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BRIEF COMMUNICATION

Heterogeneity in the Definition and Clinical Characteristics of Dumping Syndrome: a Review of the Literature

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Abstract

Background No real consensus regarding the definition of dumping syndrome (DS) seems to exist and few subtyping is used in clinical practice. Knowledge is needed for correct design of trials and establishment of uniform treatment strategies. The aim of this study is to explore the distribution of clinical characteristics related to the subtypes of DS.

Methods A comprehensive search was performed in Cochrane, Google Scholar, PubMed, and ResearchGate. Data were collected on the definition and diagnostics of DS used in each study.

Results Twenty-seven clinical trials were included. Seventeen articles clearly provided a definition of DS and ten of these differentiated between early and late DS. Diagnose of DS was based on clinical symptoms (24 articles), hemodynamic parameters (e.g., tachycardia, hypotension; 9 articles), and biochemical analysis (e.g., blood sugar level; 12 articles). Questionnaires were used in 13 articles. A total of 67 different symptoms were correlated with dumping syndrome. Two symptoms were exclusively correlated with early and nine with late DS. Nine articles differentiated between early and late dumping based on timing since the last meal. Hypoglycemia was correlated with late DS in ten articles.

Conclusions This study reveals a vast heterogeneity in the definition and clinical characteristics of DS after RYGB. We feel that a standardized definition is required to provide a firm parameter in the evaluation and setup of clinical trials. A better understanding and description of the definition and diagnostic criteria of DS after RYGB is crucial to improve scientific reporting.

Keywords RYGB · Dumping · Syndrome · Definition · Heterogeneity · Review

Introduction

Long-term durability of weight loss and effective remission and prevention of type 2 diabetes, hypertension, and dyslipidemia is reported after Roux-en-Y gastric bypass (RYGB) [1]. While these beneficial metabolic effects of RYGB on the long-term prevent cardiovascular disorders and ultimately reduce mortality, the altered homeostasis also gives rise to the development of several side effects. Of these, dumping syndrome (DS) is one of the most challenging complications to handle after bariatric surgery. Since an increasing number of RGYB is being performed, we expect this complication to become a great challenge in future clinical practice.

In 2014, the Interdisciplinary European Guidelines on Metabolic and Bariatric Surgery (IFSO-EC, EASO, and EASO OMTF) published guidelines which recommend basic workup for all patients [2]. However, no real definition of dumping syndrome was used in these guidelines.

Recent studies have confirmed that the pathophysiology of DS after RYGB is heterogeneous [3]. In this paper, we aim to identify and discuss the diverse definitions and diagnostic modalities over time used in clinical trials. Furthermore, we studied the distribution and clinical characteristics of the subtypes of DS.

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Methods

A systematic review was performed following guidelines provided by the Cochrane Handbook for Systematic Reviews of Interventions [4]. Furthermore, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used for the evaluation of this study [5].

Literary Search

A comprehensive search was performed using individual search strings in PubMed, Cochrane database, Embase, Google Scholar, and Web of Science. In Cochrane and PubMed, the Mesh term "Dumping Syndrome" was used and results were filtered for clinical trial. For all others, dumping syndrome was entered as a keyword and manual screening was performed for each result individually. For each result, titles and abstracts were reviewed for relevance and when approved, articles were obtained. Articles other than clinical trials were excluded as well as articles written in another language than English, retracted articles, and trial protocols (Table 1). Screening of articles was done by two people (BG and TL) and if no consensus was reached between these two, a third party was addressed. Search strategy is illustrated in Fig. 1.

Screening of Definition

In each selected article, the used definition of DS was extracted and summed up in a database. Afterwards, these definitions were separated in different groups:

1. No definition of DS was mentioned
2. Definition was mentioned
    a. Distinction was made between early and late dumping.

For each eligible article, the parameters used to diagnose and/or define DS were listed.

Results

A total of 27 clinical trials were included in this review. Consensus for inclusion was reached for all articles, so no third party was addressed. Seventeen articles clearly provided a definition of DS and 10 of these 17 explicitly differentiated between early and late DS (Table 2). Ten articles did not provide a definition whatsoever [14, 23–31].

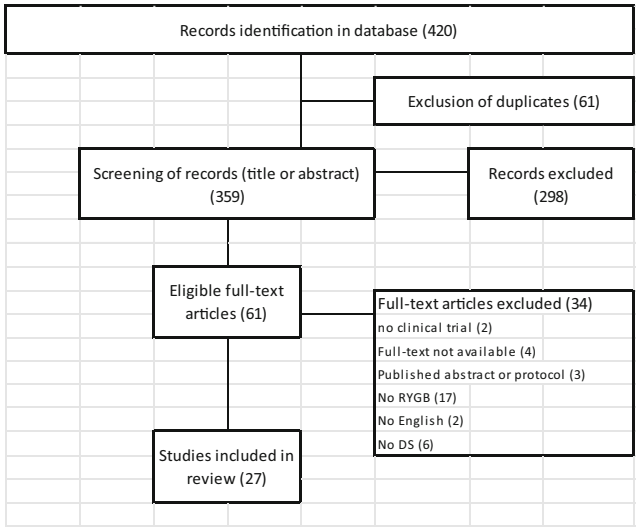

Fig. 1 Outline of search strategy and selection of articles. *DS* Dumping syndrome; *RYGB* Roux-en-Y Gastric Bypass

Diagnose of DS was based on symptomatology (24 articles), hemodynamic parameters (e.g., tachycardia, hypotension; 9 articles) and biochemical analysis (e.g., blood sugar level; 12 articles).

Questionnaires were used in 13 articles: dumping severity score [32] (2 articles), Sigstad [33](-like) score (7 articles), Dumping Symptom Rating Scale [34] (3 articles), or dumping syndrome survey [14] (1 article). In case of differentiation between early and late, hypoglycemia was correlated with late DS in ten articles. The term "post-RYGB hypoglycemia" was used in five articles for late DS. Hypoglycemia was correlated with non-differentiated DS in three articles. The term "post-vagotomy" was used in one article.

A total of 67 different symptoms were correlated with dumping syndrome (Table 3). Of these, two symptoms were exclusively correlated with early DS: "stomach cramp" (2 articles) and "stop feeling" (2 articles). Nine symptoms were exclusively associated with late DS; "difficult to/loss of concentration" (2 articles), "hunger" (6 articles), "fainting" (1 article), "tremor" (4 articles), "irritability" (2 articles), "drowsiness" (2 articles), and "aggression" (2 articles).

Table 1 Inclusion and exclusion criteria used in search strategy. *RYGB* Roux-en-Y gastric bypass, *DS* dumping syndrome

Inclusion criteria	Exclusion criteria
Clinical trials	Study design other than clinical trial
DS	No RYGB
English full text	Dumping syndrome not mentioned as an outcome measure or as a detected complication
Publish date between January 7, 2007 and January 8, 2018	

Table 2 A total of 27 clinical trials were included in this review with 17 articles clearly providing a definition of DS and 10 of these 17 explicitly differentiated between early and late DS

Differentiation		Ref
Early	Late	
"...abdominal pain, flushing and/or sweating occurring 15–60 min after a meal..."	"...hypoglycemic syndrome: sweating, shakiness, loss of concentration, hunger, and fainting, linked with severe hypoglycemia (plasma glucose < 55 mg/dl) appearing 1–3 h after a meal and relieved by normalization of the plasma glucose levels (Whipple triad); use of medication such as acarbose, diazoxide, octreotide, or any drug interfering with glucose metabolism"	[6]
"...clinically characterized by postprandial sweating, flushing, dizziness, weakness, tachycardia, palpitations, diaphoresis, and lassitude..."		[7]
"Early dumping occurs within an hour after eating, when the emptying of food into the small intestine triggers rapid fluid shifts into the intestinal lumen and the release of gastrointestinal hormones, resulting in gastrointestinal and vasomotor symptoms."	"Late dumping occurs between 1and 3 h after carbohydrate ingestion and is caused by an exaggerated insulin release, resulting in hypoglycemia."	[8]
"In patients who have dumping syndrome, high-osmolarity foods pass rapidly through the small-volume gastric pouch and cause an osmotic overload on entering the small intestine. This osmotic overload brings fluid into the lumen of the small intestine, resulting in a vagal reaction."		[9]
"...dumping syndrome, a group of symptoms associated with food emptying too quickly into the small intestine following surgery to remove or bypass the stomach, such as Roux-en-Y gastric bypass (RYGB).... early dumping syndrome, which tends to occur soon after eating..."	"...late dumping, a type of reactive hypoglycemia which tends to occur 1 to 3 h afterward..."	[10]
"Dumping syndrome, a group of symptoms associated with food emptying too quickly into the small intestine."		[11]
"...dumping syndrome leading to hyperinsulinemic hypoglycemia due to changes in the hormonal milieu of the gut..."		[12]
"Early DS comprises both gastrointestinal symptoms (such as abdominal pain, diarrhea, borborygmi [rumbling sound due to the fluid flow], nausea, and bloating) and vasomotor symptoms (such as tiredness, a need to lie down after meals, palpitations, perspiration, tachycardia and hypotension)."	"Late DS, which we prefer to label reactive hypoglycemia (RH), occurs 1–3 h after ingestion of a meal and includes symptoms such as perspiration, palpitations, hunger, fatigue, confusion, aggression, tremor, and syncope."	[13]
"Early symptoms occurs about 10–30 min postprandial and comprise both GI and vasomotor symptoms. GI symptoms include abdominal pain, diarrhea, borborygmi, nausea, and bloating. Vasomotor symptoms include fatigue, a desire to lie down after meals, facial flushing, palpitations, perspiration tachycardia, hypotension, and syncope."	"Late symptoms (which we prefer to label as late postprandial symptoms rather than dumping symptoms) occur 1–3 h after ingestion of a meal and include symptoms like perspiration, palpitations, hunger, fatigue, confusion, aggression, tremor, and syncope."	[14]
"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. DS is associated with rapid delivery of nutrients into the small intestine and subsequent release of vasoactive substances, incretins, and hormones, causing both gastrointestinal and vasomotor symptoms within the first 30 min after a meal."		[15]
"Severe dumping syndrome was defined as more than 3 episodes of postprandial diarrhea per week."		[16]
"...rapid transit of nutrients to the distal gut has also been proposed to account for increased postprandial gastrointestinal (GI) symptoms, which in severe cases, responsible for "dumping syndrome"..."		[17]
"Early dumping occurs within the first hour after a meal as a result of rapid nutrients emptying to the small intestine, thus causing an osmotically driven fluid movement from the intravascular components to the intestinal lumen. The induced intestinal distention and decreased circulating blood volume result in gastrointestinal symptoms, including abdominal pain, borborygmi, and nausea, and in vasomotor symptoms, including fatigue, fascial flushing, and palpitations."	"Late dumping occurs within 1–3 h after a meal as a result of a hyperinsulinemia induced hypoglycemic response. This reactive hypoglycemia is characterized by autonomic symptoms, including tremor, sweating, and palpitation, and neuroglycopenic symptoms, including confusion, inability to concentrate, and altered levels of consciousness."	[18]
"...early DS (DS occurring 15 min to 1 h after a meal ingestion) are mainly GI and they are caused by osmotically driven fluid shifts from the blood to the lumen."	"...late DS (DS occurring 1 to 3 h following a meal) are mainly vasomotor. They are caused by reactive hypoglycemia that is induced by a surge in insulin secretion that overcompensates for the glucose load delivered to the portal circulation."	[19]
"...dumping syndrome occurs after anastomosis of the small intestine to the gastric remnant of a gastrectomy. Early symptoms are digestive and adrenergic (the classical dumping syndrome)."	"...the late components comprise adrenergic and neuroglucopenic signs..."	[20]
	"Late dumping syndrome occurs as a side effect of proximal Roux-en-Y gastric bypass and has a reported incidence of up to 70% after oral glucose intake as shown by the oral glucose tolerance test (OGTT).In clinical practice, however, symptoms vary greatly in severity. The pathogenesis of late dumping is still unclear; it has been suggested that fast influx of undigested carbohydrates into the small bowel causes rapid resorption, triggering a surge in incretin secretion and thus inducing an exaggerated insulin response. As a consequence, blood glucose falls to hypoglycemic levels."	[21]
"Early dumping is caused by faster nutrition release to the intestine, which leads to osmotically driven fluid shifts from the blood to the lumen and, thus, vasomotor symptoms. The marked increased secretion of gastrointestinal hormones, such as glucagon-likepeptide1 (GLP-1), after RYGB probably contributes to early dumping."	"Late dumping occurs 1–3 h after eating and is caused by hyperinsulinemia and is therefore characterized by symptoms of hypoglycemia-like weakness, sweating, and dizziness."	[22]

Time between the meal and the onset of symptoms was stipulated in ten articles. In case of differentiation, the start of symptoms correlated with early DS was stated somewhere between 10 and 60 min after a meal. Late DS was said to start somewhere between 1 and 3 h. One article, in which no differentiation was made, stated that symptoms should arise within the first 30 min after a meal.

Table 3 Clinical or biochemical parameters used to diagnose or define dumping syndrome

Correlated with early DS	"abdominal pain," "flushing," "diarrhea," "bloating," "nausea," "cramping," "cramps," "near syncope," feeling faint or shaky," "fainting esteem," "vomiting," "fullness," "desire to lie," "sit down," "will lie down or sit," "palor," "paleness," "borborygm," "tiredness," "cold sweats," "stomach cramp," "stop-feeling"
Correlated with late DS	"shakiness," "difficulty to/loss of concentration," "hunger," "fainting," "severe hypoglycemia (plasma glucose < 55 mg/dl) 1–3 h after meal," "weakness," "exhaustion," "tremor," "irritability," "drowsiness," "unconsciousness," "confusion," "aggression"
Correlated with DS, both late and/or early, in case of baseline differentiation	"sweating occurring 15–60 min after meal," "sweating," "diaphoresis," "sweatiness," "perspiration," "dizziness," "vertigo," "palpitations," "fatigue," "physical fatigue" "exhaustion," "syncope," "loss of consciousness," "fainting"
Correlated with DS, both late and/or early, in case of no baseline differentiation	"tachycardia," "rapid pulse," "lassitude," "hypoglycemia," "shaking," "severe diarrhea," "lightheadedness," "somnolence," "gurgling," "headache," "headaches," "belching," "eructation," "recumbency," "restlessness," "breathlessness or dyspnea," "sleepiness," "sleep," "listlessness," "heart attack symptoms," "pre-shock," "shock," "drowsiness," "yawning," "falling asleep," "feeling off warmth," "warm," "feeling hot," "clammy skin," "meteorism," "cloudy vision," "blurred vision," "cold," "disorientation," "slurred speech," "seizure," "agitated," "agitation," "lethargic," "regurgitation," "abdominal distention," "anxiety"

Discussion

The goal of this systematic review was to explore the different definitions and parameters used in literature. We hypothesized that there is a vast heterogeneity for both. We state that it was not realistic to include all publications, so differentiation was made to only include high-quality publications in order to obtain an optimal study design.

The exact underlying mechanisms of early and late DS are yet to be identified. Probably, a multifactorial etiology is responsible for this phenomenon. Few have tried to study the pathophysiology of this complication and most are older studies.

Early DS involves rapid gastric emptying and was first described in 1913 by Hertz [35]. In 1922, the term "dumping stomach" was stated by Mix [36], and in the early 1950s, these symptoms were brought together under the so-called "post-gastrectomy" or "post-vagotomy syndrome" [37]. The loss of the pyloric muscle and/or vagotomy was the suggested underlying mechanism [38]. Although dumping syndrome and post-gastrectomy syndrome have similar clinical properties, there are very important distinctions between the early twentieth century gastrectomy patient and the today's bariatric patient. Most likely, a combination of hyperosmolar nutrient fluid shift from the intravascular to the interstitial compartment and the concomitant release of multiple GI hormones is responsible [39]. Gastric emptying studies have been used to support the diagnose; however, in most cases, dietary changes give immediate (< 7–15 weeks) relieve and further investigation is considered unnecessary.

In current literature, late DS is sometimes synonymized with "post-gastric bypass hypoglycemia". It was first described in German literature in 1933, and biochemical analysis was first published in 1947 by Gilbert and Dunlop [40]. It is assumed to be the result from hypoglycemia following a postprandial insulin peak and concomitant rapid delivery of undigested carbohydrates [41] [42]. The underlying physiological culprit seems to involve an exaggerated endogenous glucagon-like peptide-1 (GLP-1) response [43]. Especially when presented as a late, fulminant and/or refractory complication with an abrupt beginning, these patients should not be labeled DS purely based on suggestive symptomatology. Detailed (pancreatic) analysis is justified to exclude other rare causes of hyperinsulinemic hypoglycemia, i.e., nesidioblastosis or (multifocal) insulinoma.

In our study, we observed a large amount of heterogeneity between studies describing clinical symptoms for DS after RYGB. Although clinical signs appear to dominate the picture of DS, several studies were able to demonstrate clear associations between hemodynamic parameters or laboratory results. Presumably, the diagnosis of DS should depend on a combination of both clinical symptoms and objectifiable parameters. Therefore, we feel that current scoring systems (e.g., Sigstad, dumping severity score) may be insufficient to identify DS as a stand-alone diagnostic tool.

Besides anamnestic, clinical, and biochemical work-up, there might be place for additional diagnostic imaging. In an expert consensus document on gastric and intestinal motility disorders, Keller et al. [44] state that provocation tests using gastric emptying studies (99mTc-labeled scrambled eggs scintigraphy, 13C-octanoic acid gastric emptying breath test) and liquid or solid meal tests remain helpful in clinical cases with unclear symptoms and findings. In patients with typical symptoms after surgery, however, gastric emptying tests usually add little to the diagnosis.

Based on this study, we feel researchers should downsize the number of associated parameters relating to the definition of dumping syndrome until a correct and validated diagnostic tool is agreed upon. The first step should be to declare outcomes with a corresponding definition. In order to maximize transparency and diminish bias, this should be registered on an approved trial registry combined with a Delphi survey.

Conclusion

This study reveals a vast heterogeneity in the definition and clinical characteristics of DS after RYGB. We feel that a standardized definition is required to provide a firm parameter in the evaluation and setup of clinical trials. To enable comparison between studies and settings, authors should be clear about their choice of definition. A better understanding and description of the definition and diagnostic criteria of DS after RYGB is crucial to improve scientific reporting, evaluation of clinical data, and setup of treatment strategies.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Statement This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Statement Does not apply.

Appendix I – syntaxes used for the search in the different available databases

Embase.com

exp. dumping syndrome/co, di, dm, dt, ep, et, pc, si, su, th [Complication, Diagnosis, Disease Management, Drug Therapy, Epidemiology, Etiology, Prevention, Side Effect, Surgery, Therapy]

Cochrane

MeSH descriptor: [Dumping Syndrome] explode all trees

Web of science

TS = (dumping AND syndrome)

PubMed publisher

("Dumping Syndrome"[Mesh]) AND "Gastric Bypass"[Mesh]

Google scholar

allintitle: "dumping syndrome" and "gastric bypass".

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