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Influence of diet, exercise and serum vitamin D on sarcopenia in post-menopausal women

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Abstract

Purpose—To investigate the effects of 12 months of dietary weight loss and/or aerobic exercise on lean mass and the measurements defining sarcopenia in postmenopausal women, and to examine the potential moderating effect of serum 25-hydroxyvitamin D (25(OH)D) and age.

Methods—439 overweight and obese postmenopausal women were randomized to: diet modification (N=118); exercise (N=117), diet+exercise (N=117), or control (N=87). The diet intervention was a group-based program with a 10% weight loss goal. The exercise intervention was 45 mins/day, 5 days/week of moderate-to-vigorous intensity aerobic activity. Total and appendicular lean mass were quantified by dual Xray absorptiometry (DXA) at baseline and 12 months. A skeletal muscle index (SMI=appendicular lean mass (kg)/m^2) and the prevalence of sarcopenia (SMI<5.67 kg/m^2) were calculated. Serum 25(OH)D was assayed using a competitive chemiluminescent immunoassay.

Results—Dietary weight loss resulted in a significant decrease in lean mass, and a borderline significant decrease in appendicular lean mass and SMI compared to controls. In contrast, aerobic

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exercise significantly preserved appendicular lean mass and SMI. Diet + exercise attenuated the loss of appendicular lean mass and SMI compared to diet alone, and did not result in significant loss of total- or appendicular lean mass compared to controls. Neither serum 25(OH)D nor age were significant moderators of the intervention effects.

Conclusions—Aerobic exercise added to dietary weight loss can attenuate the loss of appendicular lean mass during weight loss, and may be effective for the prevention and treatment of sarcopenia among overweight and obese postmenopausal women.

Keywords

caloric restriction; weight loss; 25-hydroxyvitamin D; ageing

INTRODUCTION

Weight gain leading to overweight and obesity is associated with a proportional increase in lean tissue. However, excess weight is not necessarily protective against the age-related decline in muscle mass known as sarcopenia (31). As such, the term sarcopenic-obesity has been coined to describe the simultaneous presence of both obesity and low muscle mass, which confers a higher risk of functional impairment and physical disability than sarcopenia alone (30).

While weight loss among obese individuals is recommended for chronic disease prevention (14), the prudence of weight loss among overweight and obese older adults has been debated over concerns about the potentially deleterious concurrent loss of muscle and bone mass (8, 20, 27, 40). The relative loss of lean mass compared to fat mass represents a significantly greater percentage of weight loss in older compared to younger adults (27). Thus, accelerated muscle loss with weight loss is a particularly justified concern in older persons with a body phenotype of sarcopenic-obesity. Whether, and how, weight loss can be achieved in persons with or at risk of sarcopenia without the detrimental loss of lean mass has not been demonstrated.

Difficulty remains in identifying sarcopenia in research and clinical settings given that no formal, universally accepted definition yet exists. Baumgartner was the first to use a dichotomous method whereby sarcopenia was defined as height-adjusted appendicular muscle mass (muscle mass/height^2) two standard deviations or more below the mean of a young reference population, as measured by dual X-ray absorptiometry (DXA) (2). Several other approaches have used similar types of cut-points but have relied on other measurement tools such as bioelectrical impedance and computed tomography (13), have adjusted for total weight rather than height (17) or used residuals from linear regression models (26). Ongoing efforts are being made to establish a definition based on pathophysiology and associated risk; however, the process needed to disentangle the complex inter-relationships involved makes this difficult (9, 39).

Although muscle loss is a consequence of aging, considerable interindividual differences exist owing to a variety of lifestyle and other factors. Serum 25-hydroxyvitamin D (25(OH)D), the most common indicator of whole-body vitamin D status, is positively associated with lean mass, physical performance and muscle strength (11, 16, 18), while intervention studies have demonstrated improvements in physical functioning and reduced risk of falls in older adults after vitamin D supplementation (7). Vitamin D receptors are present in human skeletal muscle (5, 35) and previous studies have linked vitamin D receptor polymorphisms to reduced muscle mass and function in older adults, suggesting that vitamin D does play a role in sarcopenia. Yet, there remains little consensus on the mechanisms underlying the observed associations (12). Whether vitamin D status moderates

the effect of weight loss by caloric restriction or exercise on lean mass by supporting muscle preservation remains unknown.

The purpose of this study was to investigate the effects of 12 months of weight loss through caloric restriction and/or exercise interventions on lean mass and on measurements defining sarcopenia (e.g. appendicular lean mass and skeletal muscle index) among postmenopausal women, and to investigate the potential moderating effects of serum 25(OH)D status and age. We hypothesized that women with high 25(OH)D will preserve a greater amount of lean mass than women with low 25(OH)D.

PARTICIPANTS & METHODS

Design Overview

The Nutrition and Exercise in Women (NEW) study, conducted from 2005–2009, was a 12-month randomized controlled trial testing the effects of caloric restriction and/or exercise on circulating hormones and other outcomes. Study procedures were reviewed and approved by the Fred Hutchinson Cancer Research Center Institutional Review Board in Seattle, WA, and all participants provided informed written consent.

Participants

Participants were overweight or obese (BMI ≥25.0 kg/m^2 or ≥23.0 kg/m^2 if Asian-American) postmenopausal women (50–75 y), recruited through media and mass mailings. Specific exclusion criteria included: >100 min/week of moderate physical activity; diabetes, fasting blood glucose ≥126mg/dL or use of diabetes medications; postmenopausal hormones use within 3 months; history of serious medical condition(s); alcohol intake >2 drinks/day; current smoking; contraindication to the study interventions (e.g. abnormal exercise tolerance test); current or planned participation in another weight loss program; use of weight loss medications; or any additional factors that might interfere with the measurement of outcomes or intervention success (e.g. inability to attend facility-based sessions).

Randomization & Interventions

Eligible women were randomized to one of four study arms: 1) reduced-calorie dietary modification (N=118); 2) moderate-to-vigorous intensity aerobic exercise (N=117); 3) combined diet and exercise (N=117); or 4) control (no intervention) (N=87). Computerized random assignment was stratified according to BMI (≥ or <30.0 kg/m^2) and participants' self-reported race/ethnicity (White, Black, other). To achieve a proportionally smaller number of women assigned to the control group, we used permuted blocks randomization with blocks of 4, wherein the control assignment was randomly eliminated from each block with a probability of approximately 1 in 4.

The interventions have been previously described in detail (10). Briefly, the dietary intervention was modified from the Diabetes Prevention Program (DPP)(19) and Look AHEAD (Action for Health in Diabetes) (33) lifestyle behavior change programs with goals of: 1200–2000 kcal/day, <30% daily energy intake from fat, and 10% loss of baseline weight within 6 months with weight maintenance thereafter. Participants met individually with a dietitian on at least two occasions, followed by weekly group (5–10 women) meetings for 6 months, and monthly group meetings thereafter, in addition to phone or email contact. The women were weighed at each visit and both the dietitian and participant tracked this on a graph. Women were asked to keep a daily food journal for at least six months or until they reached their individual weight loss goal (10%). Journals were collected by the dietitian and returned with feedback after being analyzed. Journaling, weekly weight loss and the total number of sessions attended were used as measures of adherence to the diet intervention.

The exercise intervention began with 15 minute sessions at 60–70% maximal heart rate (determined by baseline exercise treadmill testing) on 3 days/week and progressed incrementally to the target 70–85% maximal heart rate for 45 minutes, 5 days/week, by the 7^{th} week after enrollment where it was maintained for the remainder of the study. Participants attended three supervised sessions/week at the study facility and exercised 2 days/week at home. Facility-based exercise consisted of treadmill walking, stationary cycling and use of other aerobic machines, while a variety of home exercises were encouraged including walking/hiking, aerobics and bicycling. Women wore Polar heart rate monitors (Polar Electro, Lake Success, NY) during both facility and home exercise sessions to assist with attaining their target heart rate. In addition, they recorded the mode and duration of exercise, and peak heart rate achieved. At home, women also recorded their relative perceived exertion. Activity logs were completed by each participant and were reviewed weekly by study staff in order to monitor compliance and to intervene when needed. Activities of ≥4 metabolic equivalents (METs) (1) were counted towards the prescribed target of 225 mins/week of moderate-to-vigorous aerobic exercise. A small amount of resistance training and stretching to strengthen joints and limit injury was recommended, though not required. Sixty-eight percent (n=159) of women randomized to exercise intervention reported doing strength training an average of once per week but duration was not recorded.

Participants randomized to diet+exercise received the diet intervention in separate sessions and were instructed not to discuss diet during supervised exercise. The control group was requested not to change their diet or exercise habits for 12 months.

Outcomes & Follow-Up

All study measures were obtained and analyzed by trained personnel who were blinded to the participants' randomization status.

Demographic information, medical history, dietary intake (via a validated 120-item self-administered food frequency questionnaire that assessed nutrient intake over the previous 6 months (29)), supplement use, physical activity patterns (via a modified, interview-administered Minnesota Physical Activity Questionnaire describing the previous 12 months (38)), and average pedometer (Accusplit, Silicon Valley, CA) daily step count over 1 week were collected at baseline and 12 months. Cardiorespiratory fitness (VO_2max) was assessed using a maximal graded treadmill test according to a modified branching protocol (28). Heart rate and oxygen uptake were continuously monitored with an automated metabolic cart (MedGraphics, St. Paul, MN).

Body Composition Assessment

Participants wore a hospital gown without shoes for anthropometric measurements. Body mass index (BMI=kg/m^2) was calculated from weight and height, measured to the nearest 0.1 kg and 0.1cm, respectively, with a balance beam scale and stadiometer. Waist circumference was measured to the nearest 0.5 cm at the minimal waist. Body composition was measured on a DXA whole-body scanner (GE Lunar, Madison, WI; Encore 2004 software, v. 8.80.001), including total body bone-free lean mass Appendicular lean mass was calculated as the sum of the upper and lower limb muscular masses. Appendicular lean mass was normalized to height by calculating a skeletal muscle index: [SMI= appendicular lean mass (kg)/height (m^2)], and used to determine the prevalence of sarcopenia SMI ≤5.67 kg/m^2 according to current consensus recommendations (9).

Fasting venous blood samples (50 mL) were collected during clinic visits prior to randomization and at 12 months. Participants consumed only water for 12 hours prior and

did not exercise for 24 hours preceding the blood draw. Blood was processed within 1 hour and samples were stored at −70°C.

Serum 25(OH)D was assayed by direct, competitive chemiluminescent immunoassay using the DiaSorin LIAISON 25-OH Vitamin D Total assay (Heartland Assays, Inc., Ames, IA). Samples were analyzed in batches such that each participant's baseline and 12-month samples were assayed simultaneously, the number of samples from each intervention group was approximately equal, participant randomization dates were similar, and sample order was random. The intra- and inter-assay coefficients of variation (CV) were 8.2% and 11.0%, respectively.

Statistical Analysis

All statistical analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC). For the main analyses, missing data were imputed by multiple imputation (PROC MI). Body composition variables were imputed based on baseline values of the variable of interest, age, race/ethnicity and BMI. Five imputed datasets were created (32) and results were combined (PROC MIANALYZE). For all other analyses, only available data were used. Differences in baseline characteristics between groups were tested using t-tests and Chi-square or Fisher exact tests for frequency comparisons as appropriate. Pearson correlation coefficients were calculated between age, 25(OH)D, body fat, lean mass, appendicular lean mass and SMI.

Mean changes in lean mass, appendicular lean mass and SMI from baseline to 12 months within each intervention group were computed and compared to controls using the generalized estimating equations (GEE) modification of linear regression to account for intra-individual correlation over time. Age, race/ethnicity, baseline BMI, vitamin D intake (food + supplements), % calories from protein and % weight loss were examined as covariates. Additional comparisons between the diet and exercise groups to the diet +exercise group were also performed. Adjustment for multiple comparisons was made via Bonferroni correction (two-sided alpha 0.05/5=0.01). The intervention effects were examined based on the assigned treatment at randomization, regardless of adherence or study retention (i.e. intent-to-treat). The effect of vitamin D status was investigated by repeating the main analyses after stratification according to the median split (25(OH)D ≤ or >22ng/mL) and the following serum 25(OH)D concentrations: <20 ng/mL, 20–30 ng/mL, >30 ng/mL(15). Season of randomization (March-May, June-August, September-November, December-February) was also included as a covariate in this model. Similarly, potential differences in younger compared to older women were also compared in stratified analyses (50–60 y, 60–75 y) and tested for a significant interaction effect.

RESULTS

Participants

At 12-months, 397 participants underwent a DXA scan; 371 completed a treadmill test; 39 did not complete the study. One participant was missing baseline blood measures and is excluded from this analysis. The flow of participants through the NEW trial and a comparison of baseline participant characteristics between randomized groups have been previously published (10). As reported previously (24), the mean serum 25(OH)D concentration among participants was 22.5 ng/mL (range: 4.1–57.0 ng/mL). Serum 25(OH)D varied according to season of randomization; however the frequency of randomization by season did not differ across groups (chi square p=0.29). Serum 25(OH)D was inversely correlated with % body fat (r = −0.12, p=0.01) and positively associated with

lean mass (r = 0.11, p=0.02), but was not significantly correlated with appendicular lean mass (r = −0.09, p=0.06) or SMI (r = −0.09, p=0.07) at baseline.

Prevalence of Sarcopenia

Table 1 shows participant characteristics by sarcopenic status. At baseline, 76 (17.4%) participants met the criteria for sarcopenia (SMI ≤5.67). Women with sarcopenia, compared to women without sarcopenia, had a lower mean BMI (31.4 vs 28.2 kg/m^2, p<0.0001) and waist circumference (90.2 vs. 95.4 cm, p<0.0001), less lean mass (36.0 vs. 41.2 kg, p<0.0001), and a higher mean % body fat (48.5 vs. 47.0%, p=0.006) (Table 1). No significant differences in VO_2max, pedometer steps per day, % calories from fat or protein, use of vitamin D supplements, or serum 25(OH)D were detected by sarcopenic status.

Intervention Fidelity

At 12 months, the mean weight change was −2.4% (p=0.03) in the exercise group, −8.5% (p<0.001) in the diet group, and −10.8% (p<0.001) in the diet+exercise group, compared to −0.8% among controls (10). Women randomized to exercise alone participated in moderate-to-vigorous activity for a mean 163.3 mins/week, while women randomized to diet+exercise participated for 171.5 mins/week. Both groups significantly increased average pedometer steps/day (+3202 steps/d and +4038 steps/d, respectively) and VO_2max (+0.17 and +0.12 L/min, respectively) compared to baseline. Daily % calories from fat decreased in both the diet (−6.7%) and diet+exercise (−8.0%) groups. In both diet groups, women attended an average of 27 diet counseling sessions (86%).

Intervention Effects

After 12 months, lean mass decreased significantly in the diet group compared to controls (−1.1 kg vs. −0.1 kg, p<0.001), with a borderline significant decrease in appendicular lean mass and SMI (p=0.02 and p=0.01, respectively) (Table 2). In contrast, aerobic exercise significantly preserved appendicular lean mass (p=0.003) and SMI (p=0.004) compared to controls, despite no change in total lean mass. No significant changes in lean mass (p=0.20), appendicular lean mass (p=0.90) or SMI (p=0.68) were detected between the diet+exercise group and controls after 12 months. Compared to the diet alone group, the reductions in appendicular lean mass and SMI were smaller in the diet+exercise group (p<0.01). None of the results were meaningfully changed after further adjustment for total % weight loss or for % body fat loss rather than BMI.

Among women who met the criteria for sarcopenia at baseline, 3 cases (14%) in the control group, one case (8%) in the diet group, 8 cases (50%) in the exercise group, and 6 cases (35%) in the diet+exercise group no longer met the criteria for sarcopenia by 12 months. Conversely, the incidence rates of sarcopenia among women who did not meet the criteria at baseline were: 10% (n=6) in the control group, 12% (n=11) in the diet alone group, 7% (n=6) in the exercise group, and 9% (n=8) in the diet+exercise group (Table 3). Although both the exercise and exercise + diet interventions were associated with a lower risk of incident sarcopenia compared to controls, the relative risk estimates were not statistically significant after adjustment for age, ethnicity, and % weight loss.

Baseline vitamin D status did not significantly affect the loss of lean mass, appendicular lean mass or SMI in any intervention group (Table 4), and no significant interaction effect was detected when serum 25(OH)D was stratified and tested using a median split (25(OH)D ≤ or >22 ng/mL)(results not shown). No significant interaction effects were observed according to age (<60 y, ≥60 y) (Table 5).

DISCUSSION

Given the increased risk of disability, frailty and fracture risk associated with sarcopenia (10–12), the potential loss of lean mass can be a deterrent to prescribed weight loss for overweight and obese older adults. Yet, behavioral lifestyle changes leading to modest weight loss of 5–10% is generally sufficient to yield significant improvements in a variety of chronic disease risk factors (14). Thus, the effects of different lifestyle interventions for obesity treatment on lean mass in older populations are of particular clinical importance.

In this study of overweight and obese postmenopausal women, 12 months of aerobic exercise resulted in a small but significant increase in appendicular lean mass and SMI compared to a net loss among controls. In contrast, 12 months of dietary weight loss (without exercise) resulted in a significant loss of lean mass, and a borderline significant decrease in appendicular lean mass and SMI compared to controls. The combination of dietary weight loss + exercise attenuated the loss of appendicular lean mass and SMI compared to diet alone, and did not result in the significant loss of total- or appendicular lean mass compared to controls, while still achieving significant and meaningful weight loss and accompanying metabolic improvements (10, 23). While resistance exercise is typically considered the best approach for preserving muscle mass with ageing, its utility for promoting weight loss, especially in older women, is not known. Our data suggest that aerobic exercise has some benefit for maintaining lean body mass when combined with dietary weight loss. Future studies should investigate whether the addition of resistance training, and at what dose, may confer additional benefits for the preservation of muscle mass and function, as well as bone during weight loss.

Although serum 25(OH)D was positively associated with lean mass at baseline, vitamin D status did not appear to significantly influence the loss of total lean mass or appendicular lean mass in any intervention group. In the control group, diet group, and diet+exercise group, women with serum 25(OH)D >30 ng/mL lost quantitatively less lean mass than those with lower baseline values; however the groups may have been too small to detect a significant relationship. Vitamin D receptors are present in human skeletal muscle (5, 35), and serum 25(OH)D concentrations have been positively associated with physical performance and overall physical fitness in cross-sectional studies of older women (11, 37). Further, vitamin D_3 supplementation has been shown to increase muscle strength in older adults with low vitamin D (21, 25); however, the mechanisms underlying the effect of vitamin D on muscle strength are not fully understood.

The prevalence of sarcopenia increases with advancing age, as does the rate of muscle loss (41). We observed a greater loss of lean mass over 12 months in older women, regardless of intervention assignment; however, the intervention effects on lean mass did not differ according to age, suggesting that aerobic exercise is equally effective in preventing the loss of lean mass in older compared to middle aged women. Additional studies will be required to determine whether similar effects are seen in women older than 75 years.

For the purpose of this study, we opted to use the DXA-based approach first described by Baumgartner et al.(2), with the SMI cut-off suggested in a more recent international consensus definition of sarcopenia (9). The use of DXA for precise assessment of total and regional lean mass is a study strength. Additional strengths include the relatively large size and adequate statistical power to examine differences in lean mass in women assigned to diet vs. exercise vs. both combined, as well as excellent intervention adherence and study retention. A limitation is that we did not measure muscle function. A growing body of related research suggests that muscle function, independent of muscle size, is an important determinant of physical functioning and risk of disability (36). Several groups including the

European Working Group on Sarcopenia in Older People (EWSOP) (6) and the International Sarcopenia Consensus Conference Working Group (9) have recently recommended using the presence of both low muscle mass *and* low muscle function (strength or performance) to identify sarcopenia. Future studies should examine the effects of weight loss and various exercise regimens on this aspect of sarcopenia, as well as the extent to which changes in muscle mass are associated with functional outcomes.

The etiology of sarcopenia is complex with multiple contributing factors over the lifespan, including early life developmental influences, diet, physical inactivity, chronic disease, specific drug treatments, and the ageing process (22, 34). Several mechanisms have been implicated in the onset and progression of sarcopenia, including endocrine factors such as insulin resistance, inflammation, changes in sex hormones, disuse, motor neuron loss, inadequate nutrition or nutrient malabsorption, and cachexia (4, 22). Exercise may directly and indirectly influence the sarcopenic process through several of these mechanisms. Further research is needed to disentangle the complex and interrelated pathways influencing the development of sarcopenia, and to establish better exercise prescriptions to minimize its negative consequences.

This study demonstrates that regular aerobic exercise is effective for the prevention and management of muscle loss among postmenopausal women undergoing weight loss, and that aerobic exercise added to a dietary weight loss program should be considered as a viable strategy to mitigate the potentially adverse effects of weight loss among older overweight and obese women. These observations are particularly important given that the loss of lean mass experienced during weight loss is not fully recovered with weight regain (3). The potential for a disproportionate regain in fat mass among older adults means that unsuccessful weight loss maintenance could further increase the risks associated with sarcopenic-obesity and underscores the importance of incorporating regular exercise into weight loss programs for older adults. Higher serum 25(OH)D levels do not appear to protect against the loss of lean mass during weight loss in this population.

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Table 1

Characteristics of study women with sarcopenia and without sarcopenia at baseline

Variable	No Sarcopenia		Sarcopenia		P*
	N	MEAN (SD) or %	N	MEAN (SD) or %	
Age (year)	362	57.9 (5.0)	76	58.0 (5.0)	0.9
Ethnicity (%)					0.04
Non-Hispanic White	300	82.9	72	94.7	
Non-Hispanic Black	34	9.4	1	1.3	
Hispanic	11	3	1	1.3	
Other (American Indian, Asian, or Unknown)	17	4.7	2	2.6	
Weight (kg)	362	85.0 (11.9)	76	77.0 (8.8)	<.0001
BMI (kg/m^2)	362	31.4 (4.0)	76	28.2 (2.5)	<.0001
Waist circumference (cm)	362	95.4 (10.3)	76	90.2 (7.6)	<.0001
Body fat (%)	362	47.0 (4.4)	76	48.5 (3.8)	0.006
Lean mass (%)	362	48.8 (4.3)	76	47.0 (3.6)	0.001
Lean mass (kg)	362	41.2 (4.8)	76	36.0 (3.3)	<.0001
Appendicular lean mass (kg)	362	17.5 (2.0)	76	14.7 (1.2)	<.0001
SMI (kg/m^2)	362	6.5 (0.6)	76	5.4 (0.2)	<.0001
Pedometer steps/day (7 day average)	353	5671 (2300)	74	6050 (2147)	0.19
VO^{2}max (ml/kg/min)	362	22.9 (4.0)	76	23.1 (1.2)	0.77
Average Dietary Intake (FFQ)					
Total calories (kcal/day)†	352	1966 (634)	74	1794 (631.8)	0.03
% calories from fat‡	352	34.3 (6.9)	74	34.5 (7.0)	0.85
% calories from protein	352	17.4 (3.2)	74	17.4 (2.7)	0.96
Baseline Dietary Vit D intake (μg/d)	352	6.2 (3.9)	74	5.6 (3.6)	0.23
12-mo Dietary Vit D intake (μg/d)	308	5.9 (3.5)	65	5.2 (3.3)	0.11
Regular users of Vitamin D containing supplements					
Baseline users (%)	183	50.8	35	46.1	0.45
Mean daily intake among baseline users (IU/day)	172	514.4 (313.6)	33	608.2 (527.2)	0.17
Serum 25-hydroxy Vit D (ng/mL)	362	22.6 (9.2)	75	21.8 (7.1)	0.48

Sarcopenia was defined according to a Skeletal Muscle Index <5.67 (ref 14).

† Daily kcal values derived from FFQ truncated <600 kcal & >4000 kcal

* P value: t-test for mean comparison; Chi-square or fisher exact test for frequency comparison.

Table 2

12-month change in lean mass, appendicular lean mass (ALM)[†] and Skeletal Muscle Index (SMI)[⍰] among participants, stratified by intervention arm.

	Lean Mass (kg)				ALM (kg)				SMI (kg/m^2)			
	Baseline Mean (SD)	12 mo Mean (SD)	%Δ	p*	Baseline Mean (SD)	12 mo Mean (SD)	%Δ	p*	Baseline Mean (SD)	12 mo Mean (SD)	%Δ	p*
Control	40.6 (5.3)	40.5 (5.2)	**−0.04**		17.2 (2.4)	17.0 (2.4)	**−1.2**		6.25 (0.7)	6.16 (0.7)	**−1.5**	
Exercise	40.2 (5.3)	40.2 (4.8)	**−0.07**	**0.14**	17.1 (2.3)	17.1 (2.3)	**−0.12**	**0.003**	6.27 (0.7)	6.29 (0.7)	**0.4**	**0.004**
Diet	40.7 (5.1)	39.6 (4.6)	**−2.9**	**<0.001**	17.1 (2.1)	16.6 (2.1)	**−3.1**	**0.02**	6.32 (0.6)	6.12 (0.6)	**−3.2**	**0.01**
Diet + Exercise	39.6 (4.3)	39.0 (3.8)	**−1.5**	**0.20**[e]	16.8 (2.0)	16.6 (2.0)	**−1.4**	**0.90**[d,e]	6.31 (0.7)	6.24 (0.7)	**−1.0**	**0.68**[d]

*GEE model. P value comparing the change from baseline to 12 months between each intervention group versus controls, adjusted for age ethnicity, baseline BMI, %calories from protein, total vitamin D intake, and % weight loss.

†ALM = arms + legs lean mass, measured by DXA

⍰SMI = ALM/height (m)^2

[d]p<0.01 comparing diet+ exercise to diet alone

[e]p<0.01 comparing diet+ exercise to exercise alone

Table 3

Relative odds (95% Confidence Interval) of SMI ≤5.67 at 12 months among women without sarcopenia at baseline

	Incident cases (n)	Odds (95% CI)*
Control	6	1.00
Diet	11	0.62 (0.18–2.12)
Exercise	6	0.61 (0.18–2.05)
Diet + Exercise	8	0.39 (0.11–1.44)

* Logistic regression models adjusted for age, ethnicity and % weight loss.

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Table 4

Baseline and 12-month change (mean, 95% CI) values for lean mass, appendicular lean mass (ALM) and SMI inpostmenopausal women according to intervention group, stratified by baseline serum 25(OH)D.

	Serum 25-hydroxyvitamin D						
	<20 ng/mL		20–29.9 ng/mL		≥30 ng/mL		p_{trend}*
	Baseline	12 mo Δ	Baseline	12 mo Δ	Baseline	12 mo Δ	
Control	n=35	n=32	n=35	n=33	n=17	n=15	
lean mass	35.6 (37.7, 41.4)	−0.55 (−1.22, 0.13)	40.5 (38.7, 42.2)	0.38 (−0.30, 1.06)	42.8 (40.9, 44.6)	0.04 (−0.87, 0.94)	0.75
ALM	16.6 (15.8, 17.5)	−0.30 (−0.55, 0.05)	17.4 (16.6, 18.5)	−0.21 (−0.53,0.10)	17.9 (17.0, 18.7)	−0.20 (−0.65, 0.25)	0.80
SMI	6.1 (5.9, 6.4)	−0.11 (−0.20, −0.02)	6.3 (6.1, 6.5)	−0.07 (−0.18,0.04)	6.4 (6.2, 6.6)	−0.09 (−0.254, 0.06)	0.74
Exercise	n=59	n=53	n=38	n=32	n=20	n=20	
lean mass	41.0 (39.6, 42.5)	0.32 (−0.21, 0.86)	40.0 (38.4, 41.5)	0.52 (−0.16, 1.21)	38.1 (36.3, 40.0)	−0.11 (−0.96, 0.73)	0.82
ALM	17.5 (16.8, 18.1)	0.29 (0.03, 0.55)	17.1 (16.4, 17.8)	0.05 (−0.24, 0.35)	16.1 (15.3, 16.8)	−0.05 (−0.37, 0.28)	0.44
SMI	6.4 (6.2, 6.6)	0.11 (0.02, 0.21)	6.32 (6.0, 6.4)	0.01 (−0.09, 0.12)	6.1 (5.9, 6.3)	−0.05 (−0.19, 0.10)	0.32
Diet	n=48	n=41	n=52	n=47	n=17	n=15	
lean mass	41.9 (40.3, 43.6)	−0.83 (−1.28, 0.39)	40.3 (39.1, 41.5)	−1.12 (−1.65,−0.58)	38.8 (37.3, 40.2)	−0.3− (−1.15, 0.37)	0.56
ALM	17.6 (17.0, 18.2)	−0.47 (−0.73, −0.21)	17.0 (16.4, 17.5)	−0.63 (−0.83,−0.43)	16.3 (15.5, 17.1)	−0.35 (−0.68, −0.01)	0.99
SMI	6.5 (6.3, 6.6)	−0.18 (−0.28, −0.08)	6.3 (6.1, 6.4)	−0.25 (−0.33,−0.18)	6.2 (5.9, 6.5)	−0.11 (−0.24, 0.01)	0.98
Diet + Exercise	n=45	n=40	n=46	n=42	n=25	n=25	
lean mass	40.3 (38.9, 41.6)	−0.99 (−1.70, −0.29)	39.3 (38.0, 40.6)	−0.48 (−1.00, 0.04)	39.4 (38.3, 40.5)	0.29 (−0.23, 0.82)	0.21
ALM	17.0 (16.4, 17.5)	−0.34 (−0.64, −0.05)	16.8 (16.1, 17.4)	−.33 (−0.59,−0.08)	16.8 (16.2, 17.4)	0.15 (−0.12, 0.43)	0.06
SMI	6.4 (6.2, 6.6)	−0.13 (−0.24, −0.02)	6.3 (6.1, 6.6)	−0.11 (−0.21,−0.01)	6.2 (6.0, 6.4)	0.09 (−0.01, 0.19)	0.02

Analysis completed using all available data.

*ptrend: trend across serum 25(OH)D categories within each intervention arm, adjusted for age, ethnicity, baseline BMI, total vitamin D intake, % calories from protein, and season of randomization.

Table 5

12-month change (mean, 95% CI) in lean mass, appendicular lean mass (ALM) and skeletal muscle index (SMI) among participants, stratified by age.

	Age <60y		Age ≥60 y		
	Baseline	**12 month Δ**	**Baseline**	**12 month Δ**	
Control	n=62	n=57	n=25	n=23	
lean mass	40.9 (39.6, 42.2)	0.02 (−0.56, 0.59)	39.6 (37.6, 41.7)	−0.23 (−0.75, 0.28)	
ALM	17.4 (16.8, 18.0)	−0.29 (−0.51, −0.07)	16.6 (15.7, 17.6)	−0.13 (−0.48, 0.22)	
SMI	6.3 (6.1, 6.5)	−0.10 (−0.17, −0.02)	6.1 (5.9, 6.4)	−0.07 (−0.19, 0.05)	
Exercise	n=80	n=71	n=37	n=34	$p_{interaction}$*
lean mass	40.7 (39.5, 41.8)	0.38 (−0.11, 0.87)	39.2 (37.7, 40.7)	0.11 (−0.44, 0.66)	0.16
ALM	17.3 (16.8, 17.8)	0.23 (0.00, 0.45)	16.7 (16.0, 17.4)	−0.03 (−0.28, 0.22)	0.67
SMI	6.3 (6.2, 6.4)	0.09 (0.00, 0.17)	6.2 (6.0, 6.4)	0.02 (−0.12, 0.09)	0.67
Diet	n=83	n=74	n=34	n=29	
lean mass	40.9 (39.8, 42.0)	−0.73 (−1.07, −0.39)	40.3 (38.8, 41.9)	−1.38 (−2.12, −0.63)	0.54
ALM	17.3 (16.8, 17.8)	−0.50 (−0.67, −0.33)	16.7 (16.2, 17.2)	−0.60(−0.90, −0.30)	0.94
SMI	6.3 (6.2, 6.5)	−0.19 (−0.25, −0.12)	6.3 (6.1, 6.5)	−0.26 (−0.38, −0.13)	0.87
Diet + Exercise	n=79	n=72	n=38	n=36	
lean mass	39.6 (38.7, 40.5)	−0.36 (−0.78, 0.06)	39.7 (38.3, 41.1)	−0.70 (−1.39, −0.01)	0.59
ALM	16.9 (16.4, 17.3)	−0.11 (−0.29, 0.07)	16.7 (16.1, 17.3)	−0.45 (−0.77, −0.12)	0.33
SMI	6.3 (6.1, 6.4)	−0.03 (−0.10, 0.04)	6.4 (6.2, 6.7)	−0.16 (−0.28, −0.03)	0.49

Analysis completed using all available data.

*pinteraction: pvalue comparing difference in baseline to 12 months change in between age strata in each intervention group versus controls, adjusted for ethnicity,