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The effect of diabetes mellitus on age-associated lean mass loss in 3153 older adults

J. S. W. Lee^{*,†,‡}, T. W. Auyeung^{§,¶}, J. Leung^{**}, T. Kwok^{*}, P. C. Leung^{**}, and J. Woo^{*}

^{*} Division of Geriatrics, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China

[†] Department of Medicine and Geriatrics, Shatin Hospital, Hong Kong, China

[‡] CADENZA Project, A Jockey Club Initiative for Seniors, Hong Kong, China

[§] Department of Medicine and Geriatrics, Pok Oi Hospital, Hong Kong, China

[¶] The S. H. Ho Centre of Geriatrics and Gerontology, The Chinese University of Hong Kong, Hong Kong, China

^{**} Jockey Club Centre for Osteoporosis Care and Control, The Chinese University of Hong Kong, Hong Kong, China

Abstract

Aims—Diabetes mellitus may be associated with excessive lean mass loss. Other diabetes-related conditions may also play a role. We assessed body composition changes associated with diabetes in older adults with adjustment for diabetes-related co-morbidities.

Methods—Three thousand, one hundred and fifty-three community-living adults aged ≥ 65 years were examined for lifestyle factors, diabetes-related medical conditions and body composition by dual energy X-ray absorptiometry at baseline and 4 years later. Body composition changes were compared between participants with diabetes and those without diabetes. Multivariate linear regression was used to examine the relationship between appendicular lean mass loss and confounders.

Results—Appendicular lean mass loss in men with diabetes was two times that of men without diabetes (-1.5% in ‘no diabetes’ vs. -3.0% in ‘diabetes’) and in women with diabetes was 1.8 times that of those without diabetes (-1.9% in ‘no diabetes’ vs. -3.4% in ‘diabetes’) over 4 years. Men with diabetes also had higher total body mass loss and higher total body fat loss than men without diabetes. Women with diabetes had higher total body mass loss but total body fat loss was similar. After adjusting for age, body mass index, diabetes-related conditions, lifestyle factors and total body mass loss, diabetes remained an independent predictor of appendicular lean mass loss in both men and women.

Conclusion—Diabetes was associated with higher body mass loss and higher appendicular lean mass loss in older adults. In men, diabetes was also associated with total body fat loss.

Keywords

diabetes; elderly; muscles; sarcopaenia

Correspondence to: Jenny S. W. Lee, Division of Geriatrics, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong. jennylee@cuhk.edu.hk.

Competing interests

Nothing to declare.

Introduction

Diabetes mellitus becomes more prevalent with ageing (1–5) and is associated with significant disability in older adults (6–9). With ageing, fat increases while muscle decreases (10), resulting in sarcopaenia, an important component of frailty (11–13). Diabetes was associated with higher fat mass and lower muscle mass in older adults in a cross-sectional study in a Western population (14). In the Chinese population, however, diabetes was associated with higher muscle mass (15), yet its association with disability remained similar (16,17). There is a variety of mechanisms by which diabetes can act synergistically with ageing to accelerate muscle loss (13), but longitudinal studies on how diabetes affected body composition and muscle loss were few. Only one cohort has reported longitudinal data in muscle loss among older adults with diabetes at 3 years (18) and 6 years (19). In these reports, diabetes was associated with more appendicular muscle loss over time in older White and Black adults.

Diabetes commonly coexists with hypertension, heart disease, stroke, atherosclerosis and obesity. These conditions could predispose to sarcopaenia directly or they might have done so through their association with diabetes (13,20). Identification of the independent risk factors of sarcopaenia may facilitate early intervention to sarcopaenia-associated frailty.

We examined the effect of diabetes on muscle loss and concurrent body composition changes over 4 years and studied whether this effect of diabetes is independent of other diabetes-related conditions in a large cohort of well-functioning older adults. We hypothesized that diabetes was an independent risk factor for muscle loss in older people, irrespective of the effect of other diseases commonly coexisting with diabetes.

Subjects and methods

Between August 2001 and December 2003, 4000 community-dwelling ethnic Chinese men and women aged 65 years or over were recruited by notices in elderly social centres and housing estates to attend a health check in the School of Public Health of the Chinese University of Hong Kong. We excluded those who (i) were unable to walk independently, (ii) had had bilateral hip replacements, (iii) were not competent to give informed consent and (iv) had medical conditions which made it unlikely that they would survive the follow-up period of 4 years (in the judgment of the study physicians). The sample was stratified to have equal numbers in three age groups: 65–69, 70–74 and 75 years or above. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong.

The Questionnaire

A questionnaire containing information regarding demographics, lifestyle, physical activity level and medical history was administered by trained interviewers. Smokers were classified by 'having ever smoked more than five packs of cigarettes in the past', 'smoking currently' or 'never smoked'.

Physical activity level was assessed using the Physical Activity Scale of the Elderly(21), which measured the number of hours per day spent in leisure, household and occupational physical activities over the previous 7 days. Activity weights for items were based on the amount of energy spent and each item score was calculated by multiplying the weight with activity frequency. A summary score reflected the daily physical activity level.

Medical diagnoses

Medical diagnoses were based on the subjects' report of their physician's diagnoses, supplemented by medications brought to the interviewers. Diabetes was defined by either self-report (ever being told by a physician that the patient had diabetes) or being on hypoglycaemic agents, which were brought to the study centre for confirmation. Stroke, heart disease and hypertension were defined by self-reporting. Heart disease included coronary heart disease, heart failure and myocardial infarction. Self-report diseases have been recognized as a valid method for collecting medical diagnoses in large-scale studies (22,23). Peripheral vascular disease was defined as the ankle-brachial index (the ratio of the systolic blood pressure of the posterior tibial artery to that of the brachial artery) being < 0.9 (24).

Physical measurements

Body weight was measured, with subjects wearing a light dressing gown, using the Physician Balance Beam Scale (Health-O-Meter, Arlington Heights, IL, USA). Height was measured using the Holtain Harpenden stadiometer (Holtain Ltd, Crosswell, UK). Blood pressure was measured on both sides at the arm and at the posterior tibial artery. The lower ankle-brachial index measurement of the two was used for analysis. Hip circumference (the maximum circumference around the buttocks posteriorly and the symphysis pubis anteriorly) and waist circumference (the narrowest circumference around the trunk between the rib cage and the pelvis) were measured with a flexible measuring tape to the nearest millimeter. Waist-hip ratio was taken to be high if > 0.9 in men and > 0.85 in women (25).

Body composition

We measured total body mass, body fat and lean mass by dual-energy X-ray absorptiometry using a Hologic QDR 2000 densitometer (Hologic Delphi, software version 11.2; Hologic Inc, Bedford, USA) at baseline and 4 years later. Appendicular lean mass was calculated by the sum of lean mass measured in the four limbs, with the operator adjusting the cut lines of the limbs according to specific anatomical landmarks as described by Heymsfield *et al.* (26). In delineating the trunk for measurement of the trunk fat, a line was drawn just below the chin to separate the head from the trunk. Another line was drawn between the head of the humerus and the scapula through the glenoid fossa to separate the arm from the trunk, and another passed through the femoral necks and just below the ischium to separate the pelvis from the leg. The Hologic Body composition step phantom was scanned daily to ensure proper calibration for fat and non-fat compartments. The maximum coefficient of variation for fat and lean mass is 1.47% and 0.84%, respectively.

Statistical methods

Data analysis was performed using statistical package SAS, version 9.1 (SAS Institute, Inc., Cary, NC, USA). As body composition differs with gender, all statistical tests were carried out separately for men and women. Characteristics of subjects with diabetes and those without were compared. Two-samples independent *t*-tests were used for continuous variables and χ^2 -tests for categorical variables. Body composition changes at 4 years were compared by using analysis of covariance (ANCOVA), adjusting for age. Multivariate linear regressions were used to examine the relationship between appendicular lean mass loss and diabetes, adjusting for age, physical activity, smoker status, BMI and diabetes-related conditions (low ankle-brachial index, hypertension, heart disease and stroke) and total body mass loss, in different models. All tests were two-sided and a *P*-value of < 0.05 was taken as statistically significant.

Results

Four thousand participants had a baseline dual-energy X-ray absorptiometry measurement and 3153 (74.95%) returned for the 4th-year dual-energy X-ray absorptiometry measurements. Among those who did not return, 248 (6.2%) had died and 599 (15.0%) defaulted. Those who did not return were older, had lower physical activity, lower total body mass, lower appendicular lean mass and were more likely to have an ankle-brachial index measurement < 0.9 at baseline. Women who did not return were more likely to have high waist-hip ratio and men who did not return were more likely to be current smokers and have a history of stroke. A similar proportion of participants with diabetes did and did not return for the 4th-year measurement.

At baseline, adults with diabetes were more likely to have hypertension, heart disease, low ankle-brachial index and high waist-hip ratio (Table 1). In both men and women, there was no difference in physical activity scores among those with or without diabetes. Among the 3153 subjects with both baseline and 4th-year dual-energy X-ray absorptiometry measurements, 442 (14.0%) had diabetes. Both men and women with diabetes had higher total body lean mass and total lean mass % (total lean mass/total body mass) than those without diabetes, but participants with diabetes had lower appendicular lean mass to total body lean mass ratios.

Changes in body composition over time are presented in Table 2. Participants both with and without diabetes had significant loss of total body mass and appendicular lean mass after 4 years, irrespective of gender ($P < 0.001$). Appendicular lean mass loss per year in our male participants was 69.5 g/year (without diabetes) vs. 150.3 g/year (with diabetes) and in our female participants was 64.5 g/year (without diabetes) vs. 118.8 g/year (with diabetes). Those with diabetes had higher total body mass loss than those without diabetes (-2.3 vs. -0.9% in men, $P < 0.001$; -2.4 vs. -1.2% in women, $p = 0.005$). Participants both with diabetes and without diabetes lost total body lean mass, trunk lean mass and appendicular lean mass over time, but those with diabetes had higher loss than those without. Men without diabetes lost appendicular lean mass at a rate of 1.5% over 4 years, while women without diabetes lost appendicular lean mass at a rate of 1.9% over the same period. The difference in lean mass loss was more marked in the limbs (-3.0 vs. -1.5% in men, $P < 0.001$; -3.4 vs. -1.9% in women, $P < 0.001$) than in the trunk (-2.7 vs. 1.9% in men, $P = 0.003$; -2.5 vs. -1.9% in women, $P = 0.034$).

Multivariate analyses

Table 3 shows the relationship of appendicular lean mass loss over time in relation to diabetes, adjusted for age, physical activity, smoking status, BMI, total body mass change and diabetes-related conditions. The appendicular lean mass loss in men and women with diabetes was higher than those without diabetes by 1.380 and 1.387%, respectively. The difference was attenuated after additional adjustment for total body mass loss over the same period in model 2, but association between diabetes and appendicular lean mass loss remained significant. Having diabetes was associated with an additional 0.85% of appendicular lean mass loss in men and 0.96% loss in women. Total body mass loss over time was strongly associated with appendicular lean mass loss in men and women irrespective of diabetes status [2.664% (0.086%) per additional 5 kg total body mass loss in men, $P < 0.001$; 2.635% (0.089%) in women, $P < 0.001$]. There was no significant interaction effect between age and diabetes ($P > 0.30$) on appendicular lean mass change, in either men or women. Further adjustment for changes in the Physical Activity Scale of the Elderly over four years (model 3) showed that the effect of diabetes was only slightly attenuated. The change in the physical activity score was significant in the multivariate model only in men but not in women.

Discussion

Our results suggest that diabetes is associated with increased lean mass loss and, in particular, appendicular lean mass loss in older adults over a period of 4 years. This concurs with the findings of Park *et al.* (18,19), in which a similar association was found in White and Black older adults. Diabetes was associated with a higher prevalence of disability and a more rapid decline in functions (9,23). As appendicular lean mass was associated with poorer physical function in old age (10,27), it is possible that higher appendicular lean mass loss in diabetes contributes partly to this phenomenon.

There was a loss of total body mass in participants both with and without diabetes over time. The magnitude of body mass loss was higher among our participants with diabetes. Diabetes-associated weight loss has been previously reported (28) and was found to be associated with adverse health outcomes. Low body mass and weight loss have also been reported as risk factors for mortality, disability and institutionalization in old age (28–30). Our results suggest that diabetes is associated with excessive loss of weight through excessive loss of both body fat and lean mass, especially in men.

In our cohort, diabetes was consistently associated with appendicular lean mass loss in both men and women, independent of the diabetes-related conditions studied (low ankle–brachial index, high BMI, heart disease, stroke and hypertension). The average appendicular lean mass loss difference between participants with diabetes and those without diabetes was 1.6% per 4 years (0.40% per year) in men and 1.5% per 4 years (0.38% per year) in women. This difference was comparable with or slightly greater than that reported in White and Black populations (18), which averaged approximately 1% per 3 years (0.33% per year), with men and women considered together. Absolute appendicular lean mass loss in our male participants was 69.5 g/year (without diabetes) vs. 150.3 g/year (with diabetes) and in our female participants was 64.5 g/year (without diabetes) vs. 118.8 g/year (diabetes). In term of absolute weight, this loss was lower than that in White and Black populations, as estimated from the report by Park *et al.* (193.3 g/year without diabetes vs. 246.7 g/year with diabetes, with men and women taken together) (18), but their baseline total body mass and appendicular lean mass were much higher than in our results. Unfortunately, as no separate data for men and women and White and Black populations were available, the effect of diabetes on appendicular lean mass in different ethnic groups in each of the genders could not be directly compared at present. As lean mass, especially appendicular lean mass, is associated with activities of daily living (27), and Asians have a greater increase in diabetes prevalence in comparison with other populations (2), the impact of diabetes on appendicular lean mass loss may lead to a higher diabetes-related healthcare burden in Asian populations.

In our cohort, the absolute amount of total lean mass, appendicular lean mass and total lean mass % were higher in participants with diabetes, but the relative proportion of lean mass in the limbs (appendicular lean mass/total lean mass) was lower in participants with diabetes. A higher lean mass in diabetes was also found in White and Black populations (18). Increased fat infiltration of muscles in diabetes (13) might account for the higher total lean mass when measured by dual-energy X-ray absorptiometry, which could not distinguish between muscle and muscle infiltrated by fat. Whether diabetes causes higher fat infiltration in trunk lean mass (e.g. internal organs) when compared with appendicular lean mass could not be answered using dual-energy X-ray absorptiometry measurements.

There were multiple possible mechanisms of more rapid loss of appendicular lean mass observed in older adults with diabetes, most of which involved alterations in protein synthesis and protein breakdown in muscles. Lower bioavailable testosterone and insulin-like growth factor 1 in older men with diabetes might contribute to lower protein synthesis,

while higher pro-inflammatory cytokines and higher angiotension II levels might contribute to increased muscle breakdown, resulting in loss of muscle mass (13,20).

While physical activities had been associated with muscle mass in older populations (31), physical activities as reflected by the Physical Activity Scale of the Elderly score used in this study only mildly attenuated the association between appendicular lean mass loss and diabetes, and only in men. This score captures all activities, including activities of daily living, such as shopping, walking and doing home chores, and was not used exclusively for resistive or aerobic exercise. This might have limited its association with the decline in muscle mass.

Our study had several limitations. We had no data regarding control or the duration of diabetes. The diagnoses relied on self-report, although this had been recognized as a valid method for collecting medical diagnoses in large studies (22,23). Weight loss could not be classified as intentional or unintentional. We were unable to demonstrate causality between diabetes and the observed weight and muscle losses. A higher than expected proportion of participants did not return for the 4th-year assessment, which might have biased our results towards more healthy older adults. The cohort consisted of community-dwelling and well-functioning older adults; hence, the results should not be generalized to those who are more frail.

Conclusion

Diabetes was associated with higher body mass loss and appendicular lean mass loss in older Chinese adults. In men, diabetes was also associated with higher total body fat loss. Diabetes-associated muscle loss may contribute to diabetes-related frailty in older adults.

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Table 1

Comparison of baseline characteristics between subjects with diabetes (DM) and without diabetes (no DM)

	Men				Women			
	No DM (n = 1344)		DM (n = 222)		No DM (n = 1367)		DM (n = 220)	
	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	P-value of t-test/ χ^2 -test	P-value	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	P-value of t-test/ χ^2 -test	P-value
Age	71.7 (4.7)	72.0 (4.6)		0.439	72.0 (5.1)	72.4 (4.9)		0.235
PASE score	100.7 (50.1)	100.1 (54.5)		0.864	86.8 (33.6)	88.1 (32.1)		0.601
Body mass index (kg/m ²)	23.3 (3.1)	24.7 (2.8)		<0.001	23.9 (3.4)	24.3 (3.3)		0.104
Total body mass (kg)	61.4 (9.1)	64.9 (8.2)		<0.001	54.4 (8.4)	55.6 (8.5)		0.052
Total body fat mass (kg)	15.1 (4.6)	16.6 (4.3)		<0.001	19.2 (5.1)	19.0 (5.1)		0.629
Total body lean mass (kg)	44.2 (5.3)	46.1 (4.8)		<0.001	33.8 (4.0)	35.1 (4.3)		<0.001
Trunk fat mass (kg)	8.5 (3.0)	9.9 (2.8)		<0.001	9.9 (2.9)	10.2 (2.7)		0.141
Trunk lean mass (kg)	21.6 (2.7)	22.7 (2.5)		<0.001	17.0 (2.1)	17.9 (2.3)		<0.001
Appendicular fat mass (kg)	5.7 (1.8)	5.9 (1.8)		0.171	8.5 (2.5)	8.0 (2.7)		0.007
Appendicular lean mass (kg)	19.3 (2.6)	19.9 (2.3)		<0.001	13.8 (1.9)	14.3 (2.0)		0.002
Total lean mass/total body mass (%)	71.3 (4.1)	72.5 (4.7)		0.001	62.6 (5.0)	63.6 (5.0)		0.005
Appendicular lean mass/total body lean mass (%)	43.5 (1.5)	43.2 (1.5)		0.003	40.9 (1.6)	40.5 (1.7)		0.004
Smoker status				0.364				0.434
Never smokers	506 (37.7%)	86 (38.7%)			1249 (91.4%)	199 (90.5%)		
Ex-smokers	686 (51.0%)	118 (53.2%)			94 (6.9%)	19 (8.6%)		
Current smokers	152 (11.3%)	18 (8.1%)			24 (1.8%)	2 (0.9%)		
Hypertension	499 (37.1%)	148 (66.7%)		<0.001	540 (39.5%)	154 (70.0%)		<0.001
Stroke	50 (3.7%)	21 (9.5%)		<0.001	46 (3.4%)	8 (3.6%)		0.837
Heart disease	222 (16.5%)	53 (23.9%)		0.008	209 (15.3%)	48 (21.8%)		0.015
ABI < 0.9	40 (3.0%)	7 (3.2%)		0.888	101 (7.4%)	24 (10.9%)		0.073

	Men				Women			
	No DM (<i>n</i> = 1344)		DM (<i>n</i> = 222)		No DM (<i>n</i> = 1367)		DM (<i>n</i> = 220)	
	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	<i>P</i> -value of <i>t</i> -test/ χ^2 -test	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	Mean (SD)/frequency (%)	<i>P</i> -value of <i>t</i> -test/ χ^2 -test
High gender-specific waist-hip ratio	839 (62.4%)	174 (78.4%)	1086 (79.5%)	< 0.001	195 (88.6%)			0.001

ABI, ankle-brachial index; PASE, Physical Activity Scale for the elderly.

Table 2

Comparison of body composition changes over 4 years between subjects with diabetes (DM) and without diabetes (no DM)

Body composition changes at 4 years	Men						Women					
	No DM (<i>n</i> = 1344)			DM (<i>n</i> = 222)			No DM (<i>n</i> = 1367)			DM (<i>n</i> = 220)		
	Mean (SD)	%*		Mean (SD)	%*		Mean (SD)	%*		Mean (SD)	%*	
Difference												
	Mean (SE)	%*		Mean (SE)	%*		Mean (SE)	%*		Mean (SE)	%*	
Total body mass (g)	-576 (2977) [§]	-0.9		-1482(3147) [§]	-2.3		-670 (2923) [§]	-1.2		-1297 (2882) [§]	-2.4	
Total body fat mass (g)	107 (2130)	0.7		-269(1997)	-1.6		-70 (2155)	-0.4		-332 (2109) [‡]	-1.8	
Total body lean mass (g)	-709 (1540) [§]	-1.6		-1,251(1912) [§]	-2.7		-606 (1311) [§]	-1.8		-957 (1313) [§]	-2.8	
Trunk fat mass (g)	-22 (1381)	-0.3		-291(1318) [‡]	-3.0		-107 (1304) [‡]	-1.1		-262 (1286) [§]	-2.6	
Trunk lean mass (g)	-398 (913) [§]	-1.9		-604(1083) [§]	-2.7		-324 (757) [§]	-1.9		-443 (743) [§]	-2.5	
Appendicular fat mass (g)	137 (830) [§]	2.4		35 (771)	0.6		43 (926)	0.5		-58 (952)	-0.7	
Appendicular lean Mass (g)	-278 (836) [§]	-1.5		-601 (1030) [§]	-3.0		-258 (683) [§]	-1.9		-475 (694) [§]	-3.4	

* % change from baseline;

[†] $P < 0.05$;[‡] $P < 0.01$;[§] $P < 0.001$, age adjusted P -value compared with baseline.[¶] P -value of ANCOVA, age adjusted for DM vs. no DM within gender.

Table 3

Multivariate linear regression models showing relationship between appendicular lean mass (ALM) % change over time and diabetes, adjusted for age, physical activity, smoking status, BMI, total body mass change and diabetes-related conditions

	ALM % change over 4 years (SE)	
	Men (n = 1566)	Women (n = 1587)
Diabetes (vs. no diabetes)		
Model 1	−1.380 (0.326) [‡]	−1.387 (0.360) [‡]
Model 2	−0.846 (0.256) [†]	−0.962 (0.289) [‡]
Model 3	−0.783 (0.256) [†]	−0.951 (0.289) [†]

* $P < 0.05$;

[†] $P < 0.01$;

[‡] $P < 0.001$.

Model 1: adjusted for age, Physical Activity Scale of the Elderly(PASE) score, smoker status (never, ex- and current), low ankle–brachial index, stroke, hypertension, heart disease, BMI

Model 2: additionally adjusted for total body mass % change over 4 years.

Model 3: additionally adjusted for PASE score change over 4 years.