

HHS Public Access

J Nutr Health Aging. Author manuscript; available in PMC 2022 March 02.

Published in final edited form as:

Author manuscript

J Nutr Health Aging. 2015 November ; 19(9): 913-921. doi:10.1007/s12603-015-0523-y.

Effects of Changes in Regional Body Composition on Physical Function in Older Adults: A Pilot Randomized Controlled Trial

Adam J. Santanasto, PhD, MPH^a, Anne B. Newman, MD, MPH^a, Elsa S. Strotmeyer, PhD, MPH^a, Robert M. Boudreau, PhD^a, Bret H. Goodpaster, PhD^b, Nancy W. Glynn, PhD^a ^aCenter for Aging and Population Health, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA

^bDivision of Endocrinology and Metabolism, Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA

Abstract

Background/Objective: Obesity exacerbates age-related physical disability; however, observational studies show that any weight loss in old age is associated with greater risk of mortality. Conversely, randomized controlled trials in older adults show that weight loss is beneficial. The discrepancy may be due to weight loss intention and differential changes to regional body composition. The purpose of this research was to evaluate the independent role of regional body composition remodeling in improving physical function.

Design: Pilot Randomized Controlled Trial

Setting: Community based research center

Participants: Thirty-six community dwelling, overweight to moderately obese (BMI 28.0–39.9 kg/m²) older adults (age 70.6±6.1yrs)

Intervention: Physical activity plus weight loss (PA+WL, n=21) or PA plus successful aging (SA) education. PA consisted primary of treadmill walking supplemented w/ lower extremity resistance and balance training. The WL program was based on the Diabetes Prevention Project and aimed at achieving a 7% weight loss by cutting calories, specifically those from fat.

Measurements: At baseline, 6- and 12-months, body composition was measured using computerized tomography and dual x-ray absorptiometry. Abdominal visceral (VAT) and thigh intermuscular (IMAT) adipose tissue were quantified. Physical function was assessed using the short physical performance battery (SPPB).

Results: Separate multivariable linear regression models with both groups combined demonstrated that decreases in IMAT and VAT were significantly associated with improvements

Corresponding Author: Nancy W. Glynn, PhD, 130 DeSoto Street, A531 Crabtree Hall Pittsburgh, PA 15261, 412.383.1309 (phone), 412.624.7397 (fax), glynnn@edc.pitt.edu.

Current affiliation and address for Dr. Goodpaster: Sanford/Burnham Medical Research Institute, Metabolic Disease Program. Orlando, Florida, United States

Conflict of Interest: AJS, ABN, ESS, RMB, BHG and NWG have no conflicts of interest to declare. *Ethics Statement:* This study was approved by the University of Pittsburgh's Institutional Review Board. All participants signed informed consent after demonstrating a basic understanding of the role and responsibilities of a study participant.

in SPPB (P < 0.05) independent of change in total fat mass. PA+WL improved SPPB scores from baseline (0.8 ± 1.4 , P < 0.05), whereas PA+SA did not; however no intergroup difference was detected. Of note, these effects were mainly achieved during the intensive intervention phase.

Conclusion: Decreases in IMAT and VAT are important mechanisms underlying improved function following intentional weight loss plus physical activity.

Keywords

weight loss; physical activity; intermuscular fat; visceral fat; physical function

INTRODUCTION

Obesity exacerbates physical disability in older adults(1) and is associated with several chronic health conditions including diabetes, heart disease, and osteoarthritis(2). However, observational studies show that weight loss in old age, regardless of starting weight, is associated with mortality(3–4), but most of this weight loss is unintentional. Conversely, long term follow-up of a randomized controlled trial(5) showed no association between intentional weight loss and mortality. Weight loss in combination with physical activity also improves physical function in obese older adults to a greater degree than physical activity alone, weight loss alone, and usual care(6). Nevertheless, controversy still exists as to whether older adults should lose weight(7).

Part of the discrepancy between the effects of intentional and unintentional weight-loss on health outcomes may be attributable to differential changes in regional body composition. Visceral adipose tissue (VAT) and intermuscular adipose tissue (IMAT) both increase with age. (8–9). VAT is strongly associated with higher levels of proinflammatory cytokines(10), type-2 diabetes(11) and the metabolic syndrome(12), which negatively affect muscle performance(13). Further, increasing IMAT levels are strongly related to longitudinal gait-speed decline(14) and higher IMAT levels are associated with higher levels of inflammation(15), poorer muscle power(16) and physical function(17). Therefore, decreases to regional body composition, specifically VAT and fat infiltration into muscle (myosteatosis), may better explain the relationship between weight loss and physical function than change in total body weight or fat mass.

Intentional weight loss with physical activity may target these particularly harmful fat depots. Few studies have specifically examined change in regional body composition following intentional weight loss and/or physical activity in older adults(18–21), but those that have seem to support this hypothesis. Further, only one study in older women has directly examined the relationship between decreases in regional body composition and improved physical function, but did not account for total fat mass change(21). To understand the mechanisms underlying improvements in physical function following weight loss and physical activity, it is important to investigate the relationship between changes to physical function and regional body composition.

We previously reported that 6-months of physical activity plus weight loss (PA+WL) improves physical function in older adults, while physical activity plus successful aging

(PA+SA) does not(19). The purpose of this research was to evaluate the independent role of regional body composition remodeling in improving physical function after 12-months of PA+WL or PA+SA. We hypothesized that decreases in VAT and IMAT would be related to improved function independent of change in total fat mass. We also report the overall 12-month effects of PA+WL and PA+SA on physical function and body composition.

METHODS

Participant Recruitment and Screening

Community-dwelling, overweight to moderately obese (body mass index (BMI) 28.0-39.9 kg/m^2), mostly sedentary men and woman age 60 and older were recruited to participate in a one-year, pilot randomized controlled trial called the Wellness for Elders through Lifestyle and Learning (WELL) Study. A flow chart describing screening, randomization and follow-up is provided in Figure 1. Participants were recruited via mass mailings and those who were interested (n=193) were telephone screened for initial eligibility, which has been described in detail elsewhere(19). Briefly, telephone exclusion criteria included: inappropriate age and BMI ranges, regular exercise 3x/week and 90min/week in the past month, having lost more than 10lbs in the past 4 months, taking medication for obesity or unwillingness to be randomized into either intervention group. Those who were interested and eligible (n=39) attended two baseline screening visits. Participants who were: 1. unable to walk 400m in <15 minutes without an assistive device, 2. deemed by the study nurse practitioner to have severe medical condition(s) precluding safe participation in a diet and/or exercise intervention, or 3. had significant cognitive impairment (known diagnosis of dementia or Modified Mini-Mental State Exam score <80) were also excluded. A total of 36 individuals were randomized into either the Physical Activity plus Weight Loss (PA+WL, n=21) or Physical Activity plus Successful Aging (PA+SA, n=15) group. Randomization was stratified by age and sex, which resulted in a slight imbalance between groups. This study was approved by the University of Pittsburgh Institutional Review Board and all participants provided written informed consent.

Physical Activity Program

All enrollees participated in a physical activity program consisting primarily of treadmill walking, supplemented with lower extremity resistance training using ankle weights and balance exercises(19,22). Participants were asked their Rating of Perceived Exertion on the Borg Scale (6–20)(23) after each activity and intensity was titrated to maintain a rating of 13 ("somewhat hard"). Exercise sessions were designed to be 60–75 minutes, with an emphasis on treadmill walking of at least 150 min/week by week 9. If the participant could spend the majority of the time walking, they were permitted to complete the ankle weight and balance exercises at home. Participants were given ankle weights to take home only after demonstrating their ability to perform exercises properly. Ankle weight load could be increased by 0.51b increments up to a maximum of 20lbs and exercises performed included: a standing leg curl, knee (quadriceps) extension, side hip raise and a toe stand. An unweighted wide leg squat was also performed by getting in and out of a chair with arms crossed.

The program was divided into three phases: adoption (weeks 1–8), transition (weeks 9–24), and maintenance (weeks 25–52), designed to transition exercise out of the clinic setting and into the participant's daily routine. During the adoption phase, participants were required to attend 3 center-based exercise sessions per week. For the transition phase, center-based sessions were reduced to 2 sessions per week with the third session to be conducted at home. During the maintenance phase, participants were invited to attend 1 *optional* exercise session per week; but, were expected to engage in physical activity at least three 3 per week. Rather than assigning participants specific days and times to exercise, an open-door policy was utilized and session length was not capped. Home exercise logs were maintained and collected weekly during all phases of the intervention.

Weight Loss Intervention

Participants in PA+WL (n=21) attended 24 weekly, 2 bi-monthly, and 5 monthly sessions lead by a nutritionist. Strategies to achieve the recommended caloric intake were discussed and performance in the weight loss intervention was evaluated. Based on baseline weight, according to the Diabetes Prevention Program(24), participants were assigned one of the following daily goals: 1200 calories and 33 fat grams, 1500 calories and 42 fat grams, 1800 calories and 50 fat grams, or 2000 calories and 55 fat grams. Total daily fat intake was limited to ~25% of total calories and emphasis was placed on consuming of mono- and polyunsaturated fats while limiting saturated fat and cholesterol. In addition, participants were instructed to include at least 5 servings of fruits or vegetables and 6 servings of grains, especially whole grains, in their daily diet. The goal was to achieve a 7% reduction in body weight by 6-months and to maintain the weight loss for the remainder of the trial. To aid weight loss, participants were weighed once per week and kept food records for at least 6 days/week during the first 6 months and once per month thereafter.

Successful Aging (SA) Health Education Intervention

The PA+SA group (n=15) attended 60-minute, once monthly successful aging health education workshops to control for attention. The sessions were based on "The Ten Keys to Healthy $Aging^{TM}$ "(25) and the comparison intervention program developed for the Lifestyle Interventions and Independence for Elders Pilot Study(22).

Clinical Measurements

All measures were collected at baseline (BL), 6- and 12-months. Body height (cm) and weight (kg) were measured and used to calculate BMI (kg/m²). Waist circumference (cm) was measured as previously described using the Gulick II tape measure (Country Technology Inc., Gray Mills, WI) (19). Participants also completed questionnaires on socio-demographics, medical history, and physical activity was measured using the Community Healthy Activities Model Program for Seniors (CHAMPS) Physical Activity questionnaire(26). PA levels from the CHAMPS were calculated as minutes/week of moderate intensity (3 METs).

Physical Performance Measures

The Short Physical Performance Battery (SPPB)(27), which included a 4m walk, chair stands and balance tests, and time (s) to complete a usual paced 400m walk(19), were used to assess physical function.

Dual Energy X-ray Absorptiometry (DXA)

Total body fat mass, percent body fat, and total body lean mass (excluding bone) were measured using DXA (Hologic QDR 4500, software version 12.3; Bedford, MA)(28).

Computed Tomography (CT)

CT scans (9800 Advantage, General Electric, Milwaukee, WI) were used to quantify crosssectional areas (CSA) of total, VAT and subcutaneous abdominal adipose tissue, as well as CSA of mid-thigh muscle, total thigh adipose tissue, IMAT and muscle density (a surrogate marker of intramyocellular lipid content) using established methods(11,18–19) and commercially available software (Slice-O-Matic, Tomovision, Montreal, Canada).

Statistical Analyses

Univariate statistics included means and standard deviations. Changes from baseline to 12-months were calculated and the statistical significance of both within and between group changes were determined using parametric and nonparametric tests where appropriate. Generalized Estimating Equations with an unstructured correlation matrix were used to quantify the relationship between 6- and 12-month changes in body composition with change in SPPB. Six and 12-month change scores, as opposed to values by time interactions, were used in the models due to the small sample size. Intervention groups were pooled for these analyses to address the aim of determining mechanisms regarding body composition remodeling. The effect of adjusting for intervention assignment and the significance of its beta coefficient were also assessed.

To correspond with GEE analyses, baseline characteristics include those who completed at least a 6-month visit (n=35). Baseline characteristics of the entire cohort (n=36) and sixmonth change data (n=35) are published elsewhere(19). Twelve month change data include the 32 participants who completed the trial and key baseline characteristics of completers (n=32) and non-completers (n=4) were compared. In addition to those lost to follow-up, two participants in each group were missing thigh or abdominal CT scans at all time points due to metal deposits in the body. Analyses were conducted with SAS v9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Baseline Characteristics

There were no significant baseline differences between the PA+WL and PA+SA groups in regard to demographic, anthropometric, body composition and PA, except total abdominal fat (P=0.04), which was higher in PA+WL (Tables 1 & 2). The PA+WL group also tended to have lower baseline SPPB scores and slower 400m walk times compared to the PA+SA group (both P=0.08, Figure 3).

There were no significant differences between completers (n=32) and those lost to follow-up (n=4) for any baseline measure except total thigh and subcutaneous thigh fat (both *P*<0.01), which were higher in those lost to follow-up. Those lost to follow-up also tended to have lower SPPB (10.0±1.3 vs. 11.3±1.0, *P*=0.07) and slower 400m walk times (406.2±60.5s vs. 348.8±45.5s, *P*=0.08, data not shown).

Intervention Adherence

PA+WL and PA+SA groups adhered, defined as percent attendance, similarly to the PA intervention during all phases of the intervention: adoption (79.2±19.5% vs. 77.7±12.1%, P=0.50), transition (60.4±27.7% vs. 66.3±26.4%, P=0.50), maintenance (16.3±14.8% vs. 14.3±12.3%, P=0.65) and total (51.3±19.7% vs. 52.2±15.8%, P=0.87). Likewise, minutes walked during the PA sessions was similar between PA+WL and PA+SA during all phases: adoption (28.5±9.0 vs. 29.3±8.3min, P=0.80), transition (34.6±16.7 vs. 38.2±13.7min, P=0.24), maintenance (37.8±21.2vs. 37.3±12.6min, P=0.64) and total (32.1±13.6 vs. 34.0±10.3min, P=0.42).

Adherence to the weight loss intervention was defined as the percentage of those meeting the weight loss goal and mean weight reduction. At 12-months, 39% (7/18) of participants achieved and maintained their 7% weight loss goal. The PA+WL group achieved a $5.5\pm6.8\%$ weight reduction at 12-months.

Change in Anthropometrics and Body Composition (DXA)

PA+WL significantly decreased body weight from BL to 12-months and to a greater degree than PA+SA (Table 2). PA+WL resulted in a 5-fold greater percent decrease in total body fat mass compared to lean mass (-13.1% vs. -2.5%, Table 2). PA+SA also resulted in greater decreases in total fat compared to lean mass.

Change in Body Composition (CT)

Significant 12-month decreases in total, subcutaneous and visceral abdominal adipose tissue were found for PA+WL, but not PA+SA (Table 2 and Figure 2). Additionally, significant between-group differences were observed for changes in VAT and total abdominal adipose tissue CSA, but not abdominal subcutaneous adipose tissue (Table 2). The PA+WL group lost a greater proportion of VAT compared to subcutaneous abdominal adipose tissue whereas PA+SA gained a small amount of VAT and lost 8.7% of baseline subcutaneous abdominal fat (Table 2 and Figure 2).

PA+WL resulted in significant 12-month decreases in subcutaneous and total adipose tissue CSA of the thigh while PA+SA did not; however, no significant intergroup differences existed (Table 2). PA+WL experienced a 2-fold greater percent decrease in IMAT compared to subcutaneous adipose tissue in the thigh (Table 2 and Figure 2). A 12-month decrease in IMAT (-1.8 ± 2.6 cm², -14.5%, *P*=0.03) was found in the PA+SA group, but no other fat depots decreased significantly. Neither group significantly increased thigh muscle density (Table 2). Decreases in thigh muscle CSA were observed in both groups, with PA+WL reaching significance. PA+WL reduced the proportion of total fat CSA twice as much as

thigh muscle CSA (-13.7% vs. -5.0%), whereas PA+SA resulted in equal proportions of total thigh fat and muscle loss (-2.4% vs. -2.5%, Table 2).

Intervention Effect on Physical Performance

PA+WL significantly increased SPPB scores from baseline to 12-months (0.8 ± 1.4 , P=0.03), with most of the improvement occurring between baseline and 6-months (0.6 ± 1.4 , P=0.06, Figure 3, Panel A). PA+SA improved SPPB scores marginally from baseline to 6-months, but this improvement did not reach statistical significance (0.5 ± 0.9 , P=0.13, Figure 3 Panel A) and diminished by 12-months. Though the magnitude of 12-month SPPB improvement was greater and statistically significant for PA+WL, between group difference did not reach statistical significance (P=0.27). Further, a sensitivity analysis adjusting for baseline waist circumference, weight, total body fat and baseline 400m walk time did not change the interpretation of the between group comparison for change in SPPB score.

PA+WL significantly improved 400m walk time from baseline to 6-months; but, this improvement depreciated by 12-months (Figure 3 and Panel B). PA+SA showed no change in 400m walk time from baseline to 6-months and actually declined overall from baseline to 12-months, yet there were no significant intergroup differences between 400m walk time at either 6- (22.0 ± 48.7 s, *P*=0.20) or 12-months (31.6 ± 62.4 s, *P*=0.17). Further, a sensitivity analysis adjusting for baseline waist circumference, weight, total body fat and baseline 400m walk score did not change the interpretation of the between group comparison for change in 400m walk time.

Relationship between Changes in Body Composition and SPPB

Intervention groups were combined for these analyses. After adjustment for age, sex, race, baseline body composition and SPPB, 6- and 12-month decrease in IMAT, subcutaneous adipose of the thigh, total thigh fat, VAT and total abdominal fat were all significantly related to 6- and 12-month improvements in SPPB (Table 3). An increase in muscle density was also associated with an increase in SPPB score after adjustment for covariates (Table 3). Models for IMAT and muscle density were also adjusted for total thigh muscle CSA. After adjustment for change in total fat mass, change in VAT and IMAT remained significant predictors of improved SPPB score (both *P*=0.04). Decreases in subcutaneous abdominal fat and total thigh muscle CSA were not significantly related to improvements in SPPB before or after adjustment for change in total fat.

After adjustment for covariates, 6- and 12-month change in total fat mass from DXA was significantly related to 6- and 12-month change in SPPB, while change in total lean mass was not (Table 3). Adjusting for intervention assignment had little to no effect on any model involving CT or DXA measures and the coefficient corresponding to randomization assignment was not significant in any model.

DISCUSSION

A key and novel finding of this research was that decreases in IMAT and VAT were significantly associated with improvements in SPPB independent of decrease in total fat mass. These findings support our hypotheses that losing fat mass improves function and

more importantly, the region where the fat is lost matters. This research also expands upon cross-sectional work showing that IMAT and VAT are associated with worse muscle or physical performance and adverse health conditions that may negatively affect muscle or physical performance (10,17,29). Consistent with our results, a recent WL+PA intervention study in obese older women showed that decreases in IMAT and subcutaneous fat of the calf were associated with improved walking performance (21). However, no relationship between changes in thigh IMAT and improved walking performance were observed. This difference may be attributable to their participants being about 7 years younger and 3.5 kg/m² more obese.

Although there were no statistically significant differences between the PA+WL and PA+SA group regarding improvement in SPPB or 400m walk time, the PA+WL group showed significant improvements in SPPB from BL to 12-months, while the PA+SA group did not. As previously shown, these effects were mainly achieved during the more intensive phase of the intervention(19) and improvement in 400m walking time for PA+WL was only partially sustained during the maintenance phase. The lack of sustained or continued improvement during the maintenance phase suggests that better efforts are needed to maintain long-term improvements in function(30–31). However, the benefits of PA should not be understated, as this cohort was relatively high functioning and the PA+SA group maintained their function. The suggestion that PA+WL improved function to a greater degree than PA+SA is in agreement with previous research in obese older adults demonstrating that diet plus exercise is more effective at improving physical function than either exercise or diet alone (6,32).

Interestingly, PA+WL appeared to preferentially target IMAT and VAT as opposed to subcutaneous fat, as the PA+WL group lost twice the proportion of IMAT and VAT compared to subcutaneous fat of both the thigh and abdomen. This is consistent with previous studies exhibiting that WL induced via caloric restriction, exercise or in combination results in decreases in IMAT and VAT(20,33-35). For example, in older adults both exercise- and caloric restriction-induced WL have been shown to reduce IMAT and VAT to a greater degree than subcutaneous thigh and abdominal fat, respectively(33). Importantly, exercise-induced WL resulted in greater decreases in IMAT and VAT compared to caloric restriction(33). Additionally, while the PA+WL group lost significant amounts of total and thigh lean mass, they lost over 5-times the proportion of total fat and twice the proportion of thigh fat compared to lean mass. This is in agreement with previous work comparing WL+PA to WL alone, which showed that PA was necessary to preserve lean mass(36). Although our study was not designed to test this hypothesis (no WL only), our results taken into consideration with the findings of Murphy(33) and Chomentowski(36) et al., suggest that physical activity in addition to weight loss, compared to weight loss alone, may result in more optimal body composition remodeling. Future work will examine particular factors driving the body composition remodeling, including changes to specific nutrient intake.

The biological mechanisms by which decreasing these specific fat depots may improve physical performance are unclear. VAT is strongly associated with insulin resistance independent of overall adiposity as well as with higher levels of proinflammatory cytokines(10–12). Therefore, decreases in VAT may result in improvements in metabolic

and inflammatory states, which may positively affect muscle and physical performance. Similarly, IMAT and muscle density are related to insulin resistance and the metabolic syndrome(11,37–38); therefore, decreasing IMAT and muscle density levels may result in a more optimal metabolic state, leading to improved muscle and physical function. Further, higher IMAT levels have also been linked to higher levels of inflammation(15). Intervention trials examining the specific relationships between decreases in IMAT, muscle density, and VAT with change in inflammatory and metabolic markers, and how they impact physical function in older adults are needed.

The current study has several strengths. First, physical function was measured objectively using validated and widely used performance measures rather than self-report. The gold standard method of CT was used to measure regional body composition and DXA was implemented because it is widely used and validated, allowing for comparison with other studies. The statistical method used took into account both 6- and 12-month data, thus all participants, except for the one in PA+SA who dropped out before 6-months, contributed to the main analyses. Limitations include the lack of WL only and true control groups, which would have enabled us to examine the exclusive effects of weight loss, physical activity and the combination of both. PA was measured via self-report, which introduces recall bias. Although function was performance based, SPPB score has a ceiling and the walk was usual paced; implementing a higher level task, such as a fast paced 400m walk, may have been more sensitive to changes in this higher functioning cohort. Further, the PA+SA group had a higher SPPB score at baseline, which would have made them more susceptible to the ceiling effect. The PA+WL group had 3 participants dropout between the 6- and 12-month clinic visits whereas the PA+SA group had 1 participant before beginning the intervention. Those lost to follow-up had higher amounts of subcutaneous and total thigh fat. However, it is unlikely that this would have affected the main results concerning the relationship between changes in body composition and physical function in an intention to treat analyses; as those who dropped out likely experienced decreases in function and increases in fat depots. Finally, participants in this study were volunteers and not a random sample of the population, limiting the generalizability of this study. Specifically, participants were mostly white females, relatively healthy and high functioning, thus these findings may not be generalizable to minority, male or frailer older adults.

In conclusion, decreases in IMAT and VAT, regardless of intervention assignment and independent of decreases to total fat mass, were significantly related to improved physical function. Therefore, targeting these fat depots may be of particular importance when aiming to improve physical function or prevent physical disability in older adults. Further, physical activity seems to target IMAT, as opposed to subcutaneous fat, and is likely necessary to optimize body composition remodeling during intentional weight loss. Additionally, weight loss in conjunction with physical activity resulted in significant improvements in physical function after 12-months, whereas physical activity plus successful aging did not. This study provides important and novel insights into mechanisms, related to body composition remodeling, by which moderate physical activity and intentional weight loss improve physical function in older adults.

Acknowledgements:

This work was supported by a Center for Disease Control cooperative agreement (1 U48 DP000025). ClinicalTrials.gov identifier: NCT00714506

REFERENCES

- Al Snih S, Ottenbacher KJ, Markides KS, Kuo Y, Eschbach K, Goodwin JS (2007) THe effect of obesity on disability vs mortality in older americans. Archives of internal medicine 167:774–780. doi:10.1001/archinte.167.8.774 [PubMed: 17452539]
- Villareal DT, Apovian CM, Kushner RF, Klein S (2005) Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Am J Clin Nutr 82:923–934. [PubMed: 16280421]
- Miller S, Wolfe R (2008) The danger of weight loss in the elderly. J Nutr Health Aging 12:487–491. doi:10.1007/bf02982710 [PubMed: 18615231]
- Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP (2001) Weight change in old age and its association with mortality. J Am Geriatr Soc 49:1309–1318. doi:10.1046/ j.1532-5415.2001.49258.x [PubMed: 11890489]
- Shea MK, Nicklas BJ, Houston DK, Miller ME, et al. (2011) The effect of intentional weight loss on all-cause mortality in older adults: results of a randomized controlled weight-loss trial. The American Journal of Clinical Nutrition 94:839–846. doi:10.3945/ajcn.110.006379 [PubMed: 21775558]
- Villareal DT, Chode S, Parimi N, Sinacore DR, et al. (2011) Weight Loss, Exercise, or Both and Physical Function in Obese Older Adults. New England Journal of Medicine 364:1218–1229. doi:10.1056/NEJMoa1008234
- Waters DL, Ward AL, Villareal DT (2013) Weight loss in obese adults 65 years and older: a review of the controversy. Exp Gerontol 48:1054–1061. doi:10.1016/j.exger.2013.02.005 [PubMed: 23403042]
- Kuk JL, Lee S, Heymsfield SB, Ross R (2005) Waist circumference and abdominal adipose tissue distribution: influence of age and sex. The American Journal of Clinical Nutrition 81:1330–1334. [PubMed: 15941883]
- Delmonico MJ, Harris TB, Visser M, Park SW, et al. (2009) Longitudinal study of muscle strength, quality, and adipose tissue infiltration. The American Journal of Clinical Nutrition 90:1579–1585. doi:10.3945/ajcn.2009.28047 [PubMed: 19864405]
- Schrager MA, Metter EJ, Simonsick E, Ble A, Bandinelli S, Lauretani F, Ferrucci L (2007) Sarcopenic obesity and inflammation in the InCHIANTI study. Journal of Applied Physiology 102:919–925. doi:10.1152/japplphysiol.00627.2006 [PubMed: 17095641]
- Goodpaster BH, Krishnaswami S, Resnick H, Kelley DE, et al. (2003) Association Between Regional Adipose Tissue Distribution and Both Type 2 Diabetes and Impaired Glucose Tolerance in Elderly Men and Women. Diabetes Care 26:372–379. doi:10.2337/diacare.26.2.372 [PubMed: 12547865]
- Goodpaster BH, Krishnaswami S, Harris TB, Katsiaras A, et al. (2005) Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. Archives of internal medicine 165:777–783. doi:10.1001/archinte.165.7.777 [PubMed: 15824297]
- Park SW, Goodpaster BH, Strotmeyer ES, Kuller LH, et al. (2007) Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes: the health, aging, and body composition study. Diabetes Care 30:1507–1512. doi:10.2337/dc06-2537 [PubMed: 17363749]
- Beavers KM, Beavers DP, Houston DK, Harris TB, et al. (2013) Associations between body composition and gait-speed decline: results from the Health, Aging, and Body Composition study. The American Journal of Clinical Nutrition. doi:10.3945/ajcn.112.047860
- 15. Addison O, Drummond MJ, Lastayo PC, Dibble LE, Wende AR, McClain DA, Marcus RL (2014) Intramuscular fat and inflammation differ in older adults: The impact of frailty and inactivity. J Nutr Health Aging 18:532–538. doi:10.1007/s12603-014-0019-1 [PubMed: 24886741]

- Hilton TN, Tuttle LJ, Bohnert KL, Mueller MJ, Sinacore DR (2008) Excessive Adipose Tissue Infiltration in Skeletal Muscle in Individuals With Obesity, Diabetes Mellitus, and Peripheral Neuropathy: Association With Performance and Function. Physical Therapy 88:1336–1344. doi:10.2522/ptj.20080079 [PubMed: 18801853]
- Tuttle LJ, Sinacore DR, Mueller MJ (2012) Intermuscular Adipose Tissue Is Muscle Specific and Associated with Poor Functional Performance. Journal of Aging Research 2012:7. doi:10.1155/2012/172957
- Goodpaster BH, Chomentowski P, Ward BK, Rossi A, et al. (2008) Effects of physical activity on strength and skeletal muscle fat infiltration in older adults: a randomized controlled trial. J Appl Physiol 105:1498–1503. doi:10.1152/japplphysiol.90425.2008 [PubMed: 18818386]
- Santanasto AJ, Glynn NW, Newman MA, Taylor CA, Brooks MM, Goodpaster BH, Newman AB (2011) Impact of Weight Loss on Physical Function with Changes in Strength, Muscle Mass, and Muscle Fat Infiltration in Overweight to Moderately Obese Older Adults: A Randomized Clinical Trial. Journal of Obesity 2011. doi:10.1155/2011/516576
- Avila J, Gutierres J, Sheehy M, Lofgren I, Delmonico M (2010) Effect of moderate intensity resistance training during weight loss on body composition and physical performance in overweight older adults. European Journal of Applied Physiology 109:517–525. doi:10.1007/ s00421-010-1387-9 [PubMed: 20169360]
- 21. Manini TM, Buford TW, Lott DJ, Vandenborne K, et al. (2013) Effect of Dietary Restriction and Exercise on Lower Extremity Tissue Compartments in Obese, Older Women: A Pilot Study. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. doi:10.1093/gerona/ gls337
- Rejeski WJ, Fielding RA, Blair SN, Guralnik JM, et al. (2005) The lifestyle interventions and independence for elders (LIFE) pilot study: Design and methods. Contemporary Clinical Trials 26:141–154. [PubMed: 15837437]
- 23. Borg G (1998) Borg's Perceived exertion and pain scales. Champaign, IL: Human Kinetics.
- 24. (1999) The Diabetes Prevention Program. Design and methods for a clinical trial in the prevention of type 2 diabetes. Diabetes Care 22:623–634. doi:10.2337/diacare.22.4.623 [PubMed: 10189543]
- 25. Newman AB, Bayles CM, Milas CN, McTigue K, et al. (2010) The 10 Keys to Healthy Aging: Findings From an Innovative Prevention Program in the Community. Journal of Aging and Health 22:547–566. doi:10.1177/0898264310363772 [PubMed: 20495156]
- Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL (2001) CHAMPS physical activity questionnaire for older adults: outcomes for interventions. Med Sci Sports Exerc 33:1126– 1141. [PubMed: 11445760]
- 27. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, et al. (1994) A Short Physical Performance Battery Assessing Lower Extremity Function: Association With Self-Reported Disability and Prediction of Mortality and Nursing Home Admission. Journal of Gerontology 49:M85–M94. doi:10.1093/geronj/49.2.M85 [PubMed: 8126356]
- 28. Visser M, Fuerst T, Lang T, Salamone L, Harris TB (1999) Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study--Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol 87:1513–1520. [PubMed: 10517786]
- Visser M, Goodpaster BH, Kritchevsky SB, Newman AB, et al. (2005) Muscle Mass, Muscle Strength, and Muscle Fat Infiltration as Predictors of Incident Mobility Limitations in Well-Functioning Older Persons. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 60:324–333. doi:10.1093/gerona/60.3.324
- 30. Fielding RA, Rejeski WJ, Blair S, Church T, et al. (2011) The Lifestyle Interventions and Independence for Elders Study: Design and Methods. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 66A:1226–1237. doi:10.1093/gerona/glr123
- Pahor M, Guralnik JM, Ambrosius WT, et al. (2014) Effect of structured physical activity on prevention of major mobility disability in older adults: The life study randomized clinical trial. JAMA. doi:10.1001/jama.2014.5616
- 32. Rejeski W, Brubaker PH, Goff DC Jr, et al. (2011) Translating weight loss and physical activity programs into the community to preserve mobility in older, obese adults in poor cardiovascular

health. Archives of internal medicine 171:880–886. doi:10.1001/archinternmed.2010.522 [PubMed: 21263080]

- 33. Murphy JC, McDaniel JL, Mora K, Villareal DT, Fontana L, Weiss EP (2012) Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. Journal of Applied Physiology 112:79–85. doi:10.1152/ japplphysiol.00355.2011 [PubMed: 22016371]
- 34. Marcus R, Addison O, Kidde J, Dibble L, Lastayo P (2010) Skeletal muscle fat infiltration: Impact of age, inactivity, and exercise. J Nutr Health Aging 14:362–366. doi:10.1007/s12603-010-0081-2 [PubMed: 20424803]
- 35. Janssen I, Fortier A, Hudson R, Ross R (2002) Effects of an Energy-Restrictive Diet With or Without Exercise on Abdominal Fat, Intermuscular Fat, and Metabolic Risk Factors in Obese Women. Diabetes Care 25:431–438. doi:10.2337/diacare.25.3.431 [PubMed: 11874926]
- 36. Chomentowski P, Dubé JJ, Amati F, Stefanovic-Racic M, Zhu S, Toledo FGS, Goodpaster BH (2009) Moderate Exercise Attenuates the Loss of Skeletal Muscle Mass That Occurs With Intentional Caloric Restriction–Induced Weight Loss in Older, Overweight to Obese Adults. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 64A:575–580. doi:10.1093/gerona/glp007
- Miljkovic I, Zmuda JM (2010) Epidemiology of myosteatosis. Curr Opin Clin Nutr Metab Care 13:260–264. doi:10.1097/MCO.0b013e328337d826 [doi] [PubMed: 20179586]
- Gallagher D, Kuznia P, Heshka S, Albu J, et al. (2005) Adipose tissue in muscle: a novel depot similar in size to visceral adipose tissue. The American Journal of Clinical Nutrition 81:903–910. [PubMed: 15817870]





Screening, Randomization and Follow-Up Flow Chart



Figure 2. 12-Month Changes in Specific Fat Depots of the Thigh and Abdomen Measured by Computed Tomography.

Data are presented as mean percent change in cross-sectional area, except muscle density, which was measured in Hounsfield units. The PA+WL group experienced significant decreases in all depots (all P<0.05) except muscle density – which increased slightly in both groups. The PA+SA group experienced a significant decrease in IMAT only (P<0.05). A significant intergroup difference exists for change in VAT only (P<0.05). *Denotes a significant change from baseline (P<0.05). Abbreviations: SUBQ: subcutaneous, VAT: visceral adipose tissue, IMAT: intermuscular adipose tissue, BL: baseline, PA+WL: physical activity plus weight loss, PA+SA: physical activity plus successful aging education.



Time Point

Figure 3. Short Physical Performance Battery Score (Panel A) and 400 Meter Walk Time (Panel B) by Time Point and Intervention Group

Panel A. Change in SPPB score by time point and stratified by intervention group. Data are means and the error bars represent standard errors. The PA+WL group experienced a near significant improvement from baseline to 6-months (0.6 ± 1.3 , *P*=0.06, n=21) and this change became significant at 12-months (0.8 ± 1.4 , *P*=0.03, n=18). The PA+SA group did not experience any significant changes, but there were no significant intergroup differences in regard to change in SPPB score. *Denotes a significant change from baseline (*P*<0.05). Abbreviations: SPPB: short physical performance battery, PA+WL: physical activity plus

weight loss, PA+SA: physical activity plus successful aging education. **Panel B**. Time to walk 400m at usual pace in seconds, by time point and stratified by intervention group. Data are means and the error bars represent standard errors. The PA+WL group experienced a significant improvement (P<0.05) from baseline to 6-months, but this improvement reverted back to non-significance at 12-months. The PA+SA group did not show any significant changes and there were no significant intergroup differences in regard to 6- or 12-month change in 400m walk time. *Denotes a significant change from baseline (P<0.05). Abbreviations: PA+WL: physical activity plus weight loss, PA+SA: physical activity plus successful aging education

Table 1.

Baseline and Demographic Characteristics by Intervention Group

	PA + WL (n= 21)	PA + SA (n=14)	P-value
Age	70.6 (5.9)	69.9 (6.2)	0.83
Gender			>0.99
Male	4 (19.1)	2 (14.3)	
Female	17 (81.0)	12 (85.7)	
Race			0.19
White	19 (90.5)	10 (71.4)	
African American	2 (9.5)	4 (28.6)	
Education			0.48
High School/GED	13 (61.9)	9 (64.3)	
College	6 (28.6)	2 (14.3)	
Other/Refused	2 (9.5)	3 (21.4)	
Household Income (yearly)			0.79
<\$50,000	13 (61.9)	9 (64.3)	
>\$50,000	3 (14.3)	3 (21.4)	
Don't Know/Refused	5 (23.8)	2 (14.3)	

Values are Mean (SD) or N (%). Abbreviations: PA+WL: physical activity plus weight loss, PA+SA: physical activity plus successful aging education

Table 2.

Mean Baseline and 12-month Changes in Anthropometric Measures, Body Composition and Physical Activity by Intervention Group

	PA + WL (Baseline n = 21, Change n = 18)			PA + SA (Baseline and Change n = 14)		
	BL Value or 12-month Change	Percent Change	p-value *	BL value or 12-month Change	Percent Change	p-value *
Anthropometric						
Waist Circumference, cm						
Baseline	108.8 (7.2) [†]			104.3 (8.3)		0.12
12-month Change	-2.5 (7.8)	-2.1	0.18	0.1 (10.5)	0.2	0.62
Body Weight, kg						
Baseline	89.8 (10.0)			85.3 (6.8)		0.21
12-month Change	$-4.9 (6.1)^{\$}$	-5.5	0.002	$-0.8(3.0)^{\$}$	-1.0	0.32
BMI, kg/m ²						
Baseline	33.6 (3.3)			32.0 (3.1)		0.22
12-month Change	-1.7 (2.3) <i>§</i>	-5.2	0.002	$-0.2 (1.1)^{\$}$	-0.6	0.71
DXA						
Percent Body Fat						
Baseline	43.0 (5.4)			42.2 (5.4)		0.65
12-month Change	-2.9 (3.4) [§]	-7.2	< 0.001	$-0.8(1.6)^{-1}$	-1.8	0.09
Total Fat Mass, kg						
Baseline	38.0 (5.9)			35.7 (6.7)		0.56
12-month Change	$-4.8 \ (4.6)^{\$}$	-13.1	< 0.001	-1.2 (2.2) [§]	-3.2	0.06
Total Lean Mass, kg						
Baseline	48.2 (7.6)			46.2 (5.4)		0.63
12-month Change	-1.2 (1.7)	-2.5	0.01	-0.1 (1.2)	-0.2	0.81
Abdominal CT \ddagger						
Total Fat, cm ²						
Baseline	661.5 (134.1)			561.9 (97.1)		0.04
12-month Change	-81.5 (104.8) [§]	-11.0	0.006	-26.5 (77.8) [§]	-5.9	0.24
Visceral Fat, cm ²						
Baseline	217.7 (61.3)			178.7 (49.7)		0.10
12-month Change	-34.8 (40.4) [§]	-15.1	0.004	-1.0 (29.3)§	2.1	0.91
SUBQ Fat, cm ²						
Baseline	443.7 (124.5)			382.4 (93.7)		0.07
12-month Change	-46.7 (62.8)	-8.2	0.02	-24.8 (63.8)	-8.7	0.19
Right Thigh CT \ddagger						
Total Fat, cm ²						
Baseline	150.8 (52.4)			134.4 (47.8)		0.39
12-month Change	-19.1 (24.4)	-13.7	0.007	-3.4 (7.8)	-2.4	0.15

	PA + WL (Baseline n = 21, Change n = 18)			PA + SA (Baseline and Change n = 14)		
	BL Value or 12-month Change	Percent Change	p-value *	BL value or 12-month Change	Percent Change	p-value *
SUBQ, cm ²						
Baseline	133.2 (52.8)			115.9 (46.9)		0.37
12-month Change	-15.4 (23.7)	-12.3	0.02	-1.5 (7.5)	-0.7	0.49
IMAT, cm ²						
Baseline	12.5 (3.6)			13.9 (5.5)		0.60
12-month Change	-3.2 (2.2)	-23.6	< 0.001	-1.8 (2.6)	-14.5	0.03
Muscle Mass, cm ²						
Baseline	102.3 (23.2)			101.5 (21.8)		0.90
12-month Change	-5.0 (6.4)	-5.0	0.008	-2.1 (5.7)	-2.5	0.21
Muscle Density, HU						
Baseline	39.6 (3.1)			39.9 (3.3)		0.69
12-month Change	0.7 (1.5)	1.8	0.11	0.2 (1.4)	0.6	0.55
Physical Activity, min/week						
Baseline	198.6 (227.7)			337.5 (306.6)		0.22
12-month Change [#]	-29.2 (243.4)		0.91	49.3 (336.9)		0.62

 † Values are mean \pm Standard Deviation.

* *P-values* denote significance of between group differences for baseline rows and 12-month within group changes for change rows.

 $^{\$}$ Denotes a significant between group difference for 12-month change, P < 0.05.

 $t_{\rm Two}$ participants in each group are missing thigh or abdominal CT scans due to metal deposits in the body.

#Six participants are missing percent change data due to a 0 baseline value.

Abbreviations: PA+WL: physical activity plus weight loss, PA+SA: physical activity plus successful aging education, BL: baseline, BMI: body mass index, DXA: dual energy x-ray absorptiometry, CT: Computed Tomography SUBQ: subcutaneous, IMAT: intermuscular adipose tissue, HU: Hounsfield units.

Table 3.

6- and 12-Month Change in Regional Body Composition Predicting 6- and 12-Month Change in SPPB Score using GEE

Variable [*]	Std ß (SE)	P-value	Adjusted for Std β (SE)	Fat Mass, DXA <i>P-value</i>
Intermuscular Fat **	-0.41 (0.14)	< 0.01	-0.34 (0.17)	0.04
Muscle Density **	0.22 (0.10)	0.04	0.13 (0.14)	0.37
Thigh Subcutaneous Fat	-0.31 (0.11)	< 0.01	-0.26 (0.21)	0.21
Total Thigh Fat	-0.34 (0.11)	< 0.01	-0.36 (0.28)	0.20
Abdominal Subcutaneous Fat	-0.18 (0.10)	0.09	-0.16 (0.11)	0.12
Visceral Adipose Tissue	-0.45 (0.16)	< 0.01	-0.41 (0.15)	< 0.01
Total Abdominal Fat	-0.33 (0.12)	0.01	-0.42 (0.11)	< 0.01
Thigh Muscle CSA	0.10 (0.18)	0.56	0.22 (0.13)	0.08
Lean Mass, DXA	-0.07 (0.08)	0.36	-	-
Fat Mass, DXA	-0.33 (0.14)	0.02	-	-
Total Mass, DXA	-0.27 (0.14)	0.06	-	-

* Models are adjusted for age, sex, race, randomization group, time point, baseline body composition (models adjusted for Fat Mass are also adjusted for baseline fat mass) and SPPB scores.

** Models are also adjusted for baseline thigh muscle cross-sectional area.

Abbreviations: Std: standardized, SE: standard error, : change, DXA: dual energy x-ray absorptiometry, GEE: generalized estimating equations

Author Manuscript