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## Original article

# Dumping symptoms is triggered by fat as well as carbohydrates in patients operated with Roux-en-Y gastric bypass

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#### Abstract

**Background:** Dumping syndrome after Roux-en-Y gastric bypass (RYGB) is traditionally associated with the consumption of refined carbohydrates, but the role of dietary fat is unclear.

**Objectives:** This study compares symptoms after consumption of a carbohydrate-rich or fat-rich beverage to determine perceived symptoms, glycemic control, and pulse rate.

**Setting:** University hospital.

**Methods:** We assessed perceived symptoms (Sigstad's Dumping Index) and glycemic control (P-glucose and S-insulin) as well as autonomic nervous system activity (reflected by arterial pulse rate) after a standardized liquid meal test (440 kcal/300 mL carbohydrates [CARB] or fat [FAT]) in a randomized crossover blinded setting. Blood samples were drawn before and 1, 15, 30, and 60 minutes after finishing each meal and the area under the curve (AUC) was calculated.

**Results:** Twelve patients  $42 \pm 10$  months after undergoing RYGB were studied. AUC differed between drinks for glucose (P = .003) and insulin (P = .005). Pulse rate increased more after CARB than after FAT (P = .01). AUC for perceived symptoms in the Sigstad's Dumping Index were similar after meals (P = .79), yet the pattern of type of symptoms differed.

**Conclusion:** In patients with RYGB, a meal with predominant fat content resulted in as much perceived dumping symptoms as a carbohydrate-profiled meal. As expected, an increase in glucose and insulin levels were found only after carbohydrate intake and the pulse rise was more pronounced for carbohydrates than fat. Dietary counseling in patients undergoing RYGB should address dietary fat as well as traditional information about carbohydrates to avoid dumping symptoms. (Surg Obes Relat Dis 2017;13:1159–1164.) © 2017 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords:

Gastric bypass; Dumping syndrome; Dietary carbohydrates; Dietary fats

Dumping syndrome (DS) is a well-known phenomenon after gastric surgery, likely due to the absence or non-functioning pylorus allowing food to pass directly into the intestine [1,2]. DS is associated with rapid delivery of

Refined carbohydrate-rich foods have been described as causing DS, and dietary advice has focused on avoiding carbohydrates [1–9]. However, when patients who had undergone Roux-en-Y gastric bypass (RYGB) were asked about which foods they avoid to prevent or relieve

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nutrients into the small intestine and subsequent release of vasoactive substances, incretins, and hormones, causing both gastrointestinal and vasomotor symptoms within the first 30 minutes after a meal [1,2].

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symptoms, they indicated fatty foods (55%) to a higher degree than sugar-rich foods (36%) [10].

In this study, we assessed DS by perceived symptoms, glucose and insulin levels, and autonomic response in a group of RYGB patients during a standardized liquid isocaloric meal challenge, containing either a carbohydrate- (CARB) or a fat-rich meal (FAT) in a randomized crossover. Six nonobese, nonoperated healthy volunteers served as controls.

#### Methods

Participants/recruitment, study design and ethics

Twelve adult patients (11 females) who had undergone laparoscopic RYGB [11] were invited to participate, as well as 6 healthy nonoperated volunteers (5 females). Patients were recruited from an ongoing study that validated a questionnaire to measure the dumping syndrome over time [10]. Sixteen of a total of 22 patients who reached their 2-year follow-up visit in the validation study were asked about participating in this study based on a summary of dumping symptom rating scale (DSRS) total index (severity multiplied by frequency). The patients were ranked in respect to the DSRS total index; we invited those who had the highest and lowest index. One patient could not be reached, one had recently undergone surgery for stomach ulcers and adhesions, one had depression, and a fourth could not imagine drinking cream. There was a good spread of results of the DSRS total index.

The study was conducted according to the principles of the Declaration of Helsinki. The regional ethical review board approved the study protocol (Dnr: S 060-09), and all patients gave written informed consent.

### Surgery

All operations were primary RYGB procedures completed laparoscopically. The technique, as described in detail elsewhere [11], included an antecolic-antegastric Roux-en-Y construction with a 10 to 20 mL gastric pouch and a 100 to 150 cm Roux limb. The gastrojejunostomy was created by stapling the jejunum to the posterior wall of the gastric pouch using a 45 mm 3.5-mm-staple linear cutting stapler. The remaining defect was hand-sutured.

## Study day procedures

Patients arrived in the laboratory the morning after an 8-hour overnight fast with the instruction not to eat or drink anything after midnight. Patients consumed the drinks on 2 different days, thus requiring 2 study visits. An antecubital venous cannula was inserted, and blood samples were drawn immediately before a liquid test meal and 1, 15, 30, and 60 minutes after finishing the meal. At each time point, pulse rate, blood pressure, and symptom scores were assessed.

CARB contained 440 kcal in 300 mL and consisted of 113 g Resource Addera Plus (Nestlé HealthCare Nutrition), 113 g

Nutrical (Nutricia Nordica AB), and 98 g cold water. The nutritional content was 99.5 g carbohydrate (95 % of energy content), .1 g fat, and 5.7 g protein. FAT contained 420 kcal in 300 mL and consisted of 113 g fresh cream and 118 g cold water. The nutritional content was 3.4 g carbohydrates, 45.2 g fat (94.5 % of energy content), and 2.4 g protein. CARB and the FAT were tested in a randomized crossover order on the basis of a random selection table and served in non-transparent cups, prepared by assisting personnel. The patients were asked to finish the drink as quickly as possible and not to reveal the contents to the investigator.

## Blood parameters

Samples were immediately centrifuged and stored in a -20°C freezer until analyzed with an automated glucose analyzer (Abbott laboratories, Chicago, IL) and an automated insulin assay (Abbott laboratories, Chicago, IL).

## Pulse rate and blood pressure

Pulse rate (beats/min) and blood pressure were recorded at each test point using a digital blood pressure recorder also displaying pulse rate (Cardiocap, DRE Waveline, Louisville, KY).

## Perceived symptoms

Perceived symptoms were assessed at each test point with the Sigstad's Dumping Index [12], which is used in provocation tests or direct measurements (Appendix 1). Different symptoms are given a score depending on severity and summarized into a total score. A total score ≥7 is suggestive of DS, and the maximum score possible is 25. The original Sigstad's Dumping Index was used for Tables 1 and 2. However, some symptoms of Sigstad's scale were considered to assess the same qualities and were merged under one heading for Table 3:

- 1. Desire to lie or sit down was merged with
- 2. Weakness, exhaustion and 3. Sleepiness, drowsiness, apathy, falling asleep, entitled **Tiredness**
- 1. Palpitations were merged with 2. Breathlessness,
  - 3. Dyspnea, and 4. Restlessness
- 1. **Bloating** was merged with 2. Abdominal fullness, meteorism and 3. Borborygmia

Hence, the difference in symptom levels was examined for the 2 drinks without assessing the severity (i.e., each symptom received 1 point).

#### Statistical analysis

All data are expressed as mean and 95% confidence interval or SD. Wilcoxon signed ranks test was used for the fasting (F) value and area under the curve (AUC). The nonobese reference group is presented without any

Table 1 Sigstad's dumping index (mean, 95% CI). Number of subject's with dumping syndrome according to Sigstad's original dumping index  $\geq$ 7 at the different time points

	RYGB CARB	RYGB FAT	Reference CARB	Reference FAT	P-value
Sigstad's Dumping Index mean (95% CI)					
AUC	178 (87,269)	161 (65,257)	76	86	.790
No of patients with Sigstad's Dumping Index $\geq 7$					
Fasting	0	0	0	0	
1 min	1	0	0	0	
15 min	4	3	0	0	
30 min	2	2	0	0	
60 min	1	1	0	0	

RYGB = Roux-en-Y gastric bypass; CARB = carbohydrate-rich meal; FAT = fat-rich meal; CI = confidence interval; AUC = area under the curve.

statistical comparisons to the surgical group. Results were considered significant for 2-tailed *P*-values < .05. All the statistical analyses were carried out using SPSS, version 20 (SPSS Inc. Chicago, IL).

#### Results

#### **Participants**

Twelve RYGB patients, aged 42 (7) years, were examined 42 (10) months after surgery after an overnight fast on 2 separate study days, with an average of 12 days (range 1–37) between the test days. Preoperatively, body mass index (BMI)  $(kg/m^2)$  was 47.1 (4.3), and BMI at the test date was 32.6 (6.8) with percent BMI loss of 67.8 (26.2). The reference group (n = 6) had a mean age of 44 (8) years and a BMI of 24.3 (1.0). Preoperatively, the 12 patients had

Table 2 Sigstad's dumping index for the twelve patients with dumping syndrome according to Sigstad's original criteria for dumping syndrome,  $\geq 7$ , marked in bold

	CA	RB				FA	Γ			
	F	1	15	30	60	F	ı	15	30	60
Patie	nts									
1	0	9	8	8	0	0	2	12	13	0
2	0	3	10	6	0	0	1	5	2	1
3	0	2	7	3	0	0	1	8	12	2
4	0	0	0	3	0	0	0	0	0	0
5	0	1	1	1	0	0	1	1	1	0
6	0	0	3	3	3	1	6	8	0	0
7	0	4	3	4	0	0	4	4	5	0
8	0	0	1	0	0	0	0	0	1	1
9	1	0	8	6	0	0	2	3	3	2
10	0	0	0	2	3	0	0	0	1	3
11	0	0	2	0	0	0	0	0	0	3
12	3	1	3	13	8	0	1	0	2	8
Refe	rences									
1	0	0	0	0	0	1	1	2	3	3
2	0	0	0	0	2	0	3	1	3	3
3	0	0	0	0	0	0	1	0	0	1
4	0	1	1	4	2	1	3	4	4	3
5	2	1	0	0	0	0	1	1	1	1
6	1	2	2	2	2	1	1	1	1	0

CARB = carbohydrate-rich meal; FAT = fat-rich meal.

following co-morbidities: 1 tablet-treated type 2 diabetes, 2 hypertension, 1 sleep apnea, 4 joint problems, 3 asthma, 1 polycyclic ovary syndrome, 1 Mb Dercum, and 1 hypothyroidism. At the time of the study, the patient with preoperative diabetes had normalized blood glucose; patients with high blood pressure were free of medication; and the patients with joint problems, asthma, sleep apnea, and polycyclic ovary syndrome were improved.

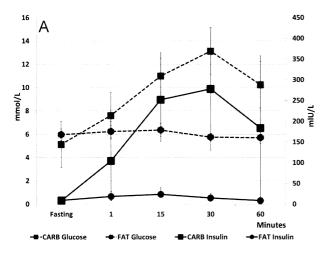
#### Glycemic control

There was a significant difference in fasting values for P-glucose, CARB 5.1 (.8) versus FAT 6.0 (.5) mmol/L, but not between S-insulin (P=.53) between the study days. Neither the P-glucose nor S-insulin increased significantly after FAT; however, glucose rapidly rose after CARB with a subsequent increase in insulin (Fig. 1). AUC differed between drinks for glucose (P=.003) and insulin (P=.005). There was no significant difference between symptomatic (Sigstad's Dumping Index  $\geq 7$ ) and asymptomatic patients in terms of AUC for glucose with FAT (P=.068) or CARB (P=.686) or insulin with FAT (P=.593) or CARB (P=1.000).

Table 3 Number of subjects (n = 12) and references (n = 6) who reported any symptoms according to the modified Sigstad's scale, (each symptom received 1 point) during the whole test except fasting, each patient may have symptoms repeated at the various time points

Symptoms	RYGB (r	n = 12	Reference $(n = 6)$	
	CARB	FAT	CARB	FAT
Tiredness	21	13	12	10
Palpitations	3	0	0	0
Dizziness	5	1	0	0
Headache	1	2	13	5
Sweating and cold sweating	2	3	3	0
Nausea	7	19	1	20
Bloating	18	24	11	21
Regurgitation	8	9	1	7
Pain	1	6	0	2
Diarrhea	0	1	0	0

RYGB = Roux-en-Y gastric bypass; CARB = carbohydrate-rich meal; FAT = fat-rich meal.



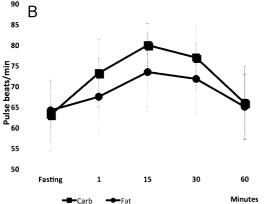


Fig. 1. (A) Glucose (dashed lines) and insulin (solid lines) mean (SD) for carbohydrate-rich (squares) and fat-rich drink (circles). (B) Pulse (beats/min) mean (SD) for carbohydrate-rich drink (squares) versus fat-rich drink (circles).

#### Pulse rate and blood pressure

There was no difference in pulse rate (P=.70) or systolic (P=.58) or diastolic (P=.86) blood pressure at baseline. However, pulse rate increased more after CARB than FAT, AUC, (P=.01) (Fig. 1b). The Wilcoxon sign rank test showed no differences in AUC for diastolic blood pressure between the 2 drinks; neither was there a difference in AUC for systolic blood pressure (P=.59). There was no significant difference between symptomatic (Sigstad's Dumping Index  $\ge 7$ ) and asymptomatic patients in terms of the AUC for pulse with FAT (P=.273) or CARB (P=.893), systolic blood pressure with FAT (P=.144) or CARB (P=.345), or diastolic blood pressure with FAT (P=.273) or CARB (P=.686).

## Perceived symptoms

There was no difference in Sigstad's Dumping Index at baseline (P = .41). Furthermore, there was no difference in Sigstad's Dumping Index calculated as AUC between drinks (P = .79) (Table 1). Three of the 12 patients perceived symptoms after both beverages (Table 2). The most

frequently reported symptoms after the CARB were tiredness and bloating; for FAT, they were tiredness, bloating, and nausea (Table 3). The number of patients reporting regurgitation was similar (n=5 for each beverage). Although pulse increased significantly more after CARB, only 3 of the 12 patients stated that they were aware of the palpitations. Symptoms that were less frequently reported were dizziness, headache, sweating and cold sweating, pain, and diarrhea (Table 3). No subject experienced preshock, shock, "almost fainting," syncope, unconsciousness, or vomiting during the test. None of the drinks caused dumping syndrome in the control group according to Sigstad's criteria ( $\geq 7$ ).

#### Discussion

When provoking patient's several years after undergoing gastric bypass with a glucose-rich and a fat-rich drink, we found that fat yielded as many symptoms as did carbohydrates, despite the fact that the latter altered glucose, insulin, and pulse rate significantly more.

Although the Sigstad's dumping score did not differ between the test meals, some specific symptoms did. FAT caused more nausea and bloating (including abdominal fullness, meteorism, and borborygmia) in comparison to CARB. Fat appears to be difficult to digest and absorb after gastric bypass surgery [13,14] and is shown to be particularly potent in inducing meal-related hormonal signals in health, functional dyspepsia, and obesity and after RYGB surgery [15–20]. Earlier studies have shown that nonoperated patients with fat intolerance complain of early satiety, bloating, and nausea, similar to patients with DS [20].

When the stomach is bypassed, as in RYGB, food passes rapidly into the jejunum, implying that the symptoms are particularly pronounced after this type of surgery [21]. However, the control group also experienced symptoms according to Sigstad's Dumping Index AUC both after FAT and after CARB (Tables 2 and 3). Fat increases glucagonlike peptide 1 release more than carbohydrates [17,18] and protein do [19], and because glucagon-like peptide 1 increases nausea and decreases the motivation to eat [22], this may explain why nausea was more pronounced after FAT than after CARB. Preference for fat decreases after gastric bypass [23,24], which seems to be a learned effect consistent with conditioned avoidance (i.e., arising over time) [25]. Because the effect is likely to be learned, it implies that reduction in fat intake is due to negative experiences, which can have gustatory and/or be related to a negative feedback mechanism from having dumping symptoms. Being sensitive to fat does not necessarily mean that DS is a complication. RYGB surgery aims to reduce energy intake, and patients themselves often look positively on the DS as they believe that it helps them to gain control of food intake [26].

In the present study, the fatty drink also affected the heart rate and blood pressure. It is known that fat can affect blood

pressure and pulse after a direct catheter infusion in the small intestine [27], which can be compared to the RYGB construction where beverage and food pass quickly into the small intestine. Pulse rate was significantly increased after CARB compared to FAT, but the change was not sufficient for patients to become aware of it and indicate this as a symptom on the Sigstad's Dumping Index.

The study was thus underpowered to show differences in specific symptoms. In addition, Sigstad's Dumping Index has several weaknesses: first, it is designed for diagnoses other than monitoring physiologic changes after gastric bypass; second, several symptoms are similar; and finally, 2 symptoms give negative points (Appendix 1). That 2 symptoms (regurgitation and vomiting) give negative points is understandable, as these symptoms should relieve the burden of DS. However, they are still symptoms that indicate DS.

## Conclusion

Although a carbohydrate provocation causes greater changes in blood glucose, insulin, and pulse rate in comparison with fat, the perceived symptoms are similar at up to 60 minutes postprandial in patients after RYGB as measured by Sigstad's Dumping Index. Fat and carbohydrates induced different symptom patterns; nausea and bloating were more common after fat. Healthcare professionals should address both fat and refined carbohydrates when counseling for early dumping syndrome in RYGB patients.

#### **Disclosures**

The study has been funded by grants from the Western Region in Sweden, VGFOUGSB-527641, and Swedish Nutrition Foundation.

# Appendix 1

Sigstad's scoring system for dumping syndrome A total score ≥7 is suggestive of dumping syndrome

Pre-shock, shock	+5	
"Almost fainting," syncope, unconsciousness	+4	
Desire to lie or sit down	+4	
Breathlessness, dyspnea	+3	
Weakness, exhaustion	+3	
Sleepiness, drowsiness, apathy, falling asleep	+3	
Palpitation	+3	
Restlessness	+2	
Dizziness	+2	
Headaches	+1	
Feeling of warmth, sweating, pallor, clammy skin	+1	
Nausea	+1	
Abdominal fullness, meteorism	+1	
Borborygmia	+1	
Regurgitation	-1	
Vomiting	-4	
Total		$\sum$

#### References

- [1] Berg P, McCallum R. Dumping syndrome: a review of the current concepts of pathophysiology, diagnosis, and treatment. Dig Dis Sci 2016;61(1):11–8.
- [2] 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(10):583–90.
- [3] Sugerman HJ, Starkey JV. Birkenhauer R. A randomized prospective trial of gastric bypass versus vertical banded gastroplasty for morbid obesity and their effects on sweets versus non-sweets eaters. Ann Surg 1987;205(6):613–24.
- [4] Mallory GN, Macgregor AM, Rand CS. The influence of dumping on weight loss after gastric restrictive surgery for morbid obesity. Obes Surg 1996;6(6):474–8.
- [5] Ukleja A. Dumping syndrome: pathophysiology and treatment. Nutr Clin Pract 2005;20(5):517–25.
- [6] Karamanolis G, Tack J. Nutrition and motility disorders. Best Pract Res Clin Gastroenterol 2006;20(3):485–505.
- [7] Hammer HF. Medical complications of bariatric surgery: focus on malabsorption and dumping syndrome. Dig Dis 2012;30(2):182–6.
- [8] Amri R, Bordeianou LG, Sylla P, Berger DL. Obesity, outcomes and quality of care: body mass index increases the risk of wound-related complications in colon cancer surgery. Am J Surg 2014;207 (1):17–23.
- [9] 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(12):1162–6.
- [10] Laurenius A, Olbers T, Naslund I, Karlsson J. Dumping syndrome following gastric bypass: validation of the dumping symptom rating scale. Obes Surg 2013;23(6):740–55.
- [11] Olbers T, Lönroth H, Fagevik-Olsén M, Lundell L. Laparoscopic gastric bypass: development of technique, respiratory function, and long-term outcome. Obes Surg 2003;13(3):364–70.
- [12] 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(6):479–86.
- [13] Odstrcil EA, Martinez JG, Santa Ana CA, et al. The contribution of malabsorption to the reduction in net energy absorption after long-limb Roux-en-Y gastric bypass. Am J Clin Nutr 2010;92 (4):704–13.
- [14] Lutz TA, Bueter M. The physiology underlying Roux-en-Y gastric bypass: a status report. Am J Physiol Regul Integr Comp Physiol 2014;307(11):R1275–91.
- [15] Feinle-Bisset C. Upper gastrointestinal sensitivity to meal-related signals in adult humans - relevance to appetite regulation and gut symptoms in health, obesity and functional dyspepsia. Physiol Behav 2016;162:69–82.
- [16] Khodarahmi M, Azadbakht L. Dietary fat intake and functional dyspepsia. Adv Biomed Res 2016;5:76.
- [17] Herrmann C, Göke R, Richter G, Fehmann HC, Arnold R, Göke B. Glucagon-like peptide-1 and glucose-dependent insulin-releasing polypeptide plasma levels in response to nutrients. Digestion 1995:56 (2):117–26.
- [18] Maffeis C, Surano MG, Cordioli S, Gasperotti S, Corradi M, Pinelli L. A high-fat vs. a moderate-fat meal in obese boys: nutrient balance, appetite, and gastrointestinal hormone changes. Obesity (Silver Spring) 2010;18(3):449–55.
- [19] Beckman LM, Beckman TR, Sibley SD, et al. Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass surgery. JPEN J Parenter Enteral Nutr 2011;35(2):169–80.
- [20] Lin HC, Van Citters GW, Zhao XT. Waxman A. Fat intolerance depends on rapid gastric emptying. Dig Dis Sci 1999;44(2):330–5.
- [21] le Roux CW, Aylwin SJ, Batterham RL, et al. Gut hormone profiles following bariatric surgery favor an anorectic state, facilitate

- weight loss, and improve metabolic parameters. Ann Surg 2006;243 (1):108-14.
- [22] Scholtz S, Miras AD, Chhina N, et al. Obese patients after gastric bypass surgery have lower brain-hedonic responses to food than after gastric banding. Gut 2014;63(6):891–902.
- [23] Laurenius A, Larsson I, Melanson KJ, et al. Decreased energy density and changes in food selection following Roux-en-Y gastric bypass. Eur J Clin Nutr 2013;67(2):168–73.
- [24] le Roux CW, Bueter M, Theis N, et al. Gastric bypass reduces fat intake and preference. Am J Physiol Regul Integr Comp Physiol 2011;301(4):R1057–66.
- [25] Mathes CM, Letourneau C, Blonde GD, le Roux CW, Spector AC. Roux-en-Y gastric bypass in rats progressively decreases the proportion of fat calories selected from a palatable cafeteria diet. Am J Physiol Regul Integr Comp Physiol 2016;310 (10):R952–9.
- [26] Laurenius A, Engström M. Early dumping syndrome is not a complication but a desirable feature of Roux-en-Y gastric bypass surgery. Clin Obes 2016;6(5):332–40.
- [27] Gentilcore D, Hausken T, Meyer JH, Chapman IM, Horowitz M, Jones KL. Effects of intraduodenal glucose, fat, and protein on blood pressure, heart rate, and splanchnic blood flow in healthy older subjects. Am J Clin Nutr 2008;87(1):156–61.