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Early Declines in Physical Function among Aging Adults with Type 2 Diabetes

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Abstract

Aims—Type 2 (T2DM) diabetes is associated with reduced physical function and early disability. We hypothesized that changes in physical function occur early and differ by age. Our aims were to determine and compare differences in and predictors of physical function in older and younger adults with T2DM.

Methods—Eighty adults completed six-minute walk distance (6MWD) tests, wore wrist actigraphy for 5 days and completed diabetes health and symptom surveys. Comparative and bivariate analyses were completed to assess differences between age groups determined by serial Box's M-plot analyses.

Results—6MWD was low (476.9 ± 106.2 m), and negatively associated with female gender, age, neuropathic pain, diabetes duration, BMI, poor sleep quality, and fatigue and positively with habitual activity and education ($p < 0.05$). Covariance matrices changed at age 59. In subjects age < 58 , 6MWD was predicted by gender, sleep quality, and neuropathic pain ($R^2 0.593$, $p < 0.001$). In those age ≥ 59 , 6MWD was predicted by diabetes duration, education, and habitual activity ($R^2 0.554$, $p < 0.001$). There were no shared predictors of 6MWD between groups.

Conclusions—T2DM is associated with early declines in physical function; the predictors of which change in mid-life. Therapies to maintain or improve physical function should be tailored by age, pain symptoms, and habitual activity levels.

Keywords

Six-minute walk distance; Physical Function Testing; Physical Activity; Diabetes Complications

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1. Introduction

Type 2 diabetes (T2DM) affects over 29 million people in the United States and 422 million worldwide, and is significantly associated with aging. The prevalence of T2DM is expected to increase significantly as the United States faces an unprecedented number of adults aged 65 years or older. The Centers for Disease Control and Prevention (CDC) reports that, by 2050, the number of U.S. adults aged 65 years or older will number 89 million, doubling the number of older adults in 2010. Increasing age and diabetes are significant independent predictors of disability and loss of independence (Bardenheier et al., 2015; Centers for Disease Control and Prevention, 2013; de Rekeneire & Volpato, 2015; Dhamoon, Moon, Paik, Sacco, & Elkind, 2014; Ferrucci et al., 2000; Gregg et al., 2000; Palmer, Espino, Dergance, Becho, & Markides, 2012; Wong et al., 2013; Wong et al., 2016; Wray, Ofstedal, Langa, & Blaum, 2005). Poor physical function is thought to be the major link between diabetes and disability. Type 2 diabetes (T2DM) is strongly associated with reduced physical function assessed via physical performance tests, including the six-minute walk test distance (6MWD), the short physical performance battery (SPPB), the timed up and go test, and gait analyses (Roman de Mettelinge, Cambier, Calders, Van Den Noortgate, & Delbaere, 2013; Sayer et al., 2005; Strotmeyer et al., 2008; Wu et al., 2003). Poor muscle quality and decreased strength may explain part of the reduced physical function seen in diabetes (de Rekeneire & Volpato, 2015; IJzerman et al., 2012; Kalyani, Metter, Egan, Golden, & Ferrucci, 2015; Kalyani et al., 2013; Park et al., 2006; Sayer et al., 2005; Volpato et al., 2012).

Declining physical function among older adults with T2DM have also been associated with glucose control (Kalyani et al., 2015), diabetic peripheral neuropathy (Strotmeyer et al., 2008), obesity (Wong et al., 2016), and participating in < 30 minutes/day of moderate physical activity (Palmer et al., 2012). Declines in physical function likely begin at an earlier age in adults with diabetes than their non-diabetic counterparts; however, most studies of changes in physical function are in patients over age 65, and few addressed predictors of poor physical function in younger, midlife adults with T2DM. Of the few studies that included midlife adults, Bardenheier (Bardenheier et al., 2015) reported that from age 50, adults with diabetes developed disability 6–7 years earlier, and spent about 1–2 more years in a disabled state, than adults without diabetes, but that study did not assess specific variables associated with this decline (Bardenheier et al., 2015). Latiri reported that decreased 6MWD in adults over 40 years with T2DM was associated with female gender, obesity, and leisure time physical activity (Latiri et al., 2012).

There is a gap in our knowledge of when changes in physical function begin and if predictors of physical function status remain stable across the adult lifespan in those with T2DM, limiting our ability to develop effective therapies to be initiated at an optimal time to reduce disability and loss of independence. We hypothesize that changes in physical function occur early and that predictors of physical function differ by age. Thus, the aim of this study was to determine physical function differences in older and younger adults with T2DM and when these changes occur. Additionally, we compared differences in predictors of physical function in the older and younger cohort.

2. Subjects

Subjects were recruited in a large Midwestern city in the United States through flyer distribution and internet-based bulletin boards and a large Veteran's Affairs Hospital, between September of 2012 and December of 2013. Subjects were considered eligible if they were aged 45 years or older, with a history of type 2 diabetes for ≥ 6 months. Subjects were excluded if they were unable to ambulate without assistance or had type 1 diabetes.

3. Materials and Methods

All study methods were approved by the Institutional Review Boards of the participating institutions. Upon written, informed consent, subjects completed three visits over 6 days. Health and demographic information collected included anthropometric measurements (height, weight, and waist circumference), and glucose control [A1C (A1CNow+™ Bayer Healthcare, Sunnyvale, CA)].

Physical function was measured using the six-minute walk test (6MWT) (Guyatt et al., 1985) a common field test shown to be reliable, valid, and safe in adults (including elderly adults) with a variety of medical conditions, including diabetes (Alfonso-Rosa, Del Pozo-Cruz, Del Pozo-Cruz, Sanudo, & Rogers, 2014; Dunbar et al., 2015; Ekman, Klintonberg, Bjorck, Norstrom, & Ridderstrale, 2013; Enright, 2003; Enright et al., 2003; Mangeri, Montesi, Forlani, Dalle Grave, & Marchesini, 2014; Pariser, Ann Demeuro, Gillette, & Stephen, 2010). The 6MWT has been shown to reflect the capacity for usual daily activities (Zeballos & Weisman, 2002) and walking ability (Ekman et al., 2013). Subjects completed the 6MWT according to established guidelines (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002; Enright, 2003; Enright et al., 2003). Because participant performance of the 6MWT is highly responsive to motivation (Guyatt et al., 1984), testing instructions, coaching, and time of testing were all standardized and distractions were minimized to decrease measurement error from outside influences.

Subjects wore a wrist accelerometer (Actiwatch-Score® Philips Respironics, Bend, OR) for measurement of objective habitual physical activity and objective sleep quality. The Actiwatch has been found to be acceptable for assessing sleep quality (e.g., sleep efficiency, wake after sleep onset [WASO], total sleep time), total movement volume, and patterns of activity during waking hours in aging women (Lambiase, Gabriel, Chang, Kuller, & Matthews, 2014). Data were collected continuously over six consecutive days. The device was sensitive to motion in all directions and was worn on the nondominant wrist of the participant. Epochs were recorded in 30-second intervals per the device specifications and then compressed into 1-minute epochs for determination of activity counts/minute. Non-wear time was identified as any bout of consecutive activity counts of 0 per minute lasting 90 minutes that was not classified as Sleep/Rest time by the software. Data were considered valid if wear time was ≥ 600 min/day.

Diabetes-related neuropathic pain was measured using the Diabetes Symptom Checklist-Revised (DSC-R) (Grootenhuis, Snoek, Heine, & Bouter, 1994), a 34-item tool that measures the occurrence and perceived burden of physical and psychological symptoms

related to T2DM and its complications. The questionnaire has been found to be reliable in adults with both T1DM and T2DM (Naegeli, Stump, & Hayes, 2010).

Fatigue symptoms were assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS), computerized adaptive testing (CAT) version for Fatigue (Fatigue CAT). Both reliability and validity of PROMIS were demonstrated in a representative sample ($n \sim 21,000$) of the U.S. population, which included adults with diabetes. In those reporting diabetes with a comorbid condition (versus those without), scores were all significantly worse for pain behavior and interference, fatigue, anger, anxiety, depression, physical function, and social role satisfaction (Rothrock et al., 2010). The fatigue item bank evaluates a range of self-reported symptoms, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Fatigue CAT assesses fatigue over the past seven days. Within the PROMIS framework, fatigue is considered a measure of both physical health and mental health (Carle, Riley, Hays, & Cella, 2015).

3.1. Data Management and Statistical Analyses

Statistical analyses were conducted using SPSS 21 (Chicago, IL). Descriptive data analyses (i.e., independent t test, Mann-Whitney U test) were conducted to present sample characteristics of participants. Correlation analyses were performed for uncovering the strongest predictors of physical function (6MWD). A series of Box's M tests were used to assess for significant changes in covariance structure by age. Subjects were then divided into groups by age (≤ 58 vs. > 59 years). Linear regression analyses were performed by age group to determine strengths and differences in predictors between groups.

Accelerometer data were compared with daily diaries of self-reported sleep, wake, and non-wear times. Data were excluded for diary self-reported non-wear time. Sleep time was not included in the analyses (Fritschi et al., 2016).

4. Results

A total of 144 individuals inquired about the study. Of the 144 inquiries, 139 individuals were screened for eligibility, and 135 met the inclusion criteria. Of those, 25 refused to participate due to travelling distance, requirements of the study, or amount of reimbursement. Additionally, three participants did not show up for their study visits, and 27 were excluded due to missing or incomplete data.

Eighty subjects completed the study (age 58.0 ± 8.2 years, 70% non-White, duration of diabetes 8.8 ± 7.2 years). They were generally obese (BMI 33.6 ± 6.8 kg/m²) and inactive, accumulating only 5.8 ± 9.3 minutes of moderate activity per day as measured by the Actiwatch (Fritschi et al., 2016). There is little consensus regarding choice of activity count thresholds for determination of light, moderate, or vigorous intensity activity; however, a threshold of ≥ 200 AC/min is considered to be indicative of physical inactivity or sedentary behavior (Lopes et al., 2009).

The average 6MWD was 471.9 ± 108.8 meters (Table 1). Most (70%) used metformin to control their glucose levels, while 35% used insulin alone or in combination with other glucose-lowering agents. Diabetes-related health complications were common; 30% reported a history of depression, 68% hypertension, 16% some form of retinopathy, 30% foot problems, and 26% obstructive sleep apnea (but only 58% of those with sleep apnea were using treatment).

Among the entire sample, bivariate analyses of factors related to physical function as measured by 6MWD showed significant associations (all $p < 0.05$) with female gender ($r = -0.301$), age ($r = -0.273$), neuropathic pain symptoms ($r = -0.250$), years since diabetes diagnosis ($r = -0.218$), habitual physical activity during waking hours (avg. AC/min [$r = 0.317$]), BMI ($r = -0.293$), years of education ($r = 0.340$), sleep quality (WASO, $r = -0.302$), and fatigue ($r = -0.255$). Glucose control was not associated with 6MWD (data not shown).

A series of exploratory Box's M tests were run to test for differences in the covariance matrices across ages. We found that from age 55 through 58, the covariance matrices began to change significantly, but these differences were no longer significant after age 58. Thus, we divided groups using 59 years as our cutoff criterion. Compared to subjects aged 59 years, the younger group (age 58 years) had longer 6MWD (502.9 vs 439.6 meters), shorter duration of diabetes (6.8 vs. 10.6 years), and higher A1C (8.2 vs. 7.2%; all $p < 0.05$). There were no other significant differences (Table 1).

We ran a second set of bivariate analyses with the sample divided by age (age 58 vs. age 59). Covariance matrices between groups differed in the key predictors of 6MWD. Among those aged < 58 years, female gender ($r = -0.470$), neuropathic pain ($r = -0.491$), BMI ($r = -0.529$), years of education ($r = 0.343$), and sleep quality indicators (average sleep efficiency [$r = 0.319$], WASO [$r = -0.351$]) were significant predictors of 6MWD (all $p < 0.05$). In contrast, among the older group (age 59 years), years since diabetes diagnosed ($r = -0.481$), habitual physical activity ($r = 0.507$), fatigue ($r = -0.370$), and years of education ($r = 0.410$) were significant predictors of 6MWD (all $p < 0.05$). Only years of education was significant in both groups (Tables 2 and 3).

We then performed a series of linear regression models by group and included all significant predictors from the correlation analyses. The regression models significantly predicted 6MWD in both groups. In the younger group (age 58), only gender and neuropathic pain symptoms explained $> 50\%$ of the variance in 6MWD ($F = 9.4$, $R^2 = 0.605$, adjusted $R^2 = 0.540$, $p < 0.001$). Years of education, sleep quality (sleep efficiency, WASO) and BMI did not retain significance in the model. In the older group (age 59), years of education, habitual physical activity, and years since diabetes diagnosis significantly predicted 6MWD ($F = 8.717$, $R^2 = 0.555$, adjusted $R^2 = 0.491$, $p < 0.001$). Only fatigue symptoms lost significance in the model.

We performed a final set of regression analyses, using only those predictors with a significance level of $p < 0.1$. The final model for the age 58 years included gender, WASO, and neuropathic pain symptoms. The model was significant at $p < 0.001$ and each variable retained its significance at $p < 0.05$. Together, the variables accounted for over 50% of the

variance in 6MWD (R^2 0.593, adjusted R^2 0.563, $F = 19.4$, $p < 0.001$). In the older group (age ≥ 59 years), the years since diabetes diagnosis, years of education, and objectively measured habitual physical activity remained significant (all $p < 0.01$) and accounted for over 50% of the variance in 6MWD (R^2 0.554, adjusted R^2 0.508, $F = 12.03$, $p < 0.001$; Tables 4 and 5). There were no shared predictors of 6MWD between adults aged ≥ 58 and ≥ 59 years with T2DM.

5. Discussion

The primary finding in this study was that physical function as measured by the 6MWD was significantly reduced in all subjects compared to nondiabetic people, with an average distance of 476.9 ± 106.2 m, which correlates to an estimated peak VO_2 of 15.92 ml/kg/min (Ross, Murthy, Wollak, & Jackson, 2010). These scores are significantly lower than population norms when age- and sex-matched (Casanova et al., 2011). The functional impairment was even more striking in the group ≥ 59 years of age suggesting that declines in physical function may start in mid-life rather than an older age. We were further able to identify a variety of health and demographic factors that predicted 6MWD, but these were significantly different between age groups ≥ 58 and ≥ 59 years, suggesting that sometime during midlife, strategies for maintaining physical function will need to change. The diabetes health and sociodemographic factors associated with 6MWD were not stable across midlife years. Years of education was the only significant predictor of 6MWD in both groups. In the later regression analyses, education only remained significant in the older group. The reason for this remains unknown, but it is plausible that higher education, including college experience, offers opportunities and experiences to engage in more activity or use a gym. It is also possible that educated adults are more likely to have higher-wage jobs that would enable them to join fitness facilities or live in safe, walkable neighborhoods. They may also have participated in more health-promoting activities throughout the years. Neuropathic pain symptoms, sleep quality (WASO), and gender accounted for $> 50\%$ of the variance in 6MWD among the younger group, while in the older group, years of education, duration of diabetes, and objectively measured habitual physical activity were the only factors significantly and positively related to 6MWD.

The 6MWD scores in our subjects were similar to those from a trial of muscle strength, mobility, and quality of life in T2DM adults with and without diabetic peripheral neuropathy (DPN) (Ijzerman et al., 2012). Ijzerman reported that adults with T2DM with and without DPN had poorer muscle strength than matched healthy controls, and this was linked to poorer physical performance in the 6MWT (Ijzerman et al., 2012). The authors reported no differences in muscle strength or 6MWD between patients with and without DPN; however, both measures were significantly lower than matched non-DM controls. We found that symptoms of DPN were strongly predictive of 6MWD, but only in the younger group.

Ijzerman also reported lower quality of life scores, including vitality, in patients with diabetes (Ijzerman et al., 2012). The present study did not measure muscle strength, but the 6MWDs lower than the population norm suggest a reduction in overall fitness levels.

Several possible reasons have been suggested for the lower physical function status in adults with T2DM. Kalyani found that aging adults with diabetes had reduced quadriceps strength and power and that this was related to slower walking speeds (Kalyani et al., 2013). Data from the Health, Aging, and Body Composition study revealed that T2DM was associated with excessive loss of muscle mass, especially in women. CT scans revealed rapid loss of thigh muscle mass was related to T2DM, and significantly lower in women (Park et al., 2009). Earlier findings from the same cohort revealed that muscle strength in aging adults with diabetes was lower than matched controls and was related to poor glycemic control and duration of diabetes (Park et al., 2006). While we did not measure muscle strength directly, we found that glucose control was not associated with physical function (6MWD) in either group, and duration of diabetes only predicted 6MWD in the older group. These findings indicate that patients with T2DM age < 59 who have neuropathic pain, low levels of education, and sleep problems may experience an accelerated loss of physical function and that particular attention should be directed towards these patients to reduce declines in physical function and limit loss of independence.

5.1. Limitations

This was a cross-sectional study with a small sample, which does not allow for generalization, nor temporal associations. We did not measure aerobic capacity, but we did find differences between the groups in 6MWD, which has been associated with peak oxygen consumption (Ross et al., 2010). Participants were in fairly good blood glucose control, which may have contributed to the lack of association between glucose control and physical function.

5.2. Summary and Conclusion

Our findings suggest that individuals with diabetes experience early declines in physical function and the predictors of those declines change in mid-life. This supports previous studies indicating the importance of physical activity and exercise in maintaining or improving physical function in aging adults, and offers evidence for initiating therapies earlier to address the potential decline in physical function early in midlife in patients with diabetes. Therapies to maintain or improve physical function may need to be tailored based on age, pain symptoms, and habitual physical activity level.

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Highlights

- Little is known of predictors of physical function in aging adults with T2DM, and if those predictors change across age.
- In 80 adults with type 2 DM (age 45–81) many biobehavioral factors predicted physical function (6-minute walk distance), but differed significantly those equal to or under age 58, or equal to or older than age 59.
- Female gender, poor sleep quality, and neuropathic pain predicted lower 6MWD in participants age 58.
- Years of education, habitual physical activity, and years since diabetes diagnosis predicted 6MWD in those aged 59 years.
- This is the first paper to demonstrate how different factors significantly predict physical function status among different age groups in T2DM.

Table 1

Health characteristics and demographics

	Total Group (<i>n</i> = 80) <i>n</i> (% or SD)	Age 58 Years (<i>n</i> = 47) <i>n</i> (% or SD)	Age 59 Years (<i>n</i> = 33) <i>n</i> (% or SD)	Significance
Gender (% male)	53 (53%)	21 (44.7%)	17 (51.5%)	$\chi^2 = .363$, 0.651
Race				
Caucasian	24 (30%)	10 (41.7%)	14 (58.3%)	
Black	46 (57.5%)	31 (67.4%)	15 (32.6%)	
Other	10 (12.5%)	6 (12.8%)	3 (9%)	
Hispanic Ethnicity	9 (11.3%)	6 (66.7%)	3 (33.3%)	$\chi^2 = .363$, 0. NS
Currently Employed	40 (50%)	31 (79.5%)	8 (20.5%)	$\chi^2 = .14.15$, 0.001
Veteran status	12 (15%)	1 (8.3%)	11 (33.3%)	$\chi^2 = .15.37$, <0.001
Current Smoker	19 (23.8%)	13 (28.3)	4 (12.1%)	$\chi^2 = 3.88$, NS
Age (years)	58.0 (8.2)	52.5 (4.2)	66.0 (5.7)	<0.001
Diabetes duration (years)	8.8 (7.2)	6.8 (5.9)	10.6 (7.9)*	0.058
A1C (%)	7.6 (2.1)	8.2 (2.3)	7.2 (1.5)	0.030
A1C (mmol/mol)	60 (23)	66 (25.1)	55 1(6.4)	0.30
Diabetes Medications				
Insulin (Any)	25 (31.8%)	17 (36.1%)	8 (24.2%)	$\chi^2 = 1.54$, NS
Sulfonylureas	16 (20%0	9 (19.1%)	7 (21.2%)	$\chi^2 = .052$, NS
Glucophage	60 (75%)	35 (74.5%)	25 (75.8%)	$\chi^2 = .139$, NS
BMI	33.6 (6.8)	33.9 (7.7)	33.2 (5.4)	0.649
Education (years of school)	14.5 (2.8)	14.4 (2.9)	14.7 (2.6)	0.680
Activity-related Factors				
6 Minute Walk Distance (meters)	471.9 (108.8)	502.9 (89.1)	439.6 (118.2)	0.021
Habitual Physical Activity (Average activity counts/minute)	309.1 (99.8)	322.2 (96.6)	290.4 (102.7)	0.162
Self-reported Symptoms				
#x02003;Fatigue	51.0 (8.6)	51.5 (8.7)	50.3 (8.6)	0.560
#x02003;Neuropathic Pain Symptoms	0.90 (1.2)	1.1 (1.3)	0.64(1.0)	0.118
Self-reported Cardiovascular Health				
Hypertension	57 (71.3%)	29 (61.7%)	28 (84.8%)	$\chi^2 = .027$, <.05
Coronary Artery Disease	11 (13.8%)	5 (10.6%)	6 (18.2%)	$\chi^2 = 1.045$, NS

Table 2

Bivariate correlations in subjects 58 Years ($n = 47$)

	6MWD (meters)	Female Gender	Neuropathic Pain Symptoms	Habitual Physical Activity	Fatigue	Years of Education	Years since DM Diagnosis	Body Mass Index
Female gender	-.470**							
Neuropathic pain symptoms	-.491**	.251						
Habitual physical activity	.080	-.055	-.061					
Fatigue (PROMIS)	-.204	.204	.338**	-.213				
Years of education	.343*	-.191	-.396**	-.217	-.038			
Years since DM diagnosis	.204	-.258	.302*	.012	-.049	-.152		
Body Mass Index	-.529**	.429**	.483**	-.133	.397**	-.287	-.091	
Wake after sleep onset (mins)	-.351*	.244	.040	.088	.168	-.299*	-.243	-.020
Sleep efficiency (%)	.319*	-.237	-.142	.191	-.138	.147	.283	-.246

* $p < .05$,** $p < .001$

Table 3

Bivariate correlations in subjects 59 years ($n = 33$)

	6MWD (meters)	Female Gender	Neuropathic Pain Symptoms	Habitual Physical Activity	Fatigue	Years of Education	Years since DM Diagnosis	Body Mass Index
Female Gender	-.187							
Neuropathic Pain Symptoms	-.068	-.078						
Habitual Physical Activity	.507**	-.070	.302					
Fatigue (PROMIS)	-.374*	.277	.267	-.365*				
Years of Education	.410*	.080	-.524**	.031	-.357*			
Years since DM diagnosis	-.481**	.189	-.021	-.303	.190	.067		
Body Mass Index	-.030	.175	.094	-.220	.157	-.091	-.196	
Wake after sleep onset (mins)	-.210	.037	.178	-.190	.178	-.267	-.000	.374*
Average Sleep Efficiency	-.028	.063	-.089	.070	-.083	.086	.008	-.447**

* $p < .05$,** $p < .01$.

Table 4Final linear regression model predicting six-minute walk distances in subjects 58 years old ($n = 47$)

Characteristic	B	SE	t	p
Female gender	−64.274	19.26	−3.34	0.002
Average wake after sleep onset	−.521	0.223	−2.34	0.025
Neuropathic pain symptoms	−32.98	7.01	−4.70	0.000

$F = 19.434$, $p < 0.001$. $R^2 = 0.593$, adjusted $R^2 = 0.563$

Table 5Final linear regression model predicting six-minute walk distances in subjects 59 years old ($n = 33$)

Characteristic	B	SE	t	p
Years of education	20.29	5.93	.755	0.002
Habitual physical activity	-0.542	0.200	-2.714	0.009
Years since diabetes diagnosis	-31.697	6.742	-4.701	< 0.001

 $F = 12.030$, $p < 0.001$. $R^2 = 0.554$, adjusted $R^2 = 0.508$.