Fat Mass Loss Predicts Gain in Physical Function With Intentional Weight Loss in Older Adults

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Background. Clinical recommendation of weight loss (WL) in older adults remains controversial, partially due to concerns regarding lean mass loss and potential loss of physical function. The purpose of this study is to determine the independent associations between changes in fat and lean mass and changes in physical function in older, overweight, and obese adults undergoing intentional WL.

Methods. Data from three randomized-controlled trials of intentional WL in older adults with similar functional outcomes (short physical performance battery and Pepper assessment tool for disability) were combined. Analyses of covariance models were used to investigate relationships between changes in weight, fat, and lean mass (acquired using dual-energy x-ray absorptiometry) and changes in physical function.

Results. Overall loss of body weight was $-7.8 \pm 6.1$ kg ($-5.6 \pm 4.1$ kg and $-2.7 \pm 2.4$ kg of fat and lean mass, respectively). In all studies combined, after adjustment for age, sex, and height, overall WL was associated with significant improvements in self-reported mobility disability ($p < .01$) and walking speed ($p < .01$). Models including change in both fat and lean mass as independent variables found only the change in fat mass to significantly predict change in mobility disability ($\beta_{fat} = 0.04; p < .01$) and walking speed ($\beta_{fat} = -0.01; p < .01$).

Conclusions. Results from this study demonstrate that loss of body weight, following intentional WL, is associated with significant improvement in self-reported mobility disability and walking speed in overweight and obese older adults. Importantly, fat mass loss was found to be a more significant predictor of change in physical function than lean mass loss.

Key Words: Physical function—Weight loss—Fat mass—Lean mass—Aging.

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By 2030, older adults are projected to comprise nearly 20% of the U.S. population (1). Aging is associated with declines in physical function (2,3), and such declines consistently predict future disability, institutionalization, and mortality (4–6). Health care costs associated with sarcopenic disability are significant, accounting for $18.5 billion in direct health care costs in 2000 (7). Given the increasing number of older adults, coupled with the economic and emotional burden related to age-associated loss of physical function, identification of modifiable functional decline risk factors is of considerable public health interest.

Over one third of adults aged 60 years and older in the United States are considered to be obese (8), and importantly, obesity is known to exacerbate age-related declines in physical function (9,10). Despite this knowledge, clinical recommendation of weight loss (WL) in this population remains controversial. Reluctance stems, in large part, from epidemiologic evidence linking loss of weight in late life to increased mortality (11), and physiologic evidence showing a simultaneous loss of fat and muscle (or lean) mass (which may be associated with the development of adverse health events and disability in older adults; 12,13) during intentional WL via caloric restriction (CR; 14).

Despite these concerns, limited data exist addressing the potential benefits and risks of intentional weight loss on physical function in older adults (15,16). Some studies show that WL improves function, despite loss of lean mass. A recent, small, randomized controlled trial (RCT) comparing exercise and intentional WL to exercise alone found additional improvements in lower extremity function associated with WL (over exercise alone) (17). Importantly, functional improvement was strongly and inversely correlated with change in fat mass ($r = -.34$ to $-.50$) but not with change in lean mass ($r = -.003$; 17). Similarly, the combination of hypocaloric dieting and exercise training improved muscle strength and quality, despite significant lean mass loss.
loss, with greater fat loss associated with greater gains (18). However, additional data that directly compare the effects of lean versus fat mass lost during intentional WL on functional outcomes in older adults are needed in order to further understanding of the health risks and benefits of WL in this population.

Therefore, the purpose of this study was to determine the independent associations between changes in fat and lean mass and changes in several measures of physical function in older, overweight, and obese adults undergoing intentional WL. Three RCTs of intentional WL in older adults who completed a standard battery of physical function tests pre- and postintervention were combined so that consistency of relationships and overall effects could be investigated in a broad-based population of older adults. We hypothesized that intentional weight, and especially fat mass, loss would result in improved physical function, despite a concomitant loss of lean mass.

**Methods**

**Participants**

This analysis included 271 older (≥50 years) adults enrolled in three separate WL trials at Wake Forest University between 2003 and 2010 (19–21). All studies assessed common measures of physical function and body composition before and after intentional WL. Design details of each study were previously published (19–21). Table 1 provides descriptions of each study, including sample size, distribution by sex, age, intervention duration, initial body mass index, and targeted WL strategy and goal.

Briefly, the Cooperative Lifestyle Intervention Program (CLIP) was an RCT of physical activity and WL on mobility in overweight and obese older adults with, or at risk for, cardiovascular disease. The study was conducted within the community infrastructure of Cooperative Extension Centers, and participants were randomized to one of three interventions:

- **Physical activity, WL + physical activity**, or a successful aging education control arm. The primary outcome was time to complete a 400-m walk. The Diet, Exercise, and Metabolism for Older Women (DEMO) study was an RCT comparing the effects of (i) CR alone, (ii) CR plus moderate intensity aerobic exercise, and (iii) CR plus vigorous-intensity exercise on the loss of abdominal adipose tissue and improvement in cardiovascular disease risk factors in overweight and obese postmenopausal women. Lastly, the Optimizing Body Composition for Function in Older Adults (OPTIMA) study tested the hypotheses that pioglitazone treatment decreases multiple ectopic fat depots and resistance training reduces lean appendicular tissue loss during WL in older, nondiabetic overweight and obese men and women.

Only arms of the RCTs where participants were randomized to intentional WL were included in this analysis. Further, because all included RCTs originally examined the effects of WL and exercise on various health outcomes, 202 of 271 included participants also underwent exercise training. All participants provided written informed consent and studies were approved by the university Institutional Review Board.

**Measurements**

All physical function and body composition measures were completed by trained blinded personnel at the Wake Forest Geriatric Clinical Research Center.

**Physical function.**—A common battery of both objective and self-reported physical function were collected in all studies.

Short physical performance battery.—The short physical performance battery (SPPB) consists of a 4-meter walk (m/s), repeated chair stands (sec), and three hierarchical standing balance tests (score, 0–4; 6). Each of the three performance measures is assigned a categorical score ranging
from 0 to 4, with 4 indicating the highest level of performance and 0 the inability to complete the test. A summary score ranging from 0 (worst performers) to 12 (best performers) is calculated by adding walking speed, chair stands, and balance scores.

Pepper assessment tool for disability.—The Pepper assessment tool for disability self-administered questionnaire consists of 19 items that include a range of activities that assess mobility, activities of daily living, and instrumental activities of daily living. Responses are made on a five-point Likert scale ranging from 1 (“usually did with no difficulty”) to 5 (“unable to do”), or a box can be checked that reads “usually did not do for other reasons” (22). The mobility subscale includes six items of the Pepper assessment tool for disability, and a mean scale score is calculated by summarizing across and then dividing by the six items.

Body composition.—Body mass was measured in kilograms (kg) on a standard calibrated scale, and height was measured in centimeters using a stadiometer. Body mass index was calculated as body mass in kg divided by height in meters squared. Total body fat and lean mass were assessed using dual-energy x-ray absorptiometry (Hologic Delphi A 11.0 QDR, Bedford, MA).

Statistical Analysis

Means and proportions were calculated by study and overall for baseline characteristics. Change in physical function parameters include (i) the Pepper assessment tool for disability mobility subscale score (1–5, score); (ii) walking speed (m/s); (iii) time (s) to complete five chair stands; and (iv) total SPPB score. Measurements of body mass include total weight (kg), total body fat mass (kg), and total lean mass (kg). Change from baseline to follow-up was calculated by taking the follow-up measurement minus the baseline measurement for both physical function and body mass measurements.

Within each study and overall, a series of analysis of covariance models to investigate relationships between changes in total, fat, and lean mass and changes in physical function dependent variables were fit. Initially, change in physical function was regressed on change in body mass predictor variables. Each analysis of covariance model contained a term for study, change in body mass, and the interaction between study and change in body mass. This model was used to obtain study specific estimates of the relationship between change in body mass and change in function. If the interaction term was not significant, a reduced model was fit without the interaction term, allowing estimation of the overall association between change in body mass and change in function. This series of models was fit both unadjusted and adjusted for age, sex, height, and study.

To determine the joint effect of change in total body fat and total body lean mass on change in physical function, both variables were entered into the model controlling for study, age, sex, and height. $R^2$ values were used to assess the percent of variation explained by the predictor variables in each model. Sensitivity analyses were performed to determine if the estimated relationships between change in body mass variables and change in physical function were dependent on the elapsed time between measurements. These analyses were performed by defining an additional variable representing the elapsed time between measurements and exploring for an interaction between this variable and the variable representing the change in body mass.

RESULTS

Participant Characteristics and Changes in Body Composition and Physical Function

Table 2 provides descriptive statistics for participant characteristics at baseline as well as change in physical function and in body mass and composition by study and overall ($n = 271$). Across all studies, the mean age of participants was $65.4 \pm 6.8$ years, with the majority being white and female. The overall loss of body weight was $-7.84 \pm 6.1$ kg, and the amount of fat mass lost was slightly greater than twice the amount of lean mass lost ($-5.6 \pm 4.1$ kg vs $-2.7 \pm 2.4$ kg, respectively). In each study, the loss of both fat and lean mass was statistically significant ($p < .001$ for both fat and lean mass for all studies and combined) and overall, follow-up physical function measures were improved over baseline.

Relationships Between Changes in Physical Function and Body Composition

Modeling results for the relationships between change in each dependent variable (physical function) and change in each independent variable (body composition) by study and for all studies combined are presented in Table 3. No interaction between individual study and change in mass for any physical function outcome measure was observed. In all studies combined, after adjustment for age, sex, height, and study, the magnitude of overall WL was associated with improvements in self-reported mobility disability and walking speed (both $p < .01$) but not with improvements in chair stand time or overall SPPB score. Changes in both fat and lean mass were each inversely associated with changes in mobility disability and walking speed (both $p < .05$), indicating that greater losses of fat and lean mass were both associated with more improvement in self-reported mobility disability and faster walking speed. Sensitivity analyses yielded similar results.

Changes in fat and lean mass were correlated in all studies combined (overall $r = .59$) and in each individual study ($r = .69$ for Cooperative Lifestyle Intervention Program;
r = .38 for Diet, Exercise, Metabolism, and Obesity in Older Women; r = .37 for Optimizing Body Composition for Function in Older Adults). Thus, models containing the change in both fat and lean mass were examined to investigate the independent contributions of each on changes in physical function. With both variables in the models, only the change in fat mass remained a significant predictor of change in mobility disability ($\beta_{[\text{fat}]} = 0.04, p < .01$ and $\beta_{[\text{lean}]} = 0.01, p = .62; R^2 = .11$) and walking speed ($\beta_{[\text{fat}]} = -0.01, p = .01$ and $\beta_{[\text{lean}]} = -0.003, p = .64; R^2 = .09$).

Inclusion of both change in fat and lean mass as predictor variables showed the loss of fat mass ($\beta_{[\text{fat}]} = -0.07, p = .01$), but gain in lean mass ($\beta_{[\text{lean}]} = 0.11, p = .02$) were significantly associated with improvements in SPPB score. However, when one overly influential observation (measured to have gained 3.9 kg of lean and lost 2.4 kg of fat mass) was excluded from this analysis, the relationship between change in lean mass and change in SPPB score was slightly attenuated ($\beta_{[\text{lean}]} = 0.09; p = .06$).

Figure 1a–c graphically depict expected changes in physical function measures by change in total body, fat, and lean mass. Results are scaled so that physical function measures can be presented together. Specifically, change in the outcome is expressed per 5 kg of loss of total body fat, and lean mass for walking speed, mobility disability and SPPB score. For chair stand time (s), change is expressed per 1 kg loss in total body, fat, and lean mass. Data from all studies combined show that for every 1 kg loss of body mass, walking speed increased by 0.006 m/s. This effect is magnified when considering loss of fat mass (independent of lean mass loss), where every 1 kg loss of fat mass predicts a 0.01 m/s increase in walking speed.

### Table 2. Characteristics of Participants Overall and by Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>CLIP (N = 98)</th>
<th>DEMO (N = 85)</th>
<th>OPTIMA (N = 88)</th>
<th>Overall (N = 271)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>66.8 ± 4.6</td>
<td>58.3 ± 5.4</td>
<td>70.6 ± 3.6</td>
<td>65.4 ± 6.8</td>
</tr>
<tr>
<td>Female (%)</td>
<td>67 (68.4)</td>
<td>85 (100.0)</td>
<td>40 (45.5)</td>
<td>192 (70.8)</td>
</tr>
<tr>
<td>Non-white (%)</td>
<td>14 (14.3)</td>
<td>32 (37.6)</td>
<td>10 (11.4)</td>
<td>56 (20.7)</td>
</tr>
<tr>
<td>Baseline BMI (kg/m²)</td>
<td>33.1 ± 4.1</td>
<td>32.9 ± 3.6</td>
<td>32.7 ± 5.4</td>
<td>32.9 ± 4.4</td>
</tr>
<tr>
<td>Physical function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPPB (score, 1–12)</td>
<td>9.9 ± 1.4</td>
<td>10.7 ± 1.0</td>
<td>9.0 ± 1.0</td>
<td>9.8 ± 1.3</td>
</tr>
<tr>
<td>ΔSPPB (score, 1–12)</td>
<td>0.66 ± 1.3</td>
<td>0.43 ± 1.1</td>
<td>0.64 ± 1.4</td>
<td>0.59 ± 1.3</td>
</tr>
<tr>
<td>Walking speed (m/s)</td>
<td>1.1 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>ΔWalking speed (m/s)</td>
<td>0.06 ± 0.2</td>
<td>-0.01 ± 0.2</td>
<td>0.06 ± 0.2</td>
<td>0.04 ± 0.2</td>
</tr>
<tr>
<td>Chair stand (s)</td>
<td>14.6 ± 3.9</td>
<td>13.1 ± 2.7</td>
<td>17.7 ± 5.3</td>
<td>15.2 ± 4.5</td>
</tr>
<tr>
<td>ΔChair stand (s)</td>
<td>-1.70 ± 3.9</td>
<td>-1.27 ± 2.7</td>
<td>-1.57 ± 5.8</td>
<td>-1.53 ± 4.4</td>
</tr>
<tr>
<td>PAT-D mobility (score, 1–5)</td>
<td>1.8 ± 0.7</td>
<td>1.4 ± 0.6</td>
<td>1.3 ± 0.5</td>
<td>1.6 ± 0.7</td>
</tr>
<tr>
<td>ΔPAT-D mobility (score, 1–5)</td>
<td>-0.23 ± 0.7</td>
<td>-0.09 ± 0.4</td>
<td>-0.13 ± 0.3</td>
<td>-0.16 ± 0.6</td>
</tr>
<tr>
<td>Body mass and composition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total mass (kg)</td>
<td>92.79 ± 16.1</td>
<td>89.3 ± 11.4</td>
<td>95.1 ± 16.0</td>
<td>92.4 ± 14.9</td>
</tr>
<tr>
<td>ΔTotal mass (kg)</td>
<td>-7.26 ± 7.1</td>
<td>-10.73 ± 5.3</td>
<td>-5.92 ± 4.6</td>
<td>-7.84 ± 6.1</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>36.5 ± 8.9</td>
<td>38.9 ± 6.7</td>
<td>35.3 ± 9.3</td>
<td>36.9 ± 8.5</td>
</tr>
<tr>
<td>ΔFat mass (kg)</td>
<td>-4.78 ± 4.9</td>
<td>-7.94 ± 3.4</td>
<td>-4.16 ± 2.7</td>
<td>-5.56 ± 4.1</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td>52.6 ± 11.4</td>
<td>48.2 ± 5.5</td>
<td>56.1 ± 11.4</td>
<td>52.3 ± 10.4</td>
</tr>
<tr>
<td>ΔLean mass (kg)</td>
<td>-2.48 ± 2.9</td>
<td>-3.64 ± 1.9</td>
<td>-2.04 ± 2.0</td>
<td>-2.69 ± 2.4</td>
</tr>
</tbody>
</table>

Note: Data are presented as means ± SD or n (%) Change is defined as follow-up minus baseline value. BMI = body mass index; Δ = change.

### Table 3. Adjusted Longitudinal Changes in Physical Function by Change in Body Mass and Composition

<table>
<thead>
<tr>
<th>Variable</th>
<th>PAT-D Mobility (score)</th>
<th>Walking Speed (m/s)</th>
<th>Chair Stand (s)</th>
<th>SPPB (score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predictor</td>
<td>β</td>
<td>p Value</td>
<td>β</td>
<td>p Value</td>
</tr>
<tr>
<td>Change in weight</td>
<td>Overall</td>
<td>0.0198 &lt;.01* .06</td>
<td>-0.0060 &lt;.01* .07</td>
<td>0.0506 .32 .01</td>
</tr>
<tr>
<td></td>
<td>CLIP</td>
<td>0.0268 &lt;.01*</td>
<td>-0.0082 &lt;.01* .09</td>
<td>0.0539 .43</td>
</tr>
<tr>
<td></td>
<td>DEMO</td>
<td>-0.0016</td>
<td>-0.0067 .09</td>
<td>-0.0261 .80</td>
</tr>
<tr>
<td></td>
<td>OPTIMA</td>
<td>0.0207 .13</td>
<td>0.0003 .94</td>
<td>0.1248 .25</td>
</tr>
<tr>
<td>Change in fat mass</td>
<td>Overall</td>
<td>0.0432 &lt;.01* .11</td>
<td>-0.0107 &lt;.01* .09</td>
<td>0.1253 .12 .02</td>
</tr>
<tr>
<td></td>
<td>CLIP</td>
<td>0.0501 &lt;.01*</td>
<td>-0.0136 &lt;.01* .01</td>
<td>0.1275 .22</td>
</tr>
<tr>
<td></td>
<td>DEMO</td>
<td>0.0243 .29</td>
<td>-0.0102 .10</td>
<td>-0.0013 .99</td>
</tr>
<tr>
<td></td>
<td>OPTIMA</td>
<td>0.0367 .11</td>
<td>-0.0018 .79</td>
<td>0.2798 .13</td>
</tr>
<tr>
<td>Change in lean mass</td>
<td>Overall</td>
<td>0.0453 &lt;.01* .05</td>
<td>-0.0122 &lt;.02* .06</td>
<td>0.0584 .65 .01</td>
</tr>
<tr>
<td></td>
<td>CLIP</td>
<td>0.0526 .02*</td>
<td>-0.0186 .01*</td>
<td>0.0187 .92</td>
</tr>
<tr>
<td></td>
<td>DEMO</td>
<td>0.0090 .84</td>
<td>-0.0185 .11</td>
<td>0.2028 .48</td>
</tr>
<tr>
<td></td>
<td>OPTIMA</td>
<td>0.0487 .12</td>
<td>0.0060 .53</td>
<td>0.0262 .92</td>
</tr>
</tbody>
</table>

Note: Models are adjusted for age, sex, height, and study. Change is defined as follow-up value minus baseline value. * indicates statistical significance. CLIP = Cooperative Lifestyle Intervention Program; DEMO = Diet, Exercise, Metabolism, and Obesity in Older Women; OPTIMA = Optimizing Body Composition for Function in Older Adults; PAT-D = Pepper assessment tool for disability; SPPB = short physical performance battery.
Recommendation of intentional WL remains controversial for older adults due, in part, to concerns regarding functional impairment that may accompany the loss of lean mass. Results from this study demonstrate that loss of total body mass with intentional WL is associated with significant improvements in self-reported mobility disability and walking speed in overweight and obese older adults. Importantly,
when jointly modeled, fat mass loss was found to be a more significant predictor of change in physical function than lean mass loss. Findings contribute to our understanding of the health ramifications of the loss of lean mass during WL and suggest that physical function is improved following intentional total body and fat mass loss, despite a concomitant loss in lean mass. Moreover, our findings show that physical function improves in relation to the amount of fat mass lost independent of the amount of lean mass lost.

The relative amount of lean versus fat mass loss observed in this analysis is similar to what has been previously reported for older adults (14,23), with approximately two thirds of total body mass losses coming from fat and one third coming from lean tissue. Although it is intuitive that significant loss of lean mass from intentional WL may lead to loss in physical function, our findings and others suggest that this is not the case. This is supported by evidence showing that lean mass is not the most important factor underlying age-related declines in physical function (24–29). Muscle strength, for example, is associated with increased risk of mobility loss (24) and mortality (25), independent of lean mass. Importantly, greater fat mass, especially when deposited intramuscularly, is associated with lower muscle strength and physical performance (26,27) and with increased loss of strength and function over time independent of lean mass (28,29). Furthermore, in agreement with our findings, intentional WL resulting in reduced fat mass is associated with improved physical function in older adults, even when accompanied by significant lean mass loss (18,30). Therefore, several lines of evidence implicate muscle quality (ie, defined as strength/mass), rather than quantity, as the key factor explaining functional performance in older adults.

Although causal mechanisms by which loss of adipose tissue contributes to better physical function have not been fully elucidated, the association we observed between loss of fat mass and improvement in walking speed and mobility may be partially explained by the inflammatory nature of adipose tissue. Several cytokines are secreted from adipose tissue (31), and excessive fat accumulation can induce a pro-inflammatory state. Chronic inflammation is associated with lower muscle strength (32) and predicts disability in the elderly (33,34), potentially by impairment of muscle fiber contractility (35). Weight, and specifically fat, loss decreases systemic inflammation (36) and may provide a biologic mechanism to explain why fat mass loss (beyond decreased inertia associated with total body mass loss) is associated with gains in gait speed and improved self-reported mobility disability.

Although loss of total body and fat mass were associated with statistically significant changes in mobility and gait speed, it is important to consider our findings in light of clinically meaningful functional improvements. A recent meta-analysis exploring the relationship between gait speed and mortality found increments of 0.1 m/s in gait speed predictive of increased survival (37). Based on our modeling results, a 10 kg loss in fat mass would be needed to elicit a 0.1 m/s increase in gait speed. Thus, the 5.5 kg average loss in fat mass in the adults we analyzed would be expected to improve gait speed by 0.05 m/s. Although survival does increase across the full range of gait speeds (37), and gait velocity gain that results in transition to a higher class of ambulation yields better function and quality of life (38), it is important to recognize that substantial fat mass loss may be needed to achieve improvements in walking speed associated with reduced mortality. Additionally, it is worth noting that significant associations were not observed between weight/fat mass loss and chair stand time or SPPB score. Although overall estimates were in the expected direction, due to large variances for both outcome measures, we were unable to assert statistical significance. A larger sample size may be required to improve the precision of the regression estimates and clarify observed relationships.

Lastly, although intentional WL was achieved in all included studies, modalities to achieve WL differed substantially. Diet, Exercise, Metabolism, and Obesity in Older Women represents the most controlled of the trials, with all participants receiving 5 months of individually prescribed and prepared hypocaloric meals and two thirds receiving structured aerobic exercise (19). In Optimizing Body Composition for Function in Older Adults, participants used meal replacements and nutrition counseling to elicit WL, and half of included participants were further randomized to participate in a resistance training program (21). Cooperative Lifestyle Intervention Program was the most translatable study included, where community-dwelling participants were provided nutrition education along with lifestyle modification, including a moderate intensity walking intervention on most days of the week (20). Despite study-specific differences, it is worth noting that nearly all participants received some form of exercise training as a part of their WL strategy. Regular exercise is known to improve physical functioning as well as attenuate the loss of skeletal muscle mass that occurs with CR in older adults (39); therefore, results may not apply to WL interventions that do not include an exercise training component.

In conclusion, findings from this study show that fat mass loss predicts improvements in gait speed and mobility with intentional WL in older adults. Because lean mass loss was not associated with changes in any of the functional measures, fat mass reduction seems to trump concomitant lean mass loss during intentional WL in older adults. Future studies need to identify whether changes in specific fat depots are more predictive of functional improvement than reductions in total body fat mass or whether similar findings would be observed in RCTs of WL without concomitant exercise training.

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