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ORIGINAL CONTRIBUTIONS

Use of Magnetic Resonance Imaging to Quantify Fat and Steatosis in the Pancreas in Patients after Bariatric Surgery: a Retrospective Study

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Abstract

Introduction Pancreatic steatosis (PS) has both metabolic consequences and local effects on the pancreas itself. Magnetic resonance imaging (MRI) is the most reliable non-invasive method for diagnosing PS. We investigated the impact of metabolic syndrome (MS) on the presence of PS, differences in individuals with and without PS, and the metabolic effects of bariatric procedures.

Methods Changes in anthropometric and basic biochemistry values and MS occurrence were evaluated in 34 patients with obesity who underwent a bariatric procedure. After the procedure, patients underwent MRI with manual 3D segmentation mask creation to determine the pancreatic fat content (PFC). We compared the differences in the PFC and the presence of PS in individuals with and without MS and compared patients with and without PS.

Results We found no significant difference in the PFC between the groups with and without MS or in the occurrence of PS. There were significant differences in patients with and without PS, especially in body mass index (BMI), fat mass, visceral adipose tissue (VAT), select adipocytokines, and lipid spectrum with no difference in glycemia levels. Significant metabolic effects of bariatric procedures were observed.

Conclusions Bariatric procedures can be considered effective in the treatment of obesity, MS, and some of its components. Measuring PFC using MRI did not show any difference in relation to MS, but patients who lost weight to BMI < 30 did not suffer from PS and had lower overall fat mass and VAT. Glycemia levels did not have an impact on the presence of PS.

Keywords Obesity · Bariatric surgery · Metabolic syndrome · Pancreatic steatosis

Introduction

Pancreatic steatosis is characterized by increased accumulation of fat in the pancreas [1, 2]. The most common causes are obesity and metabolic syndrome (MS), but other etiological factors include alcohol abuse and, very rarely, certain congenital syndromes or viral diseases [3]. The term non-alcoholic fatty pancreatic disease (NAFPD) refers to pancreatic steatosis that develops as a result of obesity and MS [4]. The diagnosis of pancreatic steatosis is based on non-invasive examination, and quantification of lipid content in the pancreas by magnetic resonance imaging (MRI) is considered the most reliable approach (Fig. 1) [5]. Epidemiological studies have reported a 16% prevalence of pancreatic steatosis in the adult population [6].

In clinical practice, pancreatic steatosis is especially important due to its association with type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), cardiovascular disease, acute pancreatitis, and pancreatic tumors [7]. Pancreatic steatosis is associated with dysfunction and a decrease in the number of beta cells, as well as lipotoxicity, insulin resistance, and inflammation. All of these circumstances can potentiate the development of T2DM [8].

Key points
No difference in pancreatic fat in persons with or without metabolic syndrome.
Lower BMI, fat mass, and visceral adipose tissue correspond to lower pancreatic fat.
Bariatric procedures are effective in the treatment of obesity and metabolic syndrome.

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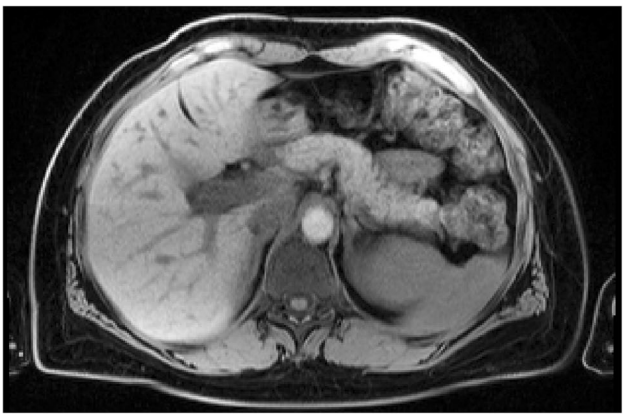

Fig. 1 T1-weighted MRI of the pancreas

Through toxic actions on the pancreatic parenchyma, pancreatic steatosis can aggravate the course of acute pancreatitis with fatty infiltration of pancreatic acini and, subsequently, contribute to destructive changes in the glandular parenchyma [9]. Several studies have reported a higher prevalence of pancreatic steatosis in patients with pancreatic carcinoma, and steatosis is an independent risk factor for the development of pancreatic carcinoma and pancreatic intraepithelial neoplasia [10, 11].

Previous studies measuring the pancreatic fat fraction using MRI have shown a significant positive correlation with BMI, waist circumference, and the number of MS criteria met. In addition, fat accumulation in the pancreas is higher than the fat accumulation in the liver and muscle tissue [12].

Obesity and MS are the most common etiological factors leading to the deposition of lipids in parenchymal organs [13]. Current evidence indicates that NAFPD is significantly associated with an increased risk of MS and its components [14]. Due to this close association between obesity and MS, one can assume that, in addition to reducing BMI, bariatric surgery could affect MS and its components, which was previously confirmed by a meta-analysis of bariatric surgery outcomes [15].

A previous study reported significantly higher pancreatic fat content measured by MRI in patients with T2DM and obesity compared to patients with or without obesity without diabetes, which dramatically decreased after bariatric surgery; a major decrease in insulin resistance and reversal of T2DM were also observed [16].

The present study aimed to investigate potential differences in the presence of NAFPD in the groups with and without MS using MRI with fat–water separated Dixon imaging. We also compared the anthropometric data and biochemical characteristics of patients with and without pancreatic steatosis to identify factors that correlate with pancreatic steatosis and possibly contribute to it. Our secondary aim was to evaluate the effect of bariatric surgery and changes in the presence of MS.

Methods

The study was approved by the Ethics Committee at the Faculty of Medicine, University of Ostrava, in accordance with the ethical standards of the Helsinki Declaration of 1975, as amended in 2013. The study had a retrospective, observational, and open-label design (ClinicalTrials.gov registration: NCT02893891). A retrospective observational study of patients following bariatric procedures was carried out between March 2020 and January 2021 at the Obesity Research Center of the Faculty of Medicine, University of Ostrava, and at the Bariatric Surgery Center, Department of Surgery, Vitkovice Hospital, Ostrava. From all patients who underwent surgery at our center, we selected patients who met the entry criteria and were also willing to participate in a more time-consuming project.

Inclusion criteria were age 18–65 years and BMI $>$ 40 kg/m^2 or $\geq$ 35 kg/m^2 with comorbidities, as per International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) criteria. Exclusion criteria were BMI $>$ 50 kg/m^2, prior major gastrointestinal surgery, diagnosis of gastric or duodenal ulcers, and gastrointestinal disease associated with resorption disorder. All patients were examined by specialists in internal medicine and psychology and received nutritional consultations prior to surgery. Enrollment into individual cohorts was at the recommendation of an interdisciplinary team.

Metabolic Syndrome Identification

When diagnosing MS, we followed the so-called harmonized definition [17]. This definition is based on five risk factors for cardiovascular disease; three abnormal findings out of five would qualify a person as having MS. The individual risk factors are waist circumference $\geq$ 102 cm in men or $\geq$ 88 cm in women (Caucasian population); elevated triglycerides ($\geq$ 1.7 mmol/l), or drug treatment for elevated triglycerides as an alternate indicator; reduced HDL cholesterol ($<$ 1.0 in men and $<$ 1.3 mmol/l in women), or drug treatment for reduced HDL cholesterol as an alternate indicator; elevated blood pressure (systolic $\geq$ 130 and/or diastolic $\geq$ 85 mm Hg) or antihypertensive drug treatment in a patient with a history of hypertension; and elevated fasting glucose ($\geq$ 5.6 mmol/l) or drug treatment for elevated glucose. These criteria were used to divide the patients into two groups: with and without MS.

Identification of Possible Risk Factors for Pancreatic Steatosis

Based on a review of recent data [3, 18, 19], we identified possible risk factors associated with MS and possibly pancreatic steatosis to investigate in patients: lipid spectrum, glycemia, adipocytokines, pancreatic fat content (by MRI), and the amount of total and visceral adipose tissue (by dual-emission X-ray absorptiometry, DXA).

Blood Tests

Blood samples were collected in the morning after overnight fasting and processed within 20 min of collection. Serum concentrations of glucose, alkaline phosphatase (ALP), triglycerides, total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol were assessed using a biochemical analyzer, AU 5420 (Beckman Coulter, Inc., Brea, CA, USA). Analyses of glucose, triglycerides, total cholesterol, LDL, and HDL cholesterol had inter-assay variation coefficients of 1.9%, 2.4%, 1.5%, 1.8%, and 2.3%, respectively. Hemoglobin A1C (HbA1c) was assessed by the Tosoh G8 High Performance Liquid Chromatography Analyzer (Tosoh Corporation, Tokyo, Japan) with interassay CV of 1.6%. Serum levels of target hormones (Leptin, Adiponectin, and Resistin) were measured on Bio-Plex® MAGPIX™ instrument (BioRad, Hercules, CA) with MILLIPLEX MAP kits (Merck KGaA, Darmstadt, Germany).

Body Composition Measurements

Height was measured in centimeters and weight in kilograms using a standard scale. The scale was calibrated on a regular basis according to the standard procedures of the site, and the same scale was used for all measurements. Weights were recorded with the individuals wearing undergarments only, including no jewelry or shoes. Body composition was assessed using DXA (Discovery A; Hologic, Waltham, MA, USA). The following parameters were monitored: fat mass (kg), fat (%), lean body mass (LBM; kg), and visceral adipose tissue (VAT; kg).

Magnetic Resonance Imaging

Twenty-four months after bariatric surgery, patients underwent MRI of the pancreas with subsequent quantification of the fat content. We compared the presence of pancreatic steatosis in patients with and without MS. All data were acquired on a 1.5 T Siemens Magnetom Sempra (Siemens, Erlanger, Germany) using a 6-channel body coil placed over the upper abdomen. The protocol consisted of morphological (T1w, T2w, T1 VIBE Dixon) and T2* mapping sequences.

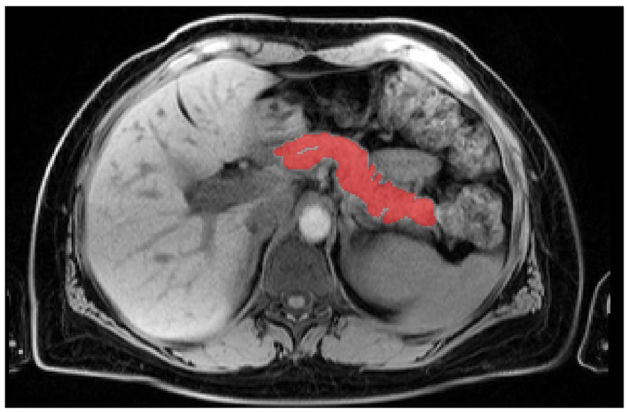

Fig. 2 Segmentation mask manually created over the pancreatic parenchyma (excluding pancreatic duct)

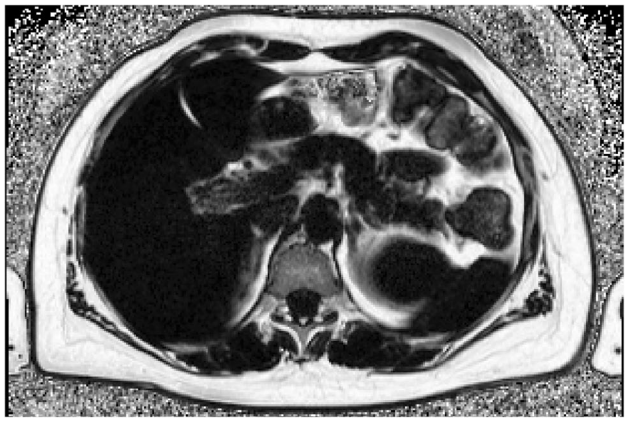

Fig. 3 Segmentation mask from Fig. 2 placed over the fat fraction map

Using ITK-SNAP software [20], manual segmentation of the pancreas was performed on transversal slices acquired from the T1-weighted sequence. Pancreatic contours and parenchyma were designated as accurately as possible on every slice, spatially defining the entire pancreas segmentation mask (Fig. 2). Special attention was paid to selecting just the pancreatic parenchyma without the surrounding fat. When the pancreatic duct could be visualized on an image, it was not included in the mask. The resulting segmentation mask was applied to the fat fraction map calculated from the Dixon sequence (Fig. 3).

The fat fraction map detailing the fat representation in the tissue (fat/fat + water) was calculated from the water and fat imagery acquired from the Dixon sequence using a custom-made script in Matlab (Matlab 2018b) (Fig. 4). The resulting value for the pancreatic fat fraction was an

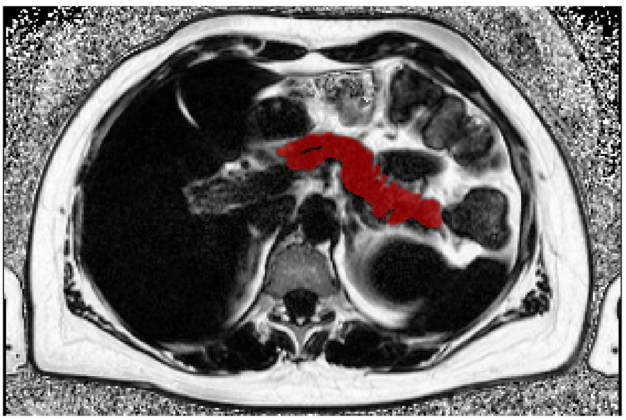

Fig. 4 Fat fraction map created using Matlab script

average representation of fat across the entire pancreatic volume.

To minimize the intra- and inter-observer errors, manual sequencing was performed in all cases by a single experienced operator. First, he performed five measurements that were not included in the analysis for perfecting and unifying the technique. Next, he performed the segmentation in all patients' imagery within a short period of time.

All MRI scans were of a quality suitable for radiological and quantitative evaluations. All MR imagery was evaluated first from the standard radiological perspective; no pancreatic pathology was found. In one patient, a 5-cm adrenal adenoma was detected, but none of the other findings were significant (cholecystolithiasis, simple hepatic, and renal cysts). Based on the literature review, the cutoff between normal and abnormally high lipid content was set to 10.4% (i.e., fat content < 10.4% was considered an absence of pancreatic steatosis and ≥ 10.4% was considered pancreatic steatosis) [6].

Statistical Analysis

Standard descriptive statistics (means, standard deviations, and medians) were used for data presentation. Significance was evaluated using t-test, ANOVA, Fisher, or Kruskal–Wallis test depending on the data characteristics; for categorical data frequencies, chi-squared test was used. All analyses were performed in R (The R Foundation for Statistical Computing Vienna, Austria) and $p \leq 0.05$ was considered significant.

Results

Patient Characteristics at the Start of the Study

Thirty-four patients were enrolled in the study. All patients underwent bariatric surgical or endoscopic procedures. The types of bariatric procedures were laparoscopic sleeve gastrectomy (LSG; $n = 20$ patients), Roux-Y bypass ($n = 1$), LSG later followed by Roux-Y bypass ($n = 1$), laparoscopic greater curvature plication (LGCP; $n = 4$), LGCP later followed by LSG ($n = 1$), partial jejuno-ileal diversion ($n = 4$), partial jejuno-colic diversion ($n = 1$), partial magnetic jejunal diversion ($n = 1$), and endoscopic gastric plication (Endomina, $n = 1$). Seven patients were male (20.6%) and 27 female (79.4%). The mean age at the time of the procedure was 44.6 ± 8.2 years. The overall mean weight before the procedure was 117 kg (± 18.7) and BMI 41.0 kg/m^2 (± 5.1).

Evaluation of Weight Reduction and Body Composition

Weight was significantly different before and after the procedure (117 ± 18.7 vs. 90.2 ± 18.4 kg, $p < 0.001$), representing an average weight loss of 26.8 kg and a significant change in BMI (41 ± 5.1 vs. 31.5 ± 6.1 kg/m^2, $p < 0.001$). The average decrease in BMI was 9.5. The total weight loss (TWL) was 22.6 ± 11.9 kg, excess weight loss (EWL) 62 ± 35.8%, and excess BMI loss (EBL) 22.9 ± 12.1%. The average waist circumference before surgery was 126.2 ± 14.9 cm, decreasing to 104 ± 16 cm at the time of the MRI ($p < 0.001$).

Analysis of the DXA data showed a significant decrease in the percentage of adipose tissue after the surgery (45.2 ± 4.7 vs. 38.5 ± 6.8%, $p < 0.001$). However, no significant differences were found in VAT (2.2 ± 0.2 kg in both groups, $p = 0.31$), systolic blood pressure (130 ± 12.4 and 128 ± 18.3 mmHg, $p = 0.563$), or diastolic pressure (82.3 ± 7.4 and 83.2 ± 11.7 mmHg, $p = 0.685$; Table 1).

Magnetic Resonance Imaging and Pancreatic Steatosis

Comparison of the Presence of Pancreatic Steatosis in Patients with and Without MS

The mean pancreatic fat content in the whole group was 14.1% (± 7%). No significant difference was observed between the MS/No-MS groups in regard to pancreatic fat content (15.1 ± 5.9 in the MS group vs. 13.3 ± 7.8 in the No-MS group; $p = 0.448$). Similarly, binary evaluation of the presence/absence of steatosis did not reveal any differences between groups (73% in the MS group vs. 58% in the No-MS group; $p = 0.566$; Table 2).

Anthropometric and Biochemistry Values in Patients with and Without Pancreatic Steatosis

When comparing the groups of patients 24 months after surgery, not on the basis of MS criteria but on the presence of pancreatic steatosis, the groups of patients with and without

Table 1 Patient characteristics before and after the bariatric procedures

Characteristic	Before bariatric procedure ($N=34$)	After bariatric procedure ($N=34$)	P-value
Male/female	7/27	7/27	-
Weight (kg)	117 ± 18.7	90.2 ± 18.4	< 0.001
Body fat (%)	45.2 ± 4.7	38.5 ± 6.8	< 0.001
Body fat (kg)	53 ± 10.3	35.2 ± 10	< 0.001
VAT (kg)	2.2 ± 0.2	2.2 ± 0.2	0.31
BMI (kg/m^2)	41.0 ± 5.1	31.5 ± 6.1	< 0.001
Waist circumference (cm)	126.2 ± 14.9	104 ± 16	< 0.001
Blood pressure systolic (mmHg)	130 ± 12.4	128 ± 18.3	0.563
Blood pressure diastolic (mmHg)	82.3 ± 7.4	83.2 ± 11.7	0.685
Presence of metabolic syndrome, yes/no	30/4	15/19	< 0.001
Presence of T2DM, yes/no	21/13	15/19	0.22
TWL (%)	-	22.6 ± 11.9	-
EWL (%)	-	62 ± 35.8	-
EBL (%)	-	22.9 ± 12.1	-

Values are given as n or mean ± standard deviation. *VAT*, visceral adipose tissue; *BMI*, body mass index; *T2DM*, type 2 diabetes mellitus; *EWL*, excess weight loss; *TWL*, total weight loss; *EBL*, excess BMI loss

Table 2 Pancreatic steatosis and pancreatic fat fraction determined by MRI

Characteristic	Overall ($N=34$)	Metabolic syndrome ($N=15$)	No metabolic syndrome ($N=19$)	P-value
Pancreatic steatosis[a]	22	11	11	0.566
No pancreatic steatosis	12	4	8	
MR fat fraction (%)	14.1 ± 7.0	15.1 ± 5.9	13.3 ± 7.8	0.448

Values are given as n or mean ± standard deviation. *MR* magnetic resonance. [a] MR fraction ≥ 10.4%

steatosis differed significantly. Differences were observed in MR fat fraction, weight, BMI, lean mass, absolute body fat, and VAT. Among biochemical parameters, there was a significant difference in total cholesterol, LDL cholesterol, and leptin values. There was no significant difference in fasting glycemia, HDL, TAG, HbA1c, or other adipocytokine (adiponectin, resistin) values. A detailed summary of all outcomes in patients with and without pancreatic steatosis is provided in Table 3.

Biochemistry Focused on Glycemic Control and Metabolic Syndrome

Before bariatric surgery, 21 (62%) patients had diabetes or elevated fasting blood glucose; after the surgery, diabetes or elevated fasting blood glucose was observed in only 15 (44%) patients. Therefore, normalization of blood glucose was observed in 6 patients ($p=0.22$).

MS was diagnosed in 30 of 34 (88%) patients prior to surgery and in 15 of 34 (44%) patients after surgery. MS regression was observed in 15 (50%) patients, whereas no improvement was observed or the improvement was not sufficient for escaping the MS criteria in the remaining 15 (50%) patients. None of the remaining four patients in whom MS criteria were not met before bariatric surgery developed MS after surgery. Changes in the presence of MS before and after surgery were significant ($p<0.001$; Table 1).

Regarding biochemical markers, a significant difference was detected in the levels of fasting glucose, triglycerides, HDL, and glycated hemoglobin before and after surgery. However, no difference was observed in the levels of ALP, cholesterol, or LDL before and after the procedure (Table 4).

Discussion

In this retrospective observational study, we examined patients by MRI to determine the pancreatic fat content, enabling the comparison of pancreatic steatosis between groups with and without MS. We also investigated the differences in groups with and without pancreatic steatosis. Our secondary goal was to evaluate the effects of bariatric surgery on anthropometric data, biochemical parameters, and the presence of MS.

Table 3 Comparison of lab values and anthropometric measures in patients with and without pancreatic steatosis

Characteristic	With pancreatic steatosis ($N=22$)	Without pancreatic steatosis ($N=12$)	P-value
Glucose (mmol/l)	5.6 ± 1.0	5.2 ± 0.5	0.074
Cholesterol (mmol/l)	5.4 ± 1.3	4.2 ± 0.7	0.001
Triglycerides (mmol/l)	1.5 ± 0.9	0.8 ± 0.3	0.005
HDL (mmol/l)	1.4 ± 0.4	1.7 ± 0.4	0.074
LDL (mmol/l)	3.5 ± 0.9	2.4 ± 0.6	< 0.001
HbA1c (mmol/mol)	39.6 ± 11.2	35.2 ± 3.7	0.099
Leptin (µg/l)	13.5 ± 9.2	5.6 ± 3.9	0.001
Adiponectin (mg/l)	62.5 ± 75.7	92.4 ± 79.9	0.301
Resistin (µg/l)	60.6 ± 23.4	57.0 ± 13.8	0.573
MR fat fraction (%)	17.4 ± 6.5	8.0 ± 1.5	< 0.001
Weight (kg)	99.1 ± 15.2	73.9 ± 11.3	< 0.001
BMI (kg/m^2)	34.2 ± 5.4	26.8 ± 4.0	< 0.001
Lean after (kg)	59.3 ± 10.6	48.4 ± 5.9	0.001
Lean after (%)	60.8 ± 7.9	63.0 ± 4.1	0.299
Fat after (kg)	38.6 ± 9.8	29.0 ± 7.2	0.003
Fat after (%)	39.2 ± 7.9	37.0 ± 4.1	0.302
VAT after (kg)	2.2 ± 0.2	2.1 ± 0.1	0.013

Values are given as mean ± standard deviation. *VAT* visceral adipose tissue

Table 4 Lab values in patients before and after bariatric surgery

Characteristic	Before bariatric procedure ($N=34$)	After bariatric procedure ($N=34$)	P-value
Glucose (mmol/l)	6.3 ± 1.7	5.5 ± 0.9	0.016
Cholesterol (mmol/l)	5.2 ± 1.0	5.0 ± 1.2	0.437
Triglycerides (mmol/l)	2.2 ± 1.7	1.2 ± 0.8	0.003
HDL (mmol/l)	1.2 ± 0.3	1.5 ± 0.4	0.002
LDL (mmol/l)	3.4 ± 0.9	3.1 ± 0.9	0.251
HbA1c (mmol/mol)	44.5 ± 13.6	38.1 ± 9.4	0.028
ALP (µkat/l)	1.3 ± 0.4	1.5 ± 0.5	0.298

Values are given as mean ± standard deviation

Weight Loss and the Effect on Metabolic Syndrome

A significant decrease in weight, BMI, waist circumference, TWL, EWL, and EBL was observed in the study group after bariatric surgery. A significant decrease in the presence of MS was recorded. These results confirm the high effectiveness of the bariatric surgery methods in treating obesity and contribute to the justification of the term "metabolic surgery" [21].

Magnetic Resonance Imaging and Pancreatic Steatosis

There are several methods for quantifying pancreatic fat using MRI, namely, in-phase and out-of-phase imaging, proton density fat fraction (PDFF) in various regions of interest of the pancreas, MRI image "biopsy," fat–water separated Dixon imaging, and MRI spectroscopy [22]. Using our method with segmentation of the whole pancreas, we wanted to minimize the risk of the effects of an uneven or patchy distribution of pancreatic fat in different areas of the pancreas [23, 24].

In the diagnosis of pancreatic steatosis, it is necessary to consider that there is no firm line for fat content defining steatosis. Ogilvie was the first to study this problem. During autopsies, he found an average pancreatic fat content of 17.1% in 19 individuals with obesity and 9.3% in 19 individuals without obesity [25]. Current non-invasive studies, however, generally indicate lower fat content. Kühn analyzed MRI data from 1367 volunteers using the PDFF technique, detecting a mean fat content of 4.4% but revealing no difference in the fat content between individuals with normal glycemia, pre-diabetes, or diabetes [26]. Another study using the same technology found a median PDFF of 5.2%. A study of 685 healthy volunteers from the general population found that 90% had pancreatic fat content between 1.8 and 10.4% and used a cutoff of 10.4% to diagnose pancreatic steatosis [6]. A large meta-analysis evaluating various methods of measuring pancreatic fat content proposed a cutoff value of 6.2% [27].

Another study using the same method for determining the pancreatic fat fraction as in the present study (T2* corrected Dixon technique) evaluated 165 patients undergoing pancreatic surgery by MRI and histological assessment of the resection specimen with measurement of fat content. The MRI-detected fat fractions ranged from 1.7 to 39.1% (median 6.5%). The MRI fat fraction showed a moderate correlation with the amount of fat in the specimen (r = 0.71, 95% confidence interval: 0.63–0.78) [22].

In our study, we did not detect a significant difference in either the pancreatic fat fraction or the presence of pancreatic steatosis between the groups with and without MS. Published studies have reported unambiguous results. Pancreatic PDFF was previously used in a study showing the correlation of pancreatic steatosis with BMI, male sex, and presence of diabetes [23]. In a large meta-analysis, a higher risk of arterial hypertension, diabetes, and MS was found in individuals with pancreatic steatosis [27]. A study using "MRI biopsy" reported a significantly higher pancreatic fat fraction in individuals with T2DM compared to those with normal glycemia (6.4 ± 0.3 vs. 5.1 ± 0.6%), noting a significant reduction in pancreatic fat content after

bariatric surgery in T2DM individuals but no such effect in those with normal glycemia [24].

A study of 267 patients used the same technique as out study for determining pancreatic fat (fat–water separated Dixon imaging), though they measured only a region of interest, not the entire pancreatic volume. They evaluated pancreatic fat fraction in relation to MS, BMI, and waist circumference [12]. The pancreatic fat fraction was 6% in patients with normal BMI, 9.4% in individuals who were overweight, and as high as 11.7% in patients with obesity. A higher degree of pancreatic steatosis was demonstrated in patients meeting multiple MS criteria, ranging from 7.8% in patients who met one criterion to 13% in patients meeting all five criteria. The average pancreatic fat fraction in patients with diagnosed MS exceeded 11%. In patients with no MS components, the pancreatic fat fraction was merely 5.4%. In addition, the association of fat accumulation in the pancreas with high BMI, waist circumference, and the number of MS criteria was stronger than that of fat accumulation in skeletal muscle and liver [12]. That study clearly demonstrated the impact of obesity and MS on pancreatic fat accumulation. Another study using the same dataset demonstrated the association between pancreatic fat fraction, incidence of T2DM, and hypertension [28].

When evaluating pancreatic fat with MRI spectroscopy, Gaborit et al. [16] found a significantly higher pancreatic triglyceride content in patients with T2DM ($23.8 \pm 3.2\%$) compared to patients with obesity (14.0 ± 3.3; $p = 0.03$) or who were lean ($7.5 \pm 0.9\%$; $p = 0.0002$). Bariatric surgery induced a major reduction in pancreatic fat ($-43.8 \pm 7.0\%$), resulting in levels comparable to lean individuals and an improvement in glucose tolerance, whereas the BMI remained highly elevated [16].

The pancreatic fat content reported in the aforementioned studies was lower than that detected in our study. One possible explanation lies in the differences in methodology—those studies generally analyzed pancreatic fat only in a few regions of interest or in several slices, whereas we evaluated the full pancreatic volume, which is more susceptible to the erroneous inclusion of pancreatic fat. This problem may have been corroborated by the fact that, in patients with T2DM, the pancreatic contours exhibited greater irregularity than in the general population and, thus, interlobular intrusions of visceral fat could have been interpreted as intrapancreatic fat [24]. The number of patients with T2DM or elevated fasting blood sugar was high in our group (44%, 15 out of 34). Our patients were also primarily patients who underwent bariatric surgery in the past and, therefore, can be expected to have pathologically higher fat content in various tissues. On the other hand, a study using the same method as us reported an even higher pancreatic fat fraction ($17.4 \pm 5.1\%$ in 277 patients with obesity) [29].

The fact that there is no gold standard for quantifying pancreatic fat is a limiting factor for a comparison of the results between studies and the methods used. The patchy nature of pancreatic fat accumulation could strongly affect the results of the MR quantification of pancreatic steatosis. Nevertheless, comparisons of various quantification methods are challenging due to the difficulty analyzing the entire pancreas using the ground truth (resected or needle biopsy samples). For this reason, the autopsy samples are used merely to characterize the histological severity of the pancreas as a whole [23].

There are three state-of-the-art methods: T2* corrected Dixon technique, intravoxel incoherent motion diffusion-weighted imaging (IVIM DWI), and PDFF. Among these, PDFF is considered the most practical and objective method because the fat fraction can be obtained quantitatively by separating water and fat using a chemical shift technique. However, it is more prevalent as a marker of hepatic steatosis because there is a lack of research done on pancreatic steatosis, similar to other techniques used in this field [30, 31]. IVIM DW imaging compensates for the downsides of traditional DWI because it is able to separate water molecule diffusion and microcirculatory perfusion-related diffusion. Changes in IVIM-derived parameters are associated with significant changes in advanced pancreatic fibrosis, which often accompanies pancreatic steatosis [22, 32].

The fact that the segmentation mask is prepared manually on the individual MR images and is, therefore, dependent on the accuracy of the contour delimitation by the examiner can be considered a limitation of the evaluation of pancreatic fat content. In our study, we did our best to minimize the inter- and intra-observer error by having a single individual perform the measurements. This examiner first gained experience on several MRI scans that were not included in the study and then he applied the technique to MRI scans of all patients. Attention was paid to evaluating all imagery within a relatively short time period to maintain uniform measurements. The quality of the MRI can also influence the overall evaluation, as lower quality images may not support accurate delimitation of the pancreas due to poorly visible borders. In addition, the pancreatic duct, which was excluded from our analysis, may not be visible in poor imagery. Acquisition of high-quality MR images may be difficult in patients with obesity [33]. It would be interesting to compare fat fraction data from pancreatic segmentations made by two or more operators. However, due to the time demands of such a task and rapid development in the field of artificial intelligence, especially image recognition and deep neural networks, we think that automated pancreatic segmentation is the way to go in the future [34]. This method would enable the evaluation of more data and accurate comparisons between different research groups. Moreover, the usage of more advanced methods, such as IVIM DWI, could provide other clinically

relevant information in patients after bariatric surgery. As our study was retrospective, we were technically limited by the clinical MRI scanner for data acquisition. This will be further investigated in our future research.

Conclusions

Bariatric procedures can be considered effective in the treatment of obesity, MS, and some of its components. Our method of pancreatic fat measurement using MRI did not find any significant differences in the pancreatic fat content between individuals with and without MS. Weight reduction reducing the BMI to < 30 kg/m^2 resulted in improvements in glucose and lipid metabolism, with no pancreatic steatosis noted in these patients. It seems that reduction of total body adipose tissue not only leads to changes in metabolic function, but could possibly also have an effect on pancreatic steatosis. However, these findings require a prospective follow-up of these types of patients.

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Declarations

Ethical Approval All procedures performed in this study were in accordance with the ethical standards of the University Hospital and Faculty of Medicine, University of Ostrava, Czech Republic, and in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2013.

Conflict of Interest The authors declare no competing interests.

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