Dumping syndrome after bariatric surgery: prevalence, pathophysiology and role in weight reduction – a systematic review

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Abstract

Background: **Dumping syndrome is a frequent and well-known adverse event after bariatric surgery and covers a dynamic spectrum of early and late dumping. Accelerated gastric emptying is generally considered to be the cause of gastrointestinal and vasomotor complaints. However, there is much uncertainty regarding the exact pathophysiology of dumping. It has been speculated that the syndrome is a desired consequence of bariatric surgery and contributes to more efficient weight loss, but supporting data are scarce.**

Methods: **A systematic search was conducted in PubMed in July-August 2021. The prevalence of dumping after the most frequently performed bariatric procedures was analyzed, as well as underlying pathophysiology and its role in weight reduction.**

Results: **Roux-en-Y gastric bypass (RYGB) is associated with the highest postoperative prevalence of dumping. The fast transit induces neurohumoral changes which contribute to an imbalance between postprandial glucose and insulin levels, resulting in hypoglycemia which is the hallmark of late dumping. Early dumping can, when received in a positive way, become a tool to maintain a strict dietary pattern, but no significant relationship to the degree of weight loss has been shown. However, late dumping is detrimental and promotes overall higher caloric intake.**

Conclusion: **Dumping syndrome is common after bariatric surgery, especially after RYGB. The pathophysiology is complex and ambiguous. Currently available data do not support dumping as a necessary condition to induce weight loss after bariatric surgery.** (Acta gastroenterol. belg., **2023**, 86, **417-427**).

Keywords: dumping syndrome, bariatric surgery, gastric bypass, sleeve gastrectomy, weight loss.

Introduction

Dumping syndrome, a frequently described phenomenon after bariatric surgery, arises from the rapid emptying or "dumping" of undigested gastric contents into the small intestine. A variety of gastrointestinal and vasomotor symptoms is induced and can be classified into early and late dumping (1). Early dumping occurs within one hour after food ingestion and is associated with hypotension, sometimes leading to syncope. Subsequently an autonomic stress response follows with symptoms of tachycardia, palpitations, flushing and sweating. This phenomenon is often accompanied by gastrointestinal symptoms such as abdominal distention, painful cramps, borborygmi, nausea and diarrhea. Late dumping commences 1 to 3 hours after a meal and consists of reactive hypoglycemia, presenting with palpitations, sweating, tremor, irritability or even unconsciousness. When accompanied with confusion and (pre)syncope, this is called neuroglycopenia. The interplay of symptoms that occur in patients with dumping varies widely. While early dumping often occurs in isolation, the combination of both early and late dumping has also been described. The solitary occurrence of late dumping is a rare phenomenon (2).

Table 1. — **Sigstad score for diagnosis of the dumping syndrome** (5)

Shock	+5
Syncope	+4
Urge to lie down	+4
Dyspnea	+3
Feeling of weakness	+3
Lethargy	+3
Palpitations	+3
Restlessness	+2
Dizziness	+2
Headache	+1
Clammy, warm skin	+1
Nausea	+1
Bloated feeling	+1
Borborygmi	+1
Eruction	-1
Vomiting	-4

Table 2. — **Arts questionnaire for differentiation between early and late dumping and estimation of symptom** (6)

Early dumping symptoms	Late dumping symptoms
Sweating	Sweating
Flushing	Palpitations
Dizziness	Hunger
Palpitations	(Pre)syncope
Abdominal discomfort	Tremor
Diarrhea	Irritability
Bloated feeling	
Nausea	

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Several diagnostic tools for dumping syndrome have been described in literature. Most evidence to establish a diagnosis is based upon the clinical presence of typical dumping complaints in patients after upper gastrointestinal surgery, recently supported by a consensus panel (3,4). Scoring systems such as the Sigstad score (Table 1) and the Arts questionnaire (Table 2) can be used to facilitate this process (5-7). Noteworthy, no questionnaire has been adequately validated (e.g. to physiological testing) as there is a significant overlap in symptoms between early and late dumping, posing an important challenge in diagnosis. A modified oral glucose tolerance test (OGTT) is useful to objectify clinical symptoms and one of the most commonly used test in clinical practice (4,8). After an overnight fast, typically 75 g glucose is given to the patient. An absolute rise in hematocrit of > 3% or an increase in heart rhythm of > 10 beats per minute, within 30 minutes after ingestion, is indicative of early dumping. Hypoglycemia (< 50 mg/dL), two to three hours after a meal, indicates late dumping. However, this test is not yet accepted as a general guideline, nor is it evident to define a certain postprandial hypoglycemia value as cutoff for late dumping, although a recent international consensus guideline supported the cut-off of 50mg/dL (4,5,9,10). To increase specificity, more often hypoglycemia in association with symptoms, relieved by carbohydrate ingestion, is used to indicate late dumping (Whipple's triad) (10). Scintigraphic radionuclide imaging to determine the rate of gastric emptying is not recommended (4). There is no absolute difference in gastric emptying between patients with and without dumping after gastric surgery, presumably because often only the initial phase of gastric emptying is accelerated (11). Establishing an unambiguous diagnostic tool to detect the dumping syndrome remains a difficulty. The occurrence of typical dumping symptoms related to food intake after bariatric surgery, appears to be the best method to diagnose the condition, whereas the OGTT can be regarded as supporting evidence.

First-line treatment of dumping consists of dietary modification (3). Patients are advised to consume small amounts of food several times a day. Fast digesting or simple carbohydrates and fatty foods should be avoided (12). Consumption of liquids during or within 30 minutes after a meal is to be discouraged to decelerate gastric emptying. Patients who fail to respond to conservative measures may benefit from pharmacological agents such as acarbose and somatostatin analogues (3). Acarbose is an alpha-glucosidase inhibitor that prevents cleavage of polymeric carbohydrates into rapidly absorbed monosaccharides. As a result, postprandial glucose absorption is decreased and less insulin and gastro-intestinal hormones are released, thus reducing symptoms of especially late dumping (13). There are no data on the effect of acarbose on early dumping syndrome. Somatostatin analogues slow down gastric emptying and intestinal transit, reduce postprandial vasodilatation and the release of gastrointestinal hormones and therefore are an effective treatment for both early and late dumping (14). It is recommended to start with immediate release formulations (e.g. octreotide 0.05-0.1mg tid) to assess efficacy and tolerability before switching to longer acting formulations such as octreotide LAR 20-30mg or lanreotide 90mg every 4 weeks. In a study evaluating octreotide LAR 82% of patients were responders (better or partly better). (6). Rarely, when the dumping proves to be refractory to these classical dietary and pharmacotherapeutic measures, continuous enteral feeding or even a surgical re-intervention, for example restoration of normal anatomy or conversion of gastric bypass to sleeve gastrectomy, may be indicated. Surgical or endoscopic restoration of the gastric restriction after bypass has also shown to improve symptoms of dumping in some patients, but post-surgical motility disorders including gastroparesis are common even if no systematic analysis is available in the literature (15-18) at present, the most effective method to achieve major, long-term weight loss in severely obese patients. Recently, severe recurrent symptomatic hyperinsulinemic hypoglycemia was described as a consequence of gastric bypass surgery (GBS Therefore, these surgical procedures are extremely rare and not recommended in the large majority of

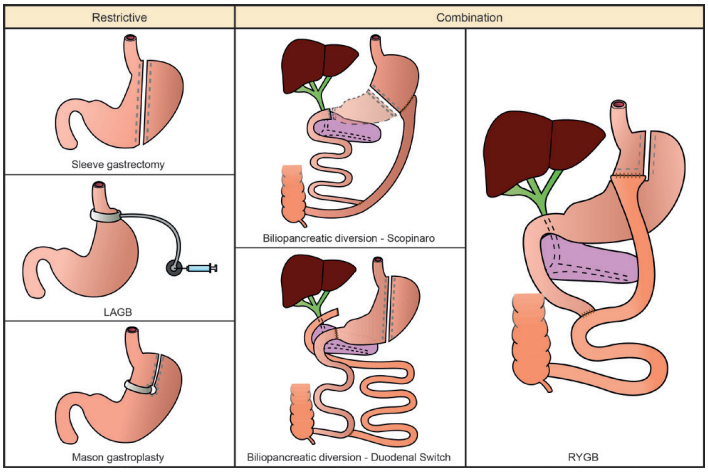

Figure 1. — Schematic overview of the most common bariatric procedures anno 2022.

patients. Fortunately, the majority of the patients with dumping suffer from relatively mild complaints, that are well controlled with strict dietary adjustments.

Dumping mainly occurs after surgery to the upper gastrointestinal tract, for example after Nissen fundoplication, Billroth gastrectomy and pyloroplasty with vagotomy. Rare cases of idiopathic dumping have been described, frequently associated with type 2 diabetes mellitus (5). Bariatric surgery is the leading cause of the dumping syndrome, with a prevalence of up to 76% after Roux-en-Y Gastric Bypass (RYGB) (19). The most popular bariatric procedure performed worldwide, is by far the sleeve gastrectomy, followed by the RYGB (20). The Laparoscopic Adjustable Gastric Banding (LAGB), the Mason gastroplasty (Vertical banded gastroplasty) and the biliopancreatic diversion, Scopinaro (BPD-S) and Duodenal Switch (BPD-DS) are less frequently performed today in Europe and America. (Figure 1). Obesity is a preventable global health issue, affecting more than 1.9 billion adults in 2016 (21). In the last decade, bariatric surgery has gained increasing popularity with 833,687 procedures registered across 61 countries in 2019, making dumping a hot topic in daily practice (20). Whether dumping is merely an undesired complication of bariatric surgery, or rather a facilitating factor in achieving sustained weight loss, is subject of ongoing debate. This systematic review examines the occurrence of dumping after the most frequent weight loss surgeries, explores the complex etiology behind the syndrome and whether or not dumping aids in achieving the intended weight reduction.

Methods

During the period of July-August 2021, a systematic literature search was conducted in the PubMed database. (Figure 2). We included the bariatric procedures most frequently performed throughout Europe and America, in the search terms. The final search term included 'dumping syndrome', combined with 'bariatric surgery', 'gastroplasty', 'biliopancreatic diversion', 'gastric bypass', 'laparoscopic adjustable gastric banding', 'roux-en-y gastric bypass', 'sleeve gastrectomy', 'vertical banded gastroplasty', 'mason gastroplasty', 'scopinaro' and 'duodenal switch'. The Mesh term 'gastrectomy' was not included because this yielded too many studies on total gastrectomy in the context of oncological etiology. Both Mesh terms and Tiab (title + abstract) were searched for. The reference list from the obtained articles was screened for relevant publications.

Results

Epidemiology

In general, we can state that early dumping occurs on average in 15.7% of patients, within six months after bariatric surgery (23). Late dumping can reach up to 25%

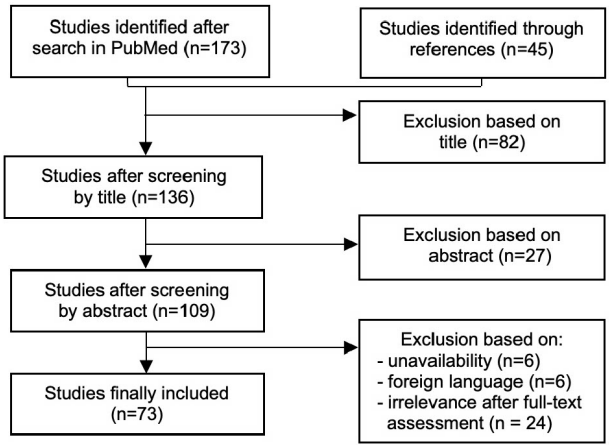

Figure 2. — PRISMA 2009 Flow Diagram (22).

in an average period of one to five years post-surgery (2,23). An extensive review analyzed the postoperative prevalence of dumping using a total of 3626 combination and 3568 restrictive procedures (24). Weight loss surgery with a combined restrictive and malabsorptive approach, in particular RYGB, is the most frequent cause of dumping. Dumping syndrome occurred in 14.6% of the combination procedures, compared to only in 0.28% of the restrictive surgeries. These percentages are generally lower than those found in other publications. An important note is that the prevalence of dumping greatly varies depending on the terminology and diagnostic method used. On average, studies using the Sigstad score obtained higher percentages of dumping compared to physiological testing or alternative questionnaires. For example, incidence rates of up to 76% have been documented after RYGB based on the Sigstad questionnaire (19).

A detailed overview of the incidence of early and late dumping is shown in Table 3. Kalarchian et al. evaluated the incidence of dumping in 87 cases, six months after RYGB, using the Sigstad score of which 35.7% had a score of > 7, suggestive of dumping (25). Emous et al. investigated the prevalence of early and late dumping separately in 351 patients two to three years after RYGB using the Arts questionnaire (7). Complaints of early and late dumping were present in 18.8% and 11.7% respectively and 7% showed a combination of both. Nielsen et al. mapped the prevalence up to 4.5 years after RYGB by means of questionnaires in 1429 patients (26). They found that early dumping was present in 9.4% of the patients, reactive hypoglycaemia after a 50 g OGTT, i.e. late dumping, in 6.6% of the cases and 3.4% showed both early and late dumping. A decreasing trend in dumping complaints is found if the intervention was performed longer ago. However, one in five patients after RYGB suffer from a long-term reduction in quality of life due to dumping syndrome (7,27,28).

After BPD, dumping appears to be less frequent based on the published data. Only 2% of 113 patients who underwent BPD-DS scored positive for dumping up to

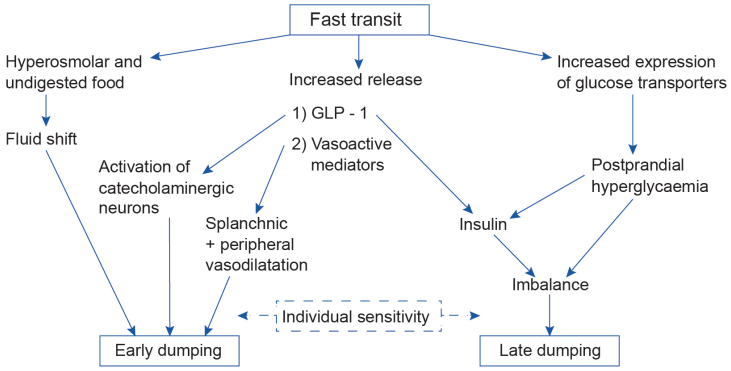

Figure 3. — Schematic representation of the pathophysiology of early and late dumping after bariatric surgery.

seven years after surgery (29). The numbers were similar for BPD-S: merely two out of 2241 patients reported a transient period of early dumping in a follow-up period of 155 months (30). It is not yet fully elucidated why the incidence of dumping after BPD is so limited when the mechanism of action is largely the same as for RYGB. A possible explanation could lie in the fact that the remaining gastric pouch after RYGB is smaller than after BPD and therefore accommodation capacity is less, resulting in faster transit after RYGB (54,39,45).

In purely restrictive weight-loss surgery, incidence rates are generally low. Six months after LAGB, 4.7% of 56 patients scored > 7 on the Sigstad score (25). During a follow-up study of 72 patients, up to three years after LAGB, only one patient reported disabling symptoms of dumping at any given time point (28). The overall incidence of dumping after sleeve gastrectomy is greater than after LAGB, presumably because sleeve surgery has more impact on gastric emptying rate (31). The gastric half emptying time after sleeve is significantly shorter compared to non-operated controls: 14 ± 12 min. vs. 35 ± 25 min. for liquids and 38 ± 19 min. vs. 78 ± 15 min. for solid food (32). In addition, the pacemaker region of the stomach, which is located near the greater curvature, is also resected in sleeve gastrectomy which may also impact on gastric motility (31). There is no role for preoperative measurement of gastric emptying rate. Tzovaras et al. assessed the incidence of dumping in 31 patients, six weeks after sleeve gastrectomy, using the Sigstad score in combination with an OGTT (34). About one third had a Sigstad score of > 7 (diagnostic for dumping) and one out of six had a score between 5 and 7 (suggestive for dumping), mainly with symptoms of early dumping. Papamargeritis et al. examined incidence of dumping in a group of 12 patients, six to twelve months after sleeve, using a 75 g OGTT combined with Sigstad and Arts questionnaire (31). At six months, 24% scored > 7 on the Sigstad score, mainly positive for early symptoms. At twelve months, there was a gradual switch with 25% of patients scoring positive for mainly late dumping. These figures for late dumping are remarkably higher than the incidence rates reported after RYGB indicated above, but the results should be interpreted with caution because of the small sample size of these studies.

Several authors suggest that the dumping syndrome occurs more frequently in patients with preoperative diabetes mellitus type 2. However, this is not confirmed by all studies. Emous et al. performed an analysis in a study of 351 patients, 96 of whom had preoperative type 2 diabetes (7). They reported no difference in prevalence of early and late dumping, two to three years after RYGB, between patients without diabetes, with postoperative normalized glycemia and with persistent diabetes. In contrast, Padoin et al. found higher rates of dumping syndrome up to one year after RYGB in 49 patients with preoperative diabetes (44.9%) vs. 54 patients without diabetes (5.6%) (35). They hypothesized that the higher incidence of early dumping in the preoperative diabetes group may be attributed to the pre-existing gastrointestinal neuropathy in the context of uncontrolled diabetes, but supporting data are lacking.

Pathophysiology

Transit

Bariatric surgery has a major influence on gastric physiology. If the pylorus is bypassed, as is the case in RYGB, the mechanism of controlled transit is altered, leading to an accelerated emptying of the remaining stomach pouch. In restrictive procedures, mainly accommodation is impaired, which has less influence on the gastric transit time as the pylorus is still in place. Nevertheless, vagal injury may occur, the effect of which is variable and depends on the degree and level at which the vagus nerve is damaged (3). When the pylorus is still intact and normal vagal innervation is lost, this can result in pyloric relaxation and loss of duodenal feedback inhibition, leading to an accelerated transit time (5).

In the commonly accepted pathophysiology of dumping, the accelerated gastric emptying plays a central role. The rapid emptying of the stomach would result in largely undigested and hyperosmolar food reaching the small intestine, resulting in a fluid shift from

Table 3. — **Overview of incidence rates of dumping after different types of bariatric surgery**

Article	Procedure	Study population	Postoperative time	Diagnostic tool for dumping	Percentage of dumping
Restrictive procedures					
Mallory et al. (1996)(19)	Mason GP	19	18-24 m	Sigstad score	0 % dumping (NS)
Monteforte et al. (2000)(24)	LAGB Mason GP (NS)	3568	NS	NS	0.28 % dumping (NS)
Kalarchian et al. (2014)(25)	LAGB	56	6 m	Sigstad score	4.7 % dumping (NS)
Kalarchian et al. (2017)(28)	LAGB	72	12, 24, 36 m	Sigstad score	One patient reported dumping at any given time point. (NS)
Papamargeritis et al. (2012)(31)	Sleeve 25 12	6w, 6m 12m	75 g OGTT + Sigstad and Arts questionnaire	> 6w, 6m: 24 % dumping, mainly ED (NS); > 12m: 25 % dumping, gradual switch to LD (NS)
Tzovaras et al. (2012)(34)	Sleeve	31	6 w	75 g OGTT + Sigstad and Arts questionnaire	29 %, mainly ED, 1 patient had LD
Lee et al. (2015)(36)	Sleeve	95	12-69 m	EHS*	17.9 % LD
Ahmad et al. (2019)(37)	Sleeve	249	NS	Sigstad score	26.5% dumping of which: > 22.5 % ED > 9.54 % LD > 7.6 % CD
Sun et al. (2019)(38)	Sleeve	122	13 m	EHS*, DSRS**	41 % ED, 66,4 % LD, 33.6 % CD
Combination procedures					
Skogar et al. (2017)(29)	BPD-DS	113	25.2-87.6 m	BAROS***	2 % dumping (NS)
Hedberg et al. (2011)(39)	BPD-DS	20	18-66 m	Self-report after patient education	55 % had rarely dumping (NS): 1 patient weekly, 2 patients monthly, 8 less than monthly
Scopinaro et al. (1998)(30)	BPD-S	2241	FU until 155 m	Self-report (NS)	2 patients had transient ED during FU
Michielsen et al. (1996)(40)	BPD-S	33	6 m	NS	6 % ED
Emous et al. (2017)(7)	RYGB	351	24-36 m	Sigstad and Arts questionnaire	18.8 % ED, 11.7 % LD, 7 % CD
Mallory et al. (1996)(19)	RYGB	137	18-24 m	Sigstad score	75.9 % dumping (NS)
Monteforte et al. (2000)(24)	RYGB	3626	NS	NS	14.64 % dumping (NS)
Kalarchian et al. (2014)(25)	RYGB	87	6 m	Sigstad score	35.7 % dumping (NS)
Nielsen et al. (2016)(26)	RYGB	1429	Till 54 m	DSRS** + EHS*	12.6 % dumping of which: > 9.4 % ED (3.4 % daily, 0.63 % ≤ monthly) > 6.6 % LD (2.36 % daily, 0.63 % ≤ monthly) > 3.4 % CD
Laurenius et al. (2013)(27)	RYGB	129	12, 24 m	DSRS**	12 % persistent ED
Kalarchian et al. (2017)(28)	RYGB	111	12, 24, 36 m	Sigstad score	> 12 m: 23.6 % monthly & 9.9 % weekly dumping (NS); > 24 m: 16 % monthly & 5.2 % weekly dumping (NS); > 36m: 15.5 % monthly & 6.3 % weekly dumping (NS)
Skogar et al. (2017)(29)	RYGB	98	26-8 m	BAROS***	13 % weekly dumping (NS)
Lee et al. (2015)(36)	RYGB	355	12-69 m	EHS*	38.6 % LD
Ahmad et al. (2019)(37)	RYGB	111	NS	Sigstad score	41.4 % dumping of which: > 35 % ED > 11.6 % LD > 9.9 % CD
Banerjee et al. (2013)(41)	RYGB	50	28-38 m	Sigstad score	42 % dumping from which 24 % ED and 18 % CD
de Zwaan et al. (2010)(42)	RYGB	59	18-35 m	Sigstad score	23 % weekly dumping, 50 % yearly dumping (NS)

Wijma et al. (2019)(43)	RYGB	46	39-54 m	MMTT**** + Arts questionnaire	26 % ED
D'Alessio et al. (2021) (44)	RYGB	213	24-86 w	Sigstad score	56.3 % dumping, 38% dumping after anterior and 78% after posterior gastro-jejunal anastomosis

GP=gastroplasty; w=weeks; m=months; NS=not further specified; ED=early dumping; LD=late dumping; CD=combined early and late dumping; *EHS=*Edinburgh Hypoglycemia Scale*(36), questions symptoms within 3 domains (autonomous, neuroglycopenia, overall malaise); **DSRS=*Dumping Symptom Rating Scale*(27), detection of early dumping, questions symptoms within 2 domains (autonomous and overall malaise) within 30 minutes after a meal and questions frequency of occurrence; ***BAROS=*Bariatric Analysis and Reporting Outcome System*(29), questions 3 symptoms within 3 domains (weight loss, quality of life, comorbidities), when presence of complications, points go down, successful procedure when ≥7/9; ****MMTT=*Mixed Meal Tolerance Test*(43), liquid meal containing carbohydrates, proteins and fat.

the intravascular compartment to the lumen, causing abdominal distention and symptoms of early dumping. Nguyen et al. compared the effect of oral glucose intake in ten patients after RYGB with a glucose infusion of the same amount, directly into the small intestine, at a controlled rate of 4 kcal/min. (45). This was compared to intestinal glucose infusion in matched non-operated control subjects. After RYGB, a very fast pouch emptying (3 ± 1 min) was recorded when glucose was taken orally. There was a significant relationship between the rate of gastric emptying and the occurrence of early dumping symptoms. In addition, gastrointestinal symptoms, occurring in the RYGB test group after oral glucose intake, were reduced when glucose was administered intestinally at a slower pace. Previously, the fluid shift was thought to be the cause of hypotension and secondary vasomotor complaints, but more recent research questions this hypothesis (3,8). The fluid shift seems too small to be the cause of pronounced hypotension (300-700 mL) and, importantly, intravenous fluid repletion did not prevent symptoms of early dumping (1,46). On the other hand, Macdonald et al. emphasized the individual sensitivity to systemic hypovolemia, making it difficult to substantiate whether or not the fluid shift plays a role in the pathogenesis (47). The etiology of the vasomotor symptoms is therefore still unclear.

The accelerated transit is thought, after an initial period of malabsorption, to trigger an upregulation of glucose transporters, causing postprandial hyperglycemia to arise over time. As discussed further, this hyperglycemia is followed by a disproportional insulin release, leading to hypoglycemia and late dumping. Z'graggen et al. showed that patients with severe hypoglycemia after gastric bypass had a relieve of symptoms after insertion of a gastric band around the gastrojejunal pouch to delay the rate of gastric emptying (15).

It is well established that bariatric surgery, by altering anatomy and innervation, causes an accelerated transit. We hypothesize this contributes to dumping syndrome through an intraluminal fluid shift, bowel distention and imbalance in postprandial glucose uptake and insulin release (Figure 3).

Incretins

Oral glucose intake in subjects after RYGB induces a significantly increased release (x2-3) of incretin hormones (45). When glucose is continuously administered intestinally, the release of these hormones was reduced to the same values as in non-operated individuals, despite a remarkably higher postprandial glycemia in operated individuals after both oral and intestinal glucose administration. This implies that accelerated transit, with rapid exposure of undigested, high-osmolar food to the L-cells in the hindgut, is at the basis of this increase in hormone production.

The incretin hormone glucagon-like peptide 1 (GLP-1) is thought to be a key player in both the early and late dumping process. GLP-1 has already shown to activate catecholaminergic neurons and sympathetic pathways through a peripheral and central mechanism (45,48). GLP-1 levels, norepinephrine release and increase in heart rate are significantly increased in patients after RYGB compared to asymptomatic individuals and correlated with symptoms of early dumping (48). Early dumping is accompanied with pronounced sympathetic stimulation and symptoms of anxiety, which could be caused by this mechanism. As mentioned above, early gastrointestinal symptoms disappear in patients after RYGB when glucose is administered through slow intestinal infusion and GLP-1 release is reduced to normal values (45).

This incretin presumably plays a vital role in the late dumping process, as GLP-1 stimulates glucose-mediated insulin release, blocks glucagon release and consequently promotes late hypoglycaemia. After RYGB, GLP-1 production is significantly increased in patients with neuroglycopenia as compared to those without neuroglycopenic symptoms (x1.4-1.7) (49,50). When the GLP-1 antagonist Exendin (9-39) was administered intravenously to subjects with neuroglycopenia, postprandial hypoglycemia could be corrected in all subjects (51,52). The GLP-1 antagonist had a much greater effect on postprandial insulin production in patients with neuroglycopenia after gastric bypass as compared to those without symptoms or to the non-operated control group. These data suggest a pathogenetic role for GLP-1 in both the early and late dumping syndrome. GLP-1 antagonists are therefore already under development as a treatment option in the dumping syndrome.

Vasoactive mediators

Vasoactive molecules, such as serotonin, enteroglucagon and many others, have been put forward in the pathogenesis of the dumping syndrome. These hormones are released to an increased extent after derivative

surgery, as noted before as a result of rapid exposure of food to the distal small intestine (5). Transfusion of venous blood from the portal circulation in dogs could transmit characteristics of early dumping such as diarrhea and tachycardia, which is indirect evidence that circulating factors, presumably gut hormones or vasoactive mediators, play a role in the pathogenesis (1,53).

The normal physiological response to food ingestion is a shift of blood to the splanchnic circulation along with a peripheral vasoconstriction (5). However, Vecht et al. noted synchronous peripheral and splanchnic vasodilatation in persons with early dumping, which was not present in asymptomatic individuals following bariatric surgery (1). The altered hormone production could be the cause of this disturbed autoregulation leading to early dumping symptoms.

Previously, serotonin and bradykinin were considered the main causative factors in early dumping. Carcinoid tumors, releasing large quantities of serotonin or bradykinin, are known to be associated with symptoms of early dumping. However, the role of serotonin is increasingly being put into question as consistently increased serotonin levels could not be demonstrated in all patients after obesity surgery with early dumping (1,55).

Several studies investigated the role of other gastrointestinal mediators such as neurotensin, vasoactive intestinal peptide (VIP), motilin and enteroglucagon. Sirinek et al. performed a pre- and post-operative analysis in eight RYGB patients after a 100 g OGTT (54) Preoperatively, the neurotensin, VIP and motilin levels were below the detection threshold (< 50 pg/mL) in all patients. Three to four months after surgery, there was a significant increase in both neurotensin and VIP with a maximum value of 350 pg/mL for both mediators. Motilin remained below the detection threshold in all patients postoperatively. Both VIP and neurotensin may contribute to post-meal splanchnic vasodilatation. Enteroglucagon strongly increased after gastric bypass and the concentration curve was consistent to the transient time course of dumping (1,55). Nevertheless, the role of enteroglucagon in dumping is contested as an enteroglucagon producing tumor does not cause dumping complaints. The enhanced production of this hormone is probably a result of the rapid transit, without an established role in the pathophysiology of dumping syndrome.

Neurohumoral adaptation

In addition to accelerated transit and an increased release of GLP-1 and vasoactive mediators, there are also important neurohumoral changes after bariatric procedures possibly contributing to dumping. As a result of the fast transit, a certain degree of malabsorption occurs. Studies, in a short time frame after bariatric surgery (on average six months), therefore often find a reduced postprandial glycemia and a reduced insulin release as compared to the preoperative situation (34,54,55). Also in most cases, shortly after the intervention, there is only transient early dumping and no late dumping is reported. Studies carried out more than one year postoperatively usually show opposite results, i.e. namely high glucose and insulin values (45,49,56). The study by Nguyen et al. included patients 2 to 12 years after RYGB (45). They noticed that the glucose peak after intestinal glucose infusion appears slower, but is eventually greater than after oral glucose intake. It is striking that the maximum glucose levels and the total glucose absorption in the operated group, both after oral administration as during intestinal infusion, are greater compared to intestinal infusion in the control group. These observations were confirmed by other groups (51,57). We can assume that glucose absorption increases over time after this derivative procedure, indicating an adaptation at a neurohumoral level of the intestine to the accelerated transit. The fast transit leads to a shorter contact time of the nutrients with the intestinal surface, eventually leading to initial carbohydrate malabsorption which would then result in an increased expression of glucose transporters (45). The fact that there is a prevalence switch from early to late dumping over time supports this hypothesis of neurohumoral adaptation (7,11,58).

Postprandial hyperglycemia after bariatric surgery can induce chronic stress on pancreatic tissue and is postulated to induce increased proliferation of beta cells, also known as nesidioblastosis (59). GLP-1, which is also elevated after RYGB, is known to have a trophic effect on beta cells and could contribute to this hypertrophy (56,60). This phenomenon would result in an unbalanced insulin production and consequently late dumping. When comparing postprandial insulin values, insulinemia in patients after RYGB is indeed significantly greater as compared to control subjects (49,52,56). Nevertheless, the hypothesis of nesidioblastosis is controversial. Several authors were not able to find a significant difference in beta-cell mass between subjects with and without neuroglycopenia (50). When looking at glucose and insulin levels in patients after RYGB, with or without neuroglycopenia, there is also no consistent difference between both groups (9,49,50,61). Goldfine et al. made the same observation, but demonstrated that the insulin to glucose ratio in the group with neuroglycopenia was significantly higher (49). This observation was confirmed by Salehi et al (51). Meier et al. hypothesized that the pathogenetic mechanism behind neuroglycopenia could lie in an unadjusted insulin release rather than an augmented insulin production itself (62). They examined the pancreatic tissue of individuals suffering from reactive hypoglycemia after gastric bypass, and compared this with the tissue of healthy subjects. There was no evidence for increased proliferation of the beta cell, but the diameter of the beta cells in patients with late dumping was larger than in non-dumping patients, compared to their current degree of insulin resistance.

The diameter correlated with the degree of their preoperative insulin resistance, indicating an inadequate hormonal adaptation to the improved insulin sensitivity after weigh loss with a persisting high insulin secretion, leading to hypoglycemia. Several authors have shown that most patients with late dumping post-RYGB had no previous history of diabetes, suggesting that decreased beta cell function and higher peripheral insulin resistance is protective (36,49,56).

The disproportional insulin release in patients with late dumping has also been attributed to a disturbed autoregulation of the pancreatic islets after gastric bypass. Several authors noticed a diminished suppression of beta-cell function in response to glycemic reduction during hyperinsulinemic hypoglycemic clamp in individuals with post-RYGB hypoglycemia as compared to matched non-operated individuals (63,64). A diminished clearance of insulin was also observed in patients with late dumping, suggesting that inherently lower clearance could predispose to higher circulating insulin levels and consequently increase risk for late dumping (51). Disturbance in alpha-cell glucagon synthesis with inadequately low glucagon synthesis during hypoglycemia was also observed after RYGB (63-67). Neural changes and GLP-1 induced dysregulation have been proposed as the underlying cause, but this needs further investigation (51,68). A dysregulation of alpha- and beta-cell homeostasis has been observed after gastric bypass, resulting in a greater insulin-glucose ratio and predisposing to late dumping.

The presence of late dumping is most likely a spectrum resulting from augmented glucose absorption, a certain degree of beta and alpha cell dysregulation, a reduced peripheral insulin resistance after weight loss and an important variability in individual sensibility to hypoglycemia.

Role in weight reduction

There remains a lot of disagreement whether the dumping syndrome is a desired or even necessary effect in the process of weight reduction. Dumping is mostly considered an unfavorable side effect and the phenomenon also occurs after gastrointestinal procedures that do not aim to reduce weight, for example after Nissen fundoplication for reflux disease (2). Many studies cannot find a correlation between dumping and the degree of weight loss (19,28,35,41-43,59,69). Especially when focusing on late dumping or a disturbed OGTT after bariatric surgery, no beneficial relationship to the evolution in body weight can be demonstrated.

Those who are in favor of a role of dumping in weight loss, emphasize the potential benefit of early dumping. They underpin the observation that the time frame in which maximum weight loss is achieved, on average 12 to 18 months after surgery, appears to coincide with the highest incidence of early dumping (41,57). The prevalence of early dumping starts to decline at around one to two years postoperatively when bariatric patients start to regain weight (41). Early dumping is hypothesized to suppress disadvantageous eating behavior through a negative conditioning mechanism and thus promote weight loss (7,41). Laurenius et al. interviewed 12 patients, on average nine years after RYGB, who, according to the Dumping Symptom Rating Scale, all suffered from moderately serious early dumping (70). The average weight loss was 30% of their preoperative weight. All participants saw dumping not as a disadvantage, but rather as a protection against weight regain. They admitted that dumping sometimes limited their daily activities, but they saw the need of it to prevent relapse into bad eating habits.

Proponents of the role of dumping in weight loss often emphasize that RYGB, the bariatric procedure after which dumping is most common, is more effective for weight loss than purely restrictive procedures (71). Mallory et al. evaluated the incidence of dumping, according to the Sigstad score, in patients 18-24 months after RYGB (n=137) or after Mason gastroplasty (n=19) and compared this to the degree of weight loss (19). Weight loss after gastric bypass was indeed significantly greater than after gastroplasty (72.5% of the excess BMI (eBMI) vs. 47.9%). Of the RYGB patients, 75.9% scored positive for dumping, while none met the criteria after Mason gastroplasty. However, within the group of RYGB patients, no link was found between dumping and the degree of weight loss. Skogar et al. performed an analysis in 98 patients after RYGB and 113 after BPD-DS, two combined restrictive and malabsorptive bariatric procedures (29). There was significantly more loss of eBMI in the BPD-DS group than after RYGB, respectively 79 ± 17% vs. 62 ± 23%, despite the fact that there was significantly more dumping present after RYGB. Thus, a factor other than dumping must be the cause of the difference in weight loss between bariatric surgeries.

As mentioned before, the emptying of the remaining gastric pouch after derivative procedures is much faster than after restrictive procedures (32,45). This gastric emptying rate appears to be positively correlated with the degree of weight loss and with the maintenance of weight reduction in the long run (72,73). The rapid gastric transit is responsible, among other things, for triggering early dumping and initiating an hormonal stimulus (45). An increased production of anorexigenic hormones, in addition to the restrictive and malabsorptive effect of bariatric surgery, has been put forward in the process of weight loss (57). An important satiety hormone is Peptide YY (PYY). This hormone is also produced by the L-cells of the small and large intestine. When food is presented to the hindgut in a quick and high-osmolar manner the production of PYY will increase and central satiety is reached more quickly (57). Several authors have shown that PYY levels are significantly higher after RYGB and are positively correlated with satiety (65,74).

Incretins are important satiety hormones and are significantly increased postprandially after obesity

surgery (45). Dirksen et al. studied the factors related to weight loss in 32 patients, one year after RYGB (57). Patients were classified into poor and good responders, depending on the loss of their preoperative eBMI. Sixteen of them had a reduction in eBMI of > 60% and were considered as good responders. Seventeen lost < 50% eBMI and were classified as poor responders. Among the good responders, the production of postprandial GLP-1 was more pronounced (x1.5; p=0.009). However, no significant difference was found in the degree of early dumping between both groups. Also, no difference in PYY production was seen between the good and poor responders, but there was a significant difference between the operated and non-operated group (x 2.5; p=0.008). GLP-1 is suspected to play a role in suppression of appetite and consequently weight reduction after bariatric surgery, but the role of PYY in weight reduction is more unlikely. In other words: GLP-1 plays a role in the emergence of dumping and as an anorexigenic hormone without the two phenomena having to be causally linked.

Therefore, a careful analysis of the literature suggests that dumping syndrome has no direct influence on weight loss after bariatric surgery. Mainly, the combination of anatomical changes, malabsorptive effects and adaptation of the neurohumoral axis have a positive effect on weight reduction. Early dumping is probably more of a co-phenomenon and not a contributing mechanism to weight loss. Nevertheless, these conclusions do not deny the fact that some people do recognize the positive effects of dumping and consider it a useful tool in maintaining their diet restrictions. However, this is only the case for early dumping as late dumping is known to induce a malabsorptive eating pattern (59).

Conclusion

The dumping syndrome after bariatric surgery, mainly after RYGB, is a frequent phenomenon. The clinical occurrence of typical dumping complaints, after surgery at the upper gastrointestinal tract, remains the best method to diagnose the condition. Most patients experience mild complaints that can be adequately managed through dietary modifications.

This systematic review stresses once again the multifactorial nature of dumping syndrome. The accelerated transit is acknowledged to be a crucial factor in the pathophysiology of the dumping syndrome. The anatomical changes contribute to a dyscoordination in gastrointestinal motility, hemodynamic changes, an increased release of vasoactive mediators and incretins, resulting in complaints of early dumping. Neurohumoral changes leading to an augmented glucose absorption, a certain degree of beta cell hyperfunction, a reduced peripheral insulin resistance and an individual sensitivity to hypoglycemia creates a spectrum of late dumping. Subject for debate is whether gastric bypass stimulates exuberant beta cell activity or if rather there is an inadequate adaptation of preexisting beta cell hypertrophy to the renewed metabolic state.

Based on the currently available literature we conclude that dumping syndrome does not play a vital role in the weight loss process after obesity surgery. Dumping is not to be seen as an intentional goal of bariatric surgery, but we should not present it merely as a side effect to our patients. Early dumping can, when received in a positive way, become a tool to maintain a strict dietary pattern. Late dumping, however, is detrimental and could contribute to the process of weight regain due to increased calorie load in response to postprandial hypoglycemia.

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Conflict of interest

TV has received speaker fees of Ipsen.

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