Clinical Investigation

Prognostic Value of 6-Minute Walk Test

in Stable Outpatients with Heart Failure

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The study was designed to evaluate the prognostic value of the 6-minute walk test in stable outpatients with heart failure.

We prospectively studied 43 patients (6 women and 37 men) who had chronic heart failure secondary to ischemic heart disease or idiopathic cardiomyopathy. All patients had left ventricular systolic dysfunction (ejection fraction, ≤0.40), and they were in stable New York Heart Association functional class II or III heart failure. All patients were evaluated by M-mode and 2-dimensional echocardiography. At the outset, walking distances of all the patients were evaluated by the 6-minute walk test. The patients were divided into 2 groups: Group I, patients with a 6-minute walk test distance of ≤300 m; and Group II, patients with a 6-minute walk test distance of >300 m. The patients were then monitored for a period of 2 years in regard to cardiac death.

The mortality rate was significantly higher in patients with a 6-minute walk test distance of ≤300 m than in patients with a 6-minute walk test distance of >300 m (79% vs 7%; P <0.001). The death risk was found to be significantly higher in patients with a distance of ≤300 m (P=0.005). The death risk was also higher in patients whose left ventricular ejection fraction was ≤0.30 (P=0.02).

We conclude that a 6-minute walk test distance of ≤300 m is a simple and useful prognostic marker of subsequent cardiac death in patients with mild-to-moderate heart failure.
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Functional capacity provides strong independent insight into the prognosis of patients with heart failure.[1,2] Information on peak oxygen consumption (PvO_2) during cardiopulmonary exercise testing is used extensively to evaluate cardiovascular performance. Several studies have supported PvO_2 as an independent prognostic index of survival in patients with heart failure.[3,4] Similarly, a PvO_2 of <10 to 12 mL/kg per min is considered a reliable indicator for heart transplantation.[5,6] However, cardiopulmonary exercise testing is both expensive and time-consuming. In addition, approximately 30% of patients with heart failure are unable to perform a maximal symptom-limited exercise test or to tolerate the tight mask used for breath-by-breath gas analysis. The 6-minute walk test (6MWT) has been suggested as a simple, safe, and inexpensive alternative to cardiopulmonary exercise testing.[7]

The aim of the present study was to prospectively evaluate the prognostic value of the 6MWT in patients with mild-to-moderate congestive heart failure.

Key words: *Exercise test; heart failure, congestive/ mortality; 6-minute walk test; predictive value of tests; prognosis; risk factors; stroke volume*

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Patients and Methods

From January 2003 through October 2003, we studied 43 patients (6 women and 37 men) who had stable chronic heart failure secondary to ischemic heart disease or idiopathic cardiomyopathy. All patients underwent treatment for stable heart failure with angiotensin-converting enzyme (ACE) inhibitors for at least 4 weeks and with diuretics for at least 2 weeks. The mean age was 62 ± 10 years. The cause of heart failure was idiopathic dilated cardiomyopathy in 26 patients and ischemic cardiomyopathy in 17 patients. All patients had left ventricular (LV) systolic dysfunction (left ventricular ejection fraction [LVEF], ≤0.40), and all were in stable New York Heart Association (NYHA) functional class II or III heart failure. The functional capacity of 26 patients was class II and that of the remaining 17 was class III. Table I summarizes the patients' clinical characteristics.

We excluded from the study patients who had decompensated heart failure, limitation of physical activity due to factors other than exertional dyspnea and fatigue (such as arthritis), psychiatric disorders that could keep the patients from understanding

TABLE I. Clinical Characteristics of Patients

Clinical Characteristics	Values
Number of patients	43
Mean age (yr)	62.0 ± 10
Men (%)	86
Cause (%)	
Ischemic heart disease	39.5
Dilated cardiomyopathy	60.5
Mean duration of heart failure (yr)	3.1 ± 1.9
New York Heart Association class (%)	
II	60.5
III	39.5
LVDD (mm)	61.4 ± 5.4
LVSD (mm)	50.4 ± 5.7
LVEF	0.35 ± 0.06
Left atrial diameter (mm)	42.1 ± 6.1
Body surface area (m^2)	1.48 ± 0.2
Diabetes mellitus (%)	23
Systemic hypertension (%)	38
Smoker (%)	36.5
6-Minute walk distance (m)	400.2 ± 107.8
Follow-up (mo)	18.3 ± 5.5

LVDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVSD = left ventricular end-systolic diameter

the examination, anemia, and any febrile condition or infectious disease. We also excluded patients who had experienced unstable angina, myocardial infarction, coronary revascularization, or stroke within the previous 2 months. Patients with ischemic heart failure received anti-ischemic treatment (a nitrate) and anti-aggregation treatment (aspirin), in addition to ACE inhibitors and diuretics. None of the patients received β-blocker therapy. After the walk test was performed, the patients were given 6.25 mg/day of carvedilol or 25 mg/day of metoprolol succinate, and this was increased to the maximal dose tolerated.

The study conformed to good clinical practice guidelines and followed the recommendations of the Declaration of Helsinki. The protocol was approved by our local ethics committee. Informed written consent was obtained from all patients before enrollment.

We used a GE VingMed® Vivid FiVe® echocardiographic system (GE Ultrasound; Horten, Norway) with a 2.5-MHz probe. All echocardiography was performed by the same investigator. The echocardiographic study was performed in the left lateral decubitus in the parasternal long-axis and 4-chamber views. The LVEF was obtained using Simpson's biplane methods in 2-dimensional echocardiography.[8] Left ventricular end-diastolic diameter, LV end-systolic diameter, and left atrial diameter were measured with M-mode echocardiography, using a parasternal window.

The walk test was performed in an indoor corridor 25 m long, according to the recommendations of Guyatt and colleagues.[7] Patients were instructed to walk the corridor from 1 end to the other, as many times as possible within the permitted time. The test was performed under the control of a physician, who encouraged the patients with remarks such as "you are doing well." At the end of the 6 min, the physician measured the total distance walked by the patient. On the basis of the distance walked, patients were grouped into 2 different performance levels: Group I, ≤300 m; and Group II, >300 m. The patients were monitored for 2 years in regard to cardiovascular death.

Statistical Analysis

The SPSS version 11.5 statistical program (SPSS Inc.; Chicago, Ill) was used for statistical study. Continuous variables are given as mean ± standard deviation, and categorical variables are given as percentages. The χ^2 test was used for the comparison of categorical values. The Cox proportional hazards regression model was used to estimate the relative risk of cardiovascular death. Other variables used to determine basic risk were LVEF ≤0.30, age over 65 years, and ischemic cause of heart failure. Risk ratios were determined with 95% confidence intervals, according to the Cox regression model (Table II). Cardiac death curves were obtained by the Kaplan-Meier method. The log-rank test was used for comparison of the 2 curves. A value of $P < 0.05$ was considered statistically significant.

Results

Of the 43 patients studied, 13 (30%) were lost to follow-up. The average follow-up period was 18 ± 6 months.

All patients completed the 6MWT. No clinical complication was recorded during the tests or within the 5-

TABLE II. Cox Proportional Hazards Regression Model for Death

Variable	Adjusted Hazard Ratio	95% CI	*P* Value
Age >65 yr	1.14	0.20–6.44	0.88
LVEF ≤0.30	6.12	1.32–26.3	0.02
6-Minute walk distance ≤300 m	2.38	2.02–57.6	0.005
Ischemic cause	0.81	0.19–3.39	0.77

CI = confidence interval; LVEF = left ventricular ejection fraction

hour period after the tests. The mortality rate in patients whose 6MWT distance was ≤300 m was significantly higher than in patients whose 6MWT distance was >300 m (79% vs 7%; P <0.001, log-rank test). When subgroup analyses were considered, the mortality rate in patients with heart failure due to ischemia was higher (41%) than that in patients with idiopathic cardiomyopathy (23%); however, this difference was not statistically significant.

Risk of death was significantly higher in patients whose 6MWT distance was ≤300 than in patients whose 6MWT distance was >300 m (P=0.005, Cox regression model). In addition, the risk of death was higher in patients with LVEF ≤0.30 than in those with LVEF >0.30 (P=0.02). Old age and ischemic cause of heart failure were not statistically significant in regard to risk of death (P >0.05).

At the end of follow-up (18 months on average), the mortality rate was 11.5% for patients in NYHA class II and 58.8% for patients in NYHA class III; this difference was statistically significant (P=0.001). The Kaplan-Meier curve indicating death rates during follow-up is shown in Figure 1.

Discussion

Studies of Left Ventricular Dysfunction (SOLVD)[9] was the 1st large investigation (898 patients) to show a strong connection between distances walked during the 6MWT and death, in cases of NYHA class II and class III heart failure. This prognostic value, however, remains controversial. In a study of 315 moderate-to-severe heart failure patients, Opasich and colleagues[10] reported that the distance walked during the 6MWT does not provide prognostic information that can complement or replace oxygen consumption (VO_2) or the classic clinical functional class grading system. However, patients in Opasich's study did not receive the recommended "encouraging remarks," despite their having undergone two 6MWTs each, one of which was preparatory. If Opasich's patients did not approach their anaerobic thresholds during the walking exercise, such results might have been influenced by lack of encouragement.

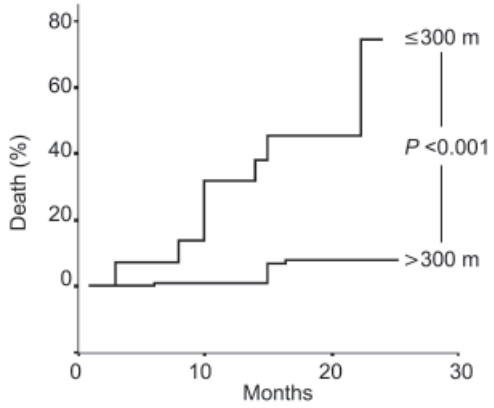

Fig. 1 *Kaplan-Meier curves for the 6-minute walk test, according to the distance walked.*

In the study by Rostagno and associates[11] of 214 patients with mild-to-moderate heart failure, the mortality rate for patients whose 6MWT distance was <300 m was significantly higher than that for patients whose 6MWT distance was ≥300 m. They concluded that a 6MWT distance of <300 m is a "simple and useful prognostic marker of subsequent cardiac death in unselected patients with mild-to-moderate congestive heart failure." Cahalin and coworkers[12] studied 45 patients referred for heart-transplantation evaluation. A 6MWT distance of <300 m predicted an increased likelihood of death or of hospitalization for inotropic or mechanical support within 6 months, but it failed to predict overall or event-free survival at a follow-up of 62 weeks. Conversely, our results suggest that a walking distance of <300 m during the 6MWT is an independent predictor of death over the long term (18 months on average) in unselected patients with mild-to-moderate heart failure.

Rubim and co-authors[13] found that, according to the receiver operating characteristics (ROC) curve, the optimal cut-off value for the distance walked was 520 m in 179 patients with mild-to-moderate heart failure. However, most of the patients in that study were in NYHA class II. Only 6 patients (3%) were in class III. In our study, 40% of the patients were in NYHA class III.

The LVEF is one of the strongest indicators of death in patients with heart failure.[13-16] The findings of our study confirm that a lower LVEF is an independent predictor of death.

While Rubim's group[13] found no difference between NYHA class I and II in 179 patients with mild or moderate heart failure, they showed that survival for patients in NYHA classes III and IV was <50%, which was significantly different when compared with patients in NYHA class I and class II. Similarly, in our study, the death rate in NYHA class III patients was significantly higher.

In 2,711 patients, Andersson and colleagues[17] showed that the mortality rate in heart failure that developed due to ischemia was higher than the mortality rate in heart failure due to other reasons. The mortality rate was also higher among our patients with ischemic heart failure, but the difference was not statistically significant. This may be attributable to the small number of patients in our study.

Recently, there have been reports of several prognostic indicators in heart failure. Anand and associates[18] reported their thesis on the value of C-reactive protein as an independent predictor of survival in patients with

heart failure. In 2004, de Groote's group[19] reported that, for patients with stable heart failure, type-B natriuretic peptide plasma levels and maximal VO_2 provide independent information for prognostic risk stratification. Despite the recent appearance of such laboratory prognostic indicators for heart failure, the distance walked in the 6MWT remains a low-cost indicator that is easy to perform and apply.

Cardiopulmonary exercise tests and the 6MWT may induce arrhythmias. When the arrhythmogenic potential of both tests was analyzed for the population studied, both methods showed a high tendency to induce arrhythmias (84.4% and 86.4%, respectively). Therefore, arrhythmias may compromise the safety of both methods—mainly that of the 6MWT, because the patient is not under continuous cardiac monitoring.[13] However, during the SOLVD study,[9] no complications were recorded for the 833 6MWTs performed. In the present study, no clinical complication was recorded within the 5-hour period after each test. We conclude that the 6MWT was a safe method for evaluating our patients.

The present study has several limitations. The major limitations are the small size of the patient group and the fact that 30% of that population was lost to follow-up. Another significant limitation is that the short duration of the study may have lowered the statistical power of the prognostic findings.

Despite these limitations, this study appears to confirm that the distance walked during the 6MWT is a highly reliable and independent predictor of cardiac death.

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