Original Article

Well-controlled versus poorly controlled diabetes in patients with obesity: differences in MRI-evaluated pancreatic fat content

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Background: Patients with obesity and poorly controlled type 2 diabetes (T2D) are at high risk of diabetic complications. This study aimed to determine the associations of visceral adipose tissue (VAT), hepatic proton-density fat fraction (PDFF), and pancreatic PDFF with poor glycemic control in patients with obesity and T2D and to evaluate the metabolic effect of bariatric surgery in patients with obesity and poorly controlled diabetes.

Methods: In this retrospective cross-sectional study, from July 2019 to March 2021, 151 consecutive obese patients with new-onset T2D (n=28), well-controlled T2D (n=17), poorly controlled T2D (n=32), prediabetes (n=20), or normal glucose tolerance (NGT; n=54) were included. A total of 18 patients with poorly controlled T2D were evaluated before and 12 months after bariatric surgery, and 18 non-obese healthy individuals served as controls. VAT, hepatic PDFF, and pancreatic PDFF were quantified by magnetic resonance imaging (MRI) using a chemical shift-encoded sequence [iterative decomposition of water and fat with echo asymmetry and least-squares estimation quantitation (IDEAL-IQ)]. Univariate analysis and multivariate regression analysis were performed.

Results: There were significant differences in VAT, hepatic PDFF, and all pancreatic PDFF between the new-onset T2D, prediabetes, and NGT groups (all $P<0.05$). Pancreatic tail PDFF was significantly higher in the poorly controlled T2D group than in the well-controlled T2D group ($P=0.001$). In the multivariate analysis, only pancreatic tail PDFF was significantly associated with increased odds of poor glycemic control [odds ratio (OR) =2.09; 95% confidence interval (CI): 1.11–3.94; $P=0.022$]. The glycated hemoglobin (HbA1c), hepatic PDFF, and pancreatic PDFF significantly decreased (all $P<0.01$) after bariatric surgery, and the values were statistically similar to those observed in the non-obese healthy controls.

Conclusions: Increased fat in the pancreatic tail is strongly associated with poor glycemic control in patients with obesity and T2D. Bariatric surgery is an effective therapy for poorly controlled diabetes and obesity, which improves glycemic control and decreases ectopic fat deposits.

Keywords: Obesity; type 2 diabetes (T2D); glycemic control; magnetic resonance imaging (MRI); bariatric surgery

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Introduction

Obesity and diabetes are 2 of the most prevalent health problems associated with severe morbidity and increased mortality (1). Individuals with obesity have a significantly higher risk of type 2 diabetes (T2D) than those with a normal body mass index (BMI) (2,3). Most patients with T2D have abnormal adiposity characterized by visceral obesity and ectopic fat deposition (4).

Poor glycemic control among patients with T2D constitutes a major public health issue and is a leading risk factor for diabetic complications (5). Many factors, including high BMI, the duration of diabetes, age, gender, and lifestyle, contribute to poor glycemic control (6,7). Glycemic control remains the primary therapeutic goal in preventing target organ damage and other complications caused by diabetes (8). For obese patients with poorly controlled T2D, additional interventions, such as bariatric surgery, may be required to achieve optimal glycemic control (9).

Excessive visceral adipose tissue (VAT) and increased ectopic fat deposits contribute to systemic inflammation, metabolic dysfunction, and insulin resistance (10). Therefore, quantifying the distribution of adipose tissue in various body parts is crucial for studying diabetes and metabolic syndrome (11).

Magnetic resonance imaging (MRI) and computed tomography (CT) are the gold standard methods for dynamically assessing body composition (12). Moreover, MRI can accurately quantify the fat content in the pancreas and liver (13-15). Several MRI studies have reported that individuals with high VAT and ectopic fat deposits are at a significantly increased risk for T2D and metabolic syndrome (16,17).

In this context, we evaluated the distribution of adipose tissue in obese patients with and without impaired glucose metabolism. Furthermore, we aimed to determine the associations between VAT, hepatic proton-density fat fraction (PDFF), and pancreatic PDFF with poor glycemic control in obese patients with T2D and to evaluate the metabolic effect of bariatric surgery in obese patients with poorly controlled diabetes. We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1083/rc).

Methods

Study design and population

This is a retrospective cross-sectional study. The clinical records of 463 consecutive obese patients who underwent abdominal MRI scans during bariatric surgery between July 2019 to March 2021 at The First Affiliated Hospital of Jinan University were reviewed. After the exclusion of 278 patients with incomplete imaging data [no iterative decomposition of water and fat with echo asymmetry and least-squares estimation quantitation (IDEAL-IQ) sequence], 185 obese patients (all >18 years) with complete imaging data were included. Diagnoses of normal glucose tolerance (NGT), prediabetes, and T2D were made based on the criteria of the American Diabetes Association (18). The diabetics included in the present study included new-onset patients without prior treatment and those treated medically for 2–4 years. For medically treated patients, those with a glycated hemoglobin (HbA1c) level equal to or less than 7% were regarded as patients with well-controlled T2D, whereas others with an HbA1c level of more than 7% were considered patients with poorly controlled T2D (19,20). All participants were Chinese and of Han ethnicity. Participants aged over 50 years or with chronic or acute viral hepatitis (hepatitis A, B, or C), pancreatic disease, insufficient image quality or incomplete clinical datasets, and BMI over 50 kg/m^2 were excluded from this study. According to the above criteria, 34 obese patients (18.4%) were excluded because of insufficient image quality and incomplete clinical datasets. Thus, the study included 28 individuals with new-onset T2D, 17 with well-controlled T2D, 32 with poorly controlled T2D, 20 with prediabetes, and 54 with NGT (*Figure 1*). Moreover, among patients with poorly controlled T2D, 18 patients were evaluated before and 12 months after bariatric surgery (laparoscopic sleeve gastrectomy), and a further 18 age- and sex-matched non-obese healthy individuals (18 kg/m^2 < BMI < 25 kg/m^2) served as controls. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University, and individual consent for this retrospective analysis was waived.

All participants underwent the following blood laboratory tests: HbA1c, fasting blood glucose (FBG), alanine aminotransferase (ALT), aspartate aminotransferase

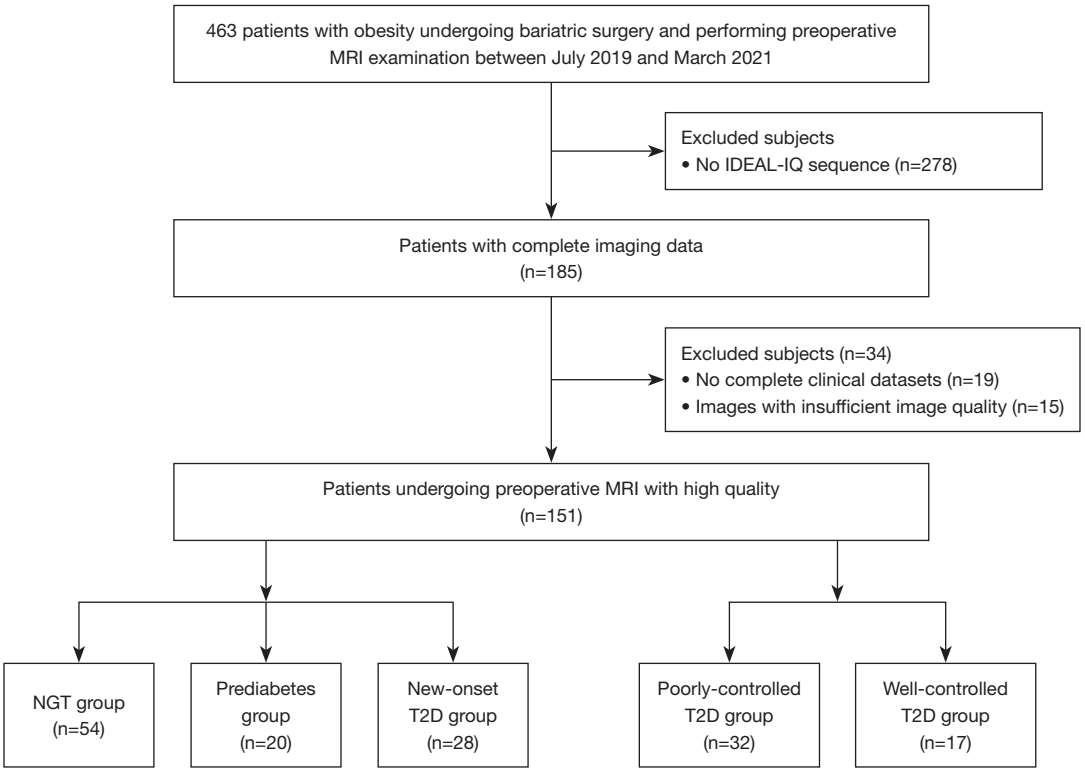

Figure 1 The flow chart of patients included in this study (n=151 patients). MRI, magnetic resonance imaging; IDEAL-IQ, iterative decomposition of water and fat with echo asymmetry and least-squares estimation quantitation; NGT, normal glucose tolerance; T2D, type 2 diabetes.

(AST), triglyceride (TG), low-density-lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), albumin (Alb), globulin (Gio), and C-reactive protein (CRP). All of these tests were performed in a standard manner. BMI was measured using the formula BMI = body weight (kg)/height^2 (m^2). All cases of obesity-related metabolic syndrome were confirmed by clinical or postoperative pathological examination.

MRI examination

All participants underwent MRI examinations using a 3.0T MRI scanner (Discovery MR750; GE Healthcare, Chicago, IL, USA). Both sequences were performed in a single breath hold (upon inspiration) to ensure optimal image quality. The MRI scan covered the diaphragm to the fourth lumbar vertebral body. Unenhanced fat-suppressed single-shot fast spin echo T2-weighted images (T2WI), gradient-recalled-echo T1-weighted images (T1WI) with in and opposed phase, and the IDEAL-IQ sequence were obtained. The IDEAL-IQ sequence had the following parameters: repetition time (TR) =15.6 ms, 6 echoes in each TR, first echo time (TE 1) =1.2–1.5 ms (increment: 1.23 ms, 6 echoes); flip angle, 8°; and slice thickness, 10 mm. The images were processed using the software provided by the manufacturer.

Anthropometric measurements

All MRI images were acquired from our institution's Picture Archiving and Communication System (PACS). For each participant, 2 consecutive axial images at the level of the L3 lumbar vertebra were processed and then averaged. A trained radiologist (YD) analyzed the MRI images, and another radiologist (YL) double-checked the results. Using Image J 1.51 (National Institutes of Health, Bethesda, MD, USA), the subcutaneous adipose tissue (SAT; cm^2) and the VAT (cm^2) were demarcated using predetermined thresholds for the signal intensity, as previously described (21).

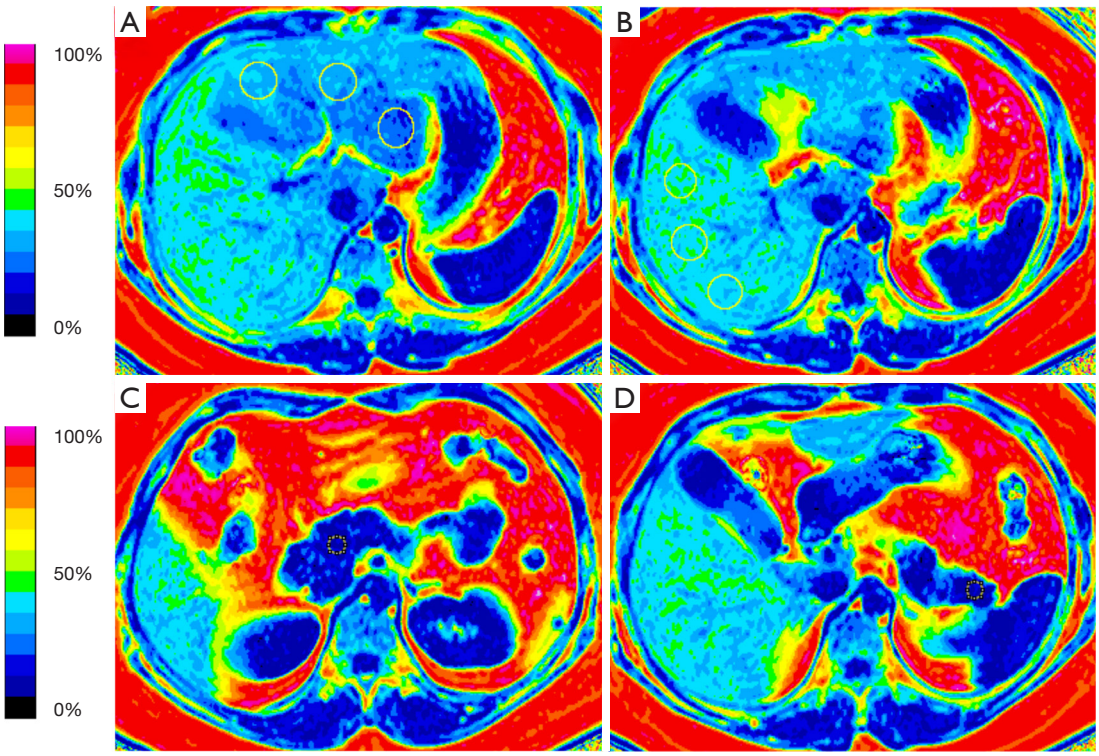

Figure 2 The ROIs (yellow circles) of the liver (A,B), pancreatic head (C), and pancreatic tail (D) in the pseudo-color map of the IDEAL-IQ sequence. The scaled color bar represents the fat content of different areas of the abdomen. ROIs, regions of interest; IDEAL-IQ, iterative decomposition of water and fat with echo asymmetry and least-squares estimation quantitation.

Measurement of hepatic PDFF and pancreatic PDFF

The IDEAL-IQ images were reviewed by a radiologist with more than 5 years of experience in abdominal imaging blinded to the patient's clinical and biochemical data. The PDFF levels of the liver and pancreas were performed on the fat fraction map using the workstation (AW 4.4; GE Healthcare). Hepatic PDFF levels were calculated by placing 2 regions of interest (ROIs) in each of the left and right lobes with an ROI of approximately 40–50 mm^2. An ROI of approximately 10–15 mm^2 was placed in each of the head, body, and tail of the pancreas, and the PDFF of each ROI was measured. Then, the average PDFF levels were calculated for the liver and pancreas. All ROIs avoided major vessels, ducts, and collecting systems (*Figure 2*).

Statistical analysis

Descriptive data were reported as means with standard deviation (SD), medians with an interquartile range, or numbers with percentages. For categorical variables, a chi-square test was used. Continuous variables were tested for normality using the Shapiro-Wilk test and, when not normally distributed, nonparametric tests were performed.

In the initial univariate analysis, data between the NGT, prediabetes, and new-onset T2D groups were compared using one-way analysis of variance (ANOVA; parametric data) or the Kruskal-Wallis H test (nonparametric data) with post hoc Holm-Bonferroni correction for multiple comparisons. Comparisons between poorly controlled T2D and well-controlled T2D groups were evaluated by using the Student's *t*-test (parametric data) and Mann-Whitney U test (nonparametric data), as appropriate.

Pancreatic tail PDFF, liver steatosis, Alb, and LDL-c distinguished poorly controlled T2D from well-controlled T2D based on the univariate analyses (all $P<0.05$). Therefore, in the next step, we used multivariate logistic regression analyses to evaluate which variables were independently associated with poorly controlled T2D.

Finally, comparisons before and after surgery were evaluated by using the paired *t*-test (parametric data) and the Wilcoxon signed-rank test (nonparametric data), as appropriate. An independent-samples *t*-test (parametric data) or Mann-Whitney U test (nonparametric data) was performed to compare continuous variables between the obese and control groups. The change after weight loss in patients with obesity for the continuous variable was calculated as the post-surgery value minus the pre-surgery value divided by the pre-surgery value, and the results were expressed as a percentage. The statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). A P value (or a P value adjusted in the Bonferroni method) <0.05 was considered statistically significant.

Results

A total of 151 obese patients with or without impaired glucose metabolism were included (*Figure 1*). The mean age of the individuals was 30 years, and 71 were female. The mean BMI was 37.8 kg/m^2.

Characteristics of the participants in the obese NGT, prediabetes, and new-onset T2D groups

Table 1 shows the characteristics of patients with obesity and NGT, prediabetes, and new-onset T2D. The BMI and CRP in the prediabetes group were significantly higher than those in the NGT group ($P_{adjusted}$=0.046 and $P_{adjusted}$<0.001, respectively). The proportions of patients with hyperlipidemia in the new-onset T2D group was significantly higher than that in the prediabetes ($P_{adjusted}$=0.003) and NGT ($P_{adjusted}$=0.01) groups.

The visceral fat, hepatic fat content, and pancreatic fat content were higher in the prediabetes and new-onset T2D groups than in the NGT group

The VAT and hepatic PDFF were significantly higher in the new-onset T2D and prediabetes groups than in the NGT group (all $P_{adjusted}$<0.05; *Figure 3*). The whole pancreas, pancreatic head, pancreatic body, and pancreatic tail PDFF in the new-onset T2D and prediabetes groups were significantly higher compared to the NGT group (all $P_{adjusted}$<0.05; *Table 1*). However, there was no significant difference in VAT, hepatic PDFF, and all pancreatic PDFF between the new-onset T2D and prediabetic groups.

Clinical characteristics of the patients in the poorly controlled T2D and well-controlled T2D groups

The characteristics of patients in the well-controlled T2D group compared to those of the poorly controlled T2D group are shown in *Table 2*. The levels of Alb, TG, and LDL-c in the poorly controlled group were significantly higher than those in the well-controlled group (P=0.02, P=0.04, and P=0.002, respectively). In addition, the proportions of patients with liver steatosis were significantly higher in the poorly controlled group than in the well-controlled group (P=0.008).

Pancreatic tail fat content was significantly higher in the poorly controlled T2D

The pancreatic tail PDFF in the poorly controlled group was significantly higher than that in the well-controlled group (P=0.001; *Table 2*). However, between groups, there was no statistically significant difference in the VAT, hepatic PDFF, whole pancreatic PDFF, pancreatic head PDFF, and pancreatic body PDFF.

Poorly controlled T2D was independently associated with pancreatic tail fat content

In the univariate logistic regression analysis, liver steatosis [odds ratio (OR) =12.92; 95% confidence interval (CI): 1.36–122.3; P=0.03], Alb (OR =1.25; 95% CI: 1.03–1.51; P=0.03), LDL-c (OR =3.93; 95% CI: 1.51–10.22; P=0.005), and pancreatic tail PDFF (OR =1.70; 95% CI: 1.13–2.54; P=0.009) were significantly associated with the presence of poorly controlled T2D.

In the multivariate analysis (*Table 3*), only pancreatic tail PDFF (OR =2.09; 95% CI: 1.11–3.94; P=0.022) was significantly associated with increased odds of poor glycemic control. In the receiver operating characteristic (ROC) curve analysis, the area under the curve (AUC) of pancreatic tail PDFF was 0.803 (95% CI: 0.682–0.925), and the optimal cutoff value was set at 5.9%, with a corresponding sensitivity of 62.5% and specificity of 100%.

The metabolic effect of bariatric surgery in obese patients with poorly controlled diabetes

Table 4 summarizes the major aspects of the patients' characteristics, including body weight, BMI, glycemic and

Table 1 The differences in clinical and anthropometric parameters among the T2D, prediabetes, and NGT groups

Variables	NGT (n=54)	Prediabetes (n=20)	New-onset T2D (n=28)	P value	Adjusted P value		
					Prediabetes *vs.* NGT	T2D *vs.* NGT	T2D *vs.* prediabetes
Age, years†	31.3 (8.9)	30.0 (7.8)	29.0 (8.3)	0.50			
BMI, kg/m^2	36.4 (31.7–41.0)	39.7 (35.0–43.6)	39.1 (35.3–43.3)	0.012	0.046	0.07	1.0
Weight, kg†	102.8 (21.9)	115.4 (19.8)	113.2 (21.7)	0.03	0.08	0.12	1.0
Height, cm†	168.6 (7.1)	170.4 (7.4)	169.3 (9.0)	0.69			
Female‡	26 (48.1)	10 (50.0)	13 (46.4)	0.90			
Liver steatosis‡	46 (85.2)	20 (100.0)	27 (96.4)	0.08			
Hypertension‡	3 (5.6)	4 (20.0)	4 (14.3)	0.17			
Hyperlipidemia‡	18 (33.3)	4 (20.0)	18 (64.3)	0.003	0.39	0.01	0.003
Glu, mmol/L	4.9 (4.7–5.4)	5.9 (5.5–6.5)	9.2 (7.2–13.5)	<0.001	<0.001	<0.001	0.01
HbA1c, %	5.5 (5.1–5.7)	6.5 (6.2–6.9)	8.7 (7.1–10.6)	<0.001	<0.001	<0.001	0.023
CRP, mg/L	4.2 (1.6–5.9)	8.0 (4.8–12.7)	4.7 (2.5–9.7)	<0.001	<0.001	0.09	0.28
ALT, U/L	34.5 (24.8–53.0)	79.5 (41.3–145.3)	67.0 (38.5–111.3)	<0.001	0.002	0.008	1.0
AST, U/L	22.5 (18.0–36.0)	51.4 (30.0–88.5)	36.0 (23.0–55.0)	<0.001	<0.001	0.009	0.58
Alb, U/L†	43.2 (3.3)	43.1 (2.9)	43.3 (3.2)	0.96			
Gio, U/L†	29.1 (3.3)	30.1 (4.8)	31.1 (4.1)	0.08			
TG, mmol/L	1.6 (1.3–2.3)	1.6 (1.4–4.1)	2.6 (1.4–4.6)	0.011	1.0	0.009	0.23
HDL-c, mmol/L	1.0 (0.9–1.2)	1.0 (0.8–1.1)	1.0 (0.9–1.1)	0.14			
LDL-c, mmol/L	3.0 (2.7–3.7)	3.0 (2.6–3.9)	3.2 (2.8–3.9)	0.40			
Hepatic PDFF, %	10.5 (5.5–19.8)	19.9 (14.2–25.0)	18.2 (14.3–22.7)	<0.001	0.004	0.002	1.0
Pancreatic PDFF, %	4.1 (2.7–5.8)	6.0 (4.3–9.1)	6.7 (5.5–10.1)	<0.001	0.005	<0.001	0.63
Pancreatic head PDFF, %	4.1 (2.9–7.3)	7.8 (4.3–11.0)	9.0 (7.6–11.6)	<0.001	0.009	<0.001	0.2
Pancreatic body PDFF, %	4.0 (2.3–5.7)	5.9 (3.6–9.4)	6.0 (4.0–11.7)	0.001	0.019	0.004	1.0
Pancreatic tail PDFF, %	3.1 (2.2–5.1)	4.9 (3.4–7.5)	4.7 (3.1–7.7)	0.004	0.016	0.026	1.0
VAT, cm^2†	145 (64.8)	193.7 (59.2)	186.9 (80.4)	0.006	0.023	0.03	1.0
SAT, cm^2†	260.9 (104.5)	388.5 (99.2)	330.7 (138.7)	0.007	0.03	0.03	1.0

Unless otherwise specified, data are medians, with interquartile ranges in parentheses. †, continuous variables are presented as the mean (SD); ‡, data are numbers of individuals, with percentages in parentheses. All comparisons were performed with the one-way analysis of variance (for parametric data) or Kruskal-Wallis tests (for nonparametric data), both with post hoc Holm-Bonferroni corrections. T2D, type 2 diabetes; BMI, body mass index; NGT, normal glucose tolerance; Glu, glucose; HbA1c, glycated hemoglobin; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Alb, albumin; Gio, globulin; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density-lipoprotein cholesterol; PDFF, proton-density fat fraction; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

patients with poor glycemic control, which was similar to the studies reported by Benoit *et al.* (33). Moreover, we found that pancreatic tail PDFF was a novel imaging marker associated with glycemic control. One possible explanation for this finding is that the density of beta islet cells in the pancreatic tail is higher (up to twice as high) than that in the pancreatic head or body (34). It has been reported that patients undergoing distal pancreatectomy are more

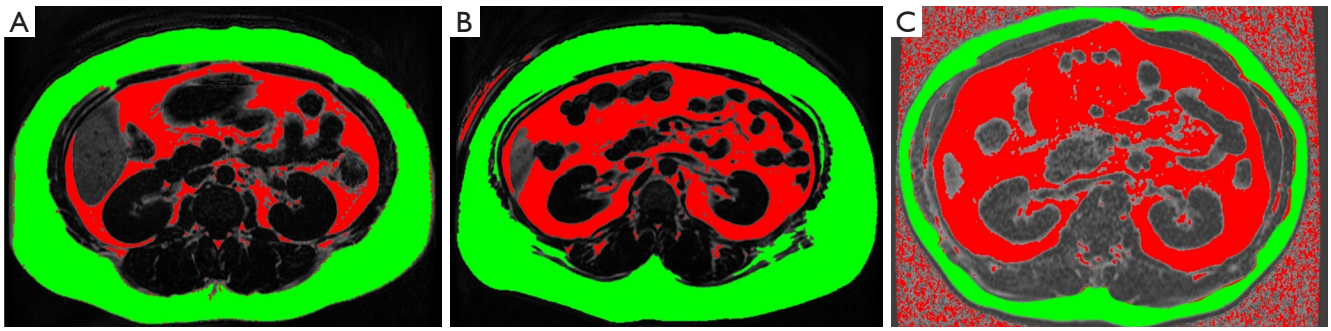

Figure 3 Axial MRI images of the abdomen in patients with obesity with NGT (A), prediabetes (B), and new-onset T2D (C). Subcutaneous and visceral fat are marked as green and red, respectively. The amount of visceral adipose tissue was significantly higher in the new-onset T2D and prediabetes groups than in the NGT group. MRI, magnetic resonance imaging; NGT, normal glucose tolerance; T2D, type 2 diabetes.

lipid parameters, hepatic PDFF, and all pancreatic PDFF, in obese patients with poorly controlled T2D and in non-obese controls. Before surgery, the obese patients had significantly higher hepatic PDFF and all pancreatic PDFF compared to the non-obese controls (all P<0.01). Values of TG and LDL-c were significantly higher in the obese patients compared than in the non-obese controls (both P<0.01).

Adiposity measures and adverse metabolic indices decreased 12 months after bariatric surgery. There was a 28.5% reduction in BMI (*Figure 4*) and a 27.8% reduction in HbA1c. The hepatic PDFF and all pancreatic PDFF significantly decreased after surgery (all P<0.01), and the values were statistically similar to those observed in the non-obese controls. Moreover, the change in BMI was associated with decreased hepatic PDFF (r=0.66; P=0.02) and pancreatic body PDFF (r=0.86; P<0.001).

Discussion

Poor glycemic control among patients with T2D constitutes a major public health issue and is a leading risk factor for diabetic complications (22,23). High BMI is closely related to poor glycemic control (24). For obese patients with poorly controlled T2D, additional interventions may be required to achieve optimal glycemic control (25). Several studies have reported significant differences in fat distribution between normal-weight and obese participants with and without T2D (16,26). However, no previous studies have investigated differences in visceral fat and ectopic fat accumulation between poorly controlled and well-controlled diabetes in obese patients. Thus, the main objective of this study was to provide more insight into the effect of abnormal adiposity on glycemic control in obese patients.

First, our findings indicated that adipose pathology might be the primary driver of obesity-related comorbidities, consistent with the findings of previous studies (27). Not all individuals classified as obese have excessive adiposity. Moreover, even among people classified as super or super-super obese, not all will have metabolic complications, such as T2D (28). In the present study, although BMI was higher in the prediabetes group than in the NGT group, there was no significant difference in BMI between the new-onset T2D and NGT groups. Conversely, some people with normal-weight or mild obesity develop metabolic complications due to ectopic adipose deposits (27). For example, compared to White populations, Asian populations tend to develop T2D at a younger age, with a lower BMI, and with relatively little weight gain, likely owing to increased insulin resistance associated with increased visceral fat and inadequate beta cell response (29). The present study showed significant differences in VAT, hepatic PDFF, and pancreatic PDFF between the new-onset T2D, prediabetic, and NGT groups in obese patients, with more ectopic fat deposition in the T2D and prediabetic groups compared to the NGT group.

Furthermore, our study demonstrated that pancreatic tail PDFF was strongly associated with poorly controlled T2D. Poor glycemic control is associated with a poor prognosis in obese patients with T2D (30,31). Poorly controlled hyperglycemia also increases the severity and mortality of patients with coronavirus disease of 2019 (COVID-19) (32). In this study, TG and LDL-c were significantly higher in

Table 2 Clinical data and anthropometric characteristics of patients with obesity and diabetes stratified according to glycemic control

Variables	Poorly controlled T2D (n=32)	Well-controlled T2D (n=17)	P value
Age, years†	39.6 (10.4)	36.8 (9.6)	0.22
BMI, kg/m^2	34.9 (32.7–38.3)	36.9 (32.7–43.1)	0.33
Weight, kg	99.0 (90.6–114.6)	98.2 (84.5–122.5)	0.99
Height, cm†	169.4 (9.5)	165.0 (10.2)	0.14
Female‡	14 (43.8)	8 (47.1)	0.83
Liver steatosis‡	31 (96.9)	12 (70.6)	0.008
Hypertension‡	15 (46.9)	7 (41.2)	0.70
Hyperlipidemia‡	16 (50.0)	8 (47.1)	0.85
Medication history‡			0.77
OHA	22 (68.8)	11 (64.7)	
OHA + insulin	10 (31.3)	6 (35.3)	
Duration of diabetes, years	3.0 (2.0–3.0)	2.0 (2.0–3.0)	0.38
Glu, mmol/L	7.5 (6.6–10.2)	5.8 (5.4–6.4)	<0.001
HbA1c, %	7.3 (7.1–8.8)	5.9 (5.7–6.4)	<0.001
CRP, mg/L	4.5 (2.0–9.0)	3.8 (2.3–6.8)	0.65
ALT, U/L	49.0 (26.5–82.0)	40.1 (17.0–74.5)	0.42
AST, U/L	26.0 (20.0–46.0)	30.0 (16.0–40.5)	0.56
Alb, U/L†	43.1 (3.4)	40.6 (3.6)	0.02
Gio, U/L	30.4 (27.9–31.9)	27.7 (27.1–30.6)	0.09
TG, mmol/L	2.8 (1.6–4.7)	1.5 (1.2–2.4)	0.04
HDL-c, mmol/L	1.0 (0.9–1.2)	0.9 (0.8–1.2)	0.34
LDL-c, mmol/L†	3.2 (0.8)	2.4 (0.7)	0.002
Hepatic PDFF, %†	15.3 (7.5)	13.6 (4.0)	0.37
Pancreatic PDFF, %	7.0 (5.8–9.0)	6.2 (5.7–6.9)	0.10
Pancreatic head PDFF, %	8.4 (6.2–10.4)	7.9 (7.6–8.7)	0.64
Pancreatic body PDFF, %	6.8 (5.4–8.6)	6.8 (5.4–7.4)	0.50
Pancreatic tail PDFF, %	6.6 (5.1–9.8)	4.7 (3.1–5.5)	0.001
VAT, cm^{2}†	196.5 (73.5)	198.7 (36.4)	0.91
SAT, cm^2	296.0 (208.8–472.7)	327.8 (217.5–515.3)	0.39

Unless otherwise specified, data are medians, with interquartile ranges in parentheses. †, continuous variables are presented as the mean (SD). ‡, data are numbers of individuals, with percentages in parentheses. All comparisons were performed with the independent-samples *t*-tests (for parametric data) or Mann-Whitney U test (for nonparametric data). T2D, type 2 diabetes; BMI, body mass index; OHA, oral hypoglycemic agent; Glu, glucose; HbA1c, glycated hemoglobin; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Alb, albumin; Gio, globulin; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density-lipoprotein cholesterol; PDFF, proton-density fat fraction; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

Table 3 Univariate and multivariate analyses of factors associated with poor glycemic control among obese patients with diabetes

Predictors	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	P value	OR	95% CI	P value
Liver steatosis	12.92	1.36–122.3	0.03	3.20	0.28–37.17	0.35
Alb	1.25	1.03–1.51	0.03	1.27	0.94–1.71	0.11
LDL-c	3.93	1.51–10.22	0.005	2.39	0.82–6.94	0.11
Pancreatic tail PDFF	1.70	1.13–2.54	0.009	2.09	1.11–3.94	0.022

OR, odds ratio; CI, confidence interval; Alb, albumin; LDL-c, low-density-lipoprotein cholesterol; PDFF, proton-density fat fraction.

Table 4 Clinical data and anthropometric parameters in obese patients with poorly controlled diabetes before and 12 months after bariatric surgery

Variables	Lean controls (n=18)	Obese surgical patient		P value			Change (%) from pre-surgery
		Pre-surgery (n=18)	Post-surgery (n=18)	Pre *vs.* Controls	Post *vs.* Controls	Pre *vs.* Post	
Age, years[†]	36.8 (6.5)	36.9 (7.5)	–	0.95	–	–	–
Female[‡]	10 (55.6)	9 (50.0)	–	0.74	–	–	–
Height, cm[†]	168.4 (8.1)	167.3 (5.5)	–	0.95	–	–	–
BMI, kg/m^2	20.7 (19.4–22.7)	39.3 (32.8–48.0)	28.8 (26.1–31.2)	<0.001	0.01	0.002	–28.5 (8.5)
Weight, kg	57.9 (53.9–64.1)	110.7 (89.1–143.5)	81.4 (71.8–88.4)	<0.001	0.001	0.003	–28.7 (8.6)
Glu, mmol/L	5.5 (5.2–5.6)	8.6 (7.2–12.4)	5.5 (5.2–5.8)	<0.001	1.0	<0.001	–39.0 (17.2)
HbA1c, %	5.5 (5.2–5.9)	7.7 (7.4–8.2)	5.6 (5.3–5.9)	<0.001	1.0	<0.001	–27.8 (–29.3, –27.3)
ALT, U/L	32.0 (30.0–33.8)	37.1 (26.8–65.3)	33.5 (30.0–35.8)	0.24	0.53	0.50	–7.5 (–45.2, 5.2)
AST, U/L	29.0 (25.3–31.8)	32.0 (23.3–41.3)	28.5 (23.5–34.5)	0.35	0.74	0.16	–11.5 (21.5)
TG, mmol/L	0.7 (0.6–0.8)	1.9 (1.5–2.1)	1.5 (1.4–1.6)	0.005	1.0	0.028	–28.6 (–30.8, –10.1)
HDL-c, mmol/L[†]	1.1 (0.1)	1.0 (0.1)	1.1 (0.1)	0.79	0.82	0.39	7.5 (4.1)
LDL-c, mmol/L[†]	2.2 (0.3)	2.9 (0.5)	2.2 (0.4)	<0.001	1.0	0.001	–23.4 (2.5)
Hepatic PDFF, %	7.8 (6.6–8.2)	11.2 (9.8–18.3)	7.8 (6.6–8.9)	<0.001	1.0	0.001	–40.6 (11.9)
Pancreatic PDFF, %	5.7 (5.0–5.9)	7.8 (6.9–9.1)	5.7 (5.3–5.9)	<0.001	1.0	<0.001	–30.1 (8.3)
Pancreatic head PDFF, %	5.7 (5.2–6.4)	9.0 (8.2–11.1)	5.9 (5.2–6.6)	<0.001	1.0	<0.001	–39.2 (6.8)
Pancreatic body PDFF, %	4.4 (3.9–5.3)	5.6 (4.7–7.6)	4.6 (4.0–5.5)	0.005	0.75	<0.001	–19.9 (12.0)
Pancreatic tail PDFF, %	4.7 (4.3–5.4)	7.3 (5.5–7.9)	4.8 (4.5–5.6)	0.002	1.0	0.003	–33.1 (–34.3, –23.3)

Unless otherwise specified, data are medians, with interquartile ranges in parentheses. [†], continuous variables are presented as the mean (SD). [‡], data are numbers of individuals, with percentages in parentheses. BMI, body mass index; Glu, glucose; HbA1c, glycated hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density-lipoprotein cholesterol; PDFF, proton-density fat fraction.

prone to develop long-term diabetes than those receiving pancreatic head resections (35,36). Therefore, potential inflammation and islet cell dysfunction in the pancreatic tail caused by steatosis may be associated with poorly controlled T2D (37).

Finally, our study indicated that bariatric surgery is an effective therapy for poorly controlled T2D and obesity. Weight loss is the most significant predictor of

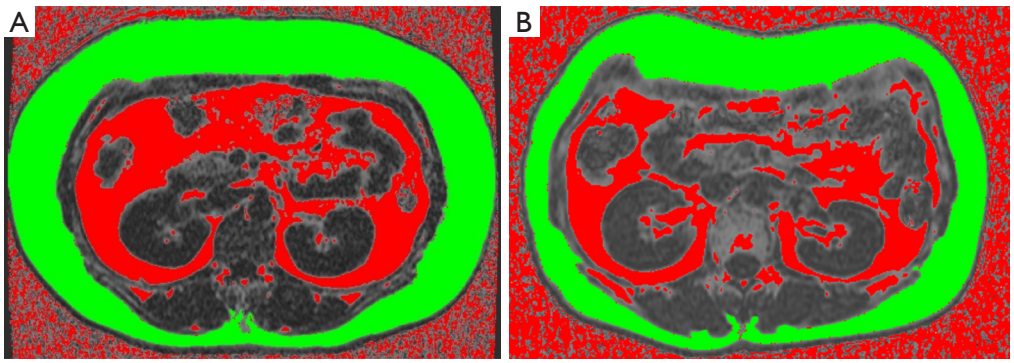

Figure 4 Axial MRI images of the abdomen in a 32-year-old man (A) before and (B) 12 months after bariatric surgery with a 37 kg weight loss (BMI decrease, 28.5%). The substantial subcutaneous (green) and visceral (red) fat accumulation seen before surgery significantly decreased after surgery. MRI, magnetic resonance imaging; BMI, body mass index.

the remission of T2D, and loss of 15% or more of body weight in the long term can have a disease-modifying effect in people with T2D (38). In the present study, obese patients with poorly controlled T2D who lost 29% of their body weight had improved glycemic control, and showed decreased pancreatic fat content 12 months after bariatric surgery. The change in BMI was associated with decreased pancreatic PDFF. However, this study did not find an association between changes in pancreatic fat content and HbA1c.

This study has several limitations. It was a retrospective study. In addition, due to the strict inclusion criteria, the sample size of this study was relatively small, which may be accompanied by type II errors. Further large, prospective studies are required to obtain more accurate findings. Finally, this was a single-center study; multicenter studies are needed to explore the consistency of results across ethnic populations.

In conclusion, the results of the present study indicate that pancreatic tail fat content is strongly associated with poor glycemic control in obese patients with T2D. Bariatric surgery is an effective therapy for obesity and poorly controlled diabetes and significantly reduces the ectopic fat content.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-1083/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1083/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University, and individual consent for this retrospective analysis was waived.

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