increases, mean value of BAFMD being 9.86±2.07% in patients with duration <5 years vs 7.94±3.13% in 6-10 years vs 7.40±2.85 in patients with >10 years duration of COPD. Also, the prevalence of abnormal BAFMD increases with the duration of COPD i.e. 53.6% in <5 years vs 87.1% in >10 years (chi-square= 10.8934, p= 0.00431).In our study, it was also found that the value of BAFMD decreases significantly with the increasing severity of COPD, mean value of BAFMD being 10.56±1.55% in GOLD stage I vs 9.70±2.57% in GOLD stage II vs 7.5±2.59% in GOLD stage III vs 6.55±2.64% in GOLD stage IV. Also, the prevalence of abnormal BAFMD increases with the severity of COPD i.e. 58.4% in GOLD stage I to as high as 92.6% in GOLD stage IV (chi-square= 10.328, p= 0.015975).Out of 24 patients who had CAD, only 1 had normal BAFMD (>10%), while remaining 23 had abnormal BAFMD (<10%), of which 83.3% patients had significantly reduced FMD i.e.<7.5% (chi-square= 36.251, p<0.0001). BAFMD was severely impaired in patients who had evidence of CAD. Mean value of BAFMD was found to be significantly low in patients who had CAD as compared to those without CAD (5.37± 2.36% vs 9.20± 2.50%).

Sancheti et al[16] found that patients with reduced BAFMD had increased prevalence of IHD and FMD was abnormal (<10%) for 100% cases with CAD (as found in Coronary angiogram). They also found that significantly higher proportion of cases with positive stress test had less %FMD and vice-versa. Chouhan et al[17]found that BAFMD was abnormal in 80% of cases of CAD. They also found that the endothelial function as assessed by FMD was significantly impaired in patients of CAD as compared to control group (6.8±5.48% vs 13.08±3.40%, with a p-value< 0.0001). Broxterman et al[18]observed that FMD was significantly lower in patients with CAD as compared to controls (5.8±9.8% vs 11.8±4.6%, with a p-value< 0.001). Fahrettin et al[19] observed that BAFMD was found to be significantly reduced in patients of CAD as compared to controls (5.03±4.24% vs 7.47±2.94%, p=0.02). Pellegrino et al[20] found that FMD significantly correlated with the impairment of coronary flow reserve (r=0.56, p<0.005). Also, the FMD was significantly lower in cases as compared to control (6.9±2.1% vs 11.4±3.4%). Gokce et al[21]in a study of 199 patients with established atherosclerotic disease suggested that BAFMD independently predicts long term cardiovascular events. Above finding was supported by evidences from various studies by- Huang et al [22](267 patients) and Brevetti et al[23] (131 patients) in cases of established atherosclerotic disease, Chan et al[24](152 patients of CAD), Hu et al[25] (279 patients admitted for acute chest pain). In a study conducted by Wu et al[26], healthy controls had significantly higher FMD values (18.88±2.31%) than patients who had risk factors but no CAD (7.85±1.66%), than those with CAD (5.91±1.07%). They also concluded that FMD has a significant association with scintigraphic CAD in his cross-sectional study with a reasonable sensitivity and specificity. A significant correlation was found between the number of thallium defects and degree of FMD impairment (r = –0.40, P < .01).

Conclusion

COPD is a major risk factor for CAD and the presence of systemic inflammation in COPD leading to endothelial dysfunction mainly explains this association. In COPD patients, we should unmask the presence of silent or subclinical CAD and target it before the patient lands in cardiac decompensation. In these patients, we should always keep in mind the possibility of CAD especially in presence of exertional dyspnea and ECG findings. We should try to rule out ACS or LVD in patients of COPD, as only a combined approach of management will help in achieving an effective outcome.BAFMD may provide clinically meaningful insight into coronary artery function and may enhance early detection of coronary artery dysfunction that precedes or underlies most of the CAD. BAFMD measurement by Color Doppler ultrasound is a very simple, cheap, non-invasive, easily available, reproducible and convenient method. So it can be used as a screening tool for atherosclerosis and hence useful in risk stratification of CAD especially in patients of COPD.

This study helps us to identify the individuals at risk of increased morbidity and mortality, warranting close monitoring and aggressive treatment to prevent/ delay complications. The overall survival and quality of life can be improved by taking this into consideration.

Limitations of the Study

- Sample size was relatively small. Only 100 cases were included.
- The sample distribution based on severity of COPD was unequal.

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