

Effects of a Hypocaloric, Nutritionally Complete, Higher Protein Meal Plan on Regional Body Fat and Cardiometabolic Biomarkers in Older Adults with Obesity

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Keywords

Weight loss · Body composition · Obesity

Abstract

Background: Whether improvements in cardiometabolic health following weight loss (WL) are associated with changes in regional body fat distribution (gluteal vs. android) is not well documented. **Methods:** Older (age: 70 ± 4 years; mean \pm SD) adults with obesity were randomized to a 6-month WL program (WL; $n = 47$), accomplished using a hypocaloric, nutritionally complete, higher protein (targeting ≥ 1.0 g/kg/day) meal plan, or a weight stability (WS; $n = 49$) program. Android, gynoid, visceral, and subcutaneous abdominal fat masses (via dual energy X-ray absorptiometry) and fasting glucose and lipid profiles were assessed at baseline and 6 months. **Results:** The WL group lost more body weight (WL:

–8.6% vs. WS: –1.7%, $p < 0.01$), resulting in a reduction in fat mass at each region only following WL (all $p < 0.05$). The decline in the ratio of android/gynoid fat mass also was significant only following WL, resulting in greater declines than WS (mean [95% CI]; WL: –0.026 [–0.040 to –0.011] vs. WS: 0.003 [–0.012 to 0.019] g, $p < 0.01$). The change in the ratio of visceral/subcutaneous abdominal fat mass was not significant in either group and did not differ between groups (WL: 0.65 [–0.38 to 1.68] vs. WS: 0.05 [–1.00 to 1.10] g, $p = 0.42$). In general, the improvements in glucose and lipid profiles were associated with declines in fat mass at the gynoid and android regions (r 's = 0.20–0.42, all $p < 0.05$), particularly the visceral depot but not the ratios. **Conclusion:** WL achieved via a hypocaloric, nutritionally complete, higher protein meal plan is effective in reducing body fat in the android, gynoid, and visceral depots, which relate to cardiometabolic improvements.

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Aging is associated with weight gain and a shift of fat storage from gluteal/femoral (gynoid) to central abdominal (android) body regions, particularly in the visceral (intra-abdominal) depot [1], which in turn increases the risk for cardiometabolic diseases [2]. Among older adults with obesity, intentional, moderate weight loss (WL; 5–10% of baseline body weight), results in clinically significant improvement in cardiometabolic risk factors, including glucose and lipid profiles [3, 4]. However, the change in the distribution of fat from android to gynoid regions with moderate WL is not well characterized, with previous evidence supporting both a decrease [5] and no change [2] in the ratio. Further, though studies consistently suggest that declines in visceral and subcutaneous abdominal fat masses are related to improvements in glucose metabolism in older adults [6, 7], others suggest that it is the overall decline in fat mass that is important, regardless of the specific depot of fat loss [2]. These data highlight the need to better understand the role of WL-associated changes in body fat distribution and their influence on cardiometabolic health as these outcomes may have important clinical implications for WL recommendations in older adults.

Protein composition of the prescribed WL diet may be a key determinant of changes in body fat distribution; yet, the macronutrient profile of WL diets are often not well described or controlled. Therefore, the purpose of this study is to determine whether random assignment to a hypocaloric, nutritionally complete, higher protein (targeting ≥ 1.0 g/kg/day) meal plan results in improved regional body fat distribution and cardiometabolic health compared to a moderate protein, weight stability program in older adults with obesity. We hypothesize that participants randomized to the WL group will experience greater reductions in android to gynoid and visceral to subcutaneous abdominal fat mass ratios and improvements in glucose and lipid profiles compared to those randomized to the weight stable (WS) group. Further, we hypothesize that greater reductions in the distribution of android to gynoid and visceral to subcutaneous abdominal fat mass ratios are associated with greater cardiometabolic improvements.

Methods

Study Participants

Older (65–79 years) men and women with obesity (body mass index [BMI] 30–40 kg/m²) and self-reported mobility disability (i.e., difficult walking 1/4 mile or climbing stairs/performing house/yard work) were recruited to participate in the Medifast[®]

for Seniors Study (NCT02730988). Detailed inclusion/exclusion criteria, along with intervention effects on change in total body composition and mobility are previously published [8]; intervention effects on regional body fat mass, and associations with biomarkers of cardiometabolic health are unique to this secondary analysis.

Interventions

Participants were randomized to a 6-month WL or a WS control program. Randomization occurred in a 1:1 allocation in 5 waves ($n = 12$ –22 participants/wave), with blocking stratified by gender. Detailed intervention descriptions can be found in the primary outcome paper [8]. Caloric deficit in the WL group was achieved through the Medifast[®] 4&2&1 Plan[®], which included a total of 4 meal replacement products, 2 lean and green meals (i.e., lean protein, non-starchy vegetables, and healthy fats), and 1 healthy snack (i.e., fruit, dairy, or grain). The diet was estimated to provide 1,100–1,300 kcal/day, 120–150 g protein (1.2–1.5 g/kg/day protein), 85–100 g carbohydrate, 30–45 g fat and targeted $\sim 10\%$ WL. In addition, WL participants also attended 12 bi-weekly behavioral counseling groups, to provide support and discuss topics pertinent to weight control led by a Registered Dietitian. Participants randomized to the WS were instructed to maintain their baseline diet throughout the study. The WS group attended 12 bi-weekly behavioral educational sessions in which they received information pertinent to healthy aging (i.e., managing medications and talking effectively to a healthcare provider) and were monitored to ensure weight stability (within $\pm 5\%$ of baseline). Bi-weekly weights were collected to track compliance to both protocols; additionally, the WL group recorded daily meal replacement product consumption.

Procedures

Body Composition

Height and weight were measured to calculate BMI. Total body fat mass, as well as regional fat mass in the android, gynoid, and visceral regions dual energy X-ray absorptiometry (iDXA, GE Medical Systems, Madison, WI, USA) were determined by DXA scans before and after the interventions. All scans were performed in accordance with manufacturer recommended positioning and analyzed by an International Society of Clinical Densitometry certified DXA technologist blinded to intervention assignment. The android area was described as the area around the waist between the mid-point of the lumbar spine and the top of the pelvis, while the gynoid area was between the head of the femur to the mid-thigh [9]. Visceral fat mass was assessed using the CoreScan algorithm (GE Medical Systems, Madison, WI, USA) [10]. Following manufacturer recommendations, subcutaneous abdominal fat mass was defined as the difference between android fat mass and visceral fat mass.

Cardiometabolic Assessments

Blood samples were collected from participants in the early morning (between 7 and 9 a.m.) following a 12-h fast at baseline and at 6 months using standard procedures [11]. Samples were sent to a clinical laboratory (LabCorp., USA) for analysis of glucose, insulin, and lipid profiles. Insulin resistance was estimated via the homeostatic model assessment (HOMA-IR), which was calculated as (fasting insulin * fasting glucose/22.5) [12].

Table 1. Effects of the weight stability and WL interventions on body composition and glucose and lipid profiles

Description	Baseline (<i>n</i> = 96), mean ± SD	Post WL (<i>n</i> = 43)		Post WS (<i>n</i> = 39)	
		mean (95% CI)	percent change	mean (95% CI)	percent change
DXA-acquired body composition					
Total fat mass, kg	44.6±7.6	36.68 (34.29–39.07) ^λ	-17.8	44.59 (42.14–47.03)	-0.0**
Android fat mass, g	4,693±1,184	3,724 (3,568–3,880) ^λ	-20.7	4,587 (4,428–4,745)	-2.3**
Gynoid fat mass, g	6,766±1,473	5,577 (5,410–5,744) ^λ	-17.6	6,612 (6,443–6,781)	-2.3**
Android/gynoid fat mass	0.710±0.183	0.684 (0.670–0.699) ^λ	-3.5	0.713 (0.698–0.729)	0.5**
Visceral abdominal fat mass, g	2,373±1,185	1,895 (1,745–2,045) ^λ	-20.1	2,324 (2,170–2,478)	-2.1**
Subcutaneous abdominal fat mass, g	2,320±813	1,829 (1,728–1,930) ^λ	-21.2	2,268 (2,165–2,370)	-2.3**
Visceral/subcutaneous abdominal fat mass	1.33±1.28	1.98 (0.95–3.01)	48.5	1.38 (0.33–2.44)	3.6
Cardiometabolic biomarkers					
Fasting glucose, mg/dL	106.5±16.2	102.77 (98.87–106.68) ^λ	-3.5	108.56 (104.47–112.64)	1.9*
Fasting insulin, uUI/mL	22.3±12.8	14.93 (12.30–17.55) ^λ	-33.2	23.55 (20.78–26.32)	5.4**
HOMA-IR	6.06±3.95	3.90 (3.06–4.75) ^λ	-35.6	6.41 (5.53–7.30)	5.9**
LDL cholesterol, mg/dL	109.6±34.1	105.22 (97.76–112.68)	-4.0	107.11 (99.32–114.90)	-2.3
HDL cholesterol, mg/dL	51.2±15.2	53.88 (50.97–56.79)	5.3	47.60 (44.52–50.68) ^λ	-7.0**
Triglycerides, mg/dL	135.7±64.0	105.79 (92.31–119.27) ^λ	-22.1	136.77 (122.72–150.82)	0.8**

Outcomes adjusted for gender and baseline value of the outcome, except for DXA, which also was adjusted for time.

Within group changes denoted with (^λ*p* < 0.05); between group intervention changes denoted with (**p* < 0.05; ***p* < 0.01).

WL, weight loss; WS, weight stable; DXA, dual energy X-ray absorptiometry; HOMA-IR, homeostatic model assessment-insulin resistance.

Statistical Analyses

Baseline descriptive statistics was calculated by group and also overall; it was presented as mean ± SD. Data were assessed for normality and transformed as appropriate (i.e., log transformation of triglycerides and visceral to subcutaneous abdominal fat mass ratio). Post intervention group-specific body composition means and 95% CIs were produced using mixed models with treatment, time, treatment by time interaction, gender, and baseline value of the outcome as covariates; estimates were produced using contrast statements at the 24-week visit. Similarly, group-specific glucose and lipid variables were produced from a general linear model, adjusted for gender and baseline value of the outcome and presented as means (95% CI). Partial correlations were used to assess relationships between body composition and cardiometabolic outcome, with baseline analyses adjusted for gender, and change analyses adjusted for gender and baseline regional body fat. All tests were performed using 2-tailed tests at a 0.05 level of significance, and data were analyzed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Participant Characteristics and Intervention

Compliance Measures

Data related to participant recruitment and retention are published previously [8]. Overall, of the 96 enrolled participants, 74% were female and 72% were Caucasian. On average, participants were 70.3 ± 3.7 years old and had obesity (body weight: 97.1 ± 14.9 kg; BMI 35.4 ±

3.3 kg/m²; total body fat: 46.6 ± 4.9%). Among those who completed the intervention (WL: *n* = 43 of 47; WS: *n* = 39 of 49), attendance to the bi-weekly educational sessions was 88 and 84%, respectively, for the WL and WS groups. Within the WL group, self-reported compliance to the meal replacement product protocol was 93%. As designed, the WL group lost significantly more body weight (-8.6 vs. -1.7%; *p* < 0.01), BMI (-9.2 vs. -1.5%; *p* < 0.01) and total body fat mass (-15.9 vs. 2.1%; *p* < 0.01) than the WS group.

Treatment effects on Regional Body Composition and Glucose and Lipid Profiles

Table 1 presents overall baseline body composition and cardiometabolic estimates, model adjusted group specific post-intervention body composition estimates and 95% CIs, and corresponding within group percentage change from baseline. The WL group lost a slightly greater percentage of android (-20.7%) than gynoid (-17.6%) fat mass, which resulted in a reduction in the android to gynoid fat mass ratio (-3.5%; *p* < 0.05). Android and gynoid fat masses and their ratio did not change with WS. The changes in android, gynoid, and the ratio of android to gynoid fat mass were greater following WL compared to WS (all *p* < 0.01). Only the WL group reduced visceral (-20.1%) and subcutaneous abdominal (-21.2%) fat masses (all *p* < 0.05), which resulted in great-

Table 2. Baseline and change in Pearson correlation coefficients between regional body fat distribution and cardiometabolic biomarkers

	Fasting glucose		Fasting insulin		HOMA-IR		LDL cholesterol		HDL cholesterol		Triglycerides	
	baseline vs. baseline	change vs. change	baseline vs. baseline	change vs. change	baseline vs. baseline	change vs. change	baseline vs. baseline	change vs. change	baseline vs. baseline	change vs. change	baseline vs. baseline	change vs. change
Total fat mass	0.18	0.21	0.14	0.42**	0.17	0.37**	-0.11	0.14	0.02	-0.25*	-0.11	0.42**
Android fat mass	0.24*	0.21	0.20*	0.40*	0.22*	0.35**	-0.13	0.21	-0.07	-0.23*	0.01	0.42**
Gynoid fat mass	0.07	0.19	0.00	0.42*	0.03	0.36**	-0.06	0.09	0.10	-0.28**	-0.17	0.43**
Android/gynoid fat mass	0.18	0.14	0.26**	0.09	0.24*	0.10	-0.11	0.33**	-0.23*	-0.12	0.15	0.20
Visceral abdominal fat mass	0.27**	0.12	0.34**	0.38**	0.33**	0.32**	-0.17	0.26*	-0.17	-0.10	0.27**	0.41**
Subcutaneous abdominal fat mass	0.02	0.20	-0.10	0.18	-0.07	0.18*	0.02	-0.03	0.09	-0.24*	-0.28**	0.16
Visceral/subcutaneous abdominal fat mass	0.06	-0.08	0.19	0.02	0.15	0.00	-0.13	0.33**	-0.17	0.03	0.16	0.19

Baseline analyses adjusted for gender, and change analyses adjusted for gender and baseline outcome measures.

* $p < 0.05$; ** $p < 0.01$.

HOMA-IR, homeostatic model assessment-insulin resistance.

er intervention effects than the WS group (all $p < 0.01$), but neither group reduced the ratio of visceral to abdominal fat mass.

Fasting glucose, insulin, HOMA-IR, and triglycerides were reduced 3.5, 33.2, 35.6, and 22.1%, respectively, with WL (all $p < 0.05$). No changes in glucose or lipid profiles were observed with WS, except a reduction in HDL cholesterol (-7.0% , $p < 0.05$). The changes in glucose, insulin, HOMA-IR, HDL cholesterol, and triglycerides were greater with WL than WS (all $p < 0.05$).

Associations between Regional Body Fat and Cardiometabolic Biomarkers

Table 2 presents baseline (adjusted for gender) and change (adjusted for gender and baseline regional body fat) in Pearson correlation coefficients in the combined groups between total and regional body fat and cardiometabolic biomarkers. Greater baseline android fat mass and the ratio of android to gynoid fat mass were generally associated with worse glucose and lipid profiles; however, gynoid fat mass was not. Within the abdominal region, it was found that greater visceral fat mass was associated with poorer glucose profiles and triglycerides, but subcutaneous fat mass alone and the ratio of visceral to subcutaneous fat mass did not.

The decrease in total, android, and gynoid fat masses each similarly predicted declines in glucose, insulin, HOMA-IR, triglycerides and increases in HDL cholesterol following the interventions (Table 2). The change in the ratio of android to gynoid fat mass did not predict the change in glucose or lipid profiles, except LDL chole-

sterol, which was stronger than the change in android or gynoid fat mass alone. Within the abdominal region, the change in visceral fat mass was associated with the change in insulin, HOMA-IR, LDL cholesterol, and triglycerides, while the change in subcutaneous abdominal fat mass was associated with HOMA-IR and HDL cholesterol (Table 2). The change in visceral to subcutaneous abdominal fat mass was only significantly associated with the change in LDL cholesterol.

Discussion

Cross-sectional associations between greater android to gynoid fat mass and cardiometabolic dysregulation in older adults, as observed in this study, are well established [13]. However, this study adds to a growing body of work investigating whether intentional, moderate WL has the ability to counter age-associated shifts in body fat deposition toward central obesity by reducing abdominal (particularly visceral) to gluteal fat mass and decreasing cardiometabolic risk factors in older adults with obesity. We report that adherence to a hypocaloric, nutritionally complete, meal plan targeting ≥ 1.0 g/kg/day of protein was effective in reducing greater android to gynoid fat mass, but not visceral to subcutaneous abdominal fat mass, and improving biomarkers of cardiometabolic health, as compared to weight stability. However, in agreement with other findings [2], we also report that greater loss of overall fat mass, independent of the specific fat depot, is associated with the greatest reductions

in cardiometabolic risk. Though these data highlight the significance of overall fat loss on cardiometabolic health, they should not detract from the need to decrease central adiposity. In accordance with our findings, previous evidence suggested that android fat reductions, from both the visceral and subcutaneous abdominal fat areas, are associated with improvements in cardiometabolic risk factors following WL in middle-aged and older adults [2, 14, 15]. Thus, identifying ways of achieving overall fat mass loss, while targeting the android region, may have clinical implications for improving WL-associated cardiometabolic health in older adults.

Little is known regarding the mechanisms of action that underlie the deposition and mobilization of regional body fat mass. Previous studies suggest a link between larger subcutaneous abdominal adipocytes and greater insulin resistance [2, 16, 17] and WL appears to reduce the size (but not number) of adipocytes [18, 19], indicating a potential role of regional storage and mobilization of acylglycerides in adipocytes following WL. However, results from these studies appear equivocal. In middle-aged women, 1 study suggested that WL results in a decline in gluteal adipocyte size, but not abdominal, so that there is an increase in the ratio of abdominal to gluteal cell size following WL [20], though another suggested a decline in the ratio due to greater reductions in abdominal than gluteal adipocyte sizes [21]. Previous studies in postmenopausal women have not found a change in the ratio with WL, despite reductions in adipocyte size at both the abdominal and gluteal regions [2, 22, 23]. Changes in both abdominal and gluteal adipocyte size, but not the ratio, have previously been linked to improvements in glucose tolerance following WL [2]. These data support the regulation of adipocytes biology (i.e., triglyceride accumulation and lipolysis) as potential therapeutic WL targets. Recent evidence suggests that certain pharmacological agents, such as thiazolidinediones, which are used in the treatment of type 2 diabetes mellitus, are linked to modifications in adipocyte differentiation [24] and visceral and intrahepatic fat accumulation [25], reinforcing this notion.

This study supports previous research that moderate WL results in a reduction in the ratio of android to gynoid fat mass [5]. The inclusion of men in these studies may partially explain variations from previous studies in older women where no change was observed [2], as sex differences in the fat distribution response to WL have been previously observed. Men show greater reductions in trunk fat mass following WL than women [5] and women have greater gluteofemoral subcutaneous adipocyte size

declines than men [18]. Further, although total body fat of the individuals in the current analysis is comparable to previous studies [2, 22], the baseline distribution of fat in participants in the current analysis differs from previous studies. Prior studies suggest that gynoid fat mass is 2 times greater than android [2], but in the current study, it was only 1.4 times greater. This may be due to racial differences between studies as our population was majority Caucasian, while others had a higher population of African Americans. Further, considering that the transition to menopause is associated with a shift of fat from the gynoid to the android regions [26], menopausal status of study participants may influence baseline body fat distribution, as well as the regional response of body fat to WL. As this is a secondary analysis, the original study was not powered to test the potential race and sex differences.

Novel strengths of the Medifast[®] for Seniors Study include utilization of a WS control group and use of DXA to acquire regional fat measures. Although protocol adherence was excellent, the design of the study does not allow us to fully disentangle the effect of the hypocaloric diet from the effect of protein. Protein composition of the WL diet may be a key determinant of changes in body fat distribution [27]. Thus, future studies are needed to decipher the relevant effects of each component on regional body fat. Additionally, we did not analyze dietary intake, which is a limitation. Therefore, detailed analyses of diet intake quantity and quality are needed in future studies to identify whether other macro- and micro-nutrients may work synergistically with protein to optimize the effectiveness of WL interventions targeting regional body fat distribution.

In summary, results from this study support a growing body of literature that reductions in body fat with a hypocaloric, nutritionally complete, higher protein meal plan, such as that of the Medifast[®] 4&2&1 Plan[®], lead to cardiometabolic health improvements in older adults with obesity, independent of the fat mass location in the android or gynoid region. More research is needed to determine the mechanism by which WL affects body fat distribution and cardiometabolic health, with the goal of identifying potential therapeutic targets and optimizing individual WL plans.

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Ethics Statement

Subjects gave their written informed consent and the study protocol was approved by Wake Forest School of Medicine's Institutional Review Board.

Disclosure Statement

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