ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CAROTID INTIMAL MEDIAL THICKNESS IN PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

General Medicine

Dr Nischitha. M.C* Senior Resident, Dept of Medicine, GMC, Chandrapur *Corresponding Author

Quadri Syeda Uzma Abdullah Senior Resident, Dept od Medicine, K B Bhabha Hospital Bandra Mumbai

Deepti P Deshmukh Professor and Head, Dept. of Medicine, IGGMC, Nagpur

ABSTRACT

Background: Pulmonary hypertension, right ventricular dysfunction, dysarrhythmia and ischemic coronary disease are known consequences of Chronic Obstructive Pulmonary Disease (COPD) progression. CIMT indirectly predicts the condition of coronary vessels also. Hence CIMT serves as biomarker of subclinical atherosclerosis. CIMT is measured by B mode ultrasonography Thus, patients with COPD may benefit from a more meticulous screening of CIMT by B Mode ultrasonography which helps in assessing the CV risk in an early stage of the lung disease and developing specific CV prevention strategies. **Methodology:** The present cross-sectional study was conducted on 100 COPD patients. Detailed history along with structured clinical and systemic examination were performed. Require investigations (X-ray / HRCT and blood investigations) performed. FEV1 was performed 15 min after administration of four doses of salbutamol sulfate (100 µg) and FVC was measured by spirometer in all cases and controls. Initial confirmation of diagnosis of COPD by post bronchodilator FEV1 <0.7 was made. Grading of COPD by GOLD guidelines was calculated. Appropriate statistical tests were used for analysis. **Results:** In majority (64(64.00%)) of patients, severity of airflow obstruction by GOLD classification was grade 3(30-49%). Majority of cases (59%) were having mMRC score of >/=2. Majority (44(44.00%)) of patients, GOLD class was B. In 34(34.00%) patients, BODE stage was 3 followed by stage 2 (30(30.00%)). In FEV1, majority (64%) of cases were having FEV1of 36-49%. Majority of cases (47%) were having 6m walk distance capacity of 150-249mt. Proportion of patients with increased {>=0.8} CIMT was significantly higher in cases as compared to controls. (Increased {>=0.8}:- 58% vs 24% respectively). (p value <0.0001). It was observed that proportion of patients with normal {<0.8} CIMT in cases was significantly higher in grade 1(>80%) (85.71%) as compared to grade 2(50-79%) (31.82%), grade 3(30-49%) (43.75%), grade 4(<30%)(14.29%). Proportion of patients with increased {>=0.8} carotid intima-media thickness(mm) in cases was significantly higher in grade 4(<30%) (85.71%) {OR (95% CI). Association between higher BMI and with increased {>=0.8} CIMT (mm) was significant. Association between lower FEV1 and with increased {>=0.8} CIMT (mm) was not significant. Lower 6m walk test (metres) and higher mMRC were significantly associated with increased {>=0.8} CIMT. **Conclusions:** COPD patients with higher stages of GOLD stages had significantly elevated carotid intima media thickness and thus depicts the severity of the disease. COPD patients with high BODE index had significantly elevated Carotid intima media thickness and thus they are more prone for cardiovascular morbidity and mortality. There should be large long-term interventional trials to investigate whether disease treatment approaches may modify the CV risk in COPD patients.

KEYWORDS

Chronic Obstructive Pulmonary Disease, carotid intimal medial thickness, GOLD Criteria, BODE criteria, FEV1, mMRC.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is currently the third leading cause of death worldwide and 90% of these deaths mostly occur in low- and middle-income countries (LMICs), even though most data are existed from high income countries. Many people suffer from this disease for years and die prematurely from it or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population. [1]

The main risk factor for COPD is tobacco smoking but other environmental exposures. Also host factors include genetic abnormalities, abnormal lung development and accelerated aging. Concomitant chronic diseases occur frequently in COPD patients [2]. Cardiovascular diseases when coexisted with COPD will lead to worst prognosis than either condition alone. In fact, mortality due to cardiac disease in patients with moderate COPD is higher than mortality attributed due to respiratory failure [3]. Pulmonary hypertension, right ventricular dysfunction, dysarrhythmia and ischemic coronary disease are known consequences of COPD progression [4].

COPD involves chronic inflammation, oxidation, endothelial dysfunction and smooth muscle proliferation which ultimately causes atherosclerotic changes of the vessel wall [5]. These atherosclerotic changes can be easily picked up in initial stages by examining the carotid intimal wall thickness. CIMT indirectly predicts the condition of coronary vessels also. Hence CIMT serves as biomarker of subclinical atherosclerosis [6]. CIMT is measured by B mode ultrasonography which is safe, cost effective, time saving, painless imaging method which is free of radiation exposure allows detailed study of carotid vessel wall changes and assess the need of medical or surgical management hence predicting the cardiovascular mortality and morbidity. According to American Heart Association (AHA) CIMT measurement is advocated as biomarker of cardiovascular outcome under class IIa/ level of evidence B [7].

COPD was significantly associated with subclinical atherosclerosis and in turn, with an increased CV risk. The risk can be correlated with severity of COPD. Thus, patients with COPD may benefit from a more meticulous screening of CIMT by B Mode ultrasonography which helps in assessing the CV risk in an early stage of the lung disease and developing specific CV prevention strategies.

AIMS AND OBJECTIVES

1. To Study Association Of Cimt With Severity Of Airflow Obstruction In Cases Of Copd As Assessed By Gold Criteria.
2. To Study Association Of Cimt With Prognosis In Cases Of Copd As Assessed By Bode Index.

MATERIALS AND METHODS

The present cross-sectional observational study was conducted at Indira Gandhi Government Medical college, Nagpur between NOV 2019 - DEC 2021. Study was started after ethical committee approval. Proper written informed consent was taken from all the cases and controls after explaining the intentions of conducting examination on them. 100 consecutive COPD patients with previously diagnosed case of COPD in steady state [no exacerbations and no medication change in the last 6 weeks], aged group between 40-80 years, attending Medicine and chest TB OPD and patients admitted to Medicine wards and 50 healthy controls who were non smokers, without any airflow obstruction as confirmed by history, examination and pulmonary function tests, were enrolled for comparison.

A detailed history along with structured clinical and systemic examination were performed. Require investigations (X-ray / HRCT and blood investigations) performed. FEV1 was performed 15 min after administration of four doses of salbutamol sulfate (100 µg) and FVC was measured by spirometer in all cases and controls. Initial

confirmation of diagnosis of COPD by post bronchodilator FEV1 <0.7 was made. Grading of COPD by GOLD guidelines was calculated. Symptoms and risk of exacerbation were assessed by ABCD assessment tool with the help of CAT assessment score, mMRC dyspnoea grading system, number of hospitalization & exacerbation needed per year. BODE index was calculated using data regarding BMI, severity of airway obstruction, mMRC dyspnoea grading system and exercise intolerance by 6-minute walk test. Cases and controls were then sent to radiology department for carotid Doppler assessment.

Statistical Analysis

Analysis was done with the use of SPSS software, ver 21.0. The presentation of the Categorical variables was done in the form of number and percentage (%). The quantitative data were presented as the means ± SD. The comparison was done using Independent t test. The comparison of qualitative variables done using Chi-Square test. Odds ratio with 95% CI was calculated for carotid intima-media thickness (mm) in cases to assess various parameters. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

The study was conducted from November 2019 to December 2021 on patients attending Medicine & Chest TB OPD /Indoor patients. 100 previously diagnosed cases of COPD in steady state were included as cases and 50 non-smokers without any airflow obstruction were included as controls. Spirometry parameters were assessed and Carotid Intimal Medial thickness was measured and results are as follows.

Table 1:- Distribution Cases And Controls According To Age (years) And Gender

Patient Variables		Cases (n=100)	Controls (n=50)	Total	P value
Age (years)	41-50	10 (10%)	4 (8%)	14 (9.33%)	0.928†
	61-70	36 (36%)	21 (42%)	57 (38%)	
	71-80	14 (14%)	6 (12%)	20 (13.33%)	
	Mean ± SD	60.8 ± 8.01	60.46 ± 7.6	60.69 ± 7.85	0.804*
	Median	60 (54.75-67.25)	62 (53.25-66)	61 (54-67)	
	Range	44-78	47-75	44-78	
Gender	Female	8 (8%)	6 (12%)	14 (9.33%)	0.427‡
	Male	92 (92%)	44 (88%)	136 (90.67%)	
Total		100 (100%)	50 (100%)	150 (100%)	

†Fisher's exact test*, Independent t test, ‡ Chi Square test

It was observed that distribution of age(years) was comparable between cases and controls. (41-50 years: 10% vs 8% respectively, 51-60 years: 40% vs 38% respectively, 61-70 years: - 36% vs 42% respectively, 71-80 years: 14% vs 12% respectively) (p value=0.928). Mean ± SD of age(years) in cases was 60.8 ± 8.01 and controls was 60.46 ± 7.6 with no significant difference between them. (p value=0.804). We found that distribution of gender was comparable between cases and controls. (Female: - 8% vs 12% respectively, Male: - 92% vs 88% respectively) (p value=0.427). It is shown in table 1.

Table 2: - Distribution Cases According To Presenting Complaints And Severity Of Airflow Obstruction By Gold Classification

Clinical Characteristics		Frequency (n=100)	Percentage
Complaints	Chest pain	3	3.00%
	Cough	28	28.00%
	Dyspnoea	45	45.00%
	Sputum	24	24.00%
Severity of airflow obstruction by GOLD classification	Grade 1(>80%)	7	7.00%
	Grade 2(50-79%)	22	22.00%
	Grade 3(30-49%)	64	64.00%
	Grade 4(<30%)	7	7.00%
Total		100	100.00%

Distribution Of Clinical Manifestations And Severity Of Airflow Obstruction In Cases

It was observed that in majority (45(45.00%)) of patients, dyspnoea was present followed by cough (28(28.00%)) and sputum (24(24.00%)). Chest pain was seen in only 3 out of 100 patients (3.00%). In majority (64(64.00%)) of patients, severity of airflow obstruction by GOLD classification was grade 3(30-49%) followed by grade 2(50-79%) (22(22.00%)). Severity of airflow obstruction by GOLD classification was grade 1(>80%) and grade 4(<30%) in only 7 out of 100 patients (7.00%) each. It is shown in table 2.

Table 3: Assessment Of Gold Variables In COPD Cases

GOLD class variables		COPD Cases (N=100)	Percentage (%)	Mean+/-SD
mMRC	<2	41	41	1.75+/-0.74
	>/=2	59	59	
No. Of Hospitalization	0	52	52	0.68+/-0.83
	>/=1	48	48	
No. Of Exacerbation	<2	34	34	1.88+/-0.83
	>/=2	66	66	
CAT Score	<10	32	32	14.43+/-5.61
	>/=10	68	68	

Out of 100 cases, majority of cases(59%) were having mMRC score of >/=2 and only 41% of cases were having mMRC score of <2 with mean value of 1.75+/-0.74. 52% of cases were never hospitalized in the present year whereas only 48% of cases were hospitalized for >/=1 in the present year with mean value of 0.68+/-0.83. Majority of cases(66%) were having exacerbation of >/=2 in a year whereas only 34% of cases were having exacerbation of >/=2 in a year with mean value of 1.88+/-0.83. Majority of cases(68%) were having CAT score of >/=10 whereas only 32% of the cases were having CAT score of <10 with mean value of 14.43+/-5.61. The table 3 shows above findings in detail.

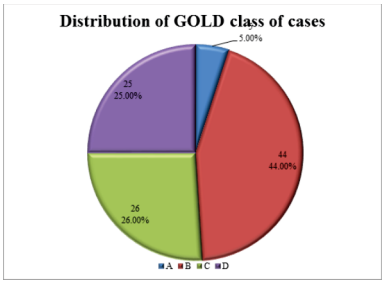

Figure 1. Distribution Of COPD Cases To Assess Symptoms/risk Of Exacerbation By Gold Class:

It was observed that in majority (44(44.00%)) of patients, GOLD class was B followed by C (26(26.00%)) and D (25(25.00%)). GOLD class was A in only 5 out of 100 patients (5.00%). It is shown in figure 1.

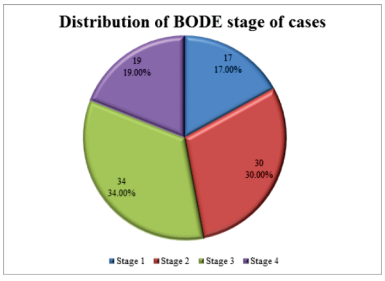

Figure 2: Distribution Of COPD Cases To Assess Prognosis By BODE Index

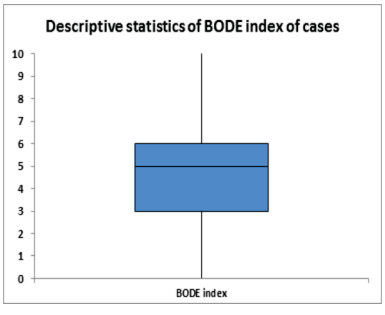

Figure 3: Descriptive Statistics Of Distribution Of COPD Cases To Assess Prognosis By BODE Index

In 34(34.00%) patients, BODE stage was 3 followed by stage 2 (30(30.00%)) and stage 4 (19(19.00%)). BODE stage was 1 in only 17 out of 100 patients (17.00%). Mean value of BODE index of cases was 4.52 ± 2.1 with median (25th-75th percentile) of 5(3-6). It is shown in table 16, figure 2 and 3.

Table 4: Assessment Of Individual BODE Index Variables In COPD Cases

BODE Variables		Total cases N=100(%)	Mean+/-SD
BMI	</=21	21(21%)	25.54±4.22
	>21	79(79%)	
FEV1(%)	</=35	9 (9%)	48.7±13.01
	36-49	64 (64%)	
	50-64	15 (15%)	
	>/=65	12 (12%)	
mMRC Score	</=2	41(41%)	1.75±0.74
	>2	59(59%)	
6m walk distance(mt)	</=149	20 (20%)	227.09±77.58
	150 to 249	47 (47%)	
	250 to 349	25 (25%)	
	>/=350	8 (8%)	

Out of 100 COPD cases, 21% people were having BMI of </=21 and 79% people were having BMI of 21 with Mean value of 25.54+/-4.22. In FEV1, majority(64%) of cases were having FEV1of 36-49%, while 15% of cases were having FEV1 of 50-64%, 12% of cases had >/= 65% and minority of cases(9%) had FEV1 of </= 35% with Mean value of 48.7+/-13.01. majority of cases(59%) were having mMRC score of </=2 whereas 41% of cases were having mMRC score of >2 with Mean value of 1.75+/-0.74. majority of cases(47%) were having 6m walk distance capacity of 150-249mt, whereas 25% of cases were having capacity of 250-349mt and 20% of cases were having a capacity of </= 149mt. Only minority of cases(8%) were having 6m walk distance capacity of >/=350mt. The mean value was found to be 227.09+/-77.58mt.

Proportion of patients with increased{>=0.8} carotid intima-media thickness(mm) was significantly higher in cases as compared to controls. (Increased{>=0.8}:- 58% vs 24% respectively). (p value <0.0001). Mean ± SD of carotid intima-media thickness(mm) in cases was 0.84 ± 0.23 which was significantly higher as compared to controls (0.71 ± 0.14). (p value <.0001) It is shown in table 5.

Comparison Of Carotid Intima-media Thickness(mm) Between Cases And Controls

It was observed that proportion of patients with normal {<0.8} carotid intima-media thickness(mm) in cases was significantly higher in grade 1(>80%) (85.71%) as compared to grade 2(50-79%) (31.82%), grade 3(30-49%)(43.75%), grade 4(<30%)(14.29%). Proportion of patients with increased {>=0.8} carotid intima-media thickness(mm) in cases was significantly higher in grade 4(<30%) (85.71%) {OR (95% CI): -18.78(1.28 to 275.01)}, grade 2 (50-79%) (68.18%) {OR(95% CI):-8.96 (1.16 to 69.06)}, grade 3 (30-49%) (56.25%) {OR (95% CI):-5.55 (0.86 to 35.90)}(p value=0.0007).

Association between higher BMI and with increased{>=0.8} CIMT (mm) was significant. Association between lower FEV1 and with increased{>=0.8} CIMT (mm) was not significant. Lower 6m walk test (metres) and higher mMRC were significantly associated with increased{>=0.8} CIMT (mm). (table 6).

Table 6: Association Of Severity Of Airflow Obstruction By Gold Classification, BODE Stage And Various Risk Factors With Cimt (mm) In COPD Cases

Variables		Normal {<0.8} (n=42)	Increased {>=0.8} (n=58)	Total	P value	Odds ratio (95% CI)
Severity of airflow obstruction (GOLD classification)	Grade 1	6 (85.71%)	1 (14.29%)	7 (100%)	0. 034†	1
	Grade 2	7 (31.82%)	15 (68.18%)	22 (100%)		8.96(1.16 to 69.06)
	Grade 3	28 43.75%)	36 (56.25%)	64 (100%)		5.55(0.86 to 35.90)
	Grade 4	1 (14.29%)	6 (85.71%)	7 (100%)		18.78(1.28 to 275.01)
BODE stage	Stage 1	11 (64.71%)	6 (35.29%)	17 (100%)	0. 0007 ‡	1
	Stage 2	17 (56.67%)	13 (43.33%)	30 (100%)		1.36 (0.40 to 4.63)
	Stage 3	13 (38.24%)	21 (61.76%)	34 (100%)		2.82 (0.85 to 9.36)
	Stage 4	1 (5.26%)	18 (94.74%)	19 (100%)		21.82(2.98 to 159.95)
Body Mass Index (kg/m²)	<=21	3 (14.29%)	18 (85.71%)	21 (100%)	0. 005†	1
	>21	39 (49.37%)	40 (50.63%)	79 (100%)		0.19(0.06 to 0.67)
FEV1 (%)	<=35	1 (11.11%)	8 (88.89%)	9(100 %)	0. 074†	1
	36-49	28 (43.75%)	36 (56.25%)	64 (100%)		0.23(0.04 to 1.41)
	50-64	5 (33.33%)	10 (66.67%)	15 (100%)		0.34(0.04 to 2.92)
	>=65	8 (66.67%)	4 (33.33%)	12 (100%)		0.09(0.01 to 0.83)
6m walk test (metres)	<=149	2 (10%)	18(90%)	20 (100%)	0. 007†	1
	150 to 249	23 (48.94%)	24 (51.06%)	47 (100%)		0.14(0.03 to 0.61)
	250 to 349	12 (48%)	13 (52%)	25 (100%)		0.15(0.03 to 0.71)
	>=350	5 (62.50%)	3 (37.50%)	8 (100%)		0.09(0.01 to 0.62)
mMRC	<2	25 (60.98%)	16 (39.02%)	41 (100%)	0. 001‡	1
	>=2	17 (28.81%)	42 (71.19%)	59 (100%)		3.75(1.62 to 8.71)
Total		42 (42%)	58 (58%)	100 (100%)	-	

† Fisher's exact test, ‡ Chi square test

DISCUSSION

COPD is a multicomponent disease with inflammation at its core leading to mortality. Systemic inflammation leads to progression of atherosclerosis and thus increases the risk of coronary artery disease, stroke and peripheral vascular diseases. CIMT is the proven measures to estimate the carotid atherosclerosis and thereby to predict the risk for coronary artery atherosclerosis and other cardiovascular diseases. Our study tries to find the association of CIMT with GOLD staging system and BODE scoring system thereby assessing the severity and prognosis of COPD respectively.

Distribution Of Age And Gender

Out of 100 patients studied 92% of patients were male and only 8% of patients were female. In the present study, it was found that most of the patients belonged to the age group 51-60 years followed by 61-70 years. The mean age of patients was 60.8 years. Lara J. Akinbami et al. studies suggested COPD prevalence was highest among women aged 65–74 (10.4%) & 75–84 (9.7%) and among men aged 75–84 (11.2%) [8]. C. Raherison et al. concluded 62% COPD patients over 40 yrs of age, with high prevalence between 40 and 64 yrs. The prevalence of COPD increases with age, with a five-fold increased risk for those aged over 65 yrs [9].

Distribution Of Severity Of Airflow Obstruction By Gold Classification

In our study, we found that 64% of COPD cases were having grade 3 followed by 22% of patients with grade 2. Only 7% of cases were having grade1 and grade 4 GOLD classification. In a study conducted by Sivakumar et al. observed majority of their cases belonging to grade 4 followed by grade 3 [10].

Distribution Of GOLD Variables In COPD Cases

In our study, out of 100 COPD cases 59% of patients were having BMI of >/=21 with mean mMRC grade of 1.75+/-0.74. There were 52% patients who never had been hospitalized in this year whereas 48% of patients were hospitalized for >/=1 per year with mean of 0.68+/-0.83. there were 66% of patients who had >/=2 exacerbations in a year whereas 34% of patients were having <2 exacerbations in a year with mean value for total number of exacerbation was 1.88+/-0.83. The CAT score was >/=10 majority (68%) of patients where only 32% of cases were having CAT score of <10 with mean value of 14.43+/-5.61.

In a study done by Jilles M Fermont et al. also found an association between number of exacerbation and hospitalization with severity of COPD as assessed by GOLD classification [11].

Distribution Of Body Mass Index Of BODE Index In COPD Cases

In our study, out of 100 cases, 79% of patients were having BMI of >21% and only 21% of patients were having BMI of </= 21 depicting the possibility of high proportion of chronic bronchitis cases rather than emphysema. Mean ± SD of body mass index(kg/m²) in cases was 25.54 ± 4.22 which was significantly lower as compared to controls (27.07 ± 3.73)(p value=0.032). In a study conducted by Sivakumar et al. found the average BMI in COPD cases were 26.12. This has been explained by them as a probability of the increased prevalence of abdominal obesity rather than the increase in whole BMI [10].

Distribution Of Severity Of Airflow Obstruction Of BODE Index In COPD Cases

In our study, majority of patients (64%) were having FEV1 36-49% and only 9% patients were having severe decrease in FEV1 of </= 35%. Mean ± SD of FEV1(%) in cases was 48.7 ± 13.01 which was significantly lower as compared to controls (81.46 ± 6.43) with a p value <0.0001. A study done by Sivakumar et al. majority of patients were having FEV1 of </=35% followed by FEV1 of 36 -49% with only minority of other 2 groups [10].

Distribution Of 6-minute Walk Distance Capacity Of BODE Index In COPD Cases

In our study, out of 100 COPD cases, 47% of patients were having 6m walking distance capacity of 150-249mts followed by 25% of patients with a capacity of 250-349mts. 20% of patients in our study were having 6m distance capacity of </=149mts and only minority of cases (8%) were having a distance capacity of >/=350mts. Frank Sciurba et al. studied 6m walk distance capacity in 761 subjects and found mean 6m distance capacity of 70.1 ± 19.2 [12].

Distribution Of CIMT In COPD Cases

In our study, 58% of the cases were having CIMT >0.8mm whereas 42% of the cases were having normal CIMT. Mean ± SD of carotid intima-media thickness(mm) in cases was 0.84 ± 0.23 which was significantly higher as compared to controls (0.71 ± 0.14).(p value <0.0001). Manal R. Hafez et al. observed that CIMT was significantly increased in the COPD group compared to the non-COPD group (0.84±0.15 vs. 0.63±0.076, p<0.001) where 64% of COPD patients and only 8.1% of non-COPD subjects had a increased CIMT. They had also found that raised CIMT in COPD patients was significantly associated with hypoxemia (p=0.008, OR=8.2), hypercapnia (p=0.04, OR=6.2), and airflow limitation (p=0.11, OR=2.1) [13]. In the study conducted by by Gestel et al. the mean carotid wall IMT was 1.07 mm. Of the patients without COPD, 23% demonstrated increased CIMT, whereas 32% of patients with mild COPD and 36% of the patients with moderate/severe COPD had increased CIMT with a P value of < 0.01 was found [14].

Association Of Severity Of Airflow Obstruction By GOLD Classification With CIMT

In our study, out of 100 cases, grade 4 was having 85.71% of cases with increased CIMT followed by grade 2 with 68.18% and grade 3 with 56.25% of cases. Only 14.29% of cases were having increased CIMT in grade 1. There was statistically significant correlation was found with p value of 0.034. In a study done by Iwamoto et al. reported a significant correlation between FEV1% and increased CIMT [15]. In a study conducted by Shivkumar et al. observed that average CIMT in stage1, stage 2, stage 3 and stage 4 were 0.723, 0.847, 0.959 and 0.998 respectively. There was a statistically significant increase in CIMT with the increase in severity of airflow limitation(p<0.004). In a study by Sandhip chindhi et al., the mean CIMT showed an increasing trend with increased severity of COPD. The mean CIMT in GOLD stages I, II, III, IV COPD were 0.96 ± 0.32, 0.98 ± 0.52, 1.16 ± 0.47, 1.20 ± 0.59, respectively with a P value for changing trend was 0.115 [16].

Association Between BODE Index With CIMT In COPD Cases

In our study, 34% of patients were comes under BODE stage 3 followed by stage 2 (30%) and stage 4 (19%). Proportion of patients with increased (>/=0.8) CIMT (mm) in cases was significantly higher in stage 2(43.33%), followed by stage 3(61.76%), and stage 4(94.74%) as compared to stage 1(35.29%). Increased BODE index was associated with increased CIMT (p value <0.0007) and thus these patients are prone for atherosclerosis and increased cardiovascular diseases. In a study done by Sivkumar et al. they found statistically significant association between increase in CIMT with the increase in BODE index in cases and controls (p<0.002) [10].

Association Of BMI Of BODE Index With CIMT

In our study, out of 100 cases, 79% of patients were having BMI of >21% and only 21% of patients were having BMI of </= 21 depicting the possibility of high proportion of chronic bronchitis cases than emphysema. Mean ± SD of BMI (kg/m²) in cases was 25.54 ± 4.22. we also found that, major proportion of patients with increased CIMT were having body mass index(kg/m²) >21(50.63%) as compared to BMI(kg/m²) <=21(85.71%) with p value=0.005. Dr. Lowie and others studied and concluded in 197 COPD patients that (mean±SD) age was 64±7 year out of which 60% were male patients, mean FEV1 found was 51±17 % predicted, mean BMI was 26.2±5.2 kg/m^2 and CIMT was 0.93±0.18 mm [17].

Association Of Fev1 Of BODE Index With CIMT

In our study, there is no statistically significant correlation found between FEV1 and CIMT with p value=0.074. In a study done by Schroeder et al. did not find an association between FEV1 and increased carotid thickness development [18]. In addition, Matsuoka et al. were also did not find FEV1 to be significantly correlated with the severity of aortic calcification [19]. However, In studies conducted by Sivkumar et al. found a statistically significant negative correlation between the CIMT and % FEV1 predicted [10].

Association Of 6 Minute Walk Distance Of BODE Index With CIMT

We found that out of 100 cases, proportion of patients with increased CIMT in cases were having significantly lower in 6m walk distance capacity(metres) 150 to 249(51.06%), 250 to 349(52%), >=350(37.50%) as compared to <=149(90%) with p value=0.007 which is statistically significant. In a study conducted by Jilles M Fermont et al. found a significant association between 6minute walk distance capacity in COPD patients with cardiovascular mortality and morbidities with c-statistic value of 0.731 where these C-statistic values indicate a moderate predictive ability of the models for the study's outcome [11]. In study done by Sivakumar et al. concluded that there was a significant increase in CIMT with the decrease in 6MWD(p<0.003) [10].

Association Of MMRC Of BODE Index With CIMT

Proportion of patients with increased CIMT in cases were having higher in MMRC >=2(71.19%) %) as compared to MMRC <2(39.02%) with a p value=0.001 which was statistically significant. No studies were found associating mMRC grading of BODE Index with raised CIMT in cases of COPD patients.

CONCLUSION

COPD patients with higher stages of GOLD stages had significantly elevated carotid intima media thickness and thus depicts the severity of the disease. COPD patients with high BODE index had significantly elevated Carotid intima media thickness and thus they are more prone for cardiovascular morbidity and mortality.

Our results support the need for large long-term interventional trials with cardiovascular end-points to investigate whether disease treatment obtained with appropriate medical and pulmonary rehabilitation approaches may modify the CV risk in COPD patients.

Limitations

Only 100 patients were included in our study and were examined at a single point of time. There is no standard reference population available and also the variation of cut off values based on age and gender was not explored. Observer bias could be possible in measuring CIMT levels by different radiologists.

The ability to generalize outcomes of this study is limited by its smaller sample size due to COVID 19 pandemic during the study, income, and geographic location, as well as the sample selection of convenience. Followup study was not done. Hence the correlation between progression of disease with CIMT level and thereby increased cardiovascular and mortality comorbidities could not be assessed.

Recommendations

CIMT is an accepted predictor for future cardiovascular events in cases of COPD independent of age, gender and cardiovascular risk factors. Measurement seems to be best applicable in patients with intermediate risk in order to readjust cardiovascular risk through various lifestyle

modifications.

A baseline spirometric evaluation and CIMT measurement with B-Mode ultrasonography should be done in all cases of COPD at their first visit and should maintain proper follow-up during their subsequent visits. Prospective studies should be done to establish protocols of follow-up of COPD patients in terms of spirometry and CIMT measurements. Preventive measures should be established on other common causes of COPD namely occupational and biomass exposures.

REFERENCES

1. Mathers CD, Loncar D. Projections of Global Mortality and Burden of Disease from 2002 to 2030. PLOS Med. 2006 Nov 28;3(11):e442.
2. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Archivos de Bronconeumología. 2023 Mar 1.
3. André S, Conde B, Fragoso E, Boléo-Tomé JP, Areias V, Cardoso J. COPD and Cardiovascular Disease. Pulmonology. 2019 May 1;25(3):168–76.
4. Balbirsingh V, Mohammed AS, Turner AM, Newnham M. Cardiovascular disease in chronic obstructive pulmonary disease: a narrative review. Thorax. 2022 Sep 1;77(9):939-45.
5. Hegele RA. The pathogenesis of atherosclerosis. Clin Chim Acta Int J Clin Chem. 1996 Mar 15;246(1–2):21–38.
6. Bauer M, Caviezel S, Teynor A, Erbel R, Mahabadi AA, Schmidt-Trucksäss A. Carotid intima-media thickness as a biomarker of subclinical atherosclerosis. Swiss Med Wkly. 2012;142:w13705.
7. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al. 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults. J Am Coll Cardiol. 2010 Dec;56(25):e50–103.
8. Akinbami LJ. Chronic Obstructive Pulmonary Disease Among Adults Aged 18 and Over in the United States, 1998–2009. 2011;(63):8.
9. Raherison C, Girodet P-O. Epidemiology of COPD. Eur Respir Rev. 2009 Dec 1;18(114):213–21.
10. Sivakumar S. To evaluate the association of subclinical atherosclerosis in chronic obstructive pulmonary disease patients with metabolic syndrome: A Hospital based case control study [Internet] [masters]. Madras Medical College, Chennai; 2018 [cited 2022 Jan 7]. Available from: http://repository-tnmgrmu.ac.in/8929/
11. Fermont JM, Fisk M, Bolton CE, MacNee W, Cockcroft JR, Fuld J, et al. Cardiovascular risk prediction using physical performance measures in COPD: results from a multicentre observational study. BMJ Open. 2020 Dec;10(12):e038360.
12. Sciurba F, Criner GJ, Lee SM, Mohsenifar Z, Shade D, Slivka W, et al. Six-Minute Walk Distance in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2003 Jun 1;167(11):1522–7.
13. Hafez M, Sobh E, Abo-Elkheir O, Sakr L. Atherosclerosis is an associated co-morbidity in patients with chronic obstructive pulmonary disease: Ultrasound assessment of carotid intima media thickness. Eurasian J Pulmonol. 2016 Nov 1;18.
14. Gestel AJR van, Kohler M, Clarenbach CF. Sympathetic Overactivity and Cardiovascular Disease in Patients with Chronic Obstructive Pulmonary Disease (COPD). Discov Med. 2012 Dec 21;14(79):359–68.
15. Iwamoto H, Yokoyama A, Kitahara Y, Ishikawa N, Haruta Y, Yamane K, et al. Airflow limitation in smokers is associated with subclinical atherosclerosis. Am J Respir Crit Care Med. 2009 Jan 1;179(1):35–40.
16. Chindhi S, Thakur S, Sarkar M, Negi PC. Subclinical atherosclerotic vascular disease in chronic obstructive pulmonary disease: Prospective hospital-based case control study. Lung India Off Organ Indian Chest Soc. 2015;32(2):137–41.
17. Vanfleteren L, Franssen F, Spruit M, Groenen M, Wouters E. Atherosclerosis in subjects with COPD is independently determined by the degree of airflow limitation. Eur Respir J [Internet]. 2012 Sep 1 [cited 2021 Nov 7];40(Supply 56).
18. Schroeder EB, Welch VL, Evans GW, Heiss G. Impaired lung function and subclinical atherosclerosis: The ARIC Study. Atherosclerosis. 2005 Jun 1;180(2):367–73.
19. Matsuoka S, Yamashiro T, Diaz A, Estépar RSJ, Ross JC, Silverman EK, et al. The relationship between small pulmonary vascular alteration and aortic atherosclerosis in chronic obstructive pulmonary disease: quantitative CT analysis. Acad Radiol. 2011 Jan;18(1):40–6.