



Original Article

Evaluation for airway obstruction in adult patients with stable ischemic heart disease



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ABSTRACT

Background: Ischemic heart disease (IHD) and chronic airway disease (COPD and Asthma) are major epidemics accounting for significant mortality and morbidity. The combination presents many diagnostic challenges. Clinical symptoms and signs frequently overlap. There is a need for airway evaluation in these patients to plan appropriate management.

Methods: Consecutive stable IHD patients attending the cardiology OPD in a tertiary care centre were interviewed for collecting basic demographic information, brief medical, occupational, personal history and risk factors for coronary artery disease and airway disease, modified medical research centre (MMRC) grade for dyspnea, quality of life-St. George respiratory questionnaire (SGRQ), spirometry and six-min walk tests. Patients with chronic airway obstruction were treated as per guidelines and were followed up at 3rd month with spirometry, six-minute walk test and SGRQ.

Results: One hundred fourteen consecutive patients with stable cardiac disease were included (Males-88, Females-26). Mean age was 58.89 ± 12.24 years, 53.50% were smokers, 31.56% were alcoholics, 40.35% diabetics, 47.36% hypertensive. Twenty five patients had airway obstruction on spirometry (COPD-13 and Asthma-12) and none were on treatment. Thirty-one patients had cough and 48 patients had dyspnea. Patients with abnormal spirometry had higher symptoms, lower exercise tolerance and quality of life. Treatment with appropriate respiratory medications resulted in increase in lung function, quality of life and exercise tolerance at 3rd month.

Conclusion: Chronic respiratory disease in patients with stable IHD is frequent but often missed due to overlap of symptoms. Spirometry is a simple tool to recognize the underlying pulmonary condition and patients respond favorably with appropriate treatment

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1. Introduction

Ischemic heart diseases (IHD) and chronic respiratory diseases account for significant morbidity and mortality throughout the world.^{1,2} The combination of the two poses many difficulties in the diagnosis as clinical symptoms like dyspnea and cough frequently overlap.³ Although both conditions have been extensively studied separately, there is sparse data addressing the combination of both diseases.⁴ It is important to identify and appropriately manage chronic obstructive airway disease in IHD patients because these patients have poor prognosis compared to presence of either disease alone.^{5–7} Indeed it is shown that poor lung function is a strong predictor of cardiac mortality.^{8,9} Younger patients with

cardiac disease might have asthma and older patients with IHD might have underlying chronic obstructive pulmonary disease (COPD), which is often overlooked. Smoking, increasing age and systemic inflammation are the shared risk factors for the development of COPD as well as coronary artery disease and both often coexist.¹⁰

There is varying prevalence rate of COPD in patients with IHD (9–51%) due to different study design, population and confirmatory test used for diagnosis, with most studies observed one-quarter to one-third of the cardiac patients had COPD.^{9,11–18} Even though spirometry is gold standard for diagnosis of COPD it is often underutilized with only one-third of cardiac patients having undergone spirometry at least once, that leads to under diagnosis of COPD in cardiac patients.^{19–21} Spirometry must be done in all patients having cardiac disease.¹¹ There is a need to know the prevalence of respiratory diseases such as asthma and COPD in patients with stable IHD in Indian population, evaluate the effect of appropriate treatment for their respiratory disease on quality of life and exercise tolerance.

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2. Methodology

Study design: We conducted a prospective study in cardiology OPD in 1800 bedded tertiary care centre, JSS medical college and University, Mysuru during February to May 2016. Consecutive adult patients with IHD attending cardiology OPD for regular follow up were screened for inclusion and exclusion criteria and patients satisfying inclusion criteria were included in the study after taking informed consent. Inclusion criteria were adult patients with stable IHD on optimal cardiac medications for at least 3 months without worsening symptoms. Exclusion criteria were patients who refused to consent, patients with contraindication for spirometry and six minute walk test as per ATS guidelines, patients unable to perform spirometry or six minute walk test, hemodynamic instability and pregnancy were excluded from the study. Patients were interviewed with questionnaire containing

basic demographic information, brief medical (drug, frequency and duration), occupational and personal history (smoking index, alcohol intake) and St. George respiratory questionnaire (SGRQ) and chest x-ray. Spirometry and 6 min walk test was performed as per guidelines provided by American Thoracic Society (ATS) and Global Initiative for Obstructive Lung Disease (GOLD).

Spirometry (Easy on PC, NDD, Medizintechnik AG, Zurich, Switzerland) was performed by a trained staff and it included measurement of forced expiratory volume in first second (FEV1) and forced vital capacity (FVC) and peak expiratory volume in seated position using American Thoracic Society guidelines (ATS) and highest measurements among best three trials which is technically acceptable and reproducible were taken. Predicted values for FVC, FEV1 and FEV1/FVC were obtained by predicted equation defined by Knudson corrected for asian population (knudson 83×0.87). Both pre and post bronchodilator tests were

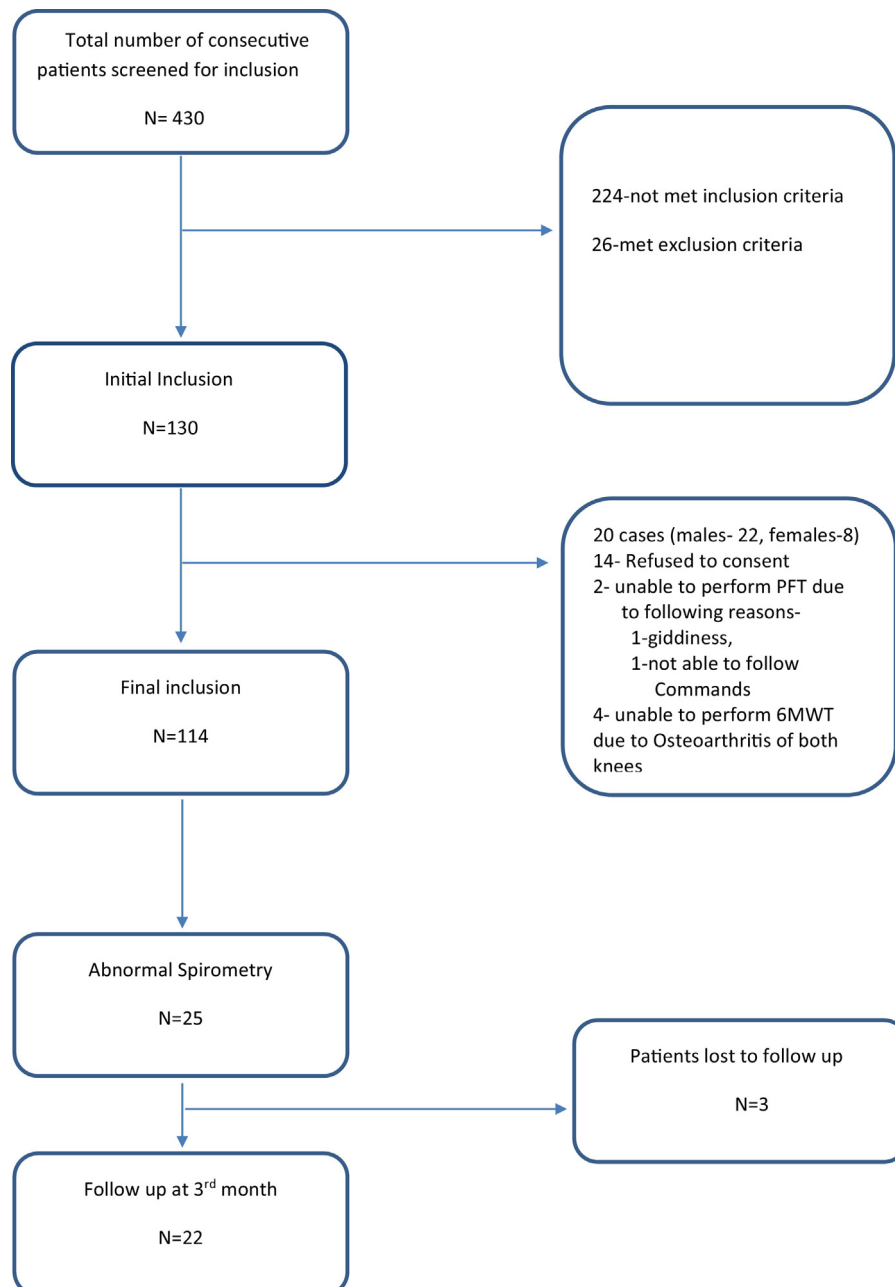


Fig. 1. Flow chart depicting flow of patients screened, included in the study and follow up at 3rd month.

performed. Post bronchodilator test was performed 15 min after inhalation of salbutamol nebulization. Pre bronchodilator test was performed to detect any reversibility. A record of FEV1/FVC ratio (post bronchodilator) <0.70 was categorized as COPD. The severity of COPD was classified as mild (FEV1 >80% of predicted), moderate (FEV1 50–80% of predicted), severe (FEV1 30–50% of predicted), very severe (FEV1 <30% of predicted) as per GOLD guidelines.²² Although true restrictive defect cannot be obtained on spirometry, a restrictive pattern was deduced from spirometry for categorization comparison only. A value of FVC less than Lower Limit of Normal (LLN) with normal FEV1/FVC ratio was labeled as having restrictive defect. Mixed pattern was labeled when there was both obstructive as well as restrictive pattern. Asthma was diagnosed as per GINA guidelines when there was significant reversibility of FEV1, more than 12% and 200 ml after bronchodilation.²³

Six minute walk test was performed by a trained physiotherapist in a 100 feet hall way after explaining the objective of the test. Vitals were recorded both before and after the test, which included pulse rate, blood pressure, respiratory rate and oxygen saturation. Patients were allowed to choose their own intensity of exercise and were allowed to stop and rest on a chair during test if required. Test was immediately stopped if patient developed any of the following: chest pain, intolerable dyspnea, leg cramps, staggering, sweating or pale appearance. Distance walked was recorded in a worksheet and percentage of predicted distance was calculated.

Echocardiography was done by single cardiologist to prevent inter observer variation –standard two dimensional views to determine left ventricular ejection fraction, right ventricular end diastolic diameter, left atrial and ventricular dimension, right ventricular systolic pressure, valve dimensions were recorded. All tests were done on the same day of visit to hospital.

We defined Stable IHD as presence of confirmed obstructive coronary artery disease without recent (<1 year) acute coronary syndrome or percutaneous intervention as per American College of Cardiology and American Heart Association task force.²⁴ We defined smoking status according to CDC as non-smokers (<100 cigarettes in life time), ex-smokers (quit >3 months back) and current smokers (quit <3 months or continuing to smoke).²⁵ All patients who were newly diagnosed with chronic respiratory diseases (COPD and asthma) were put on appropriate guideline based treatment and were followed up at 3rd month with repeat Spirometry, Six minute walk test and Quality of life questionnaire.

Ethical considerations: This study has got Institutional Ethics Committee clearance numbered JSSMC/PG/4366/2014-15 dated on 12-11-2014. Informed consent from patients was taken prior to inclusion in the study.

Statistical Analysis: Descriptive data are presented as frequencies (percentages) for discrete variables and as means (SDs) for continuous variables. For the comparisons between the two groups the Mann-Whitney *U* test was used or, when appropriate, the two-sample *t*-test. χ^2 -test was used to evaluate categorical factors. Paired *t*-test was used to know the difference between baseline and three month levels of various quantitative parameters. Correlations were performed using Pearson's correlation. All statistical tests were 2-tailed, and factors were considered statistically significant at $p < 0.05$. SPSS version 20 was used for all analysis.

3. Results

During the study period, we screened a cohort of 430 consecutive patients with cardiac disease who visited cardiology OPD. Of these, 134 patients were found to have stable IHD and were included initially in the study. Twenty patients were excluded from the study mainly because of following reasons: spirometry ATS criteria unmet, refusal to consent, unable to perform six-minute walk test. Finally 114 patients were included in the study (Fig. 1).

The baseline demographic characteristics of patients are enumerated in (Table 1). Mean age of the study population was 58.69 years, 88% of the study groups were men and 71% were smokers. Ninety-nine were on aspirin. Eighty-three patients were on beta-blockers and all were on selective beta blockers. All chest x-ray were normal, other than hyperinflated lung fields in 1.5% of COPD patients.

Abnormality in spirometry was observed in 25 (21.92%) patients. Of these, 13 patients had COPD (3 had GOLD grade1, 8 had GOLD grade2, 2 had GOLD grade3) and 12 patients had asthma (10 had mild intermittent, 3 had moderately persistent and 1 had severe persistent asthma as per GINA guidelines). Of the patients with abnormal spirometry, 88% of patients had dyspnea and 56% had cough. Three patients had no symptoms yet their spirometry showed significant bronchodilator response. Eight patients (8/13) with COPD were smokers and 2 had biomass exposures and were non-smokers. No patients with abnormal spirometry had a pulmonary evaluation or were on treatment for their underlying lung condition. Left ventricular ejection fraction and BMI was lower in patients with abnormal spirometry, which was statistically significant. There was no statistically significant effect of betablockers on spirometric abnormality. Patients with abnormal spirometry had more symptoms, poor quality of life and exercise tolerance (Table 2). There were no patients with aspirin sensitive asthma. Smokers had more symptom like cough and lower LV ejection fraction compared to non-smokers (Table 3)

We observed positive correlation between LV ejection fraction and six minute walk test and negative correlation between LV ejection fraction and SGRQ score but found no correlation between LV ejection fraction and FEV1. We observed positive correlation between FEV1 and six-minute walk test and negative correlation with SGRQ.

Follow up at 3rd month after appropriate guideline based treatment (22 patients) showed significant improvement in lung function and quality of life and exercise tolerance in COPD patients (Fig. 2). Asthmatic patients showed modest improvement in lung functions, quality of life and exercise tolerance of which only former two were statistically significant (Fig. 3).

4. Discussion

IHD and chronic respiratory diseases are important causes for mortality and morbidity throughout the world. There are diagnostic as well as therapeutic dilemma when both are concomitantly present, especially in the elderly. We conducted

Table 1
Demographic and clinical characteristics of the study population.

Characteristics	N = 114
Age in years, mean (SD)	58.89 (12.24)
Sex, male n (%)	88 (77.19)
Cough, n (%)	31 (27.19)
SOB, n (%)	48 (42.10)
Diabetes, n (%)	46 (40.35)
Hypertension, n (%)	54 (47.36)
Alcoholics, n (%)	36 (31.56)
Smoking (only male), n (%)	61 (53.50)
Pack years, mean (SD)	10.73 (16.62)
Biomass Index, mean (SD)	20.70 (54.24)
BMI, mean (SD)	23.72 (4.09)
Post PTCA, n (%)	43 (37.71)
Post CABG, n (%)	14 (12.28)
6 MWT%, mean (SD)	80.92 (11.21)
SGRQ Total, mean (SD)	537.36 (532.94)
FVC Pre(1), mean (SD)	2.65 (0.70)
FEV1 pre(1), mean (SD)	2.03 (0.65)
EF, mean (SD)	50.22 (10.64)

Table 2
Comparison of demographics and clinical characteristics in patients with normal and abnormal spirometry.

Variables	Normal spirometry n=89	Abnormal spirometry n=25	p value
Age, mean (SD)	57.83 (12.14)	62.64 (12.07)	0.083
Male sex, n (%)	67 (75.3)	21 (84)	0.430
BMI,mean (SD)	24.46 (4.23)	22 (2.83)	0.008
Pack years, mean (SD)	10 (16.78)	13.36 (16.06)	0.375
Biomass Index, mean (SD)	20.45 (47.26)	21.60 (75.26)	0.926
LV ejection fraction, n (%)	51.04 (10.66)	47.28 (10.23)	0.119
Symptom, n (%)			
Cough	17 (19.1)	14 (56)	0.001
Dyspnea	26 (29.2)	22 (88)	0.000
Questionnaires, mean (SD)			
SGRQ total	403.66 (486.71)	1013.32 (407.98)	0.000
MMRC dyspnea grade	0.22 (0.57)	1.76 (0.93)	0.000
BODE Index	0.31 (0.59)	1.64 (1.38)	0.000
Spirometry, L (SD)			
FEV1	2.19 (0.58)	1.48 (0.58)	0.000
FEV1 (% pred)	91.90 (16.40)	71.88 (21.41)	0.000
FVC	2.77 (0.65)	2.20 (0.70)	0.000
FVC (% pred)	93.37 (16.64)	84.92 (22.50)	0.041
FEV1/FVC (% pred)			
Six minute walk test (% pred)	82.63 (10.75)	74.80 (10.86)	0.002

Table 3
Comparison of symptoms, lung functions, quality of life and exercise capacity between smokers and non-smokers.

Variables	Smoker (61)	Non Smoker (53)	p value
SOB, n (%)	27 (44.3)	21 (39.6)	0.705
Cough, n (%)	22 (36.1)	9 (17)	0.034
FEV1% pred	87.26 (18.65)	87.79 (20.39)	0.885
FVC% pred	91.51 (15.82)	91.53 (20.99)	0.995
SGRQ total, n (%)	575.21 (566.36)	493.79 (493.44)	0.418
Six minute walk test, n (% pred)	81.02 (12.61)	80.80 (9.47)	0.918
LV Ejection fraction, n (%)	48.21 (10.92)	52.53 (9.91)	0.030
BODE index, mean (SD)	0.74 (1.06)	0.45 (0.99)	0.170
MMRC grade, mean (SD)	0.43 (0.82)	0.67 (0.99)	0.170

25) had pure obstruction. Thirteen patients had COPD according to the Global Initiative for Obstructive Lung Disease (GOLD) guideline criteria²² and twelve patients had asthma according to Global Initiative for Asthma(GINA) guidelines.²³ Majority of the patients with COPD had GOLD grade 2 severity (8/13). Follow up of patients with abnormal spirometry (N= 25) after appropriate treatment for 3 months showed significant improvement in lung functions, quality of life and exercise tolerance.

Most of the studies evaluating the presence of chronic obstructive airway diseases among patients with IHD have concentrated on COPD. There are lots of variations in prevalence of COPD in cardiac disease because of differences in population studied, inclusion criteria applied and diagnostic modality used. Minasian and Brenner observed the possibility of both under-diagnosis and over-diagnosis of COPD in patients with heart failure.^{26,27} Airway obstruction in patients with heart failure is a dynamic feature and can resolve after the patient becomes euvolemic.²⁶ Therefore, they recommended that spirometry should be performed only when the patient is stable. The main groups of cardiac disease patients studied for prevalence of COPD include patients with heart failure, after recovery from myocardial infarction and coronary artery disease. Since both COPD and IHD

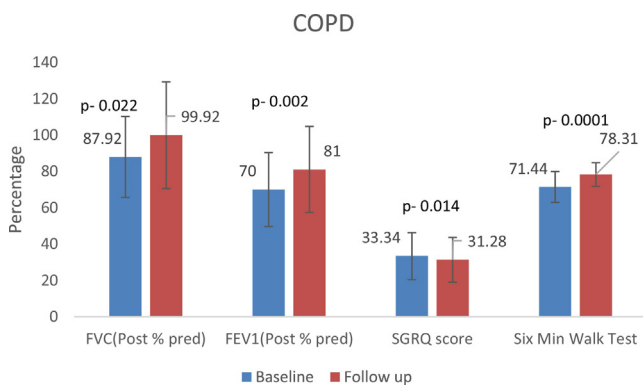


Fig. 2. Comparison of Lung functions, 6MWT and quality of Life characteristics at baseline and follow up at 3rd month of patients with COPD.

this study as there is sparse data on prevalence of obstructive airway diseases such as COPD or asthma coexisting in IHD patients in Indian population. No studies till date have observed response to appropriate guideline based therapy for COPD in stable IHD and evaluate improvements in spirometry, exercise capacity and quality of life. We found abnormal spirometry in 21.92% (25/114) of patients with stable IHD, of which 48% (12/25) had significant reversibility, 32% had mixed pattern (8/25) and 20% (5/

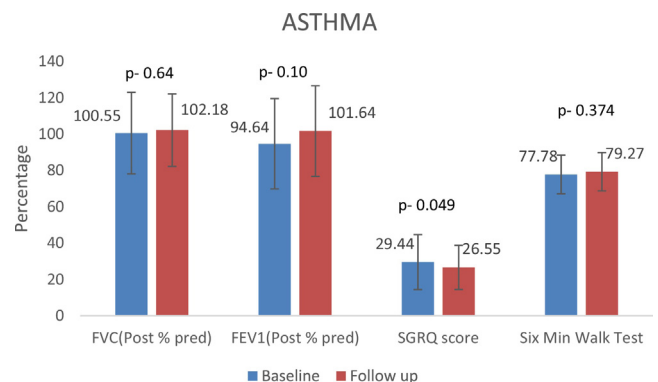


Fig. 3. Comparison of Lung functions, 6MWT and quality of life characteristics at baseline and follow up at 3rd month of patients with Asthma.

share an important common risk factor, smoking, it makes sense to evaluate for COPD in patients with IHD by the cardiologist and IHD in patients with COPD by the pulmonologist. The prevalence of COPD in heart failure patients on self-report varied from 10.6–33%^{13,28–30} and prevalence of COPD diagnosed by spirometry varied from 12 to 39.2%.^{6,16,31} A study done in Netherlands on prevalence of COPD in stable chronic heart failure found 28.3% of the cohort had COPD on spirometry and 70% of them were newly detected which highlights the proportion of missed cases of COPD in cardiac disease patients. Chronic obstructive pulmonary disease (COPD) is an important differential diagnosis in heart failure (HF). However, routine use of spirometry in outpatient HF clinics is not implemented. The aim of the present study was to determine the prevalence of airflow obstruction.³¹ Various studies on prevalence of COPD in myocardial infarction have observed a prevalence rate of (7%–15.6%).^{9,32–34} Stress Prevention Intervention (SPRINT) study observed a lower prevalence of COPD since it included patients surviving acute phase of MI. Patients with COPD who have MI have a higher mortality rates and these cases would have been missed, leading to lower prevalence of COPD (7%)³² whereas Prospective registry evaluating Myocardial infarction (PREMIER) registry included all patients who survived MI but used less strict definition of COPD which included asthma, so the prevalence of COPD was higher at 15.6%,³⁴ almost twice of what was observed in the SPRINT study. Bursi in a retrospective chart review observed in patients with MI a prevalence of COPD of 12% with a careful exclusion of asthma.⁹ In a Spanish study evaluating airflow limitation using spirometry among patients with cardiovascular disease, without cardiovascular disease in population and hospitalized patients with coronary artery disease, found airflow limitation in 19.2%, 17.5%, 33.6% respectively.³⁵ The highest prevalence of COPD was observed among patients with coronary artery disease (CAD). Hence, it would be useful for all cardiac patients to be subjected to spirometry.³³

The exact mechanism associated with link between COPD and IHD is still unclear, but COPD even in stable condition is associated with chronic low-grade inflammation which appears to play a critical role in development and progression of CAD. Supporting the evidence further it has been found that COPD patients are prone for major cardiovascular events during an exacerbation where there is increased systemic inflammatory response causing release of various cytokines, interleukins (IL-1 β , IL-6, IL-18, TNF α) and acute phase proteins (C-reactive protein). These various inflammatory mediators spill over to systemic circulation and are involved in promoting coronary atherosclerotic process and thus causing Coronary artery disease.³⁶ Along with systemic inflammation, chronic hypoxia and oxidative stress are additional important factors for progression of CAD. Patients with established CAD had higher intensity and severity of atherosclerosis in patients with COPD than the control group without COPD.³⁷ Another study observed that COPD patients had higher number of atherosclerotic lesions in primary coronary intervention (PCI) compared to those without COPD and these patients had higher mortality and repeat revascularization within 1 year of PCI.³⁸

Prognosis in presence of both COPD and IHD is worse than when either disease is present alone. PREMIER study that followed up cases of myocardial infarction found patients with COPD had two times higher risk of mortality and re-hospitalization at 1 year and lower quality of life.³⁴ COPD was a strong independent predictor of hemodynamic compromise resulting in death or cardiogenic shock in patients with acute MI.³⁹ A large cohort of patients with acute MI on long term follow up (4.7 \pm 4.6 years) observed that the prevalence of COPD increased over time and was an independent risk factor for mortality even after adjustment for age and other risk factors.⁹

Prevalence of Aspirin exacerbated respiratory tract disease is around 10% and prevalence of aspirin induced urticaria is 0.07–0.2% in general population in western population.⁴⁰ Aspirin forms the cornerstone in the management of IHD patients and hence it is very important in a small subset of patients who are sensitive to aspirin.

We found significant improvement in symptoms, lung functions, Quality of life and exercise tolerance on follow up after treatment at 3rd month. There are not many studies that have followed up IHD patients with spirometric abnormalities for assessment of response to appropriate guideline-based therapy. Both IHD and chronic respiratory disease have common symptoms such as dyspnea and are sometimes missed unless appropriate investigations are done. A better symptom improvement is expected when both the diseases are treated simultaneously than managing either disease alone. Patients with chronic heart failure alone, after careful exclusion of patients with additional COPD or asthma, still showed significant improvement in their airflow obstruction and reduction in dyspnea scores after inhaled short acting bronchodilators (salbutamol and ipratropium), prompting the investigators to suggest that even patients with isolated cardiac failure will benefit from treatment with bronchodilators.⁴¹

5. Conclusion

Presence of Chronic obstructive airway disease in patients with stable IHD is frequent (>20% subjects) but often missed due to overlap of symptoms. Spirometry is a simple tool to recognize the underlying pulmonary condition. Patients respond favorably with the institution of appropriate pulmonary therapies with significant improvement in lung function, quality of life and exercise tolerance.

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