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Body composition and lung function in cystic fibrosis: association with adiposity and normal weight obesity

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Abstract

Objectives—This study aimed to evaluate the relationship between lung function and body composition in cystic fibrosis (CF) and examine the presence of normal weight obesity (NWO), a high body fat percentage with a normal body mass index (BMI), in this population.

Research Methods & Procedures—In a pilot, cross-sectional study, 32 subjects with CF and a reference group of 20 adults without CF underwent body composition analysis with air displacement plethysmography. NWO was defined as a BMI <25 kg/m² and body fat >30% (women) or >23% (men). Lung function in subjects with CF was determined by the percentage of predicted forced expiratory volume in 1 second (FEV1% predicted).

Results—Despite lower BMI and fat-free mass index ($P<0.01$), fat mass index and percent body fat did not differ between CF subjects and the reference group. Among CF subjects, FEV1% predicted was positively associated with fat-free mass index ($\beta=6.31 \pm 2.93$, $P=0.04$) and inversely

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associated with fat mass index ($\beta = -6.44 \pm 2.93$, $P=0.04$), after adjusting for age, gender and BMI. Ten CF subjects (31%) had NWO, which corresponded with lower fat-free mass index and FEV1% predicted compared to overweight subjects ($P=0.006$ and 0.004 , respectively).

Conclusions—Excess adiposity, particularly in the form of NWO, was inversely associated with lung function in CF. Larger prospective studies should confirm these findings and determine the long-term metabolic and clinical consequences of excess adiposity in CF. As the lifespan of individuals with CF increases, nutrition screening protocols, which primarily rely on BMI, may require re-assessment.

Keywords

cystic fibrosis; body composition; obesity; diet; normal weight obesity; lung function

INTRODUCTION

As the median survival rate in patients with cystic fibrosis (CF) increases, it becomes increasingly important to identify targets for maintenance of optimal health in this aging population. Given the key role of malnutrition in the progression of CF lung disease, maintenance of adequate nutritional status, typically defined as a body mass index (BMI) goal, has been a conventional target for improved health outcomes in CF¹. However, BMI simply reflects body size (kg/m^2) and does not distinguish between the major metabolically active components of body composition (fat mass and fat-free mass). Independent of BMI or body weight, numerous studies in individuals with CF have described a preferential depletion of fat-free mass, which is associated with indexes of disease severity, including reduced lung function, increased pulmonary exacerbations, and increased inflammation²⁻⁵. Therefore, studies of body composition in CF may be more informative than use of BMI alone as a measure of optimal health.

Nutritional interventions in CF are often targeted at increasing or maintaining BMI with high-fat/high-protein diets. However, the impact of such unrestricted, high-calorie diets on body composition in adults with CF is unclear. It has been suggested that aggressive nutrition support in CF primarily restores fat mass, as opposed to fat-free mass⁵. As inflammation and an oxidative environment have been shown *in vitro* to promote adipogenesis^{6,7}, it is possible that there is preferential energy partitioning towards fat mass gain in CF driven by concomitant systemic inflammation and/or redox imbalance.

In non-CF populations, adiposity is inversely associated with lung function^{8,9}. Reports of obesity within CF populations are beginning to emerge¹⁰⁻¹². For example, an analysis of BMI trends over the past three decades showed an increase in the prevalence of overweight and obesity (from 7% to 18%) in a Toronto adult CF center¹², with a Pittsburgh pediatric CF center reporting a prevalence of up to 23%¹¹. Whether the increase in obesity prevalence has negative effects on CF morbidity is unknown; however, both overweight status and obesity are associated with increased lipid concentrations in CF¹². Furthermore, there may be a threshold above which BMI is not positively associated with lung function¹². Recently, the term normal weight obesity (NWO) has been introduced to describe the paradoxical presence of a normal weight BMI classification with a concomitant high body fat

percentage¹³. This NWO phenotype is associated with increased cardio-metabolic risk in the general population^{14,15}; however, the prevalence and clinical impact of NWO in CF is unknown.

This pilot study aimed to examine the relationship between body composition and lung function in older adolescents and adults with CF, with a specific focus on characterizing normal weight obesity in this population.

SUBJECTS AND METHODS

Study subjects

Participants were recruited as part of a parent study designed to investigate potential causes of CFRD¹⁶. Participants in the current cross-sectional analysis were 32 clinically-stable subjects with CF and a reference group of 20 non-CF subjects with available body composition data. The Emory Institutional Review Board approved the study; all participants provided written informed consent or assent, as applicable. Participants with CF were recruited during Emory CF clinic visits. Inclusion criteria for CF subjects were: age 16 yrs, confirmed CF diagnosis, and no pulmonary exacerbations within the past month. Exclusion criteria were: use of systemic glucocorticoids, pregnancy, chronic illness other than CF requiring chronic medications, chronic oxygen therapy, or post-lung transplant. Participants in the reference group were recruited as part of the parent study and consisted of healthy, non-CF volunteer students and employees at the CF center. Exclusion for the reference group were chronic illness requiring prescription medications and no acute illness in the prior three weeks of the study. Testing was conducted in the Emory University Hospital Clinical Research Network (CRN) unit of the Atlanta Clinical and Translational Science Institute (formerly General Clinical Research Center).

Body Composition

Body composition was assessed using the two-component model using air displacement plethysmography (BOD-POD®, Life Measurement Instruments, Concord, CA) with subjects wearing a bathing suit and a swim cap. Thoracic gas volume was directly measured and used for the calculation of total body volume and subsequent body density (density = mass ÷ total body volume). Percent body fat was calculated using the Siri equation¹⁷, and subsequently used to determine fat mass (kg) and fat-free mass (kg). To account for variations in stature, height-normalized indexes were determined for fat mass and fat-free mass (kg fat mass or fat-free mass ÷ height (m)²)¹⁸.

Height was measured without shoes to the nearest 0.1 cm with a manual stadiometer. Weight was measured to the nearest 0.1 kg with the BOD-POD system. BMI was calculated as kg/m². Participants with a BMI < 25, 25-29.9, and ≥ 30 kg/m² were classified as normal weight, overweight, and obese, respectively. NWO was defined as a normal weight BMI (<25 kg/m²) and % body fat >30% in women and >23% in men, according to published cut-points¹⁴. Normal weight participants with a % body fat ≥ 30% and 23% in women and men, respectively, were classified as lean.

Clinical, Analytical, and Dietary Outcomes

Clinical data, such as genotype and exocrine pancreatic sufficiency status, were obtained from the CF Patient Registry maintained by the Cystic Fibrosis Foundation. Lung function in CF subjects was assessed on the day of the study visit using conventional spirometry methods and American Thoracic Society standards. We report the percentage of predicted forced expiratory volume in 1 second (FEV₁% predicted) using the National Health and Nutrition Examination Survey as the reference population¹⁹. Lung function status was categorized based on FEV₁% predicted as moderate (<59%), mild (60-79%), or normal (≥ 80%). Dietary supplement intake was obtained through self-report or extracted from electronic medical records.

Glucose tolerance was determined with an oral glucose tolerance test (OGTT) after an overnight fast. Following a fasted blood draw, an oral glucose solution was administered (1.75 g/kg body weight to a maximum of 75 g), and subsequent blood drawn two hours later. Plasma glucose assays were performed using a standard glucose analyzer (Cardiovascular Specialty Laboratories, Atlanta, GA). According to American Diabetes Association guidelines, subjects were categorized as having normal glucose tolerance (fasting plasma glucose [FPG] < 5.56 mmol/L and 2 hour plasma glucose < 7.78 mmol/L), prediabetes (impaired fasting glucose with FPG 5.6 - 6.9 mmol/L, and/or impaired glucose tolerance with 2 hour plasma glucose 7.8 –11.0 mmol/L), or diabetes (FPG ≥ 7.0 mmol/L and/or 2 hour plasma glucose ≥ 11.1 mmol/L). Fasting plasma interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-α (TNF-α) were assayed using a Bio-Plex® multiplex system (Bio-Rad Laboratories Inc., Hercules, CA).

Three-day food records, consisting of two weekdays and one weekend day, were analyzed by a registered dietitian using the Nutrition Data System for Research software (Nutrition Coordinating Center, University of Minnesota, MN, database version 2013). Reported food intake was evaluated as a percentage of the Institute of Medicine's Dietary Reference Intakes (DRI) for energy (calculated based on a physical activity coefficient of 1.0 and individual sex, age, height, and weight) and protein (0.85 g/kg for adolescents, 0.8 g/kg for adults)²⁰. Dietary data was not available for two subjects with CF. Detailed diet intake data of CF subjects are provided in the Supplemental Data.

Statistical Methods

Descriptive statistics were performed on all variables. Differences between the CF and reference groups were determined with a two-group t-test or Fisher's exact test, as appropriate. The relationship of FEV₁% (dependent variable) with individual body composition factors (independent variable) was assessed, in separate models, using multiple linear regression analysis with age (as a continuous variable) and gender as covariates. BMI, as a continuous variable, was added as a covariate in the models for fat mass, fat-free mass, and their respective indices. Clinical and metabolic differences between the weight categories among CF subjects were determined using analysis of variance (ANOVA) with Tukey's post-hoc comparisons or the Kruskal-Wallis test if the data were not normally distributed (IL-6, IL-8, and TNF-α). Analyses were performed in JMP version 10 (SAS, Cary, NC) using two-sided tests with an alpha significance value of 0.05.

RESULTS

Demographic, clinical, and body composition characteristics of CF subjects and the non-CF reference group are shown in **Table 1**. Among the CF subjects, 44% had normal glucose tolerance, 19% had prediabetes, and 38% had CF-related diabetes. All but one CF subject had pancreatic insufficiency, 84% had at least one F508 mutation, and 82% supplemented with a general multivitamin or a multivitamin with a water-miscible formulation. The majority of CF subjects were classified as having normal lung function (62.5%); 25% and 12.5% of subjects had moderate/severe or mild lung function, respectively. The CF and reference groups did not differ in age or gender, although a higher proportion of CF subjects were Caucasian and had glucose intolerance. Height, body weight, BMI, fat-free mass, and fat-free mass index were each significantly lower in CF subjects compared to the reference group (t-test $P = 0.01$ for each). Despite lower height and BMI, there were no significant differences in fat mass, fat mass index, or percent body fat between CF subjects and the reference group.

Association between body composition and lung function in CF

In multiple linear regression analysis, after adjusting for age and gender, FEV₁% predicted was significantly and positively associated with body weight, BMI, fat mass, fat mass index, fat-free mass, and fat-free mass index (**Table 2**). After additional adjustment for BMI (**Table 2, model 2**), the positive relationships of FEV₁% predicted with fat-free mass and fat-free mass index (**Figure 1A**) remained statistically significant, and fat mass was no longer significantly associated with FEV₁% predicted. In contrast, both % body fat (**Figure 1B**) and fat mass index (**Figure 1C**) were significantly inversely associated with FEV₁% predicted after additional adjustment for BMI.

Normal weight obesity in CF

Approximately 31% of participants with CF were categorized as having NWO, and this was similar to the prevalence of NWO among the reference group (**Table 1**). Key differences in body composition within each weight category (lean, NWO, and overweight/obese) in CF subjects are highlighted in **Figure 2 (A-D)**. By definition, the overweight/obese CF subjects exhibited a higher BMI than the lean and NWO groups, and percent body fat was lower in the lean group compared to the NWO and overweight/obese groups (**Figure 2A and B**). Fat mass index increased across CF weight categories (**Figure 2C**). Fat-free mass index was lowest in the NWO group with statistically significant differences between the NWO and the overweight/obese group (**Figure 2D**). FEV₁% was lowest in the NWO group (FEV₁% mean $\pm$ SD: 66.2 $\pm$ 19.2, 81.5 $\pm$ 19.4, and 101.0 $\pm$ 12.3% in NWO, lean, and overweight/obese groups, respectively), with statistically significant differences between the NWO and the overweight/obese group ($P=0.003$, **Figure 2E**).

Additional clinical characteristics within the three body composition categories are presented in **Table 3** for CF subjects. There were no statistically significant differences in age, sex, height, CF mutation, glucose tolerance categories, or pro-inflammatory cytokines between the body composition groups. The median age of CF diagnosis was higher in the overweight/obese group, although the difference was not statistically significant ($P = 0.14$).

Multivitamin or high-calorie supplement intake did not differ between the CF groups. Three-day food records indicated no statistically significant differences in mean daily energy and macronutrient intake between body composition categories (**Supplemental Data**), although the percentage of recommended DRI for protein intake was highest in the NWO group (mean $\pm$ SD: 307.7 ± 121.1 , 228.7 ± 54.4 , and $168.2 \pm 43.0\%$ in NWO, lean, and overweight/obese groups, respectively), with statistically significant differences between the NWO and the overweight/obese group.

DISCUSSION

Body composition analyses in this single-center CF cohort of adolescents and adults in the American Southeast indicated that greater adiposity was independently associated with reduced lung function. Furthermore, approximately one-third of our subjects with CF were identified as having NWO, which was associated with diminished lung function and a lower fat-free mass index compared to overweight/obese CF subjects. These outcomes would not have been identified using BMI as the sole indicator of nutritional status, which suggests the importance of directly measuring body composition in CF patients.

Our data confirm previous studies reporting positive, independent relationships between fat-free mass and CF lung function^{2,5,21,22}. To our knowledge, the inverse relationship between adiposity and lung function has not previously been described in CF. Additional body composition studies in CF have reported either no relationship^{21,22} or a positive relationship²³ between adiposity and lung function, although previous studies have focused on younger aged subjects compared to our cohort. The negative associations of excess adiposity on lung function have been described in the non-CF literature^{8,9,24} and may reflect a restrictive mass loading effect on the thorax and upper abdomen created by adipose tissue accumulation, pro-inflammatory effects of adipose tissue, and/or general physical deconditioning²⁴. Our finding of diminished lung function in the NWO group relative to the overweight/obese group indicate that excess adiposity, coupled with low fat-free mass, may be particularly detrimental to lung function in individuals with CF. This study and others highlight the need to focus improvements in lean tissue mass, as opposed to weight and BMI, when providing clinical nutrition support to patients with CF.

Compared to the general population, adults with CF have known differences in body composition. Although CF subjects in this study exhibited lower BMI and fat-free mass index, measures of adiposity (fat mass index, percent body fat) did not differ from the non-CF reference subjects, thus reflecting a discordance between body fat and fat-free mass in CF. Previous studies have investigated the concept of a preferential depletion of fat-free mass in CF^{2,3,5}. A chronic catabolic state leading to fat-free mass depletion in CF may be attributed to multiple factors, including enhanced proteolysis due to recurrent infection and inflammation²⁵, increased energy requirements²⁶, defects in insulin secretion and insulin sensitivity²⁷, and/or negative protein and/or energy balance due to intestinal malabsorption. Underlying metabolic pathways discriminating between the three body composition categories we defined in CF subjects (lean, NWO, overweight/obese) require further investigation. It is possible that NWO in CF is a variant of sarcopenic obesity identified in cancer and other catabolic diseases²⁸. The similar pro-inflammatory cytokine concentrations

and glucose tolerance between body composition groups suggest that additional, independent factors are responsible for the body composition differences observed. For example, excess dietary intake of protein has been shown to correlate with increased adiposity in non-CF cohorts²⁹. It will be important to further characterize this sub-group of patients with NWO and to determine if NWO influences metabolic derangements over time in adults with CF.

The current study used air displacement plethysmography to measure body composition. This method has been shown to provide similar fat-free mass estimates as dual-energy X-ray absorptiometry in children and adolescents with CF³⁰. However, air displacement plethysmography is based on the two-component model of body composition which partitions body weight into fat mass and fat-free mass and is dependent on the assumption that the density of fat-free mass is constant, regardless of age, sex, race, or disease state³¹. Future studies using the four-component model in adult CF, which partitions body weight into fat, water, mineral, and protein, will be of interest to more accurately quantify body composition in CF²³.

A challenge in evaluating NWO is that there is no current consensus regarding an optimal cut-point to signify an excess percentage body fat¹³. Proposed cut-points have varied between 30-37% in women and 20-25% in men¹³. Upper tertiles of percent body fat are often used as cut-points in NWO studies. In our study, we were limited from using this method due to our small sample size. Therefore, we chose a definition for NWO based on a recently published study in the literature¹⁴. Additional limitations in this study were that: 1) the non-CF group was recruited using convenience sampling and included to serve as a reference group, as opposed to a BMI-, diabetes-, and/or race-matched control group; 2) we did not assess measures of fat distribution, which may influence metabolic risk to a greater degree than total body fat measures, or other measures that may correlate with body composition, such as intestinal absorption, basal metabolic rate, or muscle strength; 3) self-reported food intake methods are subject to reporting bias; 4) single measurements of cytokines may not fully reflect chronic inflammation; and 5) an absence of statistically significant group differences may reflect lack of power given the small samples sizes, thus this should be considered a pilot study. Finally, as this was a cross-sectional, causal relationships cannot be inferred, and results may not be generalizable to other CF populations. Nonetheless, our data are hypothesis-generating and suggest the need for larger, prospective studies on body composition, including NWO and adiposity indexes, on lung function, and the potential impact of interventions designed to increase lean tissue mass concomitant with decreased adiposity in CF.

Conclusions

In summary, this pilot study demonstrates an independent, positive relationship between measures of adiposity and lung function in individuals with CF. We further report a 30% prevalence of NWO (normal weight BMI with elevated percent body fat) in this cohort, which was associated with reduced lung function. Although additional prospective study is needed, the presence of excess adiposity may have important long-term health implications in CF and may require re-evaluation of current standards of care in regards to nutritional

monitoring and interventions in individuals with CF, especially as the population ages into an obesogenic environment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors have no conflicts of interest. JAA and AAS conceived and designed the research. All authors participated in the generation (JAA, AAS, ECM), collection (JAA, AAS, ECM), assembly (JAA, AAS, ECM), analysis (JAA), and/or interpretation of the data (JAA, AAS, ECM, TRZ). JAA drafted the initial manuscript and all authors participated in the revision. All authors read and approved the final version of the manuscript. Part of this work was presented in the 27th Annual North American Cystic Fibrosis conference in Salt Lake City, UT, October 2013.

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Abbreviations

ANOVA	analysis of variance
BMI	body mass index
CF	cystic fibrosis
CFRD	cystic fibrosis related diabetes
DRI	Dietary Reference Intake
FPG	fasting plasma glucose
FEV₁%	percentage of predicted forced expiratory volume in 1 second
IL-6	interleukin-6
IL-8	interleukin-8
NWO	normal weight obesity
OGTT	oral glucose tolerance test
TNF-α	tumor necrosis factor- α

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HIGHLIGHTS

- Fat-free mass was positively associated with lung function in cystic fibrosis (CF).
- Adiposity in CF subjects was inversely associated with lung function.
- Thirty percent of CF subjects had normal weight obesity (NWO).
- CF subjects with NWO had reduced fat-free mass and reduced lung function.
- Nutrition screening protocols that primarily rely on BMI may require re-assessment.

Figure 1. Linear regressions of FEV₁% with body composition measures, adjusted for age, gender, and BMI

A) fat-free mass index ($\beta = 6.31 \pm 2.93$, $P = 0.04$), B) percent body fat ($\beta = -1.42 \pm 0.64$, $P = 0.04$), and C) fat mass index ($\beta = -6.44 \pm 2.93$, $P = 0.04$). Triangles represent normal weight subjects, open circles represent normal weight obesity, and filled circles represent overweight/obese subjects.

Figure 2. Body composition category differences in adults with cystic fibrosis

One-way ANOVA indicated statistically significant group differences in: A) Body mass index, B) Percent body fat, C) Fat mass index, D) Fat-free mass index, and E) FEV₁% predicted (P<0.01 for all). Groups not connected by the same letter are significantly different (determined by Tukey's post-hoc comparisons).

TABLE 1

Demographic, clinical, and body composition characteristics in 32 subjects with cystic fibrosis

Variable	Cystic Fibrosis (n = 32)	Reference (n = 20)	P
Age (y)	26.1 ± 8.9	30.9 ± 8.8	0.12
Female (%)	18 (56)	8 (40)	0.39
Caucasian/White Race (%)	30 (93.8)	15 (75)	0.02
Glucose Tolerance			
Normal glucose tolerance (%)	14 (43.8)	13 (65)	0.003
Prediabetes (%)	6 (18.8)	7 (35)	
Diabetes (%)	12 (37.5)	0 (0)	
FEV ₁ (% predicted)	80.4 ± 21.5	-----	-----
Lung function status¹			
Normal (%)	20 (62.5)	-----	
Mild (%)	4 (12.5)	-----	
Moderate/severe (%)	8 (25.0)	-----	
Pancreatic insufficiency (%)	31 (96.9)	-----	-----
Age of CF diagnosis (y) ²	1.5 (0.6-5.0)	-----	-----
Genotype			
F508Homozygous (%)	18 (56.3)	-----	
F508 Heterozygous (%)	9 (28.1)	-----	
Other (%)	5 (15.6)	-----	
Height (cm)	165.6 ± 9.9	173.7 ± 11.0	0.009
Body weight (kg)	60.9 ± 11.9	74.4 ± 16.9	0.001
Body mass index (kg/m ²)	22.1 ± 2.9	24.5 ± 3.7	0.01
Fat-free mass (kg)	45.0 ± 10.0	55.5 ± 13.4	0.002
Fat-free mass index (kg/m ²)	16.2 ± 2.0	18.2 ± 2.8	0.006
Fat mass (kg)	15.9 ± 5.7	18.9 ± 7.3	0.11
Fat mass index (kg/m ²)	5.9 ± 2.2	6.3 ± 2.4	0.47
Body fat (%)	26.1 ± 7.6	25.4 ± 8.1	0.75
Body composition category			
Lean (%)	16 (50)	6 (30)	0.13
Normal weight obesity (%)	10 (31.3)	5 (25)	
Overweight/obese (%)	6 (18.8)	9 (45)	

Values are reported as mean ± SD or n (%).

¹ Lung function status defined according to FEV₁ (% predicted): <59%, moderate; 60-79%, mild; 80%, normal.² Reported as median (IQR)

TABLE 2

Multiple linear regression of FEV₁% (dependent variable) and body composition indexes, adjusting for age and sex (model 1) and age, sex, and BMI (model 2)

Independent variable ^I	Model 1 $\beta \pm \text{SE}$ (<i>P</i> -value)	Model 2 $\beta \pm \text{SE}$ (<i>P</i> -value)
Height (cm)	1.11 $\pm$ 0.68 (0.12)	-----
Body weight (kg)	1.62 $\pm$ 0.30 (<0.001)	-----
Body mass index (kg/m ²)	4.89 $\pm$ 1.03 (<0.001)	-----
Body fat (%)	0.90 $\pm$ 0.63 (0.16)	-1.42 $\pm$ 0.64 (0.04)
Fat mass (kg)	1.86 $\pm$ 0.29 (0.004)	-1.33 $\pm$ 1.09 (0.23)
Fat mass index (kg/m ²)	4.71 $\pm$ 1.76 (0.01)	-6.44 $\pm$ 2.93 (0.04)
Fat-free mass (kg)	2.67 $\pm$ 0.55 (<0.001)	1.70 $\pm$ 0.64 (0.01)
Fat-free mass index (kg/m ²)	10.05 $\pm$ 1.99 (<0.001)	6.31 $\pm$ 2.93 (0.04)

^I Individual multiple linear regression models with FEV₁% as the dependent variable and with age, sex, and BMI as covariates.

TABLE 3

Characteristics of CF subjects by weight category¹

	Lean (n = 16)	Normal weight obesity (n = 10)	Overweight/ obese (n = 6)	P ²
Age (y)	26.2 ± 9.9	25.7 ± 6.2	30.3 ± 10.2	0.57
Female (%)	9 (56)	6 (60)	3 (50)	1.00
Height (cm)	165.9 ± 10.1	163.3 ± 9.9	169.0 ± 9.3	0.55
Body weight (kg)	57.3 ± 9.8 ^a	57.3 ± 8.7 ^a	76.7 ± 9.3 ^b	0.004
F508 homozygous (%)	8 (50)	7 (70)	3 (50)	0.38
Age of CF diagnosis (y) ³	0.8 (0.1-3.3)	0.3 (0.1-4.1)	4.9 (1.9-25.8)	0.12
Glucose tolerance				
Normal glucose tolerance (%)	7 (44)	4 (40)	3 (50)	0.92
Prediabetes (%)	4 (25)	1 (10)	1 (17)	
Diabetes (%)	5 (31)	5 (50)	2 (33)	
Multivitamin supplement (%) ⁴	10 (71)	7 (88)	6 (100)	0.45
High-calorie supplement (%) ⁴	5 (36)	0 (0)	1 (17)	0.16
Fasting glucose (mg/dL)	92.7 ± 11.6	85.7 ± 17.2	87.5 ± 8.3	0.39
2-hr glucose (mg/dL)	172.6 ± 80.2	215.3 ± 110.7	178.7 ± 113.1	0.54
Interleukin-6 (pg/mL) ⁵	2.4 (0.7, 9.3)	1.6 (0.3, 4.6)	0.04 (0, 10.2)	0.50
Interleukin-8 (pg/mL) ⁵	12.1 (9.8, 17.4)	9.5 (4.9, 16.3)	11.8 (3.3, 20.5)	0.68
Tumor necrosis factor-α (pg/mL) ⁵	3.9 (2.8, 7.5)	3.6 (3.2, 4.2)	3.9 (3.2, 20.7)	0.82

¹ Reported as mean ± SD or n (%).² For all $P < 0.05$, groups not connected by the same letter are significantly different (determined by Tukey's post-hoc comparisons).³ Reported as median (interquartile range), and n = 9 and 5 in the normal weight obesity and overweight/ obese groups, respectively.⁴ General multivitamin or fat-soluble multivitamin, and n = 14 and 8 in the lean and normal weight obesity groups, respectively.⁵ Reported as median (interquartile range), and n = 9, 8, and 3 in the lean, normal weight obesity, and overweight/obese groups, respectively.