Body Composition Is Altered in Pre-Diabetic Patients With Impaired Fasting Glucose Tolerance: Results From the NHANES Survey

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Abstract

Background: Previous studies suggest that type 2 diabetes mellitus (T2DM) is associated with a loss of muscle mass but the impact of fasting blood glucose (FBG) on body composition remains underappreciated in pre-diabetic subjects. The aim of this study was to determine the influence of FBG on lean mass (LM), fat mass (FM) and their distribution (trunk vs. appendicular), separately in middle-aged men and women.

Methods: One thousand nine hundred and eleven (1,911) men (63.9 ± 11.7 years) and 1,977 women (63.7 ± 12.1 years) from the National Health and Nutrition Examination Survey (1999 - 2004) were divided into four groups: normal glucose tolerance (NGT), low impaired fasting glucose (IFG), high IFG and T2DM. Body composition was obtained from dual X-ray absorptiometry (DXA).

Results: Of the patients, 68.7% had NGT, 16.1% low IFG, 9.4% high IFG and 5.8% T2DM. After adjustment for age, body mass index, ethnicity, smoking, alcohol and physical activity (PA), no change in appendicular LM was observed between groups, but significant increases in trunk FM (in both gender) and trunk LM (in women) were found with increased glucose intolerance (T2DM > IFG > NGT), as well as significant decreases in trunk and total LM/FM ratios (T2DM < IFG < NGT) and a significant increase in trunk/appendicular FM ratio (T2DM > IFG > NGT).

Conclusions: Elevated FBG within the normal range is not associated with a significant loss of appendicular LM, but modifications in LM and FM trunk and total distribution with IFG suggest that nutritional and physical lifestyle strategies should be implemented in the pre-diabetic state.

Keywords: Type 2 diabetes mellitus; Body composition; Gender; Insulin resistance; Mobility

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Introduction

Recent studies have questioned about the impact of type 2 diabetes mellitus (T2DM) on muscle mass, but the results remain unclear and the hypothesis that T2DM is responsible for a loss of muscle mass is uncertain [1]. According to some experimental studies, insulin resistance (IR) can alter muscle protein turnover due to a disruption of intracellular insulin signaling pathways [2, 3]. This reduced metabolic response to insulin affects different key components of muscle, including mitochondria, which play a crucial role in energy production and ensure integrity of muscle [4]. Thus, in T2DM patients, IR but also the lack of insulin secretion could contribute to an altered muscle protein synthesis [5], and a progressive reduction of the muscle mass and function, favoring potential subsequent disabilities [6-9].

As part of the clinical routine, fasting blood glucose (FBG) concentrations provide through its large variability among populations a remarkable range of data spanning from normal glycemia to impaired fasting glucose (IFG) to T2DM. It has been demonstrated that higher FBG levels within the normoglycemic range constitute an independent risk factor for T2DM (i.e., subjects with IFG or impaired glucose tolerance (IGT)) [10]. Given that functional disabilities occur twice as often in T2DM patients compared with patients without T2DM [11] and that patients with pre-diabetes have a 10% annual conversion rate to T2DM [12], it seems of clinical interest to question the relationship between blood glucose homeostasis and muscle mass and function. This is particularly interesting since muscle mass and fat mass (FM) are known to act as a diabetogenic duo favoring IR and related cardiometabolic risks [13]. The impact of the glycemic status on body composition and muscle function, however, remains poorly questioned in

pre-diabetic patients.

The Third National Health and Nutrition Examination Survey (NHANES III), representative of the North American population between 1988 and 1994, revealed an inversed relationship between skeletal muscle mass index and IR, glycated hemoglobin and prevalence of pre-diabetes [14]. The NHANES III survey however used bioelectrical impedance analyzers to assess body composition, which remains an indirect method and limits the interpretation of their results. Moreover, although they adjusted their analysis for gender, males and females were pooled. Nevertheless, the sexual dimorphism in lean and fat tissue amount and distribution should be considered. While it appears necessary to conduct deeper and more precise analysis regarding this association between body composition and glucose profile, the 1999 - 2004 NHANES survey provides us with data based on dual X-ray absorptiometry (DXA) scans (as one of the gold standards for the measure of body composition). The aim of the present study was then to question the impact of FBG on total and segmental muscle mass and FM in women and men. We hypothesis that impaired FBG (pre-diabetic stages) leads to altered body composition in adults and that body composition is affected by gender. Thus, we examined the associations between FBG (across a wide spectrum of FBG from normal glucose tolerance (NGT)) to T2DM) and lean and fat tissues (both appendicular and trunk distribution), separately in men and women.

Materials and Methods

Study population

Based on a complex sampling process using the latest census techniques, 31,126 participants representative of the North American population were selected in cross-sectional studies between 1999 and 2004 [15]. Participants provided their written informed consent and the study protocol was approved by the institutional review board of the Centers for Disease Control and Prevention (CDC). The data collected were released for free access by the NHANES researchers and were downloaded from the CDC website.

Sample analysis

We restricted our analysis to NHANES participants (men and women over 45 years of age), whose records had available DXA, FBG measurement, anthropometric data (i.e., gender, age, height, weight and ethnicity), documentation of tobacco and alcohol consumption, and physical activity (PA).

Glycemic status

Based on FBG, our population was divided into four groups following the American Diabetes Association criteria as fol-

lows: 1) NGT (FBG < 5.6 mmol/L) (n = 2,677); 2) low IFG (5.6 ≤ FBG < 6.1 mmol/L) (n = 627); 3) high IFG (6.1 ≤ FBG < 7 mmol/L) (n = 367); and 4) T2DM (FBG ≥ 7 mmol/L) (n = 224) [16]. Because of the heterogeneity of antidiabetic treatments in the NHANES' population, only untreated T2DM were included. IR was expressed by homeostasis model assessment of insulin resistance (HOMA-IR) calculated by the formula HOMA-IR = glycemia (mmol/L) × insulinemia (mUI/L)/22.5 (HOMA-IR > 2.55) [17].

Anthropometric measurement and body composition

Height was measured by experienced technicians according to a standardized protocol. Weight and total body composition were measured by DXA using a Hologic QDR 400A dual photon densitometer (Hologic, Bedford, MA, USA). The DXA results were analyzed using Hologic Discovery software version 12.1 (Hologic), with a validity and reproducibility protocol previously reported [9, 18]. The body was segmented into two regions: trunk and limbs. For each region, FM and fat-free mass (FFM) were measured, with the sum of the two representing the total weight of the region. Then, bone mineral content was subtracted from FFM to define non-bone lean mass (LM). Trunk LM was calculated as the sum of trunk muscle mass and trunk visceral mass. Appendicular LM was calculated as the sum of lean soft tissue mass (fat-free, non-bone) in the arms and legs, which represents skeletal muscle mass of the limbs.

Covariate adjustments

The other characteristics analyzed included age (years) and ethnicity (Caucasian, African American, Hispanic or multiethnic). Smoking status (daily smoker, occasional or non-smoking), alcohol consumption (g/day) and PA (h/day) were also considered as potential confounders. PA was assessed using standardized questionnaires that catalogue daily household and sporting activities, which were then classified into three groups according to their intensity (low: < 3 metabolic equivalent of the task (MET); moderate: 3 - 6 METs; and vigorous: > 6 METs) to obtain the number of hours per day at each level of intensity [19].

Muscle function

The impact of FBG on muscle function was assessed by the time to complete a 20-foot walk. The walking time as a function of leg LM was also calculated [20].

Statistical analyses

Statistical analysis was performed using Stata software, version 13 (StataCorp, College Station, TX, USA). The tests were two-sided, with a type I error set at α = 0.05. Patient's char-

Table 1. Characteristics of All Participants in Men

Men	NGT (n = 1,223)	Low IFG (n = 330)	High IFG (n = 228)	T2DM (n = 130)	P-value
Age (years)	63.0 ± 11.9^b	64.9 ± 12.0^a	66.7 ± 11.5^a	$64.8 \pm 10.3^{a,b}$	< 0.0001
Height (cm)	173.4 ± 7.6	173.4 ± 7.6	173.0 ± 7.4	172.7 ± 7.5	NS
Weight (kg)	83.3 ± 16.0^c	$84.5 \pm 16.1^{b,c}$	87.4 ± 19.3^b	88.5 ± 18.0^a	< 0.0001
Body mass index (kg/m^2)	27.6 ± 4.5^c	28.0 ± 4.5^c	29.1 ± 5.7^b	29.7 ± 5.6^a	< 0.0001
Waist circumference (cm)	100.6 ± 12.2^c	102.3 ± 12.1^b	105.4 ± 14.2^a	106.4 ± 12.5^a	< 0.0001
Fasting blood glucose (mmol/L)	5.03 ± 0.4^d	5.81 ± 0.1^c	6.4 ± 0.3^b	9.3 ± 2.4^a	< 0.0001
HbA1c (%)	5.42 ± 0.4^d	5.6 ± 0.5^c	5.8 ± 0.6^b	7.5 ± 2.0^a	< 0.0001
Alcohol (g/day)	11.6 ± 25.4^a	10.8 ± 22.6^a	13.3 ± 29.3^a	5.7 ± 15.2^b	0.0002
Physical activity (PA) (h/day)					
Low intensity PA (h/day)	2.8 ± 1.6	2.8 ± 1.6	2.8 ± 1.8	2.9 ± 1.6	NS
Moderate intensity PA (h/day)	0.6 ± 1.2	0.5 ± 1.1	0.6 ± 1.2	0.6 ± 1.3	NS
Vigorous intensity PA (h/day)	0.1 ± 0.4	0.1 ± 0.3	0.1 ± 0.2	0.1 ± 0.5	NS
Ethnicity, n (%)					
Hispanic and other	325 (26.5)	99 (30.0)	63 (27.6)	45 (34.6)	0.002
Non-Hispanic White	707 (57.8)	197 (59.7)	130 (57.0)	64 (49.2)	0.001
Non-Hispanic Black	191 (15.7)	34 (10.3)	35 (15.4)	21 (16.2)	0.005
Smoking status, n (%)					
Current smoker	244 (20.0)	52 (15.8)	32 (14.0)	19 (14.6)	0.021
Occasionally	30 (2.5)	8 (2.4)	7 (3.1)	5 (3.8)	NS
Never smoker	949 (77.5)	270 (81.8)	189 (82.9)	106 (81.6)	NS
Insulin (μU/mL)	9.2 ± 6.8^c	12.0 ± 7.7^c	14.9 ± 10.3^b	20.1 ± 17.4^a	< 0.0001
HOMA-IR	2.1 ± 1.6^c	3.1 ± 2.0^c	4.3 ± 3.1^b	8.0 ± 7.1^a	< 0.0001
CRP (mg/dL)	0.4 ± 0.7	0.5 ± 1.1	0.6 ± 1.2	0.6 ± 1.4	NS

Data are mean with standard deviation or n with percentage in brackets. Groups marked with different letters (a, b, c, d) are significantly different from each other by a Tukey-Kramer pairwise comparison (P < 0.05). Groups marked with the same letters are not significantly different from each other. WC: waist circumference; FBG: fasting blood glucose; PA: physical activity; HOMA-IR: homeostasis model assessment of insulin resistance; CRP: C-reactive protein.

acteristics were presented as the mean ± standard deviation according to statistical distribution (assumption of normality assessed by using the Shapiro-Wilk test) and as the number of patients and associated percentages for categorical parameters. Comparisons between groups (NGT, low IFG, high IFG, and T2DM) were performed using the Chi-squared or Fisher's exact test for categorical variables, and ANOVA or Kruskal-Wallis test when assumptions of ANOVA were not met (normality and homoscedasticity studied by Bartlett test) for quantitative parameters. When appropriate (omnibus P-value < 0.05), a *post hoc* test for multiple comparisons was applied to take into account inflate of type I error: Tukey-Kramer test post ANOVA and Dunn after Kruskal-Wallis. The study of relationships between quantitative parameters was analyzed using correlation coefficients (Pearson or Spearman according to statistical distribution). Finally, multivariate analyses were performed by linear models using covariates determined according to univariate results and clinical relevance: age, BMI, ethnicity, alcohol and tobacco consumption, and PA. When appropriate (normality of residuals was not verified), a logarithmic transformation was proposed to achieve normality of

dependent variables.

Results

Population characteristics

The characteristics of the whole population are presented in Table 1 for men (n = 1,911), and Table 2 for women (n = 1,977). Mean BMI was 28.8 ± 5.8 kg/m^2 for women and 27.9 ± 4.7 kg/m^2 for men. Of the samples, 68.7% had NGT and 31.3% had abnormality of glucose regulation: 16.1% had low IFG, 9.4% had high IFG, and 5.8% had T2DM. Both in men and women, patients with T2DM and IFG had significantly higher BMI than those with NGT (P < 0.05). HOMA-IR significantly increases (from NGT to T2DM group) in both men and women (P < 0.05). Alcohol consumption did not differ between groups among women, while in men, T2DM group consumed less alcohol (P < 0.05). In women, low-intensity PA increases with FBG (P < 0.05), while moderate and vigorous PA decreases

Table 2. Characteristics of All Participants in Women

Women	NGT (n = 1,448)	Low IFG (n = 296)	High IFG (n = 139)	T2DM (n = 94)	P-value
Age (years)	62.8 ± 12.1[b]	65.6 ± 12.1[a]	67.0 ± 11.8[a]	66.6 ± 10.3[a]	< 0.0001
Height (cm)	159.8 ± 7.0	159.7 ± 6.5	158.3 ± 7.6	159.2 ± 7.5	NS
Weight (kg)	72.4 ± 16.7[c]	76.5 ± 17.7[b]	77.5 ± 18.0[a,b]	78.4 ± 18.0[a]	< 0.0001
Body mass index (kg/m^2)	28.3 ± 6.0[c]	29.9 ± 6.3[b]	30.8 ± 6.3[a]	30.8 ± 5.6[a]	< 0.0001
Waist circumference (cm)	94.1 ± 13.6[c]	98.9 ± 13.5[b]	101.7 ± 13.2[a]	103.1 ± 12.5[a]	< 0.0001
Fasting blood glucose (mmol/L)	5.0 ± 0.4[d]	5.80 ± 0.1[c]	6.44 ± 0.3[b]	9.4 ± 2.7[a]	< 0.0001
HbA1c (%)	5.4 ± 0.3[d]	5.6 ± 0.4[c]	5.9 ± 0.5[b]	7.4 ± 2.0[a]	< 0.0001
Alcohol (g/day)	3.6 ± 12.1	3.9 ± 13.2	3.8 ± 15.1	5.1 ± 18.9	NS
Physical activity (PA) (h/day)					
Low intensity PA (h/day)	2.8 ± 1.6[b]	3.0 ± 1.6[b]	3.0 ± 1.6[b]	2.9 ± 1.6[a]	< 0.0001
Moderate intensity PA (h/day)	0.5 ± 0.9[a]	0.4 ± 0.8[a]	0.4 ± 1.0[a]	0.6 ± 1.3[b]	< 0.01
Vigorous intensity PA (h/day)	0.08 ± 0.27[a]	0.1 ± 0.3[b]	0.03 ± 0.14[b,c]	0.02 ± 0.07[c]	< 0.05
Ethnicity, n (%)					
Hispanic and other	398 (27.5)	77 (26.0)	51 (36.7)	31 (33.0)	< 0.0001
Non-Hispanic White	827 (57.1)	171 (57.8)	64 (46.0)	37 (39.3)	< 0.0001
Non-Hispanic Black	223 (15.4)	48 (16.2)	24 (17.3)	26 (27.7)	0.001
Smoking status, n (%)					
Current smoker	186 (12.9)	52 (15.8)	32 (14.0)	19 (14.6)	NS
Occasionally	27 (1.9)	8 (2.4)	7 (3.1)	5 (3.8)	NS
Never smoker	1235 (85.2)	270 (81.8)	189 (82.9)	106 (81.6)	NS
Insulin (µU/mL)	9.2 ± 6.8[c]	13.9 ± 8.8[b]	16.0 ± 9.0[b]	21.9 ± 17.0[a]	< 0.0001
HOMA-IR	2.1 ± 1.6[c]	3.6 ± 2.3[b]	4.6 ± 2.6[b]	9.2 ± 7.8[a]	< 0.0001
CRP (mg/dL)	0.4 ± 0.7[b]	0.6 ± 0.8[b]	0.7 ± 0.9[a,b]	0.8 ± 0.9[a,b]	< 0.01

Data are mean with standard deviation or n with percentage in brackets. Groups marked with different letters (a, b, c, d) are significantly different from each other by a Tukey-Kramer pairwise comparison (P < 0.05). Groups marked with the same letters are not significantly different from each other. WC: waist circumference; FBG: fasting blood glucose; PA: physical activity; HOMA-IR: homeostasis model assessment of insulin resistance; CRP: C-reactive protein.

with FBG (P < 0.05). In men, there is no significant variation in PA between groups.

FM and LM distribution

Univariate analysis of body composition parameters is presented in Table 3 for men and women.

Multivariate analyses are presented in Figure 1 for men and Figure 2 for women. For men, appendicular LM and FM did not differ between groups. For women, appendicular LM did not differ but appendicular FM is higher in IFG groups compared to NGT and T2DM groups (P < 0.05), and higher in T2DM group compared to NGT group (P < 0.05). Concerning trunk, trunk FM is higher in high IFG and T2DM groups compared to NGT group (P < 0.05), in both men and women. In women, trunk LM is higher in IFG and T2DM groups compared to NGT group (P < 0.05). As a consequence of these results, in men, LM/FM ratios are significantly lower in high IFG and T2DM groups compared to NGT group for both trunk

(P < 0.05) and total ratios (P < 0.05). In women, the trunk and total LM/FM ratios are not significant between groups. Although the results show lower appendicular LM/FM ratios in IFG groups compared with NGT in women, this remains non-significant. In both genders, trunk/appendicular FM ratios are higher in high IFG and T2DM groups compared to NGT group (appendicular FM increases more slowly with FBG than trunk FM).

Muscle function

There is no significant difference in the absolute walking time to complete 20 feet between groups in men (6.7 ± 2.9 s for NGT, 6.7 ± 2.2 s for low IFG, 6.9 ± 2.4 s for high IFG and 6.9 ± 2.3 s for T2DM; P = 0.87), nor women (7.1 ± 3.6 s for NGT, 7.5 ± 3.9 s for low IFG, 7.7 ± 3.1 s for high IFG and 7.9 ± 3.6 s for T2DM; P = 0.31), neither using multivariate analysis. The walking time relative to leg LM was also not significant between groups in both men

Table 3. Fat Mass and Lean Mass Distribution for Each Group, Non-Adjusted for Covariates

	NGT	Low IFG	High IFG	T2DM
Men				
Appendicular LM (kg)	24.6 ± 4.4[a]	24.4 ± 4.4[a]	24.4 ± 5.1[a]	24.6 ± 5.0[a]
Appendicular FM (kg)	10.3 ± 3.5[b]	10.6 ± 3.6[a,b]	11.3 ± 4.0[a]	11.3 ± 3.9[a]
Trunk LM (kg)	27.9 ± 4.4[b]	28.3 ± 4.3[a,b]	28.7 ± 5.1[a,b]	29.2 ± 4.9[a]
Trunk FM (kg)	13.3 ± 5.1[b]	14.1 ± 5.2[b]	15.7 ± 6.0[a]	16.1 ± 5.5[a]
Total LM (kg)	55.9 ± 8.8[a]	56.1 ± 8.8[a]	56.6 ± 10.3[a]	57.3 ± 9.8[a]
Total FM (kg)	24.8 ± 8.4[b]	25.9 ± 8.6[b]	28.2 ± 9.9[a]	28.6 ± 9.1[a]
Trunk/appendicular FM	1.3 ± 0.3[b]	1.3 ± 0.2[b]	1.4 ± 0.3[a]	1.4 ± 0.3[a]
Appendicular LM/FM	2.6 ± 0.7[a]	2.5 ± 0.6[a,b]	2.3 ± 0.6[b]	2.3 ± 0.6[b]
Trunk LM/FM	2.4 ± 0.9[a]	2.2 ± 0.7[b]	2.0 ± 0.8[b]	2.0 ± 0.6[c]
Total LM/FM	2.4 ± 0.7[a]	2.3 ± 0.6[a,b]	2.2 ± 0.6[b]	2.1 ± 0.5[b]
Women				
Appendicular LM (kg)	16.6 ± 3.6[b]	17.0 ± 3.7[a]	17.22 ± 3.9[a]	17.6 ± 4.4[a]
Appendicular FM (kg)	14.9 ± 5.4[b]	16.0 ± 5.6[a]	16.20 ± 5.8[a]	15.7 ± 6.2[a,b]
Trunk LM (kg)	20.3 ± 3.3[b]	21.1 ± 3.5[a]	21.20 ± 3.6[a]	21.8 ± 3.6[a]
Trunk FM (kg)	14.7 ± 5.7[b]	16.5 ± 5.9[a]	17.13 ± 5.6[a]	17.3 ± 5.6[a]
Total LM (kg)	39.7 ± 6.8[b]	41.0 ± 7.3[a]	41.29 ± 7.6[a]	42.4 ± 8.0[a]
Total FM (kg)	30.7 ± 10.6[b]	33.6 ± 11.1[a]	34.78 ± 11.0[a]	34.1 ± 11.2[a]
Trunk/appendicular FM	1.0 ± 0.2[c]	1.0 ± 0.2[b]	1.09 ± 0.2[a,b]	1.1 ± 0.3[a]
Appendicular LM/FM	1.2 ± 0.3[a]	1.1 ± 0.3[b]	1.14 ± 0.3[a,b]	1.2± 0.3[a]
Trunk LM/FM	1.5 ± 0.6[a]	1.4 ± 0.4[b]	1.33 ± 0.4[b]	1.3 ± 0.3[b]
Total LM/FM	1.4 ± 0.4[a]	1.3 ± 0.3[b]	1.27 ± 0.3[b]	1.3 ± 0.3[a,b]

Data are mean with standard deviation, non-adjusted for covariates. Groups marked with different letters (a, b, c) are significantly different from each other by a Tukey-Kramer pairwise comparison (P < 0.05). Groups marked with the same letters are not significantly different from each other. LM: lean mass; FM: fat mass.

and women.

Discussion

The present study assessed the association between appendicular and trunk body composition and FBG levels, across a wide spectrum from NGT to T2DM in North American middle-aged men and women studied separately. After adjustment for age, BMI, ethnicity, smoking, alcohol and PA, our results show: 1) no change in appendicular LM and muscle function with the degree of glucose impairment, in both genders; 2) a significant increase in trunk FM with FBG in both genders, associated with a significant increase in trunk LM in women; 3) reduced total and trunk LM/FM ratios with FBG (significant in men but not significant in women); and 4) a significant increase in trunk/appendicular FM ratio with FBG in both genders (higher trunk FM increase compared with appendicular FM).

Overall, the present data suggest that hyperglycemia is not responsible for significant appendicular muscle modifications (neither mass nor function) in patients with pre-diabetes or T2DM. This result is consistent with a recent prospective 11-year follow-up study conducted in older adults (between 70 and 79 years old), which also missed to find association between the incidence of T2DM and muscle mass and strength, with adjusted models [21]. In the same study, unadjusted models indicate that total LM, thigh muscle areas and strength measures were associated with higher risk of T2DM, which was explained by the fact that LM is often associated with more body FM [21]. Furthermore, another recent study demonstrated that HbA1c, a marker of chronic hyperglycemia, is not related to the decreased skeletal LM and that the decrease in muscle strength may be due to other factors distinct from hyperglycemia [22]. These results are however not in line with some other previous ones suggesting that T2DM is associated with decreased muscle mass and muscle performances [6-9, 23, 24]. One of the strengths of the present study relies in the median age of 65 years, which is 10 years younger on average than subjects considered in many of these studies [6, 8, 9, 24]. Consequently, although we acknowledge that there is a physiological evidence that IR can alter muscle protein synthesis, there is a discrepancy concerning the link between glycemic status and clinical loss of muscle mass and function.

Another important result of the present study is the increase in trunk LM with FBG, which has previously been reported [7]. Trunk LM primarily represents visceral mass (i.e.,
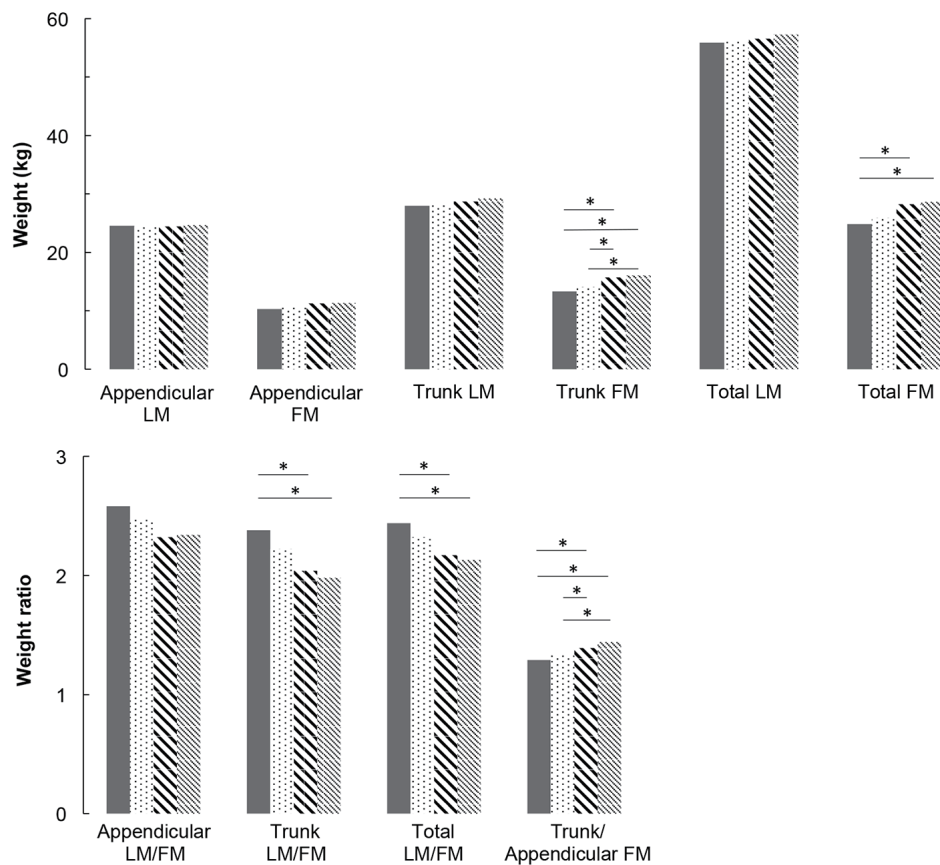
Figure 1. Lean mass and fat mass distribution adjusted for covariates (age, height, weight, ethnicity, physical activity, smoking and alcohol consumption) for men. * means that groups are significantly different from each other by a Tukey-Kramer pairwise comparison (P < 0.05).

kidneys, liver, pancreas and intestine). Early pancreatic (islet cells) and renal adaptive hypertrophy (proximal tubular and glomerular cells) are now well established in T2DM (based on both animal and human experiments) [25-28]. Chronic hyperglycemia is also associated with increased small intestinal enterocyte mass, supporting an important role of the small intestine in gluconeogenesis and the physiopathology of T2DM, as kidney and liver [29-31]. Further human studies using tomodensitometry measures are today necessary to identify the origin and the role of this increased trunk LM, which seems to occur particularly early in women.

As the trunk LM/FM ratio decreases in IFG compared to NGT groups, the present study demonstrates that the increase in trunk FM is more important than the increase in trunk LM. This modification in trunk composition begins in a pre-diabetes stage and may occur through IR, as visceral adiposity is positively associated with IFG and newly diagnosed T2DM [32]. Indeed, in the present study, IR was observed in both men and women of the IFG groups, with a significant increase in HOMA-IR from NBG subjects to subjects with T2DM. Aging and low-grade systemic inflammation (CRPus) that increase with FBG, are well-known factors associated with decreased muscle protein anabolism [33, 34]. In the present study, trunk/appendicular FM ratio significantly increases with FBG, in

other words, trunk FM increases more than appendicular FM. These results are consistent with previously published ones showing an independent association between glucose levels [35] and cardiovascular risks [36] with both higher trunk FM and lower appendicular FM.

The observed decreased total LM/FM ratio may advertise for ulterior functional consequences of T2DM, particularly given the stagnation of appendicular LM during the deterioration of glucose homeostasis [8, 9]. Moreover, although this was not significant in the present study, we observed an increasing time to complete the 20 feet walk with FBG. Indeed, it is well established that velocity is an important predictor of disability and mortality [20]. It has also previously been well demonstrated that skeletal muscle strength is an independent predictor of morbi-mortality [37], regardless of whether this loss is rapid or occurs over several years [38-40]. Given that trunk and total FM increase with FBG without increased appendicular LM, potential later functional impairments and cardiovascular diseases justify the introduction of preventive strategies [41], including nutrition counseling and exercise training, to maintain total muscle mass and decrease fat mass, prior to the onset of T2DM.

We acknowledge that this study has several limitations. First, as with any cross-sectional study, our data demonstrate
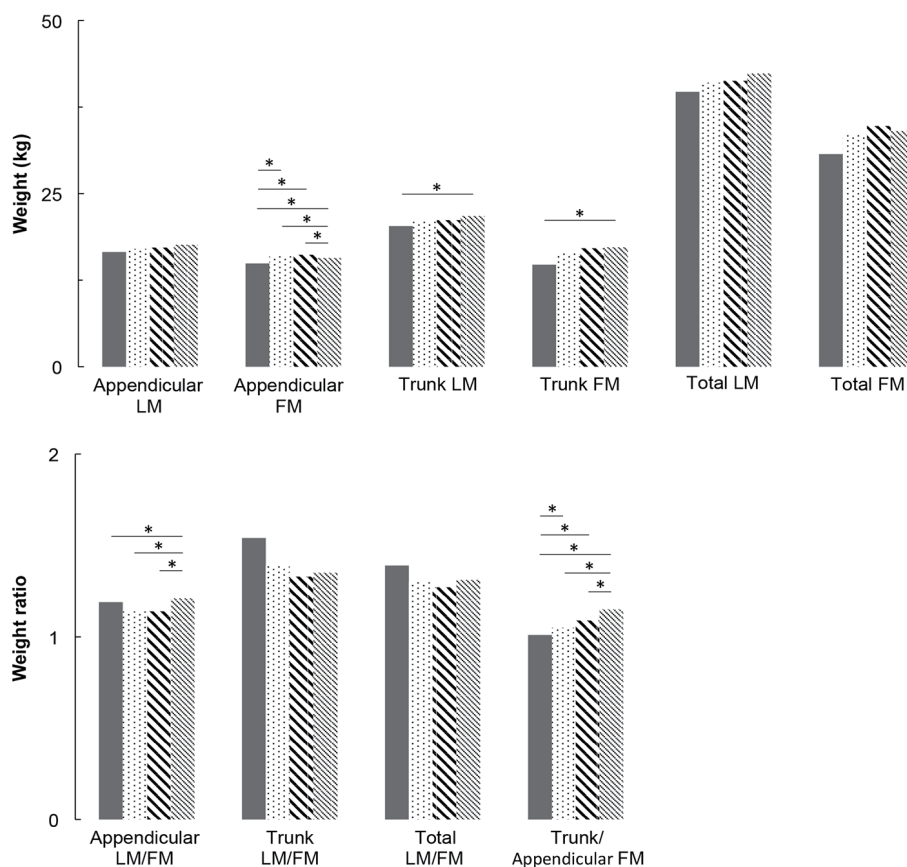
Figure 2. Lean mass and fat mass distribution adjusted for covariates (age, height, weight, ethnicity, physical activity, smoking and alcohol consumption) for women. * means that groups are significantly different from each other by a Tukey-Kramer pairwise comparison (P < 0.05).

associations but cannot prove direct effect and causal relationships. Second, the effects of other modifiers of body composition, such as hormonal status in women (premenopausal vs. postmenopausal), other chronic diseases associated with T2DM and nutritional status were not considered and may explain part of the observed results and the difference between men and women. However, in view of the mean age of our women sample, the majority were likely post-menopausal women. Further studies should investigate the role of gender on body composition because gender-related metabolic changes have previously been described between men and women [42]. Finally, as DXA measures are not able to discriminate all tissue compartments, in particular intra-abdominal versus subcutaneous tissue, coming studies may use computed tomography and magnetic resonance spectroscopy to understand the real metabolic impact of such body composition changes.

Using a large sample size (3,888 middle-aged participants) and based on objective measurements for body composition (DXA scans), the present study demonstrates that appendicular LM is maintained while trunk and total FM increase in subjects with pre-diabetes compared with NGT. Further studies are needed to question the effects of PA on the evolution of trunk LM and on trunk LM/FM ratio, in particular as soon as the pre-diabetic state begins, in order to counteract the development of progressive metabolic disorders and functional impairments, by combining nutritional and physical interventions.

Competing Interests

The authors declare that they have no competing interests.

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