

ORIGINAL ARTICLE

Determinants of the Distance Covered During a Six-Minute Walk Test in Patients with Chronic Heart Failure

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Abstract

Background: The evaluation of the functional capacity of patients with chronic heart failure (HF) by means of the distance covered in the six-minute walk test (6MWT) has assumed great importance, since the 6MWD is a predictor of mortality and hospitalization in this population, however the determinants of better distance traveled in patients with HF are little explored, especially in the Brazilian population.

Objective: To evaluate the determinants of 6MWD in patients with chronic HF.

Methods: A cross-sectional study was performed with 81 HF patients in outpatient treatment. 6MWD was used as the outcome variable and sociodemographic, clinical, physical-functional and emotional data were submitted to multiple regression analysis using the stepwise method with a significance level of 5%.

Results: Mean age of participants was 56.71 years; the 6MWD showed a bivariate correlation with age ($r = -0.27$, $p = 0.01$), maximal inspiratory pressure ($r = 0.42$, $p < 0.01$), maximal expiratory pressure ($r = 0.36$, $p < 0.01$), handgrip strength ($r = 0.38$, $p < 0.01$), Borg scale (-0.22 , $p = 0.04$), Charlson index ($r = -0.25$, $p = 0.02$) and modified Medical Research Council (mMRC) dyspnea scale ($r = -0.42$, $p < 0.01$). In the multivariate analysis, the variables gender ($p = 0.001$), age (0.004), forced vital capacity (FVC) ($p = 0.016$) and mMRC ($p = 0.001$) simultaneously explained 37% of variance in the 6MWD.

Conclusion: Higher levels of dyspnea on daily life activities, female sex, older age and lower forced vital capacity are determinants of a shorter 6MWD in patients with chronic HF. (Int J Cardiovasc Sci. 2018; [online].ahead print, PP.0-0)

Keywords: Heart Failure / physiopathology; Heart Failure / diagnosis; Walk Test / methods; Health Status Indicators; Reference Standards.

Introduction

Maximal effort test is the gold standard method for the assessment of functional capacity.¹ The six-minute walk test (6MWT), however, has become equally important to this end, and has been used as a simple, reproducible and feasible alternative. Since the 80's, the 6MWT has been widely used in clinical practice to evaluate functional capacity in heart failure (HF) patients, especially since the publication of the Studies of Left Ventricular Dysfunction (SOLVD),² showing that the distance walked was an independent predictor of mortality in patients with New York Heart Association (NYHA) classes II and III.

Functional capacity must be a priority in the management of elderly patients with cardiovascular disease. The assessment tools should have clinical applicability, be practical and efficient, since the maximal effort test is not always available. Besides, the prevalence of orthopedic and neurologic diseases has increased with population aging, which can make it difficult to perform exercise tests that require maximal effort.³

In light of this, 6MWT will become more and more present in the clinical practice, which makes it important to establish which variables may have affect its results, as well as intervention and prevention strategies for HF

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patients, aiming a better functionality and quality of life. Studies on factors associated with the 6MWT in patients with HF using multivariate analysis are scarce, especially in the Brazilian population, thus supporting the relevance of the present study.

This study aimed to identify determinants of the 6MWT in patients with chronic HF patients with NYHA classes I-III.

Methods

This was a cross-sectional study with 81 patients with chronic HF seen at the HF outpatient clinic of a referral hospital in Goiania, Goias, Brazil. Sample size was calculated using the GPower® software, using a significance level of 5%, power of 0.90, effect size of 0.59 (calculated from the determination coefficient – R^2) and number of predicting variables. A minimum of 79 patients with HF would be needed.

Inclusion criteria were: patients of both sexes aged ≥ 18 years old, with clinical diagnosis of HF, left ventricular ejection fraction (LVEF) $< 50\%$, NYHA functional class I-III, not receiving optimized treatment, and clinically stability for at least one month. Patients with acute myocardial infarction in the last month, unstable angina, stroke, musculoskeletal disorders, understanding impairment that would make it difficult to perform the tests, neoplasms or diagnosis of pulmonary diseases, pregnant women, patients using medications or ergogenic aids were excluded from the study.

Ethical aspects

All participants signed the informed consent form. The study was approved by the research ethical committee of the General Hospital of the Federal University of Goias (approval number: 883 281/2014) and of the Pontifical Catholic University of Goias (approval number: 922826/2014), following the regulatory norms and standards for research involving human subjects (Brazilian National Council, resolution number 466/2012).

Procedures

Screening of patients was performed by analysis of medical records. Eligible patients were invited to participate in the study on the visit day at the HF outpatient clinic, or later by telephone contact. All tests

were carried out by the same investigators on the same day. Questionnaires on clinical and sociodemographic data were partially completed with data obtained from medical records and complemented by interview on the visit day. The other endpoints were measured up to two weeks following the initial evaluation at a university health clinic.

The distance covered during the 6MWT (6MWD) was considered the outcome variable whereas sociodemographic, clinical, physical functional and emotional data, as well as quality of life used as exposure data.

The 6MWT was conducted following international standards.⁴ Two tests were performed on one day, with a 30-minute interval between them, for recovery of baseline heart rate (HR). The following parameters were measured immediately before the test, at the end (sixth minute) of the test and during recovery (5 minutes after the test) – HR, Borg dyspnea scale, peripheral oxygen saturation (SpO_2), systolic arterial pressure (SAP) and diastolic arterial pressure (DAP). Measurements of HR, Borg scale and SpO_2 were also made during the test (at minutes 2 and 4). The longest distance covered and the highest Borg scale rating between the two tests were considered for analysis. The distance covered was also compared with that expected one for the Brazilian population and expressed as percentage.⁵

Sociodemographic variables were age (years), sex, ethnicity (Caucasian and non-Caucasian), occupation (working or unemployed) income (Brazilian reals) (≤ 3 minimum wages and > 3 minimum wages), marital status (with a companion or single), smoking (yes or no/ex), alcohol consumption (yes or no/ex).

Clinical variables were: HF etiology (Chagasic or non-Chagasic), time of HF diagnosis (≤ 2 years or > 2 years), New York Heart Association (NYHA) functional class (class I = asymptomatic and classes II and III = symptomatic), LVEF, left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), number of medications being used, and number of hospitalizations in the past year. We also measured the Charlson comorbidity index⁶ which evaluates 19 clinical conditions combined (scores ranging from 0 to 6) and age (scores ranging from 0 to 4). The total score was the sum of clinical condition and age scores.

Resting HR was measured after 5-10-minute rest using a pulse oximeter (Onyx Nonin®), and systolic and diastolic blood pressure was measured using a

semiautomated sphygmomanometer (OMRON® HEM 711). Mean arterial pressure (MAP) was calculated using the formula: (systolic arterial pressure + 2 times diastolic pressure) divided by 3. These measures were taken during the period of rest from the 6MWT.

Height (m) and weight (kg) were measured with patients standing barefoot, using a Welmy® scale (model W300) (Sao Paulo, Brazil), and the values were used for body mass index (BMI) calculation (weight in kilograms divided by the square of height in meters).

Health-related quality of life (HRQOL) was assessed by the Minnesota Living with Heart Failure Questionnaire (MLHFQ), composed of 21 questions, that provides a total score that may range from 0 to 105, from best to worst quality of life.⁷ The total score (0-105), physical dimension (0-45) and emotional dimension (0-25) scores were used for analysis.

Dyspnea while performing activities of daily living (ADLs) was assessed by the Medical Research Council modified dyspnea scale (mMRC); scores of the items ranged from 0 to 4, in which 4 indicated the strongest limitation of ADLs due to dyspnea.⁸

Physical activity level was assessed using the short version of the International Physical Activity Questionnaire (IPAQ), validated in Brazil by Matsudo et al.,⁹ In the presente research, the participants were grouped into two groups – partially active or sedentary in one group, and active or very active in the other.

Handgrip strength (HGS) was measured using a hydraulic dynamometer (Saehan®), a validated instrument to measure isometric HGS,¹⁰ according to the American Society of Hand Therapists recommendations.¹¹ HGS was measured in the dominant hand; the mean of three measures was used for analysis. Values were expressed as percentage of predicted.¹²

Pulmonary function was measured using a portable spirometer (One Flow®; Clement Clark, United Kingdom), following the Brazilian Society of Pneumology and Phthisiology's recommendations.¹³ The following parameters were measured – forced vital capacity (FVC) in liters, forced expiratory volume in 1 second (FEV1) in liters, FEV1/FVC ratio (%). Values were expressed as percentage of predicted.¹⁴

Respiratory muscle strength was measured using a calibrated hand-held respiratory pressure meter (Globalmed® MVD300). Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were measured based on the residual volume and total

pulmonary capacity, respectively. Three reproducible measurements (less than 10% variation) were obtained; a mean of 3 to 5 measurements were taken, and the highest value was considered for analysis. The values were compared with those predicted.¹⁵

Symptoms of depression and anxiety were assessed by the Beck depression inventory (BDI)¹⁶ and Beck anxiety inventory (BAI),¹⁷ respectively. These are self-scored instruments composed of 21 items that evaluate depression and anxiety symptoms. Each item has four possible answers with scores ranging from 0 to 3 points, from absent (0) to most severe (3). The total score ranges from 0 to 63, with higher scores indicating more severe symptoms.¹⁶

Analysis of data

Statistical analysis was performed using the Statistical Package of Social Sciences (SPSS), version 23.0. Normally distributed continuous variables were presented as absolute numbers and percentages. Normality of distribution was verified by the Kolmogorov Smirnov test. The t-test for independent samples and the Mann-Whitney test was used for comparisons of normally distributed continuous variables and those without normal distribution, respectively. Bivariate correlations analysis was performed by Pearson's correlation (normally distributed variables) and Spearman's correlation (variables without normal distribution).

Multiple linear regression analysis was used to determine the predictive value of the variables on 6MWT, and the stepwise method was used for selection of the variables. All assumptions made by the multiple linear regression analysis - linear relationship, homoscedasticity, no or little multicollinearity between exposure variables were considered for selection of the model with the highest predictive value. Variables with $p < 0.10$ were excluded from the model. In addition, hierarchical multiple linear regression analysis was performed to verify the predictive value of sociodemographic, clinical, physical functional and emotional data combined. The level of significance adopted in all tests was 5%.

Results

Mean age of participants was 56.7 ± 12.4 years; 58% were younger than 60 years, 65.4% were male (Table 1).

Table 2 describes emotional, quality of life, and physical functional characteristics, Borg scale and 6MWD.

Table 1 - Clinical and sociodemographic characteristics of the study group

Variable	Mean or median n	Standard deviation or interquartile range %
Sociodemographic		
Non-caucasian	60	74.1%
Working	12	14.8%
Income < 3 minimum wages (Brazilian reais)	77	95.1%
Married / with companion	47	58%
Echocardiographic		
LVEF (%)	33.3	7.3
LVSD (mm/m ²)	54.3	6.7
LVDD (mm/m ²)	64.0	6.5
FC I	15	18.5%
FC II	60	74.1%
FC III	6	7.4%
Time of diagnosis > 2 years	59	72.8%
Number of hospitalizations	0.43	0.82
No previous hospitalization	57	29.6%
Heart rate (bpm)	66.0	60.0 - 79.5
MAP (mmHg)	94.5	13.6
BMI (kg/m ²)	25.7	23.5 - 30.1
Drugs	5.0	4.0 - 6.0
Charlson index	3.0	2.5 - 4.0
Etiology of HF		
Chagas disease	35	43.2%
Idiopathic	15	18.5%
Hypertensive	10	12.3%

LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic diameter; LVDD: left ventricular diastolic diameter; FC: functional class; MAP: mean arterial pressure.

6MWD was shorter in female participants with functional class II and III and in those with mMRC 2, 3 and 4. Although physically active subjects tended to walk a longer distance in the test, it was not statistically significant compared with the others ($p = 007$) (Table 3).

Table 2 - Emotional and physical functional characteristics, quality of life, and six-minute walk test parameters

Variable	Mean or median n	Standard deviation or interquartile range %
Emotional features		
BAI	14.0	6.2 - 23.0
BDI	10.5	7.0 - 18.0
MLHFQ		
Total QOL	35.4	21.8
Physical	17.5	7.0 - 23.0
Emotional	5.0	3.0 - 10.0
Physical activity level		
Sedentary	46	56.8%
Active	35	43.2%
mMRC		
1	42	51.9%
2	17	21%
3	9	11.1%
4	1	1.2%
MIP (cmH ₂ O)	72.6	26.0
% MIP	72.1	21.8
< 80 cmH ₂ O	49	60.5%
MEP (cmH ₂ O)	102.9	43.6
% MEP	95.8	33.6
% HGS	85.3	17.1
HGS (kgf)	31.9	8.4
% FVC	102.8	17.7
% LVEF1	95.1	22.3
FEV ₁ /CVF (%)	77.0	72.0 - 81.7
6MWD (m)	445.1	90.8
> 300 m	78	96.3%
> 450 m	47	58%
% 6MWD	79.7	14.6
Borg scale	2.0	1.25 - 4.0

BAI: beck anxiety inventory; BDI: beck depression inventory; MLHFQ: Minnesota Living with Heart Failure Questionnaire; QOL: quality of life; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; HGS: handgrip strength; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second; FVC: forced vital; LVEF: left ventricular ejection fraction; 6MWD: distance covered during the six-minute walk test.

Table 3 - Comparison of the six-minute walk distance between sexes, New York Heart Association (NYHA) functional classes, physical activity level and dyspnea on activities of daily living (Medical Research Council modified dyspnea scale, mMRC)

Variables	6MWD (mean ± SD)	p	%DTC6 (mean ± SD)	p
Male	467.7 ± 87.3*	< 0.01	81.0 ± 14.4	0.96
Female	402.3 ± 82.8		77.2 ± 14.8	
Functional class I	495.4 ± 86.8*	0.01	87.6 ± 12.1*	0.01
Functional class II and III	433.6 ± 88.3		77.9 ± 14.5	
Sedentary	429.2 ± 95.8	0.07	77.1 ± 15.6	0.06
Active	465.9 ± 80.4		83.1 ± 12.4	
mMRC (0 and 1)	472.4 ± 85.9*	< 0.01	83.9 ± 14.0*	< 0.01
mMRC (2, 3 and 4)	398.6 ± 80.4		72.7 ± 12.8	

* $p < 0.05$; 6MWD: distance covered during the six-minute walk test.

6MWD showed a moderate, significant correlation with age ($r = -0.27$; $p = 0.01$), MIP ($r = 0.42$; $p < 0.01$), MEP ($r = 0.36$; $p < 0.01$), HGS ($r = 0.38$, $p < 0.01$), Borg scale (-0.22 , $p = 0.04$), Charlson index ($r = -0.25$; $p = 0.02$) and mMRC ($r = -0.42$, $p < 0.01$).

Following the association tests and exclusion of variables by collinearity, the variables were selected in descending order of importance in the stepwise variable selection. Thereby, the following variables were included in the final model for the (dependent variable) 6MWD: mMRC ($p < 0.01$); sex ($p < 0.01$), age ($p < 0.01$) and FVC

($p = 0.01$). These variables explained 37% of the variance in the 6MWD in the study population (Table 4).

In the hierarchical model, we found that clinical and physical functional variables were the ones with the best predictive value in the 6MWT (40% and 33%, respectively) (Table 5).

Discussion

Our findings suggested four potential variables with predictive value for a shorter 6MWD: female

Table 4 - Predictors of the six-minute walk distance in heart failure patients

Models	Predictors	R ²	Beta	Standard error	t	p
1	mMRC	0.17	-0.41	11.51	-3.79	0.000
2	mMRC	0.24	-0.33	11.37	-3.14	0.002
	Sex		-0.29	20.66	-2.77	0.007
	mMRC		-0.32	10.95	-3.13	0.003
3	Sex	0.31	-0.31	19.89	-3.02	0.003
	Age		-0.26	0.76	-2.61	0.011
	mMRC		-0.35	10.63	-3.48	0.001
4	Sex	0.37	-0.36	19.68	-3.59	0.001
	Age		-0.29	0.74	-2.98	0.004
	% CVF		0.25	0.51	2.46	0.016

mMRC: Medical Research Council modified dyspnea scale; %FVC: forced vital capacity.

Table 5 - Predictors of the six-minute walk distance by hierarchical categories

Models	Predictors	R ²	Beta	Standard error	t	p		
Psychologic	BAI	0.02	-0.18	1.23	-1.20	0.234		
	BDI		0.07	1.34	0.49	0.628		
	Physical QL		-0.04	2.86	-0.11	0.911		
Quality of life	Emotional QL	0.06	0.37	4.12	1.48	0.143		
	Total QL		-0.44	1.94	-0.94	0.350		
	Age		-0.30	0.78	-2.78	0.007		
Sociodemographic	Sex	0.28	-0.29	20.24	-2.69	0.009		
	Ethnics		0.04	21.95	0.40	0.691		
	Working		0.13	26.81	1.19	0.238		
	Income		-0.01	43.58	-0.13	0.897		
	Marital status		0.24	20.15	2.19	0.032		
	Smoking		0.02	34.19	0.15	0.883		
	Alcohol consumption		-0.01	26.73	-0.14	0.893		
	Number of hospitalizations		-0.21	13.82	-1.67	0.099		
	Time of diagnosis		-0.14	26.74	-1.12	0.268		
	Chagas' heart disease		0.10	26.01	0.73	0.469		
	Number of medications		0.03	7.25	0.23	0.819		
	Clinical aspects		Charlson	0.40	-0.23	9.22	-1.76	0.084
			LVEF		0.13	1.87	0.93	0.357
LVDD		-0.04	2.09		-0.28	0.784		
BMI		-0.22	2.27		-1.65	0.104		
MAP		0.08	0.90		0.62	0.535		
HR		0.16	0.97		1.19	0.238		
mMRC		-0.37	10.00		-3.73	< 0.001		
IPAQ		0.15	18.41		1.47	0.145		
Physical functional parameters	% MIP.	0.33	0.14	0.49	1.14	0.256		
	% MEP.		0.15	0.34	1.20	0.234		
	% HGS		-0.33	0.55	-3.18	0.002		
	% FVC		0.15	0.54	1.38	0.171		
	FEV1/FVC		0.01	0.82	0.09	0.929		

BAI: Beck anxiety inventory; BDI: Beck depression inventory; QV: quality of life; LVEF: left ventricular ejection fraction; LVDD: left ventricular diastolic diameter; LVSD: left ventricular systolic diameter; BMI: body mass index; MAP: mean arterial pressure; HR: heart rate; mMRC: Medical Research Council modified dyspnea scale; IPAQ: International Physical Activity Questionnaire; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; HGS: handgrip strength; FVC-forced vital capacity; FEV1-forced expiratory volume in 1 second.

sex, older age, lower FVC and higher mMRC, which simultaneously explained 37% of the variance for the 6MWD. Additional five variables showed bivariate correlation with the 6MWD – MIP, MEP, HGS, Borg scale, and Charlson index.

Previous studies have reported several predictive variables of the 6MWD, including age, sex, weight, BMI, LVEF, anxiety, depression, quality of life, etiology of HF, functional class (NYHA), N-terminal (NT)-pro hormone BNP (NT-proBNP), glomerular filtration rate, resting HR and maximal power in the maximal effort test.¹⁸⁻²⁴

Female sex was a predictor of shorter 6MWD in a study conducted with 571 HF patients and 668 patients without HF.¹⁹ Similar findings were reported in other studies on patients with HF.^{18,22} On the other hand, Bajraktari et al.,²³ did not report any difference in the 6MWD between men and women. This result may be explained by the younger age and better cardiac function (indicated by higher LVEF) in female subjects than in men in their study.²³

With respect to age, previous studies have reported findings similar to ours. Age was found to be an independent predictive factor of the 6MWD in a study conducted in Poland,²⁰ including 243 men with HF, and in two studies from the United Kingdom^{21,22} on HF patients aged from 71 to 80.5 years.

Frankenstein et al.,¹⁹ evaluated 1,035 patients with HF, mean age of 54.9 years, and found a bivariate correlation between age and 6MWD ($r = -0.32$, $p < 0.01$), although no significant correlation was found in the multivariate analysis. In the study by Adel et al.,¹⁸ involving 40 HF patients (mean age of 55.6 years; 72.5% male), age was not associated with 6MWD. According to the authors, the small sample size contributed to these results.

Increasing age is a contributing factor to a shorter 6MWD.²⁵ In young adults, peak VO_2 decreases by 8-10% per decade, which is exacerbated with increasing age, leading to cardiovascular and pulmonary dysfunction. Besides, other factors that may negatively affect functional capacity decreases with age, such as psychological components and neuromuscular function (e.g. sarcopenia, and decrease in muscle strength, flexibility, balance and cognition).³

The effect of sex on 6MWD may be attributed to differences in biological and structural features between men and women, including higher muscle strength, muscle mass, and height in men than in women.²⁶

In studies conducted in the United Kingdom²¹ and in the Netherlands,²⁴ pulmonary function was not a

predictive variable of the 6MWD. The Dutch study showed only an association of FEV1, the FEV1/FVC ratio and total lung capacity with the distance covered by HF patients in the 6MWT. Agrawal et al.,²⁷ correlated the 6MWD with spirometric parameters in 130 patients with chronic obstructive pulmonary disease (COPD) with characteristics similar to our study regarding age (mean of 55.6 years) and sex (58.4% male) and found a correlation of the distance covered with FEV1 and FVC.

Pulmonary function may be altered in HF, particularly when combined with cardiomegaly, a condition characterized by enlargement of the heart. In this case, enlarged heart compete for intrathoracic space, causing compression of the lungs and limiting their expansion.²⁸ In a systematic review, Silva et al.,²⁸ reported an association between cardiomegaly and reduced MIP, FVC and FEV1 in HF patients.

In the present study, FVC was an independent predictor of six-minute walk distance. We did not measure cardiothoracic index in the study group for the presence of cardiomegaly. However, HF was caused by Chagas disease in most patients, a condition frequently associated with cardiomegaly. Besides, other factors may be associated with changes in pulmonary function, such as respiratory muscle weakness, chronic pulmonary congestion and pleural effusion, which decrease pulmonary compliance and increase respiratory work.²⁹ Our study group showed reduced MIP, which correlated with 6MWD. This, together with cardiomegaly, may have contributed to altered pulmonary function. Further explanation on the influence of pulmonary function on 6MWD in patients with HF is needed.

In the present study, mMRC was a predictor of 6MWD. Valadares et al.,²⁹ reported a correlation of mMRC with the London Chest Activity of Daily Living (LCAD) ($r = -0.68$, $p < 0.05$), another instrument for assessment of ADLs, that showed a strong correlation with the 6MWT ($r = -0.83$, $p < 0.05$). Camargo et al.,³⁰ found a moderate correlation between mMRC and 6MWD in 50 patients with COPD. Similar to our findings, 80% of the patients were classified as mMRC I and II, and the mean 6MWD was 435 m; nevertheless, in their study, mMRC was not a predictive factor in the multivariate analysis. Although mMRC has been rarely used in patients with HF, the instrument has been shown to be both easy to apply and easy to understand in patients with COPD. Thus, mMRC may be a fast, simple alternative tool to evaluate functional status in HF patients.

In hierarchical analysis, clinical and physical functional factors showed a greater impact on 6MWD; in contrast, sociodemographic and emotional factors showed little effect. These findings differ from previous studies showing that emotional factors, especially depression, were associated with poor functional capacity and shorter 6MWD.^{21,22,24} These discrepancies may be related to characteristics of the study population, including age, severity of HF, comorbidities such as COPD and asthma, as well as use of walking aids (not observed in our population).

This study had some limitations – the outcome measures accounted for less than half of the variance of the 6MWD, and other factors that contributed for 63% of the variance need further investigation. It is possible that physiological factors, including renal function and B-type natriuretic peptide (BNP), contribute to these differences. These factors have been frequently reported as predictive factors of the 6MWD and were not evaluated in our study. In addition, most of our patients were NYHA class I and II and in most of them had Chagas' heart disease. The possibility that the inclusion of patients with worse functional status could lead to different results cannot be ruled out.

Lack of homogeneity of the samples in the studies made it difficult to compare the results. Performance of the second 6MWT and the size of the hallway were not standardized among the studies either. In most studies, only one test was performed, and a hallway shorter than 30 meters was used in the tests. Repeated administration may influence the 6MWD, which is known as the learning effect.³¹ Also, the measurement of the HGS considered for analysis is not standardized; in this study, we decided to consider the mean of three measurements, rather than the highest measurement, since this is the most common method described in the literature.

Sex and age are expected to influence the 6MWD, regardless of the presence of HF.²⁵ Nevertheless, both pulmonary function and dyspnea on ADLs are modifiable variables that may be altered in HF. In addition, we found a bivariate correlation of the 6MWD with Borg scale, Charlson comorbidity index, MIP, MEP and HGS. These findings indicate that a careful and systematic approach by a multidisciplinary team is crucial for better outcome and impact on functional capacity of HF patients.

Most patients had a sedentary lifestyle in our study. However, although active subjects covered a longer distance during the 6MWT, it was not statistically different (despite a trend) than that in sedentary subjects.

Regular physical activity has well documented beneficial effects on peripheral muscle function, pulmonary function, exercise tolerance and quality of life, and hence is important in patients with HF.^{32,33}

Determinants of functional capacity are multifactorial, depending on demographic, socioeconomic, physiological, cultural and psychosocial factors.^{34,35} Therefore, predictive factors may differ between cultural and sociodemographic profiles. Also, in the present study, most patients had Chagas' heart disease, as the study was conducted in an endemic region of Chagas disease in Brazil. This is different from the studies cited throughout this article.

Conclusion

Four variables were identified as determinants of a shorter 6MWD in patients with chronic HF – severe dyspnea on ADLs (mMRC), female sex, older age, and lower FVC. Other variables, not explored in the present study, explain 63% of the variance in the 6MWD, indicating the multidimensionality of functional capacity in chronic HF patients.

Author contributions

Conception and design of the research: Morais ER, Rassi S. Acquisition of data: Morais ER. Analysis and interpretation of the data: Morais ER, Rassi S. Statistical analysis: Morais ER, Rassi S. Writing of the manuscript: Morais ER, Rassi S. Critical revision of the manuscript for intellectual content: Morais ER, Rassi S.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics approval and consent to participate

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Goiás (approval number: 883 281/2014) and of the Pontifical Catholic University of Goiás (approval number: 922826/2014). All the procedures in this study

were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

- Fletcher GF, Ades PA, Kligfield P, Arens R, Balady GJ, Bittner VA, et al. Exercise standards for testing and training. A scientific statement from the American Heart Association. *Circulation*. 2013; 128(8):873-934.
- Bittner V, Weiner DH, Yusuf S, Rogers WJ, Mcintyre KM, Bangdiwala SI, et al. Prediction of mortality and morbidity with a 6-min walk test in patients with left ventricular dysfunction. *J Am Med Assoc*. 1993;270(14):1702-7.
- Forman DE, Arena R, Boxer R, Mary A, Eng JJ, Fleg JL, et al. Prioritizing functional capacity as a principal end point for therapies oriented to older adults with cardiovascular disease. *Circulation*. 2017;135(16):e894-918.
- Brooks D, Solway S, Gibbons WJ. ATS statement on six-minute walk test. *Am J Respir Crit Care Med*. 2003;167(9):1287.
- Iwama AM, Andrade GN, Shima P, Tanni SE, Godoy I, Dourado VZ. The six minute walk test and the body weight-walk distance product in healthy Brazilian subjects, *Braz J Med Biol Res*. 2009;42(11):1080-85.
- Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-83.
- Carvalho VO, Guimaraes GV, Carrara D, Bacal D, Bocchi E. Validação da versão português do Minnesota Living with heart failure questionnaire. *Arq Bras Cardiol*. 2009;93(01):39-44.
- Ferris BG. Epidemiology Standardization Project (American Thoracic Society). *Am Rev Respir Dis*. 1978;118(6 Pt 2):1-120.
- Matsudo SM, Araújo T, Matsudo VR, Andrade D, Andrade E, Oliveira L, et al. Questionário Internacional de Atividade Física (IPAQ): estudo de validade e reprodutibilidade no Brasil. *Rev Bras. Ativ Fís Saúde*. 2001;6(2):5-18
- Reis MM, Arantes PMM. Medida da força de prensão manual – validade e confiabilidade do dinamômetro saehan. *Fisioter Pesq*. 2011;18(2):176-81.
- Fess EE. Grip strength. In: Casanova JS, editor. *Clinical assessment recommendations*. 2nd ed. Chicago: ASHT. p. 41-45, 1992.
- Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil*. 1985;66(2):69-72.
- Sociedade Brasileira de Pneumologia e Tisiologia. Diretrizes para testes de função pulmonar. *J Pneumol*. 2002;28(3):1-221. 1-238
- Pereira CA, Sato T, Rodrigues SC. Novos valores de referência para espirometria forçada em brasileiros adultos de raça branca. *J Bras Pneumol* 2007;33(4):397-406.
- Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res*. 1999;32(6):719-27.
- Gorenstein C, Andrade L. Validation of a Portuguese version of the Beck Depression Inventory and the State-Trait Anxiety Inventory in Brazilian Subjects. *Braz J Med Biol Res*. 1996;29(4):453-57.
- Beck AT, Epstein N, Brown G, Steer RA. The Beck Anxiety inventory. *J Consult Clin Psychol*. 1988;56:893-97.
- Adel W, Shabana A, Fakhry H, Amin Y. Predictors of Functional Capacity in Chronic Heart Failure: Echocardiography Versus Six-Minute Walk Test. *J Cardiol Curr Res*. 2015;2(4):00071.
- Frankenstein L, Remppis A, Graham J, Schellberg D, Sigg C, Nelles M, et al. Gender and age related predictive value of walk test in heart failure: Do anthropometrics matter in clinical practice? *Int J of Cardiol*. 2008;127(3):331-6.
- Wegrzynowska-Teodorczyk K, Rudzinska E, Lazorczyk M, Nowakowska K, Banasiak W, Ponikowski P, et al. Distance covered during a six-minute walk test predicts long-term cardiovascular mortality and hospitalisation rates in men with systolic heart failure: an observational study. *J Physiother*. 2013;59(3):177-87.
- Ingle L, Shelton RJ, Cleland JG, Clark AL. Poor relationship between exercise capacity and spirometric measurements in patients with more symptomatic heart failure. *J Card Fail*. 2005;11(8):619-23.
- Witham MD, Argo IS, Johnston DW, Atruthers AD, McMurdo ME. Predictors of exercise capacity and everyday activity in older heart failure patients. *Eur J Heart Fail*. 2006;8(2):203-7.
- Bajraktari G, Kurtishi I, Rxhepaj N, Tafarshiku R, Ibrahim P, Jashari F, et al. Gender related predictors of limited exercise capacity in heart failure. *Int J Cardiol Heart Vessel*. 2013;1:11-6.
- Uszko-Lencer NH, Mesquita R, Janssen E, Werter C, Rocca HPB, Pitta F, et al. Reliability, construct validity and determinants of 6-minute walk test performance in patients with chronic heart failure. *Int J Cardiol*. 2017;240:285-90.
- Enright PL. The six-minute walk test. *Respir Care*. 2003; 48(8):783-5.
- Dourado VZ, Vidotto MC, Guerra RLF. Equações de referência para os testes de caminhada de campo em adultos saudáveis. *J Bras Pneumol*. 2011;37(5):607-14.
- Agrawal MB, Awad NT. Correlation between six minute walk test and spirometry in chronic pulmonary disease. *J Clin Diagn Res*. 2015;9(8):OC01-4.
- Silva JD, Lima CSFR, Reinaux CM, Brandão DC, Andrade AD. Repercussões da cardiomegalia na função pulmonar de indivíduos adultos com insuficiência cardíaca crônica: uma revisão sistemática. *Fisioter Pesqu*. 2011;18(1):84-91.
- Valadares YD, Corrêa KS, Silva OS, Araujo CLP, Karloh M, Mayer AF. Aplicabilidade de testes de atividades de vida diária em indivíduos com insuficiência cardíaca. *Rev Bras Med Esporte*. 2011;17(5):310-4.
- Camargo LA, Pereira CAC. Dyspnea in COPD: Beyond the Modified Medical Research Council Scale. *J Bras Pneumol*. 2010; 36(5):571-8.
- Wu G, Sanderson B, Bittner V. The 6-minute walk test: how important is the learning effect? *Am Heart J*. 2003;146(1):129-33.
- Belardinelli R, Georgiou D, Cianci G, Purcaro A. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: Effects on functional capacity, quality of life and clinical outcome. *Circulation*. 1999; 99(9):1173-82.
- McKelvie RS, Teo KK, Roberts R, McCartney N, Humen D, Montague T, et al. Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). *Am Heart J*. 2002; 144(1):23-30.
- Rosa TEC, Benício MH, Latorre MR, Ramos LR. Fatores determinantes da capacidade funcional entre idosos. *Rev Saúde Pública*. 2003; 37(1):40-8.
- Lord SR, Menz HB. Physiologic, psychologic, and health predictors of 6-minute walk performance in older people. *Arch Phys Med Rehabil*. 2002;83(7):907-11.

