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Eating behavior in laparoscopic sleeve gastrectomy: Correlation between plasma ghrelin levels and hunger

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Essverhalten nach laparoskopischer „Sleeve Gastrectomy“ – Korrelationen zwischen Plasma-Ghrelin-Spiegeln und Hungerempfinden

Zusammenfassung. *Grundlagen:* Bariatrische Operationsverfahren wie das Magenband, VGB und Magenbypass haben nachgewiesenermaßen Einfluss auf das postoperative Essverhalten. Nachdem die laparoskopische „Sleeve gastrectomy“ (LSG) zu verringerten Ghrelin-Spiegeln führt, ist eine Reduktion im Hungerempfinden zu erwarten. Ziel dieser Studie war es, den Einfluss der LSG auf das Essverhalten in Korrelation Plasma-Ghrelin-Spiegeln zu bestimmen.

Methodik: In dieser prospektiven Studie von 15 morbid adipösen LSG-Patienten wurde die deutsche Version des „Self-report Three-Factor Eating Questionnaire“ (TFEQ) vor der Operation und 6 Monate postoperativ angewandt, um den Einfluss der LSG auf die drei Dimensionen des Essverhaltens: Kontrolle, Irritierbarkeit und Hungerempfinden zu bestimmen. In einer Untergruppe von 7 Patienten wurde die Korrelation zwischen Plasma-Ghrelin-Spiegeln und dem Hungerempfinden untersucht.

Ergebnisse: LSG führte zu einer Zunahme in der kognitiven Einschränkung und zu einer reduzierten Kontrolle, Irritierbarkeit. Weiters wurde eine signifikante Reduktion im Hungerempfinden nachgewiesen, welche ebenfalls mit den Ghrelin-Spiegeln korrelierte ($r = 0.834$, $p = 0.01$).

Schlussfolgerungen: LSG führt zu einem reduzierten Hungerempfinden, welches mit den ebenfalls verringerten Plasma-Ghrelin-Spiegeln korreliert. Diese Effekte können zu dem exzellenten Gewichtsverlust nach LSG beitragen.

Schlüsselwörter: Ghrelin, Hunger, Essverhalten, Sleeve gastrectomy, TFEQ.

Summary. *Background:* Bariatric procedures like gastric banding, vertically banded gastroplasty and Roux-en-Y gastric bypass have impacted on the postoperative eating behavior. Since laparoscopic sleeve gastrectomy (LSG) leads to decreased plasma ghrelin levels, a reduced sensation of hunger following surgery is expected. The aim of this study was to assess the impact of LSG on the eating behavior in correlation with plasma ghrelin levels.

Methods: This prospective study was carried out in 15 morbidly obese patients who underwent LSG. The German version of the self-report Three-Factor Eating Questionnaire (TFEQ) was applied preoperatively and at six months following surgery to assess the impact of LSG on the three dimensions of eating behavior: restraint, disinhibition and hunger. The correlation between plasma ghrelin levels and the sensation of hunger was assessed in a subset of seven patients.

Results: Following LSG, increased cognitive restraint and decreased disinhibition of eating were found. Furthermore, a significant decrease in hunger was observed with a significant correlation ($r = 0.834$, $p = 0.01$) between circulating plasma ghrelin levels and hunger scores.

Conclusions: Following LSG, a high correlation between decreased ghrelin levels and the reduced sensation of hunger was found. This may contribute to the excellent weight loss observed following laparoscopic sleeve gastrectomy.

Keywords: Ghrelin, hunger, eating behavior, sleeve gastrectomy, TFEQ.

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Introduction

Bariatric procedures like laparoscopic adjustable gastric banding (LAGB) and Roux-en-Y gastric bypass (RYGBP)

were found to be effective in weight reduction [1–6] and to improve quality of life (QoL) in the postoperative course [7–10].

A major factor contributing to the long-term success of weight reduction following bariatric procedures may be the profound changes in the eating behavior postoperatively. The self-report Three-Factor Eating Questionnaire (TFEQ) was already applied to assess the impact of LAGB, VBG and RYGBP [11–16] on three dimensions of eating behavior: cognitive restraint of eating, disinhibition of eating and susceptibility of hunger. In laparoscopic sleeve gastrectomy (LSG), another restrictive bariatric procedure [17–24], the TFEQ as a validated and reliable instrument has not been used for the evaluation of the impact on eating behavior so far. In a study of Han [25], the subjective view on appetite was assessed by the patients themselves, finding a mean reduction to 49% of the preoperative appetite at six months postoperatively.

Ghrelin, a hunger-regulating peptide hormone mainly produced in the fundus of the stomach [26–29], decreased in the postoperative course of LSG [30, 31]. LSG might, therefore, be seen as a strictly restrictive procedure augmented by the reduction of the ghrelin-producing tissue. A reduction in the sensation of hunger assessed by the self-report Three-Factor Eating Questionnaire was suspected.

The aim of this study was to determine the effects of laparoscopic sleeve gastrectomy on the eating behavior in correlation with plasma ghrelin levels.

Material and methods

A prospective study was performed in a series of 15 morbidly obese patients according to the NIH recommendations for bariatric surgery [32]. The patients underwent laparoscopic sleeve gastrectomy as first and single-step bariatric procedure; seven of them had a BMI of more than 50 kg/m² and were, therefore, considered to be super-obese. Demographic data of the study population are listed in Table 1.

Surgical method

Sleeve gastrectomy is performed laparoscopically; the patient is in a half sitting position with abducted legs. Trocars are placed left to midline about halfway between xiphoid and umbilicus (10 mm), in the epigastric (5 mm), left lateral subcostal (5 mm), right middle abdominal (12 mm), and left middle abdominal (12 mm) position. The greater

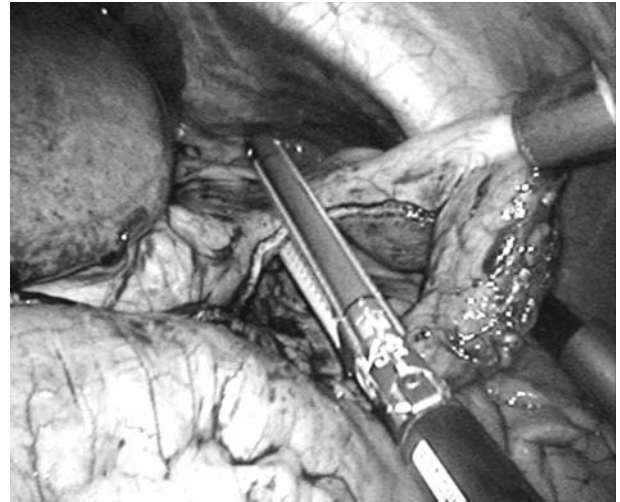


Fig. 1: Laparoscopic Sleeve gastrectomy: The stomach is reduced to a small gastric tube by resecting the main part of the corpus, antrum and the complete fundus

curvature is mobilized using the Ligasure Atlas™ (COVIDIEN), and thereafter major parts of the antrum, corpus and the complete fundus are resected from the antrum to the angle of His (Fig. 1), using 4.8-mm and 3.5-mm linear endo-staplers (Autosuture EndoGIA, COVIDIEN). The stomach is therefore reduced to a narrow gastric tube at the lesser curvature over a 48-French bougie, which is placed there to avoid stenosis. Thus, LSG can be seen as strictly restrictive bariatric procedure.

Evaluation instrument

Eating behavior was assessed preoperatively and at six months following surgery using the German version of the self-report Three-Factor Eating Questionnaire (TFEQ) developed by Stunkard and Messick [33]. The Questionnaire is a validated and reliable instrument in obesity research and eating disorders and was already applied in LAGB, VBG and RYGBP [11–16]. This questionnaire measures three dimensions of eating behavior: cognitive restraint of eating, disinhibition of eating, and susceptibility to hunger. The cognitive restraint of eating scale measures the amount of intentional restriction of food intake. The disinhibition scale concerns the inability to resist food stimuli or social and emotional eating cues. The hunger scale measures subjective feelings of hunger.

Ghrelin assay

Venous blood samples were collected in pre-chilled tubes containing aprotinin/EDTA solution at the day of hospital admission and in the outpatient clinic at six months following LSG. After centrifugation at 4°C, plasma was separated and stored at –20°C until analysis. Total plasma ghrelin levels were measured by radioimmunoassay using I¹²⁵ labeled-ghrelin as a tracer molecule, and a polyclonal antibody was raised in rabbits against full-length octanoylated human ghrelin (Peninsula Laboratories, San Carlos CA).

Tab. 1: Demographic data of the study population

N	15
Sex (f/m)	12/3
Age (years)	40.8 ± 14.3 (21.4–69.5)
Body weight (kg)	139.9 ± 20.2 (113–187)
BMI (kg/m ²)	49.3 ± 8.0 (40.7–73.5)
Superobese	7 (47%)

Statistical analysis

Results are expressed as mean \pm standard deviation. A p -value < 0.05 was considered to be significant. Differences between the preoperative and postoperative subscores of the self-report Three-Factor Eating Questionnaire and Plasma ghrelin levels were analyzed using the Mann-Whitney- U Test [34]. Pearson correlation coefficients were calculated to determine the association between hunger scores assessed by the self-report Three-Factor Eating Questionnaire (TFEQ) and plasma ghrelin levels. Statistical analysis was performed using the SPSS statistical package, version 11.0 for Max OS X (SPSS, Chicago, IL).

Results

BMI at the time of surgery was $49.3 \pm 8.0 \text{ kg/m}^2$ (range 41–73), with a proportion of super-obese patients of 47% (7/15). The mean body weight was $139.9 \pm 20.2 \text{ kg}$ (range 113–187). At six months following LSG, the patients achieved a mean excessive weight loss (EWL) on the basis of Metropolitan Tables [35] of 51%, as BMI and body

weight were reduced to mean $30.8 \pm 3.4 \text{ kg/m}^2$ and $105.3 \pm 15.7 \text{ kg}$.

The results of the Three-Factor Eating Questionnaire are summarized in Table 2. Preoperatively, the patients showed low scores for cognitive restraints, and very high scores for disinhibition of eating and hunger compared with the German norms [36]. Postoperatively, cognitive restraint must be classified as high, disinhibition of eating and susceptibility to hunger as medium and low, respectively.

In a subset of seven patients the correlation between plasma ghrelin levels and the sensation of hunger was assessed. LSG led to a significant decrease of plasma ghrelin compared with preoperative levels ($107 \pm 25 \text{ fmol/ml}$ preoperative vs. $44 \pm 11 \text{ fmol/ml}$ six months after LSG, $p = 0.001$). As shown in Fig. 2, this reduction of plasma ghrelin correlated significantly with the reduced sensation of hunger following LSG ($r = 0.834$, $p = 0.01$).

Discussion

In this study we demonstrate significant changes in all of the three dimensions of eating behavior measured by the self-report Three-Factor Eating Questionnaire comparing preoperative values to data at six months following LSG. Cognitive restraint of eating increased significantly, while disinhibition of eating and susceptibility to hunger significantly decreased. Furthermore, hunger scores highlighted a significant correlation with the Plasma ghrelin levels preoperatively and at six months following LSG.

The self-report Three-Factor Eating Questionnaire (TFEQ) is a validated instrument in research on obesity and eating disorders. It was already applied to measure the impact of bariatric procedures like LAGB, VBG and RYGBP on the three dimensions of eating behavior.

Guisado [12] applied the TFEQ to report eating behavior after VBG comparing patients with and without psychiatric disorders. Significant differences were found only in the values for disinhibition between the two groups, and not for restriction and hunger.

Three studies shed luster on the effect of LAGB on the eating behavior. Schindler [15] reported a significant increase in cognitive restraint, and a significant decrease in hunger and the disinhibition of eating in a series of LAGB patients. This corresponds to the findings of Nickel [16] and Lang [37] who found these results at three months following surgery remaining stable up to 12 months postoperatively. The same results were found in a recently published study by Burgmer [13] on eating behavior following gastric restrictive surgery (AGB and VBG). In this study postoperative disinhibition was inversely correlated with the extent of weight loss after gastric restrictive surgery.

Also in Roux-en-Y gastric bypass surgery, the TFEQ assessed a significant increase comparing preoperative and postoperative values for cognitive restraint and decreases for hunger and disinhibition of eating, as published by Boan [14]. Kalarchian [11] found significant higher values in the disinhibition and hunger scores and lower values in the cognitive restraint score of binge

Tab. 2: Three factor eating questionnaire (TFEQ) in laparoscopic sleeve gastrectomy: scores of subscales

	Preoperatively	6 months postoperatively	
Cognitive restraint	6.4 ± 4.9	12.2 ± 4.9	$p = 0.005$
Disinhibition	13.2 ± 2.4	6.5 ± 3.6	$p < 0.001$
Hunger	11.1 ± 1.9	2.4 ± 2.3	$p < 0.001$

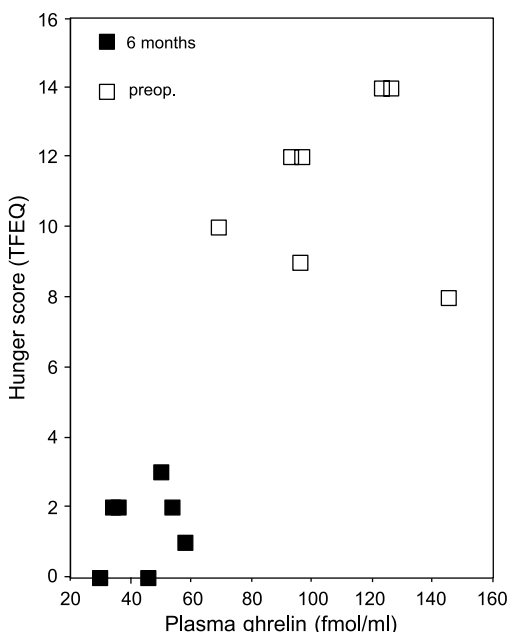


Fig. 2: Correlation between Plasma ghrelin levels and the sensation of hunger as assessed by the self-report Three-Factor Eating Questionnaire (TFEQ) in seven patients, preoperatively and at six months following LSG

eaters following gastric bypass, compared to non-binge eaters.

The correlation between Ghrelin and hunger was the cynosure in a larger series of studies. Ghrelin was found to play a role for meal initiation and induction of satiety by increased levels during fasting and rapidly decreased levels following a meal [29, 38, 39]. In rodents, exogenous administration of ghrelin leads an increase in food intake [40], while humans receiving ghrelin reported an increased perception of hunger and consumed more calories at a subsequent meal [28]. Ghrelin, mainly produced in the fundus of the stomach [26, 27] is reported to be significantly increased in diet-induced weight-loss [41].

A correlation between plasma ghrelin levels and eating behavior evaluated by the TFEQ has not been analysed in morbidly obese patients or in bariatric surgery so far. In only one study conducted on the relationship between ghrelin and the energy expenditure in healthy young normal-weight women, St. Pierre [42] found no correlation between ghrelin levels and the three dimensions of eating behavior evaluated by the TFEQ.

In bariatric surgery inconsistent effects of different surgical procedures on plasma ghrelin levels have been reported so far. Following RYGBP, a significant decrease of plasma ghrelin levels could be found comparing pre- and postoperative values [41, 43, 44]. In LAGB significantly increased levels were described [15, 44–46].

In LSG, the greater curvature and the gastric fundus as the main locus of ghrelin production are completely resected, forming a narrow gastric tube that permits oral intake of only small amounts of food. LSG might be seen as a strictly restrictive procedure augmented by the reduction of the ghrelin-producing tissue. Stable decreased plasma ghrelin levels in the early postoperative course of LSG have already been reported [30, 31]. In the present study, we found a significant correlation between the decreased plasma ghrelin levels and the reduction of the sensation of hunger assessed by the self-report Three-Factor Eating Questionnaire.

The mechanisms leading to sustained weight loss following bariatric surgery are not completely understood. But significant and lasting changes of the eating behavior in the postoperative course might contribute to the long-term success of weight loss surgery. This study underscores that LSG, as a restrictive procedure, has these desired effects on postoperative eating behavior. Until now, only short and intermediate follow-up data concerning the weight loss following laparoscopic sleeve gastrectomy have been presented. A longer follow-up has to be initiated to assess long-term weight loss and eating behavior following LSG.

Preoperative eating behavior tested for only one single type of bariatric procedure has not enunciated any significant correlation with the success of weight reduction so far [13, 47, 48]. Thus, a prospective study comparing the three different bariatric procedures as LAGB, RYGBP and laparoscopic sleeve gastrectomy in their impact on postoperative eating behavior is needed. Evaluation of preoperative eating behavior may enhance the outcome of bariatric surgery, by selecting the best procedure for each patient preoperatively.

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