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Six-Minute Walk Test as a Predictive Measure of Exercise Capacity in Adults with Type 2 Diabetes

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Abstract

Objective—The 6 Minute Walk Test (6MWT) is a measure that is routinely used to assess a response to treatment for cardiopulmonary diseases such as pulmonary fibrosis and congestive heart failure. The measure has never been verified as a valid measure of exercise capacity in the highly prevalent patient population of type 2 diabetes (T2DM). This study investigated the correlation between the 6MWT and graded exercise testing (GXT) in an effort to validate the 6MWT as a quality tool for assessing exercise capacity in adults with T2DM.

Research Design and Method—This is a secondary data analysis of Program ACTIVE II, a randomized controlled trial designed to assess the effectiveness of two behavioral interventions on depression and glycemic outcomes in adults with T2DM. The correlation of 6MWT and predicted VO₂ max (PVO₂M) using GXT was examined in a subsample of participants at the time of study enrollment and at post-intervention.

Results—PVO2M showed a significant correlation with 6MWT distance both at baseline ($r=0.57$, $p=0.014$) and post-intervention ($r = 0.66$, $p = 0.037$). The regression analysis of baseline data revealed that 6MWT distance alone explained 45% ($F = 13.03$, $p = .0024$) of the variability in PVO2M. When combined with the SF-12 physical health component score (PCS), 6MWT explained 66% ($F = 13.62$, $p < .001$) of the variance in PVO2M. After adjusting for PCS, 6MWT distance explained an additional 30% variability in PVO2M.

Conclusions—Findings from this study indicate that the 6MWT and predicted exercise capacity are significantly correlated. The 6MWT can be used to estimate exercise capacity in adults with T2DM.

INTRODUCTION

Diabetes affects more than 29.1 million, or 9.3%, of the population (1). It is estimated that 86 million, or 37% of adults in the United States, have been diagnosed with prediabetes many of which will progress to type 2 diabetes (1). In 2010, diabetes was the 7th leading cause of death. Between 2003–2006 the rate of death was 1.5 times higher from all causes in adults diagnosed with diabetes compared to adults without diabetes (1).

In addition to diet and medications, moderate-intensity exercise is the standard of care for treatment of most people with T2DM and prediabetes (2). The graded maximal exercise stress test (GXT) has long been used for the measurement of exercise capacity. However, it is not always available and is unsustainable for routine use given the extensive tools required for administration. The Six Minute Walk Test (6MWT) is used as an alternative, cost-effective method to measure exercise capacity. It has been proven to be useful as a prognostic indicator in the treatment of congestive heart failure, idiopathic pulmonary fibrosis, pulmonary artery hypertension and chronic obstructive pulmonary disease (3,4,5,6). Guidelines published by the American Thoracic Society have established standardization of the test itself (7). While the 6MWT has been used as a measurement tool in those with T2DM, to date, no studies have validated the 6MWT as an alternative to GXT in gauging exercise capacity in adults with T2DM (8).

The aim of this study was to determine the degree of correlation between the 6MWT and GXT (measured as predicted VO2 max) in order to validate the 6MWT as a quality tool for assessing exercise capacity for patients with T2DM.

METHODS

Study Design

This study is a secondary analysis of Program ACTIVE II, a multi-state randomized controlled trial designed to test the comparative effectiveness of cognitive behavioral therapy and community-based exercise on depression and diabetes outcomes. Details of the study design and methodology are published elsewhere (9). The data for this study was gathered from participants recruited from the north-central West Virginia site from 2011–2016 (9). Participants were recruited through community outreach and advertisements via physician offices, pharmacies, community centers and events, radio stations and newspapers. Potential participants were given a toll-free number to call for study information and to be screened

by a trained staff to determine eligibility. The study was approved by the Institutional Review Board at West Virginia University and informed consent was given by all participants.

Recruitment and Enrollment Procedures

Individuals with T2DM and likely Major Depressive Disorder (MDD) were screened and assessed using a multi-level approach. 1) initial phone screening of participant self-reported medical and psychiatric status; 2) permission from the participant's primary care provider for the participant to engage in low to moderate intensity exercise; 3) baseline assessment data collection including resting blood pressure prior to the 6MWT and 4) an eligibility case conference by study investigators to determine eligibility for study enrollment.

During the initial phone screening, potential participants were queried about their medical status (e.g. most recent blood pressure reading (BP), history of medical conditions, etc.). During the phone screening, potential participants who identified a recent blood pressure reading that constituted a hypertension crisis (i.e. JNC VII Stage 3 or Stage 4 hypertension) were considered to be immediately ineligible for further evaluation and were referred to their physician for follow-up care. Individuals who reported recent BP readings of less than 140/90 mm Hg or between 140/90 mm Hg and < 180/110 mm Hg and who met other eligibility criteria were given an explanatory cover letter and the PCP Permission to Participate form so that their physician could provide the study investigators with background information on relevant medical conditions and appropriateness to participate in low to moderate intensity exercise for the baseline assessment.

Criteria for study inclusion included a diagnosis of T2DM for at least 1 year, age 18 years or older, maintained ambulatory status, and a diagnosis of MDD per study psychiatric evaluation. The medical exclusion criteria included: history of diabetic ketoacidosis (DKA), continuous insulin therapy since T2DM diagnosis, hypertension exceeding 160/100 mm Hg as defined by JNC VII (11) as hypertension unsafe for exercise, cardiac events in the past year (e.g. unstable angina, diagnosed angina, percutaneous coronary angioplasty, any cardiac intervention for CAD or tachydysrhythmias), laser surgery for proliferative retinopathy in the past 6 months, history of stroke, lower limb amputation, sensory peripheral neuropathy, aortic stenosis or other severe valvular heart disease, atrial fibrillation, severe COPD (e.g., basal oxygen), class III or IV heart failure or medical instability. Data used for this study were obtained at the participant's baseline and post-intervention medical assessment.

Psychiatric exclusion criteria included: active suicidal ideation or a history of suicide attempt, bipolar depression or history of psychotic disorder and current substance abuse or dependence disorder. Participants who were currently prescribed antidepressant medications for 6 weeks or longer and who met diagnostic criteria for major depression without psychotic features were included. Participants who reported the use of a current antidepressant medication for 5 weeks or less were excluded or deferred for later screening after the 6-week period. Participants receiving psychotherapy from a mental health provider for MDD were excluded. Participants who were receiving only medication management from a psychiatrist were included.

Once the primary care physician gave clearance for participation, the patient was scheduled for the baseline assessment visit, which included completion of the 6MWT. Prior to starting the 6MWT, two parameters needed to be met for safe participation. These included an appropriate blood pressure <160/90 and blood glucose range between 80mg/dL and 300mg/dL. After informed consent, a pretest blood glucose level was measured. If the value was below 80mg/dL or greater than 300 mg/dL, the participant was treated with a snack or 8 ounces of water, respectively, and the level was repeated 15 minutes later. If this value remained outside of the determined range, the decision to reschedule the 6MWT was made. If the repeated blood glucose level remained below 80mg/dL, then it was treated and rechecked at 15-minute intervals until greater than 80mg/dL. If the repeated level remained greater than 300mg/dL then the medical director was contacted to ensure the participant received proper follow up. A resting BP was also measured. If this BP was >160/90, a second resting BP was measured. If both BP measurements were >160/90, the 6MWT was not performed and the patient was referred back to his/her primary care physician with a letter from the study Medical Director (JS). If the primary care physician deemed the individual appropriate for study participation, the 6MWT was rescheduled and resting BP measurements were taken before and after the test. Participants whose resting BP was <160/90 were permitted to complete the 6MWT. If resting BP exceeded this threshold after a second measurement, the participant was referred back to their PCP and was not eligible for participation at that time.

Measures

6 Minute Walk Test—While the standard for conducting the 6MWT at the time of study design was a distance of 30 meters (10), this study was community based and not all fitness centers had straight corridors of that distance. To be consistent among centers, the 6MWT was conducted with two cones placed 25 feet apart on a flat hard walking surface. It was explained the participants would walk for 6 minutes and they were instructed to slow down or stop if they became fatigued, but to resume once able. How to walk between and pivot at the cones was demonstrated and participant understanding of the instructions was confirmed. Each time the subject passed the starting position a lap was recorded. Using an even-toned encouraging phrase, the time remaining in the test was reported to the participant at 1 minute intervals. If the participant needed to stop during the 6-minutes he/she was reminded to lean against the wall if necessary and to continue walking whenever able. The timer was not stopped if the participant needed to rest, however, if the participant refused to continue or it was deemed unsafe to continue at the discretion of the investigator, then a chair was offered to the participant, the timer was stopped, and it was noted the test ended prematurely and the reason for doing so. Once the 6 minutes concluded, the participant was instructed to stop and remain stationary while the end point was marked. Once marked, the total distance walk was calculated in feet. Blood glucose level, BP, heart rate (HR) and the Borg Rating of Perceived Exertion (RPE) were all measured before and immediately after the test with additional BP, HR and RPE measurements 2 minutes and 4 minutes post-test. If the post-test blood glucose level was less than 80mg/dL or had dropped by more than 100mg/dL compared to prior, a snack was given and the level was rechecked. Once a blood sugar greater than 80 mg/dL was achieved, the participant was allowed to leave.

All baseline assessment data were reviewed by the Core Study Team (JS, GH and MdG and the project coordinator who conducted the assessment visit) during the eligibility case conference. Data from the 6MWT, resting blood pressure and medical history interview were reviewed. If the study team identified concerns about the subject's ability to perform low to moderate exercise safely, the participant was referred to their primary care physician for additional cardiac stress testing. The American College of Sports Medicine (ACSM) relative indication for terminating a Clinical Exercise Test was used during the 6MWT which included: drop in systolic BP $\geq$ or equal to 10 mm Hg with an increase in exercise intensity, or if the systolic BP was below the resting level before testing; and a hypertensive response (SBP of > 250 mm Hg and/or a DBP of > 115 mm Hg. (10) The team used the general standard that SBP would increase approximately 10 ± 2 mm Hg / MET. Since the 6MWT was designed to be of moderate intensity (e.g., 3 – 6 METs), the SBP may have increased anywhere between 30 – 60 mm Hg above resting levels. Any participant who had a post 6MWT SBP > 200 mm Hg and / or a DBP > 110 mm Hg and / or a drop in SBP of 10 mm Hg or more below baseline standing SBP had enrollment deferred and were referred to their PCP for BP management. Upon approval by the primary care physician, the participant could be enrolled in the study and proceeded to completing the GXT.

GXT—Prior to starting the GXT, participants were given instruction on how to walk on the motorized treadmill. Resting HR, BP and ECG were obtained in a seated position as well as a standing position. The participants performed a modified version of the Balke Standard treadmill protocol (12). The protocol consisted of a 2-minute warmup at a speed of 1.5–2.0 miles per hour with zero percent grade. The speed was then increased to 2.0–3.5 miles per hour and remained at that level for the rest of the GXT testing. By the end of the second minute the grade was raised to 2 percent and then increased by 1 percent each minute thereafter. This continued until the participant asked/motioned for the test to be terminated or if the trained technicians agreed the test should be stopped for reasons of participant safety. HR and ECG were monitored continuously during the GXT and recorded at the end of each minute. BP was measured in the left arm at the end of each minute during the GXT. Oxygen consumed (VO_2), carbon dioxide produced (VCO_2), RER ($\text{RER} = \text{VCO}_2 / \text{VO}_2$), ventilation (VE), ventilatory equivalent for CO_2 (VE / VCO_2) and O_2 (VE / VO_2), were measured continuously and calculated using 20 second averaging throughout the GXT (TrueOne 2400; ParvoMedics, Sandy, UT). Every 2 minutes the participant's rating of perceived exertion (RPE) was recorded. At termination the treadmill's speed was reduced to 1.0–1.5 miles per hour and the grade was set to 0 percent. The participant then participated in a cool down exercise at these settings for 4 minutes, if able. Predicted VO_2 max (PVO_2M) was calculated as Peak VO_2 L/min / % maximal effort based on RPE max (13), and thus exercise capacity for this study was a calculated value.

Medical history data was gathered via interview by the research nurse for T2DM-specific physiologic characteristics such as T2DM duration, prescribed diabetes treatment regimen, medical contraindications for participation, accuracy of diagnoses, and number and severity of T2DM complications.

Short Form-12 Quality of Life Measure (SF-12) is a self-administered questionnaire assessing general quality of life (14). This measure has demonstrated an internal consistency

of $r = 0.81$ – 0.88 in adults and has been validated for use in T2DM samples (15). The SF-12 Physical Components Subscale (PCS) was used as a proxy for physical limitations that could hinder exercise capacity and was therefore used as a covariate in the regression analyses to account for baseline level of physical functioning.

Blood pressures were measured via auscultation with a calibrated sphygmomanometer. Heart rate (HR) was determined via palpitation of the radial artery. Researchers counted the number of heartbeats occurring in 10 seconds and multiplied this number by 6 to arrive at a Beats Per Minute value. Blood pressure and HR were collected as outlined above for the 6MWT and the GXT. Height and weight were measured using standardized procedures.

Statistical Analysis—Data were analyzed using Statistical Analysis Software (SAS) 9.4. A simple regression analysis was performed to identify any significant predictors of PVO2M using age, gender, marital status, household income, education, PCS score, participants' use of beta-blockers, and weight individually. Only PCS score showed a significant association. We then fitted three models using PCS score only, 6MWT distance only and both covariates jointly. The univariate analysis for association with 6MWT distance showed that the homogeneity variance assumption of the general linear model was not met (See Figure 1). Therefore, we used the reciprocal of PVO2M to transform the variable to meet homogeneity of variance. We also computed Pearson correlation coefficients between PVO2M and each of the two predictors, PCS score and 6MWT distance.

RESULTS

Demographic characteristics for all participants ($N = 18$) included in this analysis are listed in Table 1. The study participants were on average 53 years of age, 72% female, mostly White (82%), married or living with partner (56%), currently employed (56%) with a HS Diploma or GED or greater educational attainment.

Baseline PVO2M was significantly correlated with the distance walked during the baseline 6MWT for the 18 participants who completed both protocols at baseline ($r = .57$; $p = .014$). In addition, PVO2M at post-intervention follow-up was correlated with 6MWT distance at the post assessment among the 10 individuals who completed both protocols at that time point ($r = .66$; $p = .037$).

The regression analysis of baseline data revealed that 6MWT distance alone explained 45% ($F = 13.03$, $p = .002$) of the variability in PVO2M while this predictor jointly with physical health (PCS) score explained 66% ($F = 13.62$, $P < .001$) of the variability in PVO2M. After adjusting for PCS, 6MWT distance explained an additional 30% variability in PVO2M. Though the unadjusted analysis of PCS score showed a significant association with PVO2M ($R^2 = 36\%$, $F = 8.35$, $p = .011$), it did not remain significant after adjusted for 6MWT distance ($p = .246$). None of the predictors (age, gender, marital status, household income, education, PCS score, and participants' use of beta-blockers) showed any significant association with PVO2M.

DISCUSSION

Physical activity is a fundamental component of disease management for adults with T2DM, yet most people with T2DM do not engage in recommended levels of physical activity. (16). Valid assessment techniques of exercise capacity that are not dependent on specialized equipment are needed for clinical providers who practice in a variety of settings. In this paper, we presented the first study to examine the validity of the 6MWT as a measure of predicted exercise capacity for adults with T2DM. We observed a significant correlation between the 6MWT and predicted exercise capacity as measured by the VO2 Max after accounting for self-reported physical ability as measured by the physical component score of the SF-12 (PCS12).

Limitations of the current study include a small sample size that limits generalizability of the findings to the entire population of patients with T2DM. Patients with T2DM have been found to be twice as likely to experience depressive symptoms as their non-diabetic peers with 1 in 4 patients reporting clinically significant depressive symptoms and 11.4% meeting criteria for MDD (17). The population in this study was selectively screened to be eligible for an exercise trial and may not be representative of all people with T2DM who may actually have even higher CV risk. In addition, the small sample size limited the number of covariates that could be used in the model thereby limiting assessment of the role of medical and physical characteristics that could influence the interaction of these two assessment measures. In order to maximize parsimony, the PCS12 was used as a proxy variable for physical characteristics. We felt it adequately represented physical limitations that could hinder exercise capacity. The fact that the regression model using post-intervention data did not reach significance is likely explained by the small sample size (n=10).

The existing literature has explored changes in the 6MWT distance to gauge the efficacy of treatment for patients with diverse pathologies involving the heart and lungs. However, this measure of exercise capacity was never validated against the gold standard of graded exercise testing (1,2,3,4). The exercise capacity for this study was ultimately a predicted maximum utilizing VO2 volume and subjective RPE indicated by the participant. Other options for determining maximal exercise capacity would have included incorporation of the heart rate or pushing these participants to their absolute maximal capacity. We decided against using heart rate target as many participants were prescribed a beta blocker medication. We elected against physically pushing these participants to their absolute max given the extremely uncomfortable and likely distressing nature of such states. In addition, these states are not generalizable or easily replicable in everyday practice.

An important consideration of validation of the 6MWT is the extent to which it is an effective screening tool for cardio-pulmonary problems. Of the 145 6MWT that were performed during the Program ACTIVE II study, three were stopped early due to the onset of signs/symptoms that could potentially be a result of clinically significant disease. These three participants were referred to their primary care physician with the results and description of their 6MWT. After referral, only one patient was found to have a true positive test as additional medical testing confirmed the presence of clinically significant coronary artery disease.

Findings from this study suggest that the 6MWT can be used to determine exercise capacity in the clinical setting. This is an efficient test that can be practically used in assessing a patient's ability to pursue exercise. Its simplicity can support the development of safe and effective exercise therapy for patients with T2DM. Utilizing this walk test, physical therapists can make more informed recommendations regarding an exercise regimen that can be tailored for each patient with hopes of maximizing adherence and improving overall disease outcomes.

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Figure 1. Scatterplot displaying the like of homogeneous variance in 6-minute walk test distance when associated with VO2 max.

Table 1

Demographic Characteristics (N = 18)

	Mean, N	SD, %
Age, y (Mean, SD)	52.8	10.2
Gender		
Female	13	72.2
Ethnicity (N=17)		
White	14	82.4
Black/African American	1	5.9
Native American	2	11.8
Education		
HS Diploma GED	5	27.8
Trade School	1	5.6
Part College	2	11.1
4-year College Degree	5	27.8
Master's or Post-Degree Education	4	22.2
Other	1	5.6
Marital status		
Married/Living with Partner	10	55.6
Divorced	5	27.8
Single	3	16.7
Income (N=16)		
0–10,000	1	6.3
21,000–40,000	8	50.0
41,000–60,000	2	12.5
61,000–80,000	3	18.8
More than 100,000	2	12.5
Current Employment (yes)	10	55.6
Health Insurance (N=17; yes)	14	82.4
Current Primary Care Provider (N=17; yes)	16	94.1
Current Diabetes Specialist (N=17; yes)	3	17.7
T2DM Duration	10.0	8.2