PREVALENCE OF ISCHEMIC ECG CHANGES IN PATIENTS WITH COPD
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ABSTRACT: Patients with chronic obstructive pulmonary disease (COPD) are at increased risk of cardiovascular disease. Electrocardiography (ECG) carries information about cardiac disease and prognosis, but studies comparing ECG characteristics between patients with and without COPD are lacking. In this study ECG characteristics of patients with COPD was tabulated; further studies can help to determine whether ECG abnormalities can be correlated to COPD severity. The present study is a retrospective study conducted within a cohort of 104 COPD patients, aged 40 years or older. All patients underwent extensive examinations, including resting 12-lead ECG and pulmonary function tests, with a primary diagnosis of COPD and were followed for electrocardiographic evidence of myocardial ischemia. Conduction abnormalities were common ECG abnormality in COPD patients (28%). The mean heart rate was higher in COPD patients (72 bpm), and QTc prolongation was less frequent in COPD patients. The prevalence of ECG abnormalities increased with severity of pulmonary obstruction. ECG abnormalities, especially conduction abnormalities are common in COPD patients, and the prevalence of ECG abnormalities increases with severity of COPD. This underlines the importance of an integrated-care approach for COPD patients, paying attention to early detection of unrecognized coexisting cardiac disorders. The aim of this study was to test the hypothesis that myocardial ischemia complicates the management of some patients with chronic obstructive pulmonary disease (COPD) exacerbations.

KEYWORDS: COPD, IHD, ECG.

INTRODUCTION: Patients suffering from chronic obstructive pulmonary disease (COPD) are at increased risk of cardiovascular morbidity and mortality1. Compared to people without COPD, they are more prone to develop ischemic heart disease, cardiac arrhythmias, and heart failure2. Moreover, most hospitalizations and deaths in COPD patients are caused by co-existence of COPD and cardiovascular disease. In addition, they share important risk factors: cigarette smoking, advanced age, inactive lifestyle, and low socioeconomic status3,4. Importantly, however, after adjusting for risk factors for CVD, including the aforementioned, COPD remains a strong independent predictor for cardiovascular events and death5. Large population-based studies also showed a strong association between lung function impairment. Patients with COPD are also at increased risk for CAD and other smoking-related illnesses.

Pathogenesis: Various studies have reported a strong link between the occurrence of COPD and the presence of CAD. The causal link between these diseases has historically been cigarette smoking, but the exact mechanisms have only recently been studied. Epidemiologic evidence supports the importance of systemic inflammation in the pathogenesis of atheroma formation and ischemic heart disease, and recent studies have indicated that patients with COPD have a prominent systemic inflammatory response6. C-reactive protein (CRP), a known marker of systemic inflammation, for
example, has been shown to be elevated in patients with both stable COPD and during exacerbations. Because elevations in CRP have been linked to CAD, it appears as though the pathogenesis of both COPD and CAD may stem from enhanced systemic inflammation. Although data supporting the use of statin therapy for primary prevention of CAD are currently lacking, there are data showing that the use of statins reduces systemic inflammation as evidenced by reductions in CRP. In addition, the observation that the use of statin therapy is associated with a significant reduction in respiratory-related mortality after a COPD exacerbation further highlights the likely importance of inflammation in this disease.

**Recognition of Disease:** Noninvasive assessment of coronary disease in COPD is problematic because patients with COPD are often ventilatory limited in exercise, and pharmacologic stress testing (including adenosine and dipyramidole) may be associated with bronchospasm.

Although recent data highlight the safety of dobutamine echocardiography in the general patient population, its safety and efficacy in COPD is not known. Hyperinflation accompanying COPD may limit the diagnostic accuracy of transthoracic echocardiography for detecting wall motion abnormalities with stress.

Recent data indicate that noninvasive 64-slice multidetector computed tomography (64-MDCT) coronary angiography has comparable diagnostic accuracy to traditional invasive quantitative coronary angiography. However, its utility for assessing CAD in COPD has not been determined. Given the increasing recognition of the potential importance of CAD to the natural history of COPD, development of noninvasive techniques to assess coronary disease in this population is required.

**Treatment:** Although β-blockade plays a pivotal role in the management of CAD, there has been longstanding concern that it may precipitate bronchospasm in COPD. However, the use of cardioselective β-blockers such as atenolol and metoprolol, appears to be safe. Camsari and colleagues examined the use of metoprolol in 50 patients with COPD (mean FEV₁, 50% of predicted) and found no adverse effects. Two recent meta-analyses examining single-dose as well as chronic β-blocker treatment in patients with reactive airway disease and COPD demonstrated no evidence of adverse respiratory effects. In addition to their role in CAD, the use of β-blockers has become standard of care for most patients with left ventricular dysfunction. Although most studies examining the use of β-blockers in heart failure have excluded patients with COPD, available evidence has shown that the use of nonselective α- and β-blockers such as carvedilol is safe in these patients, although caution should be used in patients with reversible airflow obstruction as in asthma. Given the demonstrated efficacy of these agents in CAD and heart failure, existing data suggest that these agents should not be routinely withheld in patients with concomitant COPD.

Limited data exist regarding the safety and efficacy of coronary revascularization in COPD. Prospectively collected data on 183 patients with COPD undergoing percutaneous coronary intervention revealed no increase in in-hospital adverse cardiac outcomes; however, patients with COPD had increased long-term mortality when compared with those without COPD. Likewise, surgical revascularization can be performed safely in patients with CAD and concomitant COPD, although long-term survival in patients with COPD is significantly reduced. Zhu and colleagues performed a retrospective analysis comparing conventional coronary artery bypass grafting (CABG) with off-pump CABG in COPD, and found fewer postoperative respiratory complications and a higher PaO₂/FIO₂ ratio with off-pump CABG.
AIMS & OBJECTIVES:
1. To study various Electrocardiographic (ECG) changes in patients of chronic obstructive pulmonary disease.
2. To determine the frequency of ischemic ECG changes

METHODS AND MATERIALS:
Study Population: A retrospective study was conducted inpatients of chronic obstructive pulmonary disease admitted to the Department of Medicine in KIMS Hospital, Bangalore from 15th Jan, 2012 to 15th Jan, 2013. Out of 104 cases, 20 were females and 84 were males. Most of the patients were diagnosed clinically then radiologically; ECG was performed on all patients.

Inclusion criteria were age > 40 years; postbronchodilator FEV1/FVC ratio < 0.70; and a postbronchodilator β2-agonist FEV1 reversibility of < 15%, < 200 mL, or both. Patients with all GOLD (Global Initiative for Chronic Obstructive Lung Disease) stages of severity were included in the analysis. Patients were not taken if they had evidence of another clinically significant primary respiratory disease.

Clinical Evaluation of Participants: A full medical history was taken by the attending physician for all patients, including age, sex, smoking status, pack-year history of smoking, and all medications. Comorbid conditions were established. Health status was assessed in the stable patient (no exacerbation 4 weeks before and 2 weeks following the visit) using the St. George Respiratory Questionnaire (SGRQ)\(^9\). Medical Research Council (MRC) dyspnea score was used as an objective measure of stable-state breathlessness, which is associated with level of disability.\(^10\) The presence or absence of chronic bronchitis (cough with productive sputum on most days for at least 3 months for each of the 2 previous years) also was recorded. IHD comprised stable angina, previous MI, and previous coronary artery intervention, such as bypass grafting, angioplasty, and stenting.

Postbronchodilator FEV1 and FVC were measured. BMI was calculated from height and weight at recruitment.

RESULTS: A total 104 patient with COPD were studied, out of which there were 20 females and 84 males. All electrocardiograms were scored independently using the Minnesota scoring system. Major or minor Q or QS pattern, ST junction and segment depression, T-wave items, or left bundle branch block were considered ischemic ECG changes. Thirty-seven patients had ischemic ECG changes. In addition, patients with ischemic ECG changes had higher dyspnea grades (Modified Medical Research Council (mMRC) 2.9 ± 1.1 vs. 2.6 ± 1.1, p = 0.032).

Although exacerbations in patients with comorbid IHD were more prolonged, treatment at the onset of the exacerbation was not significantly different, with the proportion of exacerbations requiring systemic corticosteroids (with IHD vs without IHD, 50% vs 39%, P = .227), antibiotics (64% vs 67%, P = .930), or hospitalization (4.1% vs 6.4%, P = .236).

DISCUSSION: This study compares differences in cardiac-disease-related ECG characteristics of COPD patients.

The prevalence of ECG abnormalities, in general, increased with GOLD stage. Consistent with large population-based studies, it was demonstrated that COPD is associated with an excess of cardiac arrhythmias, particularly atrial fibrillation\(^11\).
As arrhythmias are often intermittently present and ECGs are a snap-shot of the cardiac situation, our results could underestimate the actual prevalence of arrhythmias. Nevertheless, bradycardia (heart rate < 50 bpm) was significantly less prevalent. This could be partly attributable to the higher prevalence of beta-blocking agents used in patients without COPD compared to COPD patients.

In analogy with other studies, we showed that patients with COPD had a relatively high heart rate and that heart rate significantly increased with increasing GOLD stage12.

Next, tachyarrhythmia is a well-recognized side-effect of beta-mimetic and anticholinergic agents. As inhaled beta-mimetics as well as anticholinergic agents are central to symptom management in COPD, this could be another explanation of the increased heart rate of COPD patients. However, as 84% of the COPD patients used at least one of these medications (41% of the COPD patients used both) we were not able to determine the effect of these drugs on heart rate. Finally, another potential cause of the increased heart rate could be lung hyperinflation. Hyperinflation in COPD may lead to decrease of the ventricular size and function, with decreased stroke volume and cardiac output. As a result, this may cause an increase in heart rate and tachycardia.

Different mechanisms have been proposed to explain why COPD patients have a higher risk of cardiovascular events. One potential mechanism may relate to systemic inflammation. The increased cardiovascular risk is not only shown in COPD, but also in other systemic diseases characterized by chronic inflammation, such as rheumatic arthritis or chronic renal impairment. Epidemiologic data strongly associate systemic inflammation to atherosclerosis and ischemic heart disease13.

Furthermore, there is evidence that COPD patients have autonomic dysfunction, most likely due to chronic hypoxemia, which contributes to the development of CVD.

Soriano et al demonstrated, using the UK General Practice Research Database, that in the year following clinical COPD diagnosis, the relative risks of diagnosed angina and MI were 1.67 and 1.75, respectively, when compared with subjects without COPD.11 In a large longitudinal Canadian health database study, COPD patients were found to have higher risk ratios for angina (2.02) and myocardial infarction (1.99) compared with matched controls following adjustment for known cardiovascular risk factors. Mortality due to cardiovascular disease in COPD patients was also approximately doubled compared with controls in this study.14

In the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study, 'heart trouble' as opposed to IHD was reported in 26% of 2164 COPD patients compared with 11% of 337 smoking controls (p < 0.001), with a MI reported in 9 versus 3% (p < 0.001).15 It should be noted that the controls in this study were on average 8 years younger and with a lower smoking pack-year history. The prevalence figures were not different between GOLD stages II, III and IV.

There appears to be a relationship between the severity of COPD and cardiovascular risk. Incident cardiovascular events were more frequent in COPD patients with a lower FEV1 over a 15-year follow-up period in the ARIC study.16 This pattern was observed regardless of smoking status or whether or not the subjects had cardiovascular disease at baseline. Curkendall and colleagues stratified COPD patients in terms of descriptors found in medical records which were associated with hospital admission, including the presence of emphysema, recent nebulizer use, home oxygen, corticosteroid use, frequent bronchodilator use, pneumonia and exacerbations.17 The most severe
quintile of patients according to these criteria had higher cardiovascular morbidity and mortality (odds ratio: 1.63) than the least severe quintile.

In another large population-based study from the UK, Feary and colleagues demonstrated that the relative risk of comorbid cardiovascular disease and subsequent MI and stroke events was higher in COPD patients than the rest of the population. The burden of cardiovascular disease and events was highest in older COPD patients, given that they constitute the majority of COPD patients, intriguingly, cardiovascular risk was consistently higher in younger age groups. This may represent a group of patients with a shared susceptibility phenotype to the development of COPD and cardiovascular disease.

Data from the third National Health and Nutritional Examination Survey demonstrated that COPD patients with higher serum C-reactive protein had more cardiac injury detected on electrocardiogram (ECG), beyond shared risk factors such as age and smoking. It is a widely held belief in the field that chronic low-grade systemic inflammation is a major pathophysiological link between COPD and atherosclerotic diseases. Impaired vascular reactivity is an independent and early feature of and risk factor for atherosclerosis even before structural plaque changes are present. Endothelium-dependent and-independent vasodilatation has been found to be impaired in COPD patients without known cardiovascular disease compared with control subjects. The degree of endothelial dysfunction was related to lung function and serum C-reactive protein, providing another inflammatory link between COPD and atherosclerosis. Subclinical atherosclerosis is likely to start early in the course of COPD, as suggested by the findings of increased carotid artery intima-media thickness in middle aged smokers with airflow limitation.

Data regarding the symptomatic impact of IHD on COPD patients is lacking. It has been shown that COPD patients with heart disease (not specifically IHD) have a worse health status (assessed using the Short Form 36 questionnaire) and consume more healthcare resources.

Using The Health Improvement Network database to analyze more than 25,000 COPD patients, and the risk of acute MI has been shown to be elevated 2.3-fold in the period 1–5 days following an exacerbation. Acute exacerbations of COPD are known to involve a rise systemic inflammation beyond that already seen in the stable state, including plasma fibrinogen, itself an independent risk factor for atherosclerotic diseases. However, the presence of IHD does not appear to be a risk factor for more frequent COPD exacerbations.

AntonelliIncalzi and colleagues followed up patients after hospital admission for exacerbation of COPD, they found that median survival was shorter in those who had ECG evidence of IHD (2.19 vs 3.26 years, p = 0.027). The presence of COPD has an adverse impact on hospital admission rate and subsequent inpatient mortality in those with IHD, as well as survival following angiography.

It may be appropriate for clinicians to screen all COPD patients, or those with other risk factors, for previous silent myocardial damage with a 12-lead ECG and institute appropriate management earlier. Following potential symptoms of an acute coronary syndrome, the diagnosis of IHD may be more difficult in COPD patients as they may not be able to reach the physical threshold required for accurate exercise ECG testing. Other noninvasive alternatives such as stress echocardiograms and myocardial perfusion scans may be preferable. Coronary artery calcium scanning using CT could potentially have wider utility in COPD as a first line investigation, although further work is required to establish the optimal diagnostic pathway prior to angiography.
In conclusion diagnostic values of ECG among patients with respiratory problems suggest that COPD patients should be screened electrocardiographically in addition to other clinical investigations. Its relevance in relation to clinical outcome can be predictors of impaired survival in patients. Additional clinical research and trials are needed to form the scientific basis of our practice. In those who have a known history suggestive of IHD, we need to be aware that some of the common symptoms in COPD and cardiac failure overlap. More importantly, during a lung emergency, the patient’s cardiac status may deteriorate. It is, thus, important to carefully monitor the cardiac function of these patients during COPD exacerbations and, when necessary, use blood biomarkers and imaging studies to detect heart failure. The use of drugs related to the autonomic system may have to be closely monitored. There is merit in establishing a combined cardio-respiratory team to deal with these highly complex patients, so that they can put their knowledge together to advance the care for such patients with COPD.

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|                |   |
|----------------|---|
| Males          | 84|
| Average Age (years) | 56|
| Current or past smoker | 68|

**Signs and symptoms**

|                |   |
|----------------|---|
| Cough          | 18|
| Breathlessness | 22|
| Chest pain     | 7 |
| Rhonchi        | 47|
| Crepitations   | 52|
| FEV₁(%pred., SD) | 71(20) |
| FEV₁/FVC (SD)  | 0.85 (0.08) |
| History of Cardiac arrhythmias | 7 (2%) |
| History of Ischemic heart disease | 18 |
Medications used

| Category                  | Count | Percentage |
|---------------------------|-------|------------|
| Cardiovascular drugs      | 24    |            |
| QT prolonging drugs       | 4 (1%)|            |
| ß-blockers                | 37 (24%)|           |
| Respiratory drugs         | 22    |            |
| Inhaled corticosteroids   | 17    |            |
| Inhaled anticholinergics  | 4 (1%)|            |
| Inhaled beta-agonists     | 13    |            |

Table 1: Baseline characteristics of the study population (n=104)

| ECG characteristic                        | Count | Percentage |
|--------------------------------------------|-------|------------|
| Sinus tachycardia (>100/minute)            | 28    | 26.9%      |
| Sinus bradycardia (<50/minute)             | 3     | 2.88%      |
| Bradyarrhythmia                            | 1     | 0.96%      |
| Premature ventricular contraction          | 6     | 5.77%      |
| Premature atrial contraction               | 4     | 3.84%      |
| Atrial fibrillation                        | 25    | 24%        |
| Complete left bundle branch block          | 7     | 6.7%       |
| Right Axis Deviation                       | 65    | 62.5%      |
| Left atrial enlargement                    | 1     | 0.96%      |
| Complete right bundle branch block         | 9     | 8.65%      |
| Incomplete right bundle branch block       | 6     | 5.77%      |
| Atrio-ventricular block                    | 1     | 0.96%      |
| Right atrial enlargement                   | 27    | 26%        |
| Left ventricular hypertrophy               | 13    | 12.5%      |
| Right ventricular hypertrophy              | 19    | 18.1%      |
| Inferior Q-wave myocardial infarction      | 4     | 3.84%      |
| Anterior Q-wave myocardial infarction      | 5     | 4.81%      |
| ST segment elevation                       | 1     | 0.96%      |
| ST segment depression                      | 10    | 9.62%      |
| T-wave abnormalities                       | 10    | 9.62%      |
| Prolonged QTc interval                     | 3     | 2.88%      |

Table 2: ECG characteristics of participants
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