Predictors of 6-Minute Walk Distance Among Aging Adults With Chronic Cardiopulmonary, Metabolic, and Renal Diseases

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ABSTRACT

Background: The 6-minute walk test is a widely used measure of physical function in healthy people and patients with chronic conditions. Few reports have compared 6-minute walk distance (6MWD) across different conditions, and limited knowledge is available about how common covariates [age, sex, body mass index (BMI)] differentially affect 6MWD. Our purposes were to examine the 6MWD in persons with chronic conditions, compare walk distances with healthy controls, and identify predictors of 6MWD.

Methods: Data were aggregated from previous studies. Participants with primary diagnoses of heart failure (HF), chronic obstructive pulmonary disease (COPD), type 2 diabetes, chronic kidney disease, and peripheral artery disease (PAD) were included. Univariate and multivariate general linear models were used to estimate the impact of each condition on the 6MWD.

Results: The sample included 429 adults (48% female) aged 63 ± 9 years. Participants with HF, COPD, and PAD walked shorter distances than healthy controls (all $P < 0.01$). Predictors differed by group. In the HF group, age, Black race, and male sex negatively affected 6MWD. In the type 2 diabetes group, older age and high BMI were associated with shorter distances walked. In the chronic kidney disease group, higher BMI, Black race, and male sex negatively impacted 6MWD. No covariates were associated with 6MWD in the PAD, COPD, or control groups.

Conclusion: We found wide variation in common, nondisease-specific predictors of the 6MWD and significantly lower 6MWDs compared with healthy controls. Our findings add to our knowledge of 6MWD among aging adults with common chronic diseases. *J Clin Exerc Physiol*. 2022;11(4):140–145.

Keywords: 6-minute walk test, functional capacity, physical function, cardiovascular disease, diabetes

INTRODUCTION

The 6-minute walk test (6MWT) is a standardized, widely used functional capacity measure for evaluating the integrated abilities of the cardiovascular, pulmonary, and skeletal muscle systems to support a short period of exercise (1,2). The 6MWT can be completed in a straight long (>30 m) hallway of a clinic, hospital, or research facility. Patients are asked to walk as far as they can in 6 minutes. Healthy adults walk between 514 and 650 m (3–6), which is a significantly longer distance than patients who have cardiopulmonary disorders (7,8). Although the 6MWT is widely used, limited information is available to guide the interpretation of 6-minute walk distances (6MWDs) across patient populations with complex chronic cardiopulmonary, metabolic, and renal conditions. Improving our understanding of how different disease phenotypes relate to 6MWD is

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Conflicts of Interest and Source of Funding: None

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important for determining how to interpret physical functional ability.

The clinical relevance of the 6MWT has been established across both healthy individuals and those with a chronic condition. A short 6MWD correlates with cardiopulmonary and renal disease severity and is a significant predictor of mortality in patients with chronic diseases. For example, a 6MWD of 258 ± 81 m (mean ± standard deviation [SD]) was an independent predictor of death in patients with chronic heart failure (HF), even after controlling for covariates (7). In chronic kidney disease (CKD) patients receiving hemodialysis, survival increased ~5% for every 100 m walked during the 6MWT (9). The minimally clinically important difference for the 6MWD for patients with chronic conditions is approximately 30 m overall (10–14). For adults with chronic obstructive pulmonary disease (COPD) or HF, a 6MWD < 350 m is considered indicative of poor functional capacity with an increased risk for mortality (7,15–17).

Authors of few studies have compared 6MWDs among chronic conditions, and therefore, limited knowledge exists about how common covariates (e.g., age, sex, and body mass index [BMI]) differentially affect the 6MWD in these populations (4,18–25). Comparing 6MWDs among patients with different chronic conditions, while controlling for common health-related covariates, is important for understanding how 6MWT findings can be interpreted in different populations to estimate functional status and prognosis. The purposes of this study were to examine the 6MWD in persons with chronic cardiopulmonary [COPD, HF, peripheral arterial disease (PAD)], metabolic [type 2 diabetes (T2DM)], and renal disease (CKD), compare the walk distance with healthy controls, and identify predictors of the walk distance. We hypothesized that patients with HF, COPD, and PAD would have the shortest 6MWDs.

METHODS

We aggregated 6MWD data from published (26–30) and unpublished studies conducted by each of the present study's coauthors. Across the study protocols, stable community-dwelling older adults with primary diagnoses of T2DM, CKD, COPD, PAD, and HF, and healthy controls were recruited. All subjects could walk independently. All walk tests were conducted following the guidelines set by the American Thoracic Society and used a 100-foot corridor (2). We used SPSS 22.0 (SPSS Inc, IBM, NY, USA) for all statistical analyses. Before data analysis, we checked for missing data, normal distribution, and outliers. We removed 2 cases because of their young age.

Descriptive statistics (mean ± SD or percentage) were calculated to examine patient characteristics by group (T2DM, CKD, COPD, PAD, and HF). We also examined descriptive statistics for the combined condition group without controls and for those participants who walked <350 m. We ran univariate general linear models to determine the differences between healthy controls and each chronic condition group. We added interaction terms between diagnosis and each predictor to determine difference in the effect of predictors for each chronic condition. We included age, sex, race, and BMI as covariates. Before data analysis, we checked for missing data, normal distribution, and outliers. Outliers were assessed with boxplots. Regression diagnostics revealed a linear model with residuals that were normal and homoscedastic, and no multicollinearity appeared between predictors.

RESULTS

The sample included 429 adults (48% female) aged 63 ± 9 years who completed the 6MWT for studies led by each of the coauthors. The sample characteristics are presented in Tables 1 and 2.

Among those with chronic conditions, participants with HF (SE) = −219.3 (25.2); COPD (SE) = −97.2 (24.6), and PAD (SE) = −119.8 (35.2) had lower 6MWDs than healthy controls (all $P < 0.01$). The mean 6MWDs were not significantly different between controls and participants with T2DM (SE) = −18 (24.4) and CKD (SE) = −25.3 (25.2) (Figure 1).

In model 2, we included age, BMI, race, and sex as covariates in the analysis and interaction terms between each condition and the covariates. The same conditions (HF, COPD, and PAD) remained different from healthy controls, and all 4 covariates were significant. In the HF group, higher age, Black race, and male sex negatively affected 6MWD. In the T2DM group, higher age and higher BMI negatively affected 6MWD. In the CKD group, higher BMI, Black race, and male sex were negatively associated with 6MWD. None of the covariates were significantly associated with 6MWD in the PAD, COPD, or healthy control groups. Only the effect of sex was significantly different between groups. See Table 3.

DISCUSSION

In this novel study, we examined the impact of specific chronic conditions (T2DM, CKD, COPD, PAD, and HF) on the 6MWD. These findings are important, as we examined 6MWD across multiple common, chronic conditions, which has not been previously reported. We found wide variation in the 6MWD among the different conditions, and when compared with age-matched healthy controls, only participants with HF, COPD, and PAD had significantly lower 6MWDs. The 6MWDs among our participants with T2DM and CKD were like 6MWDs in healthy controls. We expected the HF, COPD, and PAD groups to have the shortest 6MWDs, as these patients are likely to experience activity-limiting symptoms such as dyspnea or claudication.

Common covariates, including sex, age, race, and BMI have been found to independently affect the 6MWD in both healthy subjects and patients with chronic conditions (4,6,18,19,21–25), and we report similar results. Sex, age, race, and BMI were associated with 6MWD when we included all patient groups in the model. However, when each group was assessed separately, the significant common factors differed by condition.

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TABLE 1. Chronic condition group characteristics.

Parameter	Group, N = 429						All Conditions (No Controls), n = 407	Patients With 6MWD < 350, n = 128
	Controls, n = 22	T2DM, n = 117	CKD, n = 82	PAD*, n = 15	COPD*, n = 108	HF*, n = 85		
Age, mean ± SD	60.9 ± 10.9	58.8 ± 8.6	69.1 ± 5.7	65.4 ± 7.4	65.4 ± 6.7	62.9 ± 11.4	63.7 ± 9.1	65.3 ± 8.7
BMI, mean ± SD	29 ± 6.3	33.4 ± 6.7	30.9 ± 7.2	27.1 ± 5.9	27.2 ± 4.5	33.3 ± 8.1	31.0 ± 7.1	32.5 ± 8.5
Female sex, No. (%)	11 (50)	64 (54.7)	38 (46.3)	3 (20)	36 (33.3)	44 (51.8)	185 (45.5)	60 (46.9)
Race or ethnicity, No. (%)								
White	12 (54.5)	32 (27.3)	48 (58.5)	6 (40)	102 (94.4)	13 (15.3)	195 (47.9)	44 (34.4)
Black	8 (36.4)	72 (61.5)	33 (40.2)	9 (60)	6 (5.6)	72 (84.7)	192 (47.2)	83 (64.8)
Asian	1 (4.5)	3 (2.6)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	0 (0.0)
Native American	0 (0.0)	3 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0 (0.0)
Missing	1 (4.5)	7 (6.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.7)	0 (0.0)
Latinx	1 (4.8)	14 (12)	6 (7.3)	0 (0)	0 (0)	7 (8.2)	27 (6.6)	8 (6.2)
6MWD (m), mean ± SD	494.6 ± 93.4	476.7 ± 104.3	469.3 ± 123.8	374.8 ± 63.9	397.4 ± 89.9	275.4 ± 112.9	408.4 ± 130.2	255.7 ± 73.6
6MWD < 350 m, No. (%)	1 (4.5)	13 (11.1)	14 (17.1)	5 (33.3)	32 (29.6)	63 (74.1)	127 (31.2)	

6MWD = six-minute walk distance; BMI = body mass index; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; HF = heart failure; PAD = peripheral artery disease; SD = standard deviation; T2DM = type 2 diabetes
*6MWD < than controls ($P < 0.01$)

TABLE 2. Chronic condition group severity markers.

Group and Marker	Value
Type 2 diabetes, mean ± SD, n = 117	
Hemoglobin A1c	7.7 ± 2.0
Chronic kidney disease stage, No. (%), n = 82	
2	2 (2.4)
3	67 (81.7)
4	12 (14.6)
5	1 (1.2)
Peripheral artery disease,* No. (%), n = 15	
Ankle-brachial index severity	
Mild	3 (20)
Moderate	8 (53.3)
Severe	4 (26.7)
Chronic obstructive pulmonary disease,* mean ± SD, n = 108	
Forced expiratory volumed at 1 s % adjusted	50.9 ± 17.9
Heart failure*, No. (%), n = 85	
New York Heart Association Class stage	
I	23 (27.1)
II	40 (47.1)
III	22 (25.9)

*6MWD < than controls ($P < 0.01$)

In our sample, we found male sex to be a predictor of lower 6MWD only in our HF and CKD groups. Sex was not associated with 6MWD in the other groups. Unlike our findings, most studies of 6MWD report that male sex is associated with longer 6MWD. Ferreira et al. (13) and Gravina et al. (31) reported that female sex predicted shorter 6MWD in patients with HF and CKD, respectively. Male sex has been associated with longer 6MWD among healthy adults (3,21), including reports from a study of healthy adults from 7 countries in which female sex and older age predicted short 6MWD (average female 6MWD = −571 ± 9 m compared with males) (4).

Younger age is consistently associated with longer 6MWD in healthy adults (3,21). Age was only a significant predictor of 6MWD in participants with T2DM and HF, with older age predicting shorter 6MWD in both groups. The youngest group, T2DM, had the longest 6MWD among all 5 groups. Although it is likely that older age is associated with disease progression and functional decline, we did not find a relationship between age and 6MWD in our oldest group, CKD. Younger age is associated with longer 6MWD in patients with CKD (31) and COPD (32), but we found no relationship between age and 6MWD in our CKD and COPD groups. This finding may be related to limited variability in age between the groups. It is likely age is also related to functional decline and disease severity; however, no common metric existed for disease severity among all chronic conditions. For reference, we calculated disease severity specific to each condition. We included hemoglobin A1c for

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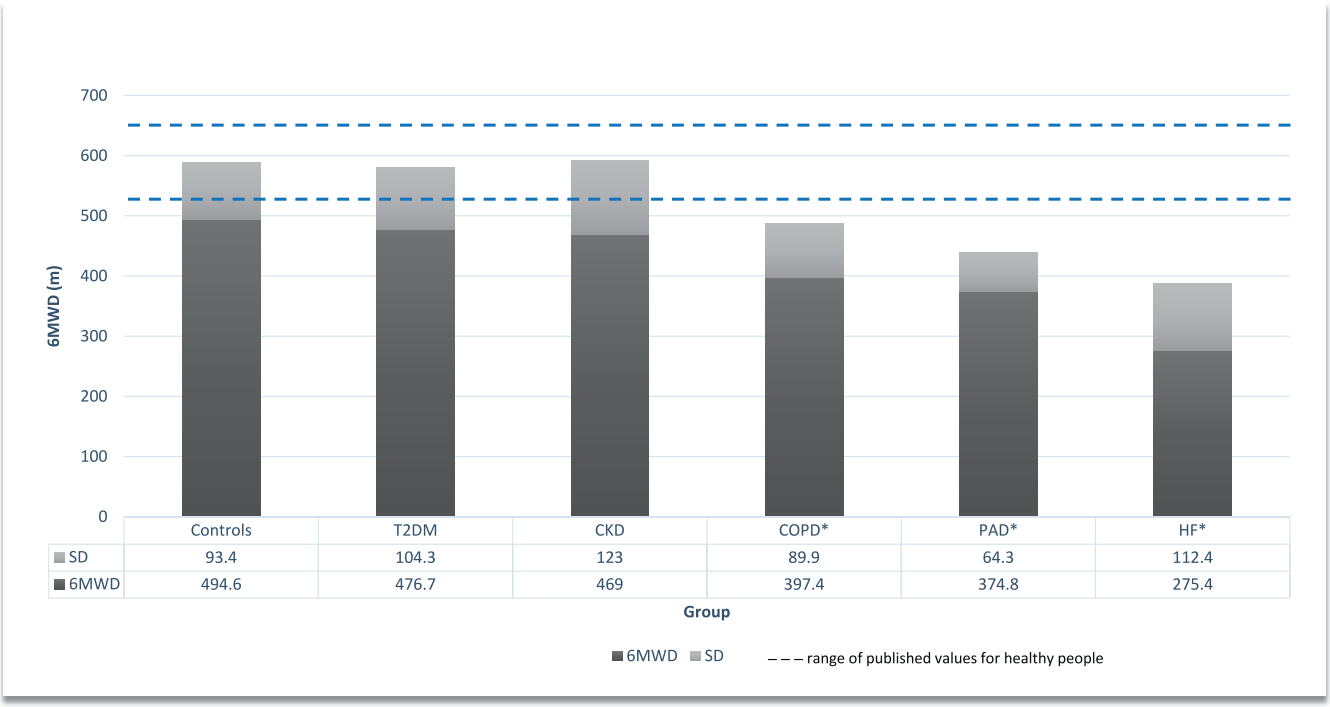

FIGURE 1. 6-minute walk distance by group.

T2DM, CKD stage for the CKD group, ankle-brachial index for the PAD group, adjusted forced expiratory volumed at 1 second (FEV1) for the COPD group, and New York Heart Association stage for the HF group (Table 2).

BMI was only a predictor of 6MWD in patients with T2DM and CKD. In both groups, the BMI was in the obese range. Hulens et al. (22) reported significantly reduced 6MWD in women with morbid obesity (BMI > 35 $kg{\cdot}m^{-2}$) compared with overweight or obese (BMI > 27.5 $kg{\cdot}m^{-2}$) women. Importantly, morbidly obese women reported a higher rating of perceived exertion, dyspnea, and musculoskeletal pain than leaner women (22). Pulmonary function was not measured in our participants with T2DM and CKD; however, reduced pulmonary function, even in the absence of pulmonary disease, may also contribute to shorter 6MWD in patients with T2DM (33–35). These factors may help to explain why BMI was a predictor of 6MWD in the T2DM and CKD groups.

None of the common covariates were associated with 6MWD among our participants with PAD. This is likely due to the small sample size of that group. Additionally, none of the covariates were associated with 6MWD among our participants with moderate to severe COPD who reported

TABLE 3. Effects of covariates on 6MWD by chronic condition (n = 419[a]).

Condition	Age	BMI	Black Race	Sex (Male)
	b (95% CI)	b (95% CI)	b (95% CI)	b (95% CI)
Control, n = 20	−2.2 (−6.9, 2.5)	−0.1 (−7.7, 7.5)	−77.5 (−174.1, 19.2)	−22.7 (−111.7, 66.2)
T2DM, n = 110	−4.1 (−6.1, −2)**	−4.4 (−7.6, −1.2)**	−32.4 (−70.7, 6.0)	30 (−8.5, 68.6)
CKD, n = 82	−2.2 (−6, 1.7)	−7.2 (−10.2, −4.2)**	−73.6 (−118, −29.2)**	−54.9 (−98.3, −11.5)*
PAD, n = 15	0.3 (−8.8, 9.3)	−3 (−11.9, 5.9)	−12.6 (−157.4, 132.1)	7.4 (−135.5, 150.2)
COPD, n = 108	−2.4 (−5.1, 0.2)	−1.1 (−5.3, 3.1)	−58.5 (−137.8, 20.7)	0.2 (−39.6, 40.1)
HF, n = 84	−3.5 (−5.4, −1.5)**	−1.3 (−4, 1.4)	−55.5 (−113, 1.9)	75.3 (33.4, 117.2)**
Group differences				
F_5	0.505	3.958	2.199	0.417
P	0.837	0.054	0.772	0.002

6MWD = six-minute walk distance; b = Beta (unstandardized); BMI = body mass index; CI = confidence interval; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; HF = heart failure; PAD = peripheral artery disease; T2DM = type 2 diabetes
*$P < 0.05$, **$P < 0.01$ for effect of covariate on 6MWD
[a]Participants missing any covariates were not included in the model

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moderate levels of dyspnea and fatigue. Our results differ from a recent study by Sánchez-Martínez et al. (8), who examined COPD disease-specific variables in their models. They reported that low 6MWD in participants with COPD was associated with those who had greater smoking pack-years, dyspnea ≥2 on the modified British Medical Research Council scale, a lower percentage of FEV1, and a higher number of hospitalizations for exacerbations (8). Importantly, Sánchez-Martínez et al. (8) also showed that 2 non-pulmonary factors were independent predictors of poor 6MWD performance: lower scores on the 5-repetition sit-to-stand test score and the percentage of mobility activities with limitations. The findings by Sánchez-Martínez et al. (8) suggest that predictive models for 6MWD should include disease-specific variables but also factors potentially responsive to interventions such as physical therapy. Studies such as these could provide understanding leading to effective interventions to reduce prevalence of poor 6MWD.

Limitations

Several limitations to our study exist. In addition to the primary diagnosis, it is likely the patients in each disease group suffered from multiple comorbidities that could affect 6MWD as well as disease-specific clinical factors such as deconditioning or muscle weakness, dyspnea, pain, or disease severity that likely affected the 6MWD. As a number of these factors were not measured in the entire sample, we were unable to determine the amount of variance these symptoms might have explained in our models. We collected only those variables that were both common to and measured in all groups. In future studies, it would be important to include symptom and clinical variables not usually associated with each disease. It may be especially useful to include measures of pain and dyspnea in all patient populations, as each of our chronic conditions is associated with poor cardiometabolic health. In addition, the PAD sample cohort was small and may not be representative of the patient population.

CONCLUSION

In conclusion, we found wide variation in the 6MWD and significantly lower 6MWDs in participants with HF, COPD, and PAD when compared with age-matched healthy controls. The 6MWDs among our participants with T2DM and CKD were like 6MWDs in healthy controls. Given that the 6MWT can be easily administered in a clinic or nonacute setting, it continues to be an effective method for evaluating functional capacity in patients with chronic conditions. Our findings highlight the importance of interpreting the 6MWD and its predictors in the context of chronic diseases.

Acknowledgments: Funding for this study was provided by the University of Illinois at Chicago, UIC Nursing Dean's fund and members of the Cardiometabolic Research Interest Group.

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