Journal of Gastroenterology and Hepatology Research

Online Submissions: http://www.ghrnet.org/index./joghr/doi: 10.17554/j.issn.2224-3992.2022.11.1061

Journal of GHR 2022 December 21; **11(5)**: 3759-3764 ISSN 2224-3992 (print) ISSN 2224-6509 (online)

ORIGINAL ARTICLE

Obesity Subtypes and Short Term Weight Loss After Vertical Sleeve Gastrectomy: A Retrospective Cohort Study

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Conflict-of-interest statement: TRS is a Consultant for Boehringer Labs and for Ethicon Endosurgery. All other authors declare that there is no conflict of interest regarding the publication of this paper.

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Received: October 23, 2022 Revised: November 23, 2022 Accepted: November 27, 2022 Published online: December 23, 2022

ABSTRACT

AIM: Vertical sleeve gastrectomy has become the most common

surgical intervention for medically-complicated obesity. This study examines the hypothesis that a clinical subtype of obesity (psychosocial factors, genetic risk, or early life endocrine disruptors termed obesogens) can identify the best candidates for vertical sleeve gastrectomy.

MATERIALS AND METHODS: This is a retrospective cohort study of 225 consecutive new individuals with medically-complicated obesity seen preoperatively in outpatient bariatric clinic in an urban community teaching hospital. Eighty-four individuals underwent sleeve gastrectomy with a minimum of 6 months of follow up.

RESULTS: Among 3 subtypes, early life obesogen exposure has been identified in 14.5% of individuals, genetic risk in 24.5% of individuals, and psychosocial factors in 61% of individuals. Percent excess weight loss (mean+/-SD) at 6 months is different among the three groups (pANOVA = 0.024). Individuals with genetic risk (38%+/-14) have significantly less weight loss (p = 0.029) than individuals with psychosocial factors (47%+/-15), while there is no difference compared to the obesogen subtype (41%+/-8.9).

CONCLUSION: The most common clinical subtype of obesity is psychosocial factors, and there is significantly higher short term weight loss after sleeve gastrectomy in individuals with psychosocial factors. Weight loss may be limited by an individual's genetic risk and early life obesogen exposure. A prospective study is required to confirm these findings.

Key words: Obesity; Bariatric Surgery; Bariatrics; Psychosocial Factors; Weight Loss

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Shah RA, Nath A, Shope TR, Lameda ILP, Brebbia JS, Koch TR. Obesity Subtypes and Short Term Weight Loss After Vertical Sleeve Gastrectomy: A Retrospective Cohort Study. *Journal of Gastroenterology and Hepatology Research* 2022; **11(5)**: 3759-3764 Available from: URL: http://www.ghrnet.org/index.php/joghr/article/view/3340

List of abbreviations

VSG: Vertical Sleeve Gastrectomy

INTRODUCTION

Temporal prevalence studies of worldwide obesity have confirmed that this epidemic continues to worsen and investigators have suggested that the scope of this problem may indeed be underestimated^[1]. The pathogenesis of the condition is multifactorial and complex but is generally considered to result from energy intake in excess to expenditure^[2]. Suggested risk factors include psychosocial factors, genetic factors, and obesogens (environmental chemicals associated with alteration of programming of fat cell development and interference of neuroendocrine pathways)^[3-5]. There has been a rise in the numbers of overweight or obese children in the United States to a prevalence of 33% by 2016^[6]. There is not an a single genetic cause or endocrine disorder as an explanation for this disorder in the majority of these children^[6], and so early life obesogens could be a pathophysiological mechanism involves in this increase in childhood obesity.

Because of insufficient weight loss in those individuals with medically-complicated obesity managed with dietary-activity programs or weight loss medications, bariatric surgical procedures have risen to prominence as the method of treatment for medically-complicated obesity^[7]. The resultant weight loss has been shown to result in improvements in the risks of associated disease processes^[8]. Vertical sleeve gastrectomy (VSG) is the most commonly performed bariatric procedure worldwide, attributed to its relative technical simplicity and physiologic anatomy without bypass or anastomosis^[9].

Preoperative factors might assist in determining which patients will receive the best postoperative benefit, which in turn could aid clinicians who counsel patients with medically-complicated obesity. We have previously shown that symptoms of irritable bowel syndrome do not predict the magnitude of weight loss after bariatric surgery^[10]. Multiple other factors have been suggested including hormonal, dietary, hereditary, exertional, and psychiatric components^[11]. However, studies assessing each of these factors remain sparse and sometimes contradictory, leading to wide practice variability in patient selection. With regard to psychosocial factors, some studies have found that weight loss was significantly associated with pre-surgical psychiatric diagnoses while other studies did not identify a clear relationship^[12].

It is therefore difficult to predict which patients with medically-complicated obesity are most likely to benefit from undergoing a VSG^[13,14]. The influence of multiple clinical predictors on weight loss remains an area of active investigation. Elucidation of these relationships could aid clinicians in a more tailored patient selection and postoperative management for those individuals with medically-complicated obesity. Our hypothesis is that clinical subtypes of obesity can identify the best candidates to counsel for a VSG.

METHODS

Study Population

All procedures performed in studies using human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for human studies was obtained from the MedStar Research Institute Human Studies Subcommittee on December 15, 2018. The Human Studies Subcommittee decided that this was a minimal risk protocol and granted a waiver of informed consent for this research study.

This is a single institution, retrospective cohort study performed in a large, urban community teaching hospital. This study includes

225 consecutive new obese subjects living in urban and suburban locations who underwent preoperative evaluation in bariatric gastrointestinal clinic from October 2018 to June 2019. Since this is a retrospective cohort study, the population standard deviation for use in a sample size calculation was unknown. Subjects (n=17) were excluded due to an absence of complete information. Eighty-four patients who had undergone VSG had been followed for at least 6 months postoperatively.

Data collection

Patient information was reviewed using the available electronic medical records. The type of bariatric surgery was recorded along with the patient's family history of obesity, the patient's height and weight at age 18, present age, sex, and present body mass index (BMI as kg/m²).

Definitions of Subtypes of Obesity

Early life obesogen exposure is defined by clinical features: mother and father both with normal weights (to exclude a genetic risk) and the individual had a BMI of $\geq 30~\text{kg/m}^2$ at age 18 years-old. Genetic risk (due to either a genetic or an epigenetic disorder) is defined by clinical features: mother and/or father is obese, and the individual had a BMI of $\geq 30~\text{kg/m}^2$ at age 18. Psychosocial factors are defined by a clinical feature: the individual had a BMI $< 30~\text{kg/m}^2$ at age 18 (in order to estimate psychosocial factors involved in an individual after age 18).

Statistical Analyses

Statistical analysis was performed using StatView for Windows, SAS Institute Inc., Cary, NC, USA. Demographic information is examined by the use of descriptive statistics.

RESULTS

Prevalence of Obesity Subtypes

As shown in Figure 1, the most common subtype of obesity is psychosocial factors (61%) followed by genetic risk (24.5%), and then early life obesogens (14.5%).

The demographics of these individuals are shown in Table 1. Using the Tukey Kramer test, as shown in Table 2, the psychosocial factors subtype was significantly older compared to the obesogens subtype or the genetic risk subtype. The psychosocial factors subtype had significantly less weight compared to the obesogens subtype or the genetic risk subtype. The psychosocial factors subtype had significantly lower BMI compared to the obesogens subtype or the genetic risk subtype. At age 18, the psychosocial factors subtype had significantly less weight compared to the obesogens subtype, which was significantly less than the genetic risk subtype. At age 18, the psychosocial factors subtype had significantly lower BMI compared to the obesogens subtype, which was significantly less than the genetic risk subtype.

Weight Loss after Vertical Sleeve Gastrectomy

Figure 2 demonstrates the mean (SD) percent excess weight loss at 6 months after VSG for the 3 obesity subtypes. There was a statistically significant difference among the 3 subtypes (pANOVA = 0.024). Using the Scheffe multiple comparison test, percent excess weight loss was greater (p = 0.029) in the psychosocial factors subtype (47 +/- 15 %) compared to the genetic risk subtype (38 +/- 14 %). There was no statistically significant difference (pANOVA = 0.24) in the decreases in BMIs at 6 months after VSG for the three subtypes:

obesogens [mean (SD): 13.0 (3.3)], psychosocial factors [mean (SD): 10.8 (5.3)], and genetic risk [mean (SD): 12.4 (4.5)]. There was no statistically significant difference (pANOVA = 0.70) in the decreases in percent total weight loss at 6 months after VSG for the three subtypes: obesogens [mean (SD): 23% (4)], psychosocial factors [mean (SD): 23% (6.8)], and genetic risk [mean (SD): 22% (6.6)].

The demographics of these individuals are shown in Table 3. Using the Tukey Kramer test, as shown in Table 4, the psychosocial factors subtype was significantly older compared to the genetic risk subtype. The psychosocial factors subtype had significantly less weight compared to the obesogens subtype or the genetic risk subtype. The psychosocial factors subtype had significantly lower BMI compared to the obesogens subtype or the genetic risk subtype.

DISCUSSION

In this patient population, psychosocial factors, as defined by weight gain leading to obesity after age 18, is the most common obesity subtype. The results did support our hypothesis that clinical subtypes of obesity can identify the best candidates for vertical sleeve gastrectomy. In this present study, individuals with the psychosocial subtype of obesity have statistically more percent excess weight loss

Table 1 Demographics of the obesity sub-types

	Obesogens	Psychosocial	Genetic Risk
No. of Subjects	30 (14.5%)	127 (61%)	51 (24.5)
Gender	6 Men (20%)	14 Men (11%)	10 Men (20%)
Gender	24 Women (80%)	113 Women (89%)	41 Women (80%)
Mean Age	41 (10)	48 (9)	36 (10)
Years (SD)	(Range 26-69)	(Range 24-68)	(Range 18-60)
Mean Weight	150.9 (34)	124 (22)	156.8 (41)
kg (SD)	(Range 96.3-216)	(Range 84.5-212)	(Range 95.4-276)
Mean BMI	54 (11)	45 (7)	57 (13)
kg/m2 (SD)	(Range 39-74)	(Range 35-86)	(Range 36-99)
Age 18 Mean	105 (22)	66.4 (11)	116 (25.5)
Weight kg (SD)	(Range 63.6-159)	(Range 44.5-93)	(Range 79.5-195)
Age 18 Mean	37 (6)	24 (3)	41 (8)
BMI kg/m² (SD)	(Range 30-50)	(Range 16-29)	(Range 30-75)

Table 2 Statistical analysis (tukey kramer tests) of the obesity subtypes.		
Age: pANOVA < .001		
Obesogens vrs Psychosocial Factors: p < .001		
Obesogens vrs Genetic Risk: p = 0.089		
Genetic Risk vrs Psychosocial Factors: p < 0.001		
Weight: pANOVA < .001		
Obesogens vrs Psychosocial Factors: p < 0.001		
Obesogens vrs Genetic Risk: p = 0.65		
Genetic Risk vrs Psychosocial Factors: p < 0.001		
BMI: pANOVA < .001		
Obesogens vrs Psychosocial Factors: p < 0.001		
Obesogens vrs Genetic Risk: p = 0.393		
Genetic Risk vrs Psychosocial Factors: p < 0.001		
Age 18 Weight: pANOVA < .001		
Obesogens vrs Psychosocial Factors: p < 0.001		
Obesogens vrs Genetic Risk: p = 0.03		
Genetic Risk vrs Psychosocial Factors: p < 0.001		
Age 18 BMI: pANOVA < 0.001		
Obesogens vrs Psychosocial Factors: p < 0.001		
Obesogens vrs Genetic Risk: p = 0.002		
Genetic Risk vrs Psychosocial Factors: p < 0.001		

after VSG at their 6 month postoperative visits. We believe that this is a major finding because a previous study of patients who underwent VSG revealed that > 90% of the patients' percent excess body weight loss occurred by their 6 month follow up visits (Mean+/-SD: 39%+/-2) compared to their 24 months postoperative visits (Mean +/- SD: 42%+/-4)^[10]. In our search of the medical literature, no other publication has yet explored the influence of early life obesogens on outcomes after bariatric surgery.

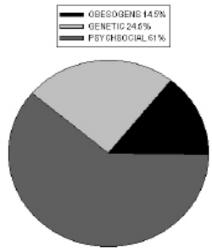


Figure 1 Percentages of individuals with obesity sub-types as defined by exposure to Early Life Obesogens, Genetic Risk, and Psycho-Social Factors.

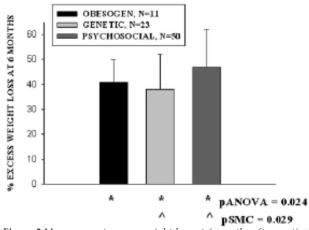


Figure 2 Mean percent excess weight loss at 6 months after vertical sleeve gastrectomy in the three obesity sub-types, early life obesogens, genetic risk, and psychosocial factors. There was a statistically significant difference among the 3 subtypes (pANOVA = 0.024). Using the Scheffe multiple comparison test, weight loss was greater in the psychosocial factors subtype compared to the genetic risk subtype (p = 0.029).

Table 3 Demographics of individuals who underwent vertical sleeve gastrectomy.

	Obesogens	Psychosocial	Genetic Risk
No. of Subjects	11 (13%)	50 (60%)	23 (27%)
Gender	2 Men (18%)	3 Men (6%)	3 Men (13%)
Gender	9 Women (82%)	47 Women (94%)	20 Women (87%)
Mean Age	42 (8.8)	47 (10)	36 (8)
Years (SD)	(Range 32-58)	(Range 24-65)	(Range 21-51)
Mean Weight	153 (36.8)	123.6 (21.3)	154 (33.6)
kg (SD)	(Range 107-216	(Range 95-212)	(Range 103-234)
Mean BMI	56 (12)	46 (8)	57 (10)
kg/m2 (SD)	(Range 39-74)	(Range 35-86)	(Range 43-80)
Mean % Excess	41 (8.9)	47 (15)	38 (14)
Weight Loss (SD)	(Range 26-54)	(Range 19-103)	(Range 14-73)

Table 4 Statistical analysis (tukey kramer tests) of individuals who underwent vertical sleeve gastrectomy

Age: pANOVA < 0.001
Obesogens vrs Psychosocial Factors: p = 0.29
Obesogens vrs Genetic Risk: p = 0.22
Genetic Risk vrs Psychosocial Factors: p < 0.001
Weight: pANOVA < .001
Obesogens vrs Psychosocial Factors: p = 0.005
Obesogens vrs Genetic Risk: p = 0.99
Genetic Risk vrs Psychosocial Factors: p < 0.001
BMI: pANOVA < .001
Obesogens vrs Psychosocial Factors: p = 0.0046
Obesogens vrs Genetic Risk: p = 0.98
Genetic Risk vrs Psychosocial Factors: p < 0.001

The term obesogen is applied to a chemical that, upon exposure, leads to increased adipose tissue accumulation. Obesogens are believed to contribute to obesity via a variety of mechanisms that include epigenetic modification, gut microbiome alteration, and interference with endocrine signaling pathways[15]. A wellcharacterized obesogen in the literature is tributyltin (TBT), which is used as a fungicide in industrial water systems and agriculture^[16]. TBT has been shown to activate peroxisome proliferator-activated receptor (PPAR) and Retinoid X Receptor leading to increased adipogenesis^[17]. In support of this concept, analysis of the National Health and Nutrition Examination Surveys database has revealed an association between urinary tin concentration and diagnosis of an obesity-related disorder, diabetes mellitus^[18]. Additional studies have shown that over 200 unique compounds have been identified in phthalates and bisphenols, which are commonly used in plastics, that stimulate preadipocyte proliferation and differentiation to adipocytes^[19]. Interestingly, the majority of these compounds were found to act via pathways other than PPAR.

While our criterion used to define an early life obesogen may be considered overly broad, the full spectrum of potential obesogens have not yet been identified and therefore would not be detected^[4]. These criterion may not exclude the effects of obesogen exposure since transgenerational effects to exposure have been demonstrated in murine models^[20]. Future studies could be directed at elucidating the mechanisms of transgenerational effects of obesogens in order to better discern the contribution of genetic predisposition versus epigenetic modifications. As obesogens are identified, interventions to reduce exposure could contribute to reducing the rising prevalence of obesity.

Genetic factors have previously been shown to play a role in weight loss after bariatric surgery. A study of 13 pairs of first-degree relatives who underwent Roux-en-Y gastric bypass were compared to unrelated cohabitating pairs^[21], and there was significantly less difference in weight loss between the related pairs (9% mean difference in related versus 26% mean difference in unrelated). Several hundred polymorphisms have been identified that contribute to obesity but, combined, these can account for only approximately 5% of the body mass index variance observed in the general population^[22]. Genetic risk factors have widely varying effects on phenotype. In an animal model, melanocortin 4-receptor deficiency has been linked to obesity^[23]. A second study in a rat model revealed that performance of sleeve gastrectomy in a melanocortin 4-receptor-deficient phenotype led to decreased weight loss compared to controls^[24].

Our definition of an individual with genetic risk could include

individuals who were exposed to epigenetic phenomena (which could be related to an environmental exposure but would nonetheless be heritable). Further investigations are presently ongoing into histone modification and non-coding RNA molecules in the development of obesity. Certainly, better understanding of genetic risks is quite important during this world-wide epidemic of obesity.

Our final category of patients were individuals who were not obese in childhood but developed obesity after 18 years of age, presumably due to the influence of psychosocial factors after age 18. These individuals were defined in this study as the psychosocial factors obesity subtype. While research has generally focused on established psychiatric diagnoses, contemporary psychological theory posits that behavioral characteristics, such as disinhibition, may be a better indicator of postoperative weight loss rather than discrete psychiatric diagnoses^[25]. Dopaminergic and opioid receptor pathways have been implicated in the pathophysiology of obesity, indicating eating behavior in this disorder may be modulated in a similar manner to drug addiction^[26]. Patients have been observed to have an increased incidence of substance dependence after bariatric surgery, attributed to 'addiction transfer' [27]. In our present study, we attempt to encompass the broader spectrum of those individuals with behavioral characteristics that predispose to obesity. Individuals with the psychosocial subtype of obesity demonstrated significantly more weight loss compared to individuals with either genetic risk or exposure to obesogens. This result may be partially attributable to psychosocial factors being the only modifiable risk factors among the three subtypes of obesity that were evaluated in this study. Psychosocial factors have a complex causal relationship to obesity. For example, individuals who undergo bariatric surgery have reported significant improvements in depression and anxiety within the first year, as well as body image, relationship fulfillment, and sexual

The limitations of our present study include the previously discussed limitations regarding the categorization of patients. In addition, this study shares the well describes weaknesses of all retrospective studies including its applicability to other patient populations. In this study, there were a small number of individuals who underwent VSG compared to the number of individuals who underwent preoperative evaluation.

Our present study supports the merits of examining the roles that subtypes of obesity play in postoperative weight loss after VSG. A larger prospective study is required to further elucidate the roles of each of these obesity subtypes in weight loss after VSG and to study potential mechanisms that could promote or hinder postoperative weight loss. This information could be useful for assisting clinicians who counsel patients with medically-complicated obesity and could be useful for optimizing postoperative care in those individuals who have a less favorable subtype of obesity.

Authorship credits

All authors listed (RS, AN, IPL, JB, TK) have contributed to: (1) conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. More specifically, AN, TS, and TK contributed to the study conception and design. Acquisition of data was completed by IPL, JB, TS and TK. Material preparation, data collection and analysis were performed by RS, AN, and TK. The first draft of the manuscript was written by RS and AN, IPL, JB, and TK revised it critically for important intellectual content. All co-authors approved the final manuscript.

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