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Original Research Article

Clinical and phonocardiographic evaluation of left ventricular function in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a term to describe a group of diseases (chronic bronchitis and emphysema). The status of left ventricular (LV) function in patients with COPD has been a controversial subject. Given the ambiguity in correlation of LV dysfunction and COPD, this study was planned to assess the relationship between LV function and COPD.
Methods: This was an observational study done in 40 adult patients with acute exacerbation of COPD. The enrolled patients were divided into 2 major groups. Group A - predominant emphysema and Group B - predominant bronchitis. Phonocardiogram (PCG), carotid pulse tracing and ECG were done to measure LV ejection time (LVET) and pre-ejection period (PEP).
Results: FEV1 impairment was greater (severe to very severe grade) in the majority (77%) of patients of group B, whereas the majority (77.2%) of group A patients had lesser degree of FEV1 impairment (mild to moderate). PEPI were observed to be prolonged and LVETI were observed to be shortened. PEP/LVET ratio was observed to be prolonged in 77.5% of patients in stable condition. PEP/LVET ratio was abnormally prolonged (>0.42) to a greater extent in patients of group B than in patients of group A.
Conclusions: LV dysfunction is commonly encountered in patients with COPD and was observed to be exaggerated during an acute exacerbation. It was maximum in patients with chronic bronchitis with cor pulmonale with CCF and lesser in patients with chronic bronchitis without cor pulmonale or CCF and least in patients with emphysema.

Keywords: Chronic obstructive pulmonary disease, Left ventricular dysfunction, Systolic time intervals

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a term to describe a group of diseases (chronic bronchitis and emphysema) all of which have in common the physiological defect of airway obstruction, which secondarily involves the cardiovascular (CV) system. The primary CV complication in this group of diseases is the development of pulmonary arterial hypertension (PAH).[1] Hypoxic vasoconstriction, acidosis, and reduction in pulmonary vascular bed because of lung destruction or pulmonary thromboembolism have been shown to contribute to the development and maintenance of PAH.[2] Right ventricular hypertrophy develops in response to this increased afterload and eventually right-sided heart failure ensues. It is well established that PAH is the principle cause of right ventricular hypertrophy and failure in COPD.[3]

The status of left ventricular (LV) function in patients with COPD has been a controversial subject since early autopsy studies demonstrated LV hypertrophy in a

significant percentage of patients dying with COPD.[4] These studies suggested that LV is adversely affected by long-standing obstructive lung disease alone, a concept in conflict with the traditional belief that chronic lung disease affects the right ventricle alone.

The measurement of systolic time intervals (STI) is a non-invasive technique which has been demonstrated to be a reliable index of LV function.[5] The three basic STI are the pre-ejection period (PEP), the left ventricular ejection time (LVET) and the total electromechanical systole (QS-2).[6] The diagnostic value of the STI for identification of LV dysfunction can be enhanced by determination of the ratio PEP/LVET. Since the PEP and LVET may identify LV dysfunction when either or both the PEPI and LVETI are still within the normal range, consequent the PEP/LVET has become the single most useful measurement of LV performance from the STI.

Alpert J et al found PEP and PEP/LVET ratios were lengthened and LVET was shortened in patients with chronic right ventricular failure.[7] Hooper RG and Whitcomb ME demonstrated that subclinical LV dysfunction is frequently present in patients with moderate obstructive lung disease. They have measured STI in 28 patients with COPD who had only moderate arterial blood gas abnormalities. They found that significant differences in pre-ejection period index (PEPI) and left ventricular ejection time index (LVETI) existed between the control subjects and the patients with the most severe lung disease. A highly significant difference in PEP/LVET existed between these two groups.[4]

STI has become one of the established "non-invasive" techniques of clinical cardiology. Indeed, the term "non-invasive" was first used in connection with the STI. It was one of the first quantitative non-invasive tests of cardiac function and remains one of the simplest and most reliable to perform. It provides a quantitative estimate of the effect of various CV disorders upon the LV. Like all non-invasive techniques, the STI has the advantage that multiple observations can be performed.[6]

The broad objectives of this study were to assess the alterations in STI, to demonstrate the presence of LV dysfunction in COPD, to assess degree of LV dysfunction in different types of COPD, to correlate LV dysfunction with severity pulmonary disease, and to evaluate degree of LV dysfunction during acute exacerbation of COPD.

METHODS

Adult patients of either gender in the age group of 30-50 years, diagnosed with acute exacerbation of COPD and admitted in Medicine wards of Indira Gandhi Medical College and Hospital, Nagpur were recruited into the study. Also, normal subjects were enrolled to serve as controls. The diagnosis of COPD was based on clinical presentation and physical examination. The patients with clinical history suggestive of organic heart disease, history of alcohol abuse, hypertension, any cardiac abnormality on physical examination, abnormal electrocardiogram (ECG), abnormal cardiac silhouette on a standard chest roentgenogram and associated co-morbidities were excluded from the study.

The enrolled patients were divided into two major groups. Group A - predominant emphysema and Group B - predominant bronchitis. Depending upon absence or presence of associated cor pulmonale with congestive cardiac failure (CCF), the patients were further divided into 2 subgroups. As no patients had cor pulmonale with CCF in group A, only patients from group B were divided into group B1 and group B2, based on the absence or presence of cor pulmonale with CCF respectively.

The demographic characteristics, clinical presentation, past medical history, family history, personal history, general examination findings and systemic examination findings of the patients were recorded into case record forms. A 12 lead ECG, chest roentgenogram, complete blood count and packed cell volume (PCV) and sputum culture were done. Lung function tests were done when the patient became stable. Forced expiratory volume (FEV1) and forced vital capacity (FVC) were measured with 13.5 litre Collins light-weight respirometer.

Simultaneous recordings of the phonocardiogram (PCG), carotid pulse tracing and ECG were made using a three-channel polygraph (ECG/phono system FD-310-Fukuda Denshi Co. Ltd. Tokyo Japan). The recordings were done at two settings, one upon admission, and the second upon discharge, when patient had become stable. Carotid pulse tracing was recorded through the same piezoelectric crystal transducer applied over the point where carotid pulse was maximally felt. LVET and PEP were measured directly from the tracings namely ECG, PCG and carotid pulse tracing. The PEP/LVET ratio was also calculated. The indices QS2I, PEPI and LVETI were obtained using standard regression equations described by Lewis RP et al.[8]

Statistical analysis

The mean value, standard deviation (SD) and standard error (SE) were calculated for each time interval. Student's t test was applied to find out the significance of difference between the mean values in different groups.

RESULTS

Total 40 patients with clinically acute exacerbation of COPD were enrolled in the study. Out of 40 patients, 28 patients (70%) were male (15 in group A and 13 in group B) and 12 patients (30%) were female (7 in group A and 5 in group B). Most patients (42.5%) were between 46 and 50 years of age, followed by 30% patients between 41 and 45 years of age. A total of 22 (55%) patients belonged to group A and 18 (45%) patients were of group

B. A total of 26 (65% patients (13, 64% patients in group A and 12, 66% patients B) were engaged in occupations involving air pollution. Cor pulmonale with CCF was present in 9 (50% of) patients in group B, while there was no patient with cor pulmonale with CCF in group A. All patients mainly presented with cough and breathlessness. Sputum production more than 100 cc/24 hrs was seen in all 18 patients in group B (9 patients each in sub groups B1 and B2) and none in group A. Edema in the feet was present in all (9) patients in group B2 and not in any other groups while weight loss was reported by 9 patients in group A and not in any other groups. All patients from group A had been symptomatic for less than 10 years. Seven patients (78%) out of 9 in group B2 had been symptomatic for more than 10 years, whereas only 1 patient (11%) out of 9 patients of group B1 had been symptomatic for more than 10 years. Patients in group A had grade II and grade III dyspnoea (77% and 23% respectively), while most of patients in group B had grade IV and grade II dyspnoea (44% and 33% respectively). Grade IV dyspnoea was seen only in patients of group B2.

54% and 72% of the patients in group A and group B respectively were smokers. Amongst them 22 (88%) were moderate smokers, of whom 9 (40%) were of group A and 13 (60%) were of group B. 20 patients (9 in group A, 5 in group B1 and 6 in group B2) had been smoking for more than 15 years duration. On clinical presentations, all the patients in group B2 showed signs of CCF (raised JVP, edema in feet and early clubbing). Cyanosis was predominantly seen in group B patients (83%) as compared to group A (27%).

All 9 patients of group B2 revealed presence of parasternal heave and right ventricular gallop (S3) rhythm and 8 out of 9 patients had diastolic shock.

All patients of group B2 had hepatomegaly. No patient was found to be anaemic. Growth on sputum culture was seen only in group B (17, 94%). Commonest organisms grown was *H. influenzae* (41%), followed by *Streptococci* (35%). Whereas, *Staphylococci* and *Klebsiella* were grown only in 12% of cases.

Table 1: Severity of COPD depending on % predicted FEV1.

Grade	Total	Group A	Group B	Group B1	Group B2
Mild (65-79% predicted FEV1)	6	5	1	1	-
Moderate (50-64% predicted FEV1)	15	12	3	3	-
Severe (35-49% predicted FEV1)	17	5	12	5	7
Very severe (<35% predicted FEV1)	2	-	2	-	2

As shown in Table 1, in group A, most patients (54%) had moderate impairment of pulmonary function, while in group B, most patients had severe impairment of pulmonary function (66%).

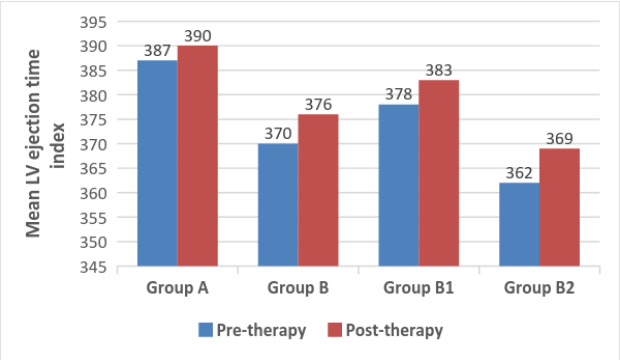

Figure 1: Left ventricular ejection time index (mean).

The mean left ventricular ejection time index (LVETI) recorded in control subjects was 408+8 ms. As shown in Figure 1, pre-therapy, this was significantly lower in both groups A and B (387 ms in group A and 370 ms in group B, $p<0.05$). A more significant decrease in LVETI was observed in group B and an especially highly significant decrease was seen in group B2 (362 ms, $p<0.05$). After therapy i.e. when the patients were symptomatically stable, there was a slight increase in LVETI in both groups, but it was greater in group B2 than in group B1 and group A. However, LVETIs did not return to normal post-therapy.

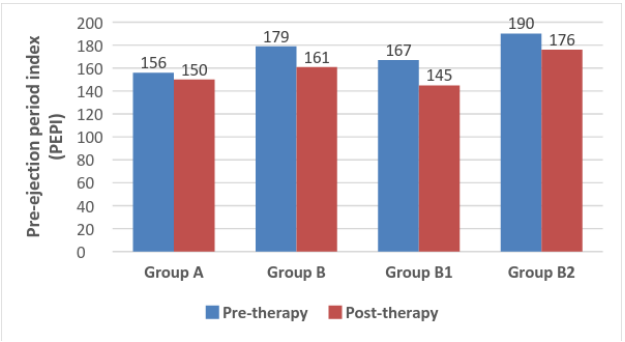

Figure 2: Pre-ejection period index (PEPI).

PEPI recorded in control subjects was 125±12 ms. As shown in figure 2, compared to control values, pre-therapy, this was significantly higher in both groups (156

in group A and 179 in group B, p<0.05). A more significant increase in PEPI was seen in group B2 (190) compared to group B1 (167) and group A (156). After therapy there was a significant decrease in PEPI in group B1 (-22, p<0.01) than group B2 (-14) and group A (-6). But, PEPI did not return to normal post-therapy.

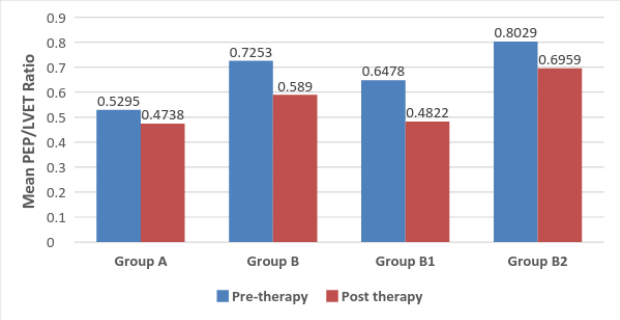

Figure 3: Mean PEP/LVET ratio in different groups.

In acute exacerbation of COPD, 39 patients (97.5%) had PEP/LVET >0.42 suggestive of presence of LV dysfunction. After recovery from acute exacerbation i.e. in stable condition, 31 patients (77.5%) had evidence of LV dysfunction. At stable condition of disease, 4 (44%) patients of group B1 and 5 (22.7%) patients of group A had no LV dysfunction.

At acute exacerbation of COPD, there was a significant increase in PEP/LVET ratio in all the groups compared to the control (0.38) as shown in figure 3. There was a greater increase in group B2 than in the other groups. Recovery i.e. decrease in PEP/LVET after therapy was significantly greater in group B patients, especially in B1 group compared to other groups. Little decrease was seen in PEP/LVET after therapy in group A patients. At acute exacerbation of COPD, increase in PEP/LVET ratio was more in male than female patients, i.e. LV dysfunction was more commonly observed in male than female patients. The recovery of PEP/LVET i.e. decrease towards normal values after therapy was smaller in male than female patients. There was no difference in PEP/LVET ratio between smokers and nonsmokers in any group. However, the extent of PEP/LVET abnormalities increased with increasing degree of airway obstruction.

Table 2: PEP/LVET ratio in acute exacerbation of COPD.

FEV1 impairment	Total	Group A	Group B	Group B1	Group B2
Mild	0.5606	0.5437	0.6452	0.6452	--
Moderate	0.5222	0.5151	0.5509	0.5509	--
Severe	0.6941	0.5500	0.7541	0.7065	0.7881
Very severe	0.8550	--	--	--	0.8550
				(p < .001)	

As shown in Table 2, mean PEP/LVET ratio in different degrees of airway obstruction was observed to be abnormally prolonged in all groups, and this was statistically significant (p <0.001). The extent of PEP/LVET prolongation was found to be 0.5606 in mild airway obstruction, to 0.5222 in moderate airway obstruction and this change was statistically not significant versus control, but the degree of PEP/LVET ratio abnormality observed in severe airways obstruction (0.6941) was found to be statistically significant (p < 0.001). Similarly, the extent of PEP/LVET ratio abnormality seen in very severe airway obstruction (0.8550) as compared to that of severe obstruction (0.6941) was also statistically highly significant (p <0 .001). Maximal abnormalities in PEP/LVET ratio were observed in patients of group B2 (0.8550).

Table 3: PEP/LVET ratio in stable COPD patients.

	Total	Group A	Group B	Group B1	Group B2
Mild	0.4481	0.4481	0.4151	0.4151	--
Moderate	0.4409	0.4572	0.3756	0.3756	--
Severe	0.5982	0.5390	0.6229	0.5597	0.6686
Very Severe	0.7934	--	--	--	0.7934

As shown in Table 3 in chronic bronchitis stable patients (group B) with mild-moderate pulmonary function impairment, there was no left ventricular dysfunction. In other patients of COPD at stable conditions, the left

ventricular dysfunction was increased with severity of disease.

The extent of recovery as observed by values of PEP/LVET ratios, was greatest in patients having mild airways obstruction (0.956-group A, 0.2301-group B1) and became lesser in moderate degree airway obstruction (0.0579-group A, 0.1753-group B1) and even lesser in patients with severe airway obstruction (0.0110-group A, 0.1312-group B) and was least in patients of group B2 (0.1201). The extent of improvement in left ventricular dysfunction after therapy progressively reduced with increasing severity of airway obstruction as observed in all groups, but the extent of recovery was better in patients of group B (0.2301 - 0.1753 - 0.1312) as compared to patients of group A (0.0956 - 0.0579 - 0.0110).

DISCUSSION

The present study was done in 40 patients with COPD admitted in medicine wards and 10 normal individuals, who served as controls. Out of 40 patients, 22 were predominantly emphysematous (group A), 18 had chronic bronchitis (group B) of which 9 were having cor pulmonale and CCF (group B2) and 9 were without evidence of cor pulmonale or CCF (group B1).

In our study, we found female: male ratio as 1:2.33. In contrast to this, in Britain it was 1:6. The higher prevalence of the disease in females in India may be related to their exposure to domestic atmospheric pollution.[9] Cough and breathlessness were the most common symptoms being present in all patients in our study as reported also by Thurlback WM.[10] Weight loss was present in 41% patients of emphysematous group. Similar observations have been reported by Thurlback.[10]

Around 63% patients had history of smoking. Similar observations have also been reported by Thurlback who found that cigarette smoking was the most commonly identified correlate with COPD.[10] In our study, the severity and duration of smoking was seen to be greater in chronic bronchitis patients than in emphysematous patients. We found a positive history of exposure to occupational air pollution in 15 patients (38%). Similar observations were reported by Will J.[11] In all 12 female patients, there was history of exposure to domestic air pollution.

Smoking could possibly be one of the factors responsible for higher prevalence of polycythemia in group B patients as compared to group A patients, in our study. Polycythemia is closely related to the degree of chronic hypoxemia between exacerbations as observed by Hyne R.[12] There is also evidence that the degree of polycythemia may be related to the amount of carboxyhaemoglobin induced by smoking and that reduction in smoking can reduce the red cell mass as observed by Calverlgy PMA et al.[13]

In our study, FEV1 was more impaired in patients with chronic bronchitis with cor pulmonale and CCF than in chronic bronchitis without cor pulmonale and least impaired in emphysematous patients. This is probably due to longer duration of symptoms in patients with chronic bronchitis with cor pulmonale and CCF (B2) group. This may be due to the fact that majority of these patients (67%) were moderate smokers and the duration of smoking was higher in this group as compared to patients of group A.

Right ventricular involvement due to COPD is well established, but the subject of left ventricular performance in COPD has been controversial and complicated.[14-19] Postmortem reports have revealed the presence of left ventricular hypertrophy in a significant percentage of patients with COPD.[14-15,20-22] The measurement of LV function was difficult and complicated until the advent of non-invasive techniques. The measurement of STI is a non-invasive technique which has been demonstrated to be a reliable index of LV function.[5,6,8]

The internally measured systolic time intervals (PEP and LVET) correlate closely with the externally recorded PEP and LVET.[23,24] In addition, a highly significant correlation between the PEP/LVET and LV ejection fraction as measured by angiography has been demonstrated in a variety of cardiac diseases.[5]

PEP prolongation, LVET shortening and an increase in PEP/LVET ratio is a characteristic pattern observed in patients with LV dysfunction, provided the patients are in sinus rhythm and do not have conduction defects or valvular heart diseases.[6,8,25] In the present study, we observed an abnormal prolongation of PEP/LVET ratio more than 0.42 in 97.5% of patients at the time of acute exacerbation while the ratio was abnormal in 77.5% patients when they were in stable condition.

The results of our study indicate that PEP/LVET ratios (LV function) become abnormal during an episode of acute exacerbation but do normalize in certain patients (20.5%) after the condition stabilizes. This reversibility of PEP/LVET ratios to normal values was not observed in patients with cor pulmonale with CCF.

Hooper RG and Whitcomb ME observed PEP/LVET ratios to be abnormal in 53.6% of their cases of stable COPD.[4]

The high incidence of abnormal PEP/LVET ratio (77.5%) observed in our study, in stable COPD patients may be because all patients in the present study had an FEV1 below 75% of predicted value, whereas in the previous study, 28.6% had an FEV1 more than 75% of predicted. In the present study, a higher percentage of patients (47.5%) had an FEV1 less than 50% of predicted, as compared to 35.7% of the patients in the previous study. The mean LVETI was significantly shortened in all

groups of patients of COPD, both during acute exacerbation and in stable condition. Significant lengthening of PEPI and shortening of LVETI have been observed by Hooper RG and Whitcomb ME and Alpert J et al in patients with stable COPD, however our results of abnormalities of PEPI and LVETI during acute exacerbation in COPD are not comparable as similar studies have not yet been published.[4,7] Of the 40 cases studied, the PEP/LVET ratio was observed to be abnormal in 97.5% patients during an acute exacerbation and abnormal in 77.5% in stable condition, thereby indicating an LV dysfunction which had occurred in 8 patients (20.5%) during an acute exacerbation and had reverted to normal after the patients regained stable condition.

The increase in PEP/LVET ratio was observed in all groups of patients of COPD and was greater during an acute exacerbation than in stable condition. Maximum increase in PEP/LVET ratio during exacerbation and stable condition was observed in patients of chronic bronchitis with cor pulmonale and CCF, group B2. The statistically significant increase in PEP/LVET ratio was observed to be smaller in patients of chronic bronchitis without CCF (group B1) and least in patients of emphysema (group A). These observations indicate that there is an increase in PEP/LVET ratio during acute exacerbation in COPD, indicating increased LV dysfunction, which occurs to a greater degree in patients with chronic bronchitis than in those with emphysema. The probable reason for this phenomenon may be the effect of hypoxia, but the oxygen uptake in patients with COPD is normal or even increased owing to the greater work of breathing. The observations of Filley GF et al revealed that there is no deficit of oxygen uptake at rest or on exercise in patients with COPD. Even in profoundly hypoxic conditions when cyanosis is present, there is no evidence of impaired oxygen uptake.[26]

Our observations in the present study showed that PEP/LVET ratio abnormalities were greater in patients of B2 group and least in patients of group A. This may probably be due to longer duration of symptoms and greater degree of FEV1 impairment observed in the patients of group B2 as compared to the patients of group A.

In this study, degree of impairment of LV function was maximum in patients with very severe airway obstruction. The degree of LV dysfunction was lesser in severe airway obstruction and still lesser in those with mild to moderate airway obstruction. These observations indicate that LV dysfunction is proportionate to the severity of airway obstruction and greater the degree of airway obstruction, greater is the severity of LV dysfunction. Similar observations have also been reported by Hooper RG and Whitcomb ME.[4]

The extent of recovery of PEP/LVET ratio was observed to be maximum in patients with mild airway obstruction, less in patients with moderate to severe airway obstruction and least in very severe airway obstruction. The degree of recovery of LV dysfunction as measured by PEP/LVET ratio was more in patients of chronic bronchitis group B as compared to patients of emphysematous group A. We also observed that as polycythemia increased, the LV dysfunction also increased. Erythrocythemia increases viscosity of blood and theoretically, it leads to elevated pulmonary arterial pressure.[12] This may be one of the reasons for increasing degree of LV dysfunction with increasing polycythaemia. The finding that the extent of PEP/LVET ratio abnormalities were nearly similar in both groups of patients, indicates that smoking alone cannot be a cause of LV dysfunction in patients with COPD.

CONCLUSION

LV dysfunction is commonly encountered in patients with COPD and was observed to be exaggerated during an acute exacerbation. It was seen to be maximum in patients with chronic bronchitis with cor pulmonale with CCF and lesser in patients with chronic bronchitis without cor pulmonale or CCF and least in patients with emphysema. Extent of recovery of LV dysfunction after therapy for acute exacerbation was more in patients with chronic bronchitis without cor pulmonale or CCF and lesser in patients of emphysema and least in patients with cor pulmonale with CCF. The extent of LV dysfunction is directly proportional to the degree of FEV1 impairment, and degree of polycythaemia.

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