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Abdominal adiposity and liver fat content 3 and 12 months after gastric banding surgery

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Abstract

Weight loss after laparoscopic adjustable gastric banding surgery (LAGB) is associated with mobilization of adipose tissue from a variety of depots. We sought to evaluate and relate abdominal and hepatic lipid deposition in an obese female population 3 and 12 months after LAGB. We related changes in these depots to markers of insulin sensitivity. Eighteen female obese subjects underwent magnetic resonance imaging and spectroscopy before and 3 and 12 months after LAGB for the quantification of abdominal subcutaneous (ABSAT) and visceral (VAT) adipose tissue areas and liver fat content (LFAT). Fasting blood free fatty acids (FFA) were analyzed. Insulin sensitivity was assessed by the homeostasis model assessment of insulin resistance index (HOMA-R). Mean weight loss 3 and 12 months after LAGB was 9.8 ± 1.1 kg and 20.0 ± 2.2 kg, respectively. Postoperatively, VAT area loss exceeded ABSAT area loss in the cohort as a whole and when divided according to preoperative liver fat stores. Three months after LAGB, reductions had occurred in VAT and ABSAT areas (both $P < .01$) and in FFA ($P < .05$). Twelve months after LAGB, further significant reductions ($P < .01$) occurred in VAT and ABSAT areas but not in FFA. No significant reduction occurred in LFAT at either time point in the group as a whole. In those with preoperative hepatic steatosis (LFAT >∼5%, n = 7), LFAT fell by 42% ($P = .036$) 3 months after LAGB, with a total reduction of 50% ($P = .027$ cf baseline) occurring by 12 months. There was an improvement in HOMA-R at 12 months (1.9 ± 0.3 cf 2.9 ± 0.5 at baseline, $P = .04$) but not 3 months (2.7 ± 0.4). Preoperatively, LFAT related significantly to VAT area ($r = 0.67$, $P = .003$) and HOMA-R ($r = 0.497$, $P = .04$) but not ABSAT area. Postoperatively at both 3 and 12 months, LFAT continued to relate to VAT area ($r = 0.63$, $P < .01$ at both time points) but not HOMA-R. The changes in LFAT and VAT area were unrelated postoperatively. Abdominal adipose tissue loss was greater from the visceral than subcutaneous depots, suggesting that insulin sensitivity may not be an important determinant of selective lipid depot loss. The lack of a significant change in liver fat in the group as a whole may relate to low preoperative liver fat stores and to high postoperative dietary fat intakes. Preoperative liver fat stores did not influence insulin sensitivity or abdominal lipid changes during weight loss. Liver fat content and VAT area interrelated more closely than either related to ABSAT area, suggesting differing regulatory pathways for fat mobilization from ABSAT and VAT depots but possibly similar pathways for storage and mobilization of fat in the liver and viscerally.

1. Introduction

The significance of adiposity varies according to its location. Abdominal obesity, indicated by an increased waist to hip ratio, is a feature of the metabolic syndrome and increases the risk of cardiovascular disease, type 2 diabetes mellitus, and other metabolic abnormalities such as hyperlipidemia and obstructive sleep apnea. On the other hand, a predominance of subcutaneous adiposity over visceral adiposity, for example, in subjects with a low waist to hip ratio, is associated with insulin sensitivity and is seen in those treated with thiazolidinediones [1].

Weight loss is associated with variable reductions in both visceral adipose tissue (VAT) and abdominal subcutaneous adipose tissue (ABSAT) depots. The relative degree of adipose tissue loss from one site over another after a weight loss intervention has been studied by several groups, although the results conflict [2-4]. The preferential loss of

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adipose tissue from one depot over another may relate to lifestyle habits such as physical activity and diet as well as familial and sex influences [5] and the mechanism of weight loss [6]. Preexisting hepatic steatosis and insulin sensitivity may also be relevant. Insulin has an antilipolytic effect in adipose tissue that is greater in subcutaneous than visceral adipose tissue such that the latter lipid depot is more vulnerable to lipolysis [5,7]. In insulin-resistant states, as occur for example with hepatic steatosis, the relative insensitivity of VAT to the actions of insulin could be more pronounced, resulting in the observed tendency toward greater loss of VAT than ABSAT during weight loss [2,8,9].

Metabolic improvements occur with weight loss and the accompanying reductions in VAT and ABSAT volumes. Although there is general consensus that visceral adiposity is responsible for many of the metabolic disturbances associated with obesity, any beneficial metabolic effect arising from loss of adipose tissue from one depot over another has not been well explored [10-12].

In recent years, the accumulation of triglyceride within hepatocytes (liver fat content [LFAT]) has been associated with features of the metabolic syndrome; and the liver is another location for lipid deposition that must be considered when evaluating the relative importance of lipid depots in determining disease risk. With the advent of noninvasive techniques to quantitate LFAT, studies have examined the relationship between LFAT and other lipid depots, again with conflicting results [13,14].

The purposes of the present study were several. Firstly, we aimed to distinguish the effect over time of a bariatric surgical procedure on weight loss from 3 important lipid depots (liver, abdominal subcutaneous layer, and viscera). As secondary aims, we examined the effect of progressive weight loss upon each patient's homeostasis model assessment (HOMA) score, a marker of their insulin sensitivity; and we sought to explain the fat loss from each depot on the basis of the subject's HOMA score and their preoperative LFAT stores.

2. Research methods and procedures

Ethics approval to conduct this study was received from the clinical research ethics committee of our institution.

2.1. Subjects

Eighteen obese female subjects (mean age, 44 years; range, 20-57) scheduled for laparoscopic adjustable gastric banding surgery (LAGB) gave their written consent to participate in this study.

Subjects that met the clinical criteria for LAGB (body mass index [BMI] >35 kg/m^2 or >30 kg/m^2 with a recognized comorbidity of obesity) were considered for enrolment in the study. Patients with a known history of diabetes mellitus or a baseline fasting blood glucose level greater than 6.0 mmol/L were excluded from the study. Because most patients who undergo this procedure are female, men were excluded from this study to improve sample homogeneity. Other reasons for exclusion were chronic conditions that were poorly controlled and contraindications to magnetic resonance studies including excessive size, claustrophobia, or the presence of metallic foreign bodies or incompatible implants. Assessments of the study cohort occurred preoperatively and 3 and 12 months post-LAGB.

2.2. Magnetic resonance

Magnetic resonance images and spectra were obtained to quantify lipid contained within the abdominal subcutaneous and visceral compartments and the liver using a Philips Intera 1.5-T magnet (Best, the Netherlands). With the subject lying supine in the magnet, a series of contiguous 10-mm–thick, T1-weighted axial images of the abdomen was taken from above the diaphragm to the symphysis pubis. Using one of these images with the liver clearly visible, an 8-cm^3 voxel was placed over a homogenous portion of liver, near a 7.6-cm surface coil that had been positioned laterally over the subject's right upper abdominal quadrant.

Liver spectra were acquired, with and without water suppression, using a predefined point-resolved spectroscopy sequence (echo time, 31 milliseconds; repetition time, 3000 milliseconds; 80 measurements; 32 measurements 1024 data points).

2.2.1. Hepatic lipid

Proton magnetic resonance spectroscopy was used for determining hepatic fat content [15,16]. Hepatic fat content was calculated from the ratio of the area under the lipid resonance in the water-suppressed sequence to that of the water resonance in the unsuppressed sequence [17] using the AMARES algorithm contained within the MRUI software program (EU project TMR, FMRX-CT97-0160, Barcelona, Spain). This method provides a numerical value for liver fat, the units of which are arbitrary (AU) but may be defined in percentage terms. An LFAT greater than 0.056 AU (5.6%) was used to identify those subjects with hepatic steatosis [17]. Sixteen complete sets of spectra were available for analysis.

2.2.2. Visceral and subcutaneous lipid

Images were transferred to a local workstation for volumetric analysis using Philips EasyVision software as previously described [18]. Briefly, a single axial image acquired at the level of the L4-5 intervertebral space was used to measure the change in abdominal adipose tissue [19].

The cross-sectional areas of both the visceral and subcutaneous fat depots were automatically computed after manual perimetry of each fat compartment. A total of 17 sets of images were analyzed. Repeated abdominal subcutaneous and visceral fat estimation using this technique gave rise to coefficients of variation of 3% and 6%, respectively [18].

2.3. Anthropometry

Body weight was measured to the nearest 0.1 kg with the subject in light clothing (shoes removed) on an upright pedestal digital scale (Seca, Birmingham, UK). Height was

measured to the nearest 0.5 cm (shoes removed) using a stadiometer (Seca). Body mass index was calculated from weight and height measurements (BMI = weight in kilograms/height in square meters). Waist circumference was measured to the nearest 0.1 cm at the narrowest point between the lower costal margin and the iliac crest using a standard metric tape measure.

2.4. Biochemistry

At each assessment, a single blood sample was collected for the analysis of plasma glucose, insulin, and free fatty acid (FFA) levels after an overnight fast. Spectrophotometry and immunoassay techniques were used to measure plasma glucose and insulin levels, respectively. Each subject's insulin sensitivity was determined from the HOMA insulin resistance index (HOMA-R) [20]. The HOMA-R has been validated against the euglycemic-hyperinsulinemic clamp for the determination of insulin sensitivity [21-23] and closely associates with the clamp technique during within-subject comparisons after weight loss [22]. Furthermore, the HOMA-R method has been used successfully in obese populations to detect improvements in insulin sensitivity resulting from weight loss [24]. Free fatty acids were measured spectrophotometrically on a Cobas Mira Plus analyzer (Roche, Basel, Switzerland).

2.5. Dietary protocol

Subjects were instructed to follow a free-fluid diet in the first 4 postoperative weeks, followed by 2 weeks of a pureed diet. Thereafter, subjects were advised to adhere to a relatively normal-consistency low-fat diet as outlined by their dietitian, avoiding certain foods known to increase risk of gastric obstruction such as fibrous vegetables and fruit, gristly meat, and white bread. Subjects were asked to complete a 4-day food record before and 3 and 12 months after gastric banding surgery. Three complete food records, analyzed using FoodWorks V. 4, Professional Edition (Xyris Software, Brisbane, Australia), were available for each of 9 subjects.

2.6. Statistical analysis

Data are presented as mean and standard error. All statistical computations were performed using the statistical package SPSS, version 12.0 (SPSS, Chicago, IL). The significance of the change in variables from baseline to postoperative assessments at 3 and 12 months was assessed using analysis of variance (ANOVA) and paired-samples *t* tests as appropriate, with significance assumed if *P* was less than .05. The significance of the difference between VAT and ABSAT depot changes was determined using ANOVA. Differences between variables measured in subjects with and without hepatic steatosis were analyzed using independent-samples *t* tests. Unless otherwise stated, reported changes in variables are absolute values. Relations between variables were assessed using Pearson correlation coefficient and assumed significant if *P* was less than .05.

3. Results

Subject characteristics preoperatively are depicted in Table 1. All subjects were obese (BMI, 39 ± 1 kg/m^2) and had normal fasting plasma glucose profiles. Mean baseline glucose and insulin concentrations were 4.6 ± 0.1 mmol/L and 13.7 ± 1.9 μU/mL, respectively. Four subjects had fasting hyperinsulinemia (plasma insulin level >15 μU/mL) at baseline. Seven subjects had hepatic steatosis as defined in the "Research methods and procedures" section [17]. These subjects had greater baseline levels of LFAT (24% ± 5%, $P <$ .01) and VAT (22 281 ± 3462 mm^2, $P < .05$) than those without hepatic steatosis (LFAT, 3% ± 1%; VAT, 13 909 ± 1957 mm^2). There were no differences in baseline body weight, waist circumference, ABSAT area, FFA, HOMA-R, or fasting insulin between those with and without preoperative hepatic steatosis.

3.1. Anthropometry

Changes in subjects' characteristics 3 and 12 months after LAGB are presented in Table 2. Mean weight loss over the 3-month postoperative period was 9.8 ± 1.1 kg ($P <$.01) of body weight. By 12 months, subjects had lost a total of 20.0 ± 2.2 kg ($P < .01$) of body weight. Waist circumference decreased by 9.5 ± 1.6 cm ($P <$.01) at 3 months, with a total reduction of 16.3 ± 2.2 cm ($P <$.01) by 12 months.

3.2. Diet

Three and 12 months after LAGB, significant reductions occurred in total energy, total fat (both $P < .01$), and saturated fat ($P < .05$) ingestion when compared with baseline intakes (data not presented). There was no significant change in these variables between 3 and 12 months. The percentage of energy intake derived from fat significantly decreased at 3 months ($P = .03$). By 12 months, the proportion of energy from fat was indistinguishable from baseline values. The percentage of saturated fat as a proportion of total dietary fat at baseline did not change after LAGB. In view of the limited sample size,

Table 1
Subject characteristics at baseline

Characteristic	
Age (y)	43 ± 3
Weight (kg)	104.9 ± 3.0
BMI (kg/m^2)	39 ± 1
Waist circumference (cm)	112.4 ± 2.8
LFAT (AU)	0.11 ± 0.03
VAT area (mm^2)	17 356 ± 2044
ABSAT area (mm^2)	60 469 ± 3079
FFA (mmol/L)	0.74 ± 0.05
Glucose (mmol/L)	4.6 ± 0.1
Insulin (μU/mL)	13.7 ± 1.9
HOMA-R	2.9 ± 0.5

Data represent mean ± SE.

Table 2
Subject characteristics 3 and 12 months after LAGB

Characteristic	3 mo	Change	12 mo	Change
Weight (kg)	95.1 ± 2.6*	−9.8 ± 1.1	85.0 ± 2.9*,‡	−20.0 ± 2.2
BMI (kg/m^2)	35 ± 1*	−4 ± 0.4	32 ± 1*,‡	−7 ± 1
Waist circumference (cm)	102.9 ± 2.0*	−9.5 ± 1.6	96.1 ± 2.4*,‡	−16.3 ± 2.2
LFAT (AU)	0.07 ± 0.02	−0.04 ± 0.02	0.06 ± 0.02	−0.06 ± 0.03
VAT area (mm^2)	13 582 ± 1602*	−3738 ± 742	10 913 ± 1273*,‡	−6344 ± 1107
ABSAT area (mm^2)	51 778 ± 2536*	−7850 ± 1657	42 860 ± 2904*,‡	−16 777 ± 2256
FFA (mmol/L)	0.57 ± 0.06†	−0.18 ± 0.07	0.49 ± 0.06*	−0.25 ± 0.08
Glucose (mmol/L)	4.8 ± 0.1	0.2 ± 0.2	4.8 ± 0.1	0.2 ± 0.2
Insulin (μU/mL)	12.7 ± 1.7	−1.1 ± 2.0	8.5 ± 1.5	−5.2 ± 1.7
HOMA-R	2.7 ± 0.4	−0.2 ± 0.5	1.9 ± 0.3†,‡	−1.0 ± 0.4

Data represent mean ± SE.
Change values determined from baseline: *$P < .01$ cf pre-LAGB; †$P < .05$ cf pre-LAGB; ‡$P < .01$ cf 3 months.

no correlations were sought between the changes in dietary variables and the changes in regional lipid depots.

3.3. Lipid depot changes

Compared with baseline, significant reductions in ABSAT and VAT areas had occurred postoperatively at 3 and 12 months (Table 2). These reductions were accompanied by a significant decrease in FFA. Plasma FFA at 12 months was not significantly different from that at 3 months after LAGB. The abdominal lipid depots changed significantly over this period; in fact, there was progressive and significant fat loss ($P < .01$) from both VAT (−20% at 3 months, −34% at 12 months) and ABSAT (−12% at 3 months, −27% at 12 months) sites (Fig. 1). When comparing these 2 depots, the relative changes were different at each time point ($P < .01$).

In the group as a whole and in those without preoperative hepatic steatosis (data not presented), there was no significant change in LFAT at either 3 or 12 months after LAGB. In the 7 subjects with preoperative hepatic steatosis, LFAT was reduced significantly at 3 months by 42% (from 0.24 ± 0.05 to 0.12 ± 0.03, $P = .036$), with a total significant reduction of 50% occurring by 12 months ($P = .027$). There was no significant change in LFAT between 3 and 12 months.

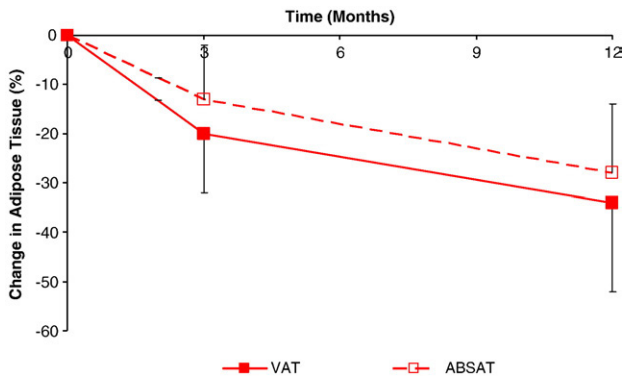

Fig. 1. Abdominal adipose tissue changes 3 and 12 months after LAGB. The VAT and ABSAT areas were determined from a single cross-sectional magnetic resonance image of the abdomen at L4. The significant ($P < .01$) differences in lipid depot areas at both time points were determined from each other and from baseline measurements (ANOVA) and are expressed in percentage terms.

The relative changes in abdominal lipid depots were compared according to preoperative LFAT stores. Regardless of the presence of preoperative hepatic steatosis, there were significant relative reductions in both ABSAT and VAT depots ($P < .05$) when 3- and 12-month data were compared with baseline levels; and a significant difference was observed when the areas of each depot were compared with each other at a similar time point. Baseline VAT area related to baseline LFAT ($r = 0.672$, $P = .003$). This relationship persisted at both 3 ($r = 0.634$, $P = .005$) and 12 months ($r = 0.626$, $P = .009$).

At baseline and throughout the study, ABSAT area did not relate to VAT area or LFAT. There was no relationship between the changes in LFAT, ABSAT area, or VAT area at 3 or 12 months.

3.4. Insulin sensitivity

Insulin sensitivity, as assessed by the HOMA-R method, had not changed from baseline at 3 months. A significant 30% improvement from baseline was present 12 months postoperatively ($P = .038$). No significant reductions occurred in either HOMA-R or fasting serum insulin levels at 3 or 12 months when the group was divided on the basis of subjects' preoperative LFAT stores. In the group as a whole, baseline HOMA-R related to baseline LFAT ($r = 0.497$, $P = .036$) and VAT area ($r = 0.596$, $P = .012$) but not to ABSAT area. After significant weight loss, these relationships did not persist.

4. Discussion

4.1. Lipid depots: changes and relationships during weight loss

This study shows that, within 3 months of LAGB, there is significant loss of lipid from VAT and ABSAT and that this loss progresses for both lipid depots over the ensuing 9 months. The proportional reduction in abdominal lipid was

greater from the visceral than from the subcutaneous compartment at 3 and 12 months.

A reduction in LFAT occurred after surgery but only in those with preoperative hepatic steatosis. Liver fat in our study was not reduced postoperatively in the group as a whole despite significant reductions, in absolute terms, in total dietary energy and fat intake. This might be due to the group's low baseline level of LFAT; but it could also be explained by the amount of fat in the diet as a proportion of total energy intake [25], which was high postoperatively (34%-36%) and not different to preoperative levels (39%).

Throughout the study, in the group as a whole, LFAT related to VAT area but not ABSAT area. Lipolysis of these 3 lipid depots may be independently regulated; or, if anything, mobilization of fat from liver and visceral sites is more closely interregulated than mobilization from subcutaneous depots.

Other nonsurgical weight loss studies investigating the response in body fat deposition [2,4,8,9,26,27] have also reported a greater reduction in visceral than abdominal subcutaneous adiposity. In some studies, statistical comparisons of the proportional reductions in VAT and ABSAT after weight loss are lacking [4,8,9,26,27]. In 1 other study, changes in VAT have only been related to changes in whole-body subcutaneous adipose tissue; and potential relations to ABSAT have not been addressed [2]. Only a few studies have examined changes in abdominal lipid deposition after surgically induced weight loss. Busetto et al [3] showed that the relative reduction in VAT was similar to ABSAT 2 and 6 months after LAGB. Although a statistical comparison was not reported, Pontiroli et al [28] reported greater relative reductions in VAT over ABSAT 1 year after LAGB. From these findings [3,28], the behavior of abdominal adiposity loss in response to LAGB intervention is not clear. The findings of the present study however support those of the latter mentioned larger study of obese insulin-resistant subjects [28]. The type of intervention does not seem to be important in determining the proportional changes in abdominal lipid depots with weight loss. The average daily caloric intake seen in the present postsurgical study (~5500 kJ) was less severe than that after a very-low-calorie diet (<3000 kJ/d), yet still promoted greater VAT than ABSAT loss [29].

Hepatic steatosis is a common finding in obese subjects [30], and few studies have reported its response to weight loss relative to abdominal adiposity changes [13,14].

We examined the impact of preoperative LFAT stores upon loss of VAT and ABSAT areas postoperatively. We found that VAT loss exceeded ABSAT loss in all subjects regardless of the presence of preoperative hepatic steatosis.

4.2. Insulin sensitivity: changes and association with VAT and LFAT

In the present study, an improvement in insulin sensitivity occurred 12 months but not 3 months after LAGB despite significant reductions in FFA, VAT, and ABSAT areas at 3 months. By 12 months, a significant change in HOMA-R was seen; and fat loss had continued from VAT and ABSAT depots. The absence of a significant change in HOMA-R 3 months after LAGB may relate to the relative insulin sensitivity of the population at baseline or to the small size of the reduction in the visceral fat depot at this time [31]. The relative insensitivity of the HOMA-R model to detect a change in insulin resistance compared with the euglycemic-hyperinsulinemic clamp [32] might also contribute to the lack of detection of an earlier change in insulin sensitivity.

The HOMA-R related to both LFAT and VAT areas preoperatively but not postoperatively. Free fatty acids and HOMA-R did not relate either pre- or postoperatively, nor were the changes in these variables related. The limited number of subjects may explain the absence of a correlation between changes in HOMA-R and VAT area. We did not perform multiple regression analysis on our limited sample size to determine interdependency of changes in LFAT, VAT area, and HOMA-R.

In conclusion, as in previous studies on more insulin-resistant, mixed-sex populations, this study showed that significant changes in abdominal lipid deposition had occurred in obese women 3 and 12 months after LAGB and that adipose tissue loss was greater from the visceral than from the subcutaneous compartment. In addition, the present study found that the lipid loss from both abdominal compartments was progressive in nature. There was no change in LFAT at either 3 or 12 months; and this may, in part, be related to the postoperative diet that remained relatively high in total and saturated fat. A significant reduction in LFAT however occurred in those with excess preoperative LFAT stores. Insulin sensitivity as measured by the HOMA-R improved by 12 months after surgery but not by 3 months. Unlike previous studies, pre- and postoperative LFAT and VAT areas related more closely to each other than either did to ABSAT area, suggesting differing regulatory pathways for fat mobilization from ABSAT and VAT but possibly similar pathways for storage and mobilization of fat in liver and viscerally. Whereas HOMA-R related to LFAT and VAT depots preoperatively, no depot was clearly related to HOMA-R postoperatively.

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