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Exocrine pancreatic insufficiency after bariatric surgery: a bariatric surgery center of excellence experience

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Abstract

Introduction Gastrointestinal symptoms such as diarrhea, bloating, abdominal pain, and nausea are common after bariatric surgery (BS) and can lead to significant morbidity. While many diagnoses can explain these symptoms, post-bariatric exocrine pancreatic insufficiency (EPI) is becoming increasingly recognized as contributor to gastrointestinal symptoms. The frequency and outcomes of EPI after BS are not well understood. We investigated the prevalence and outcomes of EPI over 18 years at a tertiary bariatric referral center.

Methods A retrospective review of patients who underwent primary or revisional BS from 2002 to 2020 was performed. Patients were included if they were suspected of having EPI or underwent fecal elastase testing (FE-1). EPI diagnosis was defined as positive FE-1 testing or improvement with empiric pancreatic enzyme replacement therapy (PERT).

Results EPI was suspected in 261 patients, and 190 were tested via FE-1 (89.5%) or empirically treated (10.5%). EPI was diagnosed in 79 (41.6%) patients and was associated with older age and lower BMI. Therapeutic PERT was given to 65 patients diagnosed with EPI, and 56 (86.2%) patients reported improved symptoms. Patients who underwent RYGB and BPD-DS were more likely to have EPI than those after SG (47.9% and 70.0% vs 17.4%, $p < 0.01$). EPI diagnosis was associated with a history chronic pancreatitis. While diarrhea and abdominal pain were the most common symptoms prompting FE-1 testing, no symptoms were significantly associated with EPI. EPI was also associated with abnormal fecal fat results and treatment with bile acid sequestrants, but not small intestinal bacterial overgrowth.

Conclusion This study highlights that exocrine pancreatic insufficiency can account to for previously unexplained GI complaints after bariatric surgery. Therefore, bariatric surgery programs should consider this diagnosis in symptomatic patients, especially following RYGB and BPD-DS. Further work to define patient factors that should prompt evaluation, optimal treatment, and prevention is necessary.

Keywords Exocrine pancreatic insufficiency · Bariatric surgery · Roux-en-Y gastric bypass · Pancreatic enzyme replacement therapy · Small intestinal bacterial overgrowth

Bariatric surgery (BS) is an important and effective tool against the rising prevalence of obesity [1]. While BS effectively treats and resolves many obesity-related medical conditions, it also improves gastrointestinal (GI) symptoms such as gastroesophageal reflux, nausea, bloating, flatulence, diarrhea, constipation, and abdominal pain [2–4]. Despite these benefits, a subset of patients (0–46%) can develop GI symptoms that, in some cases, can decrease quality of life and can be associated with malnutrition [5–8]. These symptoms tend to occur more commonly after Roux-en-Y gastric bypass (RYGB) or biliopancreatic diversion with duodenal switch (BPD-DS) compared to sleeve gastrectomy (SG) or adjustable gastric banding (AGB) [8–10].

Many patients experience GI symptoms after bariatric surgery. When symptoms are abnormal, a significant proportion can be attributed to dietary choices and maladaptive eating habits [11]. However, several reversible and

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less commonly explored causes of these symptoms include exocrine pancreatic insufficiency (EPI), clostridium difficile infection, small intestinal bacterial overgrowth (SIBO), inflammatory bowel disease, dumping syndrome, and bile acid malabsorption [12–14].

EPI results from abnormal pancreatic enzyme activity either from insufficient production, activation, or early enzyme degradation, and can occur as a primary or secondary disorder [15–17]. This condition can lead to malabsorption, maldigestion (diarrhea, steatorrhea, flatulence, etc.) and vitamin deficiencies [17–19]. While typically seen as a sequela from chronic pancreatitis or pancreatic and gastric resections, EPI has more recently been recognized as cause of GI symptoms after bariatric surgery, especially after procedures such as RYGB and BPD-DS [6, 8–10]. EPI is diagnosed by various direct and indirect methods, each with its advantages and disadvantages. Fecal elastase testing (FE-1) is the most common screening test for EPI, because it is the simplest, least expensive, and most reliable assay currently performed [20–23].

Post-bariatric EPI is thought to be multifactorial. Bariatric surgery alters GI tract anatomy and affects multiple neurohormonal signaling pathways, such as cholecystokinin which is responsible for pancreatic enzyme release. [24–26]. Little data exist on the prevalence, efficacy of treatment, or standardized management of EPI after BS. To date, only a few studies have attempted to identify patient characteristics, comorbid GI conditions, or symptoms that may predict the occurrence of EPI after BS [12, 13, 27]. Symptoms of EPI in patients who have undergone BS can be similar to known post-bariatric surgery sequelae, such as steatorrhea, weight loss, maldigestion, and malabsorption. Additionally, little is understood about the overlap between EPI and other GI disturbances such as SIBO in patients who have had BS. We report post-bariatric EPI as a cause of GI symptoms after BS, risk factors contributing to EPI diagnosis, and treatment outcomes.

Methods

A retrospective chart review of patients who received post-BS care at our institution from 2002 to 2020 was performed. This included patients who underwent primary bariatric surgery (including RYGB, SG, and AGB) at our institution as well as patients who underwent bariatric surgery (including RYGB, SG, AGB, BPD-DS, or jejunal-ileal bypass (JIB)) elsewhere. Patients who received their operation at our institution were identified through a quality improvement database AND were screened for possible EPI by electronic medical review for concurrent ICD codes for EPI, FE-1 testing, fecal fat testing, or treatment with pancreatic enzymes. Patients who received their operation elsewhere were included if they had both an ICD code indicating previous bariatric surgery AND were screened for possible EPI by electronic medical review for concurrent ICD codes for EPI, FE-1 testing, fecal fat testing, or treatment with pancreatic enzymes. A detailed review of all charts indicating concern for EPI diagnosis based on the codes listed above was performed.

Demographic data, medical history, other GI comorbid conditions, symptoms prompting testing for EPI, laboratory results, treatment type, and treatment outcomes were collected on all patients suspected of EPI and entered into a secure REDCap database [28]. This detailed review was performed by two authors (A.C., T.P.) via a screening form created in REDCap to ensure methodologic stringency when documenting patient information, including symptoms of interest that are associated with EPI including diarrhea, abdominal pain, nausea, bloating, flatulence, and weight loss as well as symptom response to treatment. This broad list of symptoms was selected for our study based on their known association with EPI [15, 16, 19] and based on other studies examining EPI in bariatric populations [13, 29, 30].

While FE-1 testing is the most clinically available test for EPI, it has known limitations, particularly increased rates of false negative results with mild disease or in post-surgical patients. Thus, multiple studies have considered EPI diagnosis if patients with significant symptoms demonstrate improvement with pancreatic enzyme replacement therapy (PERT), even when FE-1 levels may be within normal range [5, 13, 15, 18, 19, 22, 31]. We therefore defined positive exocrine pancreatic insufficiency (EPI) diagnosis as positive FE-1 testing (FE-1 < 100 µg/g = severe; 200–100 µg/g = mild/moderate) or improvement of one or more symptoms with empiric pancreatic enzyme replacement therapy (PERT) based on best available data [5, 13, 15, 18, 19, 22, 31]. We defined negative EPI as FE-1 > 200 µg/g or no symptom improvement with empiric PERT for the purposes of this study. Results from fecal fat testing (spot collection, not 3-day collection), hydrogen breath testing (HBT) for SIBO, treatment and treatment response to antibiotics for SIBO or bile acid sequestrants (BAS) were also collected when available. Similarly, based on other studies, we defined abnormal fecal fat results as increased neutral or split products [32, 33] and positive SIBO diagnosis as positive or equivocal HBT results [34]. Improvement in symptoms was defined by improvement in one or more reported GI symptoms present prior to initiation of treatment. Chi-square and Fisher's exact tests were performed on the binary and categorical data while two-sample t-tests were performed on the continuous data.

Results

EPI was suspected in 261 patients (202 after RYGB, 34 after SG, 15 after AGB and 10 after BPD-DS or JIB), and 190 patients ultimately underwent work-up for EPI via FE-1 testing (89.5%, $n=170$) or empiric treatment (10.5%, $n=20$) (Fig. 1). The median time from surgery to EPI diagnosis was 9.46 years with an interquartile range (IQR) of 11.4 years.

Patients suspected of having EPI were predominantly women (86.6%), and Caucasian (73.6%), with mean age of diagnosis at 57 ± 10.65 years. Older age ($p=0.014$), lower BMI at the time of evaluation ($p=0.020$), and greater change in BMI from the date of bariatric surgery to EPI diagnosis ($p<0.01$) were significantly associated with positive EPI diagnosis. Sex, race, ethnicity, smoking status, and alcohol use were not associated with EPI diagnosis. For demographic details see Table 1.

EPI was diagnosed in 41.6% (79/190) of patients who underwent work-up based on positive FE-1 testing or symptom improvement after empiric PERT (Table 2, Fig. 1). Of those with EPI, most patients had prior RYGB (86.1%, 68), while the remaining had BPD-DS/JIB (8.9%, 7) or SG (6.3%, 5). No patients with AGB were diagnosed with EPI by FE-1 testing or empiric treatment with pancreatic enzymes (Table 2). Patients who had RYGB ($p=0.003$) or BPD-DS ($p=0.0003$) were more likely to be diagnosed with EPI than those who had SG (47.9% RGYB, 70.0% DS/JIB vs 17.4% SG, Table 2). Though 79 patients were diagnosed with EPI, not all patients who had positive FE-1 testing received treatment. Therapeutic PERT was given to

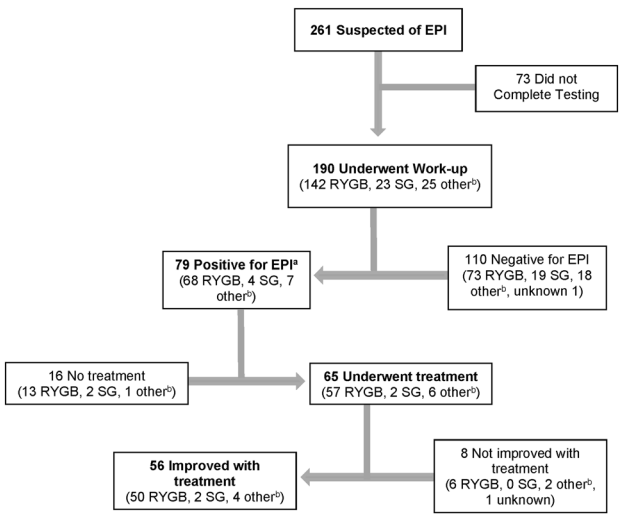

Fig. 1 Patient selection and outcomes. *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *AGB* adjustable gastric banding, *BPD-DS* biliopancreatic diversion-duodenal switch, *JIB* jejunoileal bypass, *EPI* exocrine pancreatic insufficiency, *FE-1* fecal elastase, *PERT* pancreatic enzyme replacement therapy

65 of the patients diagnosed with EPI (82.3%) and 86.2% of those treated had symptom improvement (Table 2). Of the 8 patients diagnosed with EPI whose symptoms did not improve with PERT, 6 had RYGB and 2 had BPD-DS. Four patients had RYGB performed at our institution, with creation of a 150 cm Roux limb; the operative details and limb lengths were unknown in patients who had surgery elsewhere. Thus, it is unclear whether operative anatomy may have contributed to their symptoms. All 8 patients had additional work-up for their symptoms including fecal fat testing (4/8), a trial of BAS treatment (7/8), or HBT (6/8). In total, 3 patients had improvement with BAS, 2 were treated with antibiotics for SIBO but only 2 had improvement.

The most common symptoms that prompted testing included: diarrhea (85.8%), abdominal pain (46.7%), nausea (27.6%), and bloating (13.0%). Bloating was the only symptom associated with EPI diagnosis ($p=0.011$; Fig. 2). We further examined the number of symptoms experienced by each patient and whether specific symptoms tended to improve with PERT. We found that 35.7% had one, 26.8% had two, 32.1% had three, and 5.4% had four symptoms. Of all patients, 55.4% had improvement of all symptoms and 71.4% had 50% or more of their symptoms improve. Examining response of specific symptom to PERT, patients were significantly more likely to have improvement of diarrhea (92%, $p<0.01$) abdominal pain (46%, $p=0.01$), and nausea (61%, $p=0.01$) compared to other symptoms (Fig. 3).

To examine whether clinical factors predisposed to EPI diagnosis, we then examined GI comorbidities and symptoms prompting EPI work-up, which were available for 94.6% (247/261) of our cohort. Of the GI comorbid conditions evaluated, chronic pancreatitis was found to be significantly associated with EPI diagnosis ($p=0.018$) (Fig. 4); no other GI comorbidities correlated with EPI diagnosis.

Most patients (82.6%) who underwent EPI workup also underwent fecal fat testing as a general measure of fat malabsorption. Patients diagnosed with EPI were more likely to have an abnormal fecal fat result (59.4% vs 37.1%, $p=0.004$) than those not diagnosed with EPI (Table 3). Concurrent work-up for SIBO with EPI was common (73.5%). SIBO was diagnosed in 40.1% of patients based on HBT, and in total 42.6% received empiric or therapeutic antibiotics. Treatment response was available for 42 of 49 patients who received antibiotics, and 65.9% had improvement of symptoms. EPI diagnosis was not associated with SIBO work-up, diagnosis, or treatment outcomes (Table 3).

Lastly, we examined frequency and efficacy of other treatment modalities for GI symptoms in 48 patients with EPI, namely bile acid sequestrants (BAS) for bile acid malabsorption-related diarrhea, malabsorption, or functional diarrhea (Table 3) [35, 36]. Patients diagnosed with EPI were more likely to receive BAS than those without EPI (33.3% vs 18.7%, $p=0.020$). Symptom response to BAS was available

Table 1 Patient cohort demographics by EPI suspicion and diagnosis

Demographics	Total suspected of EPI $N=261$	EPI+ $n=79$ (30.3%)	EPI $n=182$ (69.7%)	p value
Age at testing				
Mean (SD)	57.35 ± 10.65	60.19 ± 8.81	56.24 ± 11.01	0.014*
BMI at testing				
Mean (SD)	33.25 ± 7.83	31.48 ± 6.82	33.92 ± 8.07	0.020*
Change in BMI				
Mean (SD)	10.97 ± 8.25	14.53 ± 8.13	9.94 ± 7.94	0.0004*
Gender, *N* (%)				
Male	35 (13.4)	13 (4.7)	22 (8.4)	0.341[a]
Female	226 (86.6)	66 (29.2)	160 (70.1)	
Race, *N* (%)				
White	192 (73.6)	58 (30.2)	134 (69.8)	
Black	30 (11.5)	13 (43.3)	17 (56.7)	0.123[a]
Other	39 (14.9)	8 (20.5)	31 (79.5)	
Ethnicity, *N* (%)				0.590[a]
Hispanic/Latino	26 (10.0)	6 (23.1)	20 (76.9)	
Not Hispanic/Latino	226 (86.5)	71 (31.4)	155 (68.6)	
Unknown	9 (3.4)	2 (22.2)	7 (77.8)	
Smoking history, *N* (%)				
Yes	15 (5.7)	5 (33.3)	10 (66.7)	0.776[b]
No	244 (93.5)	73 (29.9)	171 (70.1)	
Alcohol use, *N* (%)				
Yes	97 (37.2)	25 (25.8)	72 (74.2)	0.185[a]
No	160 (61.3)	55 (34.3)	105 (65.6)	

EPI exocrine pancreatic insufficiency, *SD* standard deviation, *BMI* body mass index

Statistics comparing EPI + vs EPI− groups:

*$p<0.05$

[a]Chi-square test

[b]Fisher's exact test

of 43 of 48 patients. There was no association between EPI diagnosis and symptom improvement from BAS: 67.9% with EPI vs 66.7% without EPI ($p=0.96$). Of patients given both PERT and BAS ($n=25$), 48% reported symptom improvement after both treatments. Patients who improved with PERT were more likely to respond to BAS (70.6%) than those who did not improve with PERT (37.5%), but this was not significant ($p=0.194$).

Discussion

Gastrointestinal complaints are common after bariatric surgery and can lead to significant morbidity. Though previously associated with post-bariatric GI symptoms, EPI remains an underreported and undertested diagnosis. We investigated the rates of EPI after BS and its association with patient characteristics, GI comorbidities, clinical presentation, and surgery type to better understand its frequency and risk factors. Almost half of patients with suspicious GI symptoms were diagnosed with EPI and over 80% of patients with diagnosed EPI improved with PERT. Thus, our study highlights EPI as a common cause of post bariatric GI symptoms that can be diagnosed and effectively treated.

In our population, patients with a lower BMI were more likely to be diagnosed with EPI. It is unclear if this association is due to malabsorption from pancreatic insufficiency leading to excessive weight loss and malnutrition, or an inherent risk factor of EPI in lower BMI categories. Ozmen et al. found that excess weight loss (EWL) was associated with lower FE-1 levels, but this may be cofounded by the fact that EWL and FE-1 correlated with surgery type (SG, one anastomosis gastric bypass, and single anastomosis duodenal switch). Furthermore PERT therapy did not affect weight loss but did improve vitamin D deficiencies, implying that EPI itself may not be responsible for the discrepancy in weight loss [30].

Table 2 Clinical work-up of patients suspected of EPI by type of surgery

Variable	All $N=261$	RYGB $n=202$ (77.4%)	SG $n=34$ (12.9%)	AGB $n=15$ (5.7%)	BPD-DS/JIB $n=10$ (3.8%)	p value
No testing performed, N (%)	73 (27.9)	62 (30.5)	11 (32.4)	0 (0)	0 (0)	
Underwent EPI work-up, N (%)	190 (72.8)	142 (70.3)	23 (67.6)	15 (100)	10 (100)	
FE-1 testing, N (%)[a]	170 (89.5)	128 (63.4)	21 (61.8)	13 (86.7)	8 (80.0)	
Positive FE-1[b]	67 (39.4)	61 (47.7)	2 (9.5)	0 (0)	4 (50)	
Negative FE-1[b]	103 (60.5)	67 (52.3)	19 (90.5)	13 (100)	4 (50)	
Empiric PERT, N (%)[a]	20 (10.5)	14 (9.9)	2 (5.9)	1 (6.7)	3 (30.0)	
Improved[c]	12 (60)	7 (50)	2 (100)	0 (0)	3 (100)	
Not improved[c]	7 (35)	6 (42.9)	0 (0)	1 (100)	0 (0)	
Total diagnosed with EPI, N (%)[a]	79 (41.6)	68 (47.9)[d]	4 (17.4)	0 (0)[e]	7 (70)[f]	0.003[d^]*, 0.54[e#], 0.0003[f^]*
Given PERT, N (%)	65	57	2	0	6	
Improved w/PERT	56 (86.2)	50 (87.7)	2 (100)	0 (0)	4 (57.1)	g
Not improved w/PERT	8 (12.3)	6 (10.5)	0 (0)	0 (0)	3 (42.9)	

EPI exocrine pancreatic insufficiency, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *AGB* adjustable gastric banding, *BPD-DS* biliopancreatic diversion-duodenal switch, *JIB* jejunoileal bypass, *FE-1* fecal elastase, *PERT* pancreatic enzyme replacement therapy

*$p<0.05$

[a]Percentages out of those who underwent EPI workup

[b]Percentages out of those who underwent FE-1 testing

[c]Percentages out of those who underwent Empiric PERT

[d]RYGB vs SG

[e]AGB vs SG,

[f]BPD-DS/JIB vs SG

[g]Analysis not performed due to sparse data

[^]Chi-square test

[#]Fisher's exact test

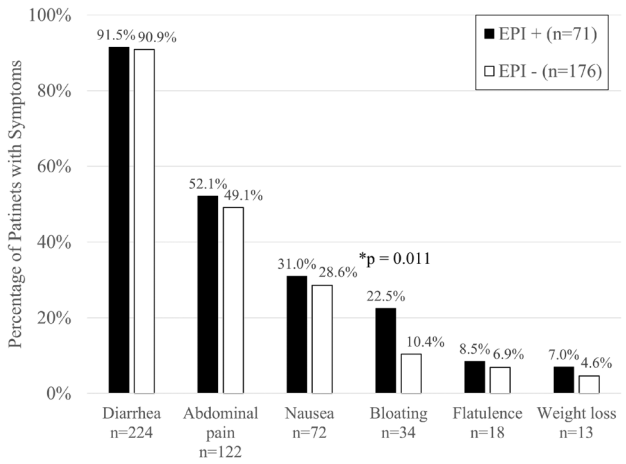

Fig. 2 Symptom frequency by EPI diagnosis. *$p<0.05$. *EPI* exocrine pancreatic insufficiency

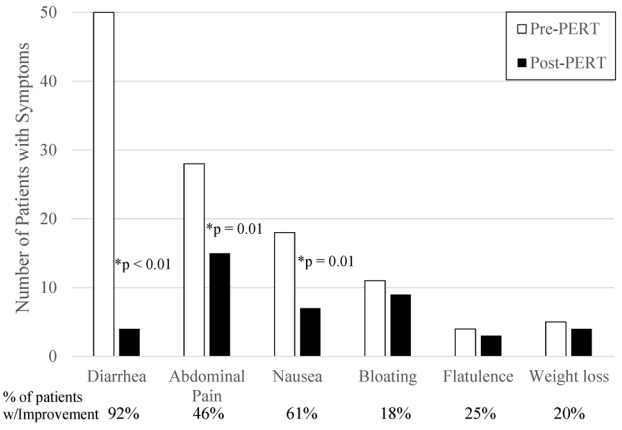

Fig. 3 Specific symptom response to PERT. *$p<0.05$. *PERT* pancreatic enzyme replacement therapy

Like prior studies, our study shows that surgery type is a predictor for EPI after BS. Of symptomatic patients, almost 50% of RYGB patients and 70% of BPD-DS patients were diagnosed with and treated for EPI. It is well known that gastric resections can result in EPI, but this has not been thoroughly evaluated in the bariatric population. In the sparse literature, studies report EPI rates between 8 and 48% after RYGB, 75% after BPD-DS and only 4% after SG [12, 13]. Patients with a history of bypass have similar

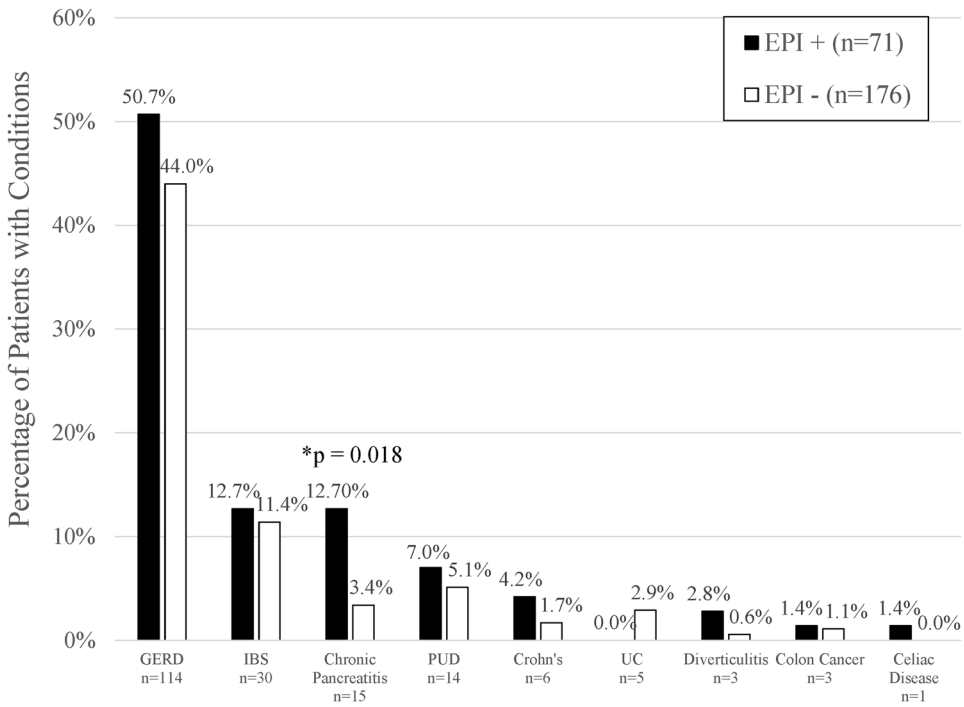

Fig. 4 Gastrointestinal comorbid conditions by EPI diagnosis. *$p < 0.05$. *EPI* exocrine pancreatic insufficiency, *GERD* gastroesophageal reflux disease, *IBS* irritable bowel syndrome, *PUD* peptic ulcer disease, *UC* ulcerative colitis

Table 3 Work-up and treatment of other gastrointestinal diagnoses by EPI diagnosis

	Total	EPI+	EPI−	*p* value
Underwent FF testing, *N* (%)	157/190 (82.6)	68/83 (81.9)	90/107 (84.1)	0.69[a]
Abnormal FF results	74/158 (45.0)	41/69 (59.4)	33/89 (37.1)	0.004[a*]
Work-up for SIBO, *N* (%)	72/98 (73.5)	38/47 (80.9)	35/51 (68.1)	0.17[a]
Abnormal HBT	29/72 (40.1)	18/38 (47.4)	11/34 (32.4)	0.19[a]
Treated with antibiotics	49/115 (42.6)	24/54 (44.4)	25/61 (41.0)	0.71[a]
Improved with antibiotics	28/42 (65.9)	16/20 (80.0)	12/22 (54.5)	0.08[b]
Treated with BAS, *N* (%)	48/190 (25.2)	28/84 (33.3)	20/106 (18.7)	0.020[a*]
Improved with BAS	29/43 (67.4)	19/28 (67.9)	10/15 (66.7)	0.93[b]

EPI exocrine pancreatic insufficiency, *FF* fecal fat, *SIBO* small intestinal bacterial overgrowth, *BAS* bile acid sequestrants

Statistics comparing EPI+ vs EPI− groups

*$p < 0.05$

[a]Chi-Square test

[b]Fisher's exact test

gastric loss, alteration of critical neurohormonal control mechanisms, and decreased contact time between food and released enzymes critical for digestion and absorption of nutrients. In 2016, Borberly et al. found that distal RYGB with longer biliopancreatic limbs and shorter common channels were associated with higher rates of EPI (48 vs 19%) [13]. These findings suggest that decreased contact time between ingested food and pancreatic enzymes may play a significant role in the development of EPI after BS. This mechanism could explain why few patients with SG had EPI. Bariatric surgery also has profound effects on the release of all gastrointestinal hormones, such as cholecystokinin and pancreatic polypeptide, [25, 37] that regulate pancreatic exocrine function. Additionally, postprandial asynchrony of pancreatic enzyme release with nutrient intake is thought to increase intraluminal destruction of pancreatic enzymes, leading to reduced digestion and absorption [5, 38]. Further studies into the exact mechanism behind development of EPI after BS is warranted.

While diarrhea was the most common symptom in our cohort, no specific symptom was associated with or predictive of EPI diagnosis. The lack of use of a standardized GI questionnaire to elicit specific GI symptoms and track improvement call for a more standardized review of

symptoms that could be predictive of EPI in the future. To counter this, identified patients were evaluated and worked-up by either the gastroenterology department or the bariatric surgery department with detailed notes focusing specifically on GI complaints. Those who received surgery at our institution received follow-up at regular intervals with longstanding advance practice providers who use a systematic method to screen for symptoms at regular intervals after surgery (2, 6, and 12 months and annually thereafter). A detailed chart review was completed by two authors using a standardized REDCap screening questionnaire to ensure detailed documentation of specific symptoms when reviewing patient medical records. In the future, determining the presence of steatorrhea, undigested foods, and other findings specific to malabsorption may be a more important predictor than diarrhea itself and should be further investigated. Standardized GI questionnaires should also be utilized to ensure a more objective assessment of GI symptom frequency and degree of improvement after treatment initiation.

The differential of patients who present with GI complaints after bariatric surgery is broad (EPI, infection, bile acid malabsorption, SIBO, autoimmune disease, cancer, etc.) and symptoms are often vague and similar across diagnoses. Given this, many of our patients underwent concurrent work-up for SIBO and fat malabsorption. Fecal fat testing can diagnose malabsorption by detecting steatorrhea but does not specifically diagnose EPI or bile acid malabsorption. Not surprisingly, patients diagnosed with EPI were more likely to have an abnormal result than those without EPI. Of patients with GI symptoms to suggest EPI, 40% were diagnosed with SIBO, with more than 47% with EPI having SIBO, indicating that concurrent disease processes are common. EPI patients were also more likely to be treated with BAS than those without EPI, but were not more likely to improve with BAS treatment when given in addition to PERT. These findings are difficult to interpret given overlap in symptoms and treatment with multiple patients taking PERT and BAS during the same interval reporting varying degrees of improvement after treatment. Additionally, testing for malabsorption and its etiology has variable reliability which further complicates diagnosis and treatment of GI complaints after BS. Meaningful and accurate fecal fat testing requires cessation of PERT, and inconvenient 3-day stool collection with strict requirements of high fat intake often not achievable for bariatric patients [39]. While we found no association between EPI and SIBO, this may just be a limitation of our sample size. The relationship between these diagnoses should be further investigated to assist with diagnostic and treatment accuracy. We have proposed a work-up and treatment algorithm for patients with GI symptoms following bariatric surgery that encompass the broad differential (Fig. 5). This and other algorithms suggested for post-bariatric diarrhea by Sollier et al. [5] may be useful in such complex patients.

EPI is diagnosed by various direct and indirect methods including secretin stimulation tests, secretin-pancreozymin test (gold standard but not clinically available), quantification of the coefficient of fat absorption via 72-h fecal fat determination (CFA), mixed C-triglyceride (C-MTG) breath test, and fecal elastase testing (FE-1) [19, 20, 23, 40–43]. All have their limitations including price, inconvenience, unavailability, and inaccuracy depending on dietary intake. Fecal elastase testing is simple, fast, inexpensive and does not require patients to alter diet or stop treatment but its accuracy, especially in mild to moderate disease, can be unreliable with high false negative rates [15, 44]. FE-1 testing specifically evaluates the amount of elastase in stool but this does not account for time in contact with nutrients and thus can underdiagnose EPI in patients with a history of intestinal bypass [44]. As a result, clinicians will often treat patients despite normal FE-1 or empirically treat for EPI without testing [19, 20, 23, 40–42], which is why we included both positive FE-1 and improvement with PERT as criteria for diagnosis.

Our findings are limited by several factors including sample size and retrospective nature. We recognize maladaptive eating habits are often a factor in patients' symptomatology [5, 45]. It is essential that patients undergo detailed investigation of their diet as part of initial work-up for GI complaints. While the patients who received surgery at our institution had detailed follow-up of their dietary history of GI symptoms, 41% of patients were not part of the institution's program and many lacked follow-up by dieticians. Thus, we chose not to include dietary history as part of this study which limits the results. The chosen definition of EPI diagnosis based on FE-1 testing and its inherent limitations may also underdiagnose its frequency. We acknowledge that including improvement with empiric PERT as criteria for EPI diagnosis to account for FE-1 testing inaccuracy in post-surgical patients introduces possible confounding bias, particularly when a standardized symptom questionnaire was not used pre- and post-treatment. This could lead to overdiagnosis or inaccurate diagnosis. Additionally, there may be patients who have EPI with normal FE-1 levels or who did not undergo testing, but failed to response to empiric PERT, who also may have been false negatives. However, these limitations would be in other studies using these definitions, which are common [19, 20, 23, 40–42]. While this is a retrospective study with symptom and comorbidity data missing in 5.3% of the patients, we had rich symptom and clinical data on a large sample size, larger in comparison to previous studies [13, 30, 46]. More detailed information like the character of diarrhea and long-term follow-up of treatment response is also lacking and should be further investigated. Surgical details such as the length of the common channel

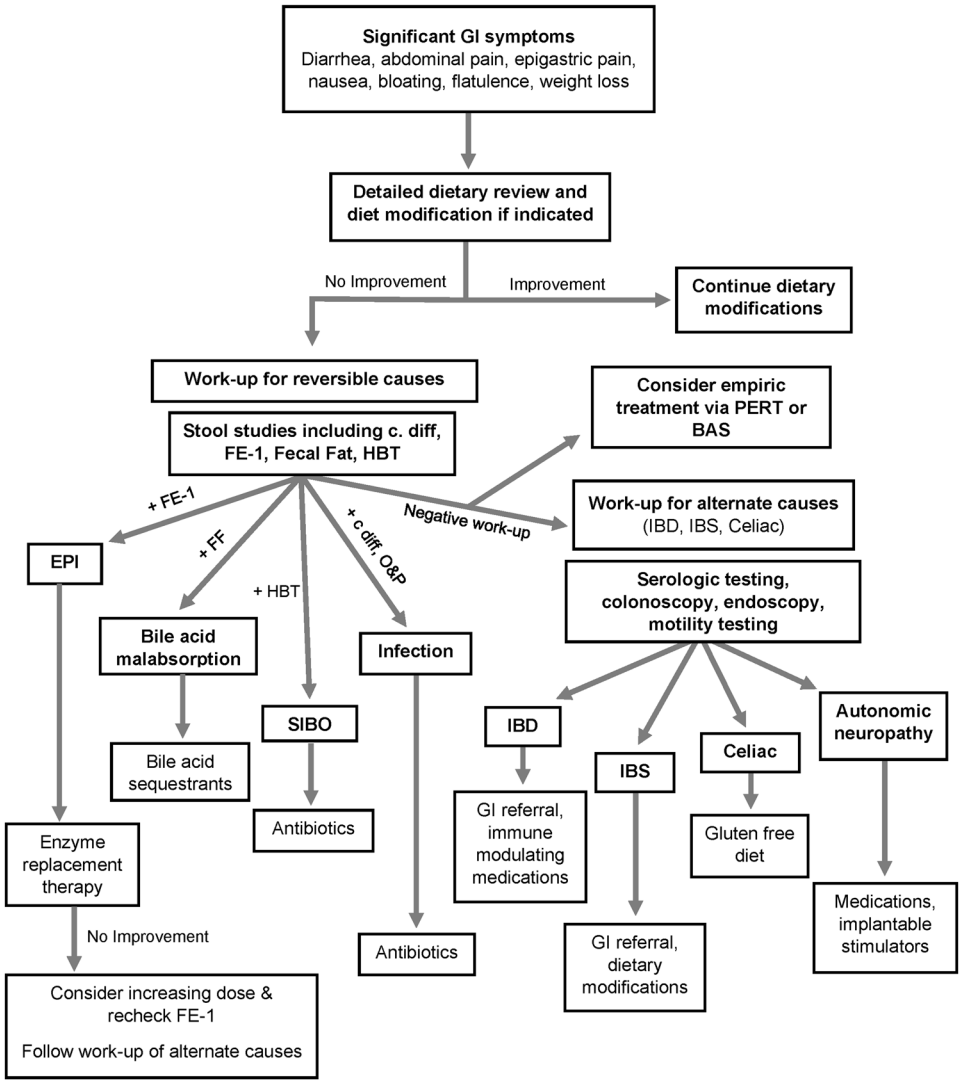

Fig. 5 Algorithm for evaluation of post-bariatric gastrointestinal symptoms. *FE-1* fecal elastase, *HBT* hydrogen breath test, *PERT* pancreatic enzyme replacement therapy, *FF* fecal fat, *BAS* bile acid sequestrants, *EPI* exocrine pancreatic insufficiency, *SIBO* small intestinal bacterial overgrowth, *O&P* ova and parasites, *IBD* inflammatory bowel disease, *IBS* irritable bowel disease

were difficult to obtain in patients who had their operation and another institution and may have provided better diagnostic information as it has been identified as an important factor in the development of EPI.

Clinicians should have a high index of suspicion for EPI in post-bariatric patients with significant GI symptoms, especially in those who have undergone anatomic bypass such as RYGB, BPD-DS, or JIB. A low threshold for empiric treatment can improve quality of life and ameliorate symptoms.

In conclusion, exocrine pancreatic insufficiency is common in patients who present with significant GI complaints after RYGB, BPD-DS, or JIB. EPI was more common in older patients with lower BMI but no symptoms or GI comorbid conditions except chronic pancreatitis were predictive of diagnosis. Our data support that when GI symptoms are present, early work-up for EPI and concurrent GI diagnoses such as SIBO is warranted. Additionally, FE-1 testing and/or treating with PERT is relatively non-invasive and can potentially address GI symptoms early to reduce patient morbidity. Further work to identify specific risk factors and characterize symptom constellation specific to EPI is necessary to identify high risk populations and allow for prevention and early treatment.

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Declarations

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