ORIGINAL ARTICLE

P-WAVE ABNORMALITIES IN PATIENTS OF STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Shriharshavardhana S V[1], Malay Sarkar[2], Arvind Kandoria[3], Rameshwar S Negi[4], Sunil Sharma[5]

Author's Affiliations: [1] Postgraduate Resident; [2]Professor & Head; [4]Associate Professor; [5]Assistant Professor, Dept of Pulmonary Medicine; [3]Professor, Dept. of Cardiology, IGMC, Shimla, Himachal Pradesh, India
Correspondence: Dr Shriharshavardhan S V Email: harsha218@gmail.com

ABSTRACT

Introduction: COPD is a common preventable and treatable disease and a major cause of morbidity and mortality globally. ECG is a very simple, widely available and convenient bedside investigation that can be used to detect various cardiac abnormalities. Electrical activities of the heart are often influenced by COPD. ECG changes like P-wave abnormalities have to be carefully assessed before coming to an inference.

Methodology: The present study was an institutional based prospective study, conducted from July 2014 to June 2015. The study was designed to assess the various ECG abnormalities in stable COPD patients and to determine echocardiography findings in relation to ECG changes.

Results: Among the P-wave abnormalities P-wave axis verticalisation (PWAV) was observed in 59(76.6%) patients. Twenty (26%) patients showed negative P-wave in V1, significant-Ptf(P-terminal force) was observed in 3(3.9%) patients. P-mitrale was seen in 18(31.2%), and P-pulmonale in 16 (20.8%) patients.

Conclusion: Though not specific, ECG may reveal various functional and structural abnormalities of the heart in relation to COPD like PWAV. PWAV may be the most commonly seen P-wave abnormalities in COPD patients. Echocardiography findings suggest that presence of P-mitrale is not conclusive of left atrial overload in patients of COPD. Echocardiography should be done routinely in all COPD patients to confirm ECG findings and to diagnose pulmonary hypertension, cor-pulmonale and other subclinical cardiovascular co-morbidities like left ventricular diastolic dysfunction.

Keywords: Chronic obstructive pulmonary disease, ECG, Echocardiography, P-wave axis verticalisation

INTRODUCTION

COPD is an important public health problem and a major cause of morbidity and mortality in both developed and developing countries. Exacerbations and Comorbidities contribute to the overall severity in individual patients.[1] Cardiovascular co-morbidities are particularly common in COPD[2]. In mild to moderate COPD, cardiovascular disease is the leading cause of hospitalization and second leading cause of mortality after lung cancer, contributing to 25% of the total COPD death.[3] However, in advanced COPD, respiratory failure is the main cause of mortality.[4] Screening for cardiovascular co-morbidities should be an important component in the management of COPD as they can worsen the clinical status and prognosis of COPD patients. COPD also influences the electrical events of the heart. ECG is a very simple, widely available and convenient bedside investigation that can be used to detect various cardiac abnormalities in COPD patients.[5] Right atrial enlargement(RAE) may be expressed as P-Pulmonale, P-wave axis verticalisation(PWAV), significant-Ptf (P-terminal force). The frontal PWAV (P-axis > 60°) has a close correlation with emphysema and may be an early finding of worsening of COPD before occurrence of other ECG changes of right heart hypertrophy and enlargement, such as P-pulmonale. Increasing verticality of the frontal P-vector correlates with increasing degree of airway obstruction, degree of depression of the diaphragm and radiographic quantification of the disease.[6-9] The Ptf is one of the P-wave indices affected by COPD, it is considered as a highly specific sign for left atrial enlargement (LAE). Amplitude of i-PV1 >1.5 mm is an established ECG criterion for RAE. The most commonly encountered type of significant-Ptf (s-Ptf) is a fully negative P-wave morphology in V1.[10] Increased Ptf in emphysema may be due to downward right atrial position caused by RA displacement, and thus the common assumption that increased P-tf implies LAE should be made with caution in patients with emphysema. Therefore, s-Ptf and verticalization of P-vectors in emphysema might be a more functional outcome of diaphragmatic depression from severe emphysema rather than RA strain or RAE. The present study was undertaken to evaluate the various

ECG and echocardiographic abnormalities in patients with stable COPD and to correlate ECG abnormalities with echocardiography findings. The objective was to know the influence of COPD on ECG changes by comparing the same with echocardiographic findings with an emphasis on P-wave abnormalities.

METHODOLOGY

Current study was conducted in the department of pulmonary medicine, IGMC, Shimla from July 2014 to June 2015. It was an observational prospective study conducted after prior approval from the ethical committee. We evaluated 77 consecutive patients with stable COPD who attended the outpatient department (OPD) of pulmonary medicine, IGMC Shimla from various places in Himachal Pradesh. All subjects were included in study after obtaining informed written consent. Non-COPD cases like bronchial asthma, pulmonary tubercuosis, lung cancer, interstitial lung disease and bronchiectasis; cases with known co-morbidities like cardiac disease, hypertension, and diabetes mellitus and patient not willing to give informed consent were excluded.The selected patients were subjected to detailed history and thorough clinical examination. We obtained chest radiography, spirometry, ECG of all subjects under study. Echocardiography was obtained in 66 patients. Eleven patients failed to get their echocardiography done. Preand postbronchodilator spirometry was performed as per ATS/ERS recommendations[11] using a spirometer (Spirolab 11) in all subjects to assess the severity of airflow limitation as per GOLD guidelines [Table 1].[1]

A single channel 12-Lead ECG machine (BPL-CARDIART 6108T) was used to record electrocardiographic characteristics. The ECG is recorded on to standard paper travelling at a rate of 25mm/s. The paper is divided into large squares, each measuring 5mm wide and equivalent to 0.2 s. Each large square is five small squares in width, and each small square is 1 mm wide and equivalent to 0.04s. The electrical activity detected by the ECG machine is measured in millivolts. Machines are calibrated so that a signal with amplitude of 1mV moves the recording stylus vertically 1cm. throughout this text, the amplitude of waveforms will be expressed as: 0.1 mV =1mm =1small square. P-pulmonale is a tall and peaked p-wave in standard lead II, III and AVF. P-wave height in lead II will be ≥2.5mm. PWAV is diagnosed by P-wave amplitude in lead III greater than its amplitude in lead I or a negative P-wave in aVL. Significant Ptf is a fully negative P-wave morphology in V1or calculated by multiplying the duration of the terminal negative phase of P-wave in V1 (in milliseconds) by its depth in millimeters. Ptf magnitude of ≥40 mm.ms, along with the presence of IAB (P-wave duration >110 ms), is considered a highly specific sign for left atrial enlargement (LAE). Amplitude of i-PV1 >1.5 mm is an established ECG criterion for RAE. [10]

A conventional echocardiography was performed using "iE33 xMATRIX " Doppler echocardiography system and parameters like Pulmonary hypertension, right atrial enlargement, left atrial enlargement, structural and functional abnormalities of right and left ventricles were noted in relation to ECG changes. Observations and results were statistically compared and analysed on their mutual relations using SPSS20 software. Chi-Square Test is applied to check the independence of variables. Chi-Square Test for independence is applied when we have two categorical variables (e.g. heart rate and severity) from a single population. It is used to determine whether there is a significant association between the two variables. We compared ECG changes with gender, age group, duration of illness, mMRC grades, GOLD stages, smoking status, SI, biomass exposure and BMI. P-value of less than 0.05 was considered statistically significant.

RESULTS

We studied the ECG characteristics in all (77) patients and echocardiography pattern in 66 patients. ECG and echocardiography findings were compared with gender, age group, duration of illness, severity of obstruction (GOLD), smoking status, smoking-index (SI) and biomass exposure. We also compared ECG findings with corresponding echocardiography findings.

Table 1: COPD severity groups by GOLD criteria (Patients with FEV_1/FVC ratio less than 0.7)

GOLD 1	Mild	$FEV_1 \geq 80\%$
GOLD 2	Moderate	$50\% \geq FEV_1 \leq 80\%$
GOLD 3	Severe	$30\% \geq FEV_1 \leq 50\%$
GOLD 4	Very Severe	$FEV_1 < 30\%$

The baseline characteristics of study population with their number and percentage are shown in [Table 2]. More number of patients(46.6%) were in the age group of 60 to 69 years. The mean age of the patients was 64.46 years. Male constituted majority of our study population. There were 58(75.3%) male and 19(24.7%) female with a male: female ratio of 3:1. Study population included patients from various places in and around Shimla and other districts of the state.

Though the duration of illness was varied from less than one year to more than 20 years, majority of the patients i.e., 66(86%) had illness for 1 to 10 years. Sixty seven (87%) of them were smokers.

Table 2: Baseline characteristics of the all study population compared to Patients with P-wave axis verticalisation

Characteristics	Study Population (%) (n=77)	Patients with P-wave axis verticalisation(n=59)
Age in years	Mean=64.46	
40-49	5 (6.5)	3
50-59	12 (15.6)	9
60-69	36 (46.6)	26
70-79	22 (28.6)	20
80-89	2 (2.7)	1
Gender		
Male	58 (75.3)	48
Female	19 (24.7)	11
Duration of Illness in Years		
<1	4 (5.2)	3
01 to 05	49 (63.6)	40
06 to 10	17 (22)	10
11 to 15	4 (5.2)	4
16 to 20	2 (2.7)	1
>20	1 (1.3)	1
mMRC grades		
Grade0	0 (0)	0
Grade1	35 (45.5)	24
Grade2	36 (46.8)	29
Grade3	6 (7.7)	6
Grade4	0 (0)	0
Smoking status		
Never Smoker	10 (13)	6
Ex Smoker	41 (53.2)	29
Current	26 (33.8)	24
Smoking Index		
Nil	10 (13)	6
<100	8 (10.3)	8
100-300	20 (26)	17
>300	39 (50.7)	28
Biomass exposure:		
Present	42 (54.5)	29
Absent	35 (45.5)	30
BMI Range (kg/m2)**:**		
Below normal: <18	31 (40.2)	24
NormalBMI:18-22.9	26 (33.8)	19
Overweight:23.0-24.9	10 (13)	8
Obesity: >25	10 (13)	8
Avg: 14.6-30.4(16.537)		
Severity(GOLD)		
Normal study	8 (10.4)	4
Mild obstruction	11 (14.3)	9
Moderate obstruction	26 (33.7)	20
Severe obstruction	14 (18.2)	11
Very severe obstruction	18 (23.4)	15

Beedi smokers were more prevalent than cigarette smokers. Nearly half of the smokers i.e., 34(44.2%) were heavy smokers with a smoking index of >300. Majority of patients were having rural background and biomass exposure was present in significant number of patients (54.5%).

Table 3: ECG Characteristics of the study population

ECG Characteristics(n=77)	No. (%)
Heart rate/min: (mean: 107.2)	
<60	5 (6.5)
60 to 100	64 (83.1)
>100	8 (10.4)
Rhythm	
Regular	73 (94.8)
Irregular	4 (5.2)
Axis	
Normal	44 (57.1)
Right	18 (23.4)
Left	13 (16.9)
North west	2 (2.6)
P- pulmonale:	24 (31.2)
Ptf-V_1(significant)	3 (3.9)
P-wave axis verticalisation(PWAV)	59 (76.6)
-ve P-wave in V_1	20 (26)
P- mitrale	18 (31.2)
QTc interval	
Normal	37 (48)
Borderline	25 (32.5)
Prolonged	15 (19.5)
Poor R-wave progression(PRWP)	23 (29.9)
Left bundle branch block(LBBB)	5 (6.5)
Left ventricular hypertrophy(LVH)	5 (6.5)
Right bundle branch block (RBBB)	2 (2.6)
Right ventricular hypertrophy(RVH)	8 (10.4)

Exposure to biomass fuel was more prevalent in female (89.5%) and a major contributor in the development of COPD among female particularly in rural areas. All of them had breathlessness as their primary symptom which was graded on the basis of mMRC (modified medical research council) classification. Most of the patients i.e. 71(92.3%) had mMRC grade 1 to 2 dyspnoea because we included only patients with stable COPD. The average BMI was 16.5kg/m^2 which is below normal. COPD patients were categorised into mild, moderate, severe and very severe groups as per GOLD criteria based on post-bronchodilator spirometry. Majority of patients 33.7% had moderate obstruction, whereas 23.4% patients had very severe obstruction. Severe obstruction and mild obstruction were seen in 14(18.2%) and 11(14.3%) patients respectively. Spirometric study was normal in 8 (10.4%) patients.

The ECG characteristics of the study population, with their number and percentage are shown in [Table 3]. Most of the patients (64) had a heart rate varying from 60 to 100 per minute with a mean of 107.2/min. It was observed that age, duration of illness, and mMRC grading had a relation with the heart rate which was statistically significant. Majority of patients had regular rhythm with only 3(3.9%) patients having an irregular rhythm. More than half (57.1%) of the patients had normal axis, 18(23.4%) patients had right axis deviation (RAD) and 13(16.9%) had left axis. Only 2(2.6%) patients had an

axis in the north western region. PWAV was observed in 59(76.6%) patients. Patients with PWAV was compared with various groups, [Table 2] summarises the same with their number and P-values. The frequency among male was significantly higher than female population in the study with 48 male and 11 female. The difference was statistically significant with P-value of 0.026. Other groups showed no statistically significant relation with PWAV.

Table 4: Echocardiography findings in the study population

Echo findings(n=66)	No. (%)
Left atrial enlargement (LAE)	2 (3.0)
Left ventricular enlargement (LVE)	5 (7.6)
Right atrial enlargement (RAE)	21 (30.9)
Right ventricular enlargement (RVE)	23 (34.8)
Left ventricular diastolic dysfunction (LVDD)	52 (76.4)
Tricuspid regurgitation (TR)	46 (70.5)
Pulmonary hypertension (PH) (TR Gradient >30)	32 (56.0)
Right ventricular dysfunction (RVD)	3 (4.5)

Twenty (26%) patients showed negative P-wave in V_1. Ptf-V_1 was measured in patients with positive P-wave in V_1. It was significant only in 3(3.9%) patients. Only one patient had absent P-wave i.e., atrial fibrillation. P-pulmonale was seen in 16 (20.8%) patients. No patient was observed to have Himalayan P-wave (amplitude >9mm). Poor R-wave progression was seen in 23(29.9%) patients. Right ventricular hypertrophy was seen in 8(10.4%) patients. QTc interval was normal in 48%, borderline in 32.5% and prolonged in 19.5%.

On echocardiography right atrial enlargement was present in 30.9% patients, right ventricular enlargement was observed in 34.8%, left ventricular diastolic dysfunction was present in 76.4%, measurable tricuspid regurgitation was observed in 70.5% patients, pulmonary hypertension was present in 56% patients. Right ventricular dysfunction, left atrial enlargement and left ventricular enlargement were not present in significant number. Echocardiography findings are summarised in [Table 4].

DISCUSSION

COPD is an important public health problem and a major cause of morbidity and mortality in both developed and developing countries. Cardiovascular co-morbidities are frequently seen in COPD patients and large studies have shown cardiovascular events as a leading cause of COPD-related mortality.[12-14]

Identification of ECG abnormalities may have significant implications in the management and outcome of patients with COPD. Though ECG can be used to screen various cardiac abnormalities, electrical activities are often influenced by the COPD changes:[5] The voluminous lungs have an insulating effect and there by diminishing the transmission of electrical potentials to the registering electrodes. The heart descends to a lower position within the thorax due to lowering of the diaphragm. This will alter the position of the heart relative to the conventional precordial electrode positions. The right ventricle and the right atrium become compromised due to a reduction of the pulmonary vascular bed and also due to chronic hypoxemia. This will result in RVH and dilatation as well as RAE.

Echocardiography plays an important role in determining cardiac changes in relation to COPD and also to detect subclinical cardiovascular abnormalities. Various studies have been done on ECG and echocardiographic abnormalities in COPD patients.[5,15,16]

Our study included a total of 77 stable COPD patients. Majority of the patients were in the age group of 60 to 69 year with mean age of 64.46 years. Majority of patients in our study were male with a male to female ratio of 3:1.PWAV was observed in significant number of patients i.e., 59(76.6%) among which 48 were male and 11 were female and the difference in their number was statistically significant with P-value of 0.026. The difference may be significant because there was male predominance in the study population and ECG findings may be masked in female because of excess soft tissue over chest compared to male. This finding is also supported by the results observed in relation to BMI. Though the association between BMI and PWAV is not statistically significant, there is definite inverse relation with BMI. We know that electrical activities of heart are better conducted in a lean thin patient than obese patient because of lack of interference by the fat tissue to the electrical waves. We can also say that emphysematous changes may be more prevalent in patients with low BMI.

Chhabra *et al.*[17] reported that PWAV is highly effective for screening emphysema and degree of verticalization provides a gross quantification of the disease. The results also showed an inverse correlation of PWAV with FEV_1. Though in our study the relation of PWAV with FEV_1 was not statistically significant the occurrence was frequent in patients showing obstruction than those showing normal study on spirometry, thus supporting the Chhabra *et al.* reports, but with the current study being prospective we could not infer on the effectiveness of PWAV for screening emphysema.

We know that both significant-Ptf with positive P-wave and negative P-wave in V_1 suggest emphysema and downward right atrial position caused by downward displacement of the diaphragm[10], but 20 (26%) patients showed negative P-wave in V_1 and only 3 (3.9%) patients had significant-Ptf suggesting that

negative P-wave in V_1 is the commonest type of significant-Ptf which is consistent with the reports by Chhabra *et al.*[10]

P-pulmonale indicates right atrial enlargement, it was seen in 24 (31.2%) patients and echocardiography revealed right atrial enlargement in 21patients which is a comparable number. ECG showed P-mitrale in a total of 18 (23.4%) patients, but only one out of 18 showed left atrial enlargement on echocardiography giving an inference that P-mitrale is nonspecific for left atrial enlargement or overload particularly in COPD patients. Similarly Ishikawa *et al.*[18]in their study concluded that twinned peaked P-wave or pseudo P-mitrale is diagnostically non-specific and its mere existence cannot imply the existence of left atrial overload. So P-pulmonale may be a reliable indicator of right atrial enlargement where as presence of P-mitrale is not conclusive of left atrial enlargement in COPD patients.

Thus change in ECG characteristics in COPD patients should be meticulously studied and compared with echocardiography findings as the ECG changes may be due to change in structure of the lung and position of the heart due to COPD rather than cardiac abnormality alone.

CONCLUSION

Cardiovascular co-morbidities are seen frequently in COPD patients and have important prognostic implication. Though not specific, ECG may reveal various functional and structural abnormalities of the heart in relation to COPD. P-wave axis verticalisation, negative P-wave in V_1, significant-Ptf and P-pulmonale are the P-wave abnormalities frequently encountered in COPD patients. Though P-wave axis verticalisation, significant-Ptf, P-mitrale all suggestive of change in structure of the lung and position of the heart due to COPD, P-wave axis verticalisation may be the most commonly seen P-wave abnormality among the three. Negative P-wave in V_1 is the frequently seen type of significant-Ptf. P- pulmonale may be suggestive of right atrial enlargement but presence of P-mitrale is not conclusive of left atrial overload particularly in patients of COPD. Echocardiography should be done routinely in all patients of COPD to confirm ECG findings and to diagnose pulmonary hypertension, cor-pulmonale and other subclinical cardiovascular co-morbidities like left ventricular diastolic dysfunction.

REFERENCES

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: http://www.goldcopd.org/. Accessed March 15th, 2016.
2. Choudhury G, Rabinovich R, MacNee W. Comorbidities and systemic effects of chronic obstructive pulmonary disease. Clin Chest Med. 2014;35(1):101–30.
3. Anthonisen NR, Connett JE, Enright PL, Manfreda J; Lung Health Study Research Group. Hospitalizations and mortality in the Lung Health Study. Am J Respir Crit Care Med. 2002 Aug 1;166(3):333-9.
4. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: Role of comorbidities. Eur Respir J. 2006 Dec;28(6):1245-57.
5. Holtzman D, Aronow WS, Mellana WM, Sharma M, Mehta N, Lim J, et al. ECG abnormalities in patients with severe versus mild or moderate chronic obstructive pulmonary disease followed in an academic outpatient pulmonary clinic. Ann Noninvasive Electrocardiol. 2011 Jan; 16(1):30-2.
6. Boushy, S.F., Aboumrad, et al, 1971; "Electrocardiogram in chronic obstructive pulmonary disease". Amer. Rev. Resp. Disease, 104: 1067-70.
7. M.K. Tandon, M.D. Feb. 1973; "Correlation of Electrocordiographic feature with Airway obstruction in chronic Bronchitis". Chest, Vol. 63, No 2: 146 –148.
8. Padmavathi and Veena Raizada. Electrocardiogram in chronic cor pulmonale. British Heart Journal 1972 ; 34 : 658-667.
9. Aktürk F, Bıyık İ, Kocaş C, Ertürk M, Yalçın AA, Savaş AU, et al. The role of ECG in evaluation of severity of chronic obstructive pulmonary disease in daily clinical practice. Tuberk Toraks 2013; 61(1):38-42.
10. Chhabra L, Chaubey VK, Kothagundla C, Bajaj R, Kaul S, Spodick DH. P-wave indices in patients with pulmonary emphysema: do P-terminal forcef and Interatrial block have confounding effects? Int J Chron Obstruct Pulmon Dis. 2013; 8:245-50.
11. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al.*; ATS/ERS Task Force. Standardisation of spirometry. Eur Respir J 2005;26:319-38.
12. Sin DD, Man SF. Why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular diseases? The potential role of systemic inflammation in chronic obstructive pulmonary disease. Circulation. 2003 Mar 25; 107(11):1514-9.
13. Sidney S, Sorel M, Quesenberry CP Jr, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. Chest 2005; 128: 2068–2075.
14. Maclay JD, MacNee W. Cardiovascular disease in COPD: Mechanisms. Chest 2013; 143: 798–807.
15. Rodman DM, Lowenstein SR, Rodman T. The electrocardiogram in chronic obstructive pulmonary disease. J Emerg Med 8 (1990) 607–15.
16. Rudski LG, Lai WW et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010 Jul; 23(7):685-713; quiz 786-8.
17. Chhabra L, Sareen P, Perli D, Srinivasan I, Spodick DH. Vertical P-wave axis: the ECG synonym for pulmonary emphysema and its severity. Indian Heart J. 2012 Jan-Feb; 64(1):40-2.
18. Ishikawa K, Pipberger HV. Critical evaluation of the twin peaked P wave ("pseudo-P mitrale") in orthogonal electrocardiograms. J Electrocardiol.1980 Apr; 13(2):181-4.