ORIGINAL ARTICLE

Isolated Acute Right Ventricular Myocardial Infarction and Ischemia in Patients with Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) increases the risk of cardiovascular disease 2-3 folds. The factors responsible for this association remain under evaluation. In this study, the prevalence of isolated right ventricular infarction (RVMI) and ischemia were compared with isolated RVMI in other patients.

Methods: This observational and analytical case-control pilot study enrolled 100 patients (82 men and 18 women) with suspected exacerbation of COPD hospitalized in the emergency department of Noor Hospital affiliated to Isfahan University of Medical Sciences, Isfahan, Iran from 2003 to 2005. Spirometry was performed with the equipment that met the American Thoracic Society performance criteria. Frequent electrocardiography (including V3R –V4R) and CK-MB enzyme assay were done.

Results: Of the 100 patients, 35 (35%) were excluded due to lack of criteria of the study. Echocardiography revealed that all patients with exacerbation of COPD had tricuspid regurgitation about 3-4 m/s, indicating moderate to severe pulmonary hypertension (PH). OF the 65 patients, 6 (9.2%) with moderate to severe pulmonary obstruction had isolated right ventricular myocardial infarction. Also, 9 (13.8%) patients had ST segment depression≥1 m in V3R and/or V4R. The difference between the patients with and without exacerbation of COPD accompanying isolated RV MI was significant.

Conclusion: Increase in the right ventricular pressure reduces the right coronary artery flow which results in ischemia, infraction and circulatory collapse. The results indicate that patients with exacerbation of COPD are at risk of isolated RV ischemia and infarction. Therefore, V3R and V4R lead should be taken.

Keywords: Chronic obstructive pulmonary disease; Right ventricular infarction; Pulmonary hypertension

Introduction

Chronic obstructive pulmonary disease COPD is a major public problem. It is the fourth leading cause of chronic morbidity and mortality in the United States.[1] In the next 20 years, chronic obstructive pulmonary disease is expected to become a leading cause of death and disability.[2-4] Considering all types of heart disease, cor pulmonale accounts for 5 to 10% of all cases.[5] Cor pulmonale increases in prevalence as airflow limitation worsens in patients with COPD. It is present in 40% with an FEV_1<1/0 L and in 70% when the FEV1 falls to 0.6 L.[5,6]

COPD is an important risk factor for atherosclerosis.[7,8] Even modest reductions in expiratory flow volumes elevate the risk of ischemic heart diseases, strokes, and sudden cardiac deaths 2 to 3 folds, independent of other risk factors.[7-9] Indeed, poor lung function has been shown to be a better predictor of all-cause and cardiac-specific mortality than established risk factors such as serum cholesterol.[8] Cardiovascular conditions are the leading cause of mortality among those with impaired lung function.[7-9] The

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mechanism or mechanisms responsible for this association, however, remain under evaluation.

Although the pathogenesis of atherothrombosis is complex and multifactorial, persistent low-grade systemic inflammation is believed to be one of the centerpieces in effecting clot formation.[10] Compelling epidemiological data link systemic inflammation to atherosclerosis, ischemic heart disease, strokes, and coronary deaths.[11,12]

The above-mentioned data are considered for patients with stable COPD. Patients with exacerbation of COPD are in high risk category for acute myocardial ischemia because of hemodynamic disorder and hypoxia. Therefore, electrocardiography (ECG) should be taken as a routine evaluation but sometimes even 12 leads ECG can not reveal acute ischemia because of isolated right ventricular (RV) involvement due to acute pulmonary hypertension. Isolated right ventricular myocardial infarction (RVMI) is uncommon and accounts for less than 3 percent of cases of myocardial infarction with acute ST-segment elevation.[13]

There are two studies with different results. In one study, COPD and RV hypertrophy predicted the increases in the RVMI with inferior myocardial infarction (MI) but in the other no such finding was reported. In both studies, no isolated RVMI and exacerbation of COPD were considered.[14,15] Therefore, we selected patients with exacerbation of COPD to determine whether exacerbation of COPD is associated with isolated RV ischemia and infarction that could be missed if V3R and V4R were not taken. Then the prevalence was determined.

Materials and Methods

In an observational and analytical pilot case-study, we evaluated 100 patients with suspected exacerbation of COPD hospitalized in the Emergency Ward, Noor Hospital affiliated to Isfahan University of Medical Sciences, Iran from 2003 to 2005. A sample was defined by clinical history with symptoms such as cough, sputum production, dyspnea and/or a history of exposure to risk factors for the disease. The diagnosis was confirmed by spirometry. Spirometry was performed with the equipment that met the American Thoracic Society performance criteria.[16] To adjust for height, age, sex, and race, we used published prediction equations for forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC).[17] We used a FEV_1-FVC ratio of <0.07 to define airflow obstruction.[18]

Mild, moderate, and severe airflow obstructions were defined as FEV_1 of >80% of predicted equivalent to stage 1 of the National Heart, Lung, and Blood Institute/World Hearth Organization Global initiative for Chronic Obstructive Lung Disease (GOLD) classification,[18] 50 to 80% of predicted (stage 2a),[17] and <50% of predicted (stages 2b and 3), respectively.[18]

In this study, for the evaluation of RV ischemia and infarction, V3R and V4R were added to 12- lead ECG and then serial ECG up to 48 hours were taken. Frequent CK-MB enzyme was measured for two days. We determined leukocyte and platelet counts, and Bun/Cr, Na/K, and arterial blood gas (ABG). Vital signs were registered. Left and right ventricular function and dimension were determined by echocardiography. Patients with LBBB, LVH, hyperkalemia and baseline ST-T changes that interfere with interpretation of ECG were excluded.

For diagnosis of isolated RV ischemia and infarction ST segment depression and elevation≥1 m in V3R and/or V4R lead associated with CK-MB rising above 2 times normal level was considered positive.[19] Patients with 12 lead ECG changes that showed ischemia or infarction were excluded because these patients were not missed by taking routine ECG. Chest radiographs (posterior/ anterior plus lateral) were taken to identify alternative diagnosis that can mimic the symptoms of an exacerbation. Statistical analysis was performed; using SPSS XI software binominal test and the results were considered statistically significant at P <.05.

Results

Of the 100 patients, 35 (35%) patients were excluded because of the following reasons: 15 (15%) patients lacked the criteria of COPD and had other causes of dyspnea and hypoxemia including asthma, pneumonia and penumothorax. Five (5%) patients did not have complete laboratory tests such as Bun/Cr, CK/MB, chest radiography, echocardiography and ABG. Also, 10 patients died (10%) and 5 (5%) referred to another hospital for ICU admission. In these patients, ABG showed Pco_2>70 mm/Hg and Pao_2<50 mm/Hg. Finally, there were 65 patients participating in this analysis (55 men and10 women). Also, in these patients, ABG showed Pco_2> 50 mm/Hg and Pao_2< 65 mm/Hg.

The average age of the participants was 56.5±0.5 years. The patients had moderate to severe air flow obstruction. Two patients with moderate obstruction and 4

with severe obstruction had ST segment elevation≥1 m in V3R and/or V4R lead (9.2%). These patients had CK-MB two times the normal level, being compatible with RV infarction that could be missed by 12 lead ECG. Of the 65 patients, 9 had ST segment depression ≥ 1 m in V3R and / or V4R lead and positive T wave.

Three patients (4.6%) with ST segment depression had CK-MB two times elevation that was considered non-ST segment elevation myocardial infarction (NSTEMI). CK-MB was also two times the normal level in 12 patients without ST-T changes, because of our including criteria (ST segment changes in V3R and/or V4R≥1 m associated with CK-M B elevation) for these patients. Other causes for CK-MB elevation such as intubation, pulmonary thromboemboli and renal failure were considered. Of the 65 patients, 10 (15.4%) had no JVP elevation because of hypovolemia. Of these 10 patients, two had RV ischemia that was elevated after fluid therapy JVP. Of the 65 patients, hypotension occurred in 15 patients (23.1%) including 5/6 patients (83.3%) with RV infarction, 4/9 patients (44.4%) with RV ischemia, and 6/47 patients (12.8%) without ECG changes. Ten patients responded to fluid therapy and five needed dobutamin concomitantly. Of the 65 patients, prerenal azotemia (Bun/Cr >20) were present in 33 patients (50.8%). From the 33 patients, 7 (21.2%) had ST segment changes in V3R and/or V4R (3 patients with ST segment elevation and 4 with ST segment depression). Five patients (7.7%) from 65 had renal azotemia.

Management of these patients was performed according to causes. Finally, the patients with ST segment changes were admitted to CCU for appropriate management. Regarding the prevalence of isolated RV MI in other patients that was 3% (13) and as compared to our finding (6/65=9.2%), binominal test indicates one-sided P=0.013.

Discussion

The results of this study confirmedhe previous reports that pulmonary function is an independent risk factor for overall cause of mortality, ischemic heart disease (IHD) and morbidity.[20,21] FEV_1 level could affect physical activity, which may prolong survival times through its influence on metabolism with decreased IHD mortality.[22] In our study, 6 out of 65 patients had the criteria of isolated RV infarction and 9 (13.8%) had RV ischemia only.

Therefore, 23% of the total patients had RV ischemia and infarction. The most important signs in these patients were hypovolemia and hypotension because 83% of the patients with isolated RV MI and 44% of patients with isolated ischemia were hypotensive. This can induce coronary artery hypoperfusion and in the presence of PH further hemodynamic disturbances can occur.

Another marker for coronary artery hypoperfusion in these patients was prerenal azotemia because all the patients with RVMI and infarction were in prerenal azotemic group. Right ventricular function in acute exacerbation of COPD is another important factor in morbidity and mortality, although the mean pulmonary arterial pressure (PPa) is between 25 and 35 in most studies on patients with stable hypoxic COPD.[23] During exacerbations, the mean PPa rose to 45 to 70 mm/Hg[6,24] due to several mechanisms that include worsened hypoxia, acidosis, and changes in pulmonary mechanics.

As previously mentioned, TR in our patients was 3-4 m/s, indicating moderate to severe PH. The sudden rise in pulmonary artery pressure reflects an abrupt increase in the right ventricular afterload, with consequent elevation of the right ventricular wall tension followed by right ventricular dilation and dysfunction.[24] As the right ventricular dilates, the interventricular septum shifts toward the left, with resultant under-filling and decreased distensibility of this chamber with under-filling of left ventricular, systemic cardiac output and declined pressure of both, potentially compromising coronary perfusion and producing myocardial ischemia and injury.[25]

Elevated right ventricular wall tension following acute exacerbation of COPD and pulmonary hypertension reduces the right coronary flow and increases the right ventricular myocardial oxygen demand, which may result in ischemia and infarction, perpetuation of which can lead to circulatory collapse and death.[26]

Because of the history of heavy smoking in COPD and acute significant rise of PA pressure during exacerbation of COPD, the right ventricle is faced with significant increased afterload; the RV being less apt to high afterload than high preload.[27]

So, this acute increase in PA pressure can compromise the right coronary and its RV branch with resultant RV ischemia and sometimes isolated RV infarction which can be diagnosed with V3R- V4R lead. Also, the other reason for infarction might be related to coronary spasm.[28] Finally, it seems that cardiovascular disease is not only the most relevant comorbidity for patients afflicted with COPD, but the

cardiovascular system may be directly damaged by the same environmental pollutants primarily affecting respiratory system.[29] Because cardiac ischemia and renal impairment are major risk factors leading to mortality of COPD patients, early diagnosis and treatment of RV ischemia and prerenal azotemia is of utmost importance. If the duration of prerenal azotemia is prolonged in these patients, it may lead to renal insufficiency and increase mortality.

This study showed that for patients with exacerbation of COPD, V3R and V4R should be taken because isolated RV infarction and ischemia could be missed by 12 lead ECG. In these patients, one of the causes of sudden death was probably cardiac ischemia and arrhythmia.[6,21] It is suggested that in patients with exacerbation of COPD, not responding to B2-agonists, anticholinergics, corticosteroid and methyl, xanthines should be evaluated for cardiac injury especially RV ischemia and infarction.

Comparing the diagnostic efficiency of the cardiac troponins versus CK-MB for MI, troponin has more sensitivity and specificity than CK- MB. Therefore, troponins assays are recommended.

With regard to the above findings, it is recommended that V3R-V4R leads should be obtained for patients with exacerbation of COPD and fluid therapy should be started immediately in the presence of prerenal azotemia and hypotension to help improve coronary perfusion and prognosis.

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