

## Determinants of the distance walked in the six-minute walk test at discharge from patients with heart failure

Determinantes da distância percorrida no teste de caminhada de seis minutos na alta hospitalar de pacientes com insuficiência cardíaca

Determinantes de la distancia recorrida en la prueba de marcha de seis minutos al alta hospitalaria de pacientes con insuficiencia cardiaca

Received: 04/28/2022 | Revised: 05/26/2022 | Accepted: 01/12/2023 | Published: 01/14/2023

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### Abstract

**Background:** The distance walked during the six-minute walk test (6MWD) is predicted measure for mortality and rehospitalization in patients with heart failure. Objective: To identify the determinants of 6MWD at discharge from patients with heart failure. **Methods:** This is a descriptive and cross-sectional clinical study. Patients aged 18 to 80 years and functional class I to II were eligible. Those who have a type of psychiatric, cognitive or locomotor disorder; atrial fibrillation; use of a fixed frequency heart pacemaker were not eligible. The following were collected from the medical records: name, age, sex, BMI (body mass index); ejection fraction of the left ventricle; hemoglobin; fasting blood glucose; etiology of stay; presence of risk factors for cardiovascular diseases; presence of infection. The muscle strength of the knee extension movement was evaluated by dynamometry, a quality of life with the Nottingham Health Profile (NHP), the previous physical activity level by the International Physical Activity Questionnaire (IPAQ) and the 6MWD. **Results:** Sixty patients from a final sample (58.3% males, mean age 56.23±10.44 years). Were selected as the variables selected from the multivariate analysis: age (p=0.057), dynamometry (p=0.004), Total NPH (p=0.017) and IPAQ (p=0.018). R=0.72 and R<sup>2</sup>=0.53 with p<0.05 and the mean of the 6MWD was 393.16±42.80 meters. **Conclusion:** In this study the determinants of 6MWD were: age, total mean knee dynamometry, total NPH and IPAQ.

**Keywords:** Heart failure; Muscle strength; Quality of life.

### Resumo

**Introdução:** A distância percorrida durante o teste de caminhada de seis minutos (DTC6) é utilizada como preditor para mortalidade e reinternações em pacientes com insuficiência cardíaca. **Objetivo:** Identificar quais os fatores

determinantes da DTC6 na alta hospitalar de pacientes com insuficiência cardíaca. Métodos: Trata-se de um estudo clínico do tipo descritivo e transversal. Pacientes com idade entre 18 a 80 anos e classe funcional de I a III foram elegíveis. Aqueles que possuíam algum tipo de transtorno psiquiátrico, cognitivo ou locomotor; fibrilação atrial; uso de marcapasso cardíaco de frequência fixa não foram elegíveis. Foram coletados dos prontuários: nome; idade; sexo; IMC (índice de massa corporal); fração de ejeção do ventrículo esquerdo; hemoglobina; glicemia em jejum; etiologia da doença; tempo de diagnóstico; tempo de internamento; presença de fatores de risco para doenças cardiovasculares; presença de infecção. A força muscular do movimento de extensão de joelhos foi avaliada pela dinamometria, a qualidade de vida com o Perfil de Saúde de Nottingham (PSN), o nível de atividade física prévio pelo Questionário Internacional de Atividade Física (IPAQ) e a DTC6. *Resultados*: sessenta pacientes fizeram parte da amostra final (58,3% do sexo masculino; idade média de 56,23±10,44 anos). As variáveis selecionadas da análise multivariada foram: Idade ( $p=0,057$ ), Dinamometria ( $p=0,004$ ), PSN total ( $p=0,017$ ) e IPAQ ( $p=0,018$ ).  $R=0,72$  e  $R^2=0,53$  com  $p < 0,05$  e a média da DTC6 foi 393,16±42,80 metros. *Conclusão*: Neste estudo os determinantes da DTC6 foram: Idade, Média total da dinamometria de joelhos, PSN total e IPAQ.

**Palavras-chave:** Insuficiência cardíaca; Força muscular; Qualidade de vida.

### Resumen

*Antecedentes*: La distancia recorrida durante la prueba de caminata de seis minutos (6MWD) se utiliza como predictor de mortalidad y reingresos en pacientes con insuficiencia cardiaca. *Objetivo*: Identificar los factores determinantes de la 6MWD al alta hospitalaria de pacientes con insuficiencia cardiaca. *Métodos*: Se trata de un estudio clínico descriptivo, transversal. Fueron elegibles pacientes de 18 a 80 años y clase funcional I a III. Quienes tuvieran algún tipo de trastorno psiquiátrico, cognitivo o locomotor; fibrilación auricular; uso de marcapasos cardíaco de frecuencia fija; no eran elegibles. De las historias clínicas se recogieron: nombre; edad; sexo; IMS (índice de masa corporal); fracción de eyección del ventrículo izquierdo; hemoglobina; glucemia en ayunas; etiología de la enfermedad; tiempo de diagnóstico; duración de la estancia; presencia de factores de riesgo de enfermedades cardiovasculares; presencia de infección. Se evaluó la fuerza muscular del movimiento de extensión de rodilla mediante dinamometría, la calidad de vida con el Perfil de Salud de Nottingham (PSN), el nivel previo de actividad física mediante el Cuestionario Internacional de Actividad Física (IPAQ) y el 6MWD. *Resultados*: sesenta pacientes formaron parte de la muestra final (58,3 varones; edad media 56,23±10,44 años). Las variables seleccionadas del análisis multivariado fueron: Edad ( $p=0,057$ ), Dinamometría ( $p=0,004$ ), PSN total ( $p=0,017$ ) e IPAQ ( $p=0,018$ ).  $R=0,72$  y  $R^2=0,53$  con  $p < 0,05$  y la media del 6MWD fue 393,16±42,80 metros. *Conclusión*: En este estudio, los determinantes de la 6MWD fueron: Edad, Dinamometría media total de rodilla, PSN total e IPAQ.

**Palabras clave:** Insuficiencia cardiaca; Fuerza muscular; Calidad de vida.

## 1. Introduction

Heart failure (HF) syndrome is the common final pathway of most heart disease. Heart failure is clinically characterized by exercise intolerance, poor quality of life and low survival rates (Bocchi et al 2009; Freitas et al., 2013).

One of the main characteristics of patients with HF is the decline in exercise capacity and quality of life (Morais et al., 2013). The six-minute walking test is a simple, safe, and well-accepted method of exercise capacity assessment in clinical practice and research (Ussavarungsi et al., 2016). The maximum walked distance on the 6MWT is associated with mortality and hospital readmissions. In addition, it is very useful in assessing the response to intervention, such as an exercise training program (Carvalho et al., 2011; Marcassa et al., 2016).

A previous study assessed the determinants of improvement in six-minute walk distance from admission to discharge in acute systolic heart failure. However, no data is available about the influence of physical variables, such as strength and previous level of physical activity on maximum walking distance at hospital discharge (Omar et al., 2017; Marcassa et al., 2016). Understanding the determinants of the maximum walked distance on the 6MWT at hospital discharge is important to plan more efficient strategies on exercise-based cardiovascular rehabilitation.

The aim of this study was to investigate the determinants of the maximum walking distance on the six-minute walking test in patients with heart failure at hospital discharge.

## **2. Methodology**

### **2.1 Study design**

This is a cross-sectional study that aimed to investigate the determinants of the maximal walking distance on the six-minute walking test in patients with heart failure at hospital discharge.

### **2.2 Population**

Eligibility criteria: stable patients with heart failure at hospital discharge between 18-80 years old, functional class (New York Heart Association - NYHA) I, II and III independently of the time of diagnosis, etiology or sex. Patients with fixed frequency pacemaker, atrial fibrillation, psychiatric disorders, cognitive or locomotor impairment that could prevent the correct performance of the six-minute walking test were not eligible.

All the patients were taking the current prescribed medication during the study protocol.

### **2.3 Patient's chart**

We collected age (years), sex, body mass index (kg/m<sup>2</sup>), left ventricle ejection fraction (%), heart failure etiology, time of diagnose (days), hospital stay (days), hemoglobina (g/dl), fasting blood glucose, infections during hospital stay, smoking (yes or no) and the presence of co-morbidities such as hypertension, diabetes, dyslipidemia.

### **2.4 Maximum isometric strength assessment**

We used a digital scale dynamometer with Kgf scale (EMG System model 432C) with an anatomic adapter for better coupling of the lower limb. The isometric strength was assessed bilaterally on knee extension. Patients remained seated in a chair with knees at 90° and hips at 110° of flexion and abducted at shoulder line. Patients performed the test under the standard verbal command "force, force, force" thus exerting a continuous isometric force for 5 seconds. Patients were instructed not to perform a Valsalva maneuver (Neves et al., 2011). Three independent measurements were performed, with an interval of one minute between them. We considered the average of the three executions.

The extensor chair used for dynamometry was financed by the Foundation for Research and Technological Innovation Support of the State of Sergipe (FAPITEC-SE).

### **2.5 Quality of life**

We used the Nottingham Health Profile (NHP) to assess quality of life. NHP is a generic instrument for assessing quality of life for patients with chronic diseases (Teixeira-Salmela et al., 2004). This questionnaire has been used in hospitalized patients (Cinarli et al., 2017).

### **2.6 Level of physical activity**

We used the short version of the International Physical Activity Questionnaire (IPAQ) to estimate the level of physical activity (Sedentary, irregularly active, active or very active) before hospital admission (Garcia et al., 2013; Binotto et al., 2014).

### **2.7 Six-minute walking test**

The six-minute walking test was performed according to the European Respiratory Society/ American Thoracic Society guideline (ATS 2002; Holland et al., 2014). We performed two tests with an interval of 30 minutes or the time enough to return heart rate and blood pressure to baseline. The tests were performed in a 30-meters flat corridor. The maximal walking

distance was checked at the end of the sixth minute. Heart rate was assessed before and at the sixth minute of the tests (ATS 2002).

## 2.8 Statistical analysis

For the sample size calculation, we used the following formula proposed by a study, for a given variance ( $\Delta r_j^2$ ) = 0.05 and a variance explained by the model ( $R^2$ ) = 50% ou 0.05,  $n = 41 + K$ . Since K was the number of variables, 15 variables were considered as potentially associated with the 6MWD to determine the final model, requiring a minimum of the 56 patients (Milton S., 1986). For all statistical analysis, we used the SPSS (Chicago II, USA) version 22.0.

Data were presented as mean and standard deviation. The univariate analysis, performed by the simple linear regression test, was used to select the variables eligible to the multivariate analysis model. We considered a level of significance < 20% ( $p < 0.20$ ) for the univariate analysis.

Non-significant variables were excluded from the multivariate analysis one by one manually following the criterion of the higher "p" value. The model was determined when all variables presented a level of significance less than 5% ( $p < 0.05$ ). The dependent variable was the maximum walking distance in the six-minute walking test.

The variables considered for univariate analysis were: age, gender, BMI, heart rate delta, left ventricular ejection fraction, hemoglobin, fasting blood glucose, heart failure etiology, diagnosis time, hospitalization time, presence of infection, presence of risk, mean between maximum isometric muscle strength of right and left knee extension (Dynamometry), NHP total score and previous level of physical activity (IPAQ).

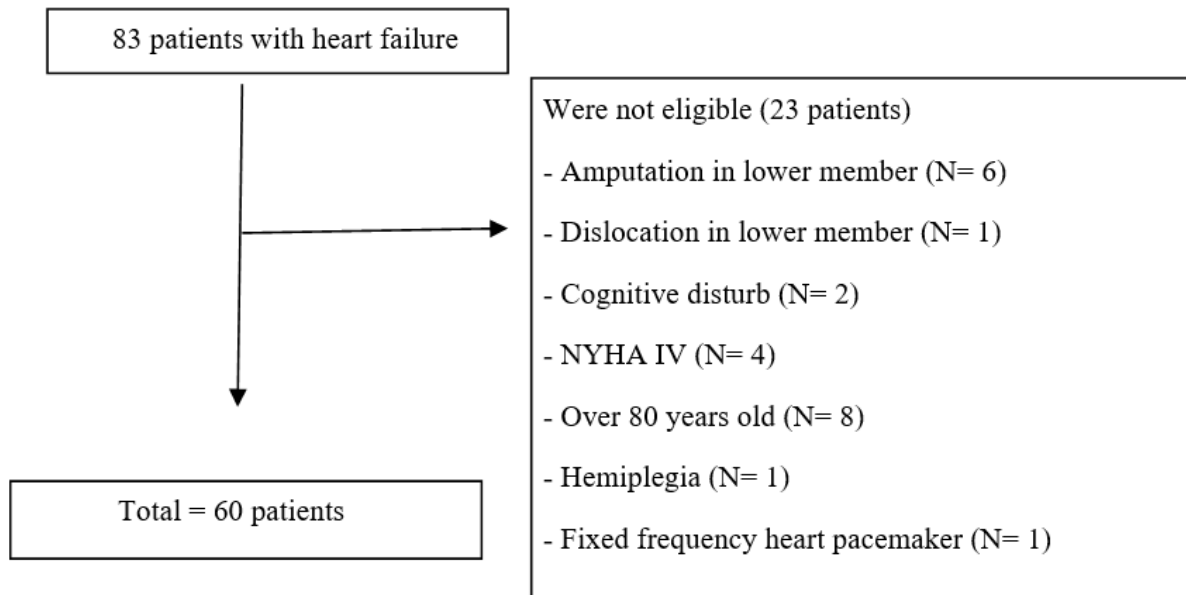
## 2.9 Ethical aspects

The project was submitted to the Ethics and Research Committee of the Federal University of Sergipe via Plataforma Brasil (Resolution no. 466 of December 12, 2012 of the National Health Council of the Ministry of Health) and was approved under the number CAAE: 40699714.6.0000.5546 and number of seem 949.539. All participants eligible for research signed the informed consent form.

## 3. Results and Discussion

Patients were assessed between September 2015 and march 2017 in a tertiary hospital (Fundação de Beneficência Hospital de Cirurgia-FBHC, Aracaju, Sergipe, Brazil) (Figure 1). The six-minute walking test was well tolerated by all 60 patients without any harm or discomfort (Tables 1 and 2). The mean maximum walking distance was  $393,16 \pm 42,80$  meters, which represents 69% of the predicted to health Brazilians (Britto et al., 2013).

**Figure 1** - Flowchart of study patients.



Source: Autors.

**Table 1** - Characterization of study participants.

Variable	Mean and Standard Deviation
Age (years)	<b>56.23 ± 10.44</b>
BMI (kg/m <sup>2</sup> )	<b>25.28 ± 2.6</b>
Hemoglobin (g/dl)	<b>13.37 ± 1.2</b>
Blood glucose (mmol/l)	<b>87.08 ± 18.89</b>
Left Ventricular Ejection Fraction (%)	<b>44.43 ± 3.6</b>
Time of hospital stay (Days)	<b>6.8 ± 2.3</b>
Diagnostic time* (Days)	<b>294.36 ± 10.00</b>
HR Initial (bpm)	<b>81.43 ± 8.8</b>
HR End (bpm)	<b>86.81 ± 7.8</b>
Δ HR (bpm)	<b>5.3 ± 4.4</b>
Gender	N (%)
Male	<b>35 (58.3)</b>
Female	<b>25 (41.7)</b>
Risk factors	N (%)
One risk factor	<b>25 (41.7)</b>
Two risk factors	<b>23 (38.3)</b>
Three risk factors	<b>11 (18.3)</b>
Four risk factors	<b>1 (1.7)</b>
Infection - n (%)	<b>4 (6.7)</b>
Etiology	N (%)
Ischemic	<b>53 (88.3)</b>
Not ischemic	<b>7 (11.7)</b>

BMI: Body Mass Index; g/dl: gram per deciliters; mmol/l: milimol per liter; HR: heart rate; Bpm: Beats per minute; \*Was presented in median. Source: Authors.

**Table 2** - Characterization of muscular strength, quality of life and level of physical activity.

Variable	Mean and Standard Deviation
<i>Dynamometry - kgf</i>	
Right Knee	<b>43.35 ± 11.08</b>
Left Knee	<b>44.17 ± 10.09</b>
Total Mean	<b>87.00 ± 22.45</b>
<i>NHP*</i>	
Energy Level	<b>9.6 ± 2.9</b>
Ache	<b>9.5 ± 2.4</b>
Emotional Reactions	<b>9.5 ± 1.2</b>
Sleep	<b>22.86 ± 3.4</b>
Social Interaction	<b>9.5 ± 1.4</b>
Physical Skills	<b>6.7 ± 2.0</b>
Total	<b>66.99 ± 7.4</b>
<i>IPAQ</i>	
	N (%)
Sedentary	<b>9 (15.0)</b>
Irregularly Active	<b>28 (46.7)</b>
Active	<b>16 (26.7)</b>
Very Active	<b>7 (11.7)</b>

Kgf: kilogram strength; NHP: Nottingham Health Profile; IPAQ: International Physical Activity Questionnaire; \*Were presented in mean and standard error. Source: Authors.

The univariate analysis showed: Age ( $p = 0.060$ ), BMI ( $p = 0.074$ ), fasting blood glucose ( $p = 0.005$ ), etiology of heart failure ( $p = 0.028$ ), presence of infection during hospital stay ( $P = 0.048$ ), maximum isometric muscle strength ( $p=0.000$ ), NHP total score ( $p = 0.000$ ) and previous level of physical activity (IPAQ) ( $p = 0.000$ ).

The following variables were withdrawn from the multivariate analysis: fasting blood glucose ( $p = 0.946$ ), heart failure etiology ( $p = 0.623$ ), BMI ( $p = 0.632$ ) and presence of infection during hospital stay ( $p = 0.222$ ).

The final variables that determined the maximum walking distance at the six-minute walking test were: age ( $p=0.057$ ), maximum isometric muscle strength ( $p=0.004$ ), NHP score total ( $p=0.017$ ) and previous level of physical activity (IPAQ) ( $p=0.018$ ) (Table 3).

**Table 3** - Independent variables selected through multiple linear regression as predictors of 6MWD.  $\beta$  – Regression Coefficient.  $R = 0,72$  e  $R^2=0,53$  with  $p < 0,05$ .

Table 3 - Selected variables in multivariate analysis.		
Variable	$\beta$	p
Constant	353.566	0.000
Age	-0.759	0.057
Total Mean Dynamometry	1.487	0.004
NHP Score Total	-0.211	0.017
IPAQ	11.804	0.018

Source: Authors.

#### 4. Discussion

Our study showed that the main determinants of maximal walking distance at six-minute walking test in individuals with heart failure at hospital discharge were age (negatively associated), maximum isometric muscle strength (knee extension), NHP total score and previous level of physical activity (IPAQ). This is the first study that aimed to investigate the determinants of maximum walking distance on the six-minute walking test at hospital discharge.

The 6MWT is a simple, safe and low cost method to assess exercise performance. Moreover, the maximum walking distance on the 6MWT is an important prognostic variable in patients with heart failure (Rubim et al., 2006). The functionality has been associated with the postoperative survival of patients at hospital discharge after cardiac surgery (Oliveira et al., 2014). Understanding the determinants of the maximum walked distance on the 6MWT at hospital discharge is important to plan more efficient strategies on exercise-based cardiovascular rehabilitation.

A previous study investigated the determinants of the maximum walking distance on the 6MWT in patients undergoing cardiac surgery at hospital discharge, where the type of cardiac surgery (valve replacement or myocardial revascularization) was found to be the main determinant factor, but it was not evaluated muscle strength<sup>19</sup>. This evaluated is considered as a predictor of muscle strains associated with the functionality of cardiac patients (Hermández-Luiz et al., 2017)

The evaluation of muscle strength has been used as a prognostic value for mortality in hospitalized patients (Santos Souza et al., 2014; Barbosa et al., 2014). The poor quality of life associated with muscle strength reduction in HF patients presents with lower scores in the functional capacity dimension (Liu et al., 2017; Pirek et al., 2017). However, after a cardiac event, patients who present a reduction in peripheral muscle strength have a tendency to gain it until the moment of hospital discharge, through a treatment directed to their dysfunctions, also improving their quality of life (Santos Souza et al., 2014; Pirek et al., 2017).

The vast majority of cardiac patients have impaired exercise capacity and approximately 50% are unable to reach current recommendations for physical activity, thus representing a risk factor for various diseases (Liu et al., 2017; Pirek et al., 2017; Bay et al., 2017). In our study, the variable that most influenced positively was the IPAQ, where 46.7% of the patients presented themselves as irregularly active, this is, the better their previous level of physical activity the higher their 6MWT. This reinforces the importance in evaluating it, since a study brings as a potential limitation the absence of this evaluating which can directly influence the functional status of these patients (Oliveira et al., 2014).

In the research the combination of independent variables was able to explain 53% of the variability of the 6MWD in the total sample. Compared with previously published studies for healthy individuals, our value is satisfactory because it is in the range of the proposed equations that explain from 30% a 66% of the variability the 6MWD (Britto et al., 2013; Iwana et al., 2009; Enright, Sherrill., 1998).

The main limitation of our study is the lack of pulmonary function assessment. However, a study found no association between pulmonary function and maximum walking distance in patients undergoing cardiac surgery at hospital discharge (Oliveira et al., 2014). Moreover, we assessed patients from just one tertiary hospital.

## 5. Conclusion

The determinants of maximal walking distance at six-minute walking test in individuals with heart failure at hospital discharge were age (negatively associated), maximum isometric knee extension strength, NHP total score and previous level of physical activity.

## Acknowledgments

The authors would like to thank the collaboration of the Fundação Beneficência Hospital Cirurgia for this study.

## Abbreviations

6MWD: Distance walked in six-minute walk test; 6MWT: Six-minute walk test; BMI: Body mass index; NHP: Nottingham Health Profile; IPAQ: International Physical Activity Questionnaire; HF: Heart failure; NYHA: New York Heart Association; HR: heart rate; Bpm: Beats per minute; Kgf: kilogram strength.

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