

# Correlation between the Six-Minute Walk Test and Subjective Functional Class in Patients with Heart Failure

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## Abstract

**Introduction:** The Six-Minute Walk Test (6MWT) is an inexpensive method to objectively evaluate physical capacity or limitation and stratify prognosis in patients with Heart Failure (HF). Since the clinical perception of symptoms may be adapted or compromised, regular evaluation from medical interviews often fails to determine functional classification. This study aimed to assess the correlation between New York Heart Association Functional Class (NYHA-FC) and the distance walked in the 6MWT. **Methods:** We conducted a cross-sectional observational study that included patients with HF with reduced ejection fraction followed up at an outpatient service of a teaching hospital, from August 2018 to April 2019. Patients in NYHA-FC I, II, or III were included. We compared NYHA-FC subjectively obtained during the consultation with the 6MWT performed after medical consultation, and the correlation between these two parameters was assessed. **Results:** The study included 70 patients with HF, 41 (58.6%) of whom were female. The mean age was  $61.2 \pm 12.7$  years. The most prevalent etiologies were dilated idiopathic cardiomyopathy (35.7%) followed by ischemic cardiomyopathy (25.7%). The mean ejection fraction was  $34.1\% \pm 9.8\%$ . The average distance walked in the 6MWT by NYHA-FC I patients was  $437.8 \pm 95.8$  meters, NYHA-FC II  $360.1 \pm 96.4$ , and NYHA-FC III  $248.4 \pm 98.3$ . Functional class measured by the 6MWT was different than that estimated by NYHA-FC in 34 patients (48.6%), 23 (32.9%) for a higher functional class and 11 (15.7%) for a lower one ( $p = 0.07$ ). Pearson's correlation coefficient between NYHA-FC and the 6MWT was  $-0.55$ . **Conclusion:** There was a moderate correlation between the subjective NYHA-FC and the 6MWT. The

6MWT revealed a different classification from NYHA-FC in almost half of the patients. Among those who presented discrepancies between methods, 6MWT reclassification towards a higher functional class was more common.

## Keywords

Heart Failure, Six-Minute Walk Test, Functional Class

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## 1. Introduction

Heart Failure (HF) is a severe clinical condition and presents high morbidity and mortality. Dyspnea and fatigue are major symptoms and cause important limitations in daily activities [1]. Evaluation of symptoms and exercise tolerance is a useful tool to inform prognosis and guide medical therapy [2]. However, different interpretations of symptoms in medical interviews can be a confounding factor for such important information.

Exercise tests are recommended for the objective evaluation of symptoms during exertion and to measure physical capacity in HF [2]. The Six-Minute Walk Test (6MWT) is a simple and inexpensive method to reproduce regular exercise by walking [2]. It consists of measuring the distance walked in six minutes, while evaluating the effects of exercise as a global organic response [3].

The 6MWT has been associated with prognosis in HF [4] [5]. However, the association between the distance walked during the test and the clinically-defined functional class is not clear [2]. The aim of this study was to assess the correlation between the 6MWT and New York Heart Association (NYHA) functional class as defined by regular medical interviews.

## 2. Methods

### 2.1. Study Design

We conducted a cross-sectional observational analytic study using interviews and the 6MWT for patients with a diagnosis of chronic heart failure who were attending on the heart failure clinic of the Hospital Santa Casa de Misericórdia de Vitória, Brazil. Eligible patients were included and submitted to the 6MWT from August 2018 to April 2019.

### 2.2. Patient Selection

We included outpatients with a previous diagnosis of HF confirmed by transthoracic echocardiography with Left Ventricle Ejection Fraction (LVEF) lower than 50% by Simpson method (mildly reduced or reduced ejection fraction). All echocardiograms had been performed by two specialized physicians using the LOGIQ E9 device from General Electric (New York City, USA).

Patients were excluded if they had decompensated HF, NYHA Functional Class

(NYHA-FC) IV, morbidities that impaired walking, such as osteoarthritis, previous stroke or severe psychiatric disorders, and any acute condition that could lead to misinterpretation of the 6MWT, such as infectious diseases, acute coronary syndromes, fever or severe pain.

All patients were screened for participation in the study during medical consultation. We estimated a minimal sample size of 83 patients for a minimal difference of 10% in change of NYHA-FC according to the 6MWT, with 90% power and 5% alpha error.

### 2.3. Data Collection

Clinical data were collected from medical registries. Clinical characteristics analyzed were age, gender, Body Mass Index (BMI), current smoking, previous hypertension, diabetes, dyslipidemia, atrial fibrillation, LVEF, etiology of HF and guideline-directed medications for improving survival in HF.

NYHA-FC was evaluated on the same day of the 6MWT by different physicians. Medical consultation was conducted first and NYHA-FC was determined subjectively, so that it would not be influenced by the result of the 6MWT. As a clinical practice, patients were considered to be at functional class I if they had no or few symptoms at ordinary exertion, class II if mild symptoms during regular daily activities, class III if marked limitation during daily exertion including less-than-ordinary activities, and class IV if they had severe limitations and/or were unable to perform any activity without symptoms.

### 2.4. Six-Minute Walk Test

The 6MWT was performed after consultation with the assistant physician, only once for each included patient. The distance walked was classified into NYHA-FC according to previous definitions [2]. Those who walked  $\geq 420$  meters were considered to be at functional class I, 340 - 419 meters at functional class II, 260 - 339 meters at functional class III, and  $<260$  meters at functional class IV. Then, this 6MWT classification and clinically-determined NYHA-FC were compared.

The 6MWT was performed by independent researchers without influence from the primary assistant physician, in a long and straight corridor located in the ambulatory section of a teaching-hospital, over a 30 meters distance. Each participant was asked to walk along the corridor as many times as possible, so that the longest possible distance was covered over six minutes. Participants were allowed to slow down or stop and rest if necessary, particularly in the case of symptoms such as severe breathlessness or fatigue. Patients were previously informed that time would run regardless any rest period they could possibly need. However, they were informed of the elapsed time and encouraged to recommence walking when symptoms subsided sufficiently. Participants were allowed to discontinue the test at any time if they wished. Moreover, the test was interrupted by the investigator immediately if the patient reported chest pain, severe breathlessness, severe loss of balance, severe sweating, or if cyanosis or severe oxygen desaturation occurred. Medical staff accompanied all tests and took clinical cautions con-

cerning any type of complications during or after the 6MWT. Otherwise, at minutes two and four during the test, an investigator informed the participants of the amount of time left and encouraged them to continue the test. At the sixth minute, the participant was advised to stop and sit down. The distance walked was measured to the nearest whole meter.

## 2.5. Statistical Analysis

NYHA-FC and reclassification from the 6MWT were compared for all patients. The Pearson Chi-Square test, Fisher test, t-student test and ANOVA were used for comparisons. The analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 23.0. P-values < 0.05 were considered as statistically significant. Pearson's correlation coefficient was used to analyze the correlation between NYHA-FC and the distance walked in the 6MWT. If Pearson's correlation coefficient is less than 0.5 it will have a weak correlation; moderate correlation if between 0.5 - 0.7; and strong correlation if above 0.70

## 3. Results

Seventy patients with HF and LVEF < 50% were included in the study, of whom 29 (41.4%) were male. Mean age was  $61.2 \pm 12.7$  years, average BMI  $28.4 \pm 7.3$  kg/m<sup>2</sup>, 48 (68.6%) had previous hypertension, 32 (45.7%) had diabetes, 52 (74.3%) had dyslipidemia, 10 (14.3%) were current smokers, 29 (41.4%) were former smokers, and three (4.3%) had chronic kidney disease. Average LVEF was  $34.1\% \pm 9.8\%$ . Regarding etiology of HF, 25 patients (35.7%) had idiopathic dilated cardiomyopathy, 18 (25.7%) had ischemic cardiomyopathy, 17 (24.3%) had alcoholic cardiomyopathy, six (8.6%) had post-chemotherapy HF (drug-induced cardiotoxicity), two (2.8%) had peripartum cardiomyopathy, one (1.4%) had hypertensive cardiomyopathy, and one (1.4%) had valvular cardiomyopathy.

Sixty-six patients (94.2%) were on treatment with the combination of a beta-blocker, spironolactone and either an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker or sacubitril-valsartan. Medications used and target doses achievement are described in **Table 1**.

Regarding clinically-determined NYHA-FC, 37 patients (52.9%) were in functional class I, 26 (37.1%) were in functional class II and seven (10.0%) were in functional class III. NYHA-FC was positively associated with advanced age (only for NYHA-FC II), male gender and high BMI, but not with diabetes and LVEF. Associations between clinical characteristics and NYHA-FC are shown in **Table 2**.

The average distance walked in the 6MWT was  $396.2 \pm 94.7$  m. Functional classification according to the distance walked is described in **Table 3**. Comparing this reclassification with clinically-determined NYHA-FC, discrepancy occurred in 34 (48.6%) patients. Discrepancy reclassified patients to a worse (higher) functional class in 23 (32.9%) patients, and to a better (lower) functional class in 11 (15.7%) patients.

**Table 1.** Use of evidence-based medications to improve survival in heart failure.

Medications	On use	Target-doses
Beta-blocker, n (%)	68 (97.1%)	41 (58.6%)
ACEI*/ARB**, n (%)	31 (44.3%)	24 (34.3%)
Sacubitril-valsartan, n (%)	35 (50.0%)	23 (32.9%)
Spirolactone, n (%)	67 (95.7%)	67 (95.7%)

\*ACEI: Angiotensin Converting Enzyme Inhibitor; \*\*ARB: Angiotensin Receptor Blocker.

**Table 2.** Association between New York heart association functional class and baseline clinical characteristics.

Characteristic	Class I	Class II	Class III	P
Male gender, n (%)	10 (27.0%)	10 (27.0%)	4 (57.1%)	0.01
Age, mean $\pm$ SD*	59.4 $\pm$ 11.9	67.5 $\pm$ 12.1	52.2 $\pm$ 12.8	0.004
Left ventricle ejection fraction, average $\pm$ SD*	36.3 $\pm$ 6.6	32.5 $\pm$ 9.9	31.4 $\pm$ 9.8	0.12
Diabetes, n (%)	18 (48.6%)	11 (42.3%)	3 (42.8%)	0.61
Body mass index, average $\pm$ SD*	28.8 $\pm$ 5.9	26.5 $\pm$ 6.9	33.2 $\pm$ 7.6	0.04

SD\*: Standard-Deviation.

**Table 3.** Reclassified functional class after the six-minute walk test and the average distances walked for each distance range.

6MWT* functional class	N (%)	Average distance, m $\pm$ SD**
I	32 (45.7)	437.8 $\pm$ 95.8
II	22 (31.4)	360.1 $\pm$ 96.4
III	13 (18.5)	248.4 $\pm$ 98.3
IV	3 (4.4)	150.1 $\pm$ 104.3

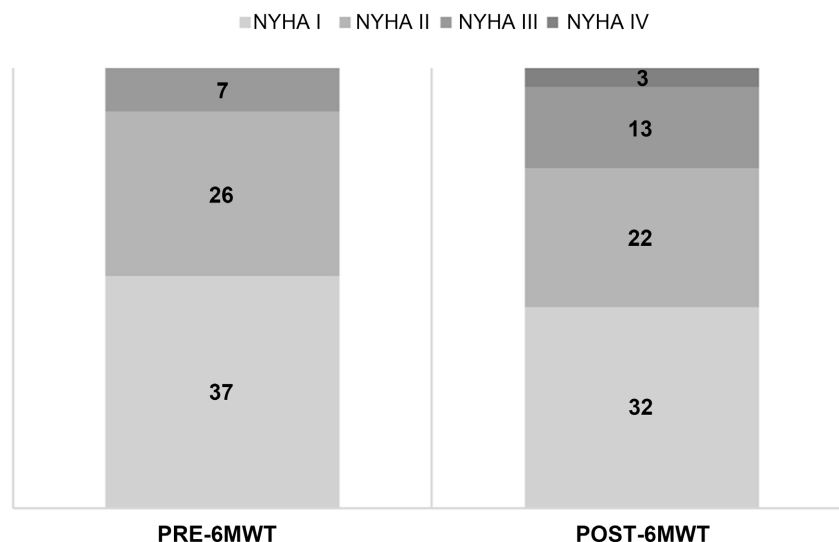
\*6MWT: Six-Minute Walk Test; \*\*SD: Standard-Deviation.

In those who were in NYHA-FC I, there was a change after the 6MWT in 13 (35.1%) patients. In those in NYHA-FC II, there was a change in 16 (61.5%), with eight (30.7%) for a worst functional class and eight (30.7%) for a better functional class. In NYHA-FC III, the modification occurred in five (71.4%) patients, two (28.6%) for a worst functional class and three (42.9%) for a better functional class. Thus, the main changes occurred in NYHA-FC II and III (**Figure 1**).

Pearson's correlation coefficient for clinically-determined NYHA-FC and functional classification according to distance walked in the 6MWT was  $-0.55$  ( $p = 0.07$ ), which demonstrates moderate correlation.

#### 4. Discussion

The NYHA classification is well established and has perpetuated for decades in



**Figure 1.** Changes in functional classes before and after 6MWT. NYHA: New York Heart Association; 6MWT: Six-Minute Walk Test.

clinical practice of HF as a quick way to obtain functional status. Relevant contemporary clinical trials, such as MERIT-HF, PARADIGM-HF and DAPA-HF, use NYHA-FC II and IV as an inclusion criteria to include new drugs in HF therapy [6] [7] [8]. Therefore, it is of great importance to correctly distinguish the NYHA-FC, since indirect evaluation can lead to biases such as low reproducibility, lack of an established pattern of questions in anamnesis and subjectivity in individual interpretations, with wide intra and inter-observer variability [9].

The 6MWT has gained space in HF, due to its easy performance and safety. It is well validated as a tool to assess functional capacity and prognosis by the total distance covered [5] [10] [11]. There is evidence of the validity and reliability of the 6MWT, especially in those patients with mild to moderate HF, as included in our study, which can be useful for outpatient follow-up [12]. However, it is noteworthy that patients with multiple comorbidities, advanced age and motor and neurological deficits may travel shorter distances, and may not truly reflect their functional capacity [12] [13]. In our study, we excluded these patients due to difficulties or impossibility in performing the 6MWT.

A systematic review involving studies that assessed NYHA-FC and 6MWT found significant heterogeneity among the studies evaluated [2]. For example, a small prospective study of patients with HF initially used self-assessed NYHA-FC; later, the evaluators (blinded for the patients' self-rating of NYH-FC) classified them, and finally these patients were submitted to the 6MWT. In that study, a moderate correlation between the self-NYHA-FC and the evaluators' classification was found, and a strong correlation between the classification attributed by the evaluator and the 6MWT was observed [14]. Our study showed only a moderate correlation between the functional class obtained by an interview in the medical office and the 6MWT in patients with stable HF in an outpatient follow-up.

Studies involving functional class and the 6MWT have showed differences mainly between classes II vs III and III vs IV [2] [11]. Thus, the subjective classification of the functional class is reliable when discriminating between mild and severe HF, however, there are flaws in defining it between mild and moderate [11]. This research found major changes in NYHA-FC after the 6MWT in patients initially classified as NYHA-FC II and III, as found by Yap *et al.* [2]. These classes are difficult to differentiate by NYHA classification, since they include patients with a wide intensity of symptoms in a grey zone, while class I represents an asymptomatic patient and class IV a patient with symptoms even at rest. In our study, there was a worsening of functional classification for these patients after the result of the 6MWT, with the NYHA-FC classification being underestimated at the office in two thirds of the cases, as opposed to the result obtained by Williams *et al.*, where the evaluators tended to attribute a higher NYHA-FC to the patients [11].

In the present study, the 6MWT was a tool responsible for objectively changing the perception of NYHA-FC in almost half of the patients. In general, it can be used as a way to complement the NYHA classification, with the purpose of improving therapeutic decisions. Our population was mostly on triple combined therapy that reduces mortality in HF (current therapy in the years 2018-2019), which includes beta-blockers, ACE inhibitors or ARBs or sacubitril-valsartan, and spironolactone [15].

## 5. Limitations and Strengths

As this is an observational and cross-sectional study, limitations inherent to this type of study must be applied here. Among them, the impossibility of determining casualty and ensuring that confounding factors will be equally distributed among groups stands out. In addition, this is an outpatient study, in which patients with motor deficits, very old age or with any sign of decompensation were excluded; therefore, our results may not be applied to a population with greater severity of HF. Still, the LVEF to determine HF with reduced or mildly reduced ejection fraction was below 50%, although new studies include HF with mildly reduced ejection fraction (40% to 49%) as a different group. We did not include this classification in our study because it did not influence substantially the initial clinical management of HF in our institution. Finally, there was no quantification of the number of patients excluded due to physical disability or non-acceptance to perform the 6MWT. This could lead to a selection bias.

## 6. Conclusion

There was a moderate correlation between the subjective NYHA-FC and the distance walked in 6MWT. A change in FC was observed after the 6MWT in almost half of the patients, especially in those initially classified as NYHA-FC II and III. Despite the established use of NYHA-FC, the 6MWT can be validated in a way that complements this classification in patients with HF.

## Ethical Considerations

The study was approved by the institution's Research Ethics Committee under the number 2.618.469. All patients read and signed the informed consent statement before inclusion in the study and agreed to participate. The study followed the ethical principles for research from the Declaration of Helsinki.

## Authors' Contributions

DMR and RRB: principal investigator, study design, data collection, analysis and manuscript preparation. GLD, LAL, PCGCL, RCS and VAA contributed to the study design and manuscript preparation. LCB, LNP, LFB, RGS, OAC and LFMB contributed to data analysis and interpretation. All authors contributed to the study design, interpretation and drafting of the article. All authors read and approve the final version of the paper.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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