



Long-Term Re-Admission after Hospital Discharge in Patients Admitted with Acute Heart Failure: The Prognostic Value of the Six-Minute Walk Test Distance

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How to cite this paper: Mandi, D.G., Naïbé, D.T., Bamouni, J., Yaméogo, R.A., Kambiré, Y., Kologo, K.J., Millogo, G.R.C., Yaméogo, N.V., Tall, A.T. and Zabsonré, P. (2018) Long-Term Re-Admission after Hospital Discharge in Patients Admitted with Acute Heart Failure: The Prognostic Value of the Six-Minute Walk Test Distance. *Open Access Library Journal*, 5: e4841.
<https://doi.org/10.4236/oalib.1104841>

Received: August 15, 2018

Accepted: September 23, 2018

Published: September 26, 2018

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Abstract

Background: We sought the value of the six-minute walk test distance in predicting re-admission in patients with chronic heart failure (CHF) in the department of cardiology, Yalgado Ouédraogo University Hospital, Ouagadougou, Burkina Faso. **Methods:** We did a prospective observational study in patients hospitalized with acute decompensated heart failure and who underwent a 6-minute walk test (6-MWT) at their discharge from hospital. The primary end-point was hospital re-admission for heart failure decompensation. **Results:** Sixty-one patients (52% females, mean age 46.9 ± 14.1 years, mean left ventricular ejection fraction $32.4 \pm 8.2\%$, mean 6-MWT distance 336.3 ± 65 meters) were followed-up for a 277.6 ± 129.8 days' period. Twenty-one patients (45.3 percent person-years) were re-admitted. Re-admitted patients had shorter 6-MWT distance ($p = 0.007$) and were more likely to die than those who were not re-admitted (RR = 1.72, 95% CI = 1.13 - 2.62, $p = 0.003$). Multivariate Cox regression analysis showed that re-admission was independently predicted by shorter 6-MWT distance ($p < 0.001$), New York Heart Association class III ($p = 0.03$), older age $p = 0.03$ and lower LVEF ($p = 0.02$). **Conclusion:** Distance covered during the six-minute walk test is an independent predictor of hospital re-admission for heart failure decompensation in patients with chronic heart failure.

Subject Areas

Cardiology

Keywords

Six-Minute Walk Test, Heart Failure, Re-Admission, Cardiac Rehabilitation, Africa

1. Introduction

Chronic heart failure (CHF) is a major public health concern [1] [2], and remains a severe disease with poor outcome despite huge progress in its management [2] [3]. Its prognosis is strongly correlated with the functional capacity [4] [5]. Assessing functional capacity is a key step for cardiac rehabilitation intervention which contributes to reducing cardiovascular events and re-hospitalizations in patients with CHF. Cardiopulmonary exercise test is known as the “gold standard” method to assess the functional capacity [6]. The value of peak oxygen uptake (VO_2) derived from the cardiopulmonary exercise testing provides an important prognostic information in patients with CHF [7]. Data have demonstrated the important prognostic value of both peak VO_2 and six-minute walk test (6-MWT) in predicting cardiac morbidity and mortality in patients with CHF [8] [9] [10]. Moreover, it has been shown that CHF patients with a 6-MWT distance < 300 meters had an increase in mortality and morbidity [11] [12] [13] [14]. However, peak VO_2 is more difficult to perform in the field, expensive and not available particularly in some low-income countries with less equipped health facilities. Conversely, the 6-MWT which is safe, simple, well accepted by the patients, and probably better correlate with patient’s symptoms [15] [16] [17], could be a low-cost alternative for the prescription of aerobic exercise in patients with CHF [18]. The assessment of the prognostic importance of 6-MWT distance is not common in Sub-Saharan African (SSA) patients with CHF. Thus, the present study aims to assess for the first time the value of the 6-MWT distance in predicting heart failure readmission in those patients in Burkina Faso.

2. Methods

2.1. Study Population

From December 1, 2013 to march 31, 2014, we prospectively enrolled into the study, consecutive patients with CHF who attended the inpatients’ unit of the department of cardiology, Yalgado Ouédraogo University Hospital. The diagnosis of heart failure was based on the guidelines of the European Society of Cardiology on the diagnosis and treatment of heart failure [19] [20]. Patients hospitalized for congestive heart failure regardless of the etiology, with random left ventricular ejection fraction (LVEF) \leq 45% and under 70 years old and who were in stable clinical condition at discharge, were included. Non-inclusion criteria

comprised acute coronary syndrome (<one month), decompensated heart failure, uncontrolled hypertension (BP > 180/100 mmHg), musculoskeletal and neurologic disorders forbidding physical exercise. We did an age cut-off of 70 years due to the fact that patients > 70 years old have more frequent physical and mental disabilities and other comorbidities which preclude walk. Enrolled patients received individualized medical treatment of heart failure accordingly [angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (93.4%), digoxin (36.1%), spironolactone (100.0%), loop diuretic (100.0%), beta blockers (4.9%), amiodarone (14.8%), antiplatelet (42.6%), vitamin K antagonists (57.4%)] including dietary prescriptions.

2.2. Six-Minute Walk Test

We used the American Thoracic Society's guidelines [21], to obtain the 6-MWT distance measurements at the time of hospital discharge. The 6-MWT was administered on a flat rectangular floor with a track length of 82 meters. The track was marked every three meters so that the total distance walked can be easily calculated. Patients were instructed to walk as far as possible at their own pace according to their tolerance to exercise in the allotted time of six minutes. The 6-MWT was performed under the control of a study physician who provided encouraging comments to the patients during the test. They were allowed to stop and rest or reduce their walking speed in case of discomfort. Prior to the test, patients observed a 10-minutes rest sitting near the starting point of the walk. The test procedures were explained to all patients in advance. After six minutes had elapsed, patients were instructed to stop walking and the total distance walked was recorded to the nearest meter (m) forward.

2.3. Study Process

On the eve of their discharge from hospital and prior to enrollment into the study, an oral informed consent was obtained from all study subjects. Thereafter, patients were assessed clinically. LVEF was obtained by echocardiography using either the Teichholz's method or Simpson's 2D formula in case of regional wall geometric or motion abnormalities and a trial fibrillation [22] as appropriate.

A pre-test was performed in order to familiarize patients with the floor. On discharge day, an enrollment 6-MWT was performed. Patients were counseled on their health and given more information on their illness and therapeutic prescriptions. Outpatient's follow-up appointments were scheduled by cardiologists every one to three months' period (depending on the severity of their symptoms) during which clinical check-ups were done and treatment adjusted as needed. Outcomes of interest included mortality and hospital readmissions resulting from worsening CHF during the observational follow-up period. Data on readmissions and deaths were collected prospectively by checking the in-hospital admission registry and patients' health records. In some cases, phone contact was used to catch those information from the patients or their relatives.

2.4. Statistical Analysis

Data on all patients consecutively enrolled during the four months' recruitment period were analyzed through EPI INFO version 7 and R version 3.2.2 software. Continuous variables were reported as means \pm SD and categorical data as percentages. Differences between variables were determined using Fisher's exact, Chi square and Student tests accordingly. The 6-MWT distance was randomly dichotomized into ≤ 300 meters and >300 meters for the curves presentations purposes. Kaplan-Meier method was used to construct curves and log-rank test to compare hospital re-admission for heart failure between 6-MWT distance stratified groups. Cox proportional hazards regression models were used to estimate the relative risk of hospital re-admissions for heart failure decompensation. We used Martingales and Schoenfeld residuals tests to assess respectively the log-linearity and proportional hazard assumptions. The backward elimination procedure according to Akaike's information criterion (AIC), [23] was used to strengthen the model. Statistical significance was defined as a two-tailed p-value of < 0.05 .

2.5. Ethical Aspects

The Research Ethics Committee of Yalgado Ouédraogo University Hospital approved the study protocol. The study was conducted in patients who gave their informed consent in accordance with the internationally established principles for Good Clinical Practice, which had their origin in the Declaration of Helsinki of the World Medical Association.

3. Results

Overall, sixty-one patients with CHF were included in analysis process. Two patients discontinued the test due dyspnea and fatigue associated with cramps. No serious adverse event occurred during the 6-MWT process and one patient was lost to follow-up. The mean age was 46.9 ± 14.1 years (extremes: 21 - 70). Thirty-two patients (52%) were female. The mean LVEF was $32.4\% \pm 8.2\%$ (extremes: 13 - 45). The mean 6-MWT distance was 336.3 ± 65 meters (extremes: 194 - 480). Patients' baseline characteristics are shown in **Table 1**.

The mean follow-up period was 277.6 ± 129.8 days (extremes: 2 - 403 days) with a total follow-up time of 16932 days (46.4 years). At the end of follow-up, 21 patients (45.3 percent person-years) were re-admitted to hospital for heart failure decompensation and 14 patients had died. Re-admitted patients had shorter 6-MWT distance ($p = 0.007$) and were more likely to die than those who were not re-admitted (RR = 1.72, 95% CI = 1.13 - 2.62, $p = 0.003$). In univariate Cox proportional hazards regression analysis, re-admission was associated with shorter 6-MWT distance both as continuous and dichotomized (≤ 300 m) variables ($p < 0.001$), older age ($p = 0.03$) and NYHA class III ($p = 0.01$) as shown in **Table 2**.

In a multivariate Cox proportional hazards model including all variables

Table 1. Baseline characteristics of all 61 patients with chronic heart failure.

Characteristic	Values
Number of patients	61
Age (years) mean \pm SD	46.9 \pm 14.1 (21 - 70)
Female sex (%)	32 (52)
NYHA class (%)	
II	46 (75.4)
III	15 (24.6)
Atrial fibrillation (%)	15 (24.6%)
LVEF (%) mean \pm SD	32.4 \pm 8.2 (13 - 45)
TAPSE (mm) mean \pm SD	16.16 \pm 4.28 (9 - 27)
SPAP (mmHg) mean \pm SD	52.1 \pm 12.4 (25 - 98)
Primary heart disease (%)	
Ischemic heart disease	10 (16.4)
Hypertensive heart disease	20 (32.8)
Peripartum cardiomyopathy	10 (16.4)
Rheumatic valvular heart disease	12 (19.6)
Others*	9 (14.8)
6-MWT distance (m) mean \pm SD	336.3 \pm 65 (194 - 480)

NYHA: New York Heart Association, LVEF: left ventricular ejection fraction; TAPSE: tricuspid annulus plane systolic excursion; SPAP: systolic pulmonary arterial pressure; *Including idiopathic dilated cardiomyopathy and myocarditis; 6-MWT: 6-minute walk test.

Table 2. Univariate Cox regression analysis predictors of re-admission in patients with chronic heart failure.

Variables	Wald test	HR	95% CI	p-value
Age (years)	4.78	1.04	1.004 - 1.079	0.03
Sex (female)	0.32	0.78	0.33 - 1.85	0.56
NYHA functional class (II/III)	6.47	3.37	1.32 - 8.61	0.01
Ischemic heart disease (%)	1.46	1.87	0.68 - 5.17	0.2
Atrial fibrillation (%)	0	1.003	0.36 - 2.77	0.99
LVEF (%)	3.28	0.95	0.89 - 1.004	0.07
TAPSE (mm)	1.78	0.93	0.84 - 1.03	0.18
6-MWT distance as continuous	12.14	0.98	0.97 - 0.99	< 0.001
6-MWT distance \leq 300 m	12.13	4.79	1.98 - 11.54	<0.001

HR: hazard ratio; CI: confident interval; NYHA: New York Heart Association, LVEF: left ventricular ejection fraction; TAPSE: tricuspid annulus plane systolic excursion; 6-MWT: 6-minute walk test.

associated with re-admission in univariate analysis, there was no violation of assumption when the dependent variable was re-admission. Both 6-MWT distance as continuous and dichotomized (\leq 300 m) variables, NYHA class III, lower

LVEF and older age independently predicted re-admission for heart failure decompensation (Table 3). The proportion of study patients re-admitted for heart failure was significantly lower in patients whose 6-MWT distance was >300 m ($p < 0.001$) during the follow-up period (Figure 1).

4. Discussion

We currently demonstrated that 6-MWT distance at the time of hospital discharge was an independent predictor of re-admission in sub-Saharan African patients with CHF. This finding is consistent with data from studies with various cut-off levels of 6-MWT distance depending of CHF patients' clinical characteristics. The SOLVD sub-study [10], was the first to show in 898 patients with

Table 3. Multivariate Cox proportional hazards ratio regression analysis predictors of re-admission in all 61 patients with chronic heart failure.

Characteristic	Re-admission (AIC = 127.48)		Re-admission with 6-MWT distance as continuous variable (AIC = 123.29)	
	HR (95% CI)	P value	HR (95% CI)	P value
6-MWT distance ≤ 300 m	5.65 (2.15 - 14.88)	<0.001	0.98 (0.97 - 0.99)	<0.001
NYHA class (II/III)	3.04 (1.10 - 8.42)	0.03	3.12 (1.13 - 8.57)	0.026
Age (years)	1.04 (1.004 - 1.08)	0.03	1.04 (1.001 - 1.08)	0.053
LVEF	2.92 (1.13 - 7.52)	0.02	4.12 (1.55 - 10.98)	0.004
Ischemic heart disease	1.55 (0.51 - 4.68)	0.43	1.74 (0.57 - 5.25)	0.32

AIC: Akaike's information criterion; HR: hazard ratio; CI: confident interval; NYHA: New York Heart Association, LVEF: left ventricular ejection fraction; 6-MWT: 6-minute walk test, p: p value.

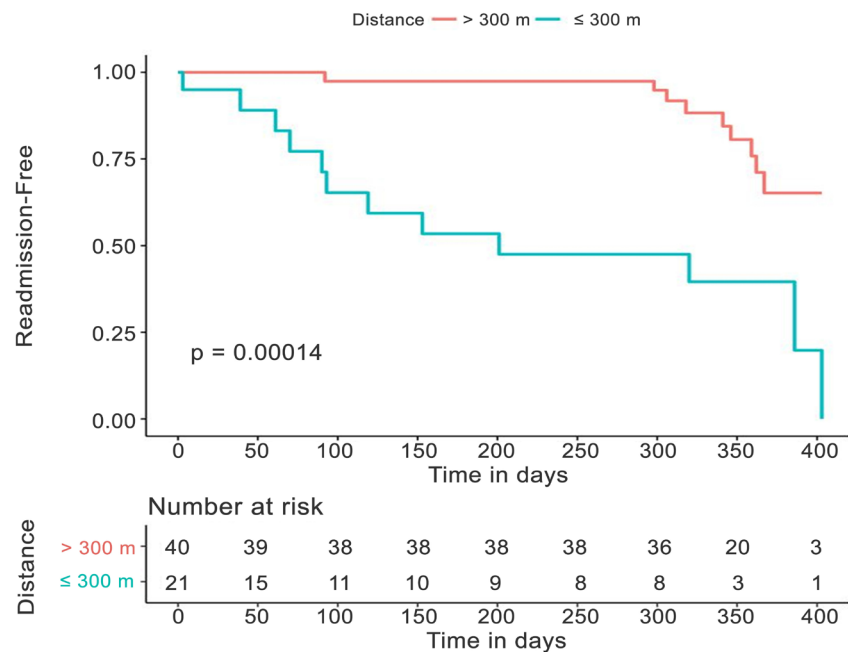


Figure 1. Kaplan-Meier readmission-free curves in patients stratified by 6-minute walk test distance ≤ 300 meters and >300 meters.

NYHA class II and III heart failure that 6-MWT distance and left ventricular ejection fraction were strongly connected with death and heart failure hospitalization rates during follow-up. In a prospective cohort study carried out by Tabata *et al.* [24] in Japan in 252 CHF patients, 103 were readmitted within 3 years. 6-MWT distance at the time of discharge was significantly shorter in re-admitted patients than non-re-admitted patients ($P < 0.001$) and was a significant predictor of re-admission ($P < 0.001$). In 1996, Cahalin *et al.* [25] conducted a study in 45 patients with advanced heart failure (age = 49 ± 8 years; LVEF = 0.20 ± 0.06) who underwent a 6-MWT during cardiac transplant evaluation and demonstrated a significant correlation ($r = 0.64$, $p < 0.001$) between peak VO_2 and the walking distance. Moreover, they noticed that a 6-MWT distance ambulated less than 300 m predicted an increased likelihood of death or pre-transplant hospital admission within six months. Similar results reported prognostic value of a shorter 6-MWT distance in the literature [26]-[31]. Alahdab *et al.* [14] prospectively evaluated the usefulness of the 6 MWT in predicting mortality and heart failure re-hospitalization in 200 American African patients with acute decompensated heart failure and found that 6-MWT distance ≤ 200 m was the strongest predictor of heart failure re-hospitalization (adjusted HR = 1.62, $p = 0.015$). Thus, 6-MWT distance could help to stratify the severity of heart failure.

However, some conflicting observations have been raised regarding the usefulness of 6-MWT in predicting outcomes in heart failure patients [32] [33]. However, these findings were mostly reported in patients without advanced HF contrasting with our study patients' baseline characteristics. To us, the 6-MWT distance remains an interesting tool that could help to evaluate outcomes in patients with CHF despite discrepancies between series.

As reported in this present study, higher NYHA class at discharge, lower LVEF and older age are well known to predict hospital re-admission for heart failure decompensation [34] [35].

Study Limitations

The small size of our study population and the lack of some variables in the analysis process such as NT-proBNP, hemoglobin concentration and renal dysfunction [27] [29] may have affected the statistical power of our findings. Compliance to medications which is known to be a risk factor for re-admission in patients with heart failure [36] was not assessed. However, these results gave a prognostic importance of the 6-MWT distance in Sub-Saharan African patients with CHF.

5. Conclusion

In Sub-Saharan African patients with CHF, shorter 6-MWT distance at the time of hospital discharge strongly predicted re-hospitalization for heart failure decompensation. Thus, the 6-MWT distance can be an indicator of the evolution of CHF patients. Those patients could greatly benefit from cardiac rehabilitation

program at least to improve their quality of life. Therefore, setting-up such cardiac rehabilitation programs in SSA health facilities is needed.

Acknowledgements

We gratefully acknowledge all subjects enrolled in this study. Many thanks to the Cardiology department medical staff members for their technical support during the study. We also thank Dr Juste Aristide GOUNGOUNGA from Aix-Marseille University (France) for his statistical support in this work.

Contributors

All authors have read and approved the final manuscript.

Conflicts of Interest

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

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