Continued Loss in Visceral and Intermuscular Adipose Tissue in Weight-Stable Women Following Bariatric Surgery

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Objective: To assess changes in total (TAT), subcutaneous (SAT), visceral (VAT), and intermuscular (IMAT) adipose tissue by whole-body MRI before surgery and at 12 months and 24 months post-surgery in a subset of participants of the Longitudinal Assessment of Bariatric Surgery-2.

Methods: From 0 to 12 months, n = 20 females and 3 males; from 12 to 24 months, n = 42 females and 7 males. Paired t-tests and GLM repeated measures examined changes in TAT, SAT, VAT, and IMAT at 12 and 24 months, with sex and age as covariates.

Results: Changes from 0 to 12 months included weight (−41.9 ± 12.1 kg; −36%), TAT (−33.5 ± 9.6 kg; −56%), SAT (−29.2 ± 8.2 kg; −55%), VAT (−3.3 ± 1.6 kg; −73%), and IMAT (−0.99 ± 0.68 kg; −50%), all P < 0.001. In females, from 12 to 24 months, despite relative weight stability (−1.8 ± 6.5 kg; −2%; P = 0.085), VAT (−0.5 ± 0.7 kg; −30%; P < 0.001) and IMAT (−0.2 ± 0.4 kg; −14%; P = 0.012) decreased further. In males, from 12 to 24 months, weight increased (5.1 ± 5.2 kg; 6%; P = 0.04) with no significant changes in TAT or sub-depots.

Conclusions: Bariatric surgery continues to induce favorable changes in body composition, i.e., persistent adipose tissue loss at 24 months in the absence of further significant weight loss.
At 12 weeks post gastric banding, losses were observed in abdominal subcutaneous fat (−20%), VAT (−15%) proportional to VAT at baseline (10), and hepatic fat (−19%) (10). Weiss et al. (6) reported reductions of 35% in VAT and 32% in SAT from a single abdominal slice at 6 months post-surgery. In this study, laparoscopic bariatric surgery procedures included Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric band (LB), duodenal switch (DS), and sleeve gastrectomy (SG). Carroll et al. (7) calculated total VAT volume (by CT) from eight abdominal slices that decreased by 22% at 6 months post-LB surgery. Using a single abdominal slice at 3 and 12 months post-LB surgery, VAT decreased by 20% and 34%, respectively (9). Korner et al. (3) using whole-body MRI in post-surgery weight-stable female patients (at 19–25 months post-LB and RYGB surgery), found that VAT was 43% lower compared to nonsurgery height, weight, and age-matched controls. Clearly, there are reductions in all measured adipose tissue depots; however, the degree of change is highly variable based on these published studies.

Obesity comorbidities such as diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea ameliorate in a significant portion of bariatric surgery patients (1) post-surgery compared to lifestyle modifications or pharmacological therapy. A clear understanding of the quantitative changes that occur in adipose tissue depots would be a first step to understand mechanisms underlying the benefits of bariatric surgery.

The aim of this study was to quantify TAT and sub-depots, namely SAT, VAT, and IMAT, using whole-body MRI prior to bariatric surgery and to describe changes in these sub-depots at 12 months and 24 months following surgery. We hypothesized that the distribution of TAT in SAT, VAT, and IMAT is different from before (T0) to 12 months (T12) and 24 months (T24) with weight loss following bariatric surgery. A secondary aim was to compare sub-depots in surgery patients at T12 and T24 to healthy non-surgery controls.

Methods

Surgery participants

Between November 2006 and February 2009, participants (n = 64) enrolled in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) at the Weill Cornell Medical College and the University of Pittsburgh Medical Center sites were invited to participate in this ancillary study (11-13). Due to a delay in recruiting relative to LABS-2, recruitment was extended through December 2009, during which an additional 41 Non-LABS-2 participants were enrolled for a total of 105 ancillary study participants, 53 from Weill Cornell and 52 from Pittsburgh. Five patients enrolled in the study did not proceed to have surgery performed due to health insurance coverage issues.

Measurements for the Weill Cornell participants were acquired at St. Luke’s-Roosevelt Hospital. Baseline measures were collected on average 1.3 week prior to surgery (T0) (range: 0-11 weeks). Postoperative measures were collected approximately 12 months later (T12) (range: 10.6-17.7 months) and 24 months later (T24). Surgery types included: RYGB, LB, biliopancreatic diversion (BPD), DS, and SG. Exclusions for entry into the study included pregnancy, claustrophobia, abnormal thyroid or cortisol levels, and self-reported use of medications known to influence body composition (such as diuretics and corticosteroids) at time of entry.

Nonsurgical controls

The surgical group was compared at one and two years post-surgery to a nonsurgical control group from a study whose design and primary findings were previously published (14). The multiethnic control group included 207 women and 87 men with mean BMI 26.0 ± 5.2 kg/m², age 41.7 ± 14.0 years, and weight 73.0 ± 16.4 kg.

Body composition measures

Subjects reported in the early morning after an 8 h fast. Subjects were weighed in a hospital gown to the nearest 0.1 kg (Weight Troy, New York, NY; and BWB 800 Tanita Corp., Pittsburgh) and height to the nearest 0.5 cm using a stadiometer (Holtain; Crosswell, Wales-New York; and Perspective Enterprises, Portage, MI, Pittsburgh).

Fat-free mass and fat mass were measured using a modified 3-compartment model (Silva 2004): Fat-3C (kg) = 2.122 × (BW/D) − 0.779 × TBW − 1.356 × BW, where BW is body weight in kg, D is body density derived from BodPod, and TBW is total body water in kg. TBW was measured using a D2O (~1 g/kg) oral dose administered after a fasting venous blood sample was taken from an antecubital vein. After 3 h, a second fasting blood sample was obtained. Body density was measured using BOD POD (Cosmed, Chicago, IL; software version 2.3) (15,16). Further details regarding body composition assessments in this cohort were recently published (17).

Magnetic resonance imaging

Total AT (TAT) including total SAT, VAT, and IMAT were measured by using whole-body multislice MRI as previously described (18,19). Subjects at both sites (New York and Pittsburgh) were placed on a 1.5 T scanner platform (GE, 6X Horizon, Milwaukee, WI) with their arms extended above their heads. The protocol involved the acquisition of 40 axial images, 10 mm in thickness and at 40 mm intervals across the whole body. SliceOmatic 4.2 image analysis software (Tomovision, Montreal, CA) was used to analyze images on a PC workstation. Estimates of MRI volume were converted to mass by using the assumed density of 0.92 kg/l for adipose tissue (20). All scans were read by the same technician at the New York Obesity Nutrition Research Center. The technical errors for three repeated readings of the same scan by the same observer for SAT, VAT, and IMAT volumes in our laboratory were 0.96%, 1.97%, and 0.65%, respectively.

Statistical analysis

Descriptive statistics, expressed as means ± SD, were calculated for subject baseline characteristics and for changes from T0 to T12 and from T12 to T24. The paired t-test was used to test the null hypothesis that the mean change from T0 to T12 and from T12 to T24 was equal to zero. Analyses were performed for males and females separately. T-tests were used to compare TAT, SAT, IMAT, and VAT between surgery group and controls. General linear models verified statistical significant differences in TAT, SAT, VAT, and IMAT between the post-bariatric surgery group and the control group after adjusting for age, sex, height, and weight.
General linear models were used to determine the contribution of age and sex in accounting for differences in TAT, SAT, VAT, and IMAT in the surgery patients. Subjects who had T0 and T12 measurements (N = 23) or T12 and T24 (N = 49) measurements were included in the analyses. Tests for preferential VAT loss were performed based on the allometric model described by Hallgreen and Hall (21). Regression models were used to investigate the relation of VAT and IMAT to TAT after weight loss. Data were analyzed using SPSS for Windows v15 (SPSS, Chicago, IL). Statistical significance was set at P < 0.05, two-tailed.

**Results**

**Baseline**

Baseline characteristics of the total study cohort (n = 100) who had bariatric surgery are presented in Table 1 by sex and surgery type. Prior to surgery, 71 participants had body sizes that extended beyond the MRI field of view and did not have an MRI performed. A total of 29 subjects had an MRI at T0, from which 23 (3 M, 20 F) had an MRI at T12; 49 (7 M, 42 F) had MRI at T12 and 24 months (T24) (81% RYGB, 19% other); and 17 (1 M, 16 F) had MRI at T0, T12, and T24. From the main study cohort, subjects with an MRI at T0 weighed less (P < 0.0001) and had a lower body mass index (BMI; P < 0.0001) than those with no MRI at T0 (Table 1). Mean % Fat for women and men at T0 was 47% and 54%, respectively and mean BMI was 45.6 kg/cm². All males and 70% of the females had RYGB surgery.

Table 2 shows baseline characteristics of subjects who had MRI at T0 and T12 (N = 23) or at T12 and T24 (N = 49). Graphical comparisons between the two groups showed that those who were larger at T0 and did not fit in MRI had a similar weight loss pattern to those who fit in MRI. Percentage fat based on a three compartment model (%Fat-3C), was higher for males and females who did not fit in the MRI at T0.

**Changes in TAT and sub-depots**

**Pre-surgery (T0) to 12 months post-surgery (T12).** Body weight, BMI, and body composition characteristics at T0 and T12 by surgery type are shown in Table 3. All males and 80% of females had RYGB. Females in the RYGB group weighed the most at baseline (115 kg, SD 14.9) and weighed less (69.8 kg, SD 11.1) at T12, compared to females who had LB and SG. Among males and females, absolute reductions occurred in body weight, TAT, and all TAT sub-deposits from T0 to T12 (females P < 0.001, males P < 0.01) (Table 4).

General linear models by sex adjusted for age showed significant losses in TAT (−35.1 kg; P < 0.001), SAT (−29.54 kg; P < 0.001), and IMAT. With respect to VAT, controlling for TAT, males had greater VAT at T0 compared to females (6.9 kg vs. 4.14 kg) and Table 2 shows baseline characteristics of subjects who had MRI at T0 and T12 and those who had MRI at T12 and T24.

**Table 1** Pre-surgery characteristics of study participants

| Race          | N (100) | Males (17%) | Females (83%) |
|---------------|---------|-------------|---------------|
| Caucasian     | 68      | 12 (70%)    | 56 (67.5%)    |
| African American | 16    | 1 (5.9%)    | 15 (18.1%)    |
| Hispanic      | 15      | 4 (23.5%)   | 11 (13.3%)    |
| Asian         | 1       | -           | 1 (1.2%)      |
| Surgery type  |         |             |               |
| RYGB          | 72      | 14 (82.4%)  | 58 (69.9%)    |
| LB            | 11      | 1 (5.9%)    | 10 (12%)      |
| BPD/DS        | 4       | -           | 4 (4.8%)      |
| SG            | 13      | 2 (11.8%)   | 11 (13.3%)    |

**Table 2** Pre-surgery characteristics of participants who had MRI at T0 and T12 and those who had MRI at T12 and T24

| Surgery type | Male (N = 3) | Female (N = 20) | Male (N = 7) | Female (N = 42) |
|--------------|--------------|-----------------|--------------|-----------------|
| Age          | 45.0 ± 20.2  | 41.6 ± 8.1      | 42.3 ± 16.8  | 43.2 ± 10.0     |
| Height (cm)  | 177.7 ± 27   | 164.2 ± 7.6     | 178.1 ± 6.5  | 165.8 ± 6.3     |
| Weight (kg)  | 130.0 ± 14.4 | 113.9 ± 14.2    | 141.5 ± 14.9 | 124.2 ± 19.3    |
| BMI (kg/m²)  | 41.2 ± 0.8   | 42.3 ± 4.9      | 44.7 ± 5.4   | 45.1 ± 5.7      |
| %Fat (3C)    | 41.6 ± 4.3   | 51.7 ± 4.4      | 50.1 ± 4.6   | 53.7 ± 4.5⁶     |
| Surgery type | N (%)        | N (%)           | N (%)        | N (%)           |
| RYGB         | 3 (100%)     | 16 (80%)        | 6 (85.7%)    | 33 (78.6%)      |
| LB           | -            | -               | 1 (2.4%)     | -               |
| BPD/DS       | -            | 2 (10%)         | -            | 5 (11.9%)       |
| SG           | -            | 2 (10%)         | 1 (14.3%)    | 3 (7.1%)        |

⁶Values are means ± SD.

**Notes:**

1. Mean % Fat for women and men at T0 was 47% and 54%, respectively.
2. Mean BMI was 45.6 kg/cm². All males and 70% of the females had RYGB surgery.
3. General linear models by sex adjusted for age showed significant losses in TAT (−35.1 kg; P < 0.001), SAT (−29.54 kg; P < 0.001), and IMAT. With respect to VAT, controlling for TAT, males had greater VAT at T0 compared to females (6.9 kg vs. 4.14 kg) and
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**Changes in TAT and sub-depots**

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TABLE 3 Adipose tissue distribution by surgery procedure before surgery (T0) and 12 months post-surgery (T12)

|                | Females | Males |
|----------------|---------|-------|
|                | RYGB (N = 16) | LB (N = 2) | SG (N = 2) | RYGB (N = 3) |
|                | T0      | T12   | T0       | T12   | T0       | T12 |
| Weight (kg)    | 115.0 ± 14.9 | 69.8 ± 11.1 | 107.8 ± 16.1 | 88.4 ± 12.1 | 110.8 ± 10.8 | 81.6 ± 8.1 | 130.0 ± 1.4 | 82.4 ± 4.9 |
| BMI (kg/m²)    | 43.4 ± 4.8 | 26.2 ± 3.4 | 38.3 ± 0.8 | 31.4 ± 1.1 | 37.5 ± 3.7 | 27.5 ± 3.0 | 41.2 ± 0.82 | 26.2 ± 1.2 |
| %Fat (30)a     | 52.4 ± 4.1b | 31.0 ± 6.2 | 50.0 ± 1.9 | 44.0 ± 1.6 | 48.6 ± 9.1 | 40.1c | 41.6 ± 4.3 | 18.7 ± 7.3 |
| TAT (kg)       | 60.9 ± 8.8 | 25.1 ± 7.9 | 57.8 ± 9.9 | 41.4 ± 4.3 | 54.6 ± 13.9 | 28.2 ± 10.3 | 55.5 ± 5.5 | 18.3 ± 4.3 |
| SAT (kg)       | 54.5 ± 8.0 | 22.9 ± 7.3 | 52.1 ± 7.7 | 37.4 ± 4.2 | 50.9 ± 13.9 | 26.7 ± 10.2 | 46.3 ± 6.1 | 16.3 ± 3.5 |
| VAT (kg)       | 4.4 ± 1.5 | 1.2 ± 0.7 | 3.9 ± 1.7 | 2.5 ± 0.5 | 2.0 ± 0.5 | 0.3 ± 0.2 | 6.9 ± 0.7 | 1.1 ± 0.7 |
| IMAT (kg)      | 2.0 ± 0.7 | 1.0 ± 0.4 | 1.7 ± 0.5 | 1.5 ± 0.4 | 1.8 ± 0.5 | 1.2 ± 0.1 | 2.3 ± 0.3 | 0.9 ± 0.2 |
| %SAT           | 89.3 ± 2.6 | 91.3 ± 3.2 | 90.4 ± 2.1 | 90.3 ± 0.7 | 93.0 ± 1.8 | 94.3 ± 1.8 | 83.2 ± 3.0 | 89.3 ± 2.8 |
| %VAT           | 7.3 ± 2.2 | 4.6 ± 2.4 | 6.8 ± 1.8 | 6.0 ± 0.7 | 3.6 ± 0.1 | 1.2 ± 0.1 | 12.6 ± 2.8 | 5.7 ± 2.3 |
| %IMAT          | 3.3 ± 0.9 | 4.1 ± 1.5 | 3.0 ± 0.3 | 3.8 ± 1.4 | 3.4 ± 1.9 | 4.5 ± 2.0 | 4.2 ± 0.4 | 5.0 ± 0.6 |

All values are means ± SD.
RYGB: Roux-en-Y gastric bypass, LB: laparoscopic adjustable gastric band, SG: sleeve gastrectomy, TAT: total adipose tissue, SAT: subcutaneous adipose tissue, VAT: visceral adipose tissue, IMAT: intermuscular adipose tissue.

Percentages are sub-depots as percentage of total adipose tissue: %SAT = (SAT/TAT) × 100, %VAT = (VAT/TAT) × 100, %IMAT = (IMAT/TAT) × 100.

*F = 2.122 × (weight/density) − 0.779 × 0.9937 × TBW – 1.356 × weight.
*N = 14 females.
*N = 1 female.

Males lost more VAT at T12 (−5.8 kg, −84%) compared to females (−2.9 kg, −70%; P = 0.002). Males had greater IMAT than females at T0. Using GLM, for subjects who had MRI at T0 and T12, sex was a significant determinant of VAT (P = 0.002), such that males lost significantly more VAT than females. Age was a significant predictor of SAT (P = 0.039) such that older subjects had higher

TABLE 4 Changes in adipose tissue distribution at 12 months post-surgery and compared to controls

|                | Surgery females (N = 20) | Control females (N = 207) | P-valueb |
|----------------|--------------------------|---------------------------|----------|
|                | T0      | T12     | Changesa | P-valuea | Percent changea |          |          |
| Weight (kg)    | 113.9 ± 14.2 | 72.8 ± 12.2 | −41.1 ± 12.8 | <0.001 | −36.1% | 68.7 ± 16.3 | 0.28 |
| TAT (kg)       | 60.0 ± 9.0 | 27.1 ± 9.0 | −32.9 ± 9.9 | <0.001 | −54.9% | 25.9 ± 11.9 | 0.68 |
| SAT (kg)       | 53.9 ± 8.1 | 24.8 ± 8.3 | −29.1 ± 8.5 | <0.001 | −54.0% | 22.1 ± 8.7 | 0.58 |
| VAT (kg)       | 4.1 ± 1.6 | 1.3 ± 0.8 | −2.9 ± 1.3 | <0.001 | −69.8% | 1.49 ± 1.2 | 0.36 |
| IMAT (kg)      | 2.0 ± 0.6 | 1.1 ± 0.4 | −0.9 ± 0.7 | <0.001 | −46.8% | 1.0 ± 0.7 | 0.92 |

|                | Control males (N = 87) | P-valueb |
|----------------|------------------------|----------|
|                | T0      | T12     | Changesa | P-valuea | Percent changea |          |          |
| Weight (kg)    | 130.0 ± 14.4 | 82.4 ± 4.9 | −47.6 ± 4.3 | 0.003 | −36.6% | 83.1 ± 11.2 | 0.92 |
| TAT (kg)       | 55.5 ± 5.5 | 18.3 ± 4.3 | −37.2 ± 7.1 | 0.012 | −67.0% | 20.7 ± 7.3 | 0.59 |
| SAT (kg)       | 46.3 ± 6.1 | 16.3 ± 3.4 | −29.9 ± 7.0 | 0.018 | −64.6% | 17.5 ± 5.7 | 0.72 |
| VAT (kg)       | 6.9 ± 0.7 | 1.1 ± 0.7 | −5.8 ± 0.8 | 0.006 | −84.1% | 2.4 ± 1.7 | 0.23 |
| IMAT (kg)      | 2.3 ± 0.3 | 0.9 ± 0.2 | −1.4 ± 0.3 | 0.012 | −60.9% | 0.8 ± 0.5 | 0.69 |

Values are means ± SD.
TAT: total adipose tissue, SAT: subcutaneous adipose tissue, VAT: visceral adipose tissue, IMAT: intermuscular adipose tissue.

Changes and percent change are for pre-surgery (T0) to 12 months post-surgery (T12).
*aBaseline (T0) versus 12 months post-surgery (T12).
*b12 months (T12) versus controls.
SAT. The change in VAT relative to TAT from T0 to T12 showed $k = 1.3 \pm 0.03$ (95% CI 1.20-1.33) when the Hallgreen and Hall model (19) was applied (Figure 1A).

**T12 to 24 months post-surgery (T24).** Body composition characteristics at T12 and T24 by surgery type are shown in Table 5. In females, those who had RYGB or SG, lost more weight and fat than females who had LB or BPD/DS. In males, those who had RYGB lost more weight and fat than males who had SG.

The pattern of weight change from T12 to T24 differed by sex (Table 6). In females ($n = 42$), despite a small and not statistically reliable change in weight ($-1.8 \pm 6.5$ kg; $P = 0.085$), there were further reductions in VAT ($-30.1\%$; $-0.5 \pm 0.7$ kg; $P = 0.001$) and IMAT ($-13.6\%$; $-0.2 \pm 0.4$ kg; $P = 0.012$), with non-statistically reliable changes in TAT ($-5.5\%$, $-1.9 \pm 6.3$ kg; $P = 0.059$). In males ($n = 7$), body weight increased ($+5.5\%$; $+5.1 \pm 5.2$ kg; $P = 0.039$) with no significant change in TAT ($+14.4\%$; $P = 0.078$) and no changes in sub-depots ($+13.8\%$ SAT, $+14.8\%$ VAT, $+17.9\%$ IMAT; Table 6).

From T12 to T24, the analyses revealed significant sex differences in change in TAT ($P = 0.025$), SAT ($P = 0.05$), VAT ($P = 0.011$), and IMAT ($P = 0.007$) for repeated measures over time, with males gaining adipose tissue in all depots and females showing adipose tissue losses. Being older (age) was associated with increased IMAT ($P = 0.046$). In females, the change in VAT relative to TAT from T0 to T24 showed $k = 1.5 \pm 0.06$ (95% CI 1.35-1.62) when the Hallgreen and Hall model (19) was applied (Figure 1B).

**Adipose tissue depots in surgery compared to nonsurgical controls**

At one year post-surgery, TAT, SAT, IMAT, and VAT were not different from nonsurgical controls (Table 4). At T24, compared to nonsurgical controls, BMI, weight, TAT, and SAT were higher ($P < 0.05$) in the bariatric surgery females while IMAT and VAT
**TABLE 5** Adipose tissue distribution by surgery type at 12 (T12) and 24 (T24) months post-surgery

|                   | Females (n = 42) | Males (n = 7) |
|-------------------|------------------|---------------|
|                   | RYGB (N = 33)    | LB (N = 5)    | BPD/DS (N = 1) | SG (N = 3) | RYGB (N = 6) | SG (N = 1) |
| **T12**           |                 |               |               |            |              |             |
| Weight (kg)       | 80.3 ± 17.9     | 98.4 ± 18.2   | 88.4          | 83.2 ± 3.9 | 90.7 ± 10.1  | 100.5       |
| BMI               | 29.0 ± 5.7      | 34.6 ± 4.3    | 33.0          | 30.4 ± 0.7 | 28.3 ± 3.4   | 33.2        |
| %Fat (3C)a        | 35.1 ± 8.6      | 47.5 ± 3.5    | 46.7          | 43.2 ± 2.7 | 26.5 ± 8.9   | 34.7        |
| TAT (kg)          | 32.6 ± 13.8     | 47.8 ± 10.9   | 37.9          | 36.8 ± 1.4 | 26.7 ± 8.5   | 38.2        |
| SAT (kg)          | 29.9 ± 12.6     | 43.3 ± 10.5   | 36.2          | 33.6 ± 0.7 | 22.8 ± 6.0   | 33.9        |
| VAT (kg)          | 1.6 ± 1.4       | 2.8 ± 0.5     | 1.1           | 2.0 ± 1.8  | 2.3 ± 1.8    | 3.2         |
| IMAT (kg)         | 1.1 ± 0.6       | 1.7 ± 0.5     | 0.6           | 1.2 ± 0.2  | 1.6 ± 0.9    | 1.1         |
| %SAT              | 91.8 ± 3.4      | 90.4 ± 1.2    | 95.7          | 91.6 ± 5.1 | 86.7 ± 5.9   | 88.7        |
| %VAT              | 4.6 ± 2.8       | 6.0 ± 1.4     | 2.9           | 5.3 ± 4.7  | 7.5 ± 4.7    | 8.4         |
| %IMAT             | 3.5 ± 1.4       | 3.6 ± 1.1     | 1.5           | 3.1 ± 0.5  | 5.8 ± 1.7    | 2.9         |
| **T24**           |                 |               |               |            |              |             |
| Weight (kg)       | 78.8 ± 19.2     | 95.2 ± 21.1   | 84.0          | 81.2 ± 14.5| 94.3 ± 12.5  | 115.1       |
| BMI               | 28.7 ± 6.3      | 33.9 ± 4.9    | 32.2          | 30.0 ± 3.3 | 29.8 ± 4.6   | 38.0        |
| %Fat (3C)a        | 35.9 ± 9.2b     | 45.5 ± 6.6    | 35.9          | 40.6 ± 10.9| 24.7 ± 13.4c | 42.7        |
| TAT (kg)          | 30.7 ± 14.1     | 46.1 ± 13.8   | 34.0          | 35.4 ± 11.5| 29.1 ± 10.4  | 51.7        |
| SAT (kg)          | 28.7 ± 13.2     | 42.2 ± 13.1   | 33.2          | 32.6 ± 11.3| 24.6 ± 7.2   | 46.8        |
| VAT (kg)          | 1.1 ± 1.2       | 2.4 ± 0.6     | 0.4           | 1.6 ± 1.8  | 2.7 ± 2.6    | 3.4         |
| IMAT (kg)         | 0.9 ± 0.4       | 1.5 ± 0.6     | 0.5           | 1.2 ± 0.3  | 1.9 ± 1.2    | 1.5         |
| %SAT              | 93.8 ± 3.2      | 91.3 ± 1.7    | 97.6          | 92.2 ± 5.5 | 86.2 ± 8.0   | 90.5        |
| %VAT              | 3.1 ± 2.6       | 5.4 ± 1.4     | 1.1           | 4.4 ± 5.1  | 7.8 ± 5.9    | 6.7         |
| %IMAT             | 3.1 ± 1.1       | 3.3 ± 0.9     | 1.3           | 3.4 ± 0.5  | 6.0 ± 2.2    | 2.8         |

Values are means ± SD.
RYGB: Roux-en-Y gastric bypass, LB: laparoscopic adjustable gastric band, BPD: biliopancreatic diversion, DS: duodenal switch, SG: sleeve gastrectomy, TAT: total adipose tissue, SAT: subcutaneous adipose tissue, VAT: visceral adipose tissue, IMAT: intermuscular adipose tissue.
Percentages are adipose tissue sub-depots as percentage of total adipose tissue: %SAT = SAT/TAT × 100, %VAT = VAT/TAT × 100, %IMAT = IMAT/TAT × 100.
%Fat (3C) = 2.122 × (weight/density) − 0.779 × 0.9937 × TBW − 1.356 × weight.

**TABLE 6** Adipose tissue depots at 12 (T12) and 24 (T24) months post-surgery and in controls

| Surgery females (N = 42) | T12 | T24 | Changesa | P-valuea | Percent changea | Controls | P-valueb |
|--------------------------|-----|-----|----------|----------|-----------------|----------|----------|
| Weight (kg)              | 82.8 ± 17.9 | 81.0 ± 19.3 | −1.8 ± 6.5 | 0.085 | −2.2% | 68.7 ± 16.3 | <0.0001 |
| TAT (kg)                 | 34.9 ± 13.6 | 33.0 ± 14.4 | −1.9 ± 6.3 | 0.059 | −5.4% | 25.9 ± 11.9 | 0.001 |
| SAT (kg)                 | 31.9 ± 12.4 | 30.7 ± 13.4 | −1.2 ± 5.6 | 0.171 | −3.7% | 22.1 ± 8.7 | <0.0001 |
| VAT (kg)                 | 1.8 ± 1.3 | 1.2 ± 1.3 | −0.5 ± 0.7 | <0.001 | −30.1% | 1.49 ± 1.2 | 0.21 |
| IMAT (kg)                | 1.2 ± 0.6 | 1.0 ± 0.5 | −0.2 ± 0.4 | 0.012 | −13.6% | 1.0 ± 0.7 | 0.71 |

| Surgery males (N = 7) | T12 | T24 | Changesa | P-valuea | Percent changea | Controls | P-valueb |
|-----------------------|-----|-----|----------|----------|-----------------|----------|----------|
| Weight (kg)           | 92.1 ± 9.9 | 97.2 ± 13.9 | 5.1 ± 5.2 | 0.039 | 5.6% | 83.1 ± 11.2 | 0.002 |
| TAT (kg)               | 28.4 ± 8.9 | 32.4 ± 12.8 | 4.0 ± 5.0 | 0.078 | 14.1% | 20.7 ± 7.3 | <0.0001 |
| SAT (kg)               | 24.4 ± 6.9 | 27.7 ± 10.7 | 3.4 ± 4.6 | 0.099 | 13.8% | 17.5 ± 5.7 | <0.0001 |
| VAT (kg)               | 2.5 ± 1.7 | 2.8 ± 2.4 | 0.4 ± 1.2 | 0.461 | 14.8% | 2.4 ± 1.7 | 0.52 |
| IMAT (kg)              | 1.5 ± 0.8 | 1.8 ± 1.1 | 0.3 ± 0.5 | 0.158 | 17.9% | 0.8 ± 0.5 | <0.0001 |

Values are means ± SD.
TAT: total adipose tissue, SAT: subcutaneous adipose tissue, VAT: visceral adipose tissue, IMAT: intermuscular adipose tissue.
ad12 months (T12) versus 24 months post-surgery (T24).
b24 months (T24) versus controls.
did not differ. In males (T24), BMI, weight, TAT, SAT, and IMAT were higher than controls whereas VAT was not different (P = 0.52) (Table 6). At T12, after adjusting for age, height, weight, and sex, the surgery group had less VAT (B = −1.385, P = 0.014) than controls whereas TAT, SAT, and IMAT did not differ. Females had more TAT (B = 11.785, P < 0.001), SAT (B = 12.194, P < 0.001), and IMAT (B = 0.421, P < 0.001) than males, with no significant group by sex interactions.

At T24, adjusting for age, height, weight, and sex, the surgery group had more TAT (B = 53.007, P < 0.001), SAT (B = 47.466, P < 0.001), and IMAT (B = 2.571, P < 0.001) than non-surgery controls. Females in the surgery group had less VAT (B = −3.752, P < 0.001; group by sex interaction) than control females. In general, females had significantly lower VAT than males (B = −0.868, P < 0.001).

**VAT and IMAT as a function of TAT in females from before to after surgery**

We investigated the relationship of VAT and IMAT with TAT in the same women at T0, T12, and T24 to ascertain how VAT (Figure 2A) and IMAT (Figure 2B) levels might vary from before to after surgery when TAT is held constant. According to our regression models (Supporting Information Table), a hypothetical 45-year-old female weighing 90 kg with 45 kg TAT would have at T0 ~3.06 kg VAT and ~1.3 kg IMAT; at T12 (using the same age, weight, and TAT parameters), this female would have ~2.42 kg VAT and ~1.45 kg IMAT, and at T24 ~1.68 kg VAT and ~1.21 kg IMAT.

**Discussion**

This study showed that bariatric surgery caused substantial and robust loss in total and regional adipose tissue at 12 and 24 months post-bariatric surgery, with continued losses between 12 and 24 months in women, when body weight change was not significant. These results indicate that bariatric surgery has an important effect on reducing adipose tissue depots even after body weight has begun to stabilize.

We found a remarkable 77% reduction in VAT at 12 months post-surgery in both men and women. Our findings are in agreement with Johansson et al. (5), where in morbidly obese women at 12 months post-surgery, weight (~33.6%), VAT (~73.1%), and SAT (~53.2%) were significantly reduced.

Hallgreen and Hall (21) described an allometric relationship between VAT and fat mass (FM), where the change in VAT is primarily determined by changes in FM and is proportional to the initial ratio of VAT to FM (defined by the differential equation dVAT/dFM = k × VAT/FM, where k is a dimensionless constant, k = 1.3 ± 0.1). This relationship has been shown to hold true for different types of weight loss intervention and for both sexes equally (21). In the current study, VAT loss relative to TAT from T0 to T12 is in agreement with Hallgreen and Hall (21), where VAT was determined by the change in TAT and by the initial VAT to TAT ratio. Using inclusion criteria of weight loss of ≥5 kg and VAT and FM loss, we found that the value of k was 1.3 ± 0.03 in both sexes. The greater absolute VAT loss in males compared to females at 12 months post-surgery is explained by a higher pre-surgery VAT to TAT ratio in males. As per Hallgreen and Hall model, the coefficients for men and women were the same indicating no sex differences in VAT loss after adjusting for the amount of TAT (or FM). However, from T0 to T24 in females, the value of k was 1.5, and was therefore greater than that proposed by the Hallgreen and Hall model, indicating increased VAT loss 2 years post-surgery in women. Remarkably, women who had bariatric surgery had significantly less VAT two years after surgery compared to BMI-matched controls.

These data emphasize the importance of longer-term longitudinal assessment of adipose tissue depots beyond the initial 12 month post-surgery period to better understand the effectiveness of bariatric surgery.
surgery in mobilizing adipose tissue depots. Bariatric surgery studies have reported improved treatment or remission of metabolic complications of obesity in males and females 6 to 12 months post-surgery (22,23). Males in the current study, by 24 months, showed significant gains in VAT and small gains in weight, VAT, SAT, and IMAT indicating unfavorable effects of weight regain that should be monitored more closely to avoid the development of obesity-related complications.

The strengths of this study include the longitudinal assessment of weight loss and specific adipose tissue depots measured by MRI (24). We report a novel finding of a preferential VAT loss in women beyond the initial 12 months post-surgery. The parent LABS trial (23) recently reported sustained weight loss at three years post-surgery in a large number of subjects with continued improvements in diabetes, hypertension, and dyslipidemia compared to pre-surgery levels. Although the parent trial did not collect measures of adipose tissue depots, it may well be that the sustained improvements in the observed risk factors are in part attributable to these reduced adipose tissue depots. Fat free mass, including skeletal muscle mass and bone mass, changes in the same cohort is being prepared for publication in a separate manuscript.

A limitation of this study was that not all participants fit in the MRI pre-surgery due the scanner field of view being less than that required to accommodate all individuals thereby limiting the sample size with pre-surgery values. The number of male participants was low, so our ability to derive stronger conclusions regarding sex differences across time was limited. A disproportionate number of participants had RYGB surgery compared to the other surgery types limited our ability to compare the effects of different surgery procedures due to inadequate sample sizes for most non-RYGB surgery types.

Conclusion
The energy restriction of bariatric surgery induces massive weight loss with continued adipose tissue mobilization from IMAT and VAT stores in women up to two years post-surgery. Males showed increases in all adipose tissue depots between 12 and 24 months post-surgery with weight regain. Studies seeking to understand weight loss and comorbidities after bariatric surgery must take into consideration all possible anatomical and AT depot pattern changes for more specific and efficient treatment in the clinical setting.

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