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Early declines in physical function among aging adults with type 2 diabetes

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ABSTRACT

Aims: Type 2 diabetes (T2DM) 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 midlife. Therapies to maintain or improve physical function should be tailored by age, pain symptoms, and habitual activity levels.

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, Lin, Zhuo, et al., 2015; Centers for Disease Control and Prevention, 2013; de Rekeneire & Volpato, 2015; Dhamoon, Moon, Paik, Sacco, & Elkind, 2014; Ferrucci, Penninx, Leveille, et al., 2000; Gregg, Beckles, Williamson, et al., 2000; Palmer, Espino, Dergance, Becho, & Markides, 2012; Wong, Backholer, Gearon, et al., 2013; Wong, Woodward, Stevenson, 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 (de Roman, Cambier, Calders, Van Den Noortgate, & Delbaere, 2013; Sayer, Dennison, Syddall, et al., 2005; Strotmeyer, de Rekeneire, Schwartz, et al., 2008; Wu, Haan, Liang, 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, Schaper, Melai, et al., 2012; Kalyani, Metter, Egan, Golden, & Ferrucci, 2015; Kalyani, Tra, Yeh, et al., 2013; Park, Goodpaster, Strotmeyer, et al., 2006; Sayer et al., 2005; Volpato, Bianchi, Lauretani, et al., 2012).

Declining physical function among older adults with T2DM has 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 min/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

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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, Elbey, Hcini, 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, Sullivan, Thompson, 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, Reilly, Gary, et al., 2015; Ekman, Klintenberg, Bjorck, Norstrom, & Ridderstrale, 2013; Enright, 2003; Enright, McBurnie, Bittner, et al., 2003; Mangeri, Montesi, Forlani, Dalle Grave, & Marchesini, 2014; Pariser, Ann Demeuro, Gillette, & Stephen, 2010). The 6MWD 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, Pugsley, Sullivan, 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/min. Non-wear time was identified as any bout of consecutive activity counts of 0 per minute lasting ≥90 min 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) and computerized adaptive testing (CAT) version for Fatigue (Fatigue CAT). Both reliability and validity of PROMIS were demonstrated in a representative sample (n ~ 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, Hays, Spritzer, 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, Park, Richardson, 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 traveling 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/m^2) and inactive, accumulating only 5.8 ± 9.3 min 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

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