Obesity Science & Practice

WILEY | THE OBESITY SOCIETY | WORLD OBESITY

SHORT COMMUNICATION OPEN ACCESS

Prolonged Water-Only Fasting Followed by a Whole-Plant-Food Diet Promotes Fat-Free Mass Recovery and Continued Fat Mass Loss in Adults With Overweight or Obesity

Sahmla Gabriel[1] | Mackson Ncube[1] | David M. Goldman[2,3] | Eugene Scharf[4] | Alan C. Goldhamer[5] | Toshia R. Myers[1]

[1]TrueNorth Health Foundation, Santa Rosa, California, USA | [2]Metabite Inc., New York, New York, USA | [3]University of Helsinki, Helsinki, Finland | [4]Mayo Clinic, Rochester, Minnesota, USA | [5]TrueNorth Health Center, Santa Rosa, California, USA

Correspondence: Toshia R. Myers (drmyers@truenorthhealth.org)

Received: 24 June 2024 | **Revised:** 17 June 2025 | **Accepted:** 13 July 2025

Funding: The authors received no specific funding for this work.

Keywords: obesity | prolonged fasting | VAT | water-only fasting | weight-loss | whole-plant-food diet

ABSTRACT

Introduction: Conventional weight-loss strategies often result in inadequate fat loss, poor sustainability, and unintended lean mass loss. Prolonged water-only fasting followed by dietary change may offer an effective alternative, but its impact on body composition remains underexplored.

Methods: This secondary analysis utilized dual-energy X-ray absorptiometry (DXA) to assess changes in fat-free mass (FFM), fat mass (FM), and bone mineral content (BMC) in adults [median (IQR) age: 62 (15) years with overweight or obesity. Participants underwent a median (IQR) of 14 (6) days of water-only fasting, followed by 6 (3) days of food reintroduction with a whole-plant-food diet and a subsequent maintenance period of 45 (5) days. Study visits occurred at baseline and at the end of each period.

Results: At end of fasting, FFM accounted for 74% of total BW lost during fasting. However, at the follow-up visit, the median (IQR) percentage change in total BW, FFM, FM, and visceral adipose tissue (VAT) mass from baseline was −8.2 (5.2), −4.4 (5.6), −14.7 (8.9), −15.8 (12.8) %, respectively. At follow-up, FM loss accounted for 67% of the total BW lost. BMC remained unchanged across all study visits.

Conclusions: This protocol produced sustained FM loss, specifically VAT mass, and FFM recovery, suggesting it may support effective weight management.

1 | Introduction

Obesity is projected to affect two billion people worldwide by 2035, contributing to increased morbidity, mortality, and economic burden [1]. Despite advances in treatment, weight management remains challenging due to low adherence, adverse events, and limited long-term efficacy of commonly prescribed interventions such as caloric restriction, exercise, surgery, and pharmacotherapy [2–6]. These challenges are further compounded by comorbidities, such as hypertension and fatty liver disease, which may complicate treatment and reduce intervention success [7]. Moreover, research indicates that abdominal obesity—specifically, the accumulation of visceral adipose tissue (VAT)—is a stronger predictor of obesity-related disease risk than obesity defined using body mass index (BMI) [8–11]. Given these limitations, there remains a critical

need for low-risk strategies that efficiently reduce body fat, particularly VAT.

Medically supervised, prolonged water-only fasting—defined as the voluntary intake of only water for periods typically lasting 7–21 days, followed by a gradual food reintroduction—is emerging as a tolerable, low-risk, and potentially effective strategy for reversing obesity, improving cardiometabolic risk factors, and restoring overall health [12–20]. Water-only fasting induces an initial weight loss of approximately 0.86 kg per day, which gradually declines to less than 0.43 kg per day as the fast progresses [20, 21]. Recent studies have reported an average total body weight (BW) reduction of approximately 10% after 10–14 days of water-only fasting, along with improvements in blood pressure and other cardiometabolic health markers [18, 22, 23]. Preliminary data also suggest that post-fast benefits were sustained or further improved one year after the intervention [20]. Moreover, participants reported enhanced palatability and increased consumption of fruits and vegetables after prolonged water-only fasting, which may support dietary changes necessary for sustaining or improving fasting-induced outcomes [24].

Weight loss during water-only fasting is primarily driven by acute adaptive mechanisms, including sodium diuresis, lipolysis, and protein catabolism [25, 26]. Briefly, the absence of exogenous glucose leads to the reduction of blood glucose and hepatic glycogen stores, resulting in dynamic changes in circulating hormone concentrations, such as reduced insulin and leptin and increased cortisol, along with increased lipolysis and free fatty acid mobilization [26, 27]. The liver converts circulating free fatty acids to ketone bodies—primarily β-hydroxybutyrate—which serve as alternative fuel for the brain and most other tissues [26]. Importantly, ketogenesis reduces the reliance on gluconeogenesis, thereby minimizing protein catabolism after an initial increase during early fasting [26]. This mechanism may explain the lack of clinically significant muscle wasting observed during medically supervised, prolonged water-only fasting [13].

Nevertheless, concerns remain that rapid weight loss induced by prolonged fasting may result in disproportionate reductions in lean tissue, particularly muscle mass, which in turn may slow metabolic rate, weaken immunity, and reduce physical strength [28]. Data on body composition changes during prolonged fasting are limited [12, 22, 29, 30]. Existing research suggests that fat-free mass (FFM) accounts for approximately two-thirds of weight loss during prolonged fasting and that FFM rapidly recovers upon food reintroduction, suggesting that much of the loss may reflect reductions in glycogen and associated fluid rather than lean tissue. However, conclusions remain uncertain due to incomplete data reporting, lack of post-fast follow-up, and the absence of research on adults with overweight or obesity. Given these inconsistencies, further research is needed to clarify the long-term effects of prolonged fasting on body composition in individuals with excess adipose tissue.

To address this topic, the immediate and sustained effects of prolonged water-only fasting followed by a whole-plant-food diet on body composition were assessed by secondary analysis of dual-energy X-ray absorptiometry (DXA) data collected from overweight or obese adults. The original study found that six weeks after fasting, participants sustained an 11% reduction in body mass index (BMI) and abdominal circumference (AC), alongside improvements in various cardiometabolic health markers [31].

2 | Methods

This study was a secondary analysis of data collected as part of a clinical trial (NCT04514146) that was approved by the TrueNorth Health Institutional Review Board in Santa Rosa, California (TNHF-2020-2VAT; April 2, 2020) and conducted according to the guidelines of the Declaration of Helsinki. The main study methods were previously published [31].

2.1 | Study Details

Participants were recruited from patients at a residential fasting center specializing in inpatient, medically supervised water-only fasting and whole-plant-food refeeding. Informed consent was obtained from all participants before enrollment and throughout the study. Forty participants were enrolled, of which 38 completed the on-site fasting and food reintroduction protocol, and the 29 participants presented here completed the full study protocol [31]. As previously described, eligibility included males and females aged 40–70 years with a BMI between 25 and 40 kg/m2 and fasting glucose < 7 mmol/L and/or hemoglobin A1c < 7% who had independently elected to undergo a medically supervised water-only fast for at least 10 consecutive days followed by the standard food reintroduction period of no less than half the duration of the fast and who were previously approved to do so by a physician. The exclusion criteria were active malignancy, active inflammatory disorders, and stroke or heart attack within the last 90 days.

Upon enrollment, participants attended study visits at baseline (BL), end of fasting (EOF), end of food reintroduction (EOR), and follow-up (FU) at approximately six weeks after the EOR. In addition to anthropometric, serology, clinical, demographic, and dietary adherence data collected as previously described [31], DXA scans were performed during each study visit. At the EOR visit, participants were provided with basic educational material on maintaining a whole-plant-food diet after returning to their home environment, but no other post-fast dietary support was provided between the EOR and FU visits. Dietary adherence was measured using a brief dietary screener specific to a whole-plant-food diet free of added salt, oil, and sugar [24]. At FU, participants reported increased consumption of whole-plant foods and decreased consumption of animal foods, dairy products, and added oil compared with BL [31]. All study data were collected and managed using REDCap electronic data capture tools hosted at the TrueNorth Health Foundation [32].

2.2 | Prolonged Water-Only Fasting and Food Reintroduction Protocol

The prolonged water-only fasting and food reintroduction protocols were detailed in the original publication [31]. The fasting

and food reintroduction protocol was implemented by non-research medical personnel at a residential, fasting facility. Briefly, after being pre-screened before arrival and, if conditionally approved to water-only fasting, potential participants were instructed to prepare by eating a diet of fresh fruits and raw or steamed vegetables *ad libitum* for two days prior to initiating the fast. While fasting, participants were instructed to consume a minimum of 1.2 L of distilled water per day and limit their physical activity. Participants were monitored twice daily by medical personnel, and serology and urinalysis were measured once weekly and as indicated. The fast was terminated with an established food reintroduction protocol consisting of five phases of gradual food introduction beginning with vegetable broths and/or fruit and vegetable juices and ending with an *ad libitum* diet of cooked and raw whole-plant-foods free of added salt, oil, and sugar with one phase for every 7–10 days of fasting lasting a minimum of half of the fasting duration [13]. Fasting lengths varied (see results below) but were no less than approximately 10 days followed by a food reintroduction period of approximately five days.

2.3 | Clinical Measurements

Clinical measurements were obtained at BL, EOF, EOR, and FU by research personnel as previously described [31]. Briefly, height was measured using a digital wall-mounted stadiometer. BW was measured using a digital body weight scale. BMI was calculated from height and weight. AC was measured at the narrowest part of the participants' midsection below the lowest palpable rib cage yet above the top of the hip/pelvic bones using a tension-sensitive, non-elastic tape. Resting SBP and DBP were measured in the morning after blood collection while in the seated position and after resting for five minutes using a digital blood pressure device.

2.4 | Dual-Energy X-Ray Absorptiometry (DXA) Measurements

Participants underwent whole-body DXA scans (Horizon Wi [S/N 303354M], Hologic) at BL, EOF, EOR, and FU by certified technicians. Measurements were taken in the morning after drinking one glass of water. The interassay coefficients of variation reported for Horizon Wi were 0.50% and 0.98% for fat-free mass (FFM) and fat mass (FM), respectively, and 7.1%, 7.2%, and 2.83% for visceral adipose tissue (VAT) mass, volume, and area, respectively [33, 34].

2.5 | Statistical Analysis

Data analysis was performed using R version 4.3.2 [35]. Medians, interquartile ranges (IQR), boxplots, histograms, and scatter plots were used to understand the data. The analysis used random intercept linear mixed-effects models with 95% confidence intervals (CI) where clinical parameters were the dependent variables, study visit the main independent variable, participant ID the grouping variable, and age and sex the control variables. The DXA and clinical measurements models were fitted in a Frequentist framework using the 'lmerTest' version 3.1.3 R package with confidence intervals obtained from 'brooms.mixed' version 0.2.9.4, while the dipstick urinalysis models were fitted in a Bayesian framework using the 'brms' 2.20.4 R package with the target average acceptance probability parameter adapt_delta set to 0.99 due to warnings about divergent transitions [36–38]. Model diagnostics were assessed as previously described for models fitted with 'lmerTest' and 'brms' [20, 31]. When lmerTest model assumptions did not hold [39], robust score equations [40] with the Satterthwaite degrees of freedom approximation [41] were employed. Complete case analysis was used to handle missing data. Regression coefficients were considered statistically significant when the 95% CI or 95% credible interval excluded 0.

3 | Results

3.1 | Participant and Visit Characteristics

This secondary analysis included a subset of male ($n = 6$) and female ($n = 23$) participants ($N = 29$), with a median (IQR) baseline age of 62.0 (15.1) years and BMI of 31.1 (6.2) kg/m^2, enrolled in a study investigating the sustained effects of water-only fasting followed by a whole-plant-food diet on cardiometabolic health (Table 1) [31]. Median (IQR) water-only fasting and food reintroduction lengths were 14 (6) and 6 (3), respectively. Dipstick urinalysis ($n = 11$) indicated that participants had median (IQR) ketone levels of 0.0 mmol/L at baseline and EOR, and 8.0 mmol/L at EOF (Supporting Information S1: Tables 1 and 2). The FU visit occurred at a median (IQR) of 45 (5) days after the completion of treatment, and the median study length was 65 days. As previously reported, total BW, BMI, and AC decreased significantly by the end of fasting (Table 1, Supporting Information S1: Table 3) [31]. Values increased minimally during food reintroduction, but overall losses were sustained for at least the next six weeks with moderate adherence to a whole-plant-food diet (Table 1, Supporting Information S1: Table 3) [31]. Participants also experienced sustained reductions in blood pressure, high sensitivity C-reactive protein (hsCRP), fatty liver index (FLI), total cholesterol, and low-density-lipoprotein (LDL) cholesterol [31].

3.2 | Changes in Fat-Free Mass and Fat Mass

Whole-body DXA measurements were used to assess body composition, including FFM, FM, and BMC, at all study visits (Table 2). These data confirmed that participants lost an estimated −8.8 kg (95% CI: −9.8, −7.7) during the fasting period (Table 3), accounting for a median 9.8% reduction in total BW (Supporting Information S1: Table 4, Figure 1A). Participants regained a minimal but statistically significant amount during food reintroduction with no additional changes at FU (Table 3, Supporting Information S1: Table 4, Figure 1A) [31]. There were no changes in BMC throughout the entire study, and therefore, changes in total BW presumably derived from FFM and FM compartments (Tables 2 and 3).

TABLE 1 | Clinical measurements by visit.

	Median (IQR)			
	BL	**EOF**	**EOR**	**FU**
Height, cm	167.5 (8.0)	167.5 (8.0)	167.5 (8.0)	167.5 (8.0)
Weight, kg	86.6 (14.9)	79.1 (15.1)	81.1 (17.1)	79.9 (16.0)
BMI, kg/m2	31.1 (6.2)	28.1 (6.2)	28.7 (6.3)	29.0 (6.7)
SBP, mmHg	121.0 (20.0)	113.0 (20.0)	110.0 (10.0)	113.0 (12.0)
DBP, mmHg	77.0 (10.0)	81.0 (12.0)	75.0 (8.0)	77.0 (9.0)
AC, cm	100.0 (10.0)	89.7 (9.0)	93.5 (8.1)	94.0 (10.5)

Note: $N = 29$ total participants; baseline.
Abbreviations: AC, abdominal circumference; BL, baseline; BMI, body mass index; cm, centimeter; DBP, diastolic blood pressure; EOF, end-of-fast; EOR, end-of-food reintroduction; FU, follow-up; IQR, interquartile range; kg, kilogram; m, meter; mm, millimeter; SBP, systolic blood pressure.

TABLE 2 | DXA measurements by visit.

	Median (IQR)			
	BL	**EOF**	**EOR**	**FU**
Total body weight, kg	86.20 (15.2)	79.30 (15.9)	81.40 (15.4)	80.20 (16.5)
Bone mineral content, kg	2.30 (0.4)	2.30 (0.4)	2.30 (0.5)	2.30 (0.4)
Total fat-free mass, kg	46.20 (13.2)	39.40 (11.3)	41.70 (12.8)	44.70 (13.8)
Fat-free mass, %	54.60 (5.9)	53.10 (7.5)	55.70 (8.6)	59.10 (8.0)
Total fat mass, kg	34.40 (11.5)	33.60 (12.2)	32.50 (11.7)	31.30 (11.3)
Total fat, %	42.50 (7.2)	43.90 (8.3)	41.10 (9.2)	38.00 (8.4)
Android fat mass, kg	3.30 (1.8)	2.90 (1.5)	2.80 (1.8)	2.80 (1.9)
Gynoid fat mass, kg	5.50 (2.0)	5.50 (1.8)	5.30 (2.0)	4.80 (1.6)
Android/gynoid ratio	1.10 (0.2)	1.10 (0.1)	1.00 (0.2)	1.00 (0.2)
Est. VAT mass, kg	0.93 (0.4)	0.83 (0.3)	0.80 (0.4)	0.78 (0.5)
Est. VAT volume, $m^3 \times 10^3$	0.90 (0.4)	0.90 (0.3)	0.90 (0.5)	0.80 (0.5)
Est. VAT area, $m^2 \times 10^2$	1.80 (0.8)	1.70 (0.7)	1.60 (0.9)	1.60 (1.0)
LMI, kg/m^2	16.70 (3.5)	14.30 (3.2)	15.20 (3.5)	15.90 (4.0)
Append LMI, kg/m^2	7.10 (1.9)	5.90 (1.5)	6.20 (1.8)	6.50 (1.6)
Bone density, kg/m^3	1104.00 (177.0)	1107.00 (183.0)	1115.00 (177.0)	1104.00 (169.0)
FFM:FM ratio	1.30 (0.4)	1.20 (0.4)	1.40 (0.5)	1.60 (0.5)

Note: $N = 29$ total participants; baseline.
Abbreviations: BL, baseline; EOF, end-of-fast; EOR, end-of-food reintroduction; Est, estimated; FU, follow-up; IQR, interquartile range; kg, kilogram; LMI, lean mass index; m, meter.

At EOF, there was a median 13.8% reduction in total FFM from baseline (Supporting Information S1: Table 4, Figure 1B), accounting for 74.5% of total BW loss (Supporting Information S1: Table 5). During the food reintroduction period, which included whole-plant foods without added salt, oil, or sugar, mean FFM significantly increased by an estimated 2.5 kg (95% CI: 1.8, 3.2) (Table 3). This upward trend continued, and by FU, the mean increase in FFM percent was an estimated 2.5% (95% CI: 1.8, 3.2) above baseline (Table 3), and FFM loss accounted for a median 31.7% of total BW loss (Supporting Information S1: Table 5). At EOF, urine specific gravity significantly increased, indicating slight physiologic dehydration, but it returned to baseline by EOR (Supporting Information S1: Table 1 and 2). There was a slight reduction in mean lean mass index (LMI) and mean appendicular LMI at FU, although the values remained within the normal range (Tables 2 and 3).

At EOF, there was a median 5.7% reduction in total FM from baseline (Supporting Information S1: Table 4, Figure 1C), accounting for 25.9% of total BW loss (Supporting Information S1: Table 5). In contrast to FFM, and despite an increase in total BW, mean FM decreased from EOF to EOR and from EOR to FU by an additional estimated −1.3 kg (95% CI: −2.0, −0.6) and −1.8 kg (95% CI: −2.5, −1.1), respectively (Table 3). At FU, there was a median 14.7% reduction in total FM (Supporting Information S1: Table 4, Figure 1C), with FM accounting for 66.9% of total BW loss (Supporting Information S1: Table 5). The median percent change from baseline in estimated VAT mass followed a similar trend, showing a 7.9% reduction at EOF that further increased to 15.8% by FU (Supporting Information S1: Table 4, Figure 1D). Moreover, by FU, the FFM-to-FM ratio had increased, while the android/gynoid ratio had decreased, indicating that participants had proportionately more FFM and less abdominal fat compared to baseline (Tables 2 and 3).

TABLE 3 | Significance of differences mixed-effects model on complete cases.

	Mean estimates (SE) [95% CI]					
	EOF - BL	**EOR - BL**	**FU - BL**	**EOR - EOF**	**FU - EOF**	**FU - EOR**
Total body weight, kg	−8.8* (0.5) [−9.8, −7.7]	−7.5* (0.5) [−8.6, −6.4]	−7.2* (0.5) [−8.3, −6.2]	1.3* (0.5) [0.2, 2.4]	1.5* (0.5) [0.4, 2.6]	0.2 (0.5) [−0.8, 1.3]
Bone mineral content, kg	−0.0 (0.0) [−0.0, 0.02]	−0.0 (0.0) [−0.0, 0.0]	−0.0 (0.0) [−0.0, 0.0]	−0.0 (0.0) [−0.0, 0.0]	−0.0 (0.0) [−0.0, 0.0]	−0.0 (0.0) [−0.0, 0.0]
Total fat-free mass, kg	−6.7* (0.4) [−7.4, −5.9]	−4.2* (0.4) [−4.9, −3.4]	−2.1* (0.4) [−2.8, −1.4]	2.5* (0.4) [1.8, 3.2]	4.6* (0.4) [3.8, 5.3]	2.0* (0.4) [1.3, 2.8]
Fat-free mass, %	−2.2* (0.3) [−2.9, −1.5]	0.1 (0.3) [−0.6, 0.8]	2.5* (0.3) [1.8, 3.2]	2.3* (0.3) [1.6, 3.0]	4.7* (0.3) [4.0, 5.4]	2.4* (0.3) [1.7, 3.1]
Total fat mass, kg	−2.0* (0.4) [−2.7, −1.3]	−3.3* (0.4) [−4.0, −2.6]	−5.1* (0.4) [−5.8, −4.4]	−1.3* (0.4) [−2.0, −0.6]	−3.1* (0.4) [−3.8, −2.4]	−1.8* (0.4) [−2.5, −1.1]
Total fat, %	2.0* (0.3) [1.3, 2.6]	−0.4 (0.3) [−1.0, 0.3]	−2.8* (0.3) [−3.4, −2.1]	−2.3* (0.3) [−3.0, −1.6]	−4.7* (0.3) [−5.4, −4.1]	−2.4* (0.3) [−3.1, −1.7]
Android fat mass, kg	−0.3* (0.0) [−0.4, −0.2]	−0.4* (0.0) [−0.5, −0.4]	−0.6* (0.0) [−0.7, −0.5]	−0.1* (0.0) [−0.2, −0.0]	−0.3* (0.0) [−0.4, −0.2]	−0.2* (0.0) [−0.3, −0.1]
Gynoid fat mass, kg	−0.3* (0.1) [−0.4, −0.1]	−0.5* (0.1) [−0.6, −0.3]	−0.9* (0.1) [−1.0, −0.8]	−0.2* (0.1) [−0.3, −0.0]	−0.6* (0.1) [−0.8, −0.5]	−0.5* (0.1) [−0.6, −0.3]
Android/gynoid ratio	−0.0 (0.0) [−0.0, 0.0]	−0.1* (0.0) [−0.1, −0.0]	−0.0* (0.0) [−0.1, −0.0]	−0.0* (0.0) [−0.1, −0.0]	−0.0* (0.0) [−0.1, −0.0]	0.0 (0.0) [−0.0, 0.0]
Est. VAT mass, kg	−0.1* (0.0) [−0.1, −0.1]	−0.1* (0.0) [−0.2, −0.1]	−0.1* (0.0) [−0.2, −0.1]	−0.0 (0.0) [−0.1, 0.0]	−0.0* (0.0) [−0.1, −0.0]	−0.0 (0.0) [−0.1, 0.0]
Est. VAT volume, m^3 x 10^3	−0.1* (0.0) [−0.1, −0.1]	−0.1* (0.0) [−0.2, −0.1]	−0.2* (0.0) [−0.2, −0.1]	−0.0 (0.0) [−0.1, 0.0]	−0.1* (0.0) [−0.1, −0.0]	−0.0 (0.0) [−0.1, 0.0]
Est. VAT area, m^2 x 10^2	−0.2* (0.0) [−0.3, −0.1]	−0.3* (0.0) [−0.4, −0.2]	−0.3* (0.0) [−0.4, −0.2]	−0.1 (0.0) [−0.2, 0.0]	−0.1* (0.0) [−0.2, −0.0]	−0.0 (0.0) [−0.1, 0.1]
LMI, kg/m^2	−2.4* (0.1) [−2.6, −2.1]	−1.5* (0.1) [−1.7, −1.2]	−0.7* (0.1) [−1.0, −0.5]	0.9* (0.1) [0.7, 1.2]	1.6* (0.1) [1.4, 1.9]	0.7* (0.1) [0.5, 1.0]
Append LMI, kg/m^2	−1.1* (0.1) [−1.2, −0.9]	−0.8* (0.1) [−0.9, −0.7]	−0.5* (0.1) [−0.6, −0.3]	0.3* (0.1) [0.1, 0.4]	0.6* (0.1) [0.5, 0.8]	0.4* (0.1) [0.2, 0.5]
Bone density$^{\zeta}$, kg/m^3	−2.4 (5.7) [−13.7, 8.8]	−0.2 (5.7) [−11.4, 11.1]	−2.0 (5.7) [−13.2, 9.2]	2.3 (5.7) [−8.9, 13.5]	0.4 (5.7) [−10.8, 11.7]	−1.9 (5.7) [−13.1, 9.4]
FFM:FM ratio	−0.1* (0.0) [−0.2, −0.0]	0.0 (0.0) [−0.0, 0.1]	0.2* (0.0) [0.1, 0.3]	0.1* (0.0) [0.1, 0.2]	0.3* (0.0) [0.3, 0.4]	0.2* (0.0) [0.1, 0.2]

Note: $N = 29$ total participants; * Statistically significant result, ζ Used robust linear mixed effects model.
Abbreviations: BL, baseline; CI, confidence interval; EOF, end-of-fast; EOR, end-of-food reintroduction; Est, estimated; FU, follow-up; kg, kilogram; LMI, lean mass index; m, meter; SE, standard error.

4 | Discussion

This secondary analysis investigated body composition changes during and after prolonged water-only fasting. The DXA data confirmed that participants lost approximately 10% of their total BW after 14 days of fasting, followed by a 1%–2% increase during the 6-day food reintroduction period, and stability throughout the 6-week maintenance period [31]. The results supported previous findings that FFM loss accounted for two-thirds of total BW lost during prolonged fasting [30] and that FFM significantly increased during the initial period of food reintroduction [22]. Notably, at the follow-up visit, FFM% increased above baseline, whereas FM loss continued at a higher rate than during fasting, ultimately accounting for nearly two-thirds of total BW loss. This indicated that acute FFM loss during prolonged fasting was transient, whereas FM loss persisted beyond refeeding, contributing to favorable body composition outcomes six weeks after the intervention.

Importantly, weight loss during fasting is primarily driven by adaptive responses, such as glycogen depletion and sodium diuresis, which result in slight but physiologically meaningful dehydration [20]. Given that DXA-derived FFM measurements, which include lean mass (e.g., skeletal muscle) as well as bodily fluids, are also highly influenced by hydration status [42], a large portion of FFM lost during fasting likely reflects changes in hydration status rather than lean tissue catabolism. Indeed, hydration and FFM were both rapidly restored upon food reintroduction in this study. Moreover, exercise has been reported to attenuate FFM loss in the context of BW reduction and may aid in FFM recovery if incorporated after the food reintroduction period [43, 44].

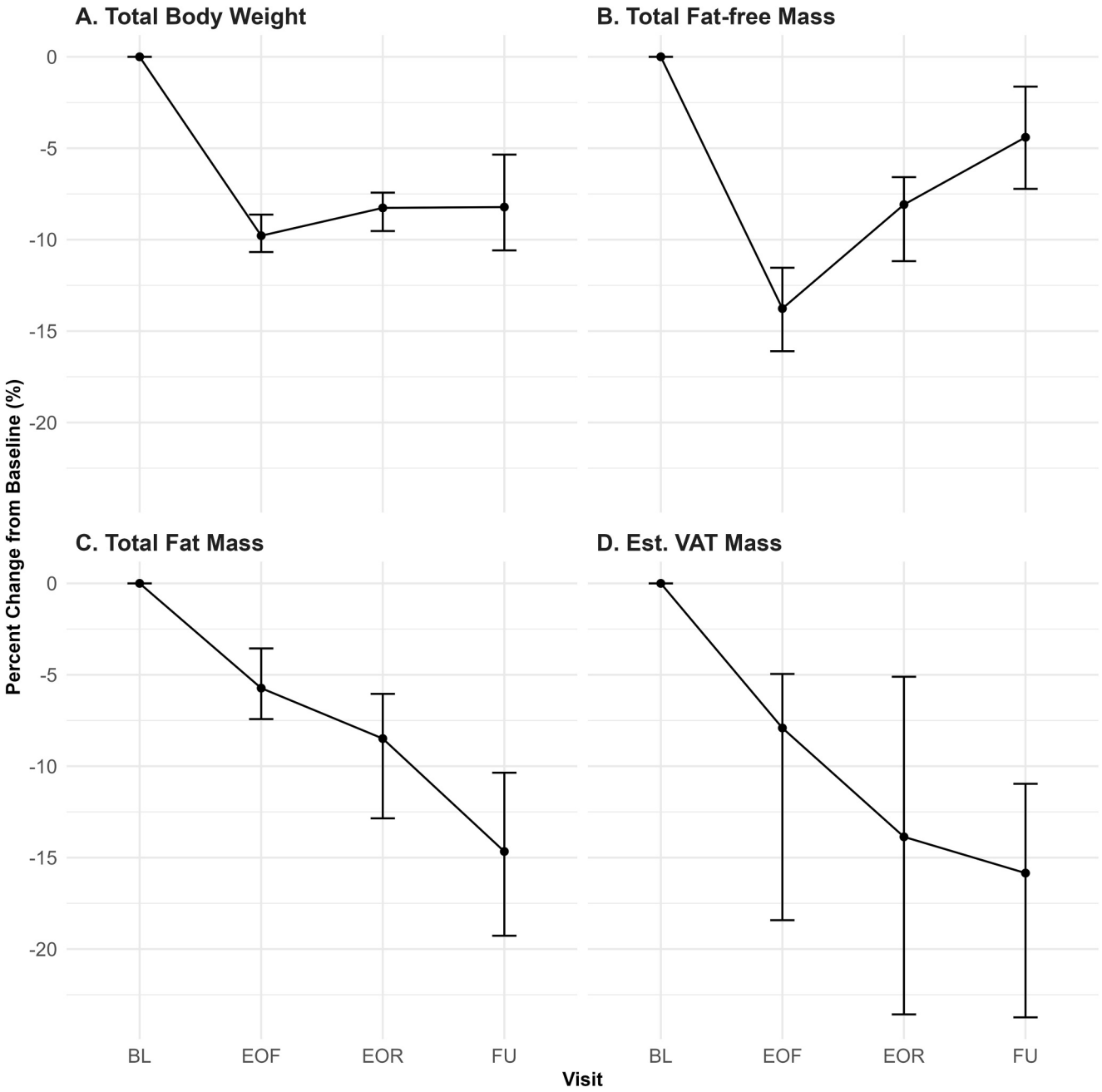

FIGURE 1 | Median percentage changes from baseline.BL, baseline; EOF, end-of-fast; VAT; visceral adipose tissue; EOR, end-of-food reintroduction; FU, 6-week, follow-up; error. %, percent

At the follow-up visit, participants had a median FM loss of 14.7% from baseline, and the majority of FM loss occurred during the food reintroduction and maintenance periods (see Supporting Information S1: Table 4). In particular, participants experienced a substantial loss of abdominal fat, represented by significant reductions in android and VAT compartments as well as in AC [31]. Reductions in visceral fat have been strongly associated with reductions in hepatic fat accumulation and enhanced metabolic function, making VAT loss a key factor in mitigating fatty liver disease and all-cause mortality [45, 46]. Further research is needed to determine whether VAT loss contributed to improved FLI and other metabolic markers in this population [31]. Moreover, the magnitude of VAT loss reported here is comparable to that observed with pharmacological and exercise interventions of substantially longer duration [47], suggesting that the intervention may be an equally effective or more time-efficient strategy for reducing visceral adiposity.

This study did not investigate the mechanisms underlying continued FM loss after food reintroduction or the extent to which a whole-plant-food diet contributed to this outcome. Nevertheless, mechanisms regulating post-fast lipolysis are unlikely to be the same mechanisms regulating lipolysis during fasting because several markers (e.g., cortisol, leptin, adiponectin) active in that process reportedly returned to baseline once exogenous glucose was reintroduced [22]. Post-fast lipolysis also appeared to continue independently of glucose metabolism, as this population experienced a transient spike in insulin and glucose upon food

reintroduction that normalized during the maintenance period [31]. Future research should examine these questions as well as whether the continued FM loss observed post-fasting eventually stabilizes or factors such as diet composition, physical activity, and individual metabolic variability further influence long-term body composition changes.

There is emerging evidence that prolonged fasting upregulates a non-canonical lipolytic pathway in humans [23], which was recently characterized as a liposomal lipolytic pathway in rodents [48, 49]. Although FGF21 has been strongly linked to fasting-induced fat oxidation and energy expenditure in rodents, it exhibited a delayed response in humans, increasing only on the 10th day of water-only fasting, leaving questions as to its precise function [50]. If FGF21 function is conserved in humans and remains elevated after food reintroduction, it could play a role in regulating post-fast fat oxidation and energy expenditure, potentially preventing cyclical FM regain. This may explain why post-fast FM loss persisted without evidence of ongoing caloric restriction, increased physical activity, or sustained ketogenesis. Future research should investigate FGF21 concentrations and non-canonical liposomal lipolysis rates after caloric intake resumes.

This study had several strengths, including the use of DXA for body composition and VAT measurements, an in-patient setting, which ensured safety and adherence monitoring through clinical assessment and laboratory evaluations, and an extended follow-up period. Nevertheless, the generalizability of these results was limited by potential selection bias due to recruitment of predominantly postmenopausal females from a single center, which may have been exacerbated by the 28% attrition at follow-up. Larger and more diverse populations would help clarify the role of demographic and clinical differences in progressive FM loss. The study also lacked a control group to determine the contribution of dietary changes to sustained outcomes and follow-up periods beyond six weeks to elucidate long-term effects.

5 | Conclusion

This preliminary analysis provided valuable insights into progressive body composition changes following prolonged water-only fasting and a whole-plant-food diet. Fasting resulted in a median 9.8% reduction in total BW. Initially, FFM loss accounted for the majority of total BW lost, but it was rapidly restored upon food reintroduction. In contrast, FM loss continued after food reintroduction and accounted for the majority of BW lost at FU, including a median 15.8% reduction in VAT mass. The observed shifts in FFM and FM highlight the need to distinguish between acute adaptations, sustained changes, and long-term health outcomes. These results warrant further investigation into prolonged water-only fasting as a potential strategy for obesity prevention and cardiometabolic health improvement.

Author Contributions

T R M, E S, and A C G conceived and designed the manuscript. S G, D G, and T R M wrote the original draft. SG collected data. M N performed analysis and prepared tables and visualizations. All authors read, reviewed, edited, and approved the final version of this manuscript.

Acknowledgments

The authors thank the study volunteers, Eve Zeiler, Natasha Thompson, and the staff at TrueNorth Health Center.

Conflicts of Interest

D.M.G. consults for Metabite, Inc. A.C.G. is owner of TrueNorth Health Center and President of the Board of the TrueNorth Health Foundation. All other authors declare no conflicts of interest.

Data Availability Statement

Data are openly available in Dryad at https://doi.org/10.5061/dryad.q2bvq83z8.

References

1. W. O. Federation, World Obesity Atlas 2024: No Area of the World Is Unaffected by the Consequences of Obesity, 2022: [cited 2024 March 2], https://www.worldobesity.org/news/world-obesity-atlas-2024#:~:text=Key%20Statistics%3A,to%201.53%20billion%20in%202035.

2. B. A. Alhamdan, A. Garcia-Alvarez, A. H. Alzahrnai, et al., "Alternate-Day Versus Daily Energy Restriction Diets: Which Is More Effective for Weight Loss? A Systematic Review and Meta-Analysis," *Obesity Science & Practice* 2, no. 3 (2016): 293–302: [published Online First: 2016/10/07], https://doi.org/10.1002/osp4.52.

3. H. Gasoyan, E. R. Pfoh, R. Schulte, P. Le, W. S. Butsch, and M. B. Rothberg, "One-Year Weight Reduction With Semaglutide or Liraglutide in Clinical Practice," *JAMA Network Open* 7, no. 9 (2024): e2433326: [published Online First: 2024/09/13], https://doi.org/10.1001/jamanetworkopen.2024.33326.

4. H. Gasoyan, E. R. Pfoh, R. Schulte, P. Le, and M. B. Rothberg, "Early- and Later-Stage Persistence With Antiobesity Medications: A Retrospective Cohort Study," *Obesity* 32, no. 3 (2024): 486–493: [published Online First: 2023/12/06], https://doi.org/10.1002/oby.23952.

5. C. M. Perdomo, R. V. Cohen, P. Sumithran, K. Clément, and G. Frühbeck, "Contemporary Medical, Device, and Surgical Therapies for Obesity in Adults," *Lancet* 401, no. 10382 (2023): 1116–1130: [published Online First: 2023/02/13], https://doi.org/10.1016/S0140-6736(22)02403-5.

6. J. M. Oppert, A. Bellicha, M. A. van Baak, et al., "Exercise Training in the Management of Overweight and Obesity in Adults: Synthesis of the Evidence and Recommendations From the European Association for the Study of Obesity Physical Activity Working Group," supplement, *Obesity Reviews* 22, no. S4 (2021): e13273: [published Online First: 2021/06/03], https://doi.org/10.1111/obr.13273.

7. S. Kloock, C. G. Ziegler, and U. Dischinger, "Obesity and Its Comorbidities, Current Treatment Options and Future Perspectives: Challenging Bariatric Surgery?," *Pharmacology & Therapeutics* 251 (2023): 108549: [published Online First: 2023/10/26], https://doi.org/10.1016/j.pharmthera.2023.108549.

8. C. M. Lee, R. R. Huxley, R. P. Wildman, and M. Woodward, "Indices of Abdominal Obesity Are Better Discriminators of Cardiovascular Risk Factors than BMI: A Meta-Analysis," *Journal of Clinical Epidemiology* 61, no. 7 (2008): 646–653: [published Online First: 2008/03/25], https://doi.org/10.1016/j.jclinepi.2007.08.012.

9. M. J. Lee and J. Kim, "The Pathophysiology of Visceral Adipose Tissues in Cardiometabolic Diseases," *Biochemical Pharmacology* 222 (2024): 116116: [published Online First: 2024/03/10], https://doi.org/10.1016/j.bcp.2024.116116.

10. A. Cesaro, G. De Michele, F. Fimiani, et al., "Visceral Adipose Tissue and Residual Cardiovascular Risk: A Pathological Link and New

Therapeutic Options," *Frontiers in Cardiovascular Medicine* 10 (2023): 1187735: [published Online First: 2023/08/14], https://doi.org/10.3389/fcvm.2023.1187735.

11. D. Rosendo-Silva, P. B. Gomes, T. Rodrigues, et al., "Clinical and Molecular Profiling of Human Visceral Adipose Tissue Reveals Impairment of Vascular Architecture and Remodeling as an Early Hallmark of Dysfunction," *Metabolism* 153 (2024): 155788: [published Online First: 2024/01/15], https://doi.org/10.1016/j.metabol.2024.155788.

12. M. Bonjour, S. Gabriel, A. C. Goldhamer, and T. R. Myers, "Medically Supervised, Water-Only Fasting Followed by a Whole-Plant-Food Diet Reduces Visceral Adipose Tissue," *International Journal of Disease Reversal and Prevention* 3, no. 2 (2021): [published Online First: 09/13/2021, https://doi.org/10.22230/ijdrp.2021v3n2a267.

13. J. S. Finnell, B. C. Saul, A. C. Goldhamer, and T. R. Myers, "Is Fasting Safe? A Chart Review of Adverse Events During Medically Supervised, water-only Fasting," *BMC Complementary and Alternative Medicine* 18, no. 1 (2018): 67: [published Online First: 2018/02/21], https://doi.org/10.1186/s12906-018-2136-6.

14. A. C. Goldhamer, N. Gershfeld, D. M. Goldman, and T. R. Myers, "Challenging Case in Clinical Practice: Long-Term Relief From Chronic Posttraumatic Headache After Water-Only Fasting and an Exclusively Plant-Foods Diet," *Alternative & Complementary Therapies* 23, no. 4 (2017): 129–131, https://doi.org/10.1089/act.2017.29117.acg.

15. A. C. Goldhamer, M. Klaper, A. Foorohar, and T. R. Myers, "Water-Only Fasting and an Exclusively Plant Foods Diet in the Management of Stage Iiia, Low-Grade Follicular Lymphoma," *BMJ Case Reports* 2015 (2015): bcr2015211582: [published Online First: 2015/12/15], https://doi.org/10.1136/bcr-2015-211582.

16. T. R. Myers, G. J. Butler, and A. Goldhamer, "Challenging Case in Clinical Practice: Total Resolution of Hydronephrosis and Ureterectasis and Partial Regression of an Unspecified Retroperitoneal Mass Following a Medically Supervised, Water-Only Fast and an Exclusively Whole-Plant-Food Diet," *Alternative & Complementary Therapies* 26, no. 1 (2020): 16–18, https://doi.org/10.1089/act.2019.29257.trm.

17. C. Rhule, S. Gabriel, T. R. Myers, and A. C. Goldhamer, "Relief of Symptoms Associated With Long COVID After Prolonged Water-Only Fasting: A Case Report," *Integrative and Complementary Therapies* 30, no. 1 (2024): 11–13, https://doi.org/10.1089/ict.2023.29112.car.

18. E. Scharf, E. Zeiler, M. Ncube, et al., "The Effects of Prolonged Water-Only Fasting and Refeeding on Markers of Cardiometabolic Risk," *Nutrients* 14, no. 6 (2022): 1183: [published Online First: 2022/03/27], https://doi.org/10.3390/nu14061183.

19. M. Watts, S. Gabriel, A. C. Goldhamer, and T. R. Myers, "Prolonged Water-Only Fasting in the Management of Hashimoto's thyroiditis: A Case Report," *Integrative and Complementary Therapies* 29, no. 6 (2023): 309–311, https://doi.org/10.1089/ict.2023.29103.mwa.

20. E. Zeiler, S. Gabriel, M. Ncube, et al., "Prolonged Water-Only Fasting Followed by a Whole-Plant-Food Diet is a Potential Long-Term Management Strategy for Hypertension and Obesity," *Nutrients* 16, no. 22 (2024): 3959: [published Online First: 2024/11/27], https://doi.org/10.3390/nu16223959.

21. P. R. Kerndt, J. L. Naughton, C. E. Driscoll, and D. A. Loxterkamp, "Fasting: The History, Pathophysiology and Complications," *Western Journal of Medicine* 137, no. 5 (1982): 379–399: [published Online First: 1982/11/01].

22. Z. Dai, H. Zhang, F. Wu, et al., "Effects of 10-Day Complete Fasting on Physiological Homeostasis, Nutrition and Health Markers in Male Adults," *Nutrients* 14, no. 18 (2022): 3860: [published Online First: 2022/09/24], https://doi.org/10.3390/nu14183860.

23. M. L. Steinhauser, B. A. Olenchock, J. O'Keefe, et al., "The Circulating Metabolome of Human Starvation," *JCI Insight* 3, no. 16 (2018): e121434: [published Online First: 2018/08/24], https://doi.org/10.1172/jci.insight.121434.

24. T. R. Myers, B. Saul, M. Karlsen, et al., "Potential Effects of Prolonged Water-Only Fasting Followed by a Whole-Plant-Food Diet on Salty and Sweet Taste Sensitivity and Perceived Intensity, Food Liking, and Dietary Intake," *Cureus* 14, no. 5 (2022): e24689: [published Online First: 2022/06/07], https://doi.org/10.7759/cureus.24689.

25. R. L. Weinsier, "Fasting--A Review With Emphasis on the Electrolytes," *Americas Journal of Medicine* 50, no. 2 (1971): 233–240: [published Online First: 1971/02/01], https://doi.org/10.1016/0002-9343(71)90152-5.

26. G. F. Cahill Jr, "Fuel Metabolism in Starvation," *Annual Review of Nutrition* 26 (2006): 1–22: [published Online First: 2006/07/20], https://doi.org/10.1146/annurev.nutr.26.061505.111258.

27. P. K. Fazeli, Y. Zhang, J. O'Keefe, et al., "Prolonged Fasting Drives a Program of Metabolic Inflammation in Human Adipose Tissue," *Molecular Metabolism* 42 (2020): 101082: [published Online First: 2020/09/30], https://doi.org/10.1016/j.molmet.2020.101082.

28. M. Ezpeleta, S. Cienfuegos, S. Lin, V. Pavlou, K. Gabel, and K. A. Varady, "Efficacy and Safety of Prolonged Water Fasting: A Narrative Review of Human Trials," *Nutrition Reviews* 82, no. 5 (2024): 664–675: [published Online First: 2023/06/28], https://doi.org/10.1093/nutrit/nuad081.

29. N. Thompson, M. Ncube, S. Gabriel, E. Zeiler, A. Goldhamer, and T. Myers, "A Preliminary Observational Study on Potential Effects of Prolonged Water-Only Fasting Followed by Whole-Plant-Food Refeeding in Normal-Weight Females," *International Journal of Disease Reversal and Prevention* 6, no. 1 (2024), https://doi.org/10.22230/ijdrp.2024v6n1a411.

30. C. Laurens, F. Grundler, A. Damiot, et al., "Is Muscle and Protein Loss Relevant in Long-Term Fasting in Healthy Men? A Prospective Trial on Physiological Adaptations," *Journal of Cachexia, Sarcopenia and Muscle* 12, no. 6 (2021): 1690–1703: [published Online First: 2021/10/21], https://doi.org/10.1002/jcsm.12766.

31. S. Gabriel, M. Ncube, E. Zeiler, et al., "A Six-Week Follow-Up Study on the Sustained Effects of Prolonged Water-Only Fasting and Refeeding on Markers of Cardiometabolic Risk," *Nutrients* 14, no. 20 (2022): 4313: [published Online First: 2022/10/28], https://doi.org/10.3390/nu14204313.

32. P. A. Harris, R. Taylor, B. L. Minor, et al., "The Redcap Consortium: Building an International Community of Software Platform Partners," *Journal of Biomedical Informatics* 95 (2019): 103208: [published Online First: 2019/05/13], https://doi.org/10.1016/j.jbi.2019.103208.

33. Y. M. Cheung, G. Roff, and M. Grossmann, "Precision of the Hologic Horizon A Dual Energy X-ray Absorptiometry in the Assessment of Body Composition," *Obesity Research & Clinical Practice* 14, no. 6 (2020): 514–518: [published Online First: 2020/11/03], https://doi.org/10.1016/j.orcp.2020.10.005.

34. E. K. Goldberg and E. B. Fung, "Precision of the Hologic DXA in the Assessment of Visceral Adipose Tissue," *Journal of Clinical Densitometry* 23, no. 4 (2020): 664–672: [published Online First: 2019/04/18], https://doi.org/10.1016/j.jocd.2019.03.005.

35. R. C. R. Team, *A Language and Environment for Statistical Computing* (R Foundation for Statistical Computing, 2023).

36. A. Kuznetsova, P. B. Brockhoff, and R. H. B. Christensen, "Lmertest Package: Tests in Linear Mixed Effects Models," *Journal of Statistical Software* 83, no. 3 (2017): 1–26, https://doi.org/10.18637/jss.v082.i13.

37. B. Bolker and D. Robinson, *Broom.Mixed: Tidying Methods for Mixed Models*. version 0.2.9.4 (R package, 2022).

38. P. Bürkner, "Brms: An R Package for Bayesian Multilevel Models Using Stan," *Journal of Statistical Software* 80, no. 1 (2017): 1–28, https://doi.org/10.18637/jss.v080.i01.

39. J. Wiley, *Multileveltools: Multilevel and Mixed Effects Model Diagnostics and Effect Sizes*, version 0.1.1 (R package, 2020).

40. M. Koller, "Robustlmm: An R Package for Robust Estimation of Linear Mixed-Effects Models," *Journal of Statistical Software* 75, no. 6 (2016): 1–24, https://doi.org/10.18637/jss.v075.i06.

41. D. Lüdecke, *Sjplot: Data Visualization for Statistics in Social Science*. version 2.8.15(R package, 2023).

42. J. Johnson and B. Dawson-Hughes, "Precision and Stability of Dual-Energy X-ray Absorptiometry Measurements," *Calcified Tissue International* 49, no. 3 (1991): 174–178: [published Online First: 1991/09/01], https://doi.org/10.1007/BF02556113.

43. J. A. L. Calbet, J. G. Ponce-Gonzalez, J. Calle-Herrero, et al., "Exercise Preserves Lean Mass and Performance During Severe Energy Deficit: The Role of Exercise Volume and Dietary Protein Content," *Frontiers in Physiology* 8 (2017): 483: [published Online First: 2017/08/10], https://doi.org/10.3389/fphys.2017.00483.

44. A. Bellicha, M. A. van Baak, F. Battista, et al., "Effect of Exercise Training on Weight Loss, Body Composition Changes, and Weight Maintenance in Adults With Overweight or Obesity: An Overview of 12 Systematic Reviews and 149 Studies," supplement, *Obesity Reviews* 22, no. S4 (2021): e13256: [published Online First: 2021/05/07], https://doi.org/10.1111/obr.13256.

45. C. L. Hanlon and L. Yuan, "Nonalcoholic Fatty Liver Disease: The Role of Visceral Adipose Tissue," *Clinics in Liver Disease* 19, no. 3 (2022): 106–110: [published Online First: 2022/04/01], https://doi.org/10.1002/cld.1183.

46. B. Yu, Y. Sun, X. Du, et al., "Age-Specific and Sex-specific Associations of Visceral Adipose Tissue Mass and Fat-To-Muscle Mass Ratio With Risk of Mortality," *Journal of Cachexia, Sarcopenia and Muscle* 14, no. 1 (2023): 406–417: [published Online First: 2022/12/01], https://doi.org/10.1002/jcsm.13142.

47. S. Rao, A. Pandey, S. Garg, et al., "Effect of Exercise and Pharmacological Interventions on Visceral Adiposity: A Systematic Review and Meta-Analysis of Long-Term Randomized Controlled Trials," *Mayo Clinic Proceedings* 94, no. 2 (2019): 211–224: [published Online First: 2019/02/04], https://doi.org/10.1016/j.mayocp.2018.09.019.

48. G. V. N. Kumar, R. S. Wang, A. X. Sharma, et al., "Non-Canonical Lysosomal Lipolysis Drives Mobilization of Adipose Tissue Energy Stores With Fasting," *Nature Communications* 16, no. 1 (2025): 1330: [published Online First: 2025/02/04], https://doi.org/10.1038/s41467-025-56613-3.

49. Y. S. Yeh, T. D. Evans, M. Iwase, et al., "Identification of Lysosomal Lipolysis as an Essential Noncanonical Mediator of Adipocyte Fasting and Cold-Induced Lipolysis," *Journal of Clinical Investigation* 135, no. 6 (2025): e185340: [published Online First: 2025/03/17], https://doi.org/10.1172/JCI185340.

50. P. K. Fazeli, M. Lun, S. M. Kim, et al., "FGF21 and the Late Adaptive Response to Starvation in Humans," *Journal of Clinical Investigation* 125, no. 12 (2015): 4601–4611: [published Online First: 2015/11/04], https://doi.org/10.1172/JCI83349.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.