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Quadriceps Strength, Quadriceps Power, and Gait Speed in Older U.S. Adults with Diabetes: Results from the National Health and Nutrition Examination Survey (NHANES), 1999–2002

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Abstract

Objectives—To examine the independent association of diabetes (and its duration and severity) with quadriceps strength, quadriceps power, and gait speed in a national population of older adults.

Design—Cross-sectional nationally representative survey.

Setting—U.S.

Participants—We examined 2573 adults ≥50 years of age in the National Health and Nutrition Examination Survey 1999–2002 who had assessment of quadriceps strength.

Methods—Diabetes was ascertained by questionnaire. Measurement of isokinetic knee extensors (quadriceps) strength was performed at 60 degrees/second. Gait speed was assessed using a 20-foot walk test. Multiple linear regression analyses were used to assess the association between diabetes status and outcomes, adjusting for potential confounders or mediators.

Results—Among older U.S. adults, those with versus without diabetes had significantly slower gait speed (0.96±0.02 versus 1.08±0.01 m/s; p<0.001). After adjusting for demographics, weight, and height, diabetes was also associated with significantly lower quadriceps strength (−4.6±1.9 Newton-meters; p=0.02), quadriceps power (−4.9±2.0 Watts; p=0.02), in addition to gait speed (−0.05±0.02 m/s; p=0.002). Associations remained significant after adjusting for physical activity and C-reactive protein. After accounting for comorbidities (cardiovascular disease, peripheral neuropathy, amputation, cancer, arthritis, fracture, COPD), diabetes was only independently

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associated with gait speed (−0.04±0.02 m/s; p=0.02). Diabetes duration in men and women was negatively associated with age-adjusted quadriceps strength (−5.7 and −3.5 Newton-meters/decade of diabetes, respectively) and power (−6.1 and −3.8 Watts/decade of diabetes, respectively) (all p ≤0.001, no significant interactions by gender). Hemoglobin A1c was not associated with outcomes accounting for body weight.

Conclusion—Compared to persons without diabetes, older U.S. adults with diabetes have lower quadriceps strength and quadriceps power that is related to the presence of comorbidities. Persons with diabetes also walk slower. Future studies should investigate the relationship of hyperglycemia with subsequent declines in leg muscle function.

Keywords

Type 2 diabetes mellitus; muscle loss; physical function; gait

INTRODUCTION

Loss of muscle strength is an important predictor of physical function and disability (1), and represents a significant public health burden associated with early mortality and increased expenditures (2–3). We have previously demonstrated that diabetes is associated with excess physical disability in older adults, especially in lower extremity mobility tasks (4). However, the relationship of diabetes to loss of muscle strength has not been fully characterized, yet has considerable implications on future strategies to preserve physical function in older persons. Previous studies of older adults have demonstrated accelerated declines in leg muscle strength among persons with diabetes, but these studies were limited to a single cohort (5–6). Further, it remains unknown whether increasing severity and/or duration of hyperglycemia is associated with proportionally greater impact on muscle strength.

Age-related reduction in lower extremity strength is associated with lower gait speed in the general population (7), and may be related to gait alterations in patients with diabetes (8). Impaired muscle performance potentially mediates the association of diabetes with lower gait speed in older adults (9). Interestingly, severe hyperglycemia and insulin resistance may also be associated with lower walking speed (10–11).

Nonetheless, whether associations of diabetes (and its duration and severity) with reduced muscle strength and gait speed are seen in a nationally representative population has not been previously explored. Although observational studies suggest protective benefits of insulin sensitizers on leg muscle mass (12), similar benefits on leg muscle strength and gait speed are unclear. The hypotheses for the present study are: 1) diabetes is independently associated with lower quadriceps strength, quadriceps power, and gait speed; 2) these associations may differ by diabetes treatment; and 3) greater hyperglycemia (i.e., diabetes duration or hemoglobin A1c) is associated with proportional greater impact on muscle outcomes in a nationally representative population of U.S. adults aged 50 years and older.

METHODS

Study Design and Population

The National Health and Nutrition Examination Survey (NHANES) uses a stratified multistage probability design to provide nationally representative estimates of the U.S. civilian non-institutionalized population (4). The present study was based on NHANES survey data from 1999–2002.

Of 4,983 potential participants aged ≥50 years screened, 4,449 participants attended the examination. For subject safety reasons (e.g., right knee pain), 550 participants were not tested which left 3899 eligible participants. 859 participants had missing data for various reasons (e.g. equipment or data capture failure). Participants with onset diabetes<25 years (more likely type 1 diabetes) were excluded (n=26). Those with a peak force velocity deviating>5 degrees/second from the goal were also excluded (n=441). Thus, our study consisted of 2,573 adults who met inclusion criteria.

The 1,326 persons eligible for testing but excluded were more likely to be 70+ years (45.9% versus 28.9%) non-Hispanic black (14.1% versus 8.8%), and female (66.8% versus 53.9%) compared to persons in our study. Consequently, the data were reweighted to adjust for these differences (see below).

Assessment of Diabetes

Participants self-reported a physician diagnosis of diabetes and age of onset. Diabetes duration was considered as 0.5 years if diagnosed within the past year.

Diabetes treatment in the past month was ascertained by asking participants and verified using the container or having participants name the drug. Treatment subgroups included: no medications, orals alone (sulfonylureas, metformin, thiazolidenediones, alpha-glucosidase inhibitors, or meglitidines), or any insulin therapy (monotherapy or combination).

Measurement of Isokinetic Quadriceps Strength and Habitual Gait Speed

A Kin Com MP isokinetic dynamometer (Chattanooga, TN) was used to assess maximum voluntary concentric muscle force of the right knee extensor (quadriceps) muscle with a goal angular velocity of 60 degrees/second (1.05 rads/second) (7, 13). Peak quadriceps strength (torque) in Newton-meters (Nm) was calculated as [PF (Newton) * mechanical arm length (cm)/100]. The mechanical arm length represented the distance from ankle to knee joint. Gravity corrections were performed (14). Peak power in Watts was calculated as [peak quadriceps strength (Newton-meter) * peak force velocity (degrees/second) * π/180] (15).

Habitual gait speed was measured using a 20-foot (6.15 meters) timed walk test. The use of a walker or cane was permitted.

Measurement of Covariates

Demographics and smoking was ascertained from the questionnaire. Height and weight were measured. Participants were asked if they did “any physical activities specifically designed to strengthen his/her muscles such as lifting weights, push-ups or sit-ups” over the past 30 days. High sensitivity C-reactive protein (CRP) was measured using Behring Nephelometer (16).

History of comorbidities including arthritis, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), and cancer (excluding non-melanoma skin cancer), and hip fracture was self-reported (4). Peripheral arterial disease (PAD) using ankle-brachial index and peripheral neuropathy using monofilament testing were defined as previously (4). Leg amputations were documented.

Hemoglobin A1c (HbA1c) measurements were performed using Primus CLC330/CLC 385 (4).

Statistical Analyses

All analyses were performed using SAS software (version 9.3, SAS Institute Inc, Cary, NC) and incorporated population-based sampling weights to obtain unbiased, nationally representative estimates from the complex NHANES sampling design (14). The NOMCAR (Not Missing Completely at Random) option accounted for variability of subjects with missing data (17). To address potential nonrandom nonresponse, revised sampling weights were created (18). Respondent sample persons were classified into 32 subgroups defined by age (50–59, 60–69, 70–79, ≥80), sex (male, female), and race/ethnicity (black, white, Mexican American and other) to calculate an adjustment factor, assuming data was missing at random within each subgroup (19).

All analyses used revised sampling weights. The Wald test compared differences in baseline characteristics by diabetes status. Linear regression models were created to assess the association of diabetes with outcomes: Model 1 adjusted for demographic factors (age, gender, race/ethnicity, education, smoking history)+weight+height; Model 2 adjusted for model 1+physical activity+CRP; Model 3 adjusted for model 2+comorbidities (self-reported CVD, PAD, arthritis, hip fracture, leg amputation, cancer, COPD, peripheral neuropathy). Regression analyses compared diabetes to no diabetes groups, and also diabetes-medication subgroups to non-diabetes.

Effect modification by gender and age strata (50–69 years, ≥70 years) was explored. However, no significant interactions were noted by age or gender for regression analyses ($p>0.05$), thus, pooled estimates are displayed.

To explore the relationship of increasing diabetes duration and severity with outcomes among persons with diabetes, weighted estimates adjusted for age and/or weight were plotted in a scatterplot (y-axis) against self-reported diabetes duration or HbA1c (x-axis) for each individual. A line was fitted and the slope was derived for men and women.

In sensitivity analysis, we excluded participants with the largest duration of diabetes (≥40 years) where data was relatively sparse.

Data are shown as mean ±standard error (SE) unless indicated.

RESULTS

As shown in Table 1, U.S. adults with diabetes were significantly older, heavier, more likely to be non-white and less likely to engage in muscle-strengthening physical activities compared to those without diabetes. Participants with versus without diabetes had significantly slower gait speed (0.96±0.02 versus 1.08±0.01 m/s; $p<0.001$) and non-significantly lower quadriceps strength (111.9±3.7 versus 114.4±0.9 Newton-meters; $p=0.52$) and quadriceps power (118.5±3.9 versus 121.2±1.0 Watts; $p=0.51$).

Though no significant crude differences in quadriceps strength or power were observed overall by diabetes status (Table 2), after accounting for demographics, weight, and height, diabetes was associated with significantly lower quadriceps strength (−4.6±1.0 Nm, $p=0.02$), lower quadriceps power (−4.9± 2.0 Watts, $p=0.02$), and reduced gait speed (−0.05±0.02 m/s, $p=0.002$) in linear regression analyses (Table 2, Model 1). Positive confounding was due primarily to differences in body weight, suggesting that at the same body weight, persons with versus without diabetes tend to have lower muscle strength. Further adjustment for physical activity and CRP minimally affected associations (Model 2). In fully adjusted models (Model 3), adjustment for comorbidities attenuated the association between diabetes and quadriceps strength (−3.2±1.9 Nm, $p=0.10$) and quadriceps power (−3.5±2.0 Watts,

p=0.09) such that they were no longer independently associated. However, though the reduction in effect (~20%) for gait speed was similar, diabetes remained independently associated with reduced gait speed in fully adjusted models (−0.037±0.02 m/s, p=0.02).

Participants with diabetes were then divided into treatment subgroups: no medications for diabetes (n=52), orals alone (n=199), or any insulin (n=68). In fully adjusted models, only insulin-users had significantly lower quadriceps strength (Table 2, Model 3; −7.7±3.3 Nm, p=0.026) and quadriceps power (−8.2±3.5 Watts, p=0.028) while oral users did not differ significantly compared to those without diabetes. However, oral alone users had reduced gait speed (Table 2, Model 3; −0.04±0.02 m/s) as did insulin users (−0.05±0.03 m/s) compared to those without diabetes but only the former group had significant differences (p=0.03 and p=0.14, respectively).

Perhaps, not surprisingly, insulin users had longer duration and higher HbA1c compared to other participants with diabetes. However, limiting analyses to those with diabetes, fully adjusted models demonstrated no differences in quadriceps strength, power or gait speed comparing each diabetes medication subgroup to those not on medications.

In men with diabetes (n=180), each year of reported diabetes was associated with reduced age-adjusted quadriceps strength of 0.57±0.17 Nm/year and power of 0.61±0.18 Watts/year (both p=0.001; Figures 1A, 1C), but not age-adjusted gait speed (0.001±0.001 m/s per year, p=0.30; Figure 1E). In women with diabetes (n=138), each year of reported diabetes was associated with reduced age-adjusted quadriceps strength of 0.35±0.09 Nm/year and power of 0.38±0.10 Watts/year (both p<0.001; Figures 1B, 1D), but not age-adjusted gait speed (0.001±0.001m/s per year, p=0.12; Figure 1F). The interaction by gender was not significant for any outcome (all p>0.05).

Persons with diabetes aged 50–69 years had more dramatic findings for age-adjusted quadriceps strength (−1.4±0.1 Nm/year) and power (−1.5±0.1 Watts/year) compared to those aged 70+ years (−0.13±0.05 Nm/year and −0.14±0.05 Watts/year, respectively). Age-adjusted gait speed was significantly reduced −0.002±0.001 m/s (p=0.01) per year of reported diabetes in those aged 50–69 years, but not aged 70+ years. Also, no significant linear association between HbA1c level and any of the outcomes were found after adjusting for body weight in either pooled or stratified analyses.

In sensitivity analysis, after excluding four participants with diabetes duration ≥40 years, the observed associations remained unchanged.

DISCUSSION

In the present study, diabetes was related to lower quadriceps strength and power after accounting for demographics and anthropometry. However, in fully adjusted models, diabetes was independently associated only with reduced gait speed, though insulin users had significantly reduced quadriceps strength and power even after accounting for comorbidities compared to those without diabetes. Among older persons with diabetes, progressively longer diabetes duration was significantly and negatively associated with age-adjusted quadriceps muscle strength and power, especially in those 50–69 years, but no associations were found between HbA1c levels and quadriceps muscle function.

Our results are similar to studies reporting decreased leg muscle strength in cross-sectional studies of older adults with diabetes (6). However, dissimilar from our findings, associations with muscle quality were independent of comorbidities. The discrepancy could be due to our inclusion of peripheral neuropathy but results were unchanged when we excluded neuropathy in fully adjusted models [data not shown]. Recently, Volpato *et al.* (2012) (9),

described significantly decreased knee extension torque using a handheld dynamometer in Italian adults with diabetes using any hypoglycemic agent. We further report decreased quadriceps strength using an isokinetic dynamometer, which has less variability compared to hand-held instruments (20), among U.S. adults with diabetes. We found most dramatic reductions in quadriceps strength among insulin-users but relatively preserved strength in oral alone users compared to those without diabetes, a novel finding. We could not distinguish whether these were medication-specific effects or reflected underlying disease characteristics. Differences between diabetes treatment subgroups were not significant, but the generalizability of this finding may be limited by statistical power.

To our knowledge, we are the first to report a progressive loss of age-adjusted quadriceps strength by up to 6 Newton-meter per decade in men and women with diabetes which is smaller but comparable to age-related declines (21). Our findings add to the study by Park, *et al.* (2006) (6) reporting that leg muscle quality is lowest in older adults (mean age~74 years) with a categorical diabetes duration ≥6 years. Interestingly, we did not observe a relationship between HbA1c levels and muscle strength as reported for muscle quality (6). This may be due to the distinction between muscle strength versus quality, with the latter accounting for muscle mass.

Our findings of reduced gait speed associated with diabetes in older U.S. adults are consistent with previous reports of slower walking speed in type 2 diabetes cohorts (8–9). However, in comparison to quadriceps strength, we found that duration of diabetes was not associated with gait speed. Other types of alterations in gait have been described in adults with diabetes, such as less efficient gait pattern (8), and were not measured in NHANES.

Potential underlying pathways include the presence of a pro-inflammatory state with insulin resistance which could reduce muscle strength (22–23); lack of participation in resistance exercises (24), or peripheral neuropathy (25). We found that associations of diabetes with lower quadriceps strength and power were not independent of comorbidities. In a future study, we hope to explore the degree to which the effect of diabetes on leg muscle strength may be mediated in part by differences in leg muscle mass (9).

Further, the association of hyperglycemia or insulin resistance with the loss of quadriceps strength has been reported even in persons without diabetes (26). Older adults with type 2 diabetes have ~50% more rapid decline in knee extensor strength than those without diabetes over three years (5) suggesting that decreased muscle strength may be a consequence of type 2 diabetes. In support of these observations, we found that diabetes duration in years was associated with a striking, progressive linear decline in quadriceps strength and power, especially in adults 50–69 years of age.

In exploratory analysis, we found that orals alone users had relatively preserved quadriceps strength compared to those without diabetes, similar to previous studies of leg muscle mass (12). Preclinical studies suggest potential benefits of the peripheral insulin sensitizer pioglitazone on improving mitochondrial function in skeletal muscle (27) which may ultimately help preserve muscle function but further studies are needed. We had limited power to separate users of peripheral insulin sensitizers or thiazolidenediones (~10% of persons with diabetes).

Strengths of our study include the rigorous data collection procedures in NHANES. We also computed adjusted sample weights to account for potential nonrandom non response present in our study and generate nationally representative estimates for the U.S. population. By examining both strength and power, we were able to obtain a more comprehensive characterization of leg muscle function in diabetes. We could investigate linear associations of diabetes duration with quadriceps strength and power given the wide range of self-

reported diabetes durations present in our participants, who were relatively younger than in previous studies (6).

Limitations to our study include the cross-sectional design, which does not allow us to infer temporality. Self-report of diabetes may have misclassified some participants with undiagnosed diabetes, who likely have intermediate muscle strength, resulting in lower mean strength reported for diabetes and no diabetes groups. Although screening for peripheral neuropathy with monofilament is useful clinically (28), nerve conduction velocities are more sensitive, and may have led to residual confounding (25). Further, our study examined a single muscle—quadriceps—but it has well-validated measurement methods and is related to mobility, functional status, and mortality (1–2). Arm strength between persons with versus without diabetes may not differ as greatly (5). Additionally, NHANES did not include measures of muscle quality, as might be ascertained through imaging the thigh muscle. We used gait speed as an objective lower extremity measure, which is linked to early mortality (29), but other measures such as chair stands were not collected. Lastly, NHANES does not include institutionalized elderly individuals, who may have lower muscle strength and gait speed than reported.

The implications of our study reporting that the presence of comorbidities is related to the lower quadriceps strength and power observed in diabetes, manifesting clinically as reduced gait speed, is that accelerated muscle loss may be related to the increased risk of adverse outcomes described in diabetes such as disability and early mortality (1–2, 30). Longitudinal studies are needed to establish directionality of relationships. Further, the role of hyperglycemia and insulin resistance in these associations needs to be better characterized in order to determine the degree to which glucose-lowering treatments and/or insulin sensitizers may offer an opportunity to preserve muscle function. Ultimately, a better understanding of accelerated muscle loss as a complication of diabetes may reduce the burden of disability in this population and impact the clinical care of older individuals.

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Sponsor's Role one.

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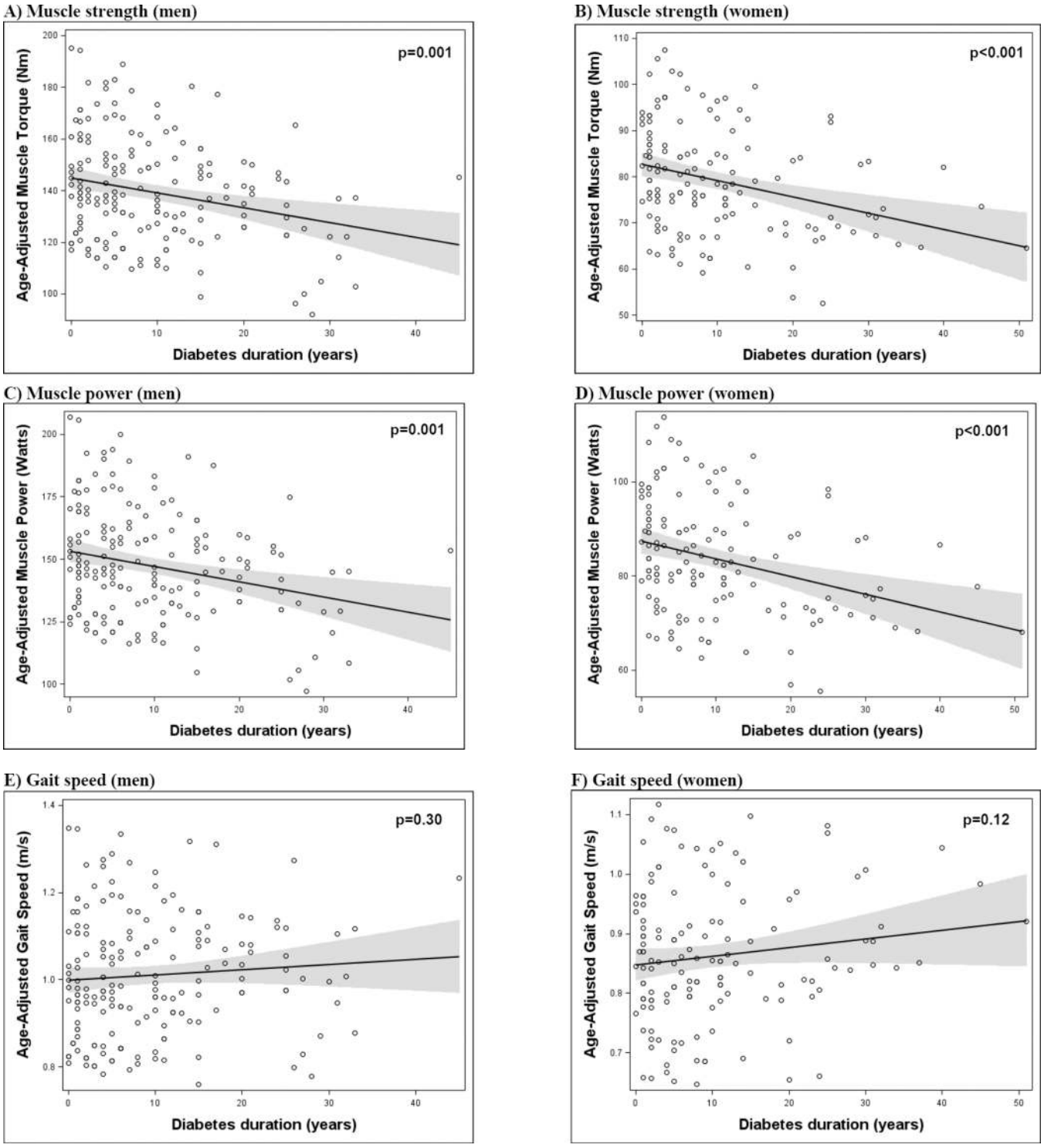

Figure 1. Association of diabetes duration with age-adjusted quadriceps muscle strength and power and gait speed in older U.S. adults

The association of self-reported diabetes duration (years) with age-adjusted quadriceps strength, quadriceps power, and gait speed in a nationally representative population of older U.S. men (Figures 1A, 1C, 1E; n=180) and women (Figures 1B, 1D, 1F; n=138) is plotted for each participant with diabetes and represented by an open circle. A fitted regression line

is shown in each figure with 95% confidence intervals represented as grey shading around the line. The negative association of years living with diabetes and age-adjusted quadriceps strength ($p \leq 0.001$) and quadriceps power ($p \leq 0.001$) are significant for both men and women.

Table 1

Characteristics of older U.S. adults by diabetes status, NHANES 1999–2002*

	All (n=2573)	Diabetes (n= 321)	No Diabetes (n = 2252)	p-value**
Demographics				
Age group				0.002
50–59 years	43.6 ± 1.2	29.9 ± 3.4	45.0 ± 1.3	
60–69 years	27.5 ± 1.3	37.5 ± 3.0	26.4 ± 1.3	
70–79 years	19.5 ± 0.8	22.4 ± 2.9	19.2 ± 0.9	
80+ years	9.4 ± 0.7	10.2 ± 2.2	9.4 ± 0.7	
Mean age (years)	63.3 ± 0.3	65.2 ± 0.7	63.1 ± 0.3	0.003
Race				<0.001
Black	8.8 ± 1.2	16.9 ± 3.4	7.9 ± 1.1	
White	78.3 ± 2.0	62.7 ± 4.5	80.0 ± 1.9	
Mexican American	3.6 ± 0.7	6.1 ± 1.5	3.3 ± 0.6	
Other	9.3 ± 1.9	14.3 ± 3.9	8.8 ± 1.7	
Gender				0.06
Male	46.1 ± 0.9	52.0 ± 3.1	45.5 ± 1.0	
Female	53.9 ± 0.9	48.0 ± 3.1	54.5 ± 1.0	
Education				<0.001
Less than high school	24.6 ± 1.6	35.6 ± 3.2	23.4 ± 1.8	
High school	25.3 ± 1.4	26.5 ± 3.6	25.2 ± 1.5	
Greater than high school	50.1 ± 1.8	37.9 ± 3.5	51.4 ± 1.9	
Lifestyle behaviors				
Smoking				0.53
Current	16.3 ± 0.9	16.4 ± 2.6	16.3 ± 0.9	
Former	38.5 ± 1.3	42.4 ± 3.8	38.1 ± 1.4	
Never	45.2 ± 1.2	41.2 ± 5.0	45.6 ± 1.2	
Muscle strengthening activities	18.2 ± 1.6	8.1 ± 1.9	19.8 ± 1.7	<0.001
Clinical history				
Arthritis	38.5 ± 1.4	48.6 ± 3.7	37.5 ± 1.5	0.006
Hip fracture	0.9 ± 0.2	1.8 ± 0.7	0.8 ± 0.2	0.08
Cancer	10.2 ± 0.7	11.3 ± 2.5	10.1 ± 0.7	0.60
COPD	8.2 ± 0.8	10.2 ± 2.2	8.0 ± 0.8	0.21
Coronary heart disease	11.1 ± 0.8	19.9 ± 3.0	10.2 ± 0.7	<0.001
Stroke	0.6 ± 0.2	2.3 ± 1.3	0.5 ± 0.2	0.01
Congestive heart failure	3.1 ± 0.4	5.2 ± 1.5	2.9 ± 0.4	0.04
Physical examination and laboratory				
Mean weight (kg)	79.0 ± 0.5	84.9 ± 1.5	78.4 ± 0.5	0.001
Mean height (cm)	167.1± 0.2	166.4 ± 0.7	167.1 ± 0.2	0.35
Mean BMI (kg/m^2)	28.2 ± 0.2	30.5 ± 0.4	28.0 ± 0.2	<0.001
Peripheral neuropathy	9.0 ± 0.7	14.3 ± 2.4	8.5 ± 0.7	0.004
Peripheral arterial disease	18.5 ± 1.0	32.0 ± 3.9	17.1 ± 0.9	<0.001

	All (n=2573)	Diabetes (n= 321)	No Diabetes (n = 2252)	p-value**
Leg amputation	3.0 ± 0.4	6.1 ± 1.7	2.7 ± 0.4	0.01
Mean CRP level (mg/dl)	0.46 ± 0.02	0.50 ± 0.04	0.45 ± 0.02	0.19

*Data are shown as % ± SEM unless otherwise indicated.

**Comparing Diabetes to No Diabetes groups.

Table 2

Linear regression models for the association of diabetes status with quadriceps muscle strength, quadriceps muscle power and gait speed in a nationally representative population of older U.S. adults[§]

	No Diabetes	Diabetes			
		All	No medications	Orals only	Any insulin
Muscle strength (Nm)					
Crude	Reference	−2.48 ± 3.8	−15.0 ± 7.2	3.7 ± 5.2	−7.8 ± 5.9
Model 1[‡]	Reference	−4.59 ± 1.92	−7.2 ± 5.2	−2.8 ± 2.5	−8.9 ± 3.7
Model 2[‡]	Reference	−4.57 ± 1.93	−7.5 ± 4.9	−1.5 ± 2.5	−10.7 ± 3.7[†]
Model 3[‡]	Reference	−3.2 ± 1.9	−6.4 ± 5.1	−0.7 ± 2.5	−7.7 ± 3.3
Muscle power (Watts)					
Crude	Reference	−2.68 ± 4.0	−16.3 ± 7.5	4.0 ± 5.5	−8.3 ± 6.3
Model 1[‡]	Reference	−4.94 ± 2.0	−8.0 ± 5.5	−3.0 ± 2.6	−9.4 ± 4.0
Model 2[‡]	Reference	−4.95 ± 2.0	−8.3 ± 5.2	−1.6 ± 2.7	−11.4 ± 3.9[†]
Model 3[‡]	Reference	−3.5 ± 2.0	−7.2 ± 5.3	−0.7 ± 2.6	−8.2 ± 3.5
Gait speed (m/s)					
Crude	Reference	−0.12 ± 0.02[†]	−0.07 ± 0.05	−0.11 ± 0.02[†]	−0.18 ± 0.04[†]
Model 1[‡]	Reference	−0.052 ± 0.02[†]	−0.03 ± 0.04	−0.06 ± 0.02	−0.08 ± 0.03
Model 2[‡]	Reference	−0.048 ± 0.02[†]	−0.03 ± 0.04	−0.05 ± 0.02	−0.07 ± 0.04
Model 3[‡]	Reference	−0.037 ± 0.02	−0.02 ± 0.04	−0.04 ± 0.02	−0.05 ± 0.03

[§]Beta coefficients ± SE are shown.

[†]p<0.01 compared to no diabetes.

[‡]Model 1: demographics (age, race, education, gender, smoking) + weight + height. Model 2: Model 1 + physical activity + CRP. Model 3: Model 2 + comorbidities (self-reported CVD, PAD, arthritis, hip fracture, amputation, cancer, COPD, peripheral neuropathy)