Original Article

Pulmonary Hypertension and Exercise Tolerance in Heart Failure Patients

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Abstract

Background: The 6-min walk test (6MWT) is a useful tool in assessing patients' outcomes: morbidity and mortality in heart failure (HF) patients. It also helps in monitoring the effect of medications being developed for treatment of pulmonary hypertension (PH) as well as response to therapeutic interventions in HF and may better reflect the functional exercise level for daily physical activities of HF patients. **Aim:** This study aims to describe how exercise tolerance of HF patients with PH may differ from that in HF patients without PH as assessed using the 6MWT. **Materials and Methods:** This was a descriptive cross-sectional study in which 65 patients each in two groups of HF patients with and without PH were sampled. All patients had their body mass index (BMI) and blood pressure assessed. In addition, all patients had echocardiography done and 6-min walk distance assessed. Data obtained were analyzed using SPSS version 23.0. **Results:** There were more females than men who participated in the study. That heart failure (HF) patients with PH walked less distance in six minutes compared to HF without PH. The total distance walked in 6 min was farther in males, younger HF patients <50 years, patients with a higher BMI, and patients with HF with reduced ejection fraction. Furthermore, a negative significant correlation was observed between mean pulmonary artery pressure (MPAP) and total distance walked in 6 min in all 130 HF patients ($r = -0.17$; $P = 0.005$) with a significant correlation between left ventricular ejection fraction ($r = 0.50$; $P < 0.001$), MPAP ($r = -0.24$; $P = 0.050$), and total distance walked in HF patients with PH. **Conclusion:** This study's findings indicate that worse outcomes await HF patients with concurrent PH. Thus, continuous monitoring of their exercise tolerance capacity using the 6MWT is of significant clinical benefit as part of their overall management.

Keywords: Echocardiography, heart failure, pulmonary hypertension, 6-min walk test

Introduction

Heart failure (HF) is a major health problem worldwide affecting all ages, races, and sexes. It affects over 20 million people worldwide, with an estimated prevalence of 2% in developed countries.[1] The prevalence of HF increases with age with about 6%–10% of people aged 65 years and above in developed countries affected.[2,3]

The 6-min walk test (6MWT) was first used in patients with heart disease in 1985 by Guyatt *et al*.[4] They applied the test six times, over 12 weeks, in 18 patients with chronic HF (CHF). The same patients also carried out the cycle ergometer test. The 6MWT and standard cycle ergometry cardiopulmonary exercise testing (CPET) are commonly used for assessing exercise capacity in patients with HF. Other measures of exercise capacity include the shuttle walk test and treadmill walk time.

The test has gained preferred because it is simple, affordable, reproducible, and well standardized.[5,6] In addition, it shows a good correlation with CPET which patients with PH may not be able to complete[7,8] and may better reflect the functional exercise level for daily physical activities of HF patients. However, this test is known to be influenced by body weight, gender, height, age, and patient motivation.

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Earlier studies have shown that the distance walked in 6 min correlates with cardiovascular morbidity and mortality, particularly for those who perform in the lowest quartile (<300–370 m).[9] It also helps in monitoring the effect of medications being developed for treatment of pulmonary hypertension (PH) as well as response to therapeutic interventions in HF[10] and used to measure physical fitness in some rehabilitation programs.[10]

Although there is abundant literature on the less common idiopathic PH, data are scarce on PH in HF or type 2 PH which is the most common type of PH. There are very few studies in West Africa on PH in HF patients and even rare studies on exercise tolerance capacity of these patients although clinicians do recommend the test.

Chikodi and Olufunke[11] evaluated the cardiovascular responses of adult Nigerians with CHF to the 6MWT. The study concluded that the 6MWT is a safe and simple instrument for demonstrating cardiovascular responses to submaximal exercise in patients with heart disease, especially in communities with limited resources.[11] Furthermore, Adedoyin *et al*.[12] suggested that the 6MWT could be useful to evaluate exercise tolerance in patients with CHF, while bicycle ergometry is more appropriate in the assessment of maximum functional capacity and has also shown a significant correlation between distance walked and VO_2[13] in CHF patients.

Furthermore, new therapeutic strategies for PH due to HF are being developed and there is need for more studies in Nigeria and Africa at large on management outcomes (as exercise tolerance is an indicator for outcome) of PH in HF patients.

This will eventually lead to better monitoring of treatment in PH in HF, thereby reducing morbidity and mortality. In particular, this study seeks to describe how exercise tolerance of HF patients with PH may differ from that in HF patients without PH as assessed using the 6MWT.

Materials and Methods

There are few works in this area. Results from this study could lead to exercise tolerance being used more freely to monitor recovery in HF patients with PH.

This study is a descriptive cross-sectional study that was carried out at the University of Benin Teaching Hospital (UBTH). The sample selection was based on convenience sampling method as patients admitted consecutively for HF were recruited for this study within a period of 6 months. Sample size was estimated using the G*Power software for comparing means of independent groups with the following parameters: minimum power = 0.90, minimum effect size = 0.5 (medium), minimum significant level = 0.05, and allocation ratio = 1. This resulted in a sample size of 130, 65 patients in each group. A total of 130 consecutively admitted HF patients (65 HF patients with and without PH in each group) who met the inclusion criteria were recruited for this study.

Patients with myocardial infarction, chronic obstructive airway disease, musculoskeletal abnormalities, ophthalmologic abnormalities (e.g., blindness), cognitive impairment, deafness, and poor echocardiographic images were excluded from the study. All patients underwent transthoracic echocardiography. The diagnosis of PH was made using estimated mean pulmonary artery pressure (MPAP) of >25 mmHg. The MPAP was derived from the pulmonary artery acceleration time (PAAT) using the following equation: "MPAP = 79–0.45 (PAAT)".[14] The PAAT was obtained from parasternal short-axis view at the level of the pulmonary valve using continuous-wave Doppler. Three measurements were taken, and the average time was taken as the PAAT. Subsequently, the 6MWT was performed for all patients and the distance walked in 6 min was recorded.

The 6MWT was carried out at the Special Investigation Unit, UBTH, with emergency crash cart readily available which included: sublingual nitroglycerin, aspirin, oxygen cylinder, Ambu bag, and an automated electronic defibrillator. The tests were carried out by two cardiologists with certification in basic and advanced life support using the ATS Statement: Guidelines for the 6MWT, March 2002.[15] The parameters that were measured in the patients include: height, weight, systolic blood pressure at rest, systolic blood pressure at 6 min, diastolic blood pressure at rest, diastolic blood pressure at 6 min, heart rate at rest, and heart rate at 6 min. A standard method was used to administer the 6MWT in a corridor of 30 m, with markings every 5 m. Patients were instructed to walk at their pace while trying to cover as much distance as possible in 6 min. The time was called out every 2 min. Participants were encouraged every 30 s with words like "You are doing well" or "Keep up the good work." During the test, patients were allowed to rest and then continue as soon as they can resume the walk. The total distance covered within 6 min was recorded. There was no adverse effect noted in any of the participants.

Statistical Analysis

Data obtained were entered into and analyzed using the IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). Categorical data were expressed as frequencies and percentages and compared using the Chi-square test. Continuous data were expressed as means (standard deviation [SD]) and compared using the independent *t*-test. A Pearson correlation test was done where applicable. $P \leq 0.05$ was considered statistically significant.

Ethical statement

Ethical clearance was obtained from the Ethics and Research Committee of the UBTH, Benin City, Edo State, on April 15, 2015.

Informed consent was obtained from patients before participation in the study.

Autonomy

Respect for respondents and confidentiality was maintained throughout the process of extracting the data.

Results

One hundred and thirty HF patients were studied. As seen in [Tables 1-5]. There were more females than males in the study, with the mean (SD) age of HF patients with PH being 56.85 (18.30) and 59.40 (16.60) in HF patients without PH.

HF with reduced ejection fraction (HFrEF) was present in 67.7% and 58.5% of patients with and without PH, respectively. About 20% of patients were obese in both groups with 36.9% and 20.0% of patients noted to be overweight. The SBP, DBP, and heart rate at rest, 1 min, and 1 min post 6MWT were not significantly different between both groups.

There was a significant difference ($P < 0.001$) between the lower total distance walked in 6 min observed in PH patients (249.90 ± 79.38) and that observed in patients without PH (310.96 ± 87.39).

The left ventricular ejection fraction (LVEF), PAAT, and body mass index (BMI) were higher in HF patients without PH while HF patients with PH had a higher MPAP.

Twenty-three and 16 patients were in NYHA Class III while 42 and 49 patients were in NYHA Class IV in patients without and with PH respectively. The total distance walked was farther in NYHA Class III patients in both groups compared to those in NYHA Class IV. There was a significant difference in the total distance walked between NYHA Class III and Class IV patients in HF patients with PH ($P < 0.001$).

There was also a statistically significant difference in the numerical values observed for MPAP ($P < 0.001$), PAAT ($P < 0.001$), and BMI ($P = 0.002$) when compared between the two groups.

In addition, there was a positive significant correlation between LVEF ($r = 0.32$; $P = 0.011$), BMI ($r = 0.33$; $P = 0.009$), weight ($r = 0.37$; $P = 0.003$), and total distance walked in 6 min in HF patients without PH.

Furthermore, there was a significant correlation between LVEF ($r = 0.50$; $P < 0.001$), MPAP ($r = -0.24$; $P = 0.050$), and total distance walked in HF patients with PH.

Furthermore, a positive significant correlation was found between BMI ($r = 0.29$; $P < 0.001$), LVEF ($r = 0.42$; $P < 0.001$), PAAT ($r = 0.34$; $P < 0.001$), and total distance walked in 6 min in the total population ($n = 130$). Furthermore, a negative significant correlation was observed between MPAP and total

Table 1: Demographic and clinical variables of patients

	Heart failure patients		χ^2	*P*
	PH absent	PH present		
Age (years)				
≤50	17 (26.2)	26 (40.0)	2.81	0.093
>50	48 (73.8)	39 (60.0)		
Sex				
Male	39 (60.0)	20 (30.8)	11.20	<0.001
Female	26 (40.0)	45 (69.2)		
BMI				
Normal	29 (44.6)	39 (60.0)	4.78	0.091
Overweight	24 (36.9)	13 (20.0)		
Obese	12 (18.5)	13 (20.0)		
LVEF				
Reduced	38 (58.5)	44 (67.7)	1.19	0.276
Normal	27 (41.5)	21 (32.3)		

LVEF: Left ventricular ejection fraction, BMI: Body mass index, PH: Pulmonary hypertension

Table 2: Total distance walked

	Heart failure patients		*t*	*P*
	PH absent	PH present		
Age (years)	59.40 (16.60)	56.85 (18.30)	0.83	0.406
LVEF	45.31 (18.24)	40.01 (21.41)	1.51	0.133
PAAT	136.65 (18.04)	97.42 (19.92)	11.77	<0.001
MPAP	16.31 (5.79)	37.84 (27.58)	−6.16	<0.001
BMI	26.62 (5.98)	23.59 (4.81)	3.18	0.002
Total distance walked in 6 min	310.96 (87.39)	244.90 (79.38)	4.48	<0.001

LVEF: Left ventricular ejection fraction, BMI: Body mass index, PAAT: Pulmonary artery acceleration time, MPAP: Mean pulmonary artery pressure, PH: Pulmonary hypertension

Table 3: Total distance walked in heart failure patients and demographic/clinical variables

	PH present	*t*	*P*
Age (years)			
≤50	263.53 (78.56)	2.40	0.019
>50	216.95 (73.47)		
Sex			
Male	251.56 (73.37)	1.02	0.314
Female	229.91 (91.77)		
BMI			
Normal	267.53 (83.62)	1.92	0.060
Overweight/obese	229.81 (75.69)		
LVEF			
Reduced	228.93 (73.67)	2.58	0.012
Normal	282.16 (82.46)		

LVEF: Left ventricular ejection fraction, BMI: Body mass index, PH: Pulmonary hypertension

Table 4: Right ventricular Doppler echocardiographic parameters in study population

	Mean±SD		*t*-test	*P*
	PH present (*n*=65)	PH absent (*n*=65)		
TRVmax	3.03±0.51	1.93±0.72	−10.91	<0.001*
RVET	266.71±90.16	295.01±31.56	2.46	0.015*
PAAT	98.62±19.56	137.78±16.56	13.07	<0.001*
PADP	17.15±6.49	12.26±5.70	−3.90	<0.001*

*P value < 0.05, SD: Standard deviation, PAAT: Pulmonary artery acceleration time, PH: Pulmonary hypertension, TRVmax: Tricuspid regurgitant velocity, RVET: Right ventricular ejection time, PADP: Pulmonary artery diastolic pressure

Table 5: Right ventricular function

	PH present ($n=65$), n (%)	PH absent ($n=65$), n (%)	Total ($n=130$), n (%)	χ^2	P
RVSD					
Present	43 (59.7)	29 (40.2)	72 (48)	10.50	0.001*
Absent	26 (33.3)	52 (66.7)	78 (52)		
RVDD					
Present	51 (63.0)	30 (37.0)	81 (54)	5.69	0.017*
Absent	30 (43.5)	39 (56.5)	69 (46)		

*P value < 0.05, PH: Pulmonary hypertension, RVSD: Right ventricular systolic dysfunction, RVDD: Right ventricular diastolic dysfunction

distance walked in 6 min in all 130 HF patients ($r = -0.17$; $P = 0.005$).

The total distance walked in 6 min was farther in males, younger HF patients <50 years, patients with a higher BMI, and patients with HFrEF. A significant difference was observed between the total distance walked when compared between the two classes of age ($P = 0.019$) and LVEF ($P = 0.012$).

Discussion

The 6MWT is a dependable tool in predicting morbidity and mortality in HF patients and a very useful prognostic tool in patients with PH.[16]

Our study showed that the total distance walked in 6 min was reduced in HF patients compared to recommended values. In addition, the distance walked was lower in HF patients with PH. The standard recommended 6-min walk distance (6MWD) has been set by earlier research at 498 m in 6 min by Lerner-Frankiel.[17] while McLaughlin *et al.*[18] set the 6MWD at 380–440 m: values not met by patients in this study indicating impaired exercise capacity.

In addition, this study showed better outcomes in younger patients, males, HF with reduced ejection fraction patients, and a normal BMI. Earlier research supports our findings of a longer 6MWD in males and younger patients than their older and female counterparts.[19]

Furthermore, our results suggest that exercise capacity is worse in HF patients with PH. Earlier research suggests that these findings may be of multiple etiologies ranging from effects of obesity, diabetes, age, and other chronic inflammatory states which cause changes resulting in decreased myocardial function[20,21] and inability of the heart to adjust proportionately to changes that occur during exercise.[22]

It is also notable that the prognostic value of the 6MWT is more practicable in the clinical setting with respect to continuous monitoring[23] although some improvements in patient test outcomes are less important compared to improvement over time. These improvements in the 6MWT though not a surety for increased survival still offer significant value as a tool for monitoring treatment success.[24,25]

An improvement in the 6MWT offers better morbidity/mortality outcomes in addition to a better quality of life.[25]

Conclusion

This study's findings indicate that worse outcomes may await HF patients with concurrent PH. Thus, continuous monitoring of their exercise tolerance capacity using the 6MWT is of significant clinical benefit as part of their overall management, especially as the 6MWT is an inexpensive, reproducible tool that can afford clinicians a better opportunity as regards monitoring and managing their patients.

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Conflicts of interest

There are no conflicts of interest.

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