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Obesity Treatment/Comorbidities

Dumping syndrome after esophageal, gastric or bariatric surgery: pathophysiology, diagnosis, and management

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Summary

Background: Dumping syndrome, a common complication of esophageal, gastric or bariatric surgery, includes early and late dumping symptoms. Early dumping occurs within 1 h after eating, when rapid emptying of food into the small intestine triggers rapid fluid shifts into the intestinal lumen and release of gastrointestinal hormones, resulting in gastrointestinal and vasomotor symptoms. Late dumping occurs 1–3 h after carbohydrate ingestion, caused by an incretin-driven hyperinsulinemic response resulting in hypoglycemia. Clinical recommendations are needed for the diagnosis and management of dumping syndrome.

Methods: A systematic literature review was performed through February 2016. Evidence-based medicine was used to develop diagnostic and management strategies for dumping syndrome.

Results: Dumping syndrome should be suspected based on concurrent presentation of multiple suggestive symptoms after upper abdominal surgery. Suspected dumping syndrome can be confirmed using symptom-based questionnaires, glycemia measurements and oral glucose tolerance tests. First-line management of dumping syndrome involves dietary modification, as well as acarbose treatment for persistent hypoglycemia. If these approaches are unsuccessful, somatostatin analogues should be considered in patients with dumping syndrome and impaired quality of life. Surgical re-intervention or continuous enteral feeding may be necessary for treatment-refractory dumping syndrome, but outcomes are variable.

Conclusions: Implementation of these diagnostic and treatment recommendations may improve dumping syndrome management.

Keywords: dumping syndrome, hyperinsulinemic hypoglycemia, pasireotide, somatostatin analogue.

Abbreviations: GLP, glucagon-like peptide; GIP, glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide; VAS, visual analogue scale; sst, somatostatin receptor subtype; OGTT, oral glucose tolerance test; GI, gastrointestinal; VIP, vasoactive intestinal peptide; LAR, long-acting release.

Introduction

Dumping syndrome is a frequent complication of esophageal, gastric or bariatric surgery. Alterations in gastric anatomy or interference with its intrinsic innervation disturb gastric emptying mechanisms and allow a substantial amount of undigested food to reach the small intestine too rapidly (1,2). Dumping syndrome is not a single disease entity but, instead, consists of a constellation of symptoms that can be categorized as early dumping or late dumping symptoms (1,2). Early dumping syndrome occurs within the first hour after a meal. Because of the hyperosmolality of the food, rapid fluid shifts occur from the plasma compartment into the intestinal lumen, resulting in hypotension and a sympathetic nervous-system response. Early dumping is characterized by gastrointestinal (GI) symptoms such as abdominal pain, bloating, borborygmi, nausea, and diarrhoea, and vasomotor symptoms such as fatigue, desire to lie down after meals, flushing, palpitations, perspiration, tachycardia, hypotension, and, rarely, syncope (1,2). In contrast, late dumping usually occurs 1 to 3 h after a meal and is a result of an incretin-driven hyperinsulinemic response after carbohydrate ingestion. Hypoglycemia-related symptoms are related to neuroglycopenia (fatigue, weakness, confusion, hunger and syncope) and autonomic/adrenergic reactivity (perspiration, palpitations, tremor and irritability) (1,2). Moreover, dumping syndrome cannot always be discretely separated into early and late dumping symptoms but, instead, is an entire disease spectrum whereby patients can develop early dumping, late dumping or both. Furthermore, early dumping symptoms may have resolved in some patients before late dumping symptoms present.

The prevalence of early and late dumping symptoms depends on the type and extent of surgery, as well as the definition of dumping syndrome used by study investigators. Thus, considerable heterogeneity may exist among different study populations, making it difficult to accurately compare results. Therefore, in acknowledgement of these differences, this systematic review includes a description of the study population where relevant. Dumping syndrome has been reported to occur in approximately 20% of patients who undergo vagotomy with pyloroplasty, in up to 40% of patients after Roux-en-Y gastric bypass or sleeve gastrectomy, and in up to 50% of patients who undergo esophagectomy (3–7). Dumping syndrome has also been reported to occur after Nissen fundoplication in children and in adults (8,9). In recent years, bariatric surgery has become the leading cause of postoperative dumping syndrome (10). Bariatric surgery results in major alterations to the anatomy and function of the GI tract (11). Various types of bariatric surgery have been used in recent years, including the Roux-en-Y gastric bypass, sleeve gastrectomy, biliopancreatic diversion, vertical banded gastroplasty and laparoscopic adjustable gastric band. The sleeve gastrectomy, vertical banded gastroplasty and the laparoscopic adjustable gastric band are restrictive procedures, in which the volume capacity of the proximal stomach is reduced. The Roux-en-Y gastric bypass and biliopancreatic diversion are considered malabsorptive procedures because they interfere with the normal digestion and absorption of food (11). After bariatric surgery, dumping syndrome has mainly been reported in patients who underwent Roux-en-Y gastric bypass and interventions involving partial gastrectomy (11). Among 450 patients who underwent a Roux-en-Y gastric bypass or sleeve gastrectomy, approximately one-third (34.2%) reported postoperative symptoms consistent with postprandial hypoglycemia (12). The mechanisms underlying dumping syndrome after bariatric surgery are numerous and remain to be fully elucidated (11).

Early dumping syndrome is the most frequent type of dumping syndrome and may occur in isolation or in association with late symptoms. Isolated late dumping (hypoglycemia as the only symptom) affects up to 25% of patients (6,13). Symptoms suggestive of early and late dumping syndrome may be severe and persist in some patients many years after surgery (7,14). Among 129 patients who underwent gastric bypass surgery, 12% reported severe fatigue after eating (half were so tired that they needed to lie down), 7% reported severe nausea and 6% severe fainting (14). Approximately, 12% had persistent dumping symptoms 1 to 2 years after surgery, especially postprandial fatigue necessitating lying down; 7% had persistent nausea and 6% had persistent fainting (14).

Dumping syndrome may result in either weight loss or weight gain. In severe cases, dumping syndrome is associated with a substantial reduction in quality of life and significant weight loss as a result of avoidance of food intake (15). Patients with severe dumping syndrome may experience weight loss of up to 30% of their preoperative weight (16). However, although it has previously been suggested that dumping symptoms might be essential for weight loss after bariatric surgery, a prospective series demonstrated that weight loss after Roux-en-Y gastric bypass was not dependent on the presence of dumping symptoms, and other studies suggest that some patients with dumping syndrome may exhibit weight gain (5,17,18). Furthermore, a Swedish nationwide cohort study of 5,040 post-gastric bypass patients demonstrated that approximately 1% were hospitalized for hypoglycemia and/or related disorders at a median of 2.7 years after surgery (19). Patients were also at increased risk for confusion, syncope, epilepsy and seizures after gastric bypass surgery (19). Symptoms can also be emotionally distressing, leading to anxiety and apprehension. Because of the large number of patients undergoing bariatric surgery, it is important to educate clinicians about how to recognize and manage dumping syndrome. Therefore, this systematic review was conducted to develop uniform guidance about the management of dumping syndrome.

Search methodology

A literature search of the PubMed database was performed to identify relevant literature published through February 2016. Search terms included 'dumping syndrome' combined with 'symptoms,' 'pathophysiology,' 'management,' 'diet,' 'pectin,' 'guar gum,' 'glucomannan,' 'acarbose,' 'somatostatin analogue,' 'octreotide,' 'lanreotide,' 'pasireotide,' 'diazoxide,' 'nifedipine,' 'glucagon-like peptide 1 (GLP-1) receptor antagonist,' 'surgery' and 'continuous enteral feeding.' The reference lists from retrieved articles were also reviewed for relevant publications. The search results were manually reviewed to eliminate commentaries and correspondence/letters related to the clinical study publications. Applying these quantitative and qualitative filters reduced the search results to approximately 160 potentially relevant citations. Each of the selected publications was reviewed for management approaches for dumping syndrome, and consensus recommendations were developed by an interdisciplinary team (endocrinologist, gastroenterologist, nutritionist and bariatric surgeon) to provide uniform practical guidance to the different specialists involved in the management of dumping syndrome. A systematic review of diagnostic approaches for dumping syndrome was not performed, but the most widely used approaches are described briefly herein. A more in-depth review of the diagnosis of dumping syndrome has recently been published (20).

Pathophysiology

The pathophysiological mechanisms involved in dumping syndrome are incompletely understood. Relatively few recent studies have been devoted to elucidating the mechanisms involved in early and late dumping syndromes, and much of our current knowledge is based on older literature (21). Symptoms of early and late dumping syndrome appear to be caused by distinct pathophysiological mechanisms.

Early dumping

Several concurrent phenomena contribute to the development of early dumping symptoms (3,22–25). Gastric surgery reduces gastric volume or removes the barrier function of the pylorus, resulting in the rapid delivery of a substantial amount of undigested solid food to the small intestine, thereby bypassing the larger part of the stomach (Fig. 1) (1). Esophageal surgery may also impair gastric retentive capacity because the accompanying vagotomy causes rapid liquid emptying. Hyperosmolar nutrients in the small bowel presumably cause a shift of fluid from the intravascular compartment (i.e. plasma) to the intestinal lumen, resulting in a reduction in plasma volume, tachycardia, and, rarely, syncope. Movement of fluid into the small bowel may also cause distention and contribute to cramp-like contractions, bloating and diarrhoea. Whether this fluid shift contributes to the pathophysiology of dumping syndrome or is mainly a consequence of this process remains unknown. In favour of the latter interpretation, intravenous fluid substitution is not effective in preventing early dumping symptoms (26). Another important mechanism involved in the pathophysiology of early dumping syndrome (and also late dumping syndrome as described below) involves the increased release of multiple GI hormones including vasoactive agents (e.g. neurotensin and vasoactive intestinal peptide [VIP]), incretins (e.g. gastric inhibitory polypeptide [GIP] and GLP-1), and glucose modulators (e.g. insulin and glucagon) (22,24,25). Enhanced release of these GI hormones may induce discoordinated GI motility and inhibit secretion, as well as elicit hemodynamic effects; for example, neurotensin and vasoactive intestinal polypeptide induce splanchnic vasodilation that results in hypotension and systemic hemoconcentration (27).

Late dumping

In contrast to the multiple pathophysiologic factors involved in early dumping syndrome, the pathophysiology of late dumping is largely attributable to the development of hyperinsulinemic or reactive hypoglycemia (3,22–25). Rapid delivery of undigested carbohydrates to the small intestine results in high glucose concentrations that induce a hyperinsulinemic response, resulting in subsequent hypoglycemia and related late dumping symptoms (28). Enteral glucose administration is known to induce enhanced insulin release relative to intravenous administration, a process known as the incretin effect. Two GI hormones are believed to play a pivotal role in the incretin effect: glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide and GLP-1. An increased GLP-1 response has been reported in patients after gastric surgery, and a positive correlation has been observed between increasing GLP-1 levels and insulin release (29). An additional study suggests that GLP-1 analogues may actually stabilize glucose levels in patients with postprandial hypoglycemia after gastric bypass surgery (30). Therefore, an exaggerated endogenous GLP-1 response appears to be the key mediator of the hyperinsulinemic and hypoglycemic effect that is characteristic of late dumping syndrome (18,29). However, the precise mechanism by which GLP-1 contributes to glucose homeostasis and late dumping syndrome is likely to be complex and remains to be fully elucidated.

Diagnosis

Population at risk

Dumping syndrome should be suspected based on the concurrent presentation of multiple suggestive symptoms

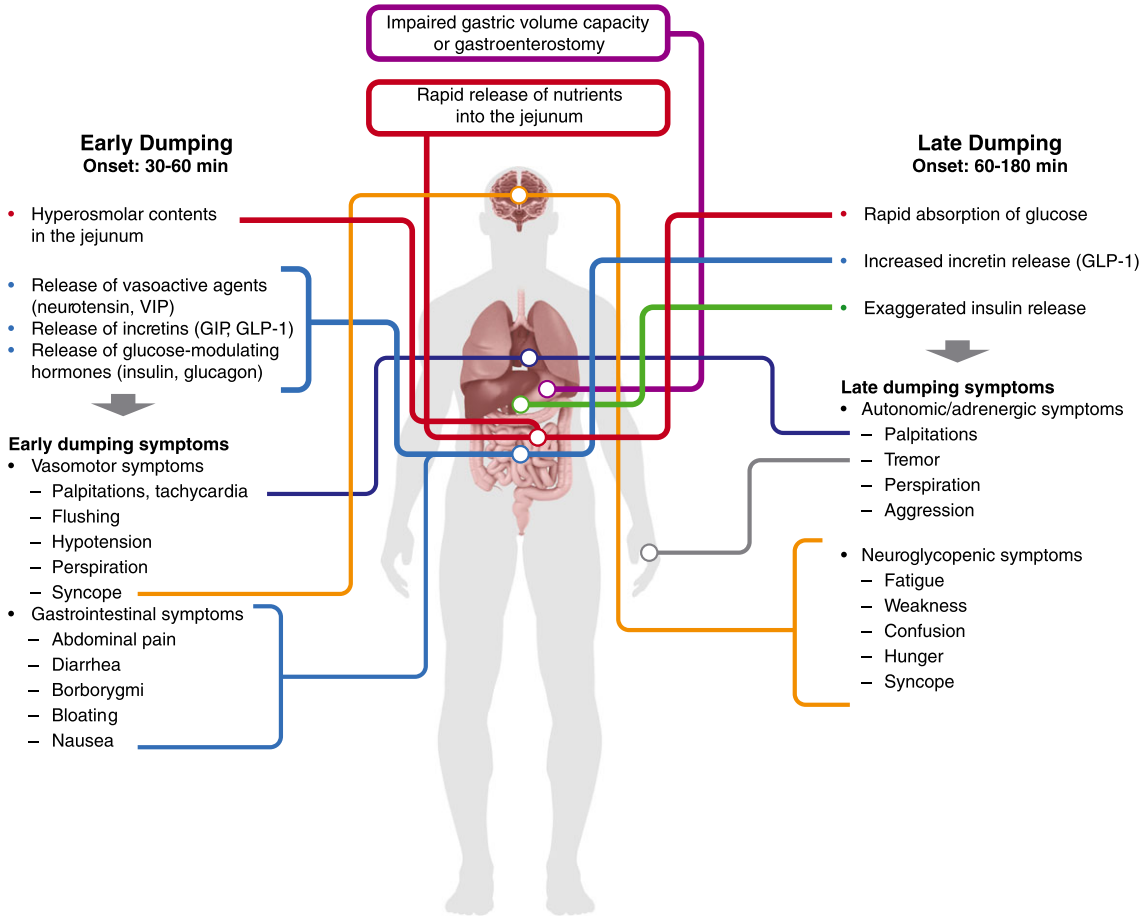

Figure 1 Pathophysiology of dumping syndrome. Abbreviations: GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide-1; VIP, vasoactive intestinal peptide.

in patients who have undergone gastric or esophageal surgery (1). A carefully obtained medical history and thorough symptom evaluation are very important for the accurate diagnosis of dumping syndrome. Profound fatigue after meal ingestion, with the need to lie down, is an important clinical clue. Various approaches can be used to confirm the presence of dumping syndrome, including symptom-based questionnaires, glycemia monitoring, oral glucose challenge testing and gastric emptying studies. An additional diagnostic evaluation may also be necessary to exclude conditions that can present with similar symptoms (e.g. postoperative complications, strictures, adhesions and insulinoma). Hypoglycemia unawareness may develop as a result of recurrent hypoglycemia, making it even more difficult to diagnose late dumping syndrome in patients who have undergone gastric bypass surgery (20).

Symptom-based questionnaires

Symptom-based questionnaires, such as the Sigstad's score and the Arts' dumping questionnaire can be used to identify patients with clinically meaningful dumping symptoms. Sigstad's score was developed to separate patients with or without postoperative dumping syndrome in the era of peptic ulcer surgery (17), while Arts' dumping questionnaire was designed to differentiate between early and late dumping symptoms. The Sigstad's scoring system assigns points to each dumping symptom, and the total points are used to calculate a diagnostic index (31). A diagnostic index >7 is suggestive of dumping syndrome whereas a score <4 suggests that other diagnoses should be considered. Patients receive an oral glucose tolerance test (OGTT) prior to using the Sigstad's scoring system to score and grade symptom severity. The primary focus of the Sigstad's scoring system is to identify early dumping by diagnosing signs and symptoms such as a high pulse rate or increased haematocrit indicative of hypovolemia. The diagnostic accuracy of the Sigstad's scoring questionnaire in bariatric patients or after upper GI cancer surgery has not been established (7). Arts *et al.* developed a dumping-severity score in which symptoms of early and late dumping (eight and six symptoms, respectively) were scored on a 4-point Likert scale (15). This

questionnaire has been tested on patients with early and late dumping, and was shown to be effective at discriminating between the two sets of symptoms and was responsive to somatostatin analogue therapy, but was never formally validated (15). A relatively recent report also describes the use of a visual analogue scale (VAS) survey to evaluate early and late dumping syndromes in more than 1,000 patients after gastrectomy for gastric cancer (32). This survey used a very low cutoff for dumping complaints (VAS score >10 mm), and a single item on the questionnaire was sufficient to label patients as symptomatic for late dumping (32).

Glycemia measurements

Single plasma glucose measurements, whether scheduled or random, can be performed during clinic visits after gastric or esophageal surgery. Although the diagnostic value of a single glucose measurement is low, its clinical value increases when evaluated in conjunction with late dumping symptoms. To date, no definitive guidance regarding cutoff values for plasma glucose has been established, but some clinicians consider plasma glucose concentrations <2.8 mmol/L (50 mg/dL) to be indicative of post-gastric bypass hypoglycemia, whereas others regard levels <3.3 mmol/L (60 mg/dL) diagnostic of hypoglycemia (33). Capillary glucose measurements (finger prick) are not considered valid because of their lack of accuracy in the hypoglycemic range. Continuous glucose monitoring may be beneficial in complex cases of dumping syndrome (34–36).

Provocative testing

Clinical suspicion of dumping syndrome can be confirmed using provocative tests such as the OGTT or mixed-meal tolerance test (37). In the glucose tolerance test, patients with suspected dumping syndrome ingest 50 g or 75 g of glucose in solution after an overnight fast. Blood glucose concentrations, haematocrit, pulse rate and blood pressure are measured before and at 30-min intervals up to 180 min after ingestion. The OGTT is considered positive for early dumping based on the presence of an early (30 min) increase in haematocrit >3% or an increase in pulse rate >10 beats/min after 30 min, the latter being regarded as the most sensitive indicator of early dumping syndrome (1). Test results are positive for late dumping based on the development of late (60–180 min postingestion) hypoglycemia (1). In the mixed-meal tolerance test, patients with suspected dumping syndrome ingest a mixed meal containing carbohydrates, fats and proteins after an overnight fast (18,38). Blood samples are collected before meal ingestion and at 30-min intervals for up to 2 h afterward to monitor glycemic and insulin profiles. The mixed-meal tolerance test is considered positive for late dumping syndrome in patients who develop hypoglycemia between 60 and 180 min after meal ingestion.

The use of provocative testing to diagnose dumping syndrome is associated with several challenges. Provocative testing can be difficult in patients with small gastric pouches as a result of gastric or bariatric surgical procedures. Furthermore, the OGTT frequently detects post-gastric bypass hypoglycemia in patients with and without symptoms, as well as in healthy individuals (20). Therefore, the diagnostic accuracy of this test is low and normative values have not been firmly established (20). As a result, clinical practice guidelines for adult hypoglycemic disorders developed by the Endocrine Society do not support the use of the OGTT for diagnosing postprandial hypoglycemia (39). The mixed meal tolerance test holds promise as a more physiologic stimulation test for the detection of post-gastric bypass hypoglycemia (20,40). Some studies demonstrate improved specificity of this test in asymptomatic patients; however, normative values have not been established for healthy individuals (20). Further validation of the mixed meal tolerance test is needed in patients with and without hypoglycemia symptoms, as well as in healthy individuals. Because there is currently no optimal approach for the diagnosis of dumping syndrome, (20) provocative testing is still commonly used in some countries to diagnose hypoglycemia in the safety of a medical testing facility.

Gastric emptying studies

The rate of gastric emptying may also be used to confirm a diagnosis of dumping syndrome. A gastric emptying scintigraphy test involves eating a bland meal that contains a small amount of radioactive material, and measuring the rate of gastric emptying at hourly intervals until 4 h after the meal. However, gastric emptying studies generally have low sensitivity and specificity, probably because the process of rapid gastric emptying occurs soon after ingestion, a phase that is not adequately assessed in most studies. Furthermore, the duration of the entire study of up to 4 h is integrated into a single value (half emptying time), which may neutralize the rapid initial emptying effect (3,15,37).

Differential diagnosis

A differential diagnosis should also be considered in patients with suspected dumping syndrome.

Early dumping

Symptoms of cramp-like contractions, bloating and diarrhoea in patients with a history of upper GI surgery may also occur as a consequence of complications such as stenosis, fistula formation, adhesions and ischemia. A marginal ulcer or gastritis is generally characterized by pain during meals, acid reflux, and nausea, and the diagnosis can

be confirmed via gastroscopy. Symptoms of stenosis or anastomoses are similar to symptoms of marginal ulcer accompanied by dysphagia, and the diagnosis can be confirmed via gastroscopy or a barium or gastrografin swallow. Internal herniation generally results in pain, sometimes colic pain, a sensation of fullness quickly after meals, sometimes ileus and vomiting and no vegetative symptoms. A diagnosis of internal herniation can be confirmed via computed tomography or diagnostic laparoscopy. The main characteristics of obstipation are a feeling of fullness, pain and defecation only once in 3 days. Symptomatic gallstone disease is characterized by colicky pain attacks, with an urge to move, nausea, and, often, vomiting. Pain generally lasts for at least 1 h. Diagnoses can be confirmed with an ultrasound showing gallbladder stones and blood testing confirming liver function abnormalities after colic.

Late dumping

A differential diagnosis of hyperinsulinemic hypoglycemia is important in patients with late dumping symptoms. Late dumping occurs during the postprandial period (1-3 h after eating). In contrast, an insulinoma, which is extremely rare, should be considered if fasting hypoglycemia occurs (i.e. not provoked by a meal) (41,42). A fast of up to 72 h (usually 48 h) in a supervised hospital setting to assess hypoglycemia and the pathological lack of decrease in insulin secretion may be indicated in case of doubt (39,41). Surreptitious use of glucose-lowering medications (e.g. sulfonylurea derivatives or insulin) should also be excluded in each case, which can be determined via a sulfonylurea and C-peptide assay, respectively. In the case of hypoglycemia resulting from exogenous insulin injection, C-peptide levels are inappropriately low at the time of hyperinsulinemic hypoglycemia. Finally, postprandial syncope may be similar to loss of consciousness, and the two conditions may be difficult to differentiate, especially in elderly patients.

Treatment

Treatment approaches for dumping syndrome include dietary modifications, pharmacologic interventions and, possibly, surgical re-intervention or continuous tube feeding. Some treatments are indicated solely for late dumping (e.g. acarbose), whereas others are potentially beneficial for both early and late dumping (e.g. somatostatin analogues). The effectiveness of some of these approaches has not been clearly established as most studies included relatively few patients and were not adequately controlled. The level of evidence and grade of recommendation, as described in Table 1, supporting the use of each of these approaches in dumping syndrome is provided.

Dietary modification (*level of evidence*: *III*; *grade of recommendation*: *B*)

Dietary modification is the initial approach used to manage dumping syndrome and is usually beneficial for a majority of patients (3,10,16,43–47). Therefore, proper patient education about dietary modification is very important and should be repeated before all subsequent treatment approaches. In addition, clinicians caring for patients after bariatric surgery should be aware of dietary approaches for the management of dumping syndrome. Clinicians should advise patients with dumping syndrome to reduce the amount of food consumed at each meal. Patients should also delay fluid intake until at least 30 min after meals. Rapidly absorbable carbohydrates should be eliminated from the diet to prevent late dumping symptoms such as hypoglycemia. Instead, patients should be advised to eat a diet consisting of high-fibre and protein-rich foods; consumption of fruit and vegetables should be encouraged whereas alcoholic beverages are better avoided. Patients should also eat slowly and chew well. Education about the glycemic index of different foods may also be helpful for patients with

Table 1 Levels of evidence and grades of recommendation

Level of evidence	Type of evidence
I	Evidence from meta-analysis of multiple, well-designed, controlled studies (randomized trials with low false-positive and low false-negative errors)
II	Evidence from at least 1 well-designed, quasi-experimental study (randomized trials with high false-positive and high false-negative errors)
III	Evidence from well-designed, quasi-experimental studies (nonrandomized, controlled, single-group, pre–post, cohort and time or matched case–control series)
IV	Evidence from well-designed, non-experimental studies (comparative and correlational descriptive and case studies)
V	Evidence from case reports
Grade of recommendation	**Level of evidence**
A	Level I evidence or consistent findings from multiple studies (level II, III or IV)
B	Level II, III or IV evidence with generally consistent findings
C	Level II, III or IV evidence with inconsistent findings
D	Little or no systematic empirical evidence

dumping syndrome. If these recommendations are not effective or are not followed properly, patients should be advised to lie down for 30 min after meals to delay gastric emptying and reduce the symptoms of hypovolemia (1,16).

Dietary supplements (*level of evidence*: *III*; *grade of recommendation*: *C*)

Dietary supplements that increase the viscosity of food (e.g. guar gum, pectin and glucomannan) slow the rate of gastric emptying and delay glucose absorption. A number of short-term studies involving the ingestion of up to 15 g of guar gum or pectin with each meal have demonstrated the efficacy of these dietary supplements in slowing gastric emptying, reducing GI hormone release, improving hyperglycemia and controlling dumping symptoms (Table 2) (48–57). A single study reported that glucomannan significantly improved glucose tolerance but had no effect on glucose absorption in children with dumping syndrome who underwent various types of gastric surgery (57). However, the palatability and tolerability of many dietary supplements are poor. Because dietary supplements are high in fibre, some patients may experience gas and bloating. Furthermore, dietary recommendations to delay fluid intake until at least 30 min after meals means that consumption of viscous, gel-forming dietary supplements with dry food may pose a choking hazard and cause bowel obstruction as a result of a delay in the transit of food through the GI tract.

Pharmacologic intervention

Pharmacologic intervention plays an important role in the management of dumping syndrome in patients who fail to respond to dietary modification. Several studies have evaluated acarbose or somatostatin analogues in patients with dumping syndrome (described in detail below). The efficacy and tolerability of other pharmacologic agents have mainly been presented as case reports, and clinical evidence supporting their use in dumping syndrome is more limited.

Acarbose (level of evidence: *III*; *grade of recommendation*: *B*)

Acarbose is an α-glycosidase hydrolase inhibitor that slows carbohydrate digestion in the small intestine, thus blunting postprandial hyperglycemia and subsequent hypoglycemia. Several small studies demonstrated that acarbose improved glucose tolerance, reduced GI hormone release, reduced the incidence of hypoglycemia and improved symptoms in patients with dumping syndrome (Table 3) (8,34,53,58–66). However, the use of acarbose as a treatment approach for

Table 2 Summary of pectin, guar Gum and glucomannan studies in dumping syndrome

Study	Design	Treatment	Results
Jenkins *et al.* (48)	Case series *N* = 9	Pectin 14.5 g, single administration before OGTT[1]	• Normalized glycemia • Prevented hypoglycemic symptoms
Jenkins *et al.* (49)	Case series *N* = 11	Pectin 14.5 g, single administration before OGTT[1]	• Significantly reduced high postprandial levels of glucose, insulin and enteroglucagon • Reduced hypoglycemia
Leeds *et al.* (50)	Case series *N* = 12	Pectin 15 g, single administration before OGTT[1]	• Improved glycemia and vasomotor symptoms • Reduced insulin levels • Prolonged gastric emptying
Lawaetz *et al.* (51)	Case series *N* = 4	Pectin 15 g, single administration before OGTT[1]	• Reduced vasomotor symptoms • Decreased levels of insulin, glucagon, neurotensin and GIP • Slowed initial gastric emptying
Andersen *et al.* (52)	Case series *N* = 5	Pectin 5 g, single administration before meal[1]	• No effect on symptoms or gastric emptying rate
Speth *et al.* (53)	Double-blind, randomized, controlled study *N* = 9	Acarbose 50–100 mg, pectin 4.2 g, acarbose 50 mg plus pectin 4.2 g, placebo, after standard breakfast	• Acarbose and acarbose plus pectin inhibited postprandial hyperglycemia and hypoglycemia • Acarbose plus pectin inhibited hyperinsulinemia • Acarbose, pectin and combination reduced hypoglycemic symptoms
Harju *et al.* (54)	Double-blind, controlled study *N* = 11	Guar gum 5 g or placebo with meals for 1 week	• Improved dumping symptoms
Harju *et al.* (55)	Double-blind, controlled study *N* = 11	Guar gum 5 g or placebo after a meal	• Slowed gastric emptying
Harju *et al.* (56)	Case series *N* = 16	Guar gum 5 g with a glucose challenge meal[1]	• Improved symptoms
Kneepkens *et al.* (57)	Case series *N* = 8	Glucomannan 1.3 g before OGTT[1]	• Significantly improved glucose tolerance • No effect on glucose absorption

[1]Efficacy was determined by comparing assessments performed before and after treatment.
Abbreviations: GIP, glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide; OGTT, oral glucose tolerance test.

Table 3 Summary of acarbose studies in dumping syndrome

Study	Design	Treatment	Results
McLoughlin *et al.* (58)	Case series $N = 10$	Acarbose 100 mg or placebo single administration before OGTT	• Improved glycemia and symptoms • Reduced increase in plasma levels of GIP and insulin • No change in gastric emptying rate
Gerard *et al.* (59)	Double-blind, randomized, controlled study $N = 24$	Acarbose 100 mg or placebo single administration before OGTT	• Improved reactive hypoglycemia • Reduced increase in plasma levels of insulin • Inhibited glucose-induced glucagon suppression
Lyons *et al.* (60)	Double-blind, randomized, controlled study $N = 13$	Acarbose 50 mg or placebo single administration before standard breakfast	• Significantly attenuated hyperglycemia • Reduced increase in plasma levels of GIP, enteroglucagon and insulin • No effect on plasma levels of neurotensin, VIP and somatostatin • No significant effect on symptoms
	$n = 9$	Acarbose 50 mg TID or placebo for 1 month	• No significant reduction in the number or severity of dumping attacks • Most patients preferred acarbose
Hasegawa *et al.* (61)	Case series $N = 6$	Acarbose 50–100 mg TID before meals for 1 month[1]	• Attenuated glucose and insulin fluctuations • Improved dumping symptoms
Ozgen *et al.* (62)	Case series $N = 21$	Acarbose 150 mg/day before meals for 2 weeks and 300 mg/day for the remainder of the 3-month treatment period[1]	• Reduced early hyperglycemic and hyperinsulinemic response • Reduced reactive hypoglycemia
Ng *et al.* (8)	Case series $N = 6$	Acarbose 12.5 mg before a meal[1]	• Improved postprandial hypoglycemia
De Cunto *et al.* (63)	Case series $N = 4$	Acarbose 25–100 mg before meals[1]	• Stabilized postprandial glucose
Valderas *et al.* (64)	Case series $N = 8$	Acarbose 100 mg before a meal[1]	• Avoided postprandial hypoglycemia • Reduced hyperinsulinemic response • Reduced GLP-1 secretion
Ritz *et al.* (34)	Case series $N = 8$	Acarbose 50–100 mg, TID for 6 weeks[1]	• Eliminated dumping symptoms • Improved CGM profile
Speth *et al.* (53)	Double-blind, randomized, controlled study $N = 9$	Acarbose 50–100 mg, pectin 4.2 g, acarbose 50 mg plus pectin 4.2 g, placebo, after standard breakfast	• Acarbose and acarbose plus pectin inhibited postprandial hyperglycemia and hypoglycemia • Acarbose plus pectin inhibited hyperinsulinemia • Acarbose, pectin and combination reduced hypoglycemic symptoms
Vilarrasa *et al.* (66)	Multicenter, retrospective, systematic case series $N = 22$	Alpha-glucosidase inhibitors[2] 50 mg/8 h orally	• 4 patients (18%) had a partial response[3]

[1]Efficacy was determined by comparing assessments performed before and after treatment.
[2]Alpha-glucosidase inhibitor not specified.
[3]Fifty percent reduction in the number and severity of hypoglycemic events.
Abbreviations: CGM, continuous glucose monitoring; GIP, glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide; GLP-1, glucagon-like peptide 1; OGTT, oral glucose tolerance test; TID, three times per day; VIP, vasoactive intestinal peptide.

dumping syndrome is limited by the fact that it affects only late dumping symptoms and may result in side effects related to carbohydrate maldigestion, such as bloating, flatulence and diarrhoea.

Somatostatin analogues (level of evidence: II; grade of recommendation: A)

Somatostatin analogues are an effective treatment option for patients with well-established dumping syndrome who fail to respond to and/or do not tolerate initial dietary modification and acarbose treatment. Somatostatin analogues target various steps in the pathophysiology of dumping syndrome, including delaying gastric emptying, delaying transit through the small intestine, inhibiting the release of GI hormones, inhibiting insulin secretion and inhibiting postprandial vasodilation (15,67–78). Somatostatin inhibition of GLP-1 secretion is mediated via activation of the somatostatin receptor subtype (sst) 5, with a lesser effect through sst2 (79). Both short-acting and long-acting formulations of somatostatin analogues have demonstrated efficacy by slowing gastric emptying, improving hypoglycemia and reducing early and late dumping symptoms (Table 4) (15,66,80–95).

Table 4 Summary of somatostatin analogue studies in dumping syndrome

Study	Design	Treatment	Results
Subcutaneous octreotide			
Hopman *et al.* (80)	Double-blind, randomized, controlled study *N* = 12	Octreotide 50 μg vs placebo before OGTT	• Improved symptoms and suppressed postprandial rise in pulse rate • Reduced peak insulin and increased nadir glycemia • Slowed GI transit
Primrose and Johnston (81)	Double-blind, randomized, cross-over, controlled study *N* = 10	Octreotide 50 μg or 100 μg vs placebo before OGTT	• Reduced early dumping and abolished late dumping symptoms • Suppressed early dumping-associated changes in haematocrit and pulse rate • Inhibited hypoglycemia
Tulassay *et al.* (82)	Double-blind, randomized, controlled study *N* = 8	Octreotide 50 μg vs placebo before OGTT	• Suppressed rise in pulse rate, haematocrit and plasma levels of VIP • Prevented postprandial hypoglycemia • Inhibited rise in plasma insulin and GIP
Geer *et al.* (83)	Double-blind, randomized, controlled study *N* = 10	Octreotide 100 μg vs placebo before OGTT	• Prevented symptom development including late hypoglycemia before OGTT • Inhibited rise in plasma levels of glucose, glucagon, pancreatic polypeptide, neurotensin and insulin • Slowed gastric emptying and GI transit
Richards *et al.* (84)	Double-blind, randomized, controlled study *N* = 6	Octreotide 100 μg vs placebo before OGTT	• Prevented symptom development • Induced phase III migrating motor complex in the small intestine • Decreased postprandial intestinal motor activity
Gray *et al.* (85)	Double-blind, randomized, cross-over, controlled study, *N* = 9	Octreotide 100 μg vs placebo before OGTT	• Suppressed symptoms and rise in pulse rate • Inhibited insulin release • Prevented hypoglycemia
Hasler *et al.* (86)	Double-blind, randomized, cross-over, controlled study, *N* = 8	Octreotide 50 μg vs placebo before OGTT	• Suppressed symptoms and rise in pulse rate • No effect on change in haematocrit, inhibition of insulin release, prevention of hypoglycemia or gastric emptying rate
Arts *et al.* (15)	Single-arm, open-label study, *N* = 30	Octreotide 50 μg for 3 days[1]	• Suppressed rise in pulse rate and haematocrit • Inhibited postprandial hypoglycemia and rise in insulin plasma levels • Improved early and late dumping symptoms
Vilarrasa *et al.* (66)	Multicenter, retrospective, systematic, case series, *N* = 13	Octreotide 50/100 μg/12 h	• 3 patients (23%) had a complete response[2] • 5 patients (38.4%) had a partial response[3]
Long-term Treatment With Subcutaneous Octreotide			
Geer *et al.* (83)	Double-blind, randomized, controlled study, *N* = 10	Octreotide 100 μg vs placebo; mean treatment period, 15 months.	• Provided sustained symptom control • Resulted in minimal side effects • Provided stable fasting plasma glucose levels, normal liver function tests and an average weight gain of 11% during a 12-month period • Most patients able to resume employment
Vecht *et al.* (87)	Single-arm, open-label study *N* = 20	Octreotide 25–200 μg; mean treatment period, 37 months[1]	• Provided early relief of early and late symptoms in all patients • Long-term effects less beneficial • Symptom relief persisted in 80% of patients at 3 months
Didden *et al.* (88)	Single-arm, open-label study, *N* = 34	Octreotide 25–50 μg; mean treatment period 93 months	• Provided early relief of early and late symptoms in all patients • Long-term effects less beneficial • 47% of patients discontinued therapy because of side effects or lack of efficacy
Long-Acting Octreotide			
Penning *et al.* (89)	Single-arm, open-label study *N* = 12	Octreotide LAR 10 mg every 4 weeks for 6 months vs subcutaneous octreotide	• Both formulations improved symptoms • Octreotide LAR was superior at increasing body weight and improving quality of life

(*Continues*)

Table 4 (Continued)

Study	Design	Treatment	Results
Arts *et al.* (15)	Single-arm, open-label study $N = 30$	Octreotide LAR 20 mg for 3 months vs subcutaneous octreotide 50 μg for 3 days	• Both formulations had a beneficial effect on dumping symptoms, hypoglycemia and pulse rate • Subcutaneous octreotide was more effective than octreotide LAR in improving hypoglycemia • Octreotide LAR was associated with significantly greater improvements in quality of life and was preferred relative to subcutaneous octreotide
Pasireotide			
Deloose *et al.* (90)	Double-blind, randomized, cross-over, controlled study, $N = 9$	Pasireotide 300 μg vs placebo for 2 weeks	• Suppressed increase in pulse rate and late hypoglycemia • Increased peak glycemia • Delayed gastric emptying

[1]Efficacy was determined by comparing assessments performed before and after treatment.
[2]Complete resolution of hypoglycemic events.
[3]Fifty percent reduction in the number and severity of hypoglycemic events.
Abbreviations: GI, gastrointestinal; GIP, glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide; LAR, long-acting release; OGTT, oral glucose tolerance test; VIP, vasoactive intestinal peptide.

Somatostatin analogues may be administered subcutaneously three times daily as a short-acting formulation or intramuscularly once every 2 to 4 weeks as a long-acting formulation. Short-acting formulations may be more effective at improving some dumping symptoms such as hypoglycemia (15,81–83,85); however, the need for repeated injections throughout the day is often a major limitation to the long-term administration of short-acting formulations. Long-acting formulations are preferred by patients because of less frequent administration and the associated improvements in quality of life (15,89). The most common adverse events associated with somatostatin analogues are diarrhoea, nausea, steatorrhea, gallstone formation and pain at the injection site. Despite the occurrence of steatorrhea, which is generally mild, patients with dumping syndrome who receive long-term somatostatin analogue therapy experience a weight gain of approximately 1% (1). Gallstone formation may influence treatment selection for dumping syndrome (96,97). Furthermore, during both short-term treatment and long-term treatment, a proportion of patients with dumping syndrome do not respond to currently available somatostatin analogues (1,15,87–89). Somatostatin analogues have not received regulatory approval for the treatment of dumping syndrome.

Pasireotide is a multireceptor-targeted somatostatin analogue with high affinity for 4 of the 5 somatostatin receptor subtypes, including sst2 and sst5. The affinity of pasireotide for sst5 is higher than that of octreotide (98,99). A recent case report demonstrated that pasireotide inhibited GLP-1 and insulin release more effectively than octreotide, resulting in improved control of postprandial hyperinsulinemic hypoglycemia after a gastric bypass (100). A pilot study also demonstrated that pasireotide suppressed the increase in pulse rate and late hypoglycemia, and delayed gastric emptying (90). However, pasireotide did not demonstrate a significant improvement in dumping symptoms, and approximately 20% of patients in the pilot study discontinued treatment because of GI events (90). A recent phase 2, dose-escalation study evaluated the pharmacokinetics, efficacy and safety of subcutaneous pasireotide followed by long-acting release (LAR) pasireotide in dumping syndrome (NCT01637272: $N = 43$) (17,101). Pasireotide effectively controlled postprandial hypoglycemia and improved changes in pulse rate and haematocrit in patients with dumping syndrome. Both subcutaneous and LAR pasireotide were well tolerated, and no new safety signals were identified (101). Another phase 2 study, which compared the efficacy, safety and quality of life of LAR lanreotide versus placebo in dumping syndrome, was recently completed, but no results have been published to date (NCT01923649) (102).

Other Pharmacologic Interventions (level of evidence: V; grade of recommendation: D)

Other pharmacologic interventions, such as diazoxide, nifedipine and exendin 9-39 have also been evaluated for the management of dumping syndrome. Diazoxide is a potassium channel activator that inhibits calcium-induced insulin release. Anecdotal evidence suggests that off-label diazoxide administered at doses ranging from 100 mg to 150 mg three times daily may be effective in the treatment of late dumping symptoms, but no effect on early symptoms is expected because of its mode of action (103). A recent multicenter, retrospective, systematic case series reported that treatment of six patients who developed

Table 5 Summary of surgical re-intervention studies for post-Roux-en-Y gastric bypass in dumping syndrome

Study	Patients	Procedure	Results
Gastric bypass reversal			
Patti *et al.* (103)	Case report $N = 1$	Gastric bypass reversal	• Ineffective in reversing hypoglycemia • Partial pancreatectomy required
Campos *et al.* (106)	Prospective study $N = 5$	Gastric bypass reversal, $N = 2$; modified sleeve gastrectomy, $N = 3$	• No postoperative episodes of neuroglycopenia • No or minimal hypoglycemic episodes • Hypocalcemia became responsive to oral replacement therapy
Lee *et al.* (107)	Case report $N = 2$	Gastric bypass reversal	• Ineffective in reversing hypoglycemia
Vilallonga *et al.* (108)	Retrospective database analysis $N = 9$	Gastric bypass reversal; patients with marked normalization of the gastrostomy tube glucose tolerance test	• No new episodes of severe hypoglycemia • 3 patients received a concomitant sleeve gastrectomy • Severe gastroesophageal reflux disease and/or chronic diarrhoea reported by some patients
Vilarrasa *et al.* (66)	Multicenter, retrospective, systematic case series $N = 3$	Gastric bypass reversal	• Hypoglycemia resolved in 2 patients (67%) • Hypoglycemia persisted in 1 patient (33%) but was controlled by alpha-glucosidase inhibitors
Rao *et al.* (109)	Case report $N = 1$	Laparoscopic gastric bypass reversal	• Marked reduction in hypoglycemia burden 9 months after reversal
Carter *et al.* (110)	Retrospective analysis $N = 3$	Sleeve gastrectomy	• Dumping symptoms and hypoglycemia resolved • 1 patient developed portal vein thrombus and seroma • 2 patients were readmitted to hospital and required supplemental nutrition
Lakdawala *et al.* (111)	Case series $N = 5$	Laparoscopic conversion to sleeve gastrectomy	• Dumping syndrome resolved • No complications were reported
Huang *et al.* (112)	Case report $N = 2$	Laparoscopic conversion to loop duodenojejunal bypass with sleeve gastrectomy	• Dumping symptoms resolved • After 6 months, the Sigstad's score decreased to 2 points • No complications were reported
Huang *et al.* (113)	Case report $N = 1$	Laparoscopic conversion to modified duodenal switch	• Dumping symptoms resolved • No complications were reported
Gastric pouch restriction			
Z'graggen *et al.* (114)	Case series $N = 10$[1]	Gastric pouch downsized; silastic (Fobi) ring around pouch, $n = 6$; adjustable band, $n = 4$	• No new hypoglycemic episodes • All had symptomatic improvement (assessed via the Sigstad score)
de Heide *et al.* (115)	Case report $N = 1$	Laparoscopic adjustable banding for pouch dilatation	• Subjective improvement in symptoms
Vilarrasa *et al.* (66)	Multicenter, retrospective, systematic case series $N = 1$	Resection of the 'candy cane' roux limb	• Patient was symptom-free 1 year after procedure
Pancreatic resection			
Patti *et al.* (103)	Case series $N = 3$	Distal pancreatectomy (80%), $n = 2$; subtotal pancreatectomy (85%), $n = 1$	• 1 patient who previously had an unsuccessful gastric bypass reversal and distal pancreatic resection required a total pancreatectomy for recurrent symptoms • 1 patient had improvements but still experienced episodes of hypoglycemia • 1 patient had no hypoglycemic episodes
Clancy *et al.* (116)	Case report $N = 2$	Distal pancreatectomy (80%), $n = 1$; subtotal pancreatectomy (95%), $n = 1$	• 80% pancreatectomy[2] unsuccessful; pancreaticoduodenectomy required • Subtotal pancreatectomy successful
Alvarez *et al.* (117)	Case report $N = 1$	Distal pancreatectomy	• Symptom-free for >10 months
Barbour *et al.* (118)	Retrospective analysis $N = 2$	Distal pancreatectomy, $n = 1$; duodenum-preserving pancreatic head resection, $n = 1$	• Symptoms resolved after distal pancreatectomy • Patient with pancreatic head resection had persistent symptoms and underwent distal pancreatectomy
Z'graggen *et al.* (114)	Case series $N = 3$[1]	Distal pancreatectomy and Fobi ring around gastric pouch, $n = 2$; distal pancreatectomy (50%–60%) and removal of pouch band, $n = 1$	• No new hypoglycemic episodes

(*Continues*)

Table 5 (Continued)

Study	Patients	Procedure	Results
Rumilla *et al.* (119)	Case series $N = 27$	Partial pancreatectomy	• 8 patients had recurrent or ongoing mild symptoms
Mathavan *et al.* (120)	Retrospective study $N = 9$	Distal pancreatectomy (80%)	• 2 patients had complete symptom resolution • 3 had occasional symptoms • 2 had frequent symptoms • 2 patients had severe symptoms refractory to medical therapy (calcium channel blockers, diazoxide and octreotide) • Both patients had extended (95%) pancreatic resection; 1 had resolution of symptoms and symptoms persisted in the second patient
Vanderveen *et al.* (105)	Retrospective chart review $N = 33$	Pancreatic resection	• Approximately 40% of patients had moderate or highly successful surgical outcomes, with an improvement in hypoglycemic symptoms
Rabiee *et al.* (121)	Case report $N = 1$	Distal pancreatectomy (85%)	• Symptoms resolved but elevated levels of GLP-1 persisted
Ceppa *et al.* (122)	Case report $N = 1$	Distal pancreatectomy	• Hypoglycemia persisted and a total pancreatectomy was required
Qintar *et al.* (123)	Case report $N = 1$	Distal pancreatectomy (80%)	• Full remission initially after surgery but hypoglycemia recurred after 6 months • Hypoglycemia recurrence well-controlled by octreotide therapy
Lee *et al.* (107)	Case report $N = 1$	Distal pancreatectomy	• Distal pancreatectomy was followed by gastric bypass reversal • Gastric bypass reversal was ineffective in reversing hypoglycemia
Vilarrasa *et al.* (66)	Multicenter, retrospective, systematic case series $N = 3$[3]	Partial pancreatectomy	• Hypoglycemia resolved in 2 patients (67%)

[1]Two additional patients ($N = 12$) with concomitant pancreatic resection excluded from the gastric pouch restriction subgroup but are included in the pancreatic resection subgroup.
[2]Resection of 80% of the total pancreatic volume starting from the pancreatic tail.
[3]Roux-en-Y gastric bypass or other malabsorptive procedure.
Abbreviation: GLP, glucagon-like peptide.

hyperinsulinemic hypoglycemia after bariatric surgery with diazoxide (168.7 ± 94 mg/day orally) resulted in a partial response (defined as a 50% reduction in the number and severity of hypoglycemic events) in three patients (50%) (66). Nifedipine, a calcium channel blocking agent, successfully controlled persistent hyperinsulinemic hypoglycemia in a case report of an adult patient with dumping syndrome that occurred after gastric bypass surgery (104). Administration of nifedipine in combination with verapamil to 10 patients who developed hyperinsulinemic hypoglycemia after bariatric surgery resulted in a partial response in five patients (50%) (66). Continuous infusion of the GLP-1 receptor antagonist exendin 9-39 has recently been shown to correct hypoglycemia after gastric bypass, which may result in a new therapeutic approach for the management of dumping syndrome. The benefit observed with exendin 9-39 therapy is consistent with the role of GLP-1 in the development of postprandial hypoglycemia after gastric bypass (18). Because these pharmacologic interventions have only been evaluated in small studies, current evidence supporting their efficacy in dumping syndrome is generally quite limited.

Surgical re-intervention or continuous enteral feeding

Despite the availability of several effective therapeutic options, some patients will continue to experience treatment-refractory dumping syndrome. Surgical re-intervention or continuous enteral feeding is additional therapeutic approaches that can be considered in this situation.

Surgical re-intervention (*level of evidence*: *IV*; *grade of recommendation*: *C*)

Most patients with postprandial hypoglycemia after Roux-en-Y gastric bypass respond to dietary modification and pharmacologic intervention. However, a subset of patients with severe post-Roux-en-Y gastric bypass hypoglycemia may respond inadequately, and surgical re-intervention may be considered. In general, surgical re-intervention procedures are largely ineffective, and some procedures (e.g. pancreatectomy) are rarely performed because of lack of effectiveness and high morbidity. A study of patients who underwent partial pancreatectomy because of noninsulinoma pancreatogenous hypoglycemia

demonstrated that nearly 90% experienced recurrent symptoms suggestive of hypoglycemia (105). Fewer than half of patients (48%) were deemed to have achieved a highly or moderately successful surgical outcome, and 25% experienced no apparent benefit (105).

Various surgical re-interventions have been used, including gastric tube placement, gastric bypass reversal with or without concomitant sleeve resection and gastric pouch restriction (Table 5) (66,103,105–123). A special consideration is the association between hypoglycemia after Roux-en-Y gastric bypass and nesidioblastosis that may result in serious and refractory neuroglycopenic symptoms, which respond to pancreatic resection and re-re section (124). Because the development of hyperinsulinemic hypoglycemia after gastric bypass surgery is not accompanied by islet hyperplasia or increased beta-cell turnover, nesidioblastosis has not been established as the cause of late dumping syndrome (125).

As shown in Table 5, approximately 24% of patients who underwent surgical re-intervention because of refractory

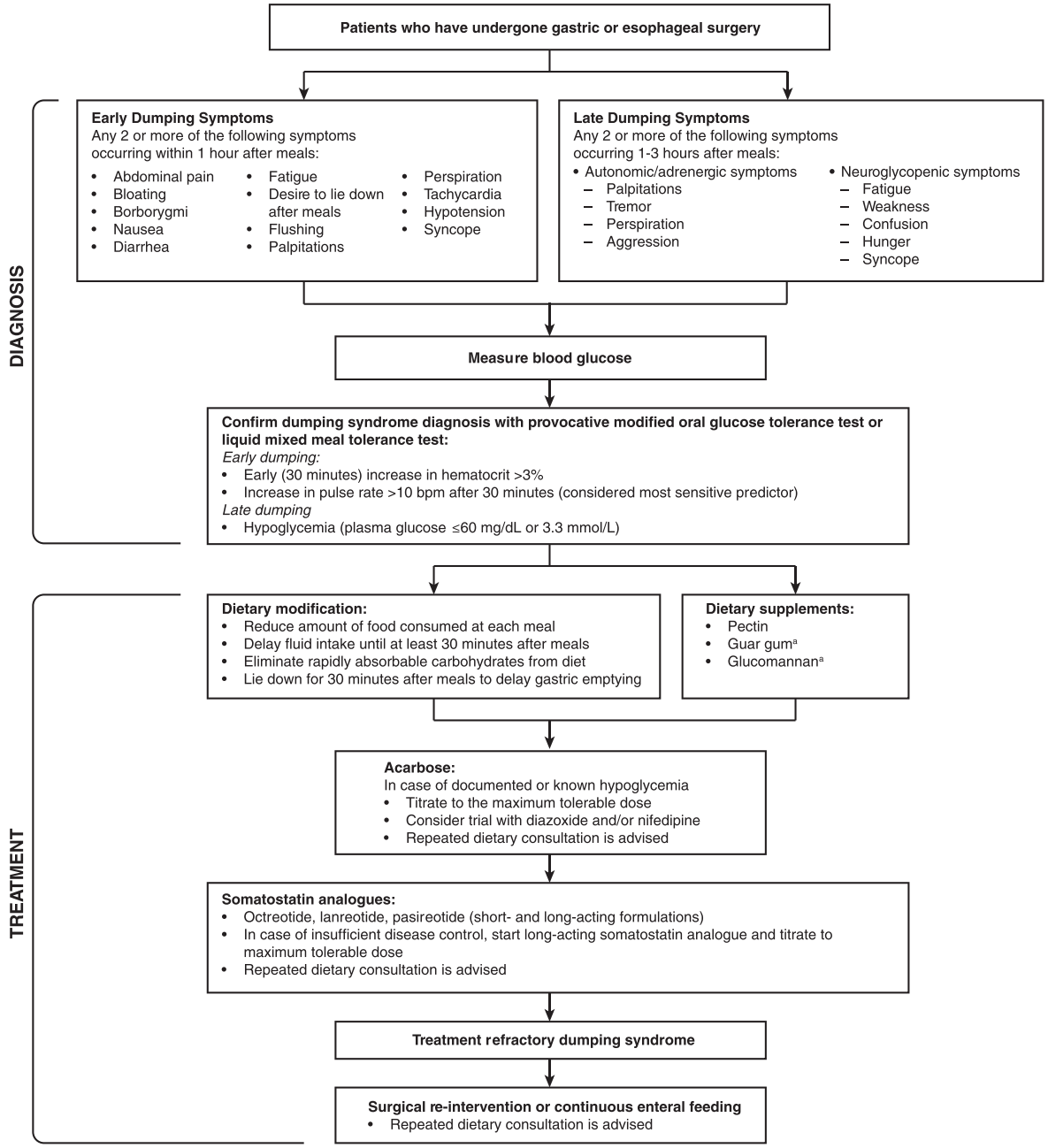

Figure 2 Recommended diagnosis and management strategies for dumping syndrome. [a]Limited evidence only.

severe post-Roux-en-Y gastric bypass hypoglycemia received a gastric bypass reversal (66,103,106–113) and approximately 9% had gastric pouch restriction (66,114,115). Pancreatic resection, the most commonly reported procedure, was performed in approximately 67% of patients (66,103,105,107,114,116–123). Some patients underwent two or more consecutive surgical re-interventions or combined re-interventions for severe hypoglycemia. The proportion of patients with symptom resolution after each procedure was generally higher for gastric bypass reversal or gastric pouch restriction than for pancreatic resection. Complications of surgical re-intervention included recurrent symptoms, diabetes and weight gain. Most surgical re-intervention studies were relatively small and presumably included highly selected patients, mean follow-up was short, and the methodology used to evaluate hypoglycemia was not consistent. Furthermore, the effectiveness of one surgical re-intervention procedure relative to another has not been evaluated in adequately controlled clinical studies. Conservative management approaches should be pursued before attempting surgical re-intervention as patients with dumping syndrome may experience symptomatic improvement over time.

Continuous enteral feeding (*level of evidence*: *V*; *grade of recommendation*: *D*)

An additional approach for the management of refractory dumping syndrome involves the provision of a constant supply of nutrients via a feeding jejunostomy. Anecdotal evidence suggests that continuous enteral feeding may be beneficial in avoiding dumping symptoms after meal ingestion; however, this approach is invasive and may impair quality of life (1,126). Restoring the original nutrient transit route via placement of a gastric tube in the remnant stomach was also reported to be effective (127). Standardized liquid meal administration via a gastric tube demonstrated complete reversal of severe metabolic abnormalities including hypersecretion of insulin and incretin hormones such as GLP-1 compared with oral administration (127). The authors of this publication also restored glucose homeostasis via the placement of a gastric tube in the remnant stomach of a patient who had undergone gastric bypass surgery (Dr. van Beek, unpublished observation). However, as these findings are based on individual case reports, clinical evidence supporting the use of continuous enteral feeding in the management of dumping syndrome is very limited.

Conclusion

Dumping syndrome is a well-known but under-recognized complication of esophageal and gastric surgery and is becoming increasingly prevalent with the rising incidence of bariatric surgery. Severe dumping syndrome, in particular, can result in disabling symptoms that impair quality of life. No medications are currently approved for the management of dumping syndrome, and most of the currently available treatments have considerable limitations, including failure to target early symptoms and poor tolerability.

Our recommendations for the diagnosis and management of dumping syndrome are based on available published clinical information and are presented in Fig. 2. Patients who have undergone esophageal or gastric surgery should be monitored for symptoms suggestive of early and late dumping. Suspected dumping syndrome should preferably be confirmed using symptom-based questionnaires, glycemia monitoring, or, probably most effectively, in a challenge using an OGTT or mixed-meal tolerance test. The differential diagnostic evaluation should also consider other postoperative conditions or complications that may present with similar symptoms. First-line management of dumping syndrome should focus on dietary modification for 3 to 4 weeks, with addition of acarbose treatment for patients who experience postprandial hypoglycemia. If dietary modification and acarbose treatment are unsuccessful, somatostatin analogue therapy should be considered in patients with dumping syndrome who are experiencing incapacitating symptoms and impairment in quality of life. Short-acting and long-acting somatostatin analogue therapy should be attempted for 2 weeks and for 2 months, respectively. Based on patient preference, long-acting somatostatin analogue formulations are probably the treatment of choice because they require less frequent administration and have less impact on quality of life compared with short-acting somatostatin analogues. However, short-acting somatostatin analogues seem to provide the most rigorous control of pulse rate and glycemia fluctuations associated with dumping syndrome. Surgical re-intervention or continuous gastric/enteral feeding may need to be considered in some patients with treatment-refractory dumping syndrome, but the outcomes of these approaches are poorly studied and tend to be more variable.

Finally, effective management of dumping syndrome requires close collaboration between specialists trained in recognizing and treating dumping symptoms, including those with expertise in gastroenterology, endocrinology, surgery and nutrition. Given the increase in bariatric procedures and, thereby, the potential for an increase in the prevalence of dumping symptoms, prospective clinical studies are needed to evaluate the occurrence of dumping syndrome and to assess the effect of early detection and treatment of clinical symptoms on weight loss and quality of life.

Conflict of interest

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References

1. Tack J, Arts J, Caenepeel P, De Wulf D, Bisschops R. Pathophysiology, diagnosis and management of postoperative dumping syndrome. *Nat Rev Gastroenterol Hepatol* 2009; **6**: 583–590.
2. Tack J, Deloose E. Complications of bariatric surgery: dumping syndrome, reflux and vitamin deficiencies. *Best Pract Res Clin Gastroenterol* 2014; **28**: 741–749.
3. Vecht J, Masclee AA, Lamers CB. The dumping syndrome. Current insights into pathophysiology, diagnosis and treatment. *Scand J Gastroenterol Suppl* 1997; **223**: 21–27.
4. McLarty AJ, Deschamps C, Trastek VF, Allen MS, Pairolero PC, Harmsen WS. Esophageal resection for cancer of the esophagus: long-term function and quality of life. *Ann Thorac Surg* 1997; **63**: 1568–1572.
5. Banerjee A, Ding Y, Mikami DJ, Needleman BJ. The role of dumping syndrome in weight loss after gastric bypass surgery. *Surg Endosc* 2013; **27**: 1573–1578.
6. Tzovaras G, Papamargaritis D, Sioka E *et al.* Symptoms suggestive of dumping syndrome after provocation in patients after laparoscopic sleeve gastrectomy. *Obes Surg* 2012; **22**: 23–28.
7. Papamargaritis D, Koukoulis G, Sioka E *et al.* Dumping symptoms and incidence of hypoglycaemia after provocation test at 6 and 12 months after laparoscopic sleeve gastrectomy. *Obes Surg* 2012; **22**: 1600–1606.
8. Ng DD, Ferry RJ Jr, Kelly A, Weinzimer SA, Stanley CA, Katz LE. Acarbose treatment of postprandial hypoglycemia in children after Nissen fundoplication. *J Pediatr* 2001; **139**: 877–879.
9. Boeckxstaens V, Broers C, Tack J, Pauwels A. Late dumping syndrome as a complication of a Nissen fundoplication in adults. *Submitted for publication*.
10. Abell TL, Minocha A. Gastrointestinal complications of bariatric surgery: diagnosis and therapy. *Am J Med Sci* 2006; **331**: 214–218.
11. Baptista V, Wassef W. Bariatric procedures: an update on techniques, outcomes and complications. *Curr Opin Gastroenterol* 2013; **29**: 684–693.
12. Lee CJ, Clark JM, Schweitzer M *et al.* Prevalence of and risk factors for hypoglycemic symptoms after gastric bypass and sleeve gastrectomy. *Obesity (Silver Spring)* 2015; **23**: 1079–1084.
13. Glasgow RE, Mulvihill SJ. Surgery for peptic ulcer disease and postgastrectomy syndromes. In: Yamada T (ed.). *Textbook of Gastroenterology Vol 1*. Wiley-Blackwell: West Sussex, UK, 2009, pp. 1060–1062.
14. Laurenius A, Olbers T, Naslund I, Karlsson J. Dumping syndrome following gastric bypass: validation of the dumping symptom rating scale. *Obes Surg* 2013; **23**: 740–755.
15. Arts J, Caenepeel P, Bisschops R *et al.* Efficacy of the long-acting repeatable formulation of the somatostatin analogue octreotide in postoperative dumping. *Clin Gastroenterol Hepatol* 2009; **7**: 432–437.
16. Ukleja A. Dumping syndrome: pathophysiology and treatment. *Nutr Clin Pract* 2005; **20**: 517–525.
17. Intra-patient dose escalation study evaluating efficacy, safety, and pharmacokinetics of pasireotide (SOM230) subcutaneous (s.c.) followed by pasireotide LAR in patients with dumping syndrome. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01637272?term=NCT01637272.
18. Salehi M, Gastaldelli A, D'Alessio DA. Blockade of glucagon-like peptide 1 receptor corrects postprandial hypoglycemia after gastric bypass. *Gastroenterology* 2014; **146**: 669–680 e662.
19. Marsk R, Jonas E, Rasmussen F, Naslund E. Nationwide cohort study of post-gastric bypass hypoglycaemia including 5,040 patients undergoing surgery for obesity in 1986-2006 in Sweden. *Diabetologia* 2010; **53**: 2307–2311.
20. Emous M, Ubels FL, van Beek AP. Diagnostic tools for post-gastric bypass hypoglycaemia. *Obes Rev* 2015; **16**: 843–856.
21. Machella TE. The mechanism of the post-gastrectomy "dumping" syndrome. *Ann Surg* 1949; **130**: 145–159.
22. Tack J. Gastric motor disorders. *Best Pract Res Clin Gastroenterol* 2007; **21**: 633–644.
23. MacGregor I, Parent J, Meyer JH. Gastric emptying of liquid meals and pancreatic and biliary secretion after subtotal gastrectomy or truncal vagotomy and pyloroplasty in man. *Gastroenterology* 1977; **72**: 195–205.
24. Mayer EA, Thompson JB, Jehn D, Reedy T, Elashoff J, Meyer JH. Gastric emptying and sieving of solid food and pancreatic and biliary secretion after solid meals in patients with truncal vagotomy and antrectomy. *Gastroenterology* 1982; **83**: 184–192.
25. Lawaetz O, Blackburn AM, Bloom SR, Aritas Y, Ralphs DN. Gut hormone profile and gastric emptying in the dumping syndrome. A hypothesis concerning the pathogenesis. *Scand J Gastroenterol* 1983; **18**: 73–80.
26. Johnson LP, Sloop RD, Jesseph JE. Etiologic significance of the early symptomatic phase in the dumping syndrome. *Ann Surg* 1962; **156**: 173–179.
27. Sirinek KR, O'Dorisio TM, Howe B, McFee AS. Neurotensin, vasoactive intestinal peptide, and Roux-en-Y gastrojejunostomy. Their role in the dumping syndrome. *Arch Surg* 1985; **120**: 605–609.
28. Eloy R, Garaud JC, Moody A, Jaeck D, Grenier JF. Jejunal factor stimulating insulin release in the isolated perfused canine pancreas and jejunum. *Horm Metab Res* 1975; **7**: 461–467.
29. Toft-Nielsen M, Madsbad S, Holst JJ. Exaggerated secretion of glucagon-like peptide-1 (GLP-1) could cause reactive hypoglycaemia. *Diabetologia* 1998; **41**: 1180–1186.
30. Abrahamsson N, Engstrom BE, Sundbom M, Karlsson FA. GLP1 analogs as treatment of postprandial hypoglycemia following gastric bypass surgery: a potential new indication? *Eur J Endocrinol* 2013; **169**: 885–889.
31. Sigstad H. A clinical diagnostic index in the diagnosis of the dumping syndrome. Changes in plasma volume and blood sugar after a test meal. *Acta Med Scand* 1970; **188**: 479–486.
32. Mine S, Sano T, Tsutsumi K *et al.* Large-scale investigation into dumping syndrome after gastrectomy for gastric cancer. *J Am Coll Surg* 2010; **211**: 628–636.
33. Ritz P, Hanaire H. Post-bypass hypoglycaemia: a review of current findings. *Diabetes Metab* 2011; **37**: 274–281.
34. Ritz P, Vaurs C, Bertrand M, Anduze Y, Guillaume E, Hanaire H. Usefulness of acarbose and dietary modifications to limit glycemic variability following Roux-en-Y gastric bypass as assessed by continuous glucose monitoring. *Diabetes Technol Ther* 2012; **14**: 736–740.

35. Hanaire H, Dubet A, Chauveau ME *et al.* Usefulness of continuous glucose monitoring for the diagnosis of hypoglycemia after a gastric bypass in a patient previously treated for type 2 diabetes. *Obes Surg* 2010; **20**: 126–129.
36. Oliveira CH, Berger K, Souza SC *et al.* Continuous glucose monitoring: a critical appraisal after one year experience. *Arq Bras Endocrinol Metabol* 2005; **49**: 983–990.
37. van der Kleij FG, Vecht J, Lamers CB, Masclee AA. Diagnostic value of dumping provocation in patients after gastric surgery. *Scand J Gastroenterol* 1996; **31**: 1162–1166.
38. Khoo CM, Muehlbauer MJ, Stevens RD *et al.* Postprandial metabolite profiles reveal differential nutrient handling after bariatric surgery compared with matched caloric restriction. *Ann Surg* 2014; **259**: 687–693.
39. Cryer PE, Axelrod L, Grossman AB *et al.* Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2009; **94**: 709–728.
40. Hogan MJ, Service FJ, Sharbrough FW, Gerich JE. Oral glucose tolerance test compared with a mixed meal in the diagnosis of reactive hypoglycemia. A caveat on stimulation. *Mayo Clin Proc* 1983; **58**: 491–496.
41. Mathur A, Gorden P, Libutti SK. Insulinoma. *Surg Clin North Am* 2009; **89**: 1105–1121.
42. Mulla CM, Storino A, Yee EU *et al.* Insulinoma after bariatric surgery: diagnostic dilemma and therapeutic approaches. *Obes Surg* 2016; **26**: 874–881.
43. Robinson FW, Pittman AC. Dietary management of postgastrectomy dumping syndrome. *Surg Gynecol Obstet* 1957; **104**: 529–534.
44. Pittman AC, Robinson FW. Dietary management of the "dumping" syndrome. Long-term follow-up. *J Am Diet Assoc* 1962; **40**: 108–110.
45. Khoshoo V, Reifen RM, Gold BD, Sherman PM, Pencharz PB. Nutritional manipulation in the management of dumping syndrome. *Arch Dis Child* 1991; **66**: 1447–1448.
46. Laurenius A, Werling M, Le Roux CW, Fandriks L, Olbers T. More symptoms but similar blood glucose curve after oral carbohydrate provocation in patients with a history of hypoglycemia-like symptoms compared to asymptomatic patients after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2014; **10**: 1047–1054.
47. Kellogg TA, Bantle JP, Leslie DB *et al.* Postgastric bypass hyperinsulinemic hypoglycemia syndrome: characterization and response to a modified diet. *Surg Obes Relat Dis* 2008; **4**: 492–499.
48. Jenkins DJ, Gassull MA, Leeds AR *et al.* Effect of dietary fiber on complications of gastric surgery: prevention of postprandial hypoglycemia by pectin. *Gastroenterology* 1977; **73**: 215–217.
49. Jenkins DJ, Bloom SR, Albuquerque RH *et al.* Pectin and complications after gastric surgery: normalisation of postprandial glucose and endocrine responses. *Gut* 1980; **21**: 574–579.
50. Leeds AR, Ralphs DN, Ebied F, Metz G, Dilawari JB. Pectin in the dumping syndrome: reduction of symptoms and plasma volume changes. *Lancet* 1981; **1**: 1075–1078.
51. Lawaetz O, Blackburn AM, Bloom SR, Aritas Y, Ralphs DN. Effect of pectin on gastric emptying and gut hormone release in the dumping syndrome. *Scand J Gastroenterol* 1983; **18**: 327–336.
52. Andersen JR, Holtug K, Uhrenholt A. Trial of pectin-enriched muffins in patients with severe dumping syndrome after gastric resection. Observations on symptoms and gastric emptying pattern. *Acta Chir Scand* 1989; **155**: 39–41.
53. Speth PA, Jansen JB, Lamers CB. Effect of acarbose, pectin, a combination of acarbose with pectin, and placebo on postprandial reactive hypoglycaemia after gastric surgery. *Gut* 1983; **24**: 798–802.
54. Harju E, Larmi TK. Efficacy of guar gum in preventing the dumping syndrome. *JPEN J Parenter Enteral Nutr* 1983; **7**: 470-472.
55. Harju E, Heikkila J, Larmi TK. Effect of guar gum on gastric emptying after gastric resection. *JPEN J Parenter Enteral Nutr* 1984; **8**: 18–20.
56. Harju E, Makela J. Reduction in symptoms after proximal selective vagotomy through increased dietary viscosity. *Am J Gastroenterol* 1984; **79**: 861–863.
57. Kneepkens CM, Fernandes J, Vonk RJ. Dumping syndrome in children. Diagnosis and effect of glucomannan on glucose tolerance and absorption. *Acta Paediatr Scand* 1988; **77**: 279–286.
58. McLoughlin JC, Buchanan KD, Alam MJ. A glycoside-hydrolase inhibitor in treatment of dumping syndrome. *Lancet* 1979; **2**: 603–605.
59. Gerard J, Luyckx AS, Lefebvre PJ. Acarbose in reactive hypoglycemia: a double-blind study. *Int J Clin Pharmacol Ther Toxicol* 1984; **22**: 25–31.
60. Lyons TJ, McLoughlin JC, Shaw C, Buchanan KD. Effect of acarbose on biochemical responses and clinical symptoms in dumping syndrome. *Digestion* 1985; **31**: 89–96.
61. Hasegawa T, Yoneda M, Nakamura K *et al.* Long-term effect of alpha-glucosidase inhibitor on late dumping syndrome. *J Gastroenterol Hepatol* 1998; **13**: 1201–1206.
62. Ozgen AG, Hamulu F, Bayraktar F *et al.* Long-term treatment with acarbose for the treatment of reactive hypoglycemia. *Eat Weight Disord* 1998; **3**: 136–140.
63. De Cunto A, Barbi E, Minen F, Ventura A. Safety and efficacy of high-dose acarbose treatment for dumping syndrome. *J Pediatr Gastroenterol Nutr* 2011; **53**: 113–114.
64. Valderas JP, Ahuad J, Rubio L, Escalona M, Pollak F, Maiz A. Acarbose improves hypoglycaemia following gastric bypass surgery without increasing glucagon-like peptide 1 levels. *Obes Surg* 2012; **22**: 582–586.
65. Moreira RO, Moreira RB, Machado NA, Goncalves TB, Coutinho WF. Post-prandial hypoglycemia after bariatric surgery: pharmacological treatment with verapamil and acarbose. *Obes Surg* 2008; **18**: 1618–1621.
66. Vilarrasa N, Goday A, Rubio MA *et al.* Hyperinsulinemic hypoglycemia after bariatric surgery: diagnosis and management experience from a spanish multicenter registry. *Obes Facts* 2016; **9**: 41–51.
67. Edmunds MC, Chen JD, Soykan I, Lin Z, McCallum RW. Effect of octreotide on gastric and small bowel motility in patients with gastroparesis. *Aliment Pharmacol Ther* 1998; **12**: 167–174.
68. Fuessl HS, Carolan G, Williams G, Bloom SR. Effect of a long-acting somatostatin analogue (SMS 201-995) on postprandial gastric emptying of 99mTc-tin colloid and mouth-to-caecum transit time in man. *Digestion* 1987; **36**: 101–107.
69. van Berge Henegouwen MI, van Gulik TM, Akkermans LM, Jansen JB, Gouma DJ. The effect of octreotide on gastric emptying at a dosage used to prevent complications after pancreatic surgery: a randomised, placebo controlled study in volunteers. *Gut* 1997; **41**: 758–762.
70. Foxx-Orenstein A, Camilleri M, Stephens D, Burton D. Effect of a somatostatin analogue on gastric motor and sensory functions in healthy humans. *Gut* 2003; **52**: 1555–1561.
71. Di Lorenzo C, Lucanto C, Flores AF, Idries S, Hyman PE. Effect of sequential erythromycin and octreotide on antroduodenal manometry. *J Pediatr Gastroenterol Nutr* 1999; **29**: 293–296.
72. Nelson-Piercy C, Hammond PJ, Gwilliam ME *et al.* Effect of a new oral somatostatin analog (SDZ CO 611) on gastric emptying, mouth to cecum transit time, and pancreatic and gut hormone release in normal male subjects. *J Clin Endocrinol Metab* 1994; **78**: 329–336.

73. von der Ohe MR, Camilleri M, Thomforde GM, Klee GG. Differential regional effects of octreotide on human gastrointestinal motor function. *Gut* 1995; **36**: 743–748.
74. Kraenzlin ME, Wood SM, Neufeld M, Adrian TE, Bloom SR. Effect of long acting somatostatin-analogue, SMS 201 995, on gut hormone secretion in normal subjects. *Experientia* 1985; **41**: 738–740.
75. Williams G, Fuessl H, Kraenzlin M, Bloom SR. Postprandial effects of SMS 201-995 on gut hormones and glucose tolerance. *Scand J Gastroenterol Suppl* 1986; **119**: 73–83.
76. Parkinson C, Drake WM, Roberts ME, Meeran K, Besser GM, Trainer PJ. A comparison of the effects of pegvisomant and octreotide on glucose, insulin, gastrin, cholecystokinin, and pancreatic polypeptide responses to oral glucose and a standard mixed meal. *J Clin Endocrinol Metab* 2002; **87**: 1797–1804.
77. Kemmer TP, Malfertheiner P, Buchler M, Friess H, Meschenmoser L, Ditschuneit H. Inhibition of human exocrine pancreatic secretion by the long-acting somatostatin analogue octreotide (SMS 201-995). *Aliment Pharmacol Ther* 1992; **6**: 41–50.
78. Hogenauer C, Aichbichler B, Santa Ana C, Porter J, Fordtran J. Effect of octreotide on fluid absorption and secretion by the normal human jejunum and ileum in vivo. *Aliment Pharmacol Ther* 2002; **16**: 769–777.
79. Chisholm C, Greenberg GR. Somatostatin-28 regulates GLP-1 secretion via somatostatin receptor subtype 5 in rat intestinal cultures. *Am J Physiol Endocrinol Metab* 2002; **283**: E311–E317.
80. Hopman WP, Wolberink RG, Lamers CB, Van Tongeren JH. Treatment of the dumping syndrome with the somatostatin analogue SMS 201-995. *Ann Surg* 1988; **207**: 155–159.
81. Primrose JN, Johnston D. Somatostatin analogue SMS 201-995 (octreotide) as a possible solution to the dumping syndrome after gastrectomy or vagotomy. *Br J Surg* 1989; **76**: 140–144.
82. Tulassay Z, Tulassay T, Gupta R, Cierny G. Long acting somatostatin analogue in dumping syndrome. *Br J Surg* 1989; **76**: 1294–1295.
83. Geer RJ, Richards WO, O'Dorisio TM *et al.* Efficacy of octreotide acetate in treatment of severe postgastrectomy dumping syndrome. *Ann Surg* 1990; **212**: 678–687.
84. Richards WO, Geer R, O'Dorisio TM *et al.* Octreotide acetate induces fasting small bowel motility in patients with dumping syndrome. *J Surg Res* 1990; **49**: 483–487.
85. Gray JL, Debas HT, Mulvihill SJ. Control of dumping symptoms by somatostatin analogue in patients after gastric surgery. *Arch Surg* 1991; **126**: 1231–1235 discussion 1235-1236.
86. Hasler WL, Soudah HC, Owyang C. Mechanisms by which octreotide ameliorates symptoms in the dumping syndrome. *J Pharmacol Exp Ther* 1996; **277**: 1359–1365.
87. Vecht J, Lamers CB, Masclee AA. Long-term results of octreotide-therapy in severe dumping syndrome. *Clin Endocrinol (Oxf)* 1999; **51**: 619–624.
88. Didden P, Penning C, Masclee AA. Octreotide therapy in dumping syndrome: Analysis of long-term results. *Aliment Pharmacol Ther* 2006; **24**: 1367–1375.
89. Penning C, Vecht J, Masclee AA. Efficacy of depot long-acting release octreotide therapy in severe dumping syndrome. *Aliment Pharmacol Ther* 2005; **22**: 963–969.
90. Deloose E, Bisschops R, Holvoet L *et al.* A pilot study of the effects of the somatostatin analog pasireotide in postoperative dumping syndrome. *Neurogastroenterol Motil* 2014; **26**: 803–809.
91. Morz R, Prager J, Pointner H. [(Influence of somatostatin (SS-14) on early dumping reaction in patients after partial gastrectomy)]. *Z Gastroenterol* 1982; **20**: 299–304.
92. Long RG, Adrian TE, Bloom SR, Somatostatin and the dumping syndrome. *Br Med J (Clin Res Ed)* 1985; **290**: 886–888.
93. Reasbeck PG, Van Rij AM. The effect of somatostatin on dumping after gastric surgery: a preliminary report. *Surgery* 1986; **99**: 462–468.
94. Sato D, Morino K, Ohashi N *et al.* Octreotide improves early dumping syndrome potentially through incretins: a case report. *Endocr J* 2013; **60**: 847–853.
95. Al-Hussaini A, Butzner D. Therapeutic applications of octreotide in pediatric patients. *Saudi J Gastroenterol* 2012; **18**: 87–94.
96. Ewins DL, Javaid A, Coskeran PB *et al.* Assessment of gall bladder dynamics, cholecystokinin release and the development of gallstones during octreotide therapy for acromegaly. *Q J Med* 1992; **83**: 295–306.
97. Moschetta A, Stolk MF, Rehfeld JF *et al.* Severe impairment of postprandial cholecystokinin release and gall-bladder emptying and high risk of gallstone formation in acromegalic patients during Sandostatin LAR. *Aliment Pharmacol Ther* 2001; **15**: 181–185.
98. Bruns C, Lewis I, Briner U, Meno-Tetang G, Weckbecker G. SOM230: a novel somatostatin peptidomimetic with broad somatotropin release inhibiting factor (SRIF) receptor binding and a unique antisecretory profile. *Eur J Endocrinol* 2002; **146**: 707–716.
99. Schmid HA. Pasireotide (SOM230): development, mechanism of action and potential applications. *Mol Cell Endocrinol* 2008; **286**: 69–74.
100. de Heide LJ, Laskewitz AJ, Apers JA. Treatment of severe postRYGB hyperinsulinemic hypoglycemia with pasireotide: a comparison with octreotide on insulin, glucagon, and GLP-1. *Surg Obes Relat Dis* 2014; **10**: e31–e33.
101. Tack J, Arts J, Aberle J *et al.* Pasireotide in Dumping Syndrome - Results from a Phase 2, International, Multicentre Study. Presented at the *23rd United European Gastroenterology Week*. Barcelona, Spain, October 24th to 28th, 2015. Poster PO262.
102. Somatuline Autogel 90 mg in dumping syndrome. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01923649?term=NCT01923649.
103. Patti ME, McMahon G, Mun EC *et al.* Severe hypoglycaemia post-gastric bypass requiring partial pancreatectomy: evidence for inappropriate insulin secretion and pancreatic islet hyperplasia. *Diabetologia* 2005; **48**: 2236–2240.
104. Guseva N, Phillips D, Mordes JP. Successful treatment of persistent hyperinsulinemic hypoglycemia with nifedipine in an adult patient. *Endocr Pract* 2010; **16**: 107–111.
105. Vanderveen KA, Grant CS, Thompson GB, et al. Outcomes and quality of life after partial pancreatectomy for noninsulinoma pancreatogenous hypoglycemia from diffuse islet cell disease. *Surgery* 2010; **148**: 1237–1245; discussion 1245-1236.
106. Campos GM, Ziemelis M, Paparodis R, Ahmed M, Davis DB. Laparoscopic reversal of Roux-en-Y gastric bypass: technique and utility for treatment of endocrine complications. *Surg Obes Relat Dis* 2014; **10**: 36–43.
107. Lee CJ, Brown T, Magnuson TH, Egan JM, Carlson O, Elahi D. Hormonal response to a mixed-meal challenge after reversal of gastric bypass for hypoglycemia. *J Clin Endocrinol Metab* 2013; **98**: E1208–E1212.
108. Vilallonga R, van de Vrande S, Himpens J. Laparoscopic reversal of Roux-en-Y gastric bypass into normal anatomy with or without sleeve gastrectomy. *Surg Endosc* 2013; **27**: 4640–4648.
109. Rao BB, Click B, Eid G, Codario RA. Management of refractory noninsulinoma pancreatogenous hypoglycemia syndrome with gastric bypass reversal: a case report and review of the literature. *Case Rep Endocrinol* 2015; **2015**: 384526.

110. Carter CO, Fernandez AZ, McNatt SS, Powell MS. Conversion from gastric bypass to sleeve gastrectomy for complications of gastric bypass. *Surg Obes Relat Dis* 2016; **12**: 572–576.
111. Lakdawala M, Limas P, Dhar S *et al.* Laparoscopic revision of Roux-en-Y gastric bypass to sleeve gastrectomy: A ray of hope for failed Roux-en-Y gastric bypass. *Asian J Endosc Surg* 2016; **9**: 122–127.
112. Huang CK, Wang MY, Das SS, Chang PC. Laparoscopic conversion to loop duodenojejunal bypass with sleeve gastrectomy for intractable dumping syndrome after Roux-en-Y gastric bypass-two case reports. *Obes Surg* 2015; **25**: 947.
113. Huang CK, Wang MY, Hsin MC, Chang PC. Conversion to modified duodenal switch for relieving intractable dumping syndrome and constipation after laparoscopic Roux-en-Y gastric bypass. *Obes Surg* 2015; **25**: 946.
114. Z'graggen K, Guweidhi A, Steffen R *et al.* Severe recurrent hypoglycemia after gastric bypass surgery. *Obes Surg* 2008; **18**: 981–988.
115. de Heide LJ, Glaudemans AW, Oomen PH, Apers JA, Totte ER, van Beek AP. Functional imaging in hyperinsulinemic hypoglycemia after gastric bypass surgery for morbid obesity. *J Clin Endocrinol Metab* 2012; **97**: E963–E967.
116. Clancy TE, Moore FD Jr, Zinner MJ. Post-gastric bypass hyperinsulinism with nesidioblastosis: subtotal or total pancreatectomy may be needed to prevent recurrent hypoglycemia. *J Gastrointest Surg* 2006; **10**: 1116–1119.
117. Alvarez GC, Faria EN, Beck M, Girardon DT, Machado AC. Laparoscopic spleen-preserving distal pancreatectomy as treatment for nesidioblastosis after gastric bypass surgery. *Obes Surg* 2007; **17**: 550–552.
118. Barbour JR, Thomas BN, Morgan KA, Byrne TK, Adams DB. The practice of pancreatic resection after Roux-en-Y gastric bypass. *Am Surg* 2008; **74**: 729–734.
119. Rumilla KM, Erickson LA, Service FJ *et al.* Hyperinsulinemic hypoglycemia with nesidioblastosis: histologic features and growth factor expression. *Mod Pathol* 2009; **22**: 239–245.
120. Mathavan VK, Arregui M, Davis C, Singh K, Patel A, Meacham J. Management of postgastric bypass noninsulinoma pancreatogenous hypoglycemia. *Surg Endosc* 2010; **24**: 2547–2555.
121. Rabiee A, Magruder JT, Salas–Carrillo R *et al.* Hyperinsulinemic hypoglycemia after Roux-en-Y gastric bypass: unraveling the role of gut hormonal and pancreatic endocrine dysfunction. *J Surg Res* 2011; **167**: 199–205.
122. Ceppa EP, Ceppa DP, Omotosho PA, Dickerson JA 2nd, Park CW, Portenier DD. Algorithm to diagnose etiology of hypoglycemia after Roux-en-Y gastric bypass for morbid obesity: case series and review of the literature. *Surg Obes Relat Dis* 2012; **8**: 641–647.
123. Qintar M, Sibai F, Taha M. Hypoglycemia due to an adult-onset nesidioblastosis, a diagnostic and management dilemma. *Avicenna J Med* 2012; **2**: 45–47.
124. Mala T. Postprandial hyperinsulinemic hypoglycemia after gastric bypass surgical treatment. *Surg Obes Relat Dis* 2014; **10**: 1220–1225.
125. Meier JJ, Butler AE, Galasso R, Butler PC. Hyperinsulinemic hypoglycemia after gastric bypass surgery is not accompanied by islet hyperplasia or increased beta-cell turnover. *Diabetes Care* 2006; **29**: 1554–1559.
126. Veit F, Heine RG, Catto-Smith AG. Dumping syndrome after Nissen fundoplication. *J Paediatr Child Health* 1994; **30**: 182–185.
127. McLaughlin T, Peck M, Holst J, Deacon C. Reversible hyperinsulinemic hypoglycemia after gastric bypass: a consequence of altered nutrient delivery. *J Clin Endocrinol Metab* 2010; **95**: 1851–1855.