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Original Research Article

Study of the diagnostic and therapeutic challenges in patients with coexistent chronic obstructive pulmonary disease and chronic heart failure

Samir Rafla, Ali Hassan Aboelhoda, Rania Ahmed Swied*, Azza Ahmed Khamis and Mohamed Saeed Elhoshy**

Alexandria University, Faculty of Medicine, Cardiology Department, Chest Department* and Research Institute**, Egypt

Corresponding Author: Samir Rafla
E-mail: smrafla@yahoo.com

Abstract

The aim of this study was to determine the impact of chronic obstructive pulmonary disease treatment on the clinical condition of patients with heart failure. Forty Patients were enrolled in this study with chronic obstructive pulmonary disease co-existent with heart failure (EF <50%). All patients enrolled in this study were males (100%). Most of the studied patients (40%) were aged between 61 and 70 years old. Definition of COPD: when FEV1 was less than 70%. About smoking: 25 patients stopped smoking (62.5%), and 15 patients didn't stop smoking (37.5%). Risk factors: 34 patients (pts) (85%) suffered from systolic hypertension, 18 pts (45%) suffered from diabetes, and 28 pts (70%) had dyslipidemia. All patients were smokers (97.5%) except 1 patient was passively smoking and 17 patients were NYHA class III (42.5%), 23 patients were NYHA class II. Average weight and height of studied patients was 88.1 ± 14.7kg and 172.5 ± 7.7cm respectively. Mean body mass index (weight/ (height) 2) was 29.2 ± 6kg/m^2. ECG findings: Among studied patients, ischemic changes in ECG were present in 37 cases (92.5%). Improvement of COPD is associated with improvement of heart failure. Cessation of smoking is the best marker of possible improvement of both diseases. The use of sympathomimetics as inhalers or tablets had no deleterious effect on cardiac function.

Keywords: Spirometry, Chronic Obstructive Pulmonary Disease (COPD), Heart Failure, Smoking, Sympathomimetic inhalers

INTRODUCTION

Heart failure and COPD are common and growing major health problems that have a great burden on patients and community (Müllerova et al., 2013). COPD is common among patients with HF and is associated with further increase in morbidity and mortality (Mentz and Felker, 2013). Several studies have addressed the prevalence of COPD in HF patients (Rutten et al., 2005). The prevalence showed by these studies ranges from 20% to 30 % (Sirak et al., 2004).

We have conducted a study aiming to evaluate possible merits of COPD treatment on clinical condition of patients with HF.

METHODS

In this prospective study all patients were subjected to

1. Thorough history taking with special emphasis on:
   - Patient complaint: grade of dyspnea, cough, wheezes, paroxysmal nocturnal dyspnea, orthopnea.
   - Cardiovascular risk factors including: age, gender, smoking status, hypertension, diabetes mellitus, dyslipidemia, family history of coronary artery disease
   - Prior myocardial infarction or Coronary Artery Bypass Graft (CABG) or coronary intervention.
   - New York Heart Association (NYHA) class.

2. Clinical examination:
All the patients were subjected to full clinical evaluation including; vital signs and detailed cardiac and pulmonary examination.

7. Laboratory investigations:
Including complete blood picture (CBC), fasting and/or random blood glucose, lipid profile, Cardiac biomarkers: serum Troponin I and CKMB, renal functions including blood urea and serum creatinine, liver functions and coagulation profile.

7. Electrocardiogram:
A standard 12 lead resting ECG was performed. Diagnostic criteria for the presence of coronary lesion is published before.

5. Radiological investigations: Plain chest x-ray (P-A view) was done for all patients.

6. Echocardiography:
Echocardiographic examinations were performed using standard equipment (HD11 XE PHILIPS) with a phased array transducer.

- Left ventricular ejection fraction (LVEF) was calculated fromtwo dimensional guided M-mode measurement of LV minor axis internal dimensions. And from apical 4-chamber images using the modified Simpson's method.
- Left ventricular diastolic function was assessed using E/A ratio, E and A velocities.
- Pulmonary artery systolic pressure by TR peak velocity: Continuous wave (CW) Doppler of the tricuspid regurgitation (TR) trace is used to measure the difference in pressures between the right ventricle and right atrium. The simplified Bernoulli equation (P = 4[Trmax] 2) is used to calculate this pressure difference using peak TR velocity. This method correlates well with PASP on right heart 2atheterization. A peak TR velocity value of ≤ 2.8 m/s is considered normal.

7. Spirometry:
- Spirometric examination with SP10W SPIROMETER was used.
- The following results were obtained: [121] FEV□ (Forced Expiratory Volume in one second), FVC: (Forced Vital Capacity), FEV□/FVC ratio& FEF 25-75%: (Forced Expiratory Flow between 25-75% of vital capacity) and PEF (peak expiratory flow).
- Precautions prior to spirometry:

Prior to performing spirometry, the patient's identification should be checked, their weight, height, age, sex, calculated body mass.

RESULTS

Forty patients were enrolled in this study with co-existent heat failure and chronic obstructive pulmonary disease. There was positive family history for cardiac diseases in 36 cases (90%), negative family in 4 cases (10%). 25 patients stopped smoking (62.5%), and 15 patients didn't stop smoking (37.5%). Among studied cases, 34 cases (85%) suffered from systolic hypertension, 18 cases (45%) suffered from diabetes, and 28 cases (70%) had dyslipidemia. All patients were smoker (97.5%) except 1 patient was passively smoking.

Distribution of patients according NYHA classification: 17 patients were NYHA class III (42.5%), 23patients were NYHA class II.

Average weight and height of studied patients was 88.10 ± 14.73kg &172.55 ± 7.71cm respectively. Mean body mass index (weight/ (height) 2 was 29.22 ± 6.06kg/ m^2.

ECG findings: Among studied patients, ischemic changes in ECG were present in 37 cases (92.5%).

ECHO Data: Baseline echo data to all patients showed ejection faction (EF) ranged from19.05 to 50.58 %in baseline echocardiography assessment with a mean 32.74 ± 9.10.

- Two months later, follow up echo showed EF ranged from1 9.36 – 56.63% with a mean 36.18 ± 10.05 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.
- Baseline echo data to all patients showed Left Ventricular Diastolic Dimension (LVDD) ranged from 54.0 – 83.0mm/m2in baseline echocardiography assessment with a mean 68.52 ± 7.50.
- Two months later, follow up echo showed LVDD ranged from 47.0 – 87.0 mm/m2with a mean 67.0 ± 9.08 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.
- Baseline echo data to all patients showed Left Ventricular systolic Dimension (LVSD) ranged from 42.0 – 81.0mm/m2in baseline echocardiography assessment with a mean 60.95 ± 8.92.
- Two months later, follow up echo showed LVSD ranged from 39.0 – 78.0mm/m2with a mean 58.05 ± 10.21showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.
- Baseline echo data to all patients showed right ventricular systolic pressure (RVSP) ranged from 18.0 – 86.0 mmHg in baseline echocardiography assessment with a mean 47.90 ± 18.76.
- Two months later, follow up echo showed (RVSP) ranged from 16.0 – 81.0mmHg with a mean 45.40 ± 18.0 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.

The European Society of Cardiology guidelines for the diagnosis Pulmonary Hypertension suggest considering: PH unlikely for TRV less than or equal 2.8 m/sec, SPAP less than or equal 36 mm Hg (assuming RAP of 5 mmHg), and no additional echocardiographic signs of PH.

1. PH possible for TRV less than or equal 2.8 m/sec and SPAP less than or equal 36 mm Hg but the presence of additional echocardiographic signs of PH or TRV of 2.9 to 3.4 m/sec and SPAP of 37 to 50 mm Hg with or without additional signs of PH.

Table 1. Descriptive analysis of the studied cases according to ECHO data (n=40)

ECHO Data	Baseline	Follow up	Test of sig.	p	Change
EF					
Min. – Max.	19.05 – 50.58	19.36 – 56.63			
Mean ± SD.	32.74 ± 9.10	36.18 ± 10.05	t= 3.247*	0.002*	3.44±6.70
Median	31.15	34.98			
LVDD					
Min. – Max.	54.0 – 83.0	47.0 – 87.0			
Mean ± SD.	68.52 ± 7.50	67.0 ± 9.08	t= 2.103*	0.042*	-1.53±4.59
Median	70.0	67.0			
LVSD					
Min. – Max.	42.0 – 81.0	39.0 – 78.0			
Mean ± SD.	60.95 ± 8.92	58.05 ± 10.21	t= 3.315*	0.002*	-2.90±5.53
Median	61.0	56.50			
RSVP					
Min. – Max.	18.0 – 86.0	16.0 – 81.0			
Mean ± SD.	47.67 ± 18.67	45.03±17.86	Z= 2.026*	0.043*	-2.65±7.45
Median	50.50	43.0			
LV mass					
Min. – Max.	176.0 – 727.0	112.0 – 639.0			
Mean ± SD.	403.53±130.59	385.4 ± 124.9	Z= 2.247*	0.025*	-18.1±47.3
Median	414.50	401.0			
DD	No. %	No. %			
No	0 0.0	0 0.0	-	-	
Yes	40 100.0	40 100.0			

T, p: t and p values for Paired t-test for comparing between pre and post
Z, p: Z and p values for Wilcoxon signed ranks test for comparing between pre and post
*: Statistically significant at p ≤ 0.05

2. PH likely for TRV > 3.4 m/sec and SPAP > 50 mm Hg with or without additional signs of PH.

• Baseline echo data to all patients showed LV mass ranged from 176.0 – 727.0g/m2 in baseline echocardiography assessment with a mean 403.5 ± 130.4

• Two months later, follow up echo showed LV mass ranged from 112.0 – 639g/m2 with a mean 385.4 ± 124.9.0 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.

• All patients showed diastolic dysfunction (DD) in addition to systolic dysfunction (100%).

• Follow up Echocardiography showed improvement in (EF & LVDD & LVSD & LV mass) with p value equal (0.002, 0.042, 0.002, 0.043, 0.025 respectively). (Table 1)

Spirometry Data

• Baseline spirometric data to all patients showed forced vital capacity (FVC) ranged from 0.55 – 2.60 liters in pre-treatment of COPD with a mean 1.31 ± 0.52.

• Two months later, follow up spirometric data showed (FVC) ranged from 0.36 – 2.84 liters with a mean 1.62 ± 0.59 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.

• Baseline spirometric data to all patients showed Forced Expiratory Volume in the first second (FEV1) ranged from 0.39 – 2.43 liters in pre-treatment of COPD with a mean 1.16 ± 0.51.

• Two months later, follow up spirometric data showed (FEV1) ranged from 0.30 – 2.50 liters with a mean 1.42 ± 0.56 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.

• .Baseline spirometric data to all patients showed Peak Expiratory Flow Rate (PEFR) ranged from 0.50-5.80L/sec in pre-treatment of COPD with a mean 2.02 ± 1.28.

• Two months later, follow up spirometric data showed (PEFR) ranged from 0.40 – 7.65liters with a mean 2.59 ± 1.58 showing obvious improvement after addition of COPD treatment to patients on anti-failure treatment.

• Baseline spirometric data to all patients showed FEV1/ FVC ratio ranged from 0.58 – 1.01in pre-treatment of COPD with a mean 0.88 ± 0.10.

• Two months later, follow up spirometric data showed FEV1/ FVC ratio ranged from 0.52 – 1.02 with a mean 0.88 ± 0.12showing nearly same ratio after addition of COPD treatment to patients on anti-failure treatment.

• Follow up spirometry showed improvement in (FVC &FEV1&PEFR) with p value equal(0.014, 0.035, 0.036,0.952 respectively) but didn't show improvement in FEV1/ FVC ratio with p value equal 0.952.

Outcome: Outcome of the studied patients was assessed by comparing follow up the echocardiographic and spirometric data to baseline data. (Table 2)

Table 2. Descriptive analysis of the studied cases according to Spirometer (n=40)

Spirometer	Baseline	Follow up	Test of sig.	p	Change
FVC(liters)					
Min. – Max.	0.55 – 2.60	0.36 – 2.84	t= 2.579*	0.014*	0.31±0.76
Mean ± SD.	1.31 ± 0.52	1.62 ± 0.59			
Median	1.23	1.60			
FEV1(liters)					
Min. – Max.	0.39 – 2.43	0.30 – 2.50	Z= 2.110*	0.035*	0.26±0.75
Mean ± SD.	1.16 ± 0.51	1.42 ± 0.56			
Median	0.98	1.39			
PEFR(L/sec)					
Min. – Max.	0.50 – 5.80	0.40 – 7.65	Z= 2.097*	0.036*	0.55±1.88
Mean ± SD.	2.05 ± 1.28	2.59 ± 1.58			
Median	1.88	2.29			
FEV1/ FVC ratio					
Min. – Max.	0.58 – 1.01	0.52 – 1.02	t= 0.061	0.952	0.0±0.15
Mean ± SD.	0.88 ± 0.10	0.88 ± 0.12			
Median	0.89	0.90			

T, p: t and p values for Paired t-test for comparing between pre and post
Z, p: Z and p values for Wilcoxon signed ranks test for comparing between pre and post
*: Statistically significant at p ≤ 0.05

Table 3. Relation between the improvement in ejection fraction and spirometric data (n=40)

EF Improvement	Improved COPD				P
	No (n= 15)		Yes (n= 25)		
	No.	%	No.	%	
Not Improved	15	100.0	0	0.0	<0.001*
Improved	0	0.0	25	100.0	

Percentage of improvement in Echocardiographic Data: Twenty five patients (62.5%) showed improvement in ejection fraction, as regards left ventricular dimensions ,nineteen patients (47.5%)showed improvement in diastolic dimensions and twenty one patients (52.5%) showed improvement in systolic dimensions, nineteen patients (47.5%) showed improvement in right ventricular systolic pressure, and twenty five patients (62.5%) showed improvement in left ventricle mass.

Percentage of improvement in spirometric Data: Twenty five patients (62.5%) showed improvement in FVC&FEV1&PEF.

All cases that improved regarding echocardiographic data showed concomitant improvement in spirometric data &none of the patients who didn't improve regarding echocardiographic data showed improvement in spirometric data. Table 3

Treatment

All forty patients were compliant on Mineralocorticoid receptor antagonists (MRA) for heart failure and long-acting beta agonists (LABA) for COPD (100%),Thirty four patients were compliant on angiotensin-converting-enzyme inhibitor (ACEI) (85%) for heart failure but 6 cases weren't compliant on ACEI (15%),Thirty eight patients were compliant on B blockers (BB)(95%) for heart failure but 2 cases weren't compliant on BB (5%), Twenty one patients were compliant on Long-acting muscarinic antagonists (LAMAs) (52.5%) for COPD but 19 patients weren't compliant on LAMAs (47.5%).

Not all patients received the same treatment as there is difference in socioeconomic status, renal functions and heart rate in ECG. LABA and LAMA are considered the safest inhalers in cardiac patients.

Relationship between smoking cessation and improvement in ejection fraction and FEV1 in studied patients

Not all studied patients were responding to our smoking cessation counseling advice in addition to other COPD treatment, only twenty four patients from the total number of the studied patient quit smoking, all patients who stopped smoking showed improvement in FEV1 and EF values in comparison to baseline values. (Table 4, Figure 1)

Table 4. Effect of smoking cessation on EF and FEV1

	Smoking cessation				X^2	p
	No (n= 15)		Yes (n= 24)			
	No.	%	No.	%		
EF						
Not Improved	15	100.0	0	0.0	39.00*	<0.001*
Improved	0	0.0	24	100.0		
FEV1						
Not Improved	15	100.0	0	0.0	39.00*	<0.001*
Improved	0	0.0	24	100.0		

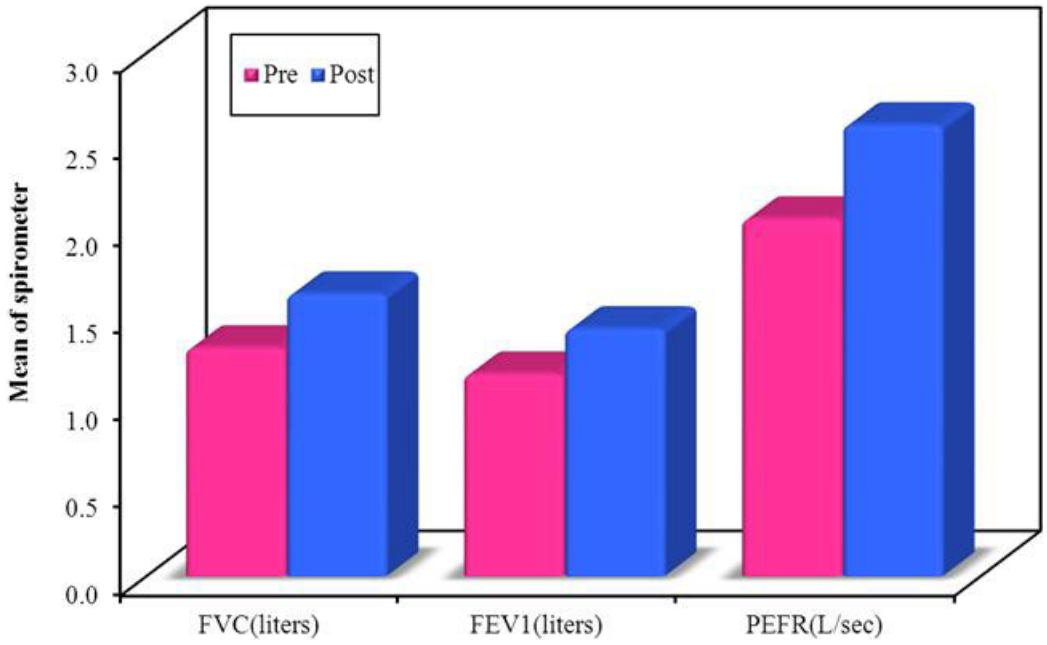

Figure 1. Descriptive analysis of the studied cases according to Spirometer (n=40)

DISCUSSION

Heart failure and COPD are common and growing major health problems that have a great burden on patients and community (Müllerova et al., 2013). COPD is common among patients with HF and is associated with further increase in morbidity and mortality (Mentz and Felker, 2013). Recognition of the impact of comorbid conditions such as COPD on the characteristics and outcomes of patients with HF may represent a first step to identify strategies to improve outcomes (Curkendall et al., 2006).

We have conducted a study aiming to evaluate possible merits of COPD treatment on clinical condition of patients with HF. Our study included 40 male patients with co-existent HF and COPD. The improvement of COPD condition was measured in terms of changes in FEV1, FVC% and PEFR while improvement of cardiac condition was measured in terms of changes in EF%, LVDD, LVSD and LV mass. We have concluded that improvement of COPD is associated with improvement of heart failure. Cessation of smoking is the best marker of possible improvement of both.

Komamura et al. completely matched our results in that treatment of COPD significantly improved cardiac condition in patients with HF. This study differed from our study in that they used spirogram, the distance of 6-minute walk (6MWD), biomarkers of heart failure and St George's Respiratory Questionnaire (SGRQ) in addition to ECHO to assess the improvement of chest and cardiac condition. They found that COPD treatment improved not only lung condition as measured by FEV1, SGRQ and 6MWD, but also caused significant improvement of HF condition as measured by ECHO and level of BNP. They also found that there was a significant correlation between the percent decrease of the plasma BNP level and the absolute change of FEV1 (Komamura et al., 2018).

Minasian et al is a study that agreed to our results

also. They included 116 patients with systolic dysfunction in their study. All of their studied patients were subjected to spirometry and Borg dyspnea measurement before and after air way obstruction treatment. They noted improvement of all spirometry components and improvement of ECHO measurements like our study. They concluded that treatment of airway obstruction may have an additional role in the management of patients with chronic HF because of their potential to improve pulmonary function (Komamura et al., 2018).

Guder et al also agreed with our results in that treatment of COPD may have a positive impact in cardiac condition in the setting of HF. However they differed from our study in two main points. First, they suggest that improvement may be a short term benefit with use of bronchodilators. Second point is that they concluded that bronchodilators may improve cardiac condition even in patients without history of COPD (Güder et al., 2014).

Uren et al in a study carried on 10 patients with airway obstruction and systolic dysfunction. They matched our results in that treating airway obstruction was associated with improvement of cardiac condition. They differed from our study in that they measured improved cardiac condition by increase in exercise capacity (Minasian et al., 2013).

Similarly Sunderrajan et al concluded that treatment of COPD had a positive impact on cardiac condition in patient with coexistent HF as it significantly improved EF%. Their study material was 30 patients with severe chronic obstructive pulmonary disease (COPD) with a mean forced expiratory volume in 1 s of 0.79±0.06 L. They used ECG-synchronized gated equilibrium radionuclide ventriculography to assess the ventricular function and it showed decreased RVEF in 27 patients and LVEF in 16 patients (Güder et al., 2014).

Similar improvements in ventricular function were noted by Matthay and colleagues, using hemodynamic and radionuclide techniques, they studied eight patients with COPD, pulmonary hypertension, and decompensated right ventricular function. They observed that the improvement of COPD resulted in a decreased pulmonary vascular resistance index, increased RVEF and cardiac index, and no change in mean pulmonary arterial pressure. Systemic vascular resistance also decreased, resulting in increased LVEF and increased cardiac index with no significant change in arterial BP (Uren et al., 1993).

The possible explanation of our results may be that treating COPD and its improvement leads to decrease work load on the heart by several mechanism. Improved oxygen delivery seen with improved COPD condition is observed by increase in Spo2 and is one of mechanisms by which COPD treatment improves cardiac condition. Improved lung volumes and decreased inflation has also its positive effect on cardiac muscle function.

However, some studies (Cazzola et al., 2005; Lipworth et al., 2016; Salpeter et al., 2005; Hawkins et al., 2009; Jabbour et al., 2010; Komamura et al., 2018) did disagree with our results. They had opposite conclusions ranged from no benefit of COPD treatment to a possible negative impact of the treatment on cardiac condition. (Hawkins et al., 2009; Cazzola et al., 2005) showed that COPD treatment was associated with increased all-cause mortality, cardiovascular death, HF hospitalization, and major adverse cardiovascular events.

The explanation why these studies had completely different results from our study may be due to the use of high doses of long acting beta agonists which have wide range of side effects on cardiac muscles that include arrhythmias, tachycardia, hypokalaemia, QT prolongation and disturbed autonomic modulation and the under use of beta-2 receptor antagonism for heart failure as their association with bronchoconstriction (Sunderrajan et al., 1983).

Otherwise recent data suggest that the prescription of beta-blockers in patients with heart disease has doubled in the last decade in both patients with and without COPD (Matthay et al., 1981; Hawkins et al., 2010).

A number of studies indicate that cardio-selective beta-blockers exert minimal impact on reversible or severe airflow obstruction. Peter Alter et al is a study carried out in Marburg, Germany and matched lung function and LV wall stress in patients with COPD, they included 641 patients with doctor diagnosis of COPD or chronic (non-obstructive) bronchitis, all of their studied patients were subjected to Spirometry/body plethysmography, Echocardiography and wall stress with availability for repeated study visits over at least 18months. They noted that there is a statistical relationship between lung function and LV wall stress in patients with COPD. These findings support the hypothesis that the development of LV impairment inpatients with COPD could be initiated or promoted at least in part, by mechanical factors exerted by the lung disorder. This study revealed the effect of COPD on the ejection fraction.

Limitations

The main limitation to our study is the relatively small number of studied patients. Not using a control group may be another limitation. Relatively short period of follow up is another limitation. So, we strongly recommend further study with larger numbers of patients and longer follow up periods.

Conflict of interest

The authors have no conflict of interest.

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