

# World Journal of *Gastroenterology*

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## Diarrhea after bariatric procedures: Diagnosis and therapy

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### Abstract

Diarrhea after bariatric procedures, mainly those with malabsorptive elements including Roux-Y Gastric

Bypass and Biliopancreatic Diversion, is common and an essential determinant of quality of life and micro- and macronutrient deficiencies. Bariatric surgery is the only sustainably successful method to address morbid obesity and its comorbidities, particularly gaining more and more importance in the specific treatment of diabetic patients. Approximately half a million procedures are annually performed around the world, with numbers expected to rise drastically in the near future. A multitude of factors exert their influence on bowel habits; preoperative comorbidities and procedure-related aspects are intertwined with postoperative nutritional habits. Diagnosis may be challenging owing to the characteristics of post-bariatric surgery anatomy with hindered accessibility of excluded segments of the small bowel and restriction at the gastric level. Conventional testing measures, if available, generally yield low accuracy and are usually not validated in this specific population. Limited trials of empiric treatment are a practical alternative and oftentimes an indispensable part of the diagnostic process. This review provides an overview of causes for chronic post-bariatric surgery diarrhea and details the particularities of its diagnosis and treatment in this specific patient population. Topics of current interest such as the impact of gut microbiota and the influence of bile acids on morbid obesity and especially their role in diarrhea are highlighted in order to provide a better understanding of the specific problems and chances of future treatment in post-bariatric surgery patients.

**Key words:** Bariatric surgery; Diarrhea; Malnutrition; Malabsorption; Steatorrhea; Dumping syndrome; Bile acids and salts; Gut microbiota; Blind loop syndrome

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**Core tip:** Bariatric surgery is the only sustainable therapy for morbid obesity and its comorbidities. Postoperative diarrhea is common and an essential determinant of quality of life and micro- and macro-

nutrient deficiencies. The distinctive anatomic changes after bariatric procedures with exclusion of various length of small bowel have a severe impact not only on diagnostic but also puts limits on therapeutic means. This review provides an overview of causes for chronic diarrhea in the particular context of post-bariatric patients, and details specific problems in diagnosis and treatment of this challenging patient population.

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## INTRODUCTION

Bariatric surgery was demonstrated to be the most efficacious method to achieve sustainable weight loss and resolution of co-morbidities among the morbidly obese. Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG) and to a lesser extent biliopancreatic diversion with duodenal switch (BPD-DS) are the most commonly applied procedures (Figure 1). Around 470000 bariatric procedures have been performed worldwide in 2013, with numbers expected to rise in the future as the threshold, currently at a body mass index of 35 kg/m<sup>2</sup>, will be lowered to 30 kg/m<sup>2</sup> in diabetic patients<sup>[1-4]</sup>. Weight loss is achieved by different mechanisms, all having various effects on bowel habits. The implied alterations of the anatomy not only affect the sensitivity and specificity of diagnostic procedures but also the pharmacodynamics and bioavailability of the used medication, potentially resulting in treatment failure<sup>[5]</sup>.

Bariatric surgery, especially BPD-DS and distal RYGB, leads to a significant change of bowel habits with enhanced frequency of malodorous flatus and diarrhea<sup>[6]</sup>. Diarrhea exposes patients at risk for fecal incontinence - up to 50% of patients after BPD-DS are affected - and has a major impact on Quality of Life as well as on nutrient and vitamin absorption<sup>[7-9]</sup>. In addition, morbid obesity per se, and in particular its associated comorbidities, broadens the spectrum of possible causes for diarrhea.

The goal of this review is to detail causes for chronic diarrhea in the specific post-bariatric surgery context, especially after RYGB, and to give a focused overview of its diagnosis and treatment, with the intention to depict the differences and difficulties compared to an evaluation for diarrhea in non-operated patients<sup>[10-12]</sup>. Reasons nonspecific for post-bariatric surgery patients, such as cancer-related diarrhea, are not covered, even though the incidence of cancer is higher in the bariatric than in the non-obese population<sup>[13]</sup>.

## EATING HABITS AND LIFESTYLE CHANGES

Bariatric surgery results in a radical change of life with lifestyle modifications eventually resulting in change of food preference, meal size and frequency. The imposed restriction, especially in the earlier postoperative period, leads to a more liquid diet with decreased fiber intake<sup>[14]</sup>. While adaptive processes towards a stable metabolism and energy intake take at least 1 year<sup>[15]</sup>, patients rarely benefit from an extensive evaluation prior to 6 mo postoperatively.

There are inconsistent data about postoperative food consumption, mainly because of self-reporting, incongruent assessment time points, changing food selection over time, and influence of nutritional counselling<sup>[16]</sup>. Overall energy intake is reduced after surgery; however, the proportion of fat, proteins and carbohydrates seems to remain constant<sup>[17]</sup>. In our practice, we observe an increased consumption of dietary and fat-reduced products in a purpose to eat "healthier". However, the use of non-absorbable sweeteners such as sorbitol in these products can lead to similar effects as carbohydrate malabsorption<sup>[18]</sup>.

## BARIATRIC PROCEDURES

### SG

Sleeve gastrectomy has become the most popular bariatric procedure in the last years. The greater curvature of the stomach is resected alongside a bougie preserving around 5 cm of antrum (Figure 1).

### Proximal and distal RYGB

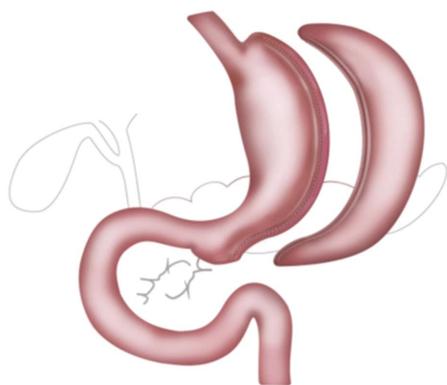
RYGB was the most popular procedure for years. A small gastric pouch is created followed by a pouch-jejunostomy, thereby forming an alimentary Roux-Y limb of up to 150 cm and a biliopancreatic limb of around 50 cm resulting in a common channel of various lengths depending on the length of whole small bowel. In distal RYGB, the length of the common channel, mostly around 100 cm, is the determined factor and the alimentary limb is of variable length (Figures 2 and 3).

### BPD-DS

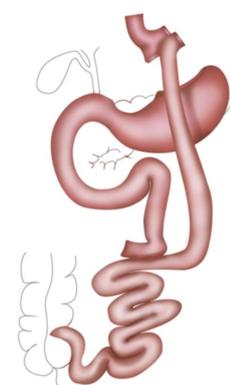
The gastric volume is reduced akin to a LSG but with a generally bigger bougie size. The duodenum is transected near the pylorus and a duodeno-jejunostomy is created to form a common channel of around 80 cm.

### Adjustable gastric banding

Adjustable gastric banding (AGB) experienced a massive decline in the past decade due to a failure of long-term weight loss. Currently it is used almost exclusively concomitant to or after RYGB to reduce pouch extensibility. Apart from vagotomy as intraoperative



**Figure 1 Laparoscopic sleeve gastrectomy.** The greater curve of the stomach is resected alongside a bougie.



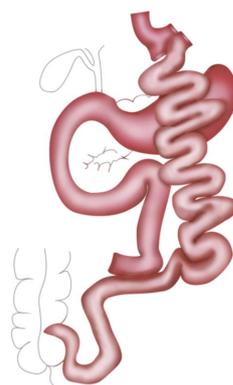
**Figure 2 Proximal Roux-Y gastric bypass.** The stomach is divided to form a small gastric pouch. Alimentary Roux-Y limbs of up to 150 cm and a biliopancreatic limbs of around 50 cm are formed; the resulting common channel is of various length depending on length of the whole small bowel.

complication, it has little influence on stool consistency, and when, patients rather tend to constipation<sup>[14]</sup>.

## BOWEL HABIT CHANGES AFTER BARIATRIC SURGERY

There is a consistent relationship between obesity and diarrhea<sup>[19]</sup>. The incidence of diarrhea in a preoperative bariatric population is around 8%<sup>[20]</sup>, being twice as high as in lean people. A possible reason for this might be a higher intake of poorly absorbed sugars<sup>[21]</sup>. Indeed, digestive symptoms in general, including diarrhea, are frequent among obese patients, both before and after bariatric surgery<sup>[22,23]</sup>.

There is a change of bowel habits after every bariatric procedure, even though the severity of symptoms differs between the individual techniques. Up to 75% of patients suffer from alterations of bowel habits and faecal transit time after RYGB<sup>[20]</sup>. Diarrhea is a common symptom after RYGB<sup>[6,20,24]</sup>, and usual after BPD<sup>[14,25]</sup>. Length of the common channel, *i.e.*, the amount of absorptive surface, seems to play a role, given the higher frequency of diarrhea in long limb/distal RYGB patients than after short limb/proximal



**Figure 3 Distal Roux-Y gastric bypass.** The same principles as in proximal RYGB are applied; however, the length of the common channel, mostly around 100 cm, is the determined factor and the alimentary limb is of variable length. RYGB: Distal Roux-Y gastric bypass.

RYGB procedures<sup>[26]</sup>, in BPD compared to RYGB<sup>[25]</sup>, and in BPD patients with shorter common channels<sup>[27]</sup>.

## SHORT BOWEL SYNDROME

Short bowel syndrome, defined by lack of absorptive surface, occurs in around 4% of patients after bariatric surgery<sup>[28]</sup>. The reported average small bowel length in obese patients ranges from 300 to 900 cm, with considerable variability between 230 cm and 1510 cm<sup>[29-31]</sup>. However, there is a remarkable intra- and interoperator variability when it comes to determination of bowel length, both in open and laparoscopic procedures<sup>[32,33]</sup>. In the most commonly performed technique, the proximal RYGB, only the lengths of the alimentary (AL) and the biliopancreatic limbs (BPL) are defined and counted through, whereas the common channel remains of variable, unknown size. While AL of 100-150 cm and BPL of 45-85 cm are commonly used<sup>[30,34,35]</sup>, there is ongoing debate about the delineation of optimal limb lengths. Nonetheless, this debate does not respect absorptive capacity of small bowel and even less its adaptation over time. Even though there is considerable progress in assessing intestinal malabsorption, no direct test with sufficient sensitivity and specificity is currently available, not to mention the diagnostic issues due to the altered anatomy after RYGB<sup>[36]</sup>. Initial treatment consists of supportive measures; surgical options are lengthening of the common channel, enteral nutrition via gastrostomy into the gastric remnant, and restitution of normal anatomy if still possible<sup>[37]</sup>. In the United States, 6.3% of home parenteral nutrition patients have a history of bariatric surgery and over two-thirds of them underwent RYGB<sup>[38]</sup>.

## MALABSORPTION OF CARBOHYDRATES (LACTOSE, FRUCTOSE)

Carbohydrates were propagated in a low-fat diet for

years; they have a good palatability and are readily available in a high-caloric liquid form<sup>[39]</sup>. Liquids transit rapidly through the intestine and produce lesser satiety than the solid form. Sugar-sweetened beverages have a considerable impact on body weight, and there is clear association between their consumption and weight gain<sup>[40,41]</sup>.

Even though a diet with a moderate amount of carbohydrates is recommended after bariatric surgery<sup>[42]</sup>, the proportion of ingested macronutrients - lipids, proteins and carbohydrates - remains constant, whereas the overall energy intake that is reduced<sup>[18]</sup>. Lack of the enzyme lactase in the intestinal mucosa leads to lactose malabsorption and intolerance with diarrhea. While symptoms are dependent on small bowel transit time, there is a poor correlation between lactose malabsorption and intolerance<sup>[18,43]</sup>. Lactase activity is diminished progressively in adulthood<sup>[44]</sup>, and the influence of bariatric surgery on this process is unclear<sup>[6]</sup>. Furthermore, there is no data on symptoms after bariatric surgery in a population of non-Western European heritage, *i.e.*, with a higher prevalence of lactase deficiency. On the other hand, a Scandinavian study found a lactose intolerance rate of 30% after jejunum-ileal bypass<sup>[45]</sup>.

Fructose as monosaccharide is widely used as a sweetener in fat-reduced, low-caloric food. In contrast to the disaccharide form, its glucose-independent absorption capacity is limited<sup>[46]</sup>. Hydrogen breath tests can be used in the diagnosis of carbohydrate malabsorption. However, 18% of patients of European descent are hydrogen non-excretors resulting in a possible false-negative result. Furthermore, the effect of excluded small bowel segments on the test accuracy has not yet been elucidated. Abstaining from or at least reducing lactose and fructose in meals might be most productive for both diagnosis and therapy, even though enzyme replacement therapies, as referred to as lactase and xylose isomerase, are available<sup>[18]</sup>.

## PROTEIN-LOSING ENTEROPATHY

Micronutrients are absorbed in the mid to distal jejunum<sup>[47]</sup>. BPD-DS and to a lesser extent distal RYGB exclude these segments and are associated with macro- and micronutrient deficiencies<sup>[9,48]</sup>. Hypoalbuminemia occurs in up to 18% of BPD-DS patients<sup>[49]</sup>, further aggravated by a protein intake of half of the recommended amount of 60-120 g protein daily in bariatric patients<sup>[47,50]</sup>. Hypoalbuminemia is associated with severe diarrhea in every fourth patient ending up with the need for parenteral nutrition<sup>[51]</sup>. The associated pathogenesis resembles the Kwashiorkor-type malabsorption of severely undernourished children resulting in a reduced production of gastric acid, pancreatic atrophy, small intestinal bowel overgrowth (SIBO) and alterations of the gut microbiota<sup>[52]</sup>. Treatment is usually initiated by employing supportive measures, rehydration and volume replacement,

together with parenteral feeding, akin to World Health Organization Treatment guidelines for children<sup>[53]</sup>. Alternatively, surgical measures, such as limb length reshaping and reversal of RYGB, may be considered.

## ENDOCRINE DISORDERS

Endocrine causes for diarrhea are rather related to morbid obesity and its comorbidities than to bariatric surgery. Ninety percent of patients with type 2 diabetes mellitus (T2DM) are overweight or obese<sup>[54]</sup>. Metabolic/ bariatric surgery, mainly RYGB, is gaining importance in the treatment of T2DM<sup>[4,55]</sup>. However, minimally symptomatic patients with T2DM may become symptomatic after RYGB. Furthermore, depending on preoperative duration and severity of T2DM, the relapse rate after a disease-free postoperative interval is reported to be up to 11%<sup>[56]</sup>. Several factors have an influence on diarrhea in T2DM-patients: dietetic, sugar-free food, association of T2DM to celiac disease<sup>[57]</sup>, and T2DM-induced disturbance of the enteric nerve system leading to altered gut motility, again resulting in SIBO and exocrine pancreatic insufficiency (EPI).

Loss of weight and fat volume after bariatric surgery<sup>[58]</sup> may require adaptation of drug apportioning otherwise leading to postoperative overdose, *e.g.*, of thyroid hormones. Thus, switch from LSG to LRYGB for gastroesophageal reflux disease requires monitoring despite absent weight change, as L-thyroxine is absorbed in the (partly excluded) small bowel<sup>[59]</sup>.

## MICROBIOTA AND SIBO

In human adults, the gut microbiota is a complex and dynamic ecosystem that coevolves with its host<sup>[60]</sup>, and remains remarkably constant slightly fluctuating around an individual core of stable colonisers. Low diversity of an individual's fecal bacteria is associated with a more pronounced overall obesity and dyslipidemia, impaired glucose homeostasis, and considerable low-grade inflammation<sup>[61]</sup>. Dietary changes, use of proton pump inhibitors or (recurrent as well as short- and long-term) antibiotic treatments may result in transient alterations of the gut microbiota composition<sup>[62,63]</sup>. It is still a matter of debate whether dietary intake or host genetics exert the stronger influence on microbial composition<sup>[64]</sup>. Not only development of obesity but also body weight reduction following bariatric surgery is, at least partly, attributed to alterations in gut microbiota. RYGB, as against SG, was demonstrated to substantially diminish the diversity of gut microbiota<sup>[65]</sup> paralleled by an increase in the proportion of Gammaproteobacteria and a decrease in Clostridia<sup>[66,67]</sup>. SG, however, was shown to cause a change in the Bacteroidetes/Firmicutes ratio, indeed, with a distinct increase in Bacteroidetes and a decline in the abundance of Firmicutes<sup>[68]</sup>. While the exact mechanisms remain unclear, change of the individual's microbiota composition is considered to be

a key factor of postoperative body weight reduction and may be one of the potential contributors to a stable weight loss after bariatric surgery<sup>[65,69]</sup>. Even though one would assume the importance of the microbiome regarding occurrence and/or resolution of diarrhea after bariatric surgery, this has not yet been elucidated. *Bacteroides*, normally increased after SG, was found to be substantially decreased in patients with idiopathic chronic diarrhea<sup>[70]</sup>. These results were confirmed by another group reporting an enrichment of *Bacteroides*, among other phyla, in controls when compared to diarrhea cases, irrespective of whether they were or not *Clostridium difficile*-associated<sup>[71]</sup>. These results cast a possible relationship between the normally observed post-bariatric shift of *Bacteroides* within the microbiota composition and diarrhea into doubt. Further studies addressing this question are warranted.

SIBO, defined as an excessive amount of bacteria in the small bowel<sup>[72]</sup>, has a prevalence of 2.5% in healthy subjects<sup>[73]</sup>, and up to 41% in obese patients, probably due to an impaired small intestinal motility<sup>[74]</sup>. In fact, side-side anastomoses with longer blind ends such as in candy cane syndrome are susceptible to SIBO<sup>[75,76]</sup>. A Brazilian group described a frequent occurrence of bacterial overgrowth in both the gastric pouch and the gastric remnant after RYGB in morbidly obese subjects, when assessed after a mean follow-up of 7.3 years<sup>[77]</sup>. These patients, however, did not complain of consistent or prolonged symptoms suggestive of SIBO, namely diarrhea, malabsorption, abdominal pain, intestinal obstruction, or extradigestive complaints (polyarthritides, dermatologic abnormalities, progressive liver insufficiency), after a mean follow-up of almost 15 years<sup>[78]</sup>. Another group reported a more than two-fold rise of SIBO after RYGB. Yet, weight loss itself does not seem to favor SIBO, given the comparable rate of bacterial overgrowth before and after exclusively restrictive surgery, such as AGB<sup>[23]</sup>. The influence of proton pump inhibitors, caloric intake and dietary composition is another topic of debate<sup>[23,79]</sup>. Diagnostic insecurities and a high prevalence of SIBO complicate the exact determination of its effects. In fact, it was shown that two thirds of patients after RYGB had digestive symptoms, but none of those were more frequent in patients with SIBO<sup>[23]</sup>. Consequences of SIBO after bariatric surgery are unclear. The nutrients escaping digestion in the small bowel due to SIBO might yield elevated levels of short- and medium-chain fatty acids through metabolization in the large bowel, implying a higher caloric uptake<sup>[80,81]</sup>. However, data on expected resulting reduced weight loss is conflicting<sup>[23,82]</sup>. The altered anatomy with excluded small bowel segments severely inflicts diagnostic measures; aspiration and culture might be impossible despite advanced endoscopic techniques, and breath testing underlies the same restrictions<sup>[83]</sup>.

## CLOSTRIDIUM DIFFICILE

Alteration of gastrointestinal climate caused by obesity, antibiotic therapy or surgery is a risk factor for *clostridium*-associated colitis<sup>[84]</sup>, even though it may occur in absence of the aforementioned factors<sup>[23]</sup>. Furthermore, it may present as a protein-losing enteropathy with hypoalbuminemia without fulminant inflammation<sup>[85]</sup>. Individual types of stool tests can yield the diagnosis. However, the high rate of asymptomatic carriers demands for a combination of symptoms and positive test results<sup>[84]</sup>. Treatment aims at reestablishing a diverse microbial flora. Long-standing medical wisdom suggested treatment with only oral antibiotics, metronidazole rather than vancomycin, and avoiding antimotility agents such as loperamid. The latter lacks substantive data<sup>[86]</sup>; the former must be questioned, at least in post-RYGB and -BPD-patients. In view of the anatomic alterations after bariatric surgery and given the pharmacokinetics of metronidazole - it is almost completely absorbed in the small bowel - intravenous vancomycin might be the preferred primary treatment option<sup>[87,88]</sup>. Fecal microbiota transplantation is a novel method to treat recurrent infections, and has also gained interest in the bariatric community due to its effects on weight loss<sup>[89]</sup>.

## ADDICTIVE DISORDERS

An "addiction-transfer" away from food may be an explanation for the increased number of impulse control disorders after bariatric surgery<sup>[90]</sup>; a quarter of the bariatric population has an eating disorder that impedes weight loss<sup>[91]</sup>. Amongst other substances, alcohol and nicotine both lead to diarrhea when consumed in excessive amounts<sup>[92]</sup>. Several cohort studies showed increased risk for alcohol abuse after bariatric surgery<sup>[93]</sup>, further complicated by a faster rise of blood alcohol concentration<sup>[94]</sup>. Preoperative history of substance misuse is associated with postoperative abuse, as for alcohol ranging up to 12%<sup>[95,96]</sup>. Furthermore, consumption of excessive amounts of (sugar-free) drops, sometimes with the purpose of covering halitosis, must be kept in mind.

## VAGOTOMY

Vagotomy during RYGB can be performed either intentionally to enhance weight loss *via* earlier satiety and lessened food intake<sup>[97,98]</sup>, as esophageal lengthening procedure concomitant to hiatal hernia repair<sup>[99]</sup> or inadvertently as intraoperative complication due to the proximity of the vagal nerves to the gastric pouch<sup>[100]</sup>. Diarrhea occurs in around 10% of patients after truncal and to a lesser extent after more distal vagotomy; severe, debilitating diarrhea occurs in 2%-3%<sup>[101]</sup>. Controversially, intentional vagotomy to

gain esophageal length in hiatal hernia repair did not lead to higher rates of side effects<sup>[98,99]</sup>. Reasons for postvagotomy diarrhea are not completely elucidated, a change of microbial climate by altered intestinal motility and gastric hypoacidity certainly plays a role<sup>[102]</sup>. Beneath the usual dietary modifications proposed for RYGB, bulking agents to decrease the water content of the stool should be introduced. A short-term trial with octreoid can be attempted, however, isolated postvagotomy diarrhea is less responsive than dumping syndrome. In severe cases, surgical options such as alteration of limb lengths or even reversal of RYGB should be discussed.

## BILE ACID MALABSORPTION

The role of bile acids in morbid obesity, its comorbidity and weight loss in post-bariatric patients experiences increased interest, as they seem to be profoundly involved in the postoperative metabolic improvement. The target of interest are FX- and TGR5-receptors and their influence on bile acid metabolism with subsequently increased hormonal - in particular incretine - answer and change of gut microbiota<sup>[103,104]</sup>.

Bile acid malabsorption results from a disturbed enterohepatic cycle and bile acid production. About 95% of bile acids are reabsorbed in the ileum, an additional small percentage is absorbed in the colon with bowel motility, medication, microbiota and food composition as influencing factors<sup>[105-107]</sup>. FXR is involved in the regulation of bile acid production, in entero- and hepatocytes<sup>[108]</sup>. BAM is categorized as either idiopathic, secondary to ileal dysfunction, such as after resection, or unrelated to ileal dysfunction, mainly due to SIBO or cholecystectomy. A disturbed synthesis in idiopathic BAM might also play role in irritable bowel syndrome (IBS)-D patients, same as in post-cholecystectomy patients<sup>[109]</sup>. Cholecystectomy concomitant to a bariatric procedure was a standard of care in the last decades<sup>[110]</sup>. BAM might further be a cause for post-vagotomy diarrhea<sup>[102]</sup>. The short common channel after BPD and distal RYGB predisposes to BAM due to reduced reabsorption rate and diminished time for bile acids to exert its effects on digestion. So far, there is no data about the rate of BAM stratified for subtypes of bariatric procedures. Bile acid malabsorption can be detected by fecal bile acid quantification, radio-labelled Selenium homotaurocholic acid testing or determination of serum-C4-concentration<sup>[111]</sup>; however, they all are expensive, rather difficult to apply in clinical practice or not standardized. Cholestyramine, a bile-acid binder, is an effective treatment with an efficacy up to 96%<sup>[112]</sup>. Due to the downsides of the above-mentioned testing procedures, it is used in diagnosis in an empirical trial<sup>[12]</sup>.

## EXOCRINE PANCREATIC INSUFFICIENCY

Gastrectomy and RYGB both can lead to secondary

EPI resulting in steatorrhea<sup>[34,113]</sup> with subsequent deficiencies of fat-soluble vitamins. Depending on type of RYGB, proximal or distal, the prevalence of EPI is up to 19%-48% respectively<sup>[34]</sup>. Changes in caloric content, composition and physical properties of meals after RYGB lead to a diminished, uncoordinated pancreatic response to nutrient stimuli<sup>[114]</sup>. The altered anatomy after RYGB leads to a shorter amount of contact time of enzymes with chyme. In addition, the degradation of pancreatic enzymes is accelerated in absence of food in the biliopancreatic limb<sup>[114]</sup>. In rare cases, left pancreatic resection for dumping syndrome or nesidioblastosis is performed, leading to primary endocrine and EPI<sup>[115]</sup>. Testing for EPI proves difficult due to altered anatomy. Direct stimulation tests require the intubation of the duodenum either in a transgastric way or *via* a double-balloon technique and measure the exocrine pancreatic response after stimulation with CCK or secretin. Indirect stimulation test, such as measurement of fecal fat or elastase-1 are cheaper, more readily available but pose other problems. The former requires the ingestion of a defined amount of fat, which proves difficult after RYGB-induced, altered perception of food. In the latter, a normal result does not preclude EPI, as only the released amount of enzymes, but not its effect on chyme is measured; the shortened contact time within the common channel is not reflected. The recommended high-fat diet, based on lipids as strongest stimulators of exocrine pancreatic response, is hard to apply in post-RYGB patients<sup>[34]</sup>. Pancreatic enzyme replacement therapy is the mainstay of EPI treatment. Substitution is adapted to symptoms<sup>[114]</sup>; if using pancrealipase, removing the acid-resistant coating is imperative as the amount of produced acid in the gastric pouch is only minimal<sup>[34]</sup>.

## DUMPING SYNDROME

Diarrhea is one of many abdominal and systemic symptoms of mostly early dumping syndrome (DS), caused by a rapid exposure of the small bowel with undigested nutrients. Prevalence of DS after RYGB is reported to be up to 75%, and after SG up to 45%. Even though bothersome at least, DS is seen not seen as complication but rather as desirable feature by a few surgeons<sup>[116]</sup>, it is thought to be an essential component of postoperative weight loss. Diagnosis relies mainly on symptom-based questionnaires like Sigstad's scoring system, together with an oral glucose tolerance test or a mixed-meal test. However, those tests have a high sensitivity, but low specificity and are complicated by the small gastric pouch<sup>[117]</sup>. First-line treatment of DS is directed at a change of diet towards a more fibre- and protein-rich regimen with a low proportion of rapid-absorbable carbohydrates. Dietary supplements such as pectin or glucomannan have a poor tolerability and may interfere with a post-bariatric diet<sup>[117]</sup>. Acarbose affects mainly late

DS, whilst diarrhea is associated rather with early DS. Somatostatin analogues are effective treatment options for both early and late DS, however, they have diarrhea as a common side effect. Total parenteral nutrition is less practical, but sometimes an inevitable option, other surgical possibilities consist in either remnant gastrectomy, reversal of RYGB or measure to enhance restriction of the pouch, such as AGB or pouch reshaping, only in very rare cases pancreatic resection have to be performed<sup>[118,119]</sup>.

## UNMASKED UNDERLYING INTESTINAL DISEASES

### Inflammatory bowel disease

The cardinal symptom of both, Crohn's disease and ulcerative colitis is diarrhea. It is unclear whether obesity and the subsequent proinflammatory state have a role in the pathogenesis of Crohn's disease<sup>[120]</sup>. Even though bariatric surgery leads to a normalization of this state, bacterial overgrowth might lead to a local activation of innate immune factors favoring inflammation<sup>[121]</sup>. Whether bariatric surgery is of benefit remains to be elucidated, case series show a favorable outcome with LSG as procedure of choice<sup>[122-126]</sup>. Even though in most instances inflammatory bowel disease will be known prior to surgery, it might be missed in pre-operative evaluation as it might occur later or is not captured, as morbid obesity seems to be associated with more colonic disease<sup>[127]</sup>. Of note, fecal calprotectin as measure for tissue inflammation is elevated after bariatric surgery<sup>[128]</sup>.

### Celiac disease

Approximately 40% of patients suffering from celiac disease (CD), traditionally associated with malabsorption and insufficient body weight, are overweight or obese at diagnosis<sup>[129,130]</sup>. They, therefore, could be potential candidates for bariatric surgery. Diarrhea is classically the hallmark of symptomatic celiac disease. However, a trend toward silent or atypical forms has been observed<sup>[131]</sup>. Triggers including pregnancy, traveller's diarrhea, gastroenteritis, and some type of gastrointestinal surgery were reported<sup>[132]</sup>. Indeed, a recent publication described the rapid onset of CD after bariatric surgery, *i.e.*, a duodenal switch procedure<sup>[133]</sup>. After all, CD should be considered as a differential diagnosis in patients presenting with persistent diarrhea after bariatric surgery.

A group of Italian surgeons suggested a preoperative work-up of specific CD tests (anti-endomysial and antitransglutaminase antibodies and total Immunoglobulin A) before bariatric procedures. Diagnosis of CD, consisting of harvesting duodenal biopsies is hindered after RYGB due to the anatomical changes involved. In these cases, exclusively serologic testing remains an option. Indeed, a negative CD specific serology does not completely exclude the diagnosis

of CD though it does make it much less likely<sup>[134]</sup>. The standard treatment of CD implementing a gluten-free diet (GFD) was shown to be successful in bariatric patients, either. In this line, a complete restoration of the intestinal mucosa within 12 mo after starting GFD was observed in a young adult with an incidentally diagnosed silent form of CD after bariatric surgery (vertical banded gastroplasty) 5 years earlier<sup>[135]</sup>. However, apart from a few case reports, little is known about onset, course, diagnosis and management of CD following bariatric surgery, particularly sleeve gastrectomy and RYGB.

### IBS

A prevalence of up to 30% of IBS fulfilling the ROME III criteria among morbidly obese patients was reported. These patients are more likely to suffer from profound alterations to quality of life and severe psychological disturbances than those without IBS<sup>[136,137]</sup>. On the other hand, a recent study of a large cohort showed that obesity is protective of a diagnosis or worsening of IBS<sup>[138]</sup>. Visceral adiposity, rather than general obesity, has been associated with an increased risk of diarrhea dominant IBS<sup>[139]</sup>. However, the association between the two entities remains unclear<sup>[140]</sup>. Increase of intra-abdominal pressure owing to excess of visceral fat, local tissue as well as systemic inflammation mediated by adipokines and cytokines originating from abdominal adipocytes<sup>[141-143]</sup>, and altered gut microbiota<sup>[144]</sup> have been suggested as possible mechanisms that link obesity and IBS. Bariatric surgery, *i.e.*, RYGB, may improve the IBS symptoms<sup>[137]</sup>. Yet, the impact of bariatric surgery on visceral hypersensitivity and outcome of IBS is still unknown. Nevertheless, it might be advisable to systematically screen IBS and other functional bowel disorders in patients eligible for bariatric surgery.

## CONCLUSION

There are a multitude of reasons for diarrhea in post-bariatric patients. Diagnosis can be challenging, as they are often intertwined and the influence of inconsistent, mood-dependent elements, must not be underestimated. The special anatomy after RYGB and BPD with excluded bowel segments complicates testing and the interpretation of results. Thus, empiric therapy of limited time will help in diagnosis and treatment.

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