ORIGINAL ARTICLE

Is Pancreatic Exocrine Insufficiency a cause of Malabsorption in Patients after Bariatric Surgery?

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ABSTRACT

Introduction It is known that afferent and efferent loop syndromes can develop following gastric surgery procedures, which can result in accelerated intestinal transit time as well as colonization by pathogenic bacteria in the upper gastrointestinal tract with inadequate stimulation and poorly synchronized pancreatic enzyme secretion. This condition is known as pancreaticocibal asynchrony and can cause pancreatic exocrine insufficiency. The aim of our study was to determine whether pancreatic exocrine insufficiency is impaired in patients after bariatric surgery. We are presenting the results of a pilot study. **Patients and methods** Patients were selected from the bariatric surgery outpatient clinic of the Slovenj Gradec General Hospital (Slovenian centre of excellence for bariatric surgery). All patients were Caucasians over 18 years of age. The eligibility criteria for surgery were determined according to European guidelines body mass index ≥40 kg/m^2 or ≥35 kg/m^2 in patients with obesity-related comorbidities). All procedures were performed by laparoscopic surgery (as Roux-en-Y or mini-omega loop gastric bypass). All patients received standard supplementation after surgery. Faecal elastase-1 (FE1) measurements were performed using the enzyme-linked immunosorbent assay method. **Results** Twenty-two consecutive patients were included in the study: 21 (95.5%) female and 1 (4.5%) male; the mean age was 42.0 ± 9.2 years, with a range of 24 to 57 years. Patients were included in the study one year after bariatric surgery. **Weight outcomes** *Body mass index pre-surgery*: 42.5±4.0 (range 34.9-49.1). *Body mass index present*: 27.4 ± 3.2 (range 23.1-34.6). *Pre-surgery weight*: 119.5±15.0 kg (range 97-149). *Lowest post-surgery weight (present weight)*: 76.7±9.6 kg (range 63-100). *Total weight loss*: 42.8±7.3 kg. Pancreatic exocrine insufficiency was present in two patients (9.1%): mild to moderate pancreatic exocrine insufficiency (FE1 191 μg/g) in a 39-year-old male and severe pancreatic exocrine insufficiency (FE1 15 μg/g) in a 52-year-old female. Serum nutritional markers were low in both patients (vitamin D, iron, selenium). **Conclusions** Our results show that pancreatic exocrine insufficiency is possible in patients one year post-surgery and could be an additional cause of malabsorption in this group of patients.

INTRODUCTION

Bariatric surgery is an established and integral part of the comprehensive management of morbidly obese patients [1]. Management of patients after bariatric surgery has been the topic of many international guidelines and review articles [2, 3, 4, 5, 6]. All bariatric surgery procedures that bypass a portion of the small intestine can produce nutritional deficiencies. Currently, the most commonly performed procedure is Roux-en-Y gastric bypass (RYGB), which bypasses the body of the stomach and the duodenum and delays the mixing of biliary and pancreatic secretions with food in the proximal small bowel [3]. Macronutrient and micronutrient deficiencies are common after RYGB. Screening and supplementation of deficiencies with iron, vitamin B12, calcium, vitamin D, folic acid and vitamin A are routinely conducted in this group of patients, especially in those who are at increased risk (those with osteoporosis and heavy menstruation) [4].

It is known that afferent and efferent loop syndromes can develop following gastric surgery procedures and can result in an accelerated intestinal transit time as well as colonization by pathogenic bacteria in the upper gastrointestinal tract with inadequate stimulation and poorly synchronized pancreatic enzyme secretion [7]. This condition is known as pancreaticocibal asynchrony and can cause pancreatic exocrine insufficiency (PEI).

The term PEI is defined as the functional limitation of pancreatic enzyme secretion regardless of its cause. The disease can exist in association with pancreatic

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illnesses (chronic pancreatitis, hereditary pancreatitis, autoimmune pancreatitis, cystic fibrosis, pancreatic carcinoma, diabetes mellitus) or as a concomitant illness (with autoimmunopathy, chronic inflammatory bowel diseases, irritable bowel syndrome, viral infections and celiac disease) [7, 8].

The main clinical consequence of PEI is fat maldigestion and malabsorption resulting in steatorrhoea. Other symptoms may also include abdominal pain, flatulence and weight loss. If left untreated, fat maldigestion may lead to low circulating levels of micronutrients, fat-soluble vitamins and lipoproteins [9].

In the last 20 years, non-invasive methods have become the gold standards for PEI detection. While faecal fat quantification is still considered to be the gold standard for the diagnosis of PEI, there are many disadvantages that limit its clinical applicability (e.g., the collection of stool over 3 days is required, which is unpleasant and cumbersome for patients and laboratory staff) [10].

Faecal elastase-1 (FE1) is a non-invasive method for diagnosing PEI. Using direct pancreatic function tests as reference standards, FE1 has an approximate sensitivity of 100% in cases of severe PEI, 77-100% for moderate PEI and 0-63% for mild PEI, with approximately 93% specificity. These studies also suggest that FE1 has greater sensitivity and specificity compared to faecal chymotrypsin [11, 12, 13, 14].

To our best knowledge, PEI has not yet been evaluated as a possible additional cause of malabsorption in patients after bariatric surgery. We also did not find any recommendations related to PEI testing in patients after bariatric surgery in the current chronic pancreatitis guidelines [15, 16].

The aim of our study was to determine whether PEI is impaired in patients after bariatric surgery.

PATIENTS AND METHODS

Patient Recruitment

Twenty-two consecutive patients who underwent gastric bypass one year ago were invited to participate in the study. All patients were Caucasians over 18 years of age who gave informed consent prior to participating in the study. They were selected from the bariatric surgery outpatient clinic of the General Hospital Slovenj Gradec (Slovenian center of excellence for bariatric surgery).

The eligibility criteria for surgery were determined according to European guidelines (body mass index (BMI) ≥40 kg/m^2 or ≥35 kg/m^2 in patients with obesity-related comorbidities) [1].

All patients received standard supplementation after surgery that included: iron III hydroxide polymaltose complex 100 mg/day, folic acid 5 mg/day, calcium carbonate 1 g/day, vitamin D (cholecalciferol) 1000 i.u./ day, vitamin B12 (hydroxocobalamin) injection into a muscle every 6 months, and multivitamin and multimineral tablets once a day.

Surgery: All procedures were performed by laparoscopic surgery (Roux-en-Y or mini- omega loop gastric bypass, depending on patients' problems with gastroesophageal reflux disease (GERD), sweet-eating habits and anatomical findings during operation).

Antecolic - antegastric RYGB was performed. A small gastric pouch (25 ml) and gastro-enteric anastomosis were made using a linear endostapler (30 mm long). Defects were closed with a running suture. In patients with BMI < 38, the Roux limb was 60 cm long and the biliopancreatic limb was 40 cm long. In patients with BMI between 38 and 48, the Roux limb was 150 cm long and the biliopancreatic limb was 60 cm long. In patients with BMI > 48, the Roux limb was 150 cm long and the biliopancreatic limb was 200 cm long. Entero-enteric anastomosis was performed using a linear endostapler and defect was closed with running suture. We randomly closed mesenteric and Peterson spaces.

Omega loop gastric bypass was performed with longer and thinner pouch stretching to the incisura angularis. In patients with BMI < 38, 38-48 and > 48, the biliopancreatic limbs were 150 cm, 200 cm and 250 cm long, respectively. Gastro-enteric anastomosis was made with a linear stapler as described above. Peterson defect was closed and an »antireflux stitch« was made.

In total, 11 (50%) patients underwent Roux-en-Y gastric bypass, and in the other 11 (50%), mini- omega loop gastric bypass was performed.

Weight outcome variables: We determined the following weight outcome variables: BMI pre-surgery and at the time of inclusion in the study; total weight loss (kg) = pre-surgery weight – lowest post-surgery weight; net weight loss (kg) = pre-surgery weight – current weight and % weight loss maintained = net weight loss/total weight loss.

Measurement of laboratory tests: Fecal elastase-1 (FE1) measurements were performed using enzyme-linked immunosorbent assay (ELISA) with a commercial kit (ScheBo Biotech, Giessen, Germany). Patients sampled a probe of their morning stool into a labelled stool tube that was transported to the central laboratory. In all patients, the stool sample was solid. The results of FE1 are expressed in μg/g stool. Levels of > 200 μg/g, 100-200 μg/g and < 100 μg/g were classified as normal exocrine pancreatic function, mild to moderate PEI and severe PEI, respectively.

In all patients, the following serologic laboratory measurements were performed: iron, vitamin B12, folic acid, magnesium, vitamin D, vitamin A, vitamin E, calcium, selenium, copper, zinc, manganese, albumin, prealbumin, cholesterol.

Radiology: Patients with confirmed PEI underwent combined MRI of the upper abdomen and magnetic resonance cholangiopancreatography (MRCP). MRI was performed on a 3.0-T MR scanner (Signa HDxt, GE) with the use of a torso phased array eight-channel surface coil. For the

assessment of the morphological features of the pancreas, the sizes, fatty infiltrations and signal intensities (SIs) on T1-weighted images in the three segments (i.e., the head, body and tail) of the pancreas were analysed. The mean values were calculated and compared to SIs of the spleen. Main and side-branch duct evaluation with MRCP was also performed to investigate signs of chronic structural changes.

Statistical Analysis

The data are shown numerically (%) as the means± standard deviations.

Ethics

This study was approved by the National Medical Ethics Committee (No. 121/01/12 of 9 February 2012). Informed consent was obtained from all individual participants included in the study.

Results

Patient characteristics: Twenty-two consecutive patients were included in the study: 21 (95.5%) female and 1 (4.5%) male; he mean age was 42.0 ± 9.2 years, with a range of 24 to 57 years. Patients were included in the study one year after bariatric surgery.

Weight outcomes: The weight outcome variables of patients are summarized in **Table 1**.

Laboratory measurements: The laboratory measurements of patients are summarized in **Table 2**.

PEI was present in two patients (9.1%): mild PEI (FE 191 μg/g) in a 39-year-old male who underwent omega gastric bypass and severe PEI (FE 15 μg/g) in a 52-year-old female following RYGB. Serum nutritional markers were low in both patients **(Table 3)**. MRI/MRCP showed normal pancreatic parenchyma in the first (male) patient and mild atrophic changes with intraductal papillary mucinous neoplasm (IPMN) of size 8.7 × 3.8 mm in the second (female) patient. She was transferred to the outpatient surgical clinic for further work-up.

DISCUSSION

The FE1 level was low in two (9.1 %) patients, suggesting that PEI as a result of pancreaticocibal asynchrony is possible in patients after bariatric surgery.

Additionally, the clinical significance of PEI was assessed in this study using a complete laboratory serum nutritional panel. None of the PEI positive patients had typical symptoms, such as abdominal pain, bloating, steatorrhoea and weight loss, which are traditionally the most important criteria for diagnosis and monitoring of treatment success. At least one serological nutritional marker was below the lower limit of normal in all of the tested patients **(Table 2)**. MRI/MRCP was performed in both patients with PEI, and no diagnostic criteria for morphological changes related to chronic pancreatitis were found. In the female patient, a side-duct IPMN of the pancreas was found, but the size of the finding was relatively small (8.7 x 3.8 mm) and is unlikely to cause such severe PEI.

The main limitation of the study is the small number of patients. We are presenting the results of a pilot study. Nevertheless, according to the first results, we can conclude that PEI is present in patients after bariatric surgery and a possible connection between pancreaticocibal asynchrony and PEI should be determined. Unfortunately, FE1 was not tested in patients before the operation.

Additionally, the use of FE1 as a diagnostic tool could also be a limiting factor because of its lower sensitivity to mild and moderate PEI [10, 11, 12, 13, 14]. Secretin magnetic retrograde cholangiopancreatography (sMRCP), which is currently used for evaluation of pancreatic exocrine function in clinical practice in some countries,

Table 1: Weight outcome variables of patients included in the study.

Parameter	Average	Minimum	Maximum	Standard Deviation
BMI pre-surgery	42.5	34.9	49.1	4
BMI present	27.4	23.1	34.6	3.2
Pre-surgery weight (kg)	119.5	97	149	15
Lowest post-surgical weight (kg)	76.7	63	100	9.6
Total weight loss (kg)	42.8	23	63	10.7

BMI body mass index

Table 2: Laboratory measurements of patients included in the study.

Parameter	Below Lower Limit of Normal n (%)
vitamin D	21 (95.4)
vitamin A	1 (4.5)
vitamin E	0 (0)
selenium	5 (22.7)
prealbumin	5 (22.7)
zinc	5 (22.7)
manganese	0 (0)
copper	1 (4.5%)
vitamin B12	0 (0)
folic acid	3 (13.6)
iron	7 (31.8)
ionized calcium	0 (0)
magnesium	0 (0)
cholesterol	3 (13.6)

n number of patients; % percentage of patients

Reference Values (units): cholesterol3.9-5.2(mmol/L); copper11-26.7(μmol/L); folicacid7.0-39.7(nmol(L); ionizedcalcium1.13-1.32(mmol/L); iron10.7-28.6(μmol/L); magnesium0.65-1.05(mmol/L); manganese3-21(μg/L); prealbumin0.2-0.4(g/L); selenium55-101(μg/L); vitaminA1.05-2.8(μmol/L); vitaminB12160.0-800.0(pg/mL); vitaminD65-165(nmol/L); vitaminE12-42(μmol/L); zinc10-19.7(μmol/L)

Table 3: Characteristics of patients with pancreatic exocrine insufficiency.

Number of patient	1	2
Age (years)	39	52
Faecal elastase level (μg/g)	191	15
Gender	male	female
Nutritional deficiencies	vitamin D, selenium	vitamin D, iron
Post-surgery BMI	24.6	30.9
Post-surgery weight (kg)	78	84
Pre-surgery BMI	39.5	45.2
Pre-surgery weight (kg)	125	123
Total weight loss (kg)	47	39

BMI body mass index; kg kilogram

could be useful for a definitive determination of pancreatic morphology and exocrine function in this group of patients [17, 18].

Standard postoperative vitamin D doses of 1000 U/day seem to be insufficient to achieve normal values.

In summary, PEI determined by FE was found in two patients after bariatric surgery.

CONCLUSIONS

Our results show that exocrine pancreatic function could be impaired in patients after bariatric surgery, which could be an additional cause of malabsorption in this group of patients.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Contributors: VM and TB designed the study and drafted the manuscript; VM, KG, BB, RB, KA recruited the patients; RS performed magnetic resonance imaging, VM, TB, KG, BB, RS wrote the manuscript, KA recruited the patients and collected the data. All authors approved the final version.

Ethics approval: National Medical Ethics Committee of the Republic of Slovenia (No. 157/02/12 of 26 March 2012).

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