ORIGINAL RESEARCH

Impact of 12-Minute Walk Test Distance on Mortality in a Group of Phase II Cardiac Rehabilitation Patients

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ABSTRACT

Background: To assess aerobic capacity in patients undergoing treatment in a cardiac rehabilitation program (CRP), the 12-minute walk test (12MWT) may be an alternative to cardiopulmonary exercise testing. The 12MWT may be a more appropriate test based on a cardiac rehabilitation (CR) patient's functional capacity. The objective of this study was to determine the impact of distance walked on a 12MWT on all-cause mortality in patients undergoing treatment in a phase II CRP.

Methods: A total of 810 phase II CR patients completed the pretreatment and posttreatment 12MWT. Patients were placed into groups based on distance completed using a half-mile (2,640 feet = 804.7 m) as the differential distance. The groups were the remained low group (LG; pre-12MWT and post-12MWT < 2,640 feet), improved group (IG; (pre-12MWT < 2,640 feet and post-12MWT ≥ 2,640 feet), and remained high group (HG; pre-12MWT and post-12MWT ≥ 2,640 feet). Covariates were assessed using Cox regression and Kaplan-Meier curves to assess mortality rates.

Results: Significant predictor variables of overall mortality included 12MWT distance, age, overweight/obesity, and diabetes. HG had significantly higher survivability than IG and LG. IG had higher survivability than LG, but results were not statistically significant. The 12MWT was a predictor of all-cause mortality when using a distance of 2,640 feet. Improvements in overall mortality related to completing 2,640 feet pre/post-12MWT, with improvement from below 2,640 feet to above 2,640 feet throughout CR, with significant improvements in mortality.

Conclusions: These results show that the 12MWT is a valid predictor of all-cause mortality in the phase II CR patient population.

Keywords: aerobic capacity, cardiac rehab, fitness testing, longevity

INTRODUCTION

Walking tests, such as the 6-minute walk test (6MWT) and 12-minute walk test (12MWT), are common assessment tools used to measure aerobic capacity in place of cardiopulmonary exercise (CPX) testing (1). CPX testing is used in many clinical settings, such as cardiac rehabilitation programs (CRPs), to predict mortality based on fitness and assist with exercise prescription (2–4). However, CPX testing requires highly trained staff, can be expensive, and requires a patient to be able to exercise at near maximal levels, making walk tests more feasible than a CPX test for many facilities. The 12MWT may be a better assessment tool than the 6MWT in most cardiac rehabilitation (CR) patients with a higher aerobic capacity due to the increased duration of the test (5).

Undergoing treatment in a CRP decreases the risk of overall mortality, having a dose-response effect based on sessions attended (6–10). In patients attending a CRP, the 12MWT has been shown to be a valid and reliable measure of aerobic capacity compared with CPX testing (11,12). Therefore, it is important to establish the effectiveness of the 12MWT as an assessment tool to predict mortality in this

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population. In this study, we aimed to determine the impact of performance on a 12MWT on overall mortality in a group of phase II CR patients.

METHODS

The University of Toledo Medical Center (UTMC) Institutional Review Board (IRB) and Bowling Green State University IRB approved the research and data collection protocols before data collection. All patients in this sample signed consent forms before undergoing treatment in the phase II CRP so that their data could be used for future research and education purposes.

In this study, we analyzed a group of patients undergoing treatment in phase II CR at the UTMC between October 1, 2004, and December 31, 2017. Patient data were extracted, collected, and collated from the UTMC-CR database.

Patients enrolled in the study completed 36 sessions of outpatient phase II CR within 6 months of admission and completed the pre-12MWT and post-12MWT. During CR sessions, patients performed 45 to 60 min of cardiovascular conditioning. Each patient's exercise prescription considered the patient's cardiac diagnosis, cardiac procedure, cardiac surgery, other comorbidities, and their performance on a CPX test and 12MWT. Exercise prescriptions were based on data from the CPX test according to the heart rate reserve (HRR) method which uses the standing resting heart rate (RHR) and the peak exercise heart rate (EHR) on the CPX test (EHR − RHR = HRR). The exercise intensity range was prescribed at 60%–85% of HRR + RHR. If a patient did not undergo a CPX test before starting CR, the training heart rate (HR) was prescribed with an upper limit of standing RHR + 20 to 30 $b\cdot min^{-1}$. The exercise prescription was gradually titrated to higher levels according to rating of perceived exertion (RPE), signs and symptoms, and normal physiologic responses. Exercise modalities included walking (treadmill and track), rowing ergometers, cycle ergometers, and recumbent steppers, all based on patient preference and maintaining their exercise prescription. The pre-12MWT was completed during the patient's first CR session, and the post-12MWT was completed between CR sessions 32 and 36. The 12MWT was administered and timed by a clinical exercise physiologist (CEP) and completed on an indoor track that measured 14 laps for a mile. Before performing the 12MWT, the patient sat quietly for 5 min. After 5 min, the RHR and blood pressure were recorded. The patient was then moved to the starting point on the track and given a lap counter set to zero. The patient was instructed to click the lap counter every time he or she went past the starting point.

The patient was given the following instructions:

> The purpose of this test is to walk as far as possible for 12 min, so don't run or jog. You will start from this point and follow the track around to the right. Twelve minutes is a long time to walk, so you will be exerting yourself. You may get out of breath or become very tired. You are permitted to slow down. If you need to stop and rest, just remain where you are until you can go on again. However, the most important thing about the test is that you walk as far as you possibly can during the 12 min.

The CEP performing the 12MWT informed the patient when 3, 6, 9, and 12 min had elapsed and offered words of encouragement at each 3-min interval. When the 12MWT was completed, the CEP marked the point where the patient stopped and recorded the number of laps performed according to the lap counter and calculated and recorded the distance walked to the nearest 50 feet. The CEP measured and recorded the patient's posttest HR, blood pressure, and RPE values.

The exclusion criteria were not completing 36 sessions of phase II CR, not completing 36 sessions within 6 months of CR admission, and not completing either the pre-12MWT or post-12MWT. The following demographic information was collected for each patient: name, sex, date of birth, age (on the date of admission), date of admission, date of discharge, primary cardiac diagnosis, secondary cardiac diagnosis (if applicable), and race. For HIPAA purposes, during analysis of data, any personal identifiers were removed. Pre-12MWT and post-12MWT distance were the primary outcome measures. HR-limiting medications, diabetes, being overweight or obese, smoking status, chronic obstructive pulmonary disease (COPD) diagnosis, and lower extremity orthopaedic limitations were covariates of interest. Mortality data were documented using information at the online obituary Website legacy.com, which is documented as a reliable and valid method to collect mortality data for research purposes (13).

A paired *t* test was used to compare the pre-12MWT and post 12MWT distance. When analyzing the 12MWT distance for all subsequent analyses, the variables were adjusted using half the standard deviation (350 feet). This was done for a more meaningful interpretation of the hazard ratios based on a larger unit of change or decrease (i.e., 350 feet versus 1 foot), making a more manageable goal for patient improvement from the pre-12MWT to the post-12MWT. One lap completed walking on the indoor track was equivalent to 350 feet. The covariates listed above were of interest because they have the potential to affect both the 12MWT performance and mortality. Outliers and normality were examined for 3 continuous variables (age, pre-12MWT distance, and post-12MWT distance). Analyses indicated that the data were normally distributed. Mahalanobis distance values were computed to identify potential multivariate outliers for the combination of the 3 continuous variables.

Bivariate linear regressions were performed to examine linearity and homoscedasticity for age with pre-12MWT and post-12MWT distances. Two preliminary Cox regression survival analyses were performed to identify variables that significantly impacted mortality to create a more parsimonious model, one for pre-12MWT distance and the other for post-12MWT distance. Additional analyses were performed to test the assumption of hazard proportionality.

Once statistically significant covariates were identified, additional Cox regression survival analyses were performed to identify variables that were not significant for survival. Kaplan-Meier (KM) survival curves were computed to determine if there were any significant changes in the rate of death based on the different distances completed. The average pretest distance walked was 2,827 feet. As a result, the distance interval used for the pre-12MWT and post-12MWT was a half-mile (2,640 feet). This distance was selected to allow facilities and patients to communicate a simple distance cutoff for improved mortality.

Three groups were created to examine improvement and mortality status for the KM curves: the remained low group (LG; pre-12MWT distance and post-12MWT distance < 2,640 feet), the improved group (IG; pre-12MWT distance < 2,640 feet and post-12MWT distance ≥ 2,640 feet), and the remained high group (HG; pre-12MWT distance and post-12MWT distance ≥ 2,640 feet). To clarify, if patients in the low category remained in the low category at posttest, they were placed in the LG. If the patients improved to the high category in the posttest, they were placed in the IG. Patients in the high category at pretest who remained in the high category at posttest were placed in the HG. Statistical significance was set at $\alpha \leq .05$. All data are presented as mean ± standard deviation. Data were analyzed using IBM SPSS version 26.0 (IBM Corp, Armonk, New York).

RESULTS

This study included 810 patients undergoing treatment in a phase II CRP. The selection process is presented in Figure 1. The following were reasons for CR referral: percutaneous coronary intervention/stent = 228, coronary artery bypass graft = 203, myocardial infarction = 176, stable angina = 81, valve procedure = 55, heart failure = 50, arrhythmia = 11, and heart transplant = 6. Three patients were identified as multivariate outliers for the variables of age, pre-12MWT distance, and post-12MWT distance. Mahalanobis distance values for these 3 patients were significant ($P < 0.001$). Upon further examination, 1 patient had an extremely low z score for age ($z = -4.04$), and the other 2 patients had extremely high z scores for the difference in pretest to posttest ($z = 3.87$ and 9.21). The 3 patients were excluded, and the final sample included the remaining 807 patients. Descriptive statistics are presented in Table 1.

Cox regression results for the pre-12MWT and post-12MWT data identified 4 significant covariates of interest in terms of mortality: pre-12MWT distance, age, diabetes, and overweight/obesity (Table 2). An additional analysis to test for the assumption of proportionality of hazards for significant covariates using pre-12MWT and post-12MWT distance as covariates was completed and found no significant interactions with time. We concluded that it was unnecessary to treat any of the covariates as time dependent. The regression coefficient statistics for the pre-12MWT and post-12MWT are shown in Table 2. The adjusted regression coefficient statistics for pre-12MWT and post-12MWT are shown in Table 3.

12MWT PREDICTION OF MORTALITY

KM curves were computed to determine survival rates based on LG, IG, and HG from post-12MWT and pre-12MWT using the half-mile criterion (see Figure 2 for KM curves and descriptive statistics). The results of the log-rank test were

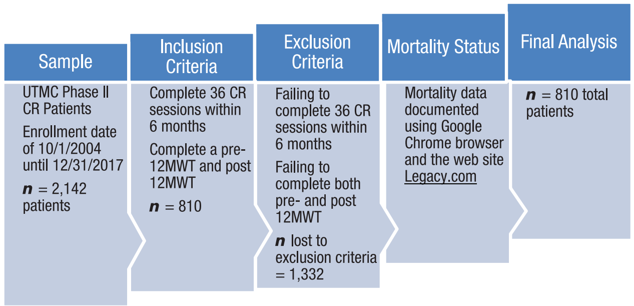


FIGURE 1. Patient sample selection process.

reported regarding differences in the survival distribution based on distance completed at pre-12MWT and post-12MWT and if there was improvement between the 2 time points. Overall comparisons for the survival distributions for LG, IG, and HG were statistically significant ($P < 0.0001$). Survival rates were calculated per group to demonstrate the remaining percentage of the population every 2 years to assess differences in mortality over 12 years (see Table 4). Pairwise comparisons between groups indicated that HG was statistically significant compared with IG and LG ($P = 0.002$ and $P < 0.0001$, respectively). However, IG was not statistically significant from LG ($P = 0.069$).

DISCUSSION

This analysis demonstrated that those who remained in the HG group had significantly higher survival rates than those who remained in the LG or moved to the IG groups. When comparing groups, the HG had an average 20% and 18% absolute higher survival rate over 12 years than the LG and IG, respectively. Although not quite reaching significance, the IG showed an average 12% higher survival rate over 10 years from the LG, suggesting improvement in aerobic fitness from CR participation may be beneficial for survival. Patients who improved by an interval of 350 feet (1 lap on the indoor track) exhibited an estimated 17% reduction in all-cause mortality.

These findings suggest that aerobic capacity should be a primary focus in this patient population. De Schutter et al. (2) completed a similar study using phase II CR patients and assessed the improvements in aerobic capacity measured by CPX test. They showed that those who made greater improvements in VO_{2peak} had lower mortality rates. We estimated each patient's aerobic capacity as determined by a 12MWT before and after CR to predict survival. A patient may demonstrate improvement because of undergoing treatment in the program, but if he or she was below the standard (e.g., walking ≤ half-mile in 12 min), he or she remained at increased risk for premature mortality. Therefore, having standard performance measures that patients can strive to achieve may assist them in improving their overall survival based on their distance walked in 12 min. This type of data allows clinicians to discuss patients' risk of premature mortality based on their distance walked early in the program. This also allows clinicians to institute exercise programming that would help them improve their survival rates by

TABLE 1. Descriptive statistics. Data presented as mean ± SD, unless noted.

Variable	Total Sample
N	807 (565 males; 242 females)
Age (y)	63.4 ± 11.3
Remained low group (LG)	126 (15.6%)
LG pre-12MWT distance (feet)	1741 ± 510[a]
LG post-12MWT distance (feet)	2037 ± 495
Improved group (IG)	165 (20.4%)
IG pre-12MWT distance (feet)	2316 ± 296[a]
IG post-12MWT distance (feet)	3086 ± 317
Remained high group (HG)	509 (63.1%)
HG pre-12MWT distance (feet)	3261 ± 414[a]
HG post-12MWT distance (feet)	3669 ± 503
Months deceased from discharge	69.8 ± 42.2
HR-limiting medications[b]	730 (90.5%)
Diabetes[b]	275 (34.1%)
Overweight/obese (BMI ≥ 25 $kg \cdot m^{-2}$)[b]	522 (64.7%)
Smoking[b]	90 (11.2%)
COPD[b]	130 (16.1%)
Lower extremity orthopedic limitations	426 (52.8%)

12MWT = 12-minute walk test; BMI = body mass index; COPD = chronic obstructive pulmonary disease; HR = heart rate.
[a]$P < 0.001$ for pre-12MWT versus post-12MWT.
[b]Data presented as number and percentage of total N with identified condition.

working toward achieving a better performance on their post-12MWT.

We report an increase in survival rates for patients who had an improvement above a half-mile over 12 years. This suggests that, while CR staff should focus on getting their patients to achieve a specific standard for aerobic capacity to improve survival, any improvement is beneficial, which is like that reported by De Schutter et al. (2).

These findings support the previous literature regarding VO_{2peak} and mortality. Authors of many studies have successfully used VO_{2peak} as a predictor variable of mortality in CR patients (2–4). Our analysis demonstrated that a field-testing method which did not directly measure VO_{2peak} (12MWT) was an effective assessment tool in predicting mortality rates in this patient population. Based on our findings, mortality rates in those who were able to walk equal to or greater than a half-mile on the pre-12MWT and post-12MWT showed significantly higher survival rates over the course of 12 years.

McGavin et al. (14,15) first used the 12MWT in clinical populations in 1976. Field-implemented walking tests are cost effective and require minimal staff and training. As compared with a CPX test which increases in speed and/or grade at intervals throughout the test, field-implemented walk tests are performed at a self-selected pace. This means that walking speed can be estimated accurately based on a patient's normal walking speed during the 12MWT. Walking speed has high validity for predicting mortality (16,17). This can be useful in deconditioned patients to determine an appropriate initial walking speed for exercise training on a treadmill during their CR sessions and for performing a CPX test on a treadmill. Field-administered walking tests are also appropriate alternatives for patients who are unable to complete a maximal CPX test based on other risk factors or

TABLE 2. Regression coefficients for pre-12MWT and post-12MWT.

Variables	Pre-12MWT		Post-12MWT	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
12MWT[a]	0.82 (0.74–0.91)	<0.001[b]		
12MWT[a]			0.82 (0.73–0.91)	<0.001[b]
Age	1.07 (1.04–1.09)	<0.001[b]	1.06 (1.04–1.09)	<0.001[b]
Sex	0.63 (0.38–1.05)	0.073	0.09 (0.39–1.07)	0.089
HR-limiting medications	1.51 (0.61–3.77)	0.374	1.62 (0.65–4.03)	0.302
Diabetes	1.74 (1.11–2.71)	0.015[b]	1.64 (1.06–2.53)	0.028[b]
Overweight/obese	0.52 (0.33–0.83)	0.006[b]	0.47 (0.29–0.76)	0.002[b]
Smoking	0.78 (0.36–1.66)	0.515	0.77 (0.36–1.65)	0.503
COPD	1.62 (0.93–2.81)	0.089	1.66 (0.96–2.89)	0.070
Orthopedic limitation	1.05 (0.66–1.65)	0.848	1.07 (0.68–1.68)	0.773

12MWT = 12-minute walk test; CI = confidence interval; COPD = chronic obstructive pulmonary disease.
[a]Each unit = 350 feet; age unit = per year; sex = male or female; HR-limiting medications, diabetes, overweight/obese, smoking, COPD, and orthopaedic limitation = yes or no.
[b]Indicates significance, $\alpha < 0.05$.

TABLE 3. Adjusted regression coefficients for pre-12MWT and post-12MWT.

Variables	Pre-12MWT		Post-12MWT	
	Adjusted Hazard Ratio (95% CI)	*P* Value	Adjusted Hazard Ratio (95% CI)	*P* Value
12MWT[a]	0.83 (0.75–0.91)	<0.001[b]	0.83 (0.75–0.91)	<0.001[b]
Age	1.07 (1.04–1.09)	<0.001[b]	1.06 (1.04–1.09)	<0.001[b]
Diabetes	1.83 (1.18–2.84)	0.007[b]	1.74 (1.12–2.71)	0.014[b]
Overweight/obese	0.51 (0.32–0.81)	0.004[b]	0.47 (0.29–0.75)	0.002[b]

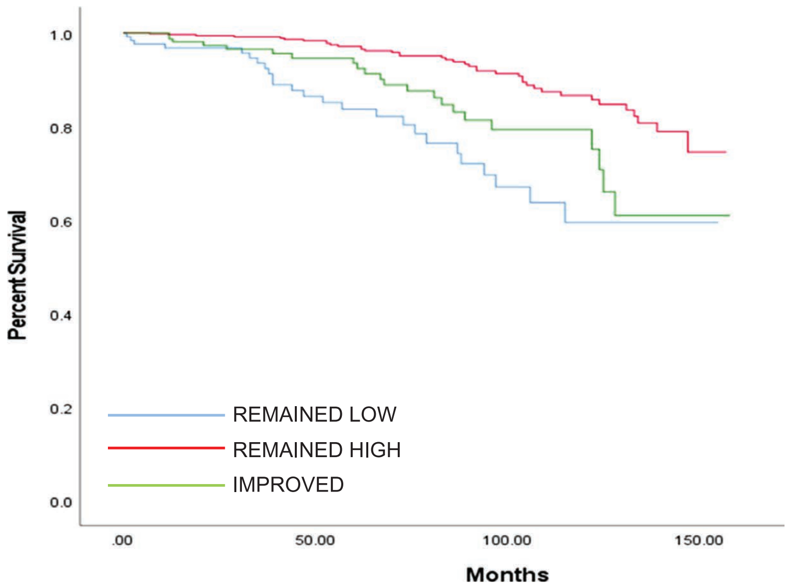
12MWT = 12-minute walk test; CI = confidence interval.
[a]Each unit = 350 feet; age unit = per year; diabetes and overweight/obese = yes or no.
[b]Indicates significance, $\alpha < 0.05$.

contraindications to maximal testing. This allows facilities that do not have the accommodations to complete VO_2 testing to still provide valuable, objective information to patients and help them plan attainable and measurable goals for themselves that can help lower their risk of premature mortality after a cardiac event or surgery.

With the significant overall increase in distance walked from pre-12MWT to post-12MWT, the results agree with the multitude of previous studies in which authors have indicated that phase II CR is an effective treatment to improve aerobic capacity after a cardiac event or cardiac surgery (18,19). Based on our patient group, the variables that were most significant in predicting mortality were walking distance, age, diabetes, and obesity/overweight. Authors of many studies have identified aerobic capacity as the leading predictor of all-cause mortality with similar results for age, diabetes, and obesity/overweight as significant predictor variables (20,21). Other measured variables that were not statistically significant included HR-limiting medications, sex, smoking status, COPD, and lower extremity orthopaedic limitations. It is well known that these variables have an impact on mortality. However, based on our findings, performance on a 12MWT was a better predictor variable of mortality. The findings of the current study can assist clinicians implementing CR programs to identify patients who are at a higher risk for mortality earlier based on their clinical assessment and performance on a 12MWT.

Limitations

While we support the use of the 12MWT to evaluate patients undergoing treatment in a CRP, caution should be exercised when using field-administered walk tests as the only method of determining a patient's aerobic capacity. Schumacher et al. (22) evaluated the validity of a 6MWT in cancer survivors. The results indicated that almost every patient's VO_{2peak} was underestimated by an average of 10 $mL \cdot kg^{-1} \cdot min^{-1}$ with the 6MWT compared with the CPX protocol. Owing to the variability of effort that could be elicited in a 6MWT based on RPE and physiological response, the authors stated that the 6MWT is not an ideal substitute for CPX testing. It was also suggested that the 6MWT was not sensitive to those who had higher aerobic capacities, such as those walking more than 1640 feet (500 m) during the test, owing to the test being of minimal stress compared with the maximal effort CPX test. While the 6MWT underpredicted VO_{2peak} in cancer



NUMBER AT RISK	0	50	100	150
REMAINED LOW	126	66	24	1
REMAINED HIGH	509	342	155	11
IMPROVED	165	90	36	5

FIGURE 2. Kaplan-Meier survival curves comparing 12-minute walk test (12MWT) distances (posttest versus pretest).

TABLE 4. Survival rate at selected intervals based on group change at post-12MWT.

Group	2-y Survival	4-y Survival	6-y Survival	8-y Survival	10-y Survival	12-y Survival
Remained low group (LG)	97%	86%	82%	70%	59%	59%
Improved group (IG)	97%	95%	90%	79%	71%	61%
Remained high group (HG)	99%	98%	95%	92%	87%	79%

12MWT = 12-minute walk test.

survivors, field-administered walk tests can still have clinical benefits in other populations. The 6MWT has been shown to have high validity and reliability in COPD and heart failure patients (5, 23–25).

In patients with a higher aerobic capacity, a 12MWT may be more appropriate due to the extended duration of the test. The 12MWT has high validity and reliability compared with VO_{2peak} measured during a CPX test in said populations (11). Unfortunately, there were not enough patients who completed both a pre-12MWT and post-12MWT and a pre-CPX and post-CPX test, preventing the comparison between the 12MWT and CPX.

While there are limitations to field-administered walking tests in some clinical populations, Schumacher et al. (22) have suggested more research on different durations of walking tests based on various clinical populations is needed. While Schumacher et al. (22) determined that the 6MWT may not be as valid and reliable in cancer patients compared with cardiac patients, the 6MWT is a common test used in COPD and chronic heart failure patients. A 6MWT may underpredict VO_{2peak} in higher-functioning cancer patients, but a 12MWT may be more reliable and valid, as seen in the phase II CR patients at UTMC.

CONCLUSIONS

Based on these data, the 12MWT is an effective assessment tool for predicting mortality in phase II CR patients. While the 6MWT is shorter and potentially easier for patients, the 12MWT is achievable in this sample and has clinical implications for mortality. This field test can be implemented at phase II CRP facilities that lack the ability to complete maximal CPX testing. Based on our findings, the 12MWT holds value especially for higher fit patients, providing helpful survival predictions that can impact exercise prescription in this population.

Further research is needed to determine the variance in primary diagnosis and distance completed on mortality to better understand preventive treatment strategies. In addition, research on all-cause mortality versus cardiac mortality prediction using a 12MWT is encouraged to assess for differences, potentially altering programming for the patient. Overall, the 12MWT can be an effective objective measure to evaluate a patient's aerobic capacity after a cardiac event and can assist in determining risk of mortality.

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