Resting Metabolic Rate, Total Daily Energy Expenditure, and Metabolic Adaptation 6 Months and 24 Months After Bariatric Surgery

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Objective: Little is known about long-term metabolic (energy expenditure) adaptation after bariatric surgery. Methods: Resting metabolic rate under basal conditions (RMR), total daily energy expenditure (TDEE), and body composition were measured in 25 participants in the Longitudinal Assessment of Bariatric Surgery-2. Results: Six months after surgery, BMI (± SD) decreased (47 ± 6 kg/m² to 37 ± 5 kg/m²), body fat went from 48% ± 6% to 40% ± 6% fat, and fat-free mass went from 67 ± 9 to 60 ± 9 kg. In absolute terms, RMR and TDEE both decreased significantly (1,730 ± 278 kcal/d vs. 1,430 ± 200 kcal/d and 2,879 ± 544 kcal/d vs. 2,369 ± 304 kcal/d), and the achieved energy balance was −1,293 ± 355 kcal/d. Sixteen of these participants underwent repeated measures at ~24 months; TDEE decreased 6 months postoperatively (2,957 ± 540 kcal/d to 2,423 ± 324 kcal/d; P = 0.0003), but at ~24 months, TDEE (2,602 ± 471 kcal/d) was not significantly different compared with month 6. The average negative energy balance from baseline to month 24 was −379 ± 131 kcal/d. Conclusions: RMR and TDEE fall precipitously in the first 6 months after bariatric surgery, but these adaptive changes were no longer significant after 2 years.

Introduction

Bariatric surgery has been shown to be effective for accomplishing durable weight loss and improved survival (1-6). There is wide variation in the amount of weight loss and regain after bariatric surgery. Pories et al. (2) reported that the percent of excess weight loss 10 years following gastric bypass was a mean of 55% with a range from 0.9% to 103%. In addition, the Longitudinal Assessment of Bariatric Surgery (LABS) consortium recently identified five weight loss trajectories following both gastric bypass and adjustable gastric banding, also demonstrating a wide variability of postoperative weight loss (7-9). Variable regain of weight occurs following all bariatric surgical procedures (7-9).

Detailed studies of the mechanism(s) of action following gastric bypass are needed in order to devise strategies for improving the outcomes of bariatric surgery. Here, we wanted to assess whether total daily energy expenditure (TDEE) and resting metabolic rate under basal conditions (RMR) change in patients undergoing bariatric surgery postoperatively compared with that measured preoperatively. Our primary hypothesis was that TDEE and RMR would decrease in patients undergoing bariatric surgery at 6 months and 24 months postoperatively compared with baseline.

Methods

Subjects

We studied patients who were enrolled in the LABS clinical trial (7), including 88% Roux-en-Y gastric bypass (none “long limb”), 8% adjustable gastric banding, and 4% biliopancreatic bypass with duodenal switch. Participants were recruited at Oregon Health & Science University. All inclusion and/or exclusion criteria matched those of LABS (7). In addition, eligible subjects were excluded if

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Author contributions: BMW, DAS, and JAL conceived the study. CES carried out the clinical study. DAS, DMT, BMW, SKMS, CES, and JAL analyzed data. JAL wrote the first draft of the manuscript, and all the authors were then involved in writing the paper and approved the submitted version. JAL is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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they were unable to walk at 2 mph for 15 minutes or weighed greater than 227 kg at the screening visit because this was the upper limit of the dual x-ray absorptiometry (DXA) scanner table. Oregon Health & Science University and Mayo Clinic Institutional Review Boards approved the study, and written informed consent was obtained.

Study design
Free-living LABS bariatric surgery patients were studied for 18-day periods on three occasions, at baseline before surgery, at 6 months, and at approximately 24 months after bariatric surgery. LABS patients followed best practice guidelines for post-bariatric-surgery care (7), which included education regarding the composition and energy content of their diets and calcium, multivitamin, and B12 supplementation. Subjects were not given an exercise prescription.

Measurements of TDEE
TDEE was measured by using doubly labeled water (DLW) at these same three time points during the study. A baseline urine was collected, and then subjects drank approximately 10 atom percent (AP) 18O water and 0.12 g of the 99.8 AP 2H water per kilogram of estimated total body water. The cup was then washed with 50 mL of tap water and drank by the subjects. Subjects were not moved prior to measurements and had not eaten since 2100 the night before. For each measurement, the face mask-equipped indirect calorimeter (Columbus Instruments, Columbus, Ohio) was calibrated by using gases of known composition. Subjects were awake, semirecumbent (10° head bed tilt), lightly clothed, and in thermal comfort (68°F-74°F) in a dimly lit, quiet room. Measurements were performed for 30 minutes, during which time subjects were not allowed to talk or move. RMR was the average of the final 25 minutes for the three consecutive days of data (days 16-18).

Measurements of body composition
Body fat was measured at the start and end of each DLW period by using DXA (13) (Discovery A (S/N 80132) Hologic; Lunar, Madison, Wisconsin). The vast majority of DXA scans were completed with the entire body captured in the field of the x-ray. In a small number of scans, subjects were unable to be captured in the field; here, the subject was scanned with the results multiplied by two for the full body estimate. Fat mass was the average of the percent DXA fat mass multiplied by the scale weight on days 0 and 14 of the TDEE protocol. The average fat-free mass (FFM) at each time point was calculated as the difference between the subject’s body weight and fat mass (FM) as determined by the two DXA.

Data and statistical analyses
Sample sizes for race other than white or surgical procedure other than Roux-en-Y were small (one or two per group), and thus analyses were performed without subcategorization. Results are reported as mean ± standard deviation (SD).

Testing for metabolic adaptation at month 6 and month 24
To test for the presence of change at both 6 months and 24 months, we performed analysis of variance (ANOVA) and post hoc paired two-sample $t$ tests, comparing RMR and total energy expenditure at baseline with month 6 RMR as well as baseline to month 24 RMR by using SPSS Statistics version 21 (IBM Corp., Armonk, New York).

The $t$ test alone cannot isolate the presence of metabolic adaptation because the difference between baseline and 6-month energy expenditure may be different because of lower metabolic rates associated with reduced weight or a change beyond the effects of reduced fat-free mass (adaptation). To determine whether metabolic rates are lower because of metabolic adaptation, we regressed a line with baseline RMR as the dependent variable and baseline fat-free mass as the independent variable in Microsoft Excel (Microsoft, Seattle, Washington). We then calculated the residuals between measured energy expenditure and that predicted from current fat-free mass by using the baseline linear relationship described above. Finally, a one-sample $t$ test was performed to determine whether the mean difference (bias) was different from zero. The one-sample $t$ test was conducted in SPSS.

Estimation of the energy deficit and energy intake
Weight change results from energy imbalance and can result from uncompensated changes in energy intake, TDEE, or both. To understand the rates of weight change over time, we applied the first law of thermodynamics by the use of energy balance models (14) to calculate the magnitude of energy deficit from body composition changes. To isolate the roles of energy intake and TDEE, we also used these models to calculate metabolizable energy intake (Ei).

\[
E_i = TDEE + ES
\]

Change in energy stores (ES) was calculated applying changes in body composition (kilograms) as measured by DXA by using the following formula:

\[
ES = 1,020 \frac{\Delta FFM}{\Delta t} + 9,500 \frac{\Delta FM}{\Delta t}
\]

From this formula, we can also calculate energy balance (the difference between metabolizable energy intake and energy expended) at 6 months and 24 months, which is equal to ES. These calculations
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**TABLE 1** Anthropometric and energetic data at baseline and 6 months post bariatric surgery

|                     | Baseline | 6 months post surgery |
|---------------------|----------|-----------------------|
|                     | Mean     | SD        | Mean     | SD        | P    |
| Age (22 women, 3 men), y | 44.5     | 10.6     | 46.1     | 5.1       | <0.001|
| BMI (kg/m²)          | 47.4     | 6.1       | 36.5     | 5.1       | <0.001|
| Weight (kg)          | 130.5    | 20.4      | 99.8     | 16.1      | <0.0001|
| Body fat (%)         | 47.9     | 5.6       | 39.6     | 6.3       | <0.001|
| Body fat (kg)        | 63.0     | 15.3      | 40.0     | 10.9      | <0.001|
| Fat-free mass (kg)   | 67.4     | 9.3       | 59.8     | 8.9       | <0.001|
| Total body water (kg)| 44.4     | 6.4       | 40.1     | 6.0       | <0.001|
| RMR (kcal/d)         | 1,730    | 278       | 1,430    | 200       | <0.0001|
| RMR residual (kcal/d)| 0        | 186       | 131      | 163       | =0.002|
| TDEE (kcal/d)        | 2,879    | 544       | 2,369    | 304       | <0.001|
| TDEE residual (kcal/d)| 0       | 420       | 227      | 339       | =0.008|

Body composition determined by using dual x-ray absorptiometry, and total body water derived from deuterium dilution. RMR determined by indirect calorimeters and TDEE by using doubly labeled water. P values are for paired analyses. Residuals calculated by predicting RMR and TDEE based on respective baseline relationships with fat-free mass before surgery. Residuals calculated as predicted – actual. Equation describing baseline relationship between fat-free mass (FFM) and RMR was RMR = 52.1 × FFM + 243 (R² = 0.55; P < 0.001). Equation describing baseline relationship between fat-free mass (FFM) and TDEE was TDEE = 37.0 × FFM + 382 (R² = 0.40; P < 0.001).

RMR, basal metabolic rate; TDEE, total daily energy expenditure.

Baseline and 6-month repeated measures of TDEE and RMR. RMR was measured before and 6 months after bariatric surgery (Table 2). In absolute terms, RMR decreased with weight loss from 1,730 ± 278 kcal/d to 1,430 ± 200 kcal/d (P < 0.001). As expected, RMR correlated with fat-free mass but not fat mass.

TDEE was measured before and 6 months after bariatric surgery (Table 2). In absolute terms, TDEE decreased with weight loss from 2,879 ± 544 kcal/d to 2,369 ± 304 kcal (P < 0.001), as did total body water (Table 2). The amount of fat loss was not predicted by initial body weight or by baseline RMR or TDEE by using linear models.

The mean measured change was 7.66 ± 3.0 kg in fat-free mass, 510 ± 433 kcal/d in TDEE, and 300 ± 203 kcal/d in RMR. The change in TDEE correlated with the change in fat-free mass (R = 0.49; P = 0.01). There was no correlation between the change in TDEE and the change in RMR or between the change in TDEE and the change in body fat. There was no association between the change in RMR and the change in body fat or fat-free mass after surgery.

Baseline, 6-month, and 24-month repeated measures

Subjects included and subjects excluded from analysis. The data presented here were derived from 16 people, 14 of whom were women, age 46 ± 11 years. Fourteen of the patients underwent Roux-en-Y gastric bypass, one completed adjustable gastric banding, and one had biliary pancreatic diversion with a duodenal switch. Of the 16 subjects, 12 identified themselves as white, 1 African American, 1 white/Native American, 1 white/African American/Native American, and 1 white/African American/“other.” The reasons that 9 of the 25 subjects did not complete the 24-month follow-up were that they chose to not repeat the measurements or could not be located for follow-up.
Baseline, 6-month, and 24-month repeated measures of body weight and body composition. As expected in these 16 patients who underwent repeated measures of body composition at 24 months postoperatively, the patients’ weight, body fat, and fat-free mass continued to decrease from postoperative months 6 through 24 (Table 2) (Figure 1). After 2 years, fat loss was highly variable (27.0 ± 6.6 [11.3-47.2] kg). The rate at which body composition changed was less between months 6 and 24 compared with baseline and month 6 (Table 2). This slowing or plateauing of the rate of weight loss was expected (7,8).

Baseline, 6-month, and 24-month repeated measures of RMR. Similar to the above, for the 16 subjects who completed the assessments through 24 months, measured RMR decreased in the first 6 months after surgery, but the change between months 6 and 24 was not significant (Table 2). Fat-free mass contributed most to the variance of RMR (Figure 2).

Baseline, 6-month, and 24-month repeated measures of TDEE. In these 16 patients, measured TDEE decreased between baseline and 24 months (2,957 ± 540 kcal/d vs. 2,602 ± 471 kcal/d).

| Table 2 Anthropometric and energetic data at baseline and 6 and 24 months post bariatric surgery |
|-----------------------------------------------|
| **Baseline** | **6 months post surgery** | **24 months post surgery** | **P (0 vs. 6 months)** | **P (6 vs. 24 months)** |
| Age (14 women, 2 men) (y) | 46.3 ± 11.2 | 37.3 ± 4.4 | 31.7 ± 9.2 | <0.0001 | 0.03 |
| BMI (kg/m²) | 47.8 ± 5.2 | 37.5 ± 4.4 | 31.7 ± 9.2 | <0.0001 | 0.05 |
| Weight (kg) | 134.5 ± 13.0 | 104.2 ± 9.9 | 96.7 ± 12.3 | <0.0001 | 0.01 |
| Body fat (%) | 47.0 ± 6.4 | 39.7 ± 7.5 | 37.6 ± 6.1 | <0.0001 | 0.02 |
| Fat-free mass (kg) | 70.8 ± 7.0 | 62.5 ± 6.9 | 60.0 ± 7.2 | <0.0001 | 0.02 |
| Total body water (kg) | 46.2 ± 4.8 | 41.7 ± 5.0 | 40.6 ± 4.8 | <0.0001 | 0.02 |
| RMR (kcal/d) | 1,792 ± 267 | 1,460 ± 192 | 1,563 ± 216 | <0.0001 | ns |
| RMR residual (kcal/d) | 13.3 ± 196 | 161 ± 139 | 3.0 ± 141 | =0.02 | ns |
| TDEE (kcal/d) | 2,957 ± 540 | 2,423 ± 324 | 2,602 ± 471 | 0.0003 | ns |
| TDEE residual (kcal/d) | 47.3 ± 410 | 273 ± 377 | 94 ± 550 | ns | ns |

Body composition determined by using dual x-ray absorptiometry, and total body water derived from deuterium dilution. RMR determined by indirect calorimeters and TDEE by using doubly labeled water. P values are for paired analyses. Residuals calculated as predicted – actual. Equation describing baseline relationship between fat-free mass (FFM) and RMR was RMR = 22.1 × FFM + 243 (R² = 0.55; P < 0.001). Equation describing baseline relationship between fat-free mass (FFM) and TDEE was TDEE = 37.0 × FFM ± 382 (R² = 0.40; P < 0.001).

RMR, basal metabolic rate; TDEE, total daily energy expenditure.
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Measured TDEE, however, did not change significantly between 6 and 24 months despite patients continuing to lose weight. TDEE and RMR did not change significantly between baseline (1.68 ± 0.31) and 6 months (1.70 ± 0.33) and 24 months postoperatively (1.70 ± 0.35).

Evidence for metabolic adaptation

To test whether RMR or TDEE displayed metabolic adaptation after surgery, energy expenditure prediction equations were developed by using baseline data. Before surgery, the relationship between RMR (kilocalories per day) and fat-free mass (FFM) (kilograms) was RMR = 22.1 × FFM + 243 ($R^2 = 0.55$; $P < 0.001$). The equation that described the relationship between fat-free mass (FFM) and TDEE at baseline was TDEE = 37.0 × FFM + 382 ($R^2 = 0.40$; $P < 0.001$).

The paired t test revealed that the 6-month RMR was significantly different from baseline ($P = 0.02$). The bias (average of the residuals) between the predicted RMR from baseline data and the 6-month RMR was $-161 ± 139$ kcal/d, indicating that, on average, RMR decreased beyond that accounted by weight loss at 6 months, which was evidence of metabolic adaptation. However, at 24 months, the bias was small ($-3 ± 141$ kcal/d) and not significantly different from zero ($P = 0.12$).

TDEE also changed more than was expected for change in body composition, but only at the 6-month assessment. The average residual between measured and predicted TDEE based on fat-free mass was significant ($-227 ± 340$ kcal/d) at 6 months but not 24 months (0 ± 555 kcal/d).

We also tested the influence of including fat mass in the TDEE prediction equation. In doing so, it was found that fat mass was a significant predictor when included along with fat-free mass, but that the coefficient for fat mass in these subjects with class III obesity was negative (i.e., TDEE decreased with increasing fat mass), and that it actually increased the estimate of metabolic adaptation at 6 months ($-454 ± 365$ kcal/d; $P < 0.001$). For the evaluation of the TDEE data at 24 months, we also tested whether using data from the 16 subjects at baseline who were present for the 24-month measurement period would change the estimate of metabolic adaptation, and it did influence the sign of the estimate, but it remained insignificant ($218 ± 480$ kcal/d).

Calculated energy deficit and energy intake

The achieved energy deficit between baseline and month 6 was $-1,293 ± 355$ kcal/d in 25 subjects, while the achieved energy deficit from month 6 to month 24 was $-93 ± 126$ kcal/d in 16 subjects, which was a 93% reduction in magnitude comparing with the estimate between baseline and month 6. The calculated energy intake was $1,111 ± 435$ kcal/d between baseline and month 6 and $2,420 ± 409$ kcal/d between month 6 and month 24.

Discussion

It is not well understood how weight loss is sustained after bariatric surgery (15-17). Our results indicate that TDEE decreases following bariatric surgery, and that the decrease at 6 months is due to both a reduction in fat-free mass (accounting for 56% of the change in TDEE), a major predictor of TDEE, and a metabolic adaptation (44%) that decreases TDEE more than the reduction in fat-free mass predicts. The decrease in TDEE was maintained at 24 months, but at that point after surgery, there was no longer evidence indicating metabolic adaptation.

Previous data have suggested that patients undergoing bariatric surgery are physically inactive (18-25), and it is often assumed that after bariatric surgery, physical activity increases. Our data and others (19,22) do not support this. Our results indicate that weight loss occurs not because of an increase in TDEE, but rather that weight loss occurs despite a reduction in TDEE. Our data support prior findings of large reductions in caloric intake despite these studies utilizing food records and dietary recall (23), which are often inaccurate (26). More accurate methods of quantitating nutrient intake, such as our energy deficit calculations combined with TDEE, following gastric bypass demonstrate evidence of a large reduction in metabolizable energy intake. It should be noted that the energy deficit/balance approach cannot isolate the influences between reduced dietary consumption and increased malabsorption, which identified 62% and 18% reductions in energy intake the first 6 months and the next 18 months after surgery, respectively. Despite the widespread popularity of gastric bypass for weight loss, the mechanisms of action remain incompletely defined.

We had a comparatively large data set to look at the short- and intermediate-term impact of bariatric surgery on human energetics (Table 1). We showed substantial variance in fat loss in our subjects as others have reported. In the first 6 months after surgery, RMR and TDEE fell precipitously by 17% and 18%, respectively. The reductions in RMR and TDEE at 6 and 24 months were due to roughly equal reductions in metabolic body size as defined by fat-free mass and metabolic adaptation during the period of rapid weight loss, which is similar to results reported by others (27). Eighteen months later (2 years postoperatively), this metabolic adaptation to short-term weight loss had started to dissipate, as both RMR and TDEE were no longer significantly less than predicted based on fat-free mass at 24 months. Because of participant dropout between 6 and 24 months, however, the power of our study was reduced.

After bariatric surgery, it appears that the energetic changes in the short term may not be sustained for even 2 years. For example, absolute RMR falls precipitously and then returns upward by 2 years. The idea of short-term energetic adaptation giving way to a longer-term change is supported by the RMR data adjusted for fat-free mass, in which the short-term decrease in RMR reverses by 2 years. These changes are mirrored by the changes in TDEE, explaining why TDEE and/or RMR is constant. It would be interesting to follow patients even longer, but we speculate that it is most likely that the trend of metabolic adaptation reverting toward zero would not change. This is consistent with the results from human energy balance studies in which energy expenditure is reduced for body composition during periods of rapid weight loss induced by negative energy balance, but it is either not significantly reduced or only slightly reduced after weight regain (28). It should be noted that our subjects were nearly in energy balance at baseline and 24 months, but energy balance was evidenced by weight stability at 24 months. The insignificant metabolic adaptation we observed at 24 months contrasts with the report from “The Biggest Loser” in which the metabolic adaptation was sustained for 6 years, although others have
suggested that this was an overstatement (29,30), and provides further evidence that weight loss induced metabolic adaptation is not permanent (30). The difference may reflect the different mechanisms of weight loss, i.e., intestinal surgery with its concurrent altered satiety feedback signaling (1), microbiome (31), or other changes versus the effect of extreme diet and exercise (32,33).

There are several studies with which to compare our data (27,34-36). Su et al. followed 11 women who underwent ileogastrectomy for 6 to 8 weeks after surgery. Over this short period of time, RMR was not affected, although TDEE significantly predicted weight loss (34). Das et al. (27) studied 30 woman before and 14 months after bariatric surgery by using DLW before and after gastric bypass. Das et al. reported that TDEE decreased following gastric bypass in proportion to the reduction in lean body mass. However, these studies could not track both the short-term (6 month) and longer-term effects of weight loss because the protocol included only one postsurgical time point. It should be noted that in our study, the TDEE and RMR values were smaller than those of Das et al. (27) despite similar body size, age, and sex distributions. It is not known whether this difference contributed to the unusual negative coefficient for fat mass at baseline and thus our finding that the use of the TDEE prediction equation using both fat mass and fat-free mass suggested a greater metabolic adaptation at 6 months than just fat mass alone. Because the sample sizes were small in both studies, we advise caution in trying to interpret the coefficients in such prediction equations.

Our studies contrast those performed in gastric bypass rats, which showed increases in TDEE and RMR, along with a 17% decrease in ad libitum food intake (37). The difference appears to be a species effect. The rat studies expressed energy expenditure as milliliters of \( O_2 \) consumed per hour per kilogram of body weight raised to the 0.75 power. Our findings were based on differences after linear adjustment for fat-free mass. We did not use the ratio of expenditure per unit of fat-free mass because the TDEE regression line did not pass through the origin, a requirement of expressing results as a ratio.

There are limitations to our study that we acknowledge. Our subjects went from a mean BMI of 48 to a BMI of 32. Even 2 years postoperatively, our subjects met criteria for obesity. If people transition to a healthy BMI, their energetic parameters might undergo further change. The studies we conducted were not large and, therefore, may have been underpowered to detect small changes. That said, the studies were arduous to conduct and represent the best available existing data to examine our stated hypothesis. A third important limitation was that most of our volunteers were women. It is impossible to say from these studies whether men would have responded differently; we respect that the impact of sex is unanswerable in this work, although it was not one of our hypotheses. Lastly, we lost one-third of our subjects to follow-up between months 6 and 24 (as might be expected). However, there is no evidence that this biased the results, as both cohorts at 6 months showed similar energetic changes and weight loss. A further question that arises that we failed to address is whether the weight loss and adaptive changes we reported were specifically a result of bariatric surgery or because of weight loss alone. Several studies (38-41) have documented how energy expenditure decreases with nonsurgical weight loss and that, during weight regain, adaptive metabolic reductions rapidly reverse even though all of the lost weight is not regained (42). Thus, the lack of metabolic adaptation we demonstrated at 24 months may be from the physiological reversal of adaptive reductions in metabolism. We cannot be certain whether the changes we document are because of bariatric surgery and/or weight loss because we did not include a weight-matched nonsurgical weight loss group because of the difficulty in achieving such large changes in weight through nonsurgical clinical methods. This is important because mechanisms specific to surgery cannot, from our data, be separated out from those of physiological weight loss (43,44).

In conclusion, RMR and TDEE fall precipitously in the first 6 months after surgery, even when data are adjusted for fat-free mass. The changes can be explained by a combination of reductions in fat-free mass and a metabolic adaptation. However, the metabolic adaptation abated sometime between 6 and 24 months, resulting in a partial absolute upward shift in energy expenditure between 6 and 24 months after surgery. If the underlying thermogenic mechanism were understood, interventions could be designed to prevent this."

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