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Poor toe flexor strength, but not handgrip strength, is associated with the prevalence of diabetes mellitus in middle-aged males

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Abstract. Previous studies suggested that reduced muscular strength was one of the potential predictor of prevalence of diabetes mellitus. The purpose of this study was to investigate the association between toe flexor strength (TFS) and handgrip strength (HGS) and the prevalence of diabetes mellitus. Cross-sectional analysis was conducted using data from 1,390 Japanese males (35–59 years). TFS and HGS were measured and medical examinations undertaken. The prevalence of diabetes mellitus was defined as fasting blood glucose ≥126 mg/dL, glycated hemoglobin ≥6.5% (48 mmol/mol), and/or current use of anti-diabetes mellitus drugs. A total of 114 participants had diabetes mellitus. TFS in participants with diabetes mellitus was significantly lower than that in persons not suffering from diabetes mellitus but HGS was not. Odds ratio (OR) and 95% confidence interval (CI) per 1-standard deviation–increase in muscular strength measurements for the prevalence of diabetes mellitus were obtained using a multiple logistic regression model. Prevalence of diabetes mellitus was inversely related to TFS (OR 0.769, 95% CI 0.614–0.963), TFS/body mass (BM) (0.696, 0.545–0.889) and TFS/body mass index (BMI) (0.690, 0.539–0.882) after adjustment of covariates. Such associations were not observed in HGS (OR 0.976, 95% CI 0.773–1.232), HGS/BM (0.868, 0.666–1.133) or HGS/BMI (0.826, 0.642–1.062). These results suggested that poor TFS was associated with an increased prevalence of diabetes mellitus independent of visceral fat accumulation, but HGS was not, in middle-aged males. TFS may be a better marker for the prevalence of diabetes mellitus than HGS.

Key words: Toe flexor, Handgrip, Muscular strength, Physical fitness, Visceral adipose tissue

SKELETAL MUSCLE plays an important role in the regulation of substrate utilization in the whole body owing to its considerable capacity for the metabolism of glucose and lipid *via* insulin- and contraction-induced signals [1]. A reduced mass of skeletal muscle and reduced fitness are related to the prevalence of diabetes mellitus, impaired glucose tolerance, and insulin resistance [2-4]. In addition, resistance exercise training can reduce the risk of type-2 diabetes mellitus significantly independent of aerobic exercise training [5, 6]. Therefore, the strength and mass of the muscle may have a role in the amelioration and/or prevention of diabetes mellitus.

Many epidemiologic studies have estimated handgrip strength (HGS) as an indicator of muscular strength which is associated with mortality, heart failure, cancer, falling, and activities of daily living [7, 8]. Several studies have demonstrated that poor HGS is associated with the prevalence of diabetes mellitus and increased level of fasting blood glucose (FBG) [9-14], but other studies have not indicate any associations [7, 15].

Recently, evidence has been accumulating that toe flexor strength (TFS) is associated with gait performances [16], jump performance [17], and the risk of falling in older persons [18, 19]. Age-related reduction of TFS is earlier and in magnitude greater than HGS [20]. Measurement of TFS is assumed to be a simple, safe and inexpensive method to evaluate muscular strength in the

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lower limbs, and may be useful for screening for health and aging-related problems. Previously, we found that TFS is inversely associated with the FBG level but that HGS is not [20]. It is likely that poor TFS is more closely associated with the prevalence of diabetes mellitus than HGS.

We designed the cross-sectional study described here to clarify the association between TFS and the prevalence of diabetes mellitus. We also investigated if HGS is associated with the prevalence of diabetes mellitus, and then compared the availability for screening for diabetes mellitus between TFS and HGS with a special focus on the accumulation of adipose tissue.

Methods

Study design and population

The present study was carried out as a part of the baseline survey of the Toyota Motor Corporation Physical Activity and Fitness Study (TMCPAFS), and was conducted from October 2015 to January 2016. Participants in the baseline study were 1,410 Japanese males, aged 35–59 years working for the Toyota Motor Corporation (Aichi, Japan). Twenty individuals were excluded because of incomplete data, so 1,390 participants were included in the present study. All participants received annual medical examinations in accordance with the Industrial Safety and Health Law of Japan.

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Toyota Memorial Hospital (Aichi, Japan). All individuals provided written consent to participate in this study.

Medical examinations

After an overnight fast of ≥11 h, participants underwent measurement of anthropometry, resting systolic blood pressure (SBP) and diastolic blood pressure (DBP), blood chemistry analyses, and computed tomography (CT). Height and body mass (BM) were measured using an automated measuring instrument (BF-220; Tanita, Tokyo, Japan), from which body mass index (BMI) was calculated. Percentage of body fat (%fat) was determined by biochemical impedance (BF-220; Tanita). Waist circumference (WC) was measured at the level of the umbilicus in a standing position while breathing normally (at the end of expiration while breathing gently). Blood samples were drawn from the antecubital vein from seated participants.

The diagnosis of diabetes mellitus

The prevalence of diabetes mellitus was defined based on meeting at least one of the following criteria: increased FBG (≥126 mg/dL); increased glycated hemoglobin (HbA1c) (≥6.5%: 48 mmol/mol); and current use of anti-diabetes-mellitus drugs.

Assessment of adipose tissues by CT

CT of the abdomen was done at the end of the expiratory phase using an Aquillion system (Toshiba Medical Systems, Tochigi, Japan). The umbilicus was assessed for areas of visceral and subcutaneous fat, which were measured in accordance with the guidelines for obesity treatment set by the Japan Society for the Study of Obesity [21]. Modified measurement levels were employed if participants possessed a clearly low umbilical body type. Image analysis software (SlimVision v4.0; Cybernet Systems, Tokyo, Japan) was used at an attenuation range of –70 Hounsfield units to –160 Hounsfield units to quantify abdominal areas of adipose tissue. The "subcutaneous fat area" (SFA) was defined as fat superficial to the abdominal and back muscles. The "visceral fat area" (VFA) was defined as intra-abdominal fat bound by the parietal peritoneum or fascia transversalis.

Biochemical assays

FBG levels were measured by the hexokinase-glucose-6-phosphate dehydrogenase method (Eiken Chemicals, Tokyo, Japan). Concentrations of HbA1c were measured by high-performance liquid chromatography. Concentrations of triglycerides (TG) were measured by enzymatic colorimetric analyses (standard methods set by the Japan Society of Clinical Chemistry and Reference Material Institute for Clinical Chemistry Standards). Total cholesterol (TC) levels were measured by the cholesterol oxidase-peroxidase method. Levels of high-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterols (LDL-C) were measured using the chemically modified enzyme method (Metaboredo® HDL-C and Metaboredo® LDL-C; Kyowa Medex, Tokyo, Japan).

Familial history of diabetes, histories of diseases, and lifestyle estimations

A self-administered questionnaire was administered to assess a familial history of diabetes mellitus (none,1; at least one parent who developed diabetes mellitus, 2), histories of stroke cardiac diseases, cancer and low back pain (none, 1; yes, 2), ≥30 min of exercise (none, 1;

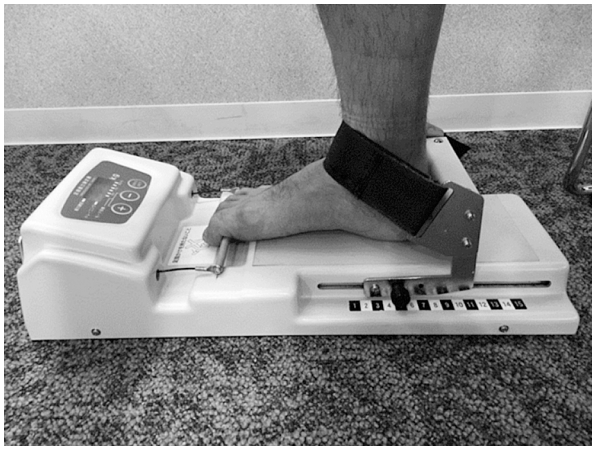

Fig. 1 Measurement of toe flexor strength using a toe grip dynamometer.

once/week, 2; 2–6 times/week, 3; every day, 4), smoking (never, 1; former, 2; current, 3), alcohol consumption (none, 1; sometimes, 2; ~3 times/week, 3; every day, 4) and sleeping time (h/day).

Measurements of muscle strength

TFS was measured using a toe grip dynamometer (T.K.K. 3364; Takei Scientific Instruments, Niigata, Japan) (Fig. 1) as described previously [20]. After sufficient training trials, maximal TFS was measured twice. Measurements were performed on right and left toes, and the mean maximum force of each toe was used in subsequent analyses.

HGS was measured using a handgrip dynamometer (T.K.K. 5401; Takei Scientific Instruments). Measurements were made in duplicate in each hand, and the mean maximum force of each hand was used in analyses.

Statistical analysis

Data are the mean ± SD. The unpaired *t*-test was used to compare mean values between participants not suffering from diabetes mellitus and participants with diabetes mellius. The prevalence of diabetes mellitus (no or yes), FBG level ≥126 mg/dL (no or yes), HbA1c level ≥6.5% (no or yes), current use of anti-diabetes-mellitus drugs (no or yes), familial history of diabetes mellitus (no or yes), history of stroke (no or yes), history of cardiac diseases (no or yes), history of cancer (no or yes), history of low back pain (no or yes), and lifestyle differences such as exercise (none, or more than once/week), alcohol consumption (none, or more than sometimes) and cigarette smoking (never, former, or current) were compared using the χ^2 test.

Relationships between 1-SD increase in muscular strength and prevalence of diabetes mellitus were analyzed using multiple logistic regression models that could estimate odds ratios (ORs) and 95% confidence intervals (CIs). Four models were used to assess these associations. The first model (Model 1) was crude. In the second model (Model 2), minimum adjustment was performed. Model 2 was adjusted for age (analyses of all measurements), height (TFS, TFS/BM, HGS and HGS/BM analyses) and BM (TFS and HGS analyses). Model 3 was adjusted for Model 2 covariates plus SBP, TG, HDL-C, LDL-C, familial history of diabetes mellitus, sleeping time, cigarette smoking, alcohol consumption, and exercise habit to exclude the effects of medical and life style characteristics. Model 4 was adjusted for Model 3 covariates plus VFA because this study tried to confirm presence or absence of effect of abdominal fat accumulation. To determine the mediation effects of the obesity parameters %fat, WC, VFA and SFA on associations between muscular strength and prevalence of diabetes mellitus, further multivariate logistic regression analyses were undertaken. In brief, the reference model, which was adjusted for the same covariates of Model 3, was adjusted further for each obesity parameter.

Differences were considered significant if $p < 0.05$. SPSS v23.0 (IBM, Armonk, NY, USA) was used for statistical analyses.

Results

Anthropometry and medical examination

Table 1 shows the characteristics of the study participants. The prevalence of diabetes mellitus in participants was 8.2%. Four participants in the diabetes mellitus group (3.5%) used insulin preparations. Age, BM, BMI, %fat, WC, VFA, SFA, FBG level, HbA1C level, SBP, DBP, TG level, familial history of diabetes mellitus, and exercise habit were significantly higher ($p < 0.05$) in participants with diabetes mellitus than participants not suffering from diabetes mellitus. Levels of TC, HDL-C and LDL-C in participants with diabetes mellitus were significantly lower ($p < 0.05$) than in participants not suffering from diabetes mellitus.

Muscular strength and prevalence of diabetes mellitus

Measurements of muscular strength are shown in Table 2. TFS, TFS/BM and TFS/BMI were significantly

Table 1 Characteristics of participants according to the prevalence of diabetes mellitus

	Total	Non-diabetes	Diabetes	p^a
Number	1,390	1,276	114	
Age (years)	48. 0 ± 8.1	47.6 ± 8.2	52.4 ± 6.6	<0.001
Height (cm)	170.5 ± 5.9	170.6 ± 5.9	169.5 ± 6.0	0.080
Body mass (kg)	67.9 ± 10.1	67.4 ± 9.6	74.2 ± 13.1	<0.001
Body mass index (kg/m^2)	23.4 ± 3.3	23.2 ± 3.1	25.8 ± 4.2	<0.001
Percentage of body fat (%)	22.4 ± 5.6	22.2 ± 5.4	25.7 ± 6.5	<0.001
Waist circumference (cm)	81.9 ± 8.9	81.3 ± 8.4	88.4 ± 10.9	<0.001
Visceral fat area (cm^2)	71.0 ± 44.9	67.7 ± 42.2	108.7 ± 56.1	<0.001
Subcutaneous fat area (cm^2)	120.5 ± 67.6	117.6 ± 65.5	152.6 ± 81.1	<0.001
Fasting blood glucose (mg/dL)	99.4 ± 15.4	96.2 ± 9.3	135.2 ± 23.1	<0.001
Glycated hemoglobin (%)	5.57 ± 0.57	5.45 ± 0.28	6.93 ± 1.04	<0.001
Systolic blood pressure (mmHg)	118.4 ± 13.8	117.7 ± 13.7	125.7 ± 12.8	<0.001
Diastolic blood pressure (mmHg)	76.9 ± 9.2	76.7 ± 9.2	79.5 ± 9.1	0.002
Triglyceride (mg/dL)	116.6 ± 88.0	114.8 ± 84.7	136.3 ± 118.1	0.012
Total cholesterol (mg/dL)	203.2 ± 31.8	204.1 ± 31.4	193.1 ± 34.9	<0.001
High-density lipoprotein-cholesterol (mg/dL)	60.7 ± 16.2	61.2 ± 16.2	54.7 ± 14.5	<0.001
Low-density lipoprotein-cholesterol (mg/dL)	126.4 ± 29.9	127.1 ± 29.6	119.2 ± 31.3	0.007
Fasting blood glucose ≥126 mg/dL (%)[b]	5.8	0.0	70.2	<0.001
Glycated hemoglobin ≥6.5 % (%)[b]	6.0	0.0	73.7	<0.001
Anti-diabetes drugs (%)[b]	4.5	0.0	54.4	<0.001
Familial history of diabetes (%)[b]	14.7	13.4	29.8	<0.001
History of stroke[b]	0.3	0.0	0.3	0.549
History of cardiac diseases[b]	2.2	2.0	3.5	0.300
History of cancer[b]	2.1	1.8	5.3	0.013
History of low back pain[b]	24.7	24.5	27.2	0.528
Sleeping time (hr)	6.2 ± 0.9	6.2 ± 0.9	6.2 ± 0.9	0.953
Never smoker (%)[b]	46.3	46.6	43.9	0.581
Former smoker (%)[b]	15.3	15.5	13.2	0.503
Current smoker (%)[b]	38.3	37.9	43.0	0.289
Alcohol consumption (%)[b]	76.7	76.6	77.2	0.895
Exercise habit (%)[b,c]	67.8	66.8	78.9	0.008

Data are the mean ± standard deviation. [a] p value from the unpaired t-test or χ^2 test. [b] p value from the χ^2 test. [c] At least one session of exercise per week.

lower in participants with diabetes mellitus than in participants not suffering from diabetes mellitus ($p < 0.05$). No significant difference was observed in absolute HGS ($p \geq 0.05$). HGS/BM and HGS/BMI in participants with diabetes mellitus were significantly lower compared with those not suffering from diabetes mellitus ($p < 0.05$).

The ORs per 1-SD increase and 95% CI in muscular strength are shown in Table 3. Overall ORs were significant with regard to TFS measurements ($p < 0.05$). No significant associations were detected in HGS ($p \geq 0.05$).

Table 2 Muscular strength according to the prevalence of diabetes mellitus

	Total	Non-diabetes	Diabetes	p^a
TFS (kg)	20.2 ± 6.0	20.3 ± 6.0	18.7 ± 6.2	0.005
TFS/BM (kg/kg)	0.301 ± 0.094	0.305 ± 0.094	0.256 ± 0.087	<0.001
TFS/BMI (kg/kg/m^2)	0.874 ± 0.275	0.886 ± 0.274	0.736 ± 0.255	<0.001
HGS (kg)	41.2 ± 5.6	41.3 ± 5.6	40.6 ± 6.1	0.198
HGS/BM (kg/kg)	0.616 ± 0.100	0.621 ± 0.098	0.560 ± 0.114	<0.001
HGS/BMI (kg/kg/m^2)	1.792 ± 0.315	1.808 ± 0.308	1.612 ± 0.346	<0.001

TFS, toe flexor strength; BM, body mass; BMI, body mass index; HGS, handgrip strength; Data are the mean ± standard deviation. [a] p value from an unpaired t-test.

HGS/BM and HGS/BMI showed significant inverse associations in Model 1 to Model 3 ($p < 0.05$). However, such associations disappeared after adjustment for the VFA (Model 4).

The mediation effects of different obesity parameters on the associations between muscular strength and the prevalence of diabetes mellitus are shown in Table 4. All TFS measurements were associated significantly with the prevalence of diabetes mellitus independent of any type of adipose-tissue accumulation ($p < 0.05$). HGS was not associated with the prevalence of diabetes mellitus. HGS/BM and HGS/BMI were not related to the prevalence of diabetes mellitus after adjustment of %fat, WC or the VFA, but the relationships remained significant after adjustment of the SFA ($p < 0.05$).

Discussion

The present study suggests that TFS can be used to predict the prevalence of diabetes mellitus in middle-aged males. One cross-sectional study also showed that poor muscular strength and power of lower-limb muscle groups are associated with the prevalence of diabetes mellitus [22]. One longitudinal study suggested that poor muscular strength (as quantified by a combination of leg and bench presses) is a risk factor for the metabolic syndrome [23]. Moreover, resistance exercise training has been shown to reduce the risk of developing diabetes mellitus [5, 6]. Based on these results, poor TFS is considered to be a potential risk factor for diabetes mellitus.

The physiologic or biochemical mechanisms underlying the associations between TFS and the prevalence of diabetes mellitus are not known. Nevertheless, it is possible that poor TFS is associated with reduced skeletal muscle volume of the whole body, which represses energy expenditure and total insulin-dependent glucose metabolism. Indeed, TFS was positively related to the lean body mass [20]. In addition, skeletal muscle has an important role in the regulation of glucose/lipid metabolism of whole body *via* insulin- and contraction-induced signals [1]. Therefore, reduced TFS-related metabolic conditions might worsen insulin resistance and lead to the development of type-2 diabetes mellitus.

Conversely, age-related loss of the strength and volume of muscle is accelerated in patients with type-2 diabetes mellitus [24, 25]. Reduced strength and volume in some muscle groups (especially those in the foot) are observed in patients with diabetes and diabetic neuropathy than in patients with diabetes mellitus but not suffering from diabetic neuropathy [2, 26, 27]. Furthermore, the patients with diabetes mellitus (especially with neuropathy) have more toe and foot deformities than persons without diabetes mellitus [28, 29]. Such abnormalities would deteriorate toe functions including flexion and extension forces, the joint motion range and flexibilities of toes.

Additionally, the protein flux, synthesis, and net balance (*i.e.*, protein synthesis minus protein breakdown) in the whole body of patients with type-2 diabetes mellitus are reduced compared with those not suffering from diabetes mellitus [30]. Oxidative stress in diabetes mellitus impairs transcriptional activity with regard to muscle repair, and reduces protein expression of creatine kinase, myosin, and transcriptional factors in skeletal muscle [31]. Carbonylated myosin protein, a characteristic of oxidative damage, has been observed in the muscles of rats with diabetes mellitus [32]. In addition, it is likely that an increased glucose level in diabetes mellitus promotes accumulation of glycated myofibrillar proteins, which impair the contraction properties of myofibrils [33]. On the basis of these results, diabetes mellitus would promote muscle atrophy and impair the produc-

Table 3 Relationship between muscular strength and the prevalence of diabetes mellitus

	β	Standard Error	OR (95% CI)[a]	*p*
TFS				
Model 1	–0.279	0.101	0.757 (0.621–0.922)	0.006
Model 2	–0.254	0.107	0.776 (0.629–0.957)	0.019
Model 3	–0.270	0.114	0.764 (0.611–0.954)	0.018
Model 4	–0.263	0.115	0.769 (0.614–0.963)	0.022
TFS/BM				
Model 1	–0.573	0.109	0.564 (0.455–0.699)	<0.001
Model 2	–0.503	0.112	0.605 (0.486–0.753)	<0.001
Model 3	–0.483	0.119	0.617 (0.489–0.779)	<0.001
Model 4	–0.362	0.125	0.696 (0.545–0.889)	0.004
TFS/BMI				
Model 1	–0.601	0.109	0.548 (0.442–0.679)	<0.001
Model 2	–0.506	0.112	0.603 (0.484–0.752)	<0.001
Model 3	–0.485	0.120	0.616 (0.487–0.779)	<0.001
Model 4	–0.372	0.125	0.690 (0.539–0.882)	0.003
HGS				
Model 1	–0.128	0.100	0.880 (0.724–1.070)	0.199
Model 2	–0.112	0.111	0.894 (0.719–1.111)	0.313
Model 3	0.017	0.117	0.931 (0.741–1.170)	0.540
Model 4	–0.025	0.119	0.976 (0.773–1.232)	0.835
HGS/BM				
Model 1	–0.639	0.105	0.528 (0.430–0.649)	<0.001
Model 2	–0.596	0.107	0.551 (0.447–0.679)	<0.001
Model 3	–0.417	0.115	0.659 (0.526–0.827)	<0.001
Model 4	–0.141	0.136	0.868 (0.666–1.133)	0.298
HGS/BMI				
Model 1	–0.664	0.106	0.515 (0.418–0.634)	<0.001
Model 2	–0.582	0.109	0.559 (0.452–0.692)	<0.001
Model 3	–0.418	0.116	0.659 (0.525–0.826)	<0.001
Model 4	–0.192	0.129	0.826 (0.642–1.062)	0.136

OR, odds ratio; CI, confidence interval; TFS, toe flexor strength; BM, body mass; BMI, body mass index; HGS, handgrip strength. [a] OR and 95% CI per 1-standard deviation increase in muscle strength measurements.

Model 1: crude.

Model 2: odds ratio adjusted for age (all), height (TFS, TFS/BM, HGS and HGS/BM) and BM (TFS and HGS).

Model 3: Model 2 + systolic blood pressure, triglyceride, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, familial history of diabetes mellitus, sleeping time, cigarette smoking, alcohol consumption, and exercise habit.

Model 4: Model 3 + visceral fat area.

Table 4 Mediation effects of different obesity parameters on the association between muscular strength and the prevalence of diabetes mellitus

Exposure	Covariates	OR (95% CI)[a]	*p*
TFS	Ref model[b]	0.764 (0.611–0.954)	0.018
	Ref model + %fat	0.766 (0.611–0.959)	0.020
	Ref model + WC	0.768 (0.613–0.961)	0.021
	Ref model + VFA	0.769 (0.614–0.963)	0.022
	Ref model + SFA	0.745 (0.596–0.932)	0.010
TFS/BM	Ref model[b]	0.617 (0.489–0.779)	<0.001
	Ref model + %fat	0.704 (0.549–0.904)	0.006
	Ref model + WC	0.724 (0.563–0.931)	0.012
	Ref model + VFA	0.696 (0.545–0.889)	0.004
	Ref model + SFA	0.662 (0.518–0.846)	0.001
TFS/BMI	Ref model[b]	0.616 (0.487–0.779)	<0.001
	Ref model + %fat	0.707 (0.550–0.910)	0.007
	Ref model + WC	0.712 (0.554–0.915)	0.008
	Ref model + VFA	0.690 (0.539–0.882)	0.003
	Ref model + SFA	0.660 (0.516–0.845)	0.001
HGS	Ref model[b]	0.931 (0.741–1.170)	0.540
	Ref model + %fat	0.937 (0.744–1.179)	0.578
	Ref model + WC	0.945 (0.747–1.194)	0.634
	Ref model + VFA	0.976 (0.773–1.232)	0.835
	Ref model + SFA	0.868 (0.687–1.097)	0.236
HGS/BM	Ref model[b]	0.659 (0.526–0.827)	<0.001
	Ref model + %fat	0.820 (0.625–1.077)	0.153
	Ref model + WC	0.933 (0.692–1.257)	0.646
	Ref model + VFA	0.868 (0.666–1.133)	0.298
	Ref model + SFA	0.726 (0.544–0.969)	0.030
HGS/BMI	Ref model[b]	0.659 (0.525–0.826)	<0.001
	Ref model + %fat	0.824 (0.629–1.081)	0.162
	Ref model + WC	0.845 (0.648–1.102)	0.213
	Ref model + VFA	0.826 (0.642–1.062)	0.136
	Ref model + SFA	0.726 (0.553–0.952)	0.021

OR, odds ratio; CI, confidence interval; TFS, toe flexor strength; BM, body mass; BMI, body mass index; HGS, handgrip strength; Ref, reference; %fat, percentage of body fat; WC, waist circumference; VFA, visceral fat area; SFA, subcutaneous fat area. [a] OR and 95% CI per 1-standard deviation increase in muscle strength measurements. [b] Reference models adjusted for age, height (TFS, TFS/BM, HGS and HGS/BM), BM (TFS and HGS), systolic blood pressure, triglyceride, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, familial history of diabetes mellitus, sleeping time, cigarette smoking, alcohol consumption, and exercise habit.

tion of muscular force.

The present study demonstrated that TFS was associated with the prevalence of diabetes mellitus whereas HGS was not. These results are consistent with epidemiologic reports showing that HGS is not associated with the risk of diabetes mellitus [15, 34]. Furthermore, the strength of lower-limb muscles in patients with diabetes mellitus is less than that in individuals not suffering from diabetes mellitus, but that of upper-limb muscles is not [2]. However, there are inconsistent reports concerning the association between HGS and diabetes mellitus. Several studies have shown that poor HGS is associated with diabetes mellitus [9-12, 14]. We further analyzed the association by focusing on adipose accumulation. The VFA as well as %fat and WC mediated the relationships between HGS/BM and HGS/BMI and the prevalence of diabetes mellitus. In contrast, these relationships remained significant after adjustment of the SFA. These results imply that the volume of visceral adipose tissue mediates the artificial association between relative HGS and the prevalence of diabetes mellitus. Studies [9-12] have shown that the association between HGS and diabetes mellitus is not adjusted by the volume of visceral abdominal tissue volume, such as the VFA. Hence, it is assumed that the association might be (at least in part) mediated by the volume of visceral abdominal tissue. HGS is associated with the prevalence of diabetes mellitus in overweight/obese (BMI ≥25 kg/m^2) persons, whereas such a relationship is not observed in non-overweight/non-obese persons [11]. Conversely, Wander *et al.* showed in a ≥10-year-prospective study, that greater HGS predicts a lower risk of type-2 diabetes mellitus but that such an association is diminished at a higher BMI [9]. They deduced that the known effects of adiposity on the risk of diabetes mellitus may override any potential benefit associated with greater HGS and its correlates. Interestingly, the relationship between obesity and the muscle strength of the hands and knees differs, and HGS cannot be considered an indicator of whole-body strength in obese persons [35]. Taken together, measurement of TFS would be a better marker for the prevalence of diabetes mellitus than that of HGS.

Another possible explanation for the inconsistent relationships of diabetes mellitus between TFS and HGS is the involvement of physical activity and/or gait speed. A lower amount of physical activity is a risk factor for type-2 diabetes mellitus [36], and gait speed is associated with the prevalence of diabetes mellitus [22, 37]. TFS is positively related to physical activity [20, 38]. In con-

trast, compared with the strength of lower limbs, HGS is lower or not associated with the amount of physical activity [20, 39]. In addition, TFS is associated with gait speed [16, 38]. Lower-limb muscle strength is a slightly better predictor of gait speed than HGS [40]. Based on these results, poor TFS might reflect diabetes mellitus more accurately than HGS through the amount of physical activity and/or gait speed.

Our study had four main limitations with respect to the generalizability and interpretation of results. First, its cross-sectional design limits the drawing of causal inferences from the relationships observed. Longitudinal studies are necessary to clarify the causal relationship. Second, the details of participants with diabetes mellitus were uncertain. The duration of diabetes mellitus and having or not having complications such as neuropathy were unidentified. Prevalence of neuropathy, which would seriously affect TFS, in patients with diabetes mellitus increases with duration of diabetes mellitus [41, 42]. This study was designed to perform in a medical examination in an institution of a corporation which was in accordance with the Industrial Safety and Health Law of Japan, but not a detailed examination in hospitals, a multiphasic health screening, or a physiological experiment. Therefore, unfortunately, it was difficult to inspect the details of participants. This was another reason that the study could not explain causal relationship. Third, the characteristics of participants in this study limited the generalizability of results. All participants were middle-aged, male, Japanese employees, so, there may have been some bias. All participants in this study worked for a manufacturing industry. Many participants engaged in jobs which required high physical demand such as assembly lines and others in office works. Degrees of age-related reduction of physical functions are at least in part dependent on occupational physical activity level [43, 44]. Occupational physical activity level affects the prevalence of type-2 diabetes mellitus [45, 46]. It was possible that such unique variation of occupational physical demands in the participants affected the results in this study. Fourth, our study did not distinguish between type-1, type-2 and other types of diabetes mellitus: pathologic processes among them differ [47]. Therefore, causality between muscle strength and the prevalence of diabetes mellitus should differ according to the type of diabetes mellitus. However, only 4 persons used insulin preparations in this study, speculating that the bias of including both types of diabetes mellitus would be very limited.

In summary, this cross-sectional study investigated the association between TFS and the prevalence of diabetes mellitus and compared such associations between TFS and HGS in middle-aged male workers. TFS, TFS/BM and TFS/BMI were reduced in persons with diabetes mellitus. Multivariate logistic regression models suggested that poor TFS measurements were associated with the prevalence of diabetes mellitus. However, HGS measurements were not related to the prevalence of diabetes mellitus after adjustment of covariates. The volume of visceral abdominal fat mediated an artificial association between relative HGS and the prevalence of diabetes mellitus but not TFS. The latter can be considered as to be a better marker of the prevalence of diabetes mellitus than HGS.

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Disclosures

None of the authors have any potential conflicts of interest associated with this research.

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