

Validity of 6-min Walk Test in Assessment of Severity among Patients with Chronic Obstructive Pulmonary Disease

Lokendra Dave¹, Vivek Rajoriya², T N Dube³, B S Yadav⁴, Nishant Shrivastava⁵, V K Sharma⁶

¹Professor and Head, Department of Tuberculosis Chest, Gandhi Medical College, Bhopal, Madhya Pradesh, India, ²Post-graduate Student, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India, ³Professor and Head, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India, ⁴Professor, Department of Cardiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India, ⁵Assistant Professor, Department of TB Chest, Gandhi Medical College, Bhopal, Madhya Pradesh, India, ⁶Ex-Professor and Head, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Abstract

Background: The 6-min walk test (6-MWT) is commonly used for evaluation of patients with cardiac or pulmonary diseases and prognostic relevance. Accordingly, the 6-MWT has been used as a primary endpoint in most randomized controlled trials of newly developed therapies in pulmonary arterial hypertension, which is the most common and progressive extrapulmonary manifestation observed among patients with chronic obstructive pulmonary disease (COPD).

Materials and Methods: Total 100 male patients who attended the chest medicine out-patient department, with the symptoms suggestive of COPD were included in this study, and the study was done to evaluate the 6-min walking distance (6-MWD) and correlated with echocardiographic findings suggestive of pulmonary hypertension as a predictor of severe COPD in these patients.

Result: All the COPD cases enrolled in the study were males, with mean age 59.5 ± 2.5 years. These patients were grouped under mild (21%), moderate (23%), and severe (56%) groups according to GOLD criteria's. The study results showed that as the COPD severity increases, the incidence of pulmonary hypertension also increases as identified by echocardiographic right ventricular systolic pressure (RVSP) and when correlated with 6-MWD, it substantially decreases as pulmonary pressures increases. The average RVSP was 59.6 ± 4.4 mmHg in severe COPD patients with mean 6-MWD 134.8 ± 4.8 m, whereas it was 47.2 ± 6.8 in moderately severe COPD with 6-MWD of 196.6 ± 5.7 m while it was 39.3 ± 5.1 in mild groups with 6-MWD of 316.4 ± 6.9 m. These values were found to be significant when they were compared to each other in different groups ($P < 0.001$).

Conclusion: 6-MWD may offer a reliable alternative method to assess the severity of COPD as it is well-correlated with the severity of pulmonary hypertension in COPD patients and may help in the follow-up of these patients.

Key words: Chronic obstructive pulmonary disease, Validity, Walk

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. The prevalence and burden of COPD are expected to increase in the future, due to continued exposure to the

risk factors and changing age structure of the world's population.^{1,2} The severity of COPD is usually assessed on the basis of a single parameter - forced expiratory volume in 1 s (FEV1). However, the patients with COPD have systemic manifestations that are not reflected by this. Hence, a multidimensional grading system, which may assess the respiratory and systemic expressions of COPD, has to be designed to predict outcome in these patients.³ BODE index has been proposed to serve this purpose in patients with COPD.⁴ The four factors that can predict the severity are the body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E), measured by the 6-min walk test (6-MWT). These variables are used to construct the BODE index,

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Corresponding Author: Dr. Lokendra Dave, Department of Tuberculosis Chest, Gandhi Medical College, Bhopal - 462 001, Madhya Pradesh, India. Phone: +91-9893155531. E-mail: drlokendradave@yahoo.com

a multidimensional 10-point scale in which higher scores indicate a worse prognosis. Accordingly, 6-MWT is one of the components for assessment of COPD patients.

COPD is associated with significant extrapulmonary (systemic) effects, among which cardiac manifestations are most common. If FEV1 <50% of predicted, cardiovascular disease accounts for approximately 50% of all hospitalization and nearly one-third of all deaths. One of these manifestations is pulmonary arterial hypertension (PAH), which adversely affects survival and exercise capacity and is associated with an increased risk of severe acute exacerbations.

The 6-MWT is commonly used for the evaluation of patients with cardiac or pulmonary diseases, as a form of submaximal exercise testing that is simple, reproducible, safe, inexpensive, applicable to everyday activities, sensitive to therapeutic interventions, and also of prognostic relevance.^{5,6}

Accordingly, the 6-MWT has been used as a primary endpoint in most randomized controlled trials of newly developed therapies in PAH.^{7,8}

The present study was done to evaluate patients of COPD with 6-MWT, and its correlation with pulmonary hypertension: Echocardiographic findings.

MATERIALS AND METHODS

After clearance and permission of the Institutional Ethical Committee, total 100 COPD patients who attended our outpatient clinic as well as indoor (from January 2013 to June 2015), at Chest Medicine Department, Gandhi Medical College, Bhopal were enrolled. The present analysis was restricted to male patients only, to improve the accuracy, as sex may be a confounding factor in many of the parameters assessed. During selection, patients with chronic lung disease other than COPD, hypertension, any known primary cardiac disease, any systemic disease that can cause pulmonary hypertension, and patients who were unable to perform spirometry, all were excluded from the study. Informed consent was obtained from all patients.

For each enrolled subject, a detailed history of dyspnea was taken, and patients were subjected to routine investigations, including complete blood count, lipid profile, blood sugar, blood urea, serum creatinine, Electrocardiogram, arterial blood gas, and chest X-ray. On the day of enrollment, height and weight were measured twice during the examination. Body mass index (BMI) was calculated by the formula - BMI = weight in kg/(height in ms).² Spirometry

was performed with spirometer equipment - RMS Helios 401 that met the American Thoracic Society performance criteria, in each of the cases on enrollment into the study and then, 20 min following the administration of 2.5 mg salbutamol nebulization. The procedure was repeated on 3 occasions every time, and the best value was taken. FEV1 (% predicted) was also noted.

Transthoracic echocardiographic assessment of pulmonary pressures was done for all the patients, on ultrasound systems (Phillips Healthcare HD7-XE Classic model) and reported according to the guidelines of the American Society of Echocardiography. The comprehensive examination included standard two-dimensional echocardiography for anatomic imaging and Doppler echocardiography for assessment of velocities. Doppler measurements were carried out over 3 heart cycles during passive expiration. Non-invasive assessment of systolic pulmonary artery pressures (sPAP) was achieved by measurement of right ventricular systolic pressure (RVSP). PAH was defined in this study as sPAP \geq 25 mmHg, according to the definition of pulmonary hypertension.^{9,10} PAH was classified into the mild, moderate, and severe category as sPAP 25-50, 50-70, and >70 mmHg, respectively.

6-MWT was performed twice with a rest of 30 min, and the average distance was taken according to ATS guidelines.¹¹ Patients were asked to walk on a level ground for maximum possible distance within the duration of 6 min. This 6-min walking distance (6-MWD) was measured and compared with RVSP/sPAP value, and any correlation, if statistically significant, was noted.

Observation

Total 100 COPD patients as cases were enrolled in the study. All the cases were males, with mean age 59.5 ± 2.5 years. These patients were grouped under mild, moderate, and severe groups according to FEV1 % of predicted and as per GOLD criteria's. There were (21%) patients, who had mild COPD, Moderate were (23%) while 56% patients had severe COPD.

The study results showed that as the COPD severity increases, the incidence of pulmonary hypertension also increases, as identified by echocardiography RVSP findings and when it was compared to 6-MWD, in same groups, the walking distance substantially decreases with increase in pulmonary pressures. The average RVSP was 59.6 ± 4.4 in severe copd patients with mean 6-MWD 134.8 ± 4.8 m, and 47.2 ± 6.8 in moderate COPD with 6-MWD of 196.6 ± 5.7 m, while it was 39.3 ± 5.1 in mild groups with 6-MWD of 316.4 ± 6.9 m. These values were found to be significantly different, when they were compared to each other, in all different three groups ($P < 0.001$) (Figure 1).

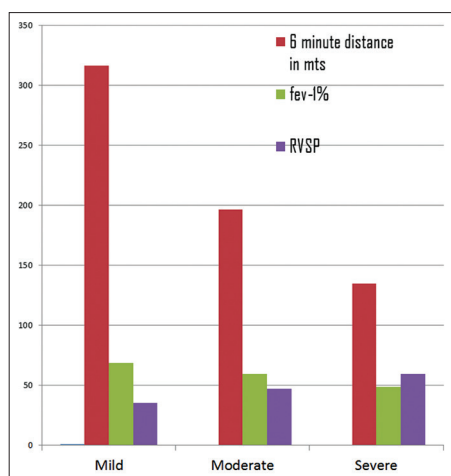


Figure 1: Mean 6 min walking distance, forced expiratory volume in 1 s % of predicted, and right ventricular systolic pressure: Comparison among groups

DISCUSSION

The natural history of COPD, being one of a progressive downhill course, PAH has generally been viewed as a late stage development occurring in patients with severe airways obstruction and a chronic hypoxemic state. The actual incidence of pulmonary hypertension in COPD is not known because it has not been screened systematically using reliable diagnostic tools (right-heart catheterization) in the wide clinical spectrum of COPD. However, indirect data suggests that the incidence of pulmonary hypertension in COPD is high.

Direct measurements of pulmonary artery pressure (P_{pa}) obtained at right-heart catheterization have been conducted only in small series of patients. In 1972, Burrows *et al.*¹² reported the hemodynamic findings in a group of 50 patients with severe COPD (FEV1/forced vital capacity [VC], 37%). The average value of mean P_{pa} was 3.46 kPa (26 mmHg), with 20% of these patients showing P_{pa} above this average value. In a series of 175 patients with severe COPD (FEV1/VC, 40%) and mild hypoxemia (arterial oxygen tension (P_{aO_2}) 8.38 kPa (63 mmHg)), reported by Weitzenblum *et al.*,¹³ the number of patients with pulmonary hypertension (mean P_{pa} >2.66 kPa (20 mmHg)) was 62 (35% of the group). The same group of investigators reported again, a similar incidence of pulmonary hypertension in a subsequent study carried out in 93 patients, 32 of them (34%) had a mean P_{pa} (20 mmHg).¹⁴

Recently, increased understanding of the pulmonary vascular pathology in PAH associated with COPD as well as the recognition that it is an important determinant of exercise limitation, dyspnea, and survival have led to renewed interest in the pathogenesis and therapeutics of this facet of COPD. Furthermore, identification of

a subset of patients of COPD who have an unusually severe form of PAH as well as the observation that pulmonary vascular changes may occur in smokers even without hypoxemia has provided additional impetus into research in PAH associated with COPD. Recently, 6-MWT has been used to evaluate and stratify performance and prognosis in pulmonary hypertension patients.⁹ Mathai *et al.*,¹⁵ retrospectively analyzed data from pulmonary hypertension: Response to tadalafil trial, in which PAH subjects were randomized to tadalafil, a phosphodiesterase type-5 inhibitor, or placebo. And found that an improvement in 6-MWT of approximately 33 m is associated with improvement in quality-of-life and hence advocated 6-MWT for assessment. More recent data do strongly suggest that the baseline 6-MWD is predictive of outcome in PAH.^{16,17}

In our study, while comparing 6-MWD and pulmonary hypertension values indirectly measured on transthoracic echocardiography (RVSP) in COPD patients, it was found that as the severity of pulmonary hypertension increases, the distance covered in 6 min decreases. This walking test proved highly acceptable to the patients, and stable, as well as reproducible results, was achieved after the two walks.

Data from the registry to evaluate early and long-term PAH disease management (REVEAL) and the French registry also demonstrate that the baseline 6-MWD is predictive of outcome in PAH.⁷ In the REVEAL registry, a baseline 6MW ≥ 440 m was associated with longer survival, whereas a 6MW of <165 m was associated with increased mortality at 1 year. In addition, multivariable analysis indicated that a greater 6 MW, among other factors, was significantly associated with improved survival and was a strong predictor of death in PAH. Same results were also cited in study by Guyatt *et al.*,¹⁸ where, they investigated the potential value of the 6-min walk as an objective measure of exercise capacity in patients with chronic heart failure, the test was administered six times over 12 weeks among 18 patients with chronic heart failure and 25 with chronic lung disease. The authors concluded that the 6 min walk is a useful measure of functional exercise capacity and a suitable measure of outcome for clinical trials in patients with chronic heart failure.

Similarly, a study done by Miyamoto *et al.*,¹⁹ where the 6-MWT was performed by 43 patients with PPH, together with echocardiography, right-heart catheterization, and measurement of plasma epinephrine and norepinephrine. Distance walked in 6 min was significantly shorter in patients with PPH than in age- and sex-matched healthy subjects (297 ± 188 versus 655 ± 91 m, $P < 0.001$).

During a mean follow-up period of 21 ± 16 months, 12 patients died of cardiopulmonary causes. Among non-invasive parameters including clinical, echocardiographic, and neurohumoral parameters, only the distance walked in 6 min was independently related to mortality in PPH by multivariate analysis. These results suggest that the 6-MWT, a submaximal exercise test, reflects exercise capacity determined by maximal cardiopulmonary exercise testing in patients with PPH, and the distance walked in 6 min also has a strong, independent association with mortality.

In our study too, it has been observed that 6-MWD can also be used to predict the severity of COPD, in terms of an indirect indicator of pulmonary hypertension. Hence, presumably, these patients can also be followed-up after using medications and oxygen therapy, whether it could be improved or not. This 6-MWT can be used to predict severity in COPD patient, in remote areas where health resources are scarce.

Limitations of the Study

1. A relatively small number of patients were studied, and this is a hospital based study and may not be representative of the general COPD patient's population. Furthermore, only male patients were included in this study, since COPD is more common among male patients. This was aimed so as to make the study group as uniform as possible. By eliminating the gender-related differences, such selection would negate the differences in 6-MWD among various patients studied, as well as in FEV1 and the patient's perception of dyspnea. Hence, perhaps the results of this study cannot be projected for female patients with COPD without further confirmation.
2. Accurate measurements of pulmonary hypertension are done by right-heart catheterization, and there may be some pitfalls in echocardiographic measurements, however, being a non-invasive method, it was preferred.
3. Patients who were not able to perform tests (pulmonary function test, 6-MWT) could not be evaluated.
4. As a cross-sectional and short study, the present study is limited in its ability to elucidate, whether improvement in 6-MWD after treatment, also reverses or improvise the other parameters analyzed?

CONCLUSION

6-MWD may offer a reliable alternative method to assess the severity of COPD, as it is well-correlated with the severity of pulmonary hypertension in COPD patients

and may probably offer help in following up of therapeutic benefits.

Since the assessment of 6-MWD requires no special instrument, It could be of great practical value in a primary health care setup, to identify individuals who need further evaluation and referral at higher center for further workup.

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