Original Article

Decreased Muscle Strength and Quality in Older Adults With Type 2 Diabetes

The Health, Aging, and Body Composition Study

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Adequate skeletal muscle strength is essential for physical functioning and low muscle strength is a predictor of physical limitations. Older adults with diabetes have a two- to threefold increased risk of physical disability. However, muscle strength has never been investigated with regard to diabetes in a population-based study. We evaluated grip and knee extensor strength and muscle mass in 485 older adults with diabetes and 2,133 without diabetes in the Health, Aging, and Body Composition study. Older adults with diabetes had greater arm and leg muscle mass than those without diabetes because they were bigger in body size. Despite this, muscle strength was lower in men with diabetes and not higher in women with diabetes than corresponding counterparts. Muscle quality, defined as muscle strength per unit regional muscle mass, was significantly lower in men and women with diabetes than those without diabetes in both upper and lower extremities. Furthermore, longer duration of diabetes (≥ 6 years) and poor glycemic control (HbA$_{1c}$ >8.0%) were associated with even poorer muscle quality. In conclusion, diabetes is associated with lower skeletal muscle strength and quality. These characteristics may contribute to the development of physical disability in older adults with diabetes. _Diabetes_ 55:1813–1818, 2006

I n the U.S., people aged 65 years and older will make up most of the diabetic population in the next 25 years. Furthermore, the proportion of the diabetic population aged 75 years and older is projected to exceed 30% by 2050 (1,2). In older adults, diabetes has been associated with a two- to threefold increased risk of developing physical disability (3–6). Moreover, we have reported the association of diabetes with subclinical functional limitation in the Health, Aging, and Body Composition (Health ABC) study (7). However, the mechanism for impaired physical function in diabetes has been poorly understood. Chronic conditions frequently combined with diabetes, such as coronary heart disease, peripheral artery disease, visual impairment, and depression, partially explained the association, but still 40% of excess risk for physical disability remained unexplained (4,6).

Low muscle strength, but not muscle mass, is associated with poor physical function in older men and women (8,9). Muscle strength measured in midlife or old age is highly predictive of functional limitations and disability up to 25 years later (10–12). However, the effects of diabetes on muscle strength and quality have never been investigated in a population-based study. Because most individuals with diabetes are obese and have bigger muscle mass and increased total body fat mass, direct comparison of their muscle strength with those without diabetes may be misleading. With the advent of body composition analysis, we are now able to precisely measure regional muscle mass and quantitatively assess in vivo skeletal muscle quality defined as maximal voluntary contractile force or torque per unit regional muscle mass of the specific body compartment (13).

In the present study, we evaluated hand grip and knee extensor strength and muscle quality in community-dwelling older adults with and without diabetes in the Health, Aging, and Body Composition Study. To evaluate the cumulative effects of metabolic derangements of diabetes on skeletal muscle function, subjects with diabetes were further categorized by the duration of diabetes and the level of glycemic control.

RESEARCH DESIGN AND METHODS

The Health ABC study included 3,075 well-functioning older adults, of whom 51.6% were women and 41.6% were black. Whites were recruited from a random sample of Medicare beneficiaries residing in zip codes from the metropolitan areas surrounding Pittsburgh, Pennsylvania, and Memphis, Tennessee. Blacks were recruited from all age-eligibles in these geographic areas. Eligibility criteria included the following: aged 70–79 years in the recruitment period from March 1997 to July 1998; self-report of no difficulty walking one-quarter of a mile or climbing 10 steps without resting; no difficulty performing basic activities of daily living; no reported use of a cane, walker, crutches, or other special equipment to ambulate; no history of active treatment for cancer in the prior 3 years; and no plan to move out of the area in the next 3 years. All individuals gave informed consent for participation in the study, and the consent forms and study protocols were approved by the institutional review boards at each field center. Among 3,075 participants, 29

(0.9%) subjects who had missing fasting plasma glucose concentrations were excluded, and 6 subjects with the onset of diabetes before age 25 were considered to have type 1 diabetes and were excluded from the analyses. Among the remaining 3,040 participants, 389 subjects (12.8%) were excluded from the knee strength test because of uncontrolled hypertension, history of stroke or aneurysm in the brain, bilateral knee joint replacement, presence of severe bilateral knee pain, or refusal by the participant. Another 33 (1.1%) who had missed body composition assessment by dual-energy X-ray absorptiometry (DEXA) were also excluded. Finally, 2,618 participants (85.1% of original cohort), including 485 (18.5%) with type 2 diabetes and 2,133 without diabetes, who had completed muscle strength test and DEXA measurements of body composition, were included in the analyses.

Diabetes assessment. Participants were considered as to have type 2 diabetes if they had *1*) a report of diagnosis as diabetes with the onset after age 25 and/or *2*) current use of oral hypoglycemic medications or insulin or *3*) a fasting plasma glucose concentration ≥7.0 mmol/l (14). We used information on reported age at diagnosis to define diabetes duration; for participants with newly diagnosed diabetes, the duration of diabetes was considered as 0. The duration of diabetes ranged from 0 to 45 years with the median of 6.0 years. Plasma glucose was measured using an automated glucose oxidase reaction (Vitros 950 analyzer; Johnson & Johnson, Rochester, NY), and a glycosylated hemoglobin (HbA$_{1c}$ [A1C]) was measured in all participants by enzymatic method (Bio-Rad, Hercules, CA).

Body composition. Body weight and height were measured in a hospital gown and without shoes on a calibrated balance-beam scale and stadiometer, respectively, and a BMI in kg/m^2 was calculated. Lean masses of the upper and lower extremities as well as the total body were assessed using DEXA (Hologic QDR 4500 software version 8.21). Bone mineral content was subtracted from the total and regional lean mass to define total nonbone lean mass, which represents primarily skeletal muscle in the extremities (15). Total body fat mass and percent body fat were also measured.

Strength assessments. Strength was measured using an isokinetic dynamometer (125 AP; Kin-Com, Chattanooga, TN) for knee extension and isometric dynamometer (Jaymar; JLW Instruments, Chicago, IL) for grip strength. For knee extension, maximal voluntary concentric isokinetic torque was assessed in Newton meters at an angular velocity of 60°/s. At least three, but no more than six, maximal efforts were allowed to produce three overlying curves, and the mean maximal torque was recorded and used for the analysis. The right leg was used unless contraindicated by pain or history of joint replacement. Isometric grip strength was assessed for each hand. Participants with severe hand pain or recent surgery were excluded. The vast majority (96%) who had leg strength testing also had grip strength testing. For these analyses, we used the maximum of the force from two trials for the right upper extremity. A measure of muscle quality (leg-specific torque, Newton meters/kg; arm-specific force, kg/kg) was created by taking the ratio of strength to the entire corresponding leg or arm muscle mass in kilograms measured by DEXA (13).

Other covariates. Sociodemographic characteristics included age, sex, race, and education. Combined chronic health conditions were summarized as the comorbidity score, which was defined as the number of the following 10 prevalent conditions: coronary heart disease, congestive heart failure, cerebrovascular disease, peripheral artery disease, knee osteoarthritis, hypertension, depression, pulmonary disease, cancer, and osteoporosis. Each condition was identified by self-report and confirmed by treatment and medication use. Self-reported poor eyesight was considered as impaired vision. Renal insufficiency was defined by serum creatinine >1.5 mg/dl in men and >1.2 mg/dl in women (16). Health-related behaviors, which included current smoking, alcohol drinking, and physical activity, were also considered as potential confounders. Level of total physical activity (kcal/week) was determined using a standardized questionnaire designed specifically for the Health ABC study (17).

Statistical analysis. Differences in means and proportions of baseline characteristics and body composition by diabetes status were tested using Student's *t* tests and χ^2 tests. Differences in muscle strength and quality between subjects with and without diabetes were also assessed by independent *t* tests. There was a significant interaction between diabetes status and sex in relation to muscle strength ($P = 0.003$). Therefore, all of the following analyses were stratified by sex. Adjustments for potential confounders were performed using multiple regression models by cumulative addition of sociodemographic factors and physical activity (model 1); plus BMI (model 2); plus smoking, alcohol drinking, combined chronic health conditions, and diabetes-related complications (model 3). To test the effects of duration and severity of diabetes on muscle strength and quality, ANOVA tests for trend were used. When overall differences were significant with ANOVA, post hoc comparisons were performed with Bonferroni adjustment. A *P* value of <0.05 was accepted as statistically significant. All of the analyses were performed using SPSS software (version 12.0.0; SPSS, Chicago, IL).

RESULTS

Among 485 older adults with type 2 diabetes, 389 (80.2%) had previously known diabetes, whereas 96 (19.8%) were newly diagnosed by fasting plasma glucose criteria. Most diabetic subjects were treated with oral hypoglycemic medications (216, 44.5%) or insulin injections (99, 20.4%), whereas one-third (170, 33.7%), including newly diagnosed subjects, were taking no diabetes medications. Participants with diabetes were more likely to be black and less educated. Older men and women with diabetes had higher weight, BMI, total body fat, and total body lean mass than nondiabetic counterparts. As expected, diabetes-related complications, such as impaired vision and renal insufficiency were twice more prevalent in those with diabetes. Older adults with diabetes also had higher comorbidity scores compared with nondiabetic subjects. Those with diabetes reported less alcohol use and less physical activity (Table 1).

Table 2 presents arm and leg muscle strength, corresponding regional muscle mass, and muscle quality by diabetes status. In men, those with diabetes showed significantly lower muscle strength in both upper and lower extremities ($P < 0.05$, each), although their arm and leg regional muscle masses were significantly greater than those without diabetes ($P < 0.001$, each). In women, absolute arm and leg muscle strength were not significantly different in those with diabetes despite greater arm and leg regional muscle mass than those without diabetes. Muscle quality was consistently lower in both upper and lower extremities in both men and women with diabetes compared with nondiabetic counterparts (all $P < 0.001$; Table 2). There was no significant difference in the relationship of diabetes to muscle quality in blacks compared with whites (P for interaction = 0.31 and 0.70 in men and 0.17 and 0.76 in women for leg and arm muscle quality, respectively).

Lower muscle quality in men and women with diabetes was slightly attenuated after adjustment for race, age, clinic site, and physical activity (Table 3, model 1). However, adjustment for BMI attenuated the difference in muscle quality by 17–37% in men and by 49–69% in women (Table 3, model 2). Adjustment for total fat mass instead of BMI gave the same result (data not shown). Further adjustments for smoking, alcohol drinking, combined chronic diseases, impaired vision, and renal insufficiency virtually eliminate the effect of diabetes on muscle quality in women. But, in men, lower muscle quality associated with diabetes remained even in the fully adjusted model (Table 3, model 3).

Muscle quality was associated with diabetes duration in both upper and lower extremities in both men and women. Those with the longer duration of diabetes (≥6 years) showed the lowest muscle quality (Fig. 1). There was also a linear trend between the level of glycemic control and muscle quality. Diabetic subjects with poor glycemic control (A1C >8.0%) had the lowest muscle quality regardless of sex and muscle groups examined (Fig. 2).

DISCUSSION

In our study, older adults with type 2 diabetes had a greater muscle mass in their arms and legs than those without diabetes. But despite this larger muscle mass, those with diabetes were either weaker (men) or not stronger (women) than those without diabetes. This finding was somewhat surprising because the quantity of

TABLE 1
Characteristics of the study population by diabetes status, according to sex

	Men			Women		
	No diabetes ($n = 1,004$)	Diabetes ($n = 273$)	P value	No diabetes ($n = 1,129$)	Diabetes ($n = 212$)	P value
Age (years)	73.7 ± 2.9	73.8 ± 2.9	0.47	73.5 ± 2.8	73.2 ± 2.8	0.19
Black (%)	32.2	45.4	<0.01	40.3	68.9	<0.01
Education <12 years (%)	24.5	32.0	0.01	19.8	37.1	<0.01
Height (cm)	173.3 ± 6.5	173.5 ± 6.1	0.63	159.6 ± 6.2	159.6 ± 5.6	0.93
Weight (kg)	80.3 ± 12.6	85.3 ± 13.8	<0.01	69.2 ± 14.1	76.9 ± 14.1	<0.01
BMI (kg/m^2)	26.7 ± 3.8	28.3 ± 4.0	<0.01	27.1 ± 5.2	30.2 ± 5.4	<0.01
Total body fat (kg)	22.8 ± 6.9	24.9 ± 7.4	<0.01	27.9 ± 9.0	31.5 ± 9.2	<0.01
Total body lean (kg)	54.9 ± 7.0	57.5 ± 7.4	<0.01	39.5 ± 5.8	43.4 ± 5.8	<0.01
Fasting glucose (mmol/l)	5.3 ± 0.5	8.5 ± 2.9	<0.01	5.1 ± 0.5	8.4 ± 3.1	<0.01
A1C (%)	6.0 ± 0.5	7.8 ± 1.5	<0.01	6.0 ± 0.5	8.0 ± 1.6	<0.01
Impaired vision (%)	18.7	28.3	<0.01	17.6	27.5	<0.01
Renal insufficiency (%)	7.5	15.9	<0.01	8.0	14.4	<0.01
Comorbidity score*	1.25 ± 1.12	1.55 ± 1.18	<0.01	1.38 ± 1.14	1.78 ± 1.27	<0.01
Smoking (current, %)	10.7	9.5	0.59	9.5	9.9	0.85
Alcohol drinking (%)	60.6	46.2	<0.01	47.4	22.6	<0.01
Physical activity (kcal/week)	5,397	4,761	0.07	4,808	4,092	<0.01

Data are means ± SD or %, except physical activity (median). *Number of combined chronic diseases, including coronary heart disease, congestive heart failure, cerebrovascular disease, peripheral artery disease, knee osteoarthritis, hypertension, depression, pulmonary disease, cancer, and osteoporosis.

muscle mass had been known as a primary determinant of muscle strength (13,18–20). We have clearly demonstrated that muscle quality was consistently lower in older adults with type 2 diabetes, regardless of sex and muscle groups examined (arm or leg). This is a novel finding possibly explaining a pathophysiological mechanism for increased risk of functional limitations and disability in older adults with type 2 diabetes, because low muscle strength or poor muscular function is predictive of physical disability (8–12). Our finding is consistent with the study in patients with type 1 diabetes (21). We have also found that lower muscle quality in older adults with diabetes was largely attenuated by adjustment for BMI, indicating that obesity might have an important role in this association. We have previously reported that skeletal muscle attenuation coefficient determined by computerized tomography was lower with increasing BMI, and it was independently associated with muscle strength and quality (22). Low muscle attenuation was also found in older adults with impaired glucose tolerance or type 2 diabetes (23). Reduced muscle attenuation values have been associated with reduced oxidative enzyme activity (24) and lower maximal aerobic capacity (25). It is possible that alterations of muscle composition with increased fat infiltration into the skeletal muscle as evidenced by low muscle attenuation in type 2 diabetes, which is also associated

with combined obesity, may result in poor muscle quality. Further research will be needed to determine whether diabetes itself or the higher levels of body fat in the diabetes is a direct cause of poor muscle quality in a prospective study.

There had been no report on skeletal muscle strength or function in type 2 diabetes until Andersen et al. (26) reported muscle weakness at the ankle and knee in a case-control study. They showed a 7–17% lower muscle strength at the ankle and knee in patients with type 2 diabetes compared with control subjects. Although control subjects were matched for sex, age, weight, height, and physical activity, it was impossible to evaluate whether muscle weakness in subjects with type 2 diabetes was due to reduced muscle mass or poor muscle quality because muscle mass was not assessed in their study. In the present study, we measured arm and leg regional muscle mass separately by DEXA. The concurrent measures of muscle mass and strength allowed us to evaluate in vivo muscle quality, which was defined as muscle strength per unit muscle mass in kilograms. This definition has been consistently used to assess muscle function in human subjects (13,27,28). The specific force of arm and specific torque of leg represent the maximal contractile capacity of each appendicular skeletal muscle group adjusted for the quantity of muscle mass. Therefore, these

TABLE 2
Comparison of arm and leg muscle strength, regional muscle mass, and muscle quality by diabetes status, stratified by sex

	Men			Women		
	No diabetes ($n = 1,004$)	Diabetes ($n = 273$)	P value	No diabetes ($n = 1,129$)	Diabetes ($n = 212$)	P value
Leg strength (Nm)	133.0 ± 32.4	128.5 ± 34.6	0.046	81.1 ± 22.0	83.8 ± 21.4	0.096
Leg muscle mass (kg)	8.7 ± 1.3	9.1 ± 1.4	<0.001	6.3 ± 1.2	7.0 ± 1.2	<0.001
Leg muscle quality (Nm/kg)	15.3 ± 3.2	14.2 ± 3.3	<0.001	13.0 ± 3.1	12.1 ± 3.2	<0.001
Hand grip strength (kg)	40.0 ± 8.9	38.7 ± 8.8	0.037	24.3 ± 6.4	25.1 ± 5.9	0.098
Arm muscle mass (kg)	3.4 ± 0.6	3.6 ± 0.6	<0.001	2.1 ± 0.4	2.3 ± 0.4	<0.001
Arm muscle quality (kg/kg)	11.7 ± 2.4	10.8 ± 2.3	<0.001	12.0 ± 2.9	11.0 ± 2.9	<0.001

Data are means ± SD. Nm, Newton meters.

TABLE 3
Multiple regression models showing the effect of diabetes on arm and leg muscle quality, stratified by sex

	Men			Women		
	β for diabetes	SE	P value	β for diabetes	SE	P value
Arm muscle quality (kg/kg)						
Unadjusted	−0.89	0.16	<0.001	−1.05	0.22	<0.001
Model 1	−0.84	0.16	<0.001	−0.85	0.22	<0.001
Model 2	−0.53	0.16	0.001	−0.43	0.21	0.043
Model 3	−0.50	0.16	0.002	−0.34	0.22	0.111
Leg muscle quality (Nm/kg)						
Unadjusted	−1.10	0.22	<0.001	−0.87	0.24	<0.001
Model 1	−1.01	0.22	<0.001	−0.61	0.24	0.011
Model 2	−0.84	0.22	<0.001	−0.19	0.23	0.404
Model 3	−0.80	0.22	<0.001	−0.15	0.24	0.524

Adjustments of covariates were performed using multiple regression analyses by cumulatively adding the following covariates into the model. Model 1, race, age, clinic site, and physical activity; model 2, model 1 + BMI; model 3, model 2 + smoking, drinking, comorbidity score, impaired vision, and renal insufficiency. Nm, Newton meters.

measures of muscle quality are a more reasonable indicator of contractile function of skeletal muscle than crude muscle strength, which is largely dependent on the quantity of muscle mass. This concept might be important, particularly for the comparison of skeletal muscle function between subjects with different body sizes like those with and without diabetes.

The discrepancy between men and women in terms of differences in absolute muscle strength can be explained by the magnitude of differences in muscle mass between those with and without diabetes. Older men with diabetes had only slightly (~4–5%) higher appendicular muscle mass than those without diabetes (Table 2). This small difference in muscle mass may not be enough to overcome poor muscle quality of diabetes, resulting in lower muscle strength in men with diabetes. But women with diabetes had moderately (~12–14%) higher appendicular muscle mass than those without diabetes, which may be enough to compensate poor muscle quality and result in absolute muscle strength comparable with the nondiabetic women. However, despite having similar muscle strength, older women with diabetes showed poor physical function in our previous report using the same cohort (7), suggesting that their strength might be insufficient to carry their heavy weight.

Another important finding of this study is a linear relationship showing that both longer duration of diabetes and poor glycemic control are associated with much poorer muscle quality (Figs. 1 and 2). These findings are consistent with our previous observation that poor glycemic control in diabetic individuals explained the association with subclinical functional limitation (7). A metabolic consequence of uncontrolled hyperglycemia is catabolism, which depending on the severity, is accompanied by muscle protein breakdown and inadequate energy use, potentially resulting in poor muscle function. Diabetes with poor glycemic control is also associated with increased systemic inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, which have detrimental effects on muscle function (29–32).

Neuropathic processes involving motor neurons might be another possible underlying mechanism for the poor muscle function in diabetes. In the mouse model, after 4 weeks of diabetes, the relative loss of torque via nerve stimulation (~43%) was greater than the force loss in the directly stimulated muscle (~24%), indicating a functional neural deficit (33). Although it is unclear in humans, a greater and selective atrophy of type IIb fibers has been observed in diabetic animal muscles (34–36), which may contribute to strength loss. In humans, the presence and severity of diabetic neuropathy has been shown to be associated with decreased muscle strength in both type 1 and type 2 diabetes (26,37). Electrophysiological studies suggest that loss of muscle strength in diabetic patients is due to incomplete reinnervation after axonal loss (38).

The present study is the first epidemiological study to assess skeletal muscle function in subjects with and without type 2 diabetes in apparently healthy, community-
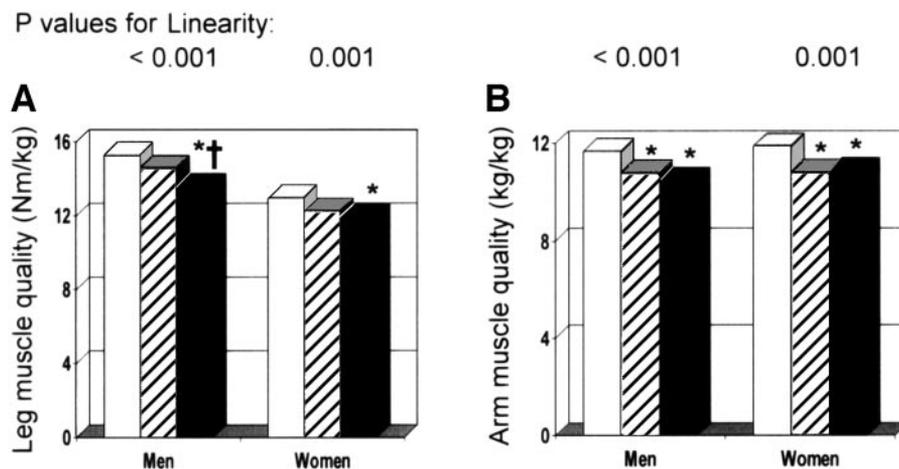
P values for Linearity:

FIG. 1. Leg (A) and arm (B) muscle quality in subjects without diabetes (□), diabetic subjects with duration <6 years (▨), and diabetic subjects with duration ≥6 years (■). *P < 0.05 compared with subjects without diabetes. †P < 0.05 compared with diabetic subjects with duration <6 years.
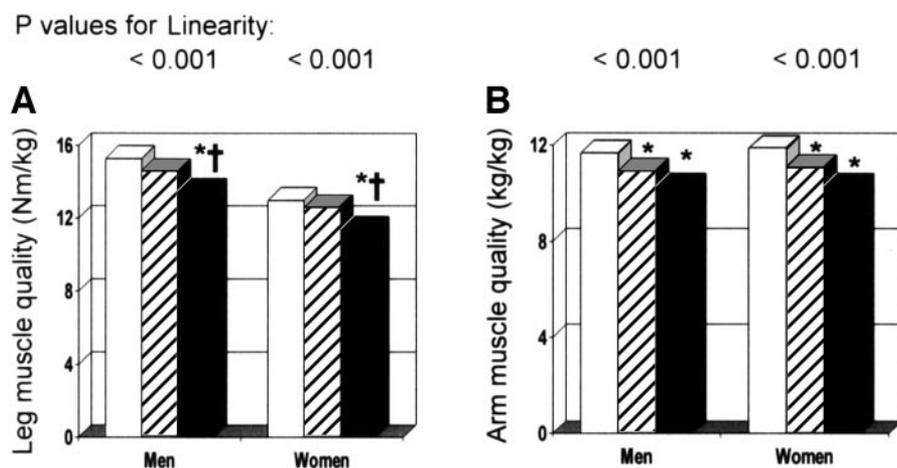
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FIG. 2. Leg (*A*) and arm (*B*) muscle quality in subjects without diabetes (□), diabetic subjects with A1C ≤8.0% (▨), and diabetic subjects with A1C >8.0% (■). *$P < 0.05$ compared with subjects without diabetes. †$P < 0.05$ compared with diabetic subjects with A1C ≤8.0%.

dwelling older adults. The population includes white and black older men and women with type 2 diabetes in various clinical stages. We found a significantly lower muscle quality in older adults with diabetes, although the difference is relatively small in magnitude. For the clinical implications, we have to consider that subjects with diabetes in this study were all well functioning without physical disability. The inclusion of asymptomatic subjects as diabetes group by fasting plasma glucose cut-point attenuated the difference in muscle quality (data not shown). In other words, older adults with diabetes seen in clinical setting might have even poorer muscle quality. It has been well established that lower muscle strength is an important contributor to disability (10–12). However, the clinical significance of poor muscle function in diabetes for the development of disability can only be answered by a prospective study.

This study has several limitations. First, this is a cross-sectional study showing only an association between type 2 diabetes and poor muscle function. It does not necessarily mean that type 2 diabetes in older adults results in poor muscle strength and quality. It is also possible that lower muscle quality is a causative factor related to the development of type 2 diabetes in older adults. However, even lower muscle quality in diabetic subjects with longer duration and poor glycemic control may suggest that poor muscle quality is likely a consequence rather than a cause of diabetes in older adults (Figs. 1 and 2). Second, we have no data on diabetic neuropathy at baseline, which may have an important mediating role in muscle weakness. Despite these limitations, this study might have important public health implications because older adults with diabetes are at increased risk of developing physical disability and potential preventive strategies are available, including resistive-training exercise program to improve skeletal muscle function in subjects with diabetes (39).

In conclusion, in community-dwelling older adults, type 2 diabetes is associated with lower skeletal muscle strength and quality. These characteristics may contribute to development of physical disability in older adults with diabetes. Prospective studies are needed to investigate whether type 2 diabetes in older adults is associated with longitudinal declines in muscle strength and to examine the relationship to the loss of muscle mass and muscle quality.

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