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Pre-clinical prediction of coronary atherosclerosis in copd by carotid artery intima media thickness

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***Abstract*---**Aim and Introduction: To determine the association between Coronary atherosclerosis in Chronic Obstructive Pulmonary Disease and Carotid Artery Intima Media Thickness. The objective of the present case control study is to determine the association between carotid atherosclerosis in COPD patients and cardiovascular morbidity. Material and methods. It was a prospective case-control observational study. 50 COPD patients and 50 age- and gender-matched non-COPD controls were studied. Carotid artery USG scanning was carried out using B-mode duplex USG for measurement of carotid artery intima - media thickness. Results. CIMT was found to be more common in COPD group patients (78%) as compared to non-COPD group patients (26%) (P value = 0.000). The mean CIMT is 1.04 0.41 mm in the COPD group and 0.71 0.24 in the COPD group with a P value of 0.0001. The mean CIMT in Gold 3 was the highest (1.10

0.48 mm), followed by Gold 4 (1.05 0.46 mm) and the minimum in Gold 1 (0.73 0.00 mm). Conclusion**.** Our study shows that COPD is associated with increased CIMT, which is a preclinical predictor of coronary atherosclerosis and cardiovascular risk. However, further studies are needed.

***Keywords*---**Carotid Intima Media Thickness (CIMT), Chronic Obstructive Pulmonary Disease (COPD), Subclinical Carotid Atherosclerosis, Coronary Atherosclerosis, and Cardiovascular Morbidity.

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease of the lungs with complex pathology involving large (chronic bronchitis) and small (bronchiolitis) airways, lung parenchyma (emphysema), and pulmonary vasculature .[1] In addition to pathology in the lungs, COPD is now believed to have a systemic feature extra pulmonary effect, and this has been recognised in the definition of COPD in guidelines .[2]A noticeable increase in the risk of cardiovascular disease in COPD is one of the extra-pulmonary effects. There is emerging evidence that hypoxia, systemic inflammation, hypercoagulable status, platelet activation, and oxidative stress in COPD patients may contribute to cardiovascular morbidity, but systemic inflammation and hypoxia are thought to be the most important factors, manifesting as atherosclerosis in the coronary vasculature and carotid arteries [3]

Atherosclerosis in the carotid artery has been noted to be strongly correlated with atherosclerosis in the coronary artery. Carotid Intima Media Thickness (CIMT) measured by high frequency Doppler ultrasound is an effective and validated method for evaluating carotid atherosclerosis, thereby preclinically predicting the burden of coronary atherosclerosis and cardiovascular risk. Various authors have found that COPD is associated with an increased carotid intima-media thickness, which in turn is an important prognostic marker of cardiovascular morbidity.

Material and Methods

Study design

A prospective case-control blinded observational study was conducted.

The research population and the research sample

The study was initiated after institutional ethics board approval and data were procured after obtaining written informed consent from each participant in the Department of Pulmonary Medicine, SCB Medical College and Hospital, Cuttack, Odisha from April 2018 to March 2019. A total number of 100 cases were included in the study. The study population was divided into two groups: (1) 50 patients were diagnosed as COPD as per GOLD guidelines (2018) and (2) an age and sex-matched non-COPD group involving 50 apparently healthy individuals. The following were the exclusion criteria: presence of other chronic lung diseases,

patients with dyslipidaemia, diabetes mellitus, essential hypertension, and patients with known cardiac diseases.

The diagnosis of COPD was based on clinical criteria like symptoms, physical examination, and risk factor exposure. The diagnosis was confirmed by post-bronchodilator spirometry, which was performed 15 minutes after the administration of 400 µg of inhaled salbutamol. Pre and Post bronchodilator spirometry was performed according to ATS recommendation using a spirometer (Schiller). The diagnosis of COPD and its severity were determined according to GOLD criteria. Investigations like CXR PA view, blood parameters like CBC, LFT, KFT, FBS/PPBS, lipid profile, CRP, 12 lead ECG, ECHO, and CIMT study were done in both the COPD and non-COPD groups.

Carotid artery Intima - Media Thickness (CIMT)

Carotid artery ultrasound scanning was carried out in the Department of Radiology using a PHILLIPS HD 7 machine with a 7.5 MHz linear superficial array probe in B-mode. Patients were examined in a supine position with their necks extended and the probe in an anterolateral position. The boundaries between the different layers of the arterial wall were demonstrated. These boundaries appeared in the longitudinal plane as two parallel echogenic lines separated by a hypoechogenic central area, and this appearance was seen on both the near and far wall of the artery. The hypo echoic arterial lumen acted as an acoustic window and allowed the double echogenic lines of the far wall to be seen more clearly. The first echo along the far wall was derived from the lumen / intima interface, while the second echogenic line represented the media/adventitia interface. At the reference site located 2 cm below the bifurcation, intima-media thickness was measured on the far wall of the right and left common carotid arteries over a length of 1 cm on a reference site. The maximum value was taken as an effective CIMT.
Normal CIMT < 0.8mm.
Increased CIMT >/= 0.8mm

Statistical analysis

The information was entered into Microsoft Excel and analysed with SPSS software version 21. Results were displayed using appropriate graphs and tables. Appropriate tests (for dependent groups or independent groups) for statistical significance would be used. A P value of 0.05 would be taken as the level of significance.

An Ethical consideration

1. Written informed consent,
2. Information sheet,
3. Confidentiality of data,
4. Ethical clearance from the institution’s ethical committee.

Results

Table 1. Demographic characteristics of COPD & healthy controls

Characteristics		COPD pts (n = 50)	Control (N = 50)	P value
Age (years) Mean ± SD		65.08 + 7.88	64.36 + 7.6	0.641
Gender (%)	Male	39 (78 %)	36 (72%)	0.644
	Female	11 (22%)	14(28%)	
Dwelling	Urban	10 (20%)	15(30%)	0.355
	Rural	40(80%)	35 (70) %	
Smoking Status	Smoker	34(68%)		
	Non-Smoker	16(32%)		
BMI (kg/m^2) Mean ± SD		22.04+5.7	24.28+2.9	0.015

Table 2. Comparison of CIMT in COPD and Non-COPD group

CIMT (Effective)	COPD GROUP N = 50 n = %	Non-COPD GROUP N = 50 n = %	p value
Normal (<0.8mm)	11 (22%)	37 (74%)	0.000
Increased (≥0.8mm)	39 (78%)	13 (26%)	
Mean CIMT (mm)	1.04 ± 0.41	0.71 ± 0.24	0.0001

TABLE 3. Relationship of mean CIMT with GOLD stages of COPD severity

Spirometry Grade	Post Bronchodilator FEV1	No. of patients N =50 N (%)	Mean CIMT in mm	Increased CIMT	Normal CIMT
Gold 1 (Mild)	≥80%	3 (6%)	0.73 ± 0.0	2 (66%)	1 (33%)
Gold 2 (Moderate)	≥50%, <80%	22 (44%)	0.98 ± 0.32	18 (81.8%)	4 (18.18%)
Gold 3 (Severe)	≥30%, <50%	17 (34%)	1.10 ± 0.48	14 (82.35%)	3 (17.64%)
Gold 4 (Very Severe)	<30%	8 (16%)	1.05 ± 0.46	5 (62.5%)	3 (37.5%)

The patient group (n = 50) was composed of 39 males and 11 females. The mean age among the cases was 65.08 years, whereas the control group consisted of 36 males and 14 females with a mean age of 64.36 years. The majority of COPD patients and control groups were males, 78% and 72%, respectively. 80% and 70% of patients were from rural areas in the COPD group and non-COPD group, respectively. Among COPD patients, 34 were smokers and 16 were non-smokers. The COPD group had a lower meanBMI as compared to the non-COPD group

(22.04 vs. 24.28). Of the patients, 44% had moderate obstruction and 34% had severe obstruction. (Table-3)

In Table-2, 39 cases (78%) had increased CIMT, whereas in the non-COPD group, 13 (26%) had increased CIMT (p = 0.000). In the COPD group, the mean average CIMT was 1.04 0.41 and in the control group it was 0.71 0.24 (p = 0.0001). The value of CIMT among the various stages of COPD showed that GOLD-3 stage 82.35% had increased CIMT, followed by GOLD stage-2 (81.81%). Table-3 shows the mean CIMT in GOLD stage-3 was the highest (1.100.48 mm), followed by GOLD-4 (1.050.46 mm) and the minimum in GOLD stage-1 (0.73 0.0).

Discussion

In our study, there was an absolute prevalence of male gender (78% in the COPD group and 72% in the non-COPD group) which was found to be more or less similar to the study by Oliveria et al. [4] where theprevalence of males was 79% and the study by Ozdemirel et al. [5] where the prevalence of males was 90.3% in the COPD group and 60% in the non-COPD group.

This study had a predominance of rural patients over urban ones (80% rural, 20% urban). The majority of patients in the COPD group were smokers (68%) and all the subjects in the non-COPD group were non-smokers. All the females in the study were non-smokers. BMI showed a significant difference between the cases and the control group (p = 0.015). In this study, 44% of patients had moderate obstruction and 34% had severe obstruction.

In our study, CIMT was raised (0.8mm) in 78% of cases among the COPD group and 26% of cases in the non-COPD group (p = 0.000), which was more or less similar to the studies by Rajani M et al [6] that is 65% in the COPD group versus 25% in the non-COPD group, Chindhi et al [7] that is 67.6% in the COPD group versus 25.8% in the non-COPD group, and Hafez et al [8] that is 64% in the COPD group versus 8.1% in the non-COPD group.

The mean CIMT in the COPD group was 1.04 0.41mm whereas that of the non-COPD group was 0.71 0.24 mm in our study, showing a significant difference (p = 0.0001). It was similar to a study by Chindhi et al. [7] who found a mean CIMT of 1.07 0.49 mm in the COPD group versus 0.75 0.33 mm in the non-COPD group. Karakas et al [3] found 0.62 0.05 mm in the COPD group versus 0.45 0.03 mm in the non-COPD group, Hafez et al [8] found 0.84 0.15 mm in the COPD group versus 0.63 0.076 mm in the non-COPD group.

In our study, we discovered that 82.35% of cases in the GOLD stages of COPD severity had increased CIMT, followed by 81.82% of cases in the GOLD-2 stages and 66% of cases in the GOLD-1 STAGE.GOLD-4 stage, 62.5% of cases had increased CIMT. Chindhi et al. [7], also found more or less similar types of results in their study, showing 69.7% of GOLD-1, 58.8% of GOLD-2, 70.5% of GOLD-3, and 71% of GOLD-4 patients have increased CIMT.

The mean CIMT in our study in GOLD-3 was highest (1.10 0.48) mm, followed by GOLD-4 (1.05 0.46) mm, GOLD-2 (0.98 0.32) mm and minimum in GOLD-1 (0.73

0.0) mm. Studies by and Chindhi et al [7] showed that there were increased CIMT values with GOLD stages of COPD according to severity. In contrast, Pobeha P et al. (2011) and Manal R Hafez et al. (2016) found no significant difference in CIMT in relation to COPD severity. They commented that it might be due to the fact that atherosclerosis of the carotid artery started early in the course of COPD. In our study, the increased CIMT in GOLD-3 and GOLD-4 stages might be due to the maximum number of cases in these stages of COPD.

Conclusion

COPD is a chronic and progressive systemic inflammatory disease. Cardiac morbidity is a major problem in COPD, leading to increased morbidity and premature mortality. Systemic inflammation is a well-recognised factor in the development of atherosclerosis and a cause of increased cardiovascular co-morbidities. Hence, it is essential to detect atherosclerosis at an early stage to prevent its impact on the adverse outcomes in COPD patients. Carotid artery intima-media thickness (CIMT) as measured by carotid duplex ultrasound is an indicator of preclinical atherosclerosis and cardiovascular disease risk. So, it should be used as a determinant of early detection of atherosclerosis and cardiovascular risk associated with COPD patients so that prompt treatment and preventive measures can be instituted to reduce cardiovascular morbidity and mortality among these patients.

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Study Limitations:

- a small population size was studied
- Single-centred study with a probability of referral bias
- Outcome assessment is not done.

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