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ORIGINAL CONTRIBUTIONS

Is There a Role for Visceral Adiposity in Inducing Type 2 Diabetes Remission in Severely Obese Patients Following Biliopancreatic Diversion with Duodenal Switch Surgery?

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Abstract
Background Severe obesity is often characterized by ectopic fat deposition, which is related to development of type 2 diabetes (T2D). Thus, resolution of T2D may not be linearly associated with weight loss. The importance of ectopic fat reduction after bariatric surgery and T2D resolution is uncertain.
Objective The aim of this pilot study is to compare body composition and body fat distribution in severely obese patients with or without T2D after biliopancreatic diversion with duodenal switch (BPD-DS) surgery in relation to diabetes resolution.
Methods Sixty-two severely obese patients were evaluated at baseline, 6, and 12 months. Of these, 40 patients underwent BPD-DS surgery. Anthropometric measurements and abdominal and mid-thigh computed tomography scans were performed at each visit.
Results Before BPD-DS surgery, obese patients with T2D had higher weight as well as greater ectopic fat deposition in the abdomen and mid-thigh level than obese patients without T2D ($p<0.05$). Resolution of T2D was 65 and 90 % at 6 and 12 months, respectively. No difference in body composition changes at 6 and 12 months could be found between patients without T2D, patients with T2D resolution, and patients who remained T2D. Resolution of T2D was associated with a greater absolute loss of visceral adipose tissue (VAT) in comparison to patients without T2D (-1175 ± 570 cm^3 vs. -729 ± 394 cm^3 at 6 months and -1647 ± 816 cm^3 vs. -1103 ± 422 cm^3 at 12 months; all $p\leq0.05$).
Conclusion Ectopic fat mobilization, particularly the absolute loss of VAT, may play a major role in T2D resolution following BPD-DS surgery, regardless of the amount of weight loss.

Keywords Severe obesity · Biliopancreatic diversion with duodenal switch surgery · Type 2 diabetes · Ectopic fat · Computed tomography scan

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Introduction

Progression in the prevalence of severe obesity [body mass index (BMI)≥40 kg/m^2] is of great concern. In 2009–2010, the prevalence of severe obesity was 33 % higher than in 1999–2000 in the USA [1]. Severe obesity is characterized by excess fat mass and could be associated with excess visceral adipose tissue (VAT) and deposition of ectopic fat (accumulation of fat at undesired sites such as the skeletal muscle, liver, and heart) [2]. Ectopic fat deposition is considered a consequence of subcutaneous fat tissue dysfunction [2], which could contribute to the metabolic disturbances related to severe obesity including type 2 diabetes (T2D) [3, 4]. Given the morbidity and the premature mortality associated with severe obesity [5], bariatric surgery is an efficient treatment for long-term weight loss management, resolution of obesity-related comorbidities in addition of being associated with decreased mortality [3, 6, 7].

Bariatric surgery can resolve T2D, often before and out of proportion to postoperative weight loss [4]. For instance, procedures with a malabsorptive component, such as the Roux-en-Y gastric bypass (RYGB) and the biliopancreatic diversion with duodenal switch (BPD-DS), may exert powerful anti-diabetic effects in comparison to restrictive procedures such as the adjustable gastric banding and sleeve gastrectomy [8]. The BPD-DS surgery is the most efficient procedure to treat T2D and is associated with a higher resolution rate at 1 year compare to RYGB (BPD-DS 59 to 95 %; RYGB 17 to 93 %) [8]. However, complete resolution is not reached in all patients and several negative predictors of T2D remission have been noted, the more consistent being diabetes duration [9–11]. Despite clinical evidence that excess body fat and body fat distribution contribute to the development of T2D, no study in the context of bariatric surgery has precisely evaluated the role of ectopic fat mobilization in relation to resolution or non-resolution of T2D 12 months after bariatric surgery.

The aim of this pilot study is to compare body composition and body fat distribution, at the abdomen and the mid-thigh level, among severely obese patient with or without T2D prior to bariatric surgery and 6 and 12 months BPD-DS in relation to diabetes resolution.

Materials and Methods

Patients and Study Design

This is a prospective study conducted at the Institut universitaire de cardiologie et de pneumologie de Québec (IUCPQ). One-hundred three white Caucasian patients (70 BPD-DS subjects and 33 control subjects) were recruited [12] and sixty-two patients (40 BPD-DS subjects and 22 control subjects) had CT scan data and were included in this analysis. Patient's refusal to the CT scan exam (n=26) and patients mispositioning (n=15) were reasons for unavailable data. Patients were included if they were between 18 and 65 years old with a BMI≥40 or ≥35 kg/m^2 with comorbidities [12]. Exclusion criteria included pregnancy, previous bariatric surgery, and a weight ≥180 kg due to the weight limitation of the computed tomography (CT) table. Patients in the group undergoing BPD-DS surgery were recruited through the bariatric surgery clinic of our Institution [13]. Severely obese controls were recruited and matched 1:2 for age and gender. All patients were evaluated at baseline and after 6 and 12 months. Anthropometric measurements and abdominal and mid-thigh CT scans were performed at each visit. For the control group, usual standard of care was strongly emphasized [14]. The study protocol was approved by the Ethics Committee of our Institution. Each patient provided written informed consent.

Bariatric Surgery Procedure and Follow-Up

The BPD-DS surgery has been performed in our Institution since 1990 [15]. It currently represents about 50 % of the bariatric procedures performed in our Institution, while during the recruitment for this study, the percent BPD-DS represented more than 80 % [16]. The BPD-DS procedure consisted of sleeve gastrectomy and ileal anastomosis 250 cm from the ileocecal valve with a common limb of a 100 cm [17]. Clinical follow-up of subjects who underwent the BPD-DS was in accordance to the guidelines of the American Society for Metabolic and Bariatric Surgery [14].

Diabetes Baseline Status and Remission Definition

Diabetes baseline status was determined from patient's biochemistry and medical record in accordance with the American Diabetes Association (ADA) guidelines [18]. According to American Diabetes Association consensus statement [19], diabetes remission was defined as fasting blood glucose under 5.6 mmol/L and a HbA1c under 6.0 % in the absence of at least 1 year's pharmacological treatment.

Anthropometric Measurements

Height was measured. Body weight, body fat, fat-free mass, and total body water were assessed using a bioelectrical impedance balance (Tanita TBF-350, Tokyo, Japan). Body mass index was calculated and expressed in kilogram per square meter.

Abdominal and Mid-Thigh Computed Tomography Scans

Computed tomography scans were performed with a GE Medical Systems HiSpeed CT/i (GE Medical System, Milwaukee, USA) during the early phase of the study (n=27 scans) and then with a Siemens Somaton DRH scanner (Siemens, Erlangen, Germany) (n=159 scans) thereafter. As described previously [20], scanning was performed at 120 kV and a 10-mm CT slice scan was acquired at (1) mid-distance between the second and the third lumbar vertebrae (L_2L_3), (2) at mid-distance between the fourth and the fifth lumbar vertebrae (L_4L_5), and (3) at mid-distance between knee joint and the iliac crest (mid-thigh) with a radiograph of the skeleton as a reference to establish the position of the scan to the nearest millimeter. Computed tomography scan images were analyzed using specialized image analysis software (Tomovision SliceOMatic 4.3 Rev-6f software, Montreal, Quebec, Canada). At the abdominal level, adipose tissue between skin and the muscle wall was defined as the subcutaneous adipose tissue (SAT) and VAT area was determined by delineating the parietal peritoneum boundary surrounding the abdominal cavity and was computed using an attenuation range of −190 to −30 Hounsfield units (HUs) [20]. Abdominal muscle was measured with an attenuation range between −29 to 130 HU [21]. Volume of VAT was estimated as from the mean of L_2L_3 and L_4L_5 cross-sectional areas multiplied by the distance separating the two slices [22]. Sagittal abdominal diameter was measured as the anterior to posterior distance at the middle part of the vertebral body. At the mid-thigh level, with a graph pen, a line was drawn at the external limit of the skeletal muscle in order to determine intermuscular adipose tissue (IMAT) [20]. Adipose tissue between skeletal muscle and skin was defined as the mid-thigh SAT [20]. Total adipose tissue areas were calculated by adding deep and SAT [23]. Normal-density muscle (low fat content muscle) was defined as the area with attenuation values between 35 and 100 HU [24]. Low-density muscle area, which is an index of TG muscle enriched (intramuscular fat), was defined as the muscle area with an attenuation range between 0 and 34 HU [24]. Total skeletal muscle areas were calculated by adding normal and low-density muscle (Fig. 1).

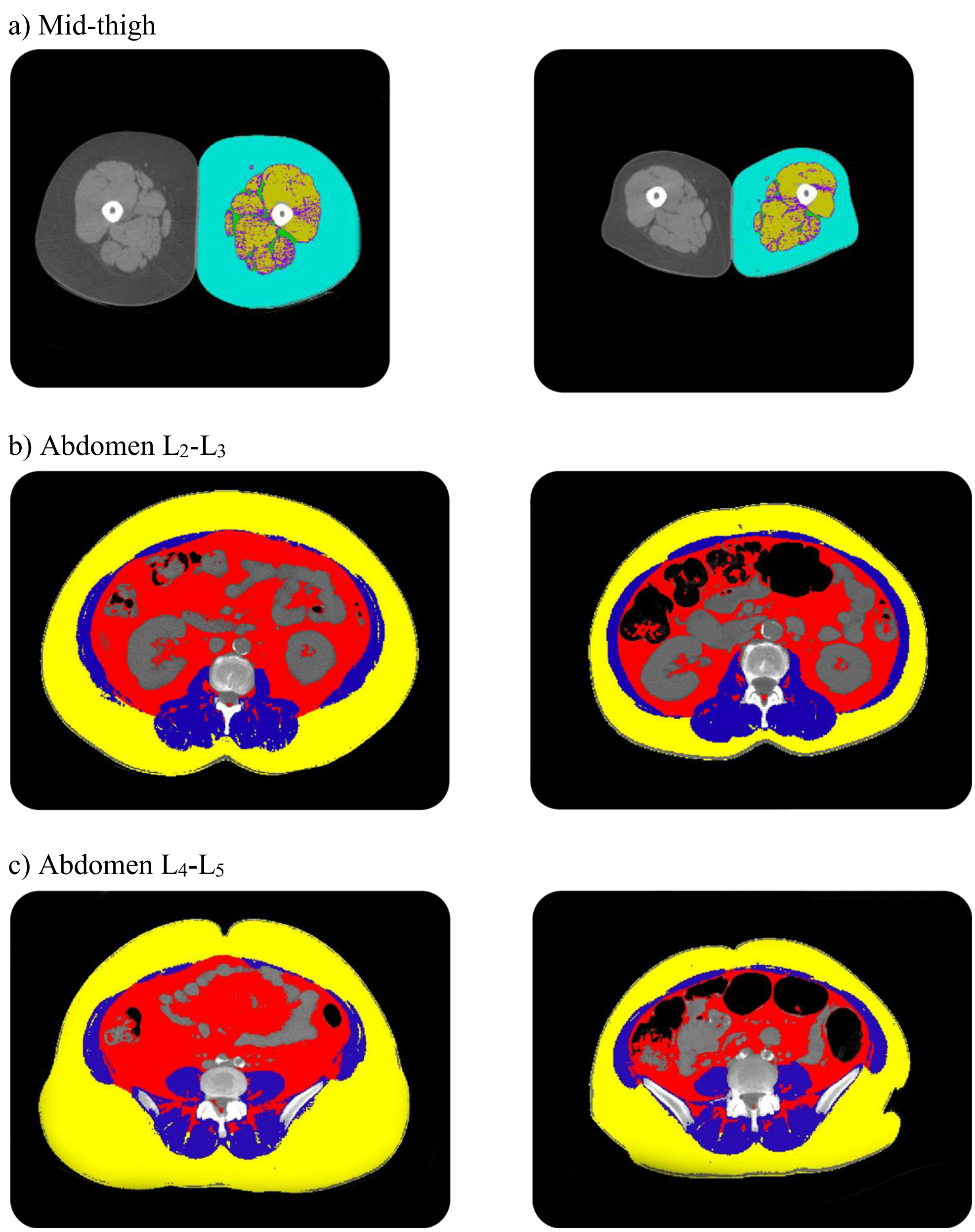


Fig. 1 Computed tomography cross-sectional abdominal and mid-thigh images, analyzed with the SliceOMatic software, at baseline (left side) and 12 months (right side) after surgery. **a** Mid-thigh. **b** Abdomen L_2L_3. **c** Abdomen L_4L_5. Mid-thigh image's color legend: *cyan*, subcutaneous adipose tissue; *green*, intermuscular adipose tissue; *purple*, low-density muscle; *yellow*, normal-density muscle. Abdominal image's color legend: *red*, visceral adipose tissue; *yellow*, subcutaneous adipose tissue; *blue*, muscle

Statistical Analyses

Data are presented as mean±standard deviation (SD) unless otherwise specified. One-way analysis of variance (ANOVA) was used to compare groups at baseline and was adjusting for potential confounding variables such as sex and baseline weight. Normality assumption was verified with the Shapiro-Wilk test on studentized residuals from ANOVA. The Brown and Forsythe's variation of Levene's test statistic was used to verify homogeneity of variances. Posteriori comparisons were performed using the Tukey's technique. Pearson correlation coefficient was used to investigate associations between changes in T2D status with body composition and body fat distribution parameters. For all 12-month statistics, T2D patients (n=2) are excluded from statistical analysis but data are presented for descriptive purpose. Statistical significance was considered at $p<0.05$. Data was analyzed using the statistical packages SAS, version 9.3 (SAS Institute Inc., Cary, NC, USA) and SPSS version 22 (Chicago, IL, USA, 2013).

Results

Patients' Characteristics

Patient's baseline characteristics (n=62) regarding diabetes status are shown in Table 1 (unadjusted p value). Patients with T2D (mean duration 4.9±4.9 years) are characterized by a lower proportion of women, a higher prevalence of hypertension as dyslipidemia, and a higher weight; all $p<0.01$. When

Table 1 Baseline characteristics in patients with and without type 2

Clinical parameters	All patients (n=62)		
	T2D patients (n=25)	Non-T2D patients (n=37)	p value
Women (n/%)	15/60	33/89	0.01
Age (years)	45.7±10.2	42.9±10.5	0.30
Comorbidities			
Hypertension (n/%)	23/92	12/32	<0.001
Dyslipidemia (n/%)	17/68	9/24	0.001
Sleep apnea (n/%)	15/60	17/46	0.28
Anthropometric measurements			
Height (m)	1.7±0.1	1.6±0.1	0.11
Weight (kg)	128.9±23.4	118.3±18.4	0.05
Body mass index (kg/m^2)	46.9±5.6	45.1±5.0	0.20
Fat mass (kg)	63.5±15.6	59.8±12.0	0.30
Body fat (%)	49.0±6.1	50.3±4.1	0.34
Fat-free mass (kg)	65.5±13.5	58.4±8.7	0.03
Total body water (kg)	47.9±9.8	42.8±6.3	0.03
Computed tomography scans			
Abdomen			
Sagittal diameter at L_4L_5 (cm)	36.9±3.4	34.0±2.8	0.001
Subcutaneous adipose tissue (cm^3)	3105±582	3545±698	0.22
Visceral adipose tissue (cm^3)	2514±807	1720±474	<0.001
Muscle (cm^3)	1110±299	974±240	0.09
Mid-thigh			
Total adipose tissue (cm^2)	255.3±64.1	281.9±48.5	0.11
Subcutaneous adipose tissue (cm^2)	240.1±64.8	270.2±49.2	0.08
Intermuscular adipose tissue (cm^2)	15.0±5.4	11.6±3.8	0.01
Total skeletal muscle (cm^2)	151.7±34.1	137.2±28.1	0.07
Low-density muscle (cm^2)	44.4±11.4	38.7±9.6	0.04
Normal-density muscle (cm^2)	94.2±24.3	83.5±17.3	0.06

Mean±standard deviation

T2D type 2 diabetes

adjusted for sex and weight, fat mass, fat-free mass, sagittal diameter, VAT, IMAT, and low-density muscle were all higher in patients with T2D (all $p<0.001$). Baseline T2D status was significantly ($p\leq0.05$) associated with greater VAT ($r=0.53$), sagittal diameter ($r=0.43$), mid-thigh IMAT ($r=0.35$), mid-thigh low-density muscle ($r=0.32$), and weight ($r=0.25$).

Table 2 Evolution in body composition and body fat distribution according to the diabetic status

A							
Changes at 6 months							
	BPD-DS group (*n*=40)				Control group (*n*=22)		
	non-T2D patients (*n*=20)	T2D resolution patients (*n*=13)	T2D patients (*n*=7)	*p* value	Non-T2D patients (*n*=16)	T2D patients (*n*=6)	*p* value
Weight (kg)	−32.5±6.8	−36.1±12.5	−33.3±15.2	0.63	−0.9±3.2	2.8±4.9	0.05
BMI (kg/m^2)	−12.4±2.2	−13.1±3.7	−12.0±4.8	0.73	−0.3±1.2	1.0±1.8	0.06
Fat mass (kg)	−25.7±5.9	−31.2±14.5	−28.5±14.3	0.38	−0.4±2.6	2.5±3.7	0.05
Body fat (%)	−10.3±4.0	−13.2±7.3	−12.9±8.3	0.33	−0.1±1.6	0.9±1.0	0.19
Mid-thigh (cm^2)							
Total adipose tissue	−94.3±29.7	−94.4±33.7	−89.9±29.6	0.94	−1.1±6.4	5.9±21.7	0.51
SAT	−90.3±28.9	−88.5±32.0	−85.4±29.4	0.31	−0.5±6.6	6.2±20.9	0.52
IMAT	−3.8±2.1	−5.9±3.1	−4.6±2.2	0.07	−0.8±2.1	−0.2±1.1	0.53
Total muscle	−28.2±14.4	−27.4±12.9	−25.2±20.9	0.90	−1.2±5.7	−0.3±1.2	0.56
Low-density muscle	−8.6±4.9	−9.3±5.0	−10.3±12.6	0.82	−0.7±4.1	2.2±4.4	0.17
Normal-density muscle	−15.3±8.2	−15.9±10.3	−12.2±12.6	0.71	−0.1±5.5	−2.4±5.4	0.39
Abdomen							
Sagittal diameter (cm)	−7.8±2.0	−8.6±3.2	−7.8±3.6	0.57	0.1±1.9	0.3±0.8	0.74
SAT (cm^3)	−1691.3±489.3	−1031.3±194.9	−1264.6±206.5	0.39	57.2±167.5	−112.6±5.1	0.21
VAT (cm^3)	−729.8±394.5*	−1175.7±570.3*	−1028.5±667.6	0.05	−11.6±146.0	102.3±199.4	0.52
B							
Changes at 12 months							
	BPD-DS group (*n*=40)				Control group (*n*=22)		
	non-T2D patients (*n*=20)	T2D resolution patients (*n*=18)	T2D patients (*n*=2)	*p* value	Non-T2D patients (*n*=15)	T2D patients (*n*=7)	*p* value
Weight (kg)	−45.5±9.9	−49.7±16.2	−28.6 and −28.8	0.34	−1.6±7.5	−0.1±2.9	0.62
BMI (kg/m^2)	−17.4±3.3	−18.0±4.8	−9.8 and −1.2	0.62	−0.6±3.1	0.1±1.0	0.59
Fat mass (kg)	−37.1±7.8	−41.4±16.9	−23.2 and −23.4	0.91	−0.8±5.6	0.6±2.1	0.54
Body fat (%)	−18.5±6.3	−20.1±10.7	−9.7 and −14.3	0.58	−0.2±2.5	−0.8±2.7	0.60
Mid-thigh (cm^2)							
Total adipose tissue	−134.3±38.0	−138.6±47.0	−68.8 and −84.8	0.79	−7.7±15.8	−3.3±17.5	0.62
SAT	−128.2±36.2	−131.3±44.9	−61.9 and −76.0	0.84	−7.3±15.1	−3.8±16.6	0.68
IMAT	−5.9±3.2	−7.3±3.5	−6.9 and −8.8	0.21	−0.1±2.2	0.4±0.9	0.64
Total muscle	−28.2±12.4	−31.4±17.6	−10.2 and −10.9	0.51	−3.2±6.9	−4.6±3.9	0.64
Low-density muscle	−12.6±6.8	−16.2±9.4	−3.3 and −6.5	0.22	−1.1±3.6	−0.3±6.4	0.74
Normal-density musclet	−10.7±8.4	−11.5±11.4	−1.7 and 1.1	0.82	−1.9±6.6	−4.4±9.2	0.45
Abdomen							
Sagittal diameter (cm)	−10.5±3.1	−12.3±3.9	−8.8 and −5.8	0.11	−0.5±2.9	0.1±1.1	0.59
SAT (cm^3)	−2134.3±678.0	−2061.8±196.2	−1818.2 and −1672.4	0.88	−12.2±417.3	123.4±312.5	0.62
VAT (cm^3)	−1103.1±422.5*	−1647.7±816.5*	−1178.9 and −979.5	0.02	−82.8±239.4	13.5±332.2	0.45

Mean±standard deviation

*$p\leq0.05$ between non-diabetic patient and patient who resolved their T2D

T2D type 2 diabetes, *BMI* body mass index, *SAT* subcutaneous adipose tissue, *VAT* visceral adipose tissue, *IMAT* intermuscular adipose tissue

Regarding T2D pharmacological treatment, 14 patients were treated with metformin, 11 patients with sulphonylurea, 6 patients with thiazolidinedione, and 5 patients with insulin.

Type 2 Diabetes Resolution

After BPD-DS surgery, T2D resolution at 6 and 12 months was 65 % (n=13) and 90 % (n=18), respectively. Patients with T2D resolution had a lower T2D duration compared to patients with persisting T2D (3.7±3.5 years vs. 9.1±5.2 years at 6 months; p=0.01; and 5.0±4.7 years. vs. 11.0±1.4 years at 12 months; p=0.05). At 12 months, no patient had insulin treatment and patients who remained with T2D (n=2) were on metformin and sulfonylurea.

Body Composition

Postoperative changes at 6 and 12 months are reported in Table 2a, b. Independently of the diabetes status, weight loss was −26.6±5.7 % at 6 months post BDP-DS with further reduction to −36.8±7.6 % in weight at 12 months (both p< 0.001), without difference according to T2D status (Fig. 2a and Table 2b). At 6 and 12 months, there was no difference regarding body composition changes including weight, BMI, body fat percentage, and fat-free mass. Interestingly, for descriptive purpose only, patients who did not resolved T2D have lost less weight, fat mass, and body fat in comparison with T2D resolution patients (Fig. 2a and Table 2b). Regarding the control group, despite statistically significant difference at 6 months for an increase in weight and fat mass (Table 2a), these differences were not observed at 12 months follow-up (Table 2b).

Ectopic Fat Mobilization

All 60 patients underwent mid-thigh CT scan but only 35 BPD-DS and 20 control patients had CT scans where data from both thighs were technically readable. Incomplete mid-thigh data was due to mispositioning on CT scan table. Correlations between both thighs were high (r≥0.98) for total adipose tissue, SAT, IMAT, total skeletal muscle, normal-density muscle, and low-density muscle; all p<0.001. Given the similarity between both thighs measurements, all patients who had either right or left mid-thigh CT scan data readable were included.

At 6 months after surgery, there were a significant difference (p=0.05) and a trend (p=0.07) toward a greater reduction in VAT and mid-thigh IMAT between patients without T2D and patients with T2D resolution (Table 2a). At 6 months, volume in VAT remained higher in patients who still had T2D in comparison with patients without T2D (p= 0.03) (Fig. 3a). Reduction of VAT at 12 months remained different between patients without T2D and patients with T2D resolution (−1103.1±422.5 cm^3 vs. −1647.7± 816.5 cm^3; p=0.03) (Table 2b). At 12 months, patients who still had T2D (n=2) had lost less VAT (−1178.9 cm^3 and −979.5 cm^3 for the two subjects, respectively) in comparison to patients who showed a resolution of their T2D (−1647.7±816.5 cm^3).

Fig. 2 For each patient, 12-month changes are presented according to T2D status. **a** Weight in kg. **b** Visceral adipose tissue in cm^3. **c** Visceral adipose tissue in %. For T2D resolution patients and for T2D patients, T2D duration is indicated at the top of the line. *Grey line* indicates T2D resolution patients. *White line* indicates non-T2D patients. *Black line* indicates T2D patients

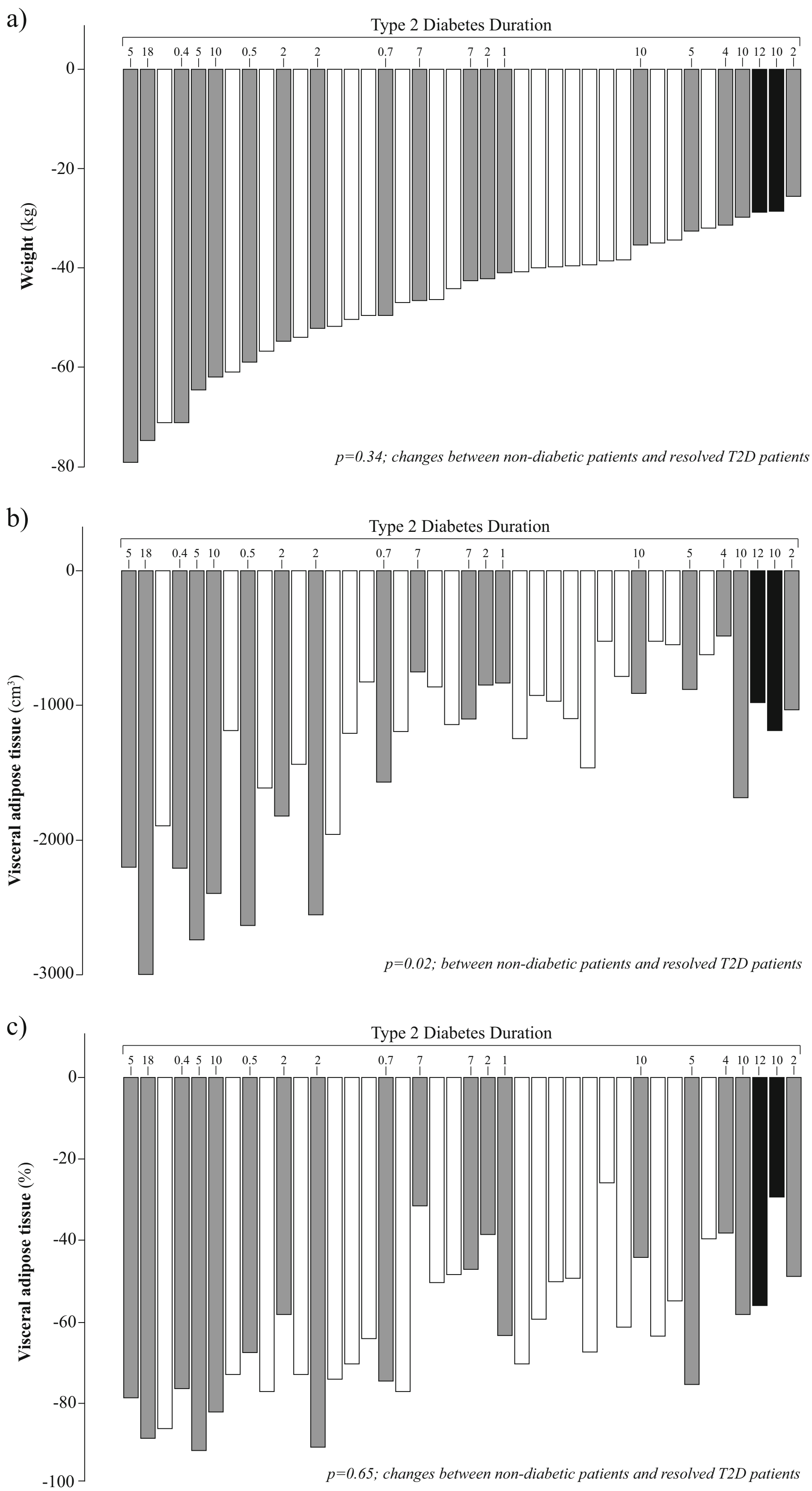
Discussion

To the best of our knowledge, this study is the first to precisely compare body composition and abdominal and mid-thigh ectopic fat deposition indices in severely obese patients with and without T2D diabetes. It is also the first to study the effect of a mixed restrictive and malabsorptive bariatric procedure on changes in body composition and ectopic fat mobilization in non-diabetic patients and in patients with T2D. Of interest, we document that one of the key correlates of T2D resolution after BPD-DS surgery is VAT mobilization, regardless of the degree of weight loss.

Severe Obesity, Type 2 Diabetes, and Ectopic fat Deposition

Type 2 diabetes is a heterogeneous disorder for which obesity, principally abdominal obesity, is considered the primary risk factor [25]. Excess visceral adiposity and ectopic fat deposition (i.e., accumulation of fat at undesired sites such as skeletal muscle) are considered consequences of subcutaneous tissue dysfunction [2] which could contribute to the development of insulin resistance and T2D. It has been estimated that the risk of developing T2D is increased 93-fold in women and 42-fold in men who are severely obese vs. individuals with healthy weight [26, 27].

In the context of severe obesity, independently of ectopic fat deposition, another important issue is the amount of total adipose tissue. As shown in Table 1, more than half of patient's weight was composed of body fat. Abdominal SAT volume was 1.2 to 2.1 times higher than VAT, and mid-thigh SAT area was 16.0- to 23.3-fold higher than IMAT. Despite the fact that the size of ectopic fat depots is quite small compared to subcutaneous fat, the former are nevertheless quite important in relationship with T2D in severely obese patients. Indeed, abdominal and mid-thigh ectopic fat depositions were more strongly associated (r=0.32 to 0.53) with diabetic status than weight (r=0.25). Furthermore, percentage of body fat and abdominal subcutaneous adipose tissue showed no


a)
Type 2 Diabetes Duration
5 18 0.4 5 10 0.5 2 2 0.7 7 7 2 1 10 5 4 10 12 10 2
Weight (kg)
0
-20
-40
-60
-80
p=0.34; changes between non-diabetic patients and resolved T2D patients
b)
Type 2 Diabetes Duration
5 18 0.4 5 10 0.5 2 2 0.7 7 7 2 1 10 5 4 10 12 10 2
Visceral adipose tissue (cm³)
0
-1000
-2000
-3000
p=0.02; between non-diabetic patients and resolved T2D patients
c)
Type 2 Diabetes Duration
5 18 0.4 5 10 0.5 2 2 0.7 7 7 2 1 10 5 4 10 12 10 2
Visceral adipose tissue (%)
0
-20
-40
-60
-80
-100
p=0.65; changes between non-diabetic patients and resolved T2D patients

significant relationship with the diabetic status before bariatric surgery.

Bariatric Surgery and Ectopic Fat Mobilization

Several studies have already assessed ectopic fat mobilization, principally abdominal and mid-thigh adiposity [28–33] with dual-energy X-ray absorptiometry [34], echographic thickness measures [28], magnetic resonance [32, 35–37], and CT scan imaging [29–31, 33]. The majority of studies have been performed in patients who underwent restrictive surgery, either adjustable gastric banding [28–30, 36] or sleeve gastrectomy [29, 31]. Only two studies have had a 12-month follow-up period [28, 29]. As expected, at 12 months after bariatric surgery, we reported a greater reduction in weight (−36 % in our study vs. −12 to −28 % in restrictive surgery studies) and in VAT (−62 % vs. −12 to −28 %) in comparison to restrictive surgery studies [28, 29]. In contrast, only three studies have included surgery with a malabsorptive component, either the RYGB surgery, and have characterized abdominal and mid-thigh adiposity changes over 12 months [32, 33, 35]. They all reported a significant weight loss (33 to 36 %) and reduction in IMAT (50 to 54 %) and in VAT (58 to 77 %) [32, 33, 35]. In our study, we reported similar 12-month reduction in body weight (36 %), IMAT (−51 %), and VAT (−62 %), all independent of the diabetic status.

Bariatric Surgery and Type 2 Diabetes Resolution

Bariatric surgery is the most efficient treatment for long-term weight loss and for resolution of T2D [3, 6, 7]. Procedures with a malabsorptive component, such as RYGB or BPD-DS surgeries, have been associated with faster and greater weight loss and with a greater impact on T2D resolution compared to restrictive surgeries [4, 38]. Studies have also shown a normalization of glucose metabolism occurring early after BPD-DS and RYGB, even before substantial weight loss [38]. Significant acute caloric restriction, increased adiponectin levels, decreased ghrelin levels, and other hormonal modifications have been suggested as weight loss-independent mechanisms responsible for short-term improvement of T2D after bariatric surgery [4, 38–40].

Early improvement in glucose metabolism does not necessarily translate into long-term success. The extent of improvement and resolution of T2D has not been found to be linearly associated with the amount of weight loss [4]. Our study showed that one of the key factors associated with T2D resolution at 6 and 12 months after BPD-DS surgery was the mobilization of VAT, regardless of the degree of weight loss. At 12 months, VAT reduction was significantly greater in patients with T2D resolution vs. non-T2D patients (−76.1±23.6 % vs. −58.2±10.1 %; p=0.03). Although it is an anecdotal finding, it is also relevant to mention that the two patients who remained with T2D (n=2) showed a lower reduction in VAT at 12 months (−56.1 and −28.6 %) than patients who showed a resolution of their T2D (−76.1±23.6 %). This difference in VAT mobilization has already been reported in a physical activity intervention study among obese patients with and without T2D [41]. Following a 26-week physical activity intervention, the magnitude of VAT loss was less important in patients with T2D (−3 %) compared to patients without T2D (−18 %). As confirmed with our study, VAT change was an important factor associated with the diabetes status, as non-T2D patients and patients with T2D resolution showing a greater decrease in abdominal fat with BPD-DS surgery compared to patients who remained with T2D.

Fig. 3 For each patient, postoperative evolutions are presented according ▶ to T2D status. Each *point* represents a given patient and *boxes* indicate the mean for the group with standard error. At 6 and 12 months follow-up, T2D resolution is according baseline status. p values at 12 months are between non-T2D patients and T2D resolution patients. *Grey color* indicates T2D resolution patients. *White color* indicates non-T2D patients. *Black color* indicates T2D patients

Diabetes duration longer than 10 years is also a recognized negative predictor of T2D remission [4, 42]. In our study, among the 6 patients with T2D duration longer than 10 years, 4 patients showed T2D resolution at 12 months, in addition to show a trend (p=0.10) toward a greater reduction in VAT compared to the 2 patients who did not show changes in diabetes status (−1995.4±906.4 cm^3 vs. −1079.2±141.0 cm^3). We acknowledge the fact that the number of patients is small but these findings may provide direction for further studies to properly investigate which of the two factors, i.e., diabetes duration or VAT mobilization, is the best predictor of T2D resolution following bariatric surgery.

Conclusion

This pilot study supports the notion that beyond weight loss, ectopic fat mobilization, mainly VAT, may play an important role in T2D resolution following BPD-DS surgery. Further researches are needed to better delineate determinants of T2D resolution, particularly to better establish whether there is a causal relationship specifically linking VAT mobilization to the resolution of T2D. Finally, to what extent diabetes duration causes prejudice to the ability of loss of adiposity/ectopic fat indices to lead to resolution of T2D will also require further studies.

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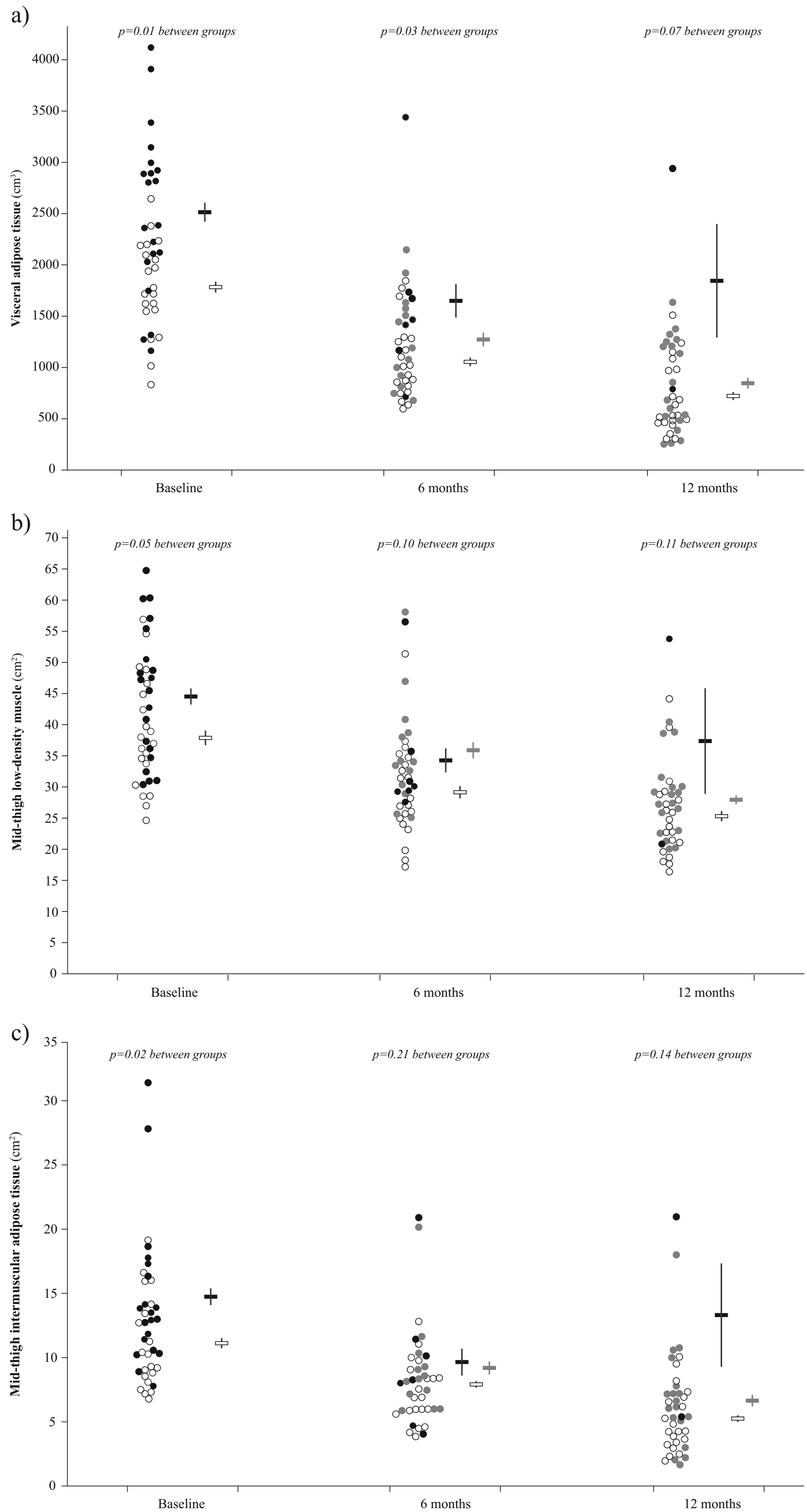
a)
p=0.01 between groups
p=0.03 between groups
p=0.07 between groups
Visceral adipose tissue (cm³)
0
500
1000
1500
2000
2500
3000
3500
4000
Baseline
6 months
12 months
b)
p=0.05 between groups
p=0.10 between groups
p=0.11 between groups
Mid-thigh low-density muscle (cm²)
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
Baseline
6 months
12 months
c)
p=0.02 between groups
p=0.21 between groups
p=0.14 between groups
Mid-thigh intermuscular adipose tissue (cm²)
0
5
10
15
20
25
30
35
Baseline
6 months
12 months

Compliance with Ethical Standards

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Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participant included in the study.

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

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