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BRIEF COMMUNICATION

Effects of Roux-en-Y Gastric Bypass Surgery on Visceral and Subcutaneous Fat Density by Computed Tomography

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Abstract We aimed to test the hypothesis that noninvasive fat density by computed tomography (CT) increases after Roux-en-Y gastric bypass (RYGB) and correlates with improved cardiometabolic risk. We examined 21 obese adults before and 12 months after RYGB and 16 obese nonsurgical controls followed for 12 months. Visceral (VAT) and subcutaneous adipose tissue (SAT) density increased after RYGB ($P<0.0001$) while remaining stable in controls ($P\geq0.1$). In RYGB subjects, 12-month increase in VAT density correlated with decreased C-reactive protein (CRP) independent of change in VAT area or BMI (both $P<0.05$). Twelve-month increase in SAT density correlated with increased HDL cholesterol independent of change in SAT area ($P=0.048$), BMI ($P=0.03$), or statin use ($P=0.002$), and 1 unit increase in SAT density had increased odds of higher total abdominal fat loss ($P=0.002$).

Keywords Obesity · Adipose tissue · Metabolic syndrome · Visceral fat · Surgery · Computed tomography

Introduction

Expansion of visceral adipose tissue (VAT) strongly correlates with increased cardiometabolic risk, while accumulation of abdominal subcutaneous adipose tissue (SAT) has more modest associations with inflammatory biomarkers [1]. Although VAT and SAT volumes are frequently measured by computed tomography (CT), fat density measures may also provide information about clinical risk [1]. CT imaging can assess fat characteristics because pixel values are measured in a scale that informs tissue radiodensity. Within the fat range [−250 to −50 Hounsfield units (HU)], lower density is associated with more lipidic content while higher density reflects increased vascularity [2]. A prior population-based cross-sectional study described associations between abdominal fat density and cardiometabolic risk markers independent of BMI and fat mass [1]. However, fat density in a severely obese population and after bariatric surgery is unknown. Bariatric surgery dramatically improves metabolic outcomes, the mechanisms of which may extend beyond weight loss and involve reductions in inflammatory adipokines secreted by VAT and SAT. This longitudinal study aimed to measure abdominal fat density by CT, before and 12 months after Roux-en-Y gastric bypass (RYGB), with the hypothesis that fat density increases after surgery and correlates with improved cardiometabolic risk markers.

Materials and Methods

Study Subjects and Protocol

This study was approved by the Institutional Review Board of Partners HealthCare, Inc., and all subjects provided written informed consent. Recruitment criteria, clinical characteristics, bone mineral density, and biochemical markers of bone formation and resorption were previously described [3]; however, no data on VAT and SAT characteristics, C-reactive protein (CRP), and serum lipids have been published. Briefly, 30 subjects scheduled for RYGB and 20 nonsurgical obese controls (all >18 years) were recruited, having similar age, sex, and weight. Exclusion criteria were weight >200 kg (due to imaging equipment limitations), pregnancy, and history of hyperthyroidism or renal disease. Nine surgical

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subjects were excluded entirely (one for not obtaining baseline abdominal CT images, one for unavailable CT images, seven for excessive CT artifact). Four nonsurgical subjects were excluded entirely for excessive CT artifact. Two nonsurgical subjects dropped out and one surgical subject was converted to sleeve gastrectomy, thus were included only in baseline analyses. The study group at baseline comprised 37 subjects (surgical n=21, nonsurgical n=16). Use of 3-hydroxy-3-methyl-glutaryl-CoA-reductase inhibitors (statins) was recorded at both visits.

Fat Depot Measures and Laboratory Data

CT scans were performed using a 16-multidetector row scanner (LightSpeedPro, General Electric, Waukesha, WI, USA) with 2.5-mm slice thickness, 120 kvP, and 100 mA. Abdominal circumference (cm), cross-sectional areas (cm^2), and mean HU for VAT, SAT, and total abdominal adipose tissue (TAT) were measured at the level of L2–3 by experienced radiologists using semi-automated tracings with density thresholds between −250 and −50 HU (Aquarius, TeraRecon Inc., San Mateo, CA, USA). Fasting serum glucose, lipids (total, HDL, and LDL cholesterol and triglycerides), and CRP were collected after an overnight fast and measured by particle-enhanced turbidimetric assay kits from Roche Diagnostics (Indianapolis, IN, USA) with a range of 1.0–200 mg/L and coefficient of variation of 1.8 %.

Statistical Analyses

Statistical analyses were conducted by Wilcoxon signed-rank test for within- and between-group comparisons. Associations were examined using Spearman's correlation. Standard least squares modeling controlled for BMI and VAT or SAT area was used to examine correlations between VAT and SAT density with other parameters. We divided 12-month TAT change into high and low TAT loss based on TAT median value and logistic regression determined odds ratios (OR) per unit change in SAT density. Analyses were performed using JMP 11 (SAS, Cary, NC, USA). P<0.05 was considered significant. Values are mean±SD.

Results

Fat Density at Baseline

Baseline characteristics of included subjects are outlined in Table 1. Subjects excluded for imaging artifacts had higher baseline weight, BMI, and abdominal circumference and lower LDL cholesterol compared to included subjects (P<0.05), with remaining parameters being similar (P>0.05).

Surgical and nonsurgical groups had similar baseline BMI and VAT and SAT densities and areas (all P≥0.6). In all subjects, VAT density correlated negatively with VAT area (r=−0.56, P=0.0003; P=0.006 after BMI adjustment). Similarly, SAT density correlated negatively with SAT area (r=−0.46, P=0.006); however, significance was lost after BMI adjustment (P=0.5). Baseline VAT density correlated negatively with CRP independent of BMI (r=−0.46, P=0.006) or VAT area (r=−0.6, P=0.003). SAT density was not associated to CRP (P=0.2).

Fat Density Increases After RYGB

Twelve months after RYGB, VAT and SAT densities increased in the surgical group (10±7 and 12±7 %, respectively, both P<0.0001) and were significantly higher than nonsurgical subjects (both P<0.001) (Table 1, Fig. 1a, b). VAT and SAT areas decreased in the surgical group (−55±21 and −43±20 %, both P<0.0001) and were significantly lower than nonsurgical subjects at 12 months (both P<0.001) (Fig. 1c, d). Surgical subjects had within-group decreased CRP (−59±64 %, P=0.0003), serum triglycerides (−27±27 %, P=0.0006), and LDL cholesterol (−15±28 %, P=0.02) and increased HDL cholesterol (40±35 %, P<0.0001), with fasting glucose (P=0.1) and total cholesterol (P=0.2) being unchanged. In nonsurgical subjects, within-group 12-month changes were not significant in all laboratory parameters (P≥0.1). Changes in fasting glucose (P=0.02), triglycerides (P=0.01), and HDL cholesterol (P=0.005) were significantly different between groups at 12 months (remaining P>0.1).

Increases in Fat Density After RYGB Correlate with Improved Metabolic Indices

Within the surgical group, 12-month increase in VAT density correlated with decreased CRP independent of change in VAT area or BMI (both r=−0.55, P<0.05). Twelve-month increase in SAT density correlated with increased HDL cholesterol independent of change in SAT area (r=0.79, P=0.048), BMI (r=0.70, P=0.03), or statin use at 12 months (r=0.77, P=0.002). We found no association between increased VAT and SAT densities with change in fasting glucose (P>0.7). In subjects from the surgical group, an increase of 1 HU in SAT density at 12 months was associated with increased odds of high TAT loss [OR 1.36 (95 % CI 1.1–1.9), P=0.002].

Discussion

Our study shows that lower VAT density correlates with higher CRP levels in morbidly obese adults, independent of

Table 1 Baseline values and change at 12 months in body composition and cardiovascular risk markers in surgical and nonsurgical subjects. Values are mean±standard deviation

	Surgical (n=21)			Nonsurgical (n=16)			P value Baseline between groups	P value 12-month change between groups
	Baseline	Change from baseline	P value Within group	Baseline	Change from baseline	P value Within group		
Age (years)	45±14	–	–	47±16	–	–	0.7	–
Gender (F:M)	19:2			14:2			0.8	
Weight (kg)	116±13	−35±14	*<0.0001*	117±15	−3±9	0.3	0.8	*<0.0001*
BMI (kg/m^2)	43±6	−13±5	*<0.0001*	43±4	−0.5±2.4	0.6	0.9	*<0.0001*
Abdominal circumference (cm)	123±6	−24±11	*<0.0001*	123±8	−2±5	0.2	1.0	*<0.0001*
VAT density (HU)	−103±6	10±8	*<0.0001*	−102±4	1±4	0.6	0.9	*0.0008*
SAT density (HU)	−110±6	14±8	*<0.0001*	−108±4	1±5	0.1	0.6	*<0.0001*
VAT area (cm^2)	204±71	−108±56	*<0.0001*	210±87	−2±22	0.3	0.9	*<0.0001*
SAT area (cm^2)	487±118	−216±120	*<0.0001*	497±103	−23±42	0.2	0.8	*<0.0001*
TAT area (cm^2)	696±116	−326±159	*<0.0001*	707±107	−24±56	0.1	0.9	*<0.0001*
CRP (mg/L)	7.6±8.0	−4.8±6.6	*0.0003*	8.3±6.6	−1.8±6	0.4	0.5	0.1
Fasting plasma glucose (mg/dl)	104±24	−8±26	0.1	90±8	5±9	0.1	0.1	*0.02*
Total cholesterol (mg/dl)	178±28	−10±35	0.2	199±42	−6±21	0.1	0.5	0.3
HDL cholesterol (mg/dl)	42±10	16±15	*<.0001*	54±13	3±8	0.2	*0.003*	*0.005*
LDL cholesterol (mg/dl)	108±25	−18±29	*0.02*	116±33	−9±17	0.2	0.3	0.2
Triglycerides (mg/dl)	154±109	−54±67	*0.0006*	141±72	−4±37	0.9	0.7	*0.01*

Italicized P-values are significant (P<0.05)

BMI or VAT area. Furthermore, in the first year after RYGB, VAT and SAT densities increase concurrent with fat loss, correlating with improved metabolic indices independent of BMI and predicting higher total fat loss.

VAT and SAT densities may be linked to adipose lipid content and vascularity. Lower CT density in adipose tissue suggests lipid-rich fat and adipocyte hypertrophy [1] and may reflect decreased vascularity of adipose tissue [2]. Importantly, adipocyte size is positively associated with insulin resistance, diabetes, and macrophage burden and is negatively associated with adiponectin secretion. Moreover, dysfunctional and hypertrophied adipose tissue has lower angiogenesis, vascular function, and capillary density [4]. This suggests that lower fat density may be a marker of tissue-level dysfunction, indicating higher lipid content and hypertrophy as well as decreased perfusion. We found that VAT and SAT densities negatively correlated with fat areas, concordant with prior research showing increased lipid and adipocyte size during fat expansion [1, 5] and decreased angiogenesis in morbid obesity [4]. Overall, increased fat CT density after RYGB likely reflects contraction of adipocyte volume as opposed to change in cell numbers.

A prior population-based study underscored the importance of density measures in abdominal fat and their relationships to cardiometabolic risk [1]. Denser fat by CT is associated with higher adiponectin and lower leptin [5], suggesting an improved metabolic state. Several studies have reported that RYGB surgery leads to increased adiponectin concurrent with decreased leptin and reductions in adipose inflammatory markers such as CRP, IL-6, and TNF-α soluble receptor-1 [6]. Although we did not obtain circulating adipocytokines, we found a 59 % decrease in CRP at 12 months that correlated with increased VAT density after RYGB, independent of VAT loss or BMI decrease. Prior evidence points towards a link between visceral fat mass and systemic inflammation, suggesting that VAT is an important site for IL-6 secretion and may regulate hepatic production of acute-phase reactants [7]. Our results support the hypothesis that density changes in VAT by CT may partly influence improvement of systemic inflammation.

Similar to a prior report [8], we documented improvements in lipid profile 12 months after RYGB. Prior evidence suggests decreased absorption of lipids after RYGB, which may reflect changes in the liver-gut axis regulating dietary cholesterol absorption [8]. In addition, we found that increased SAT density was a strong predictor of increased HDL cholesterol independent of SAT loss, BMI decrease, or statin use at 12 months. Postoperative increase in HDL cholesterol has been suggested as a promoter and strong predictor of improved microvascular function in subjects with metabolic syndrome undergoing bariatric surgery [9]. Therefore,

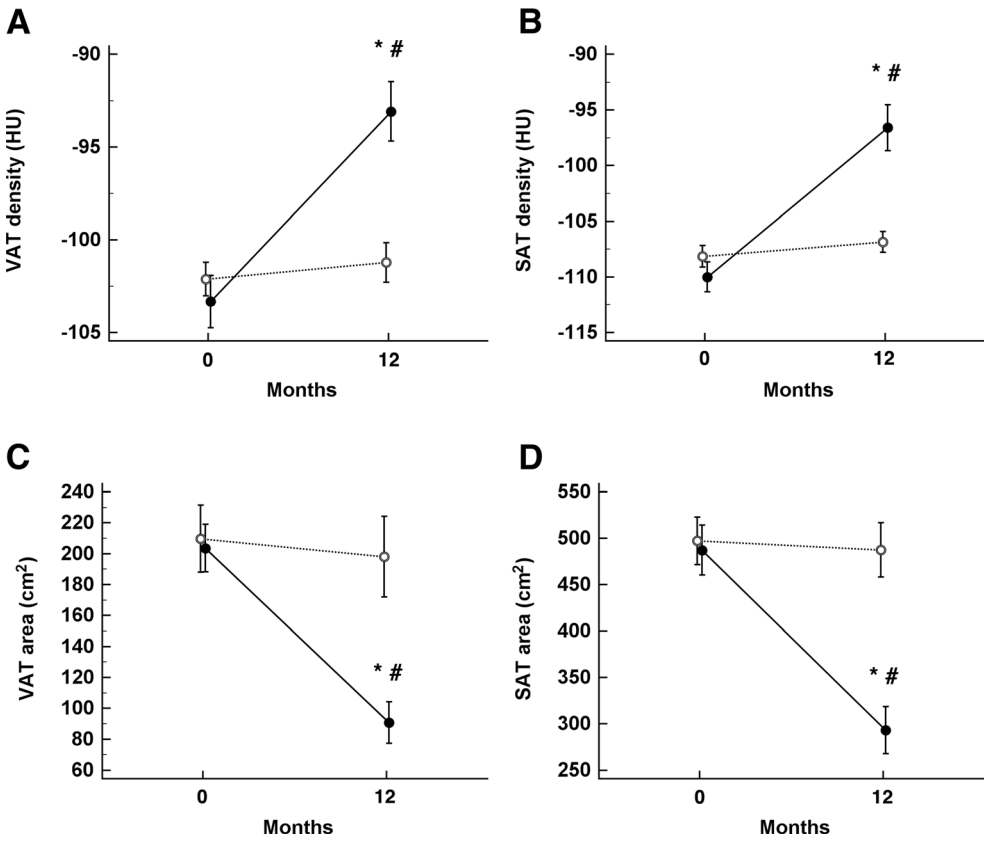

Fig. 1 **a**–**d** Change in abdominal adipose tissue density and area in obese subjects 12 months after Roux-en-Y bariatric surgery (●, *solid line*) compared to nonsurgical obese controls (◎, *dotted line*). *Asterisk* between-group, $P \leq 0.001$. *Number sign* within-group, $P < 0.0001$. *Error bars* are±SEM

increased SAT density after RYGB may reflect improved capillary recruitment because of improved HDL cholesterol. Interestingly, we observed that 12-month increase in SAT density was associated with higher total fat loss. It has been previously reported that morbidly obese adults with the lowest fat mass loss after bariatric surgery have the greatest persistence of local fibrosis within SAT despite improvement of adipocyte hypertrophy and inflammatory infiltration [10]. Whether SAT density also reflects structural changes that influence the degree of SAT loss after RYGB will require more detailed pathologic investigation.

In conclusion, CT density of abdominal fat increases after bariatric surgery and correlates with improved metabolic indices potentially serving as a noninvasive marker of change in adipose tissue characteristics.

Conflict of Interest The authors declare that they have no conflict of interest.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Statement of Human and Animal Rights Studies have been approved by the appropriate institutional and/or national research ethics committee and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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