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Original article

Correlation between the 6-minute walking test and the cardiopulmonary exercise test in individuals with heart failure

Correlação entre o teste de caminhada de 6 minutos e o teste de exercício cardiopulmonar em indivíduos com insuficiência cardíaca

Valéria Cristina de Faria[1], Ana Carolina Campos Ferreira[1], Dayana Magalhães Drummond Oliveira[1], Danielle Aparecida Gomes Pereira[1]

1. Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil

ABSTRACT

Objective: This study aimed to verify the correlation between the 6-minute walking test (6MWT) and the cardiopulmonary exercise test (CPET) in individuals with heart failure (HF), and to analyze the sensitivity of 6MWT in differentiating individuals from classes I, II, and III of the New York Heart Association (NYHA) functional classification system. Methods: Seventeen individuals (3 class I, 8 class II, and 6 class III) aged 48.09 ± 12.91 years with a left ventricular ejection fraction of 44 ± 11% and VO2peak of 25.18 ± 6.05 mL·kg-1·min-1 were assessed. Volunteers performed CPET on a treadmill; after an interval of 48 h to 6 months, they performed 6MWT. Pearson and Spearman correlations were used, and ANOVA was used to compare 6MWT variables between NYHA functional classes. An alpha of 5% was adopted as significant. Results: Significant correlations were found between distance walked in 6MWT and VO2peak (r = 0.70). Significant differences were found between NYHA functional classes regarding the distance walked in 6MWT. For walking performance, significant differences were found between NYHA classes I and II (p = 0.0001) and between classes I and III (p = 0.0001). Conclusion: The 6MWT is a simple and reliable method to assess the functional capacity of individuals with HF, proving to be a valid instrument for clinical practice.

Keywords: stress test; heart failure; 6-minute walking test.

RESUMO

Objetivo: Este estudo teve como objetivo verificar a correlação entre o teste de caminhada de 6 minutos (TC6) e o teste de exercício cardiopulmonar (TECP) em indivíduos com insuficiência cardíaca (IC), e analisar a sensibilidade do TC6 em diferenciar indivíduos das classes I, II e III do sistema de classificação funcional da New York Heart Association (NYHA). **Métodos:** Dezessete indivíduos (3 classe I, 8 classe II e 6 classe III) com idade de 48,09 ± 12,91 anos, fração de ejeção do ventrículo esquerdo de 44 ± 11% e VO2pico de 25,18 ± 6,05 mL·kg-1·min-1 foram avaliados. Os voluntários realizaram TECP em esteira; após um intervalo de 48h a 6 meses, realizaram o TC6. Correlações de Pearson e Spearman foram usadas, e ANOVA foi usada para comparar as variáveis do TC6 entre as classes funcionais da NYHA. Um alfa de 5% foi adotado como significativo. **Resultados:** Foram encontradas correlações significativas entre a distância percorrida no TC6 e o VO2pico (r = 0,70). Diferenças significativas foram encontradas entre as classes funcionais da NYHA em relação à distância percorrida no TC6. Para o desempenho da caminhada, foram encontradas diferenças significativas entre as classes NYHA I e II (p = 0,0001) e entre as classes I e III (p = 0,0001). **Conclusão:** O TC6 é um método simples e confiável para avaliar a capacidade funcional de indivíduos com IC, mostrando-se um instrumento válido para a prática clínica.

Palavras-chave: teste de esforço; insuficiência cardíaca; teste de caminhada de 6 minutos.

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Correspondence: Danielle Aparecida Gomes Pereira, E-mail: danielleufmg@gmail.com

Introduction

Heart failure (HF) is a clinical systemic syndrome characterized by cardiac dysfunction, which leads to a blood supply insufficient for metabolic needs of tissue [1]. It is the later stage of most diseases that attack the heart. These diseases are often associated with disabling symptoms, such as dyspnea and fatigue, which lead to exercise intolerance [2]. Exercise intolerance leads to a reduction of functional capacity and is directly associated with the prognosis of the disease [3]. Therefore, valid and reliable methods are vital for the prescription of appropriate exercise during the rehabilitation process of these patients.

In HF, 2 methods are most commonly used to define the degree of exercise limitation: the cardiopulmonary exercise test (CPET) and the 6-minute walking test (6MWT) [3]. The CPET is considered the gold standard for the assessment of functional capacity and prognosis of individuals with HF [4]. It is a non-invasive assessment procedure and provides important information on the individual's aerobic capacity [4]. The CPET is highly reliable in patients with HF and is a well-accepted method of assessment in this population [5].

The CPET aims to assess the clinical, hemodynamic, electromyographic, metabolic, and ventilatory responses to effort [6]. It is a test that has the primary variables oxygen consumption (VO_2), carbon dioxide (CO_2) production, respiratory rate (RR), tidal volume (VT), and heart rate (HR) [5]. With these parameters, it is possible to calculate secondary variables such as pulmonary ventilation (VE), respiratory exchange rate ($RER = VCO_2/VO_2$), expired oxygen fraction ($\%FEO_2$), carbon dioxide expired fraction ($\%FECO_2$), oxygen pulse (VO_2/FC), oxygen ventilatory equivalent (VE/VO_2), and CO_2 ventilatory equivalent (VE/VCO_2). Some of these variables have been described in the literature as predictors of the prognosis of individuals with HF. Values of VE/VCO_2 less than 35 $mL \cdot kg^{-1} \cdot min^{-1}$ indicate the worst prognosis in these individuals [1,6].

Although the CPET is the gold standard for HF, many individuals have difficulties in being evaluated by a maximum test, especially those who are more impaired, unfit, or elderly. The equipment required for this test is expensive and requires specialized staff. Furthermore, the maximum exercise performed may not reflect the difficulties of individuals with HF in performing daily activities [4]. Thus, the CPET may not be the most appropriate test to assess the functional capacity of these individuals in situations of lower effort.

The 6MWT has been proposed as another tool for the assessment of the physical capacity of individuals with HF. It is a safe, valid ($r = 0.687$, $p < 0.001$) [7], and reliable test. It is easily performed, has low costs, and predicts the survival of individuals with the disease [6]. The effort during the 6MWT is described as similar to activities of daily living, enabling the individual to determine the walking rhythm he/she tolerates; this is an advantage for those with a greater degree of impairment who would not tolerate the CPET [2,3,6,8-12]. The main variable analyzed in the 6MWT is the distance walked [6]. In addition, the speed is assessed and the hemodynamic response to effort is analyzed (HR, BP, and SpO_2).

Based on previous evidence, both the 6MWT and the CPET are indicated to assess functional capacity and establish the prognosis of individuals with HF [3,6]. However, in the Brazilian population, few studies have correlated the variables obtained in both tests [13]. In a recent study, Carvalho *et al.* [13] verified the reproducibility of the 6MWT in a sample of Brazilian individuals with HF and correlated the VO_{2peak} obtained by the CPET with the variables of the 6MWT. No correlations with other cardiorespiratory variables of important prognostic value for HF, such as VE/VCO_2, were established. Therefore, more studies that investigate the correlation between the variables used in the CPET and the 6MWT are necessary in order to confirm the similarity of the results of both tests when performed on individuals with HF. Furthermore, it is important to analyze if the existing submaximal tests, such as the 6MWT, are sensitive enough to stratify individuals with different functional capacity levels.

The present study aimed to verify the correlation between the variables used in the 6MWT and the CPET in a Brazilian sample of individuals with HF, attended at the public health service, as well as analyze if the 6MWT is sensitive enough to differentiate between individuals of the New York Heart Association (NYHA) functional classes I, II, and III.

Methods

Sample

A transversal study, approved by the Ethics in Research Committee of the *Universidade Federal de Minas Gerais* (Protocol number 050/09), was conducted. Individuals with HF having symptoms that indicated effort limitation (NYHA classes I, II and III), independent of gender and ethnic group, were included. Individuals with HF were selected by convenience in an ambulatory cardiology service associated with the institution.

The study included individuals aged between 30 and 59 years with the following characteristics: presence of HF for at least 6 months, as confirmed by the ambulatory cardiology service; clinically stable condition for at least 2 months prior to the study; left ventricular ejection fraction (LVEF) at rest <45%, recently assessed by the bidimensional echocardiogram (up to 6 months); and classification as NYHA class I, II, or III and HF stage C, according to the American College of Cardiology/American Heart Association guidelines [14]. The individuals included in the study were prescribed optimized doses of beta-blockers [15,16], ECA inhibitors [15], or angiotensin receptor blockers and had a body mass index (BMI) <30 kg/m^2.

Individuals who did not meet the criteria that define the effort test as maximum [6], who presented a peripheral oxygen saturation (SpO_2) lower than 85% during exercise, or who presented any type of complication such as the flu or a cold, hospital admission, or alterations in medication prescription between the CPET and the 6MWT were excluded from the study.

Procedures and data collection

The volunteers attended LabCare. After signing the written consent form, they were assessed by the CPET (*Medical Graphics® CPX Ultima, Miami, FL, USA*) on a treadmill (*Millenium Classic CI®, Inbramed/Inbrasport, Brazil*) using a ramp protocol [17], according to the Brazilian Cardiology Society on Ergometric Test Guidelines, in order to determine the cardiorespiratory parameters. During the test, HR was monitored by an electrocardiogram (*Welch Allyn® Cardioperfect, USA*) connected to an ergospirometer. Blood pressure was measured using a sphygmomanometer (*Diasyst®, São José dos Campos, SP, Brazil*) and a stethoscope (*Litmann Classic II S.E 3M®, USA*). SpO_2 was continuously measured by an oximeter (*Model 300 Series MEDIAD INC., California, USA*) connected to the ergospirometer. The subjective effort perception for dyspnea and lower limb fatigue was assessed by the modified Borg scale.

After a minimum interval of 48 h and a maximum of 6 months, the volunteers returned to LabCare to perform the 6MWT. The test was performed in a 30-m-long hallway, where the volunteer was instructed to walk the longest distance possible in 6 min, without running or trotting. The route was delimited by plastic cones and standard encouraging phrases, such as "very good, go on" and "let's go, continue walking as fast as possible," were given every minute [11,18]. Before and after the test, blood pressure was measured using a sphygmomanometer (*Diasyst®, São José dos Campos, SP, Brazil*) and a stethoscope (*Litmann Classic II S.E 3M.®, USA*). The subjective effort perception for dyspnea and lower limb fatigue was assessed at the end of the test by the modified Borg scale. The SpO_2 was continuously measured during the test by an oximeter (*Ohmeda Tuffsat®*), and the HR by a cardiofrequencimeter (*Polar S810®*).

The test was interrupted if any of the following criteria were observed: precordial pain, unbearable dyspnea, oxygen saturation lower than 85%, muscle cramps, limping gait, discomfort, or dizziness and paleness [19]. Two tests, with a 15-min interval between them, were performed. If the difference between the distance walked in the tests was higher than 10%, a third test was performed [11,18]. Data obtained from the 6MWT were registered in a patient identification form, which contained personal data and information on life habits.

Variables

Although the CPET provides information on the cardiorespiratory system's response to effort, the variables with higher interest for this study were VO_{2peak} (primary variable), VE/VCO_2, and PO_2 (secondary variables). The distance walked was the primary variable obtained by the 6MWT with most interest. The following variables were considered secondary variables: speed, HR, and walking performance (distance/HR). All these variables were studied in order to establish a correlation between the tests.

Statistical analysis

Data were presented as measures of central tendency and dispersion. Data distribution was analyzed by the Shapiro–Wilk test. The correlations were performed

using the Pearson correlation coefficient or the Spearman correlation coefficient, for variables with normal and non-normal distribution, respectively. One-way ANOVA was used to compare the 6MWT variables between NYHA functional classes I, II, and III. In all statistical tests, alpha values of 5% were considered significant. The software Statistical Package for the Social Sciences® (*SPSS, Chicago, IL, USA*) version 17.0 was used for data analysis.

Results

Seventeen individuals (5 women and 12 men) with HF (3 NYHA class I, 8 class II, and 6 class III) participated in the study, with an average age of 48.09 ± 12.91 years (95% CI = 39.42–56.76), LVEF of 44% ± 11% (95% CI = 0.36–0.51), and BMI of 25.86 ± 2.86 kg/m^2 (95% CI = 23.93–27.98). Data from the results obtained for the CPET and 6MWT are shown in Table I.

Table I - Results of the variables assessed in the cardiopulmonary exercise test and the 6-minute walking test (N = 17)

Variables	Mean ± SD
VO_{2peak} (mL·kg^{-1}·min^{-1})	25.28 ± 6.20
VE_VCO_2 (mL·kg^{-1}·min^{-1})	33.29 ± 3.13
PO_2 (mL O_2/bpm)	13.65 ± 7.22
RER	1.15 ± 0.08
D_6MWT (m)	622.71 ± 82.61
V_6MWT (m/minute)	103.54 ± 12.58
D/HR_6MWT (m/bpm)	4.98 ± 0.96

bpm = beat per minute; SD = standard deviation; VO_{2peak} = oxygen consumption at peak effort; VE/VCO_2 = ventilatory equivalent for carbon dioxide; PO_2 = oxygen pulse; RER = respiratory exchange rate; D_6MWT = distance walked in the 6-minute walking test; V_6MWT = velocity obtained in the 6-minute walking test; D/HR= walking performance

Significant and strong correlations were found between speed and distance walked in the 6MWT and VO_{2peak} and between walking performance (D_6MWT/PR) and PO_2 (Table 2).

Table II - Correlation between the variables of the 6-minute walking test and the cardiopulmonary exercise test

Variables	VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	VE/VCO_2	RER	PO_2 ($mL \cdot min^{-1} \cdot bpm^{-1}$)
D_6MWT	r = 0.702[a]	r = 0.169[a]	r= 0.49[a]	r = 0.352[a]
(m)	p = 0.002	p = 0.517	p= 0.853	p = 0.166
V_6MWT	r = 0.707[a]	r = 0.173[a]	r = 0.049[a]	r = 0.352[b]
(m/min)	p = 0.001*	p = 0.507	p = 0.852	p = 0.166
D/HR_6MWT	r = 0.614[a]	r = 0.356[a]	r = 0.004[a]	r = 0.847[b]
(m/bpm)	p = 0.009*	p = 0.161	p = 0.987	p = 0.0001*

bpm = beat per minute; VO_{2peak} = oxygen consumption at peak effort; VE/VCO_2 = ventilatory equivalent for carbon dioxide; RER = respiratory exchange rate; PO^2 = oxygen pulse; D_6MWT = distance walked in the six-minute walking test; V_6MWT = velocity obtained in the 6-minute walking test; D/HR = walking performance. [a] = Pearson correlation coefficient; [b] = Spearman correlation coefficient; * = $p < 0.005$

Significant differences were found between NYHA functional classes with respect to the distance walked in the 6MWT, speed obtained in the 6MWT, and walking performance (Table III).

Table III - Comparison of the variables of the 6-minute walking test between the different NYHA functional classes

Variables 6MWT	Class I	Class II	Class III	F	p
D_6MWT, mean ± SD	670.66 ± 34.12	637.40 ± 77.63†	553.33 ± 58.62#	4.99	0.023
V_6MWT, mean ± SD	111.33 ± 6.02	106.00 ± 13.00†	91.66 ± 10.01#	4.94	0.024
D_6MWT/HR (meter/bpm), mean ± SD	6.31 ± 0.27	4.54 ± 0.49*	4.37 ± 0.58#	16.70	0.005

bpm = beat per minute; SD = standard deviation; D_6MWT = distance walked in the 6-minute walking test; V_6MWT = velocity obtained in the 6-minute walking test; D/HR= walking performance. Class I = no symptomatology; Class II = symptoms during daily activities; Class III = symptoms during small efforts; F = ANOVA; * = $p < 0.05$ between classes I and II; # = $p < 0.05$ between classes I and III; † = $p < 0.05$ between classes II and III

There were no significant differences between the individuals from different NYHA functional classes in relation to age, BMI, and LVEF.

Discussion

The main finding of the present study was the strong correlation between the distance walked and the speed reached in 6MWT and the VO_{2peak} obtained in CPET; this demonstrated the ability of 6MWT to objectively assess the functional capacity of individuals with HF, especially considering that the sample represents individuals assisted by the public health service.

Standard tests are useful to compare and document changes in the functional capacity of an individual through time [2]. In individuals with HF, 6MWT has been a submaximal test widely used to assess the degree of limitation to exercise. The advantages of this test, such as simplicity, viability, and insignificant cost, have been

repeatedly reported [2,3,6,8-12]. Moreover, since it is a submaximal test in which the individual determines the walking rhythm he or she tolerates, it has been suggested that the 6MWT is highly applicable to activities of daily living.

Several authors have assessed the use and clinical applicability of the 6MWT in different populations with diverse levels of severity [6,12,20-27]. The present study assessed individuals with HF of mild severity (VO_{2max}, >20 $mL \cdot kg^{-1} \cdot min^{-1}$), according to the classification proposed by Weber [28].

The results of the present study agree with the findings of Guazzi *et al.* [3], who assessed 253 individuals with HF NYHA classes II and III. In their study, the distance walked in the 6MWT was strongly correlated with the VO_{2peak} ($r = 0.788$; $p = 0.001$), and there was a weak, but significant, correlation between the 6MWT and VE/VCO_2 ($r = 0.46$; $p = 0.001$). Moreover, the distance walked in the 6MWT decreased significantly with the progression of the functional classes proposed by Weber *et al.* [28].

Other authors have also verified these correlations by finding similar results. Cahalin *et al.* [20] assessed 45 individuals with HF and obtained correlations of moderate magnitude between the distance walked in the 6MWT and VO_{2peak} ($r = 0.64$; $p = 0.001$). According to these authors, the 6MWT was a strong predictor for the occurrence of undesirable events, such as death and hospitalization. Compared to individuals who walked longer distances, individuals who walked less than 300 meters in the 6MWT showed an increased death risk in 6 months. A study by Pulz *et al.* [27] assessed the ability of submaximal tests, such as the 6MWT and the shuttle walking test (SWT), in predicting a decrease in O_2 consumption and establishing a prognosis in individuals with HF. Significant correlations were found between VO_{2peak} and the distance walked in the 6MWT ($r = 0.76$; $p = 0.001$) and the SWT ($r = 0.79$; $p = 0.001$). The sensitivity of both tests in predicting reduced levels of O_2 consumption (VO_{2max}, <14 $mL \cdot kg^{-1} \cdot min^{-1}$) was 490 m, predominantly in individuals with mild functional impairment (Weber classes A and B), and submaximal tests were not considered good predictors of mortality in this population.

Although other authors have also reported significant correlations between the distance in the 6MWT and other cardiorespiratory variables with important prognostic value, such as VE/VCO_2 [3,20], the results of the present study did not exhibit these correlations. A larger number of individuals with HF may be necessary to reach a sufficient size to obtain statistical significance. The sample calculation of the present study considered the number of individuals necessary to establish a correlation between the 6MWT and VO_{2peak} of the CPET, the primary variables of the study.

Another CPET variable with clinical prognostic and mortality value for HF is PO_2 [29-31]. PO_2 is considered one of the most important variables assessed by ergospirometry. The variable is related to the systolic volume and the arteriovenous O_2 difference, representing an indirect index of the O_2 transport at each cardiac systole [31-33]. In our study, the walking performance variable showed a strong correlation with the PO_2 determined by ergospirometry and may be related to the tissue efficiency in using the offered O_2. In other populations, such as individuals with peripheral

obstructive arterial disease, this variable has been used to infer the cardiovascular conditioning [34] and is a variable of interest in the assessment of therapeutic interventions. Thus, if an individual is able to walk a longer distance while reaching lower HR values after physical training, it can be inferred that the physical capacity has been enhanced.

Functional capacity has shown a significant correlation with HF severity [35]. A simple and widely used method to quantify the impact of HF on the individual's daily life is the classification proposed by NYHA. According to this classification, individuals with HF can be categorized into 1 of 4 classes according to the intensity of the symptoms and the degree of limitation in performing daily activities [1]. The NYHA functional classification is a subjective estimation of the individual's real functional capacity and is significantly correlated with the objective measure of VO_2 determined by the CPET [36].

The CPET is sensitive enough to differentiate between individuals of NYHA functional classes I, II, and III [36]; however, limited data are available on the sensitivity of the 6MWT in stratifying individuals from different functional classes. In the present study, it was possible to observe significant differences between NYHA functional classes I and III, and between classes II and III in the comparisons that involved distance and speed in the 6MWT. No significant differences were found between classes I and II. This finding may be related to the fact that individuals from functional classes I and II are in the initial stages of the disease, when there are fewer repercussions for functional capacity. Another aspect that may have contributed to the limitation of the 6MWT in stratifying these individuals was the overall percentage of NYHA I individuals, which was considered relatively small (17%) when compared to the other functional classes. A significant difference was observed between classes I and II for the variable of walking performance. This finding may be explained by the fact that this variable has additional distance values compared to the HR data. This may have increased the variable's sensitivity and ability to stratify these individuals, even in initial stages of the disease when there are fewer negative repercussions for function.

One limitation of our study was that the sample was composed predominantly of individuals with HF and mild functional impairment (Weber classes A and B). Therefore, other studies are necessary to demonstrate such results in individuals with HF and moderate-to-severe functional impairment.

Conclusion

In the present study, the 6MWT correlated with the direct measure of VO_{2peak} (gold standard for functional capacity assessment) and was able to stratify individuals with different levels of functional capacity according to the classification proposed by NYHA. Thus, the 6MWT proved to be a simple and valid clinical tool for the assessment of individuals with HF, and with special external validity for individuals assisted by the public health service.

Academic affiliation
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Conflict of interest
There are no conflicts of interest.

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Authors' contribution:
Conception and design of the research: Ferreira ACC and Pereira DAG; **Data collection:** Ferreira ACC and Oliveira DMD; **Analysis and interpretation of data:** Ferreira ACC, Oliveira DMD and Pereira DAG; **Statistical analysis:** Ferreira ACC and Pereira DAG; **Manuscript writing:** Ferreira ACC and Oliveira DMD; **Critical review of the manuscript for important intellectual content:** Faria VC and Pereira DAG.

References

1. Comitê Coordenador da Diretriz de Insuficiência Cardíaca. Diretriz Brasileira de Insuficiência Cardíaca Crônica e Aguda. Arq Bras Cardiol. 2018;111(3):436-539. doi: 10.5935/abc.20180190

2. Braunschweig F, Linde C, Adamson PB, Magalski A, Erdmann E, Kjellstrom B, Bennett T. Continuous central haemodynamic measurement during the six-minute walk test and daily life in patients with chronic heart failure. Eur J Heart Fail. 2009;11:594-601. doi: 10.1093/eurjhf/hfp045

3. Guazzi M, Dickstein K, Vicenzi M, Arena R. Six-Minute Walk Test and Cardiopulmonary Exercise Testing in patients with chronic heart failure: a comparative analysis on clinical and prognostic insights. Circ Heart Fail. 2009;2:549-555. doi: 10.1161/CIRCHEARTFAILURE.109.881326

4. Bittner V. Exercise testing in heart failure. Maximal, submaximal, or both? J Am Coll Cardiol. 2003;42:123-5. doi: 10.1016/s0735-1097(03)00501-1

5. Arena R, Myers J, Guazzi M. The clinical importance of cardiopulmonary exercise testing and aerobic training in patients with heart failure. Braz J Phys Ther. 2008;12:75-87. doi: 10.1590/S1413-35552008000200002

6. Guimaraes GV, Bellotti G, Bacal F, Mocelin A, Bocchi EA. Can the Cardiopulmonary 6-Minute Walk Test reproduce the usual activities of patients with heart failure? Arq. Bras. Cardiol. 2002;78:557-60. doi: 10.1590/S0066-782X2002000600003

7. Hamilton DM, Haennel RG. Validity and reability of the 6-Minute Walk Test in a cardiac rehabilitation population. J Cardiopulm Rehabil. 2000;20:156-164. doi: 10.1097/00008483-200005000-00003

8. Pinna G, Opasich C. Reproducibility of the six-minute walking test in chronic heart failure patients. Stat Med. 2000;19:3087-94. doi: 10.1002/1097-0258(20001130)19:22<3087::aid-sim628>3.0.co;2-g

9. Enright P. The Six-Minute Walk Test. Respir Care [Internet]. 2003 [cited 2022 Feb 20];48:783-5. Available from: https://pubmed.ncbi.nlm.nih.gov/12890299/

10. Faggiano P, D´aloia A, Gualene A, Brentana L, Dei Cas L. The 6 minute walking test in chronic heart failure: indications, interpretation and limitations from a review of the literature. Eur J Heart Fail. 2004;6:687-91. doi: 10.1016/j.ejheart.2003.11.024

11. Britto RR, Sousa LAP. Teste de caminhada de seis minutos uma normatização brasileira Six Minute Walk Test – A Brazilian Standardization. Fisioter Mov [Internet]. 2006 [cited 2022 Feb 21];19:49-54. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/lil-469101

12. Rubim VSM, Neto CD, Romeo JLM, Montera MW. Valor prognóstico do teste de caminhada de seis minutos na insuficiência cardíaca. Arq Bras Cardiol. 2006;86:120-5. doi: 10.1590/S0066-782X2006000200007

13. Carvalho EEV, Costa DC, Crescêncio JC, Santi GL, Papa V, Marques F, *et al*. Insuficiência cardíaca: comparação entre o teste de caminhada de seis minutos e o teste cardiopulmonar. Heart failure: comparison between six-minute walk test and cardiopulmonary test. Arq Bras Cardiol. 2011;97:59-64. doi: 10.1590/S0066-782X2011005000056

14. Heidenreich PA, Fonarow GC, Breathett K, Jurgens CI, Pisani BA, Pozehl BJ, *et al*. 2020 ACC/AHA Clinical performance and quality measures for adults with heart failure. A report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Circ Cardiovasc Qual Outcomes. 2020;11. doi: 10.1161/HCQ.0000000000000099

15. Kell R, Haunstetter A, Dengler TJ, Zugck C, Kübler W, Hass M. Do cytokines enable risk stratification to be improved in NYHA functional class III patients? Eur Heart J. 2002;23:70-8. doi: 10.1053/euhj.2001.2780

16. Nessler J, Nessler B, Kitliński M, Gackowski A, Piwowarska W, Stepniewski M. Concentration of

BNP, endothelin 1, pro-inflamatory cytokines (TNF-α, IL-6) and exercise capacity in patients with heart failure with carvedilol. Kardiol Pol [Internet]. 2008 [cited 2022 Feb 21];66:144-51. Available from: https://pubmed.ncbi.nlm.nih.gov/18344152/

17. Pereira DAG, Vieira DSR, Samora GAR, Lopes FL, Alencar MCN, Lage SM, Pereira VF, Velloso M, Moreira MCV, Britto RR. Reprodutibilidade da determinação do Limiar Anaeróbico em Pacientes com insuficiência cardíaca. Arq Bras Cardiol. 2010;94:771-8. doi: 10.1590/S0066-782X2010005000044

18. ATS Statement: Guidelines for the six-minute walk test. Am J Cri. Care Med. 2002;166:111-7. doi: 10.1164/ajrccm.166.1.at1102

19. Rondelli RR, Oliveira AN, Corso SD, Malaguti C. Uma atualização e proposta de padronização do teste de caminhada dos seis minutos. Fisioter Mov. 2009;22:249-59.

20. Cahalin LP, Mathier MA, Semigran MJ, Dec GW, DiSalvo TG. The six-minute walk test predicts peak oxigen uptake and survival in patients with advanced heart failure. Chest. 1996;110:325-32. doi: 10.1378/chest.110.2.325

21. Miyamoto S, Nagaya N, Satoh T, Kyotani S, Sakamaki F, Fujita M, *et al*. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension. comparison with cardiopulmonary exercise testing. Am J Respir Crit Care Med. 2000;161:488-92. doi: 10.1164/ajrccm.161.2.9906015

22. Zugck C, Krüger C, Dürr S, Gerber SH, Haunstetter A, Hornig K, *et al*. Is the 6-minute walk test a reliable substitute for peak oxygen uptake in patients with dilated cardiomyopathy? Eur Heart J. 2000;21:540-4. doi: 10.1053/euhj.1999.1861

23. Demers C, McKelvie RS, Negassa A, Yusuf S. Reliability, validity, and responsiveness of the six-minute walk test in patients with heart failure. Am Heart J. 2001;142:698-703. doi: 10.1067/mhj.2001.118468

24. Opasich C, Pinna GD, Mazza A, Febo O, Riccardi R, Riccardi PG, *et al*. Six-minute walking performance in patients with moderate-to-severe heart failure Is it a useful indicator in clinical practice? Eur Heart J. 2001;22:488-96. doi: 10.1053/euhj.2000.2310

25. Rodrigues SL, Mendes HF, Viegas CAA. Six Minutes Walk Test: Study of the effect of learning in chronic obstructive pulmonary disease patients. J Bras Pneumol. 2004;30:121-5. doi: 10.1590/S1806-37132004000200008.

26. Casas JRA, Vilaro J, Rabinovich R, Mayer A, Barberà J, Roisin RR. Encouraged 6-min walking test indicates maximum sustainable exercise in COPD patients. Chest. 2005;128:55-61. doi: 10.1378/chest.128.1.55

27. Pulz C, Diniz R, Alves A, Tebexreni A, Carvalho A, Paola A, Almeida D. Incremental shuttle and six--minute walking tests in the assessment of functional capacity in chronic heart failure. Can J Cardiol. 2008;24:131-5. doi: 10.1016/s0828-282x(08)70569-5

28. Weber KT, Kinasewitz GT, Janicki JS, Fishman AP. Oxigen utilization and ventilation during exercise in patients with chronic cardiac failure. Circulation. 1982;65:1213-23. doi: 10.1161/01.cir.65.6.1213

29. Lavie CJ, Milani RV, Mehra MR. Peak exercise oxygen pulse and prognosis in chronic heart failure. Am J Cardiol. 2004;93:588-93. doi: 10.1016/j.amjcard.2003.11.023

30. Costa RV, Junior AO, Serra SM, Nóbrega ACL. Respostas ventilatórias e do pulso de oxigênio ao exercício dinâmico: correlação com a massa muscular esquelética em portadores de insuficiência cardíaca crônica avaliados pela ergoespirometria. Revista da SOCERJ [Internet]. 2005[cited 2022 Jun 13];18:283-7. Available from: http://sociedades.cardiol.br/socerj/revista/2005_04/a2005_v18_n04_art01.pdf

31. Oliveira RB, Myers J, Araujo CG, Arena R, Mandic S, Bensimhon D, *et al*. Does peak oxygen pulse complement peak oxygen uptake in risk stratifying patients with heart failure? Am J Cardiol. 2009;104:554-8. doi: 10.1016/j.amjcard.2009.04.022

32. Serra S. Considerações sobre ergoespirometria. Arq Bras Cardiol [Internet]. 1997;68:301-4. Available from: http://publicacoes.cardiol.br/abc/1997/6804/68040014.pdf

33. Stein R. Teste cardiopulmonar de exercício: noções básicas sobre o tema. Revista da Sociedade de Cardiologia do Rio Grande do Sul [Internet]. 2006 [cited 2022 June 13];15:1-4. Available from: http://sociedades.cardiol.br/sbc-rs/revista/2006/09/Artigo_01_Teste_Cardiopulmonar.pdf

34. Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT. Exercise training for claudication. The N Engl J Med. 2002;24:1941-9. doi: 10.1056/NEJMra021135

35. Mady C, Salemi VMC, Ianni BM, Ramires FJA, Arteaga E. Maximal functional capacity, ejection fraction, and functional class in chagas cardiomyopathy. are these indices related? Arq Bras Cardiol. 2005;84:152-5. doi: 10.1590/S0066-782X2005000200011

36. Russell SD, Saval MA, Robbins JL, Ellestad MH, Gottlieb SS, MD, Handberg EM, *et al*. New York Heart Association functional class predicts exercise parameters in the current era. Am Heart J. 2009;158:24-30. doi: 10.1016/j.ahj.2009.07.017