



Somatotropic Axis (GH/IGF-1) and Lipid Metabolism after Bariatric Surgery in Morbidly Obese Non-Diabetic Patients

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Abstract

Background: Growth Hormone (GH) secretion and Insulin-like Growth Factor-1 (IGF-1) production are markedly suppressed in morbidly obese patients. The postoperative variation of somatotrophic axis (GH/IGF-1) and its impact in anthropometric parameters and lipid metabolism of morbidly obese non diabetic patients is the objective of this prospective, clinical study.

Methods: 123 morbidly obese non diabetic patients with a median Body Mass Index (BMI) 47.61 Kg/m² were followed up at 1, 6 and 12 months after Laparoscopic Sleeve Gastrectomy (LSG) or Laparoscopic One Anastomosis Gastric Bypass (LOAGB). Weight loss (expressed as excess weight loss percent, EWL%), waist and hip circumference, serum GH, IGF-1 adjusted with age, total Cholesterol (CHOL), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Triglycerides (TG), Very Low Density Lipoprotein (VLDL), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB) and Lipoprotein (a) [Lp(a)], were analyzed in fasting morning serum samples.

Results: One month after LSG: BMI 41.6 kg/m² (p<0.001) and LOAGB: BMI 43.4 kg/m² (p<0.001). In the LOAGB group, significantly reduced hip circumference and ApoB in relation to an increase in GH levels were reported. Six months after LSG, significantly decreased ApoB levels related to an increase in GH levels were found, while in the LOAGB group, GH variations were positively correlated with EWL% and negatively correlated with CHOL levels. One year after LSG: BMI 30 kg/m², EWL% 70.8% (p<0.001) and LOAGB: BMI 29.9 kg/m², EWL% 72.3% (p<0.001). Only in LOAGB, the increase in GH levels was negatively correlated with Lp (a) levels and positively with ApoA1 levels.

Conclusion: GH levels seem to be improved after bariatric surgery and consequently lipid parameters, in particular Lp (a), which is difficult to be controlled with a pharmacologic intervention. LOAGB and LSG represent two long-term effective bariatric surgeries in which weight loss related to the increase in GH levels ameliorates metabolic profile and reduces cardiovascular risk factors in morbidly obese non diabetic patients.

Keywords: Growth hormone; Insulin-like growth factor-1; Lipid metabolism; Obesity; Bariatric surgery

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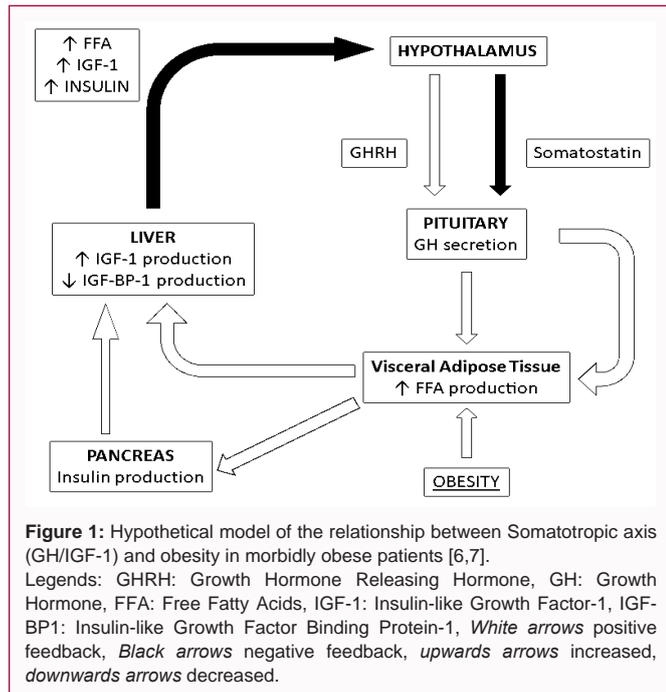
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Introduction

As Hippocrates denotes “obesity never comes alone”, meaning that it is the precursor of other diseases which directly increase the mortality in morbidly obese individuals [1]. It is worldwide accepted that obesity suppresses the frequency and the amplitude of Growth Hormone (GH) secretion followed by the reduction of Insulin-like Growth Factor-1 (IGF-1)’s production [2-4]. Somatotrophic axis (GH/IGF-1) is suppressed in the basal status and after pharmacologic inducement, in levels comparable to those found in individuals with confirmed GH deficiency [3,4]. The main factor of this suppression is considered the negative feedback that visceral adiposity and high Free Fatty Acids (FFA) levels exert to pituitary gland (Figure 1) [5,6]. It has been supported that the suppression of somatotrophic axis could further burden and maintain obesity status, due to the absence of GH lipolytic actions (Figure 1) [6,7].

Obesity and dyslipidemia are inextricably bound and dyslipidemia is one of the major causes of cardiovascular atherosclerotic disease [8,9]. Nowadays, high LDL and TG levels in relation to



low HDL levels are considered the main cardiovascular risk factors [9]. Several clinical studies have established that low concentrations of precursors lipoproteins such as ApoB, VLDL and Lp(a), are better indicators of reduced cardiovascular risk compared to LDL and TG [10,11]. ApoA1 represents the major precursor of HDL lipoprotein for the transport of cholesterol from the tissues to the liver and its final elimination from the body [10]. ApoB includes all the atherogenic particles such as VLDL, LDL and Lp(a) which transports cholesterol from the liver to cells and it is considered as a more sensible marker of coronary artery disease [10-12].

Somatotropic axis suppression seems to reverse after weight loss [13,14]. Bariatric surgery is considered the most effective mean in order to obtain a permanent weight loss, particularly when conservative means have failed [14,15].

The impact of somatotrophic (GH/IGF-1) axis variation on lipid metabolism and anthropometric parameters after two long-term effective bariatric procedures such as LSG and LOAGB is the objective of this prospective clinical study.

Materials and Methods

This is a prospective, single center, clinical study including 123 morbidly obese, non diabetic patients enrolled for evaluation before bariatric surgery. Eighty two patients underwent LSG and 41 patients LOAGB in the Laparoscopic Surgery Department of our hospital. All patients were followed up at 1, 6 and 12 months after the bariatric surgery. Informed consent was obtained from all individual participants included in the study. The inclusion criteria were: age (between 18 and 55 years) in order to limit its influence on the somatotrophic axis. The serum levels of fasting blood glucose should be <100 mg/dl. In cases of blood glucose >100 mg/dl, Oral Glucose Tolerance Test (OGTT) was performed and patients with abnormal levels were excluded from the study, in order to limit the influence of the fluctuations of blood glucose and insulin on IGF-1 levels. Patients were instructed to discontinue any drug such as statins or/and fibrates two months before surgery and until the end of the study.

The exclusion criteria used in this study were the following: history of pituitary disease, use of anticonvulsive or antipsychotic drugs, chronic renal or/and hepatic disease, chronic illnesses such as cancer, chronic inflammatory diseases, hormonal replacement therapy or use of contraceptives, history of anorexia nervosa or bulimia. We used inclusion criteria for bariatric surgery as they were proposed by the 2013 Update: Cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery [16].

In every patient, anthropometric data (body weight with light clothing, shoeless standing height, waist and hip circumference, body mass index) were recorded at 1, 6 and 12 months postoperatively and assessment of fasting (>8 hours and <14 hours) non-smoking biochemical examinations were collected. BMI (kg/m²) was calculated as weight (in kilograms) to height (in meters). Waist circumference (in centimeters) was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Hip circumference (in centimeters) was measured around the widest portion of the buttocks. All measurements were taken at the end of a normal respiration.

In every visit after the bariatric surgical procedure, the % EWL of every patient was calculated as ((preoperative body weight-current body weight)/[preoperative body weight-ideal body weight]), where the ideal body weight was estimated based on the Devine formula.

All patients weighing less than 130 kg (as the instructions of the device imposed) underwent Dual energy X-ray Absorptiometry (DEXA), in order to evaluate the variations of Body Fat (fat mass) prior to and 12 months after bariatric surgery.

Serums TG, CHOL, HDL, LDL, VLDL were measured by enzymatic colorimetric assay on Roche/Hitachi cobas c systems (Roche Diagnostics GmbH, Mannheim, Germany). ApoA1, and ApoB were measured by immunoturbidimetric assay on Roche/Hitachi cobas c systems (Roche Diagnostics GmbH, Mannheim, Germany). Lp(a) was measured by particle enhanced immunoturbidimetric assay on Roche/Hitachi cobas c systems (Roche Diagnostics GmbH, Mannheim, Germany).

GH was measured by sandwich-based immune-chemiluminescent assay on Elecsys 2010 and cobas e systems (Roche Diagnostics GmbH, Mannheim, Germany). IGF-1 was measured by enzyme-labeled chemiluminescent immunometric assay on IMMULITE 2000 IGF-1 systems (Siemens Medical Solutions Diagnostics).

Operative techniques

LSG and LOAGB were performed in a single institution by the same experienced minimally invasive surgical team. This study was approved by the Ethical Committee of the local institution.

LSG was performed with the patient placed in the supine position, with the legs apart, in a slight reverse Trendelenburg position. The pneumoperitoneum was established with the open technique, and four trocars were placed. The greater omentum was freed from the greater curvature of the stomach from a point 3 cm to 4 cm above the pylorus through the angle of His. This maneuver was accomplished with the aid of a laparoscopic shear using ultrasonic vibration. A bougie was placed to guide the gastric section (34 French). The vertical sectioning of the stomach was performed with two firings of the laparoscopic linear stapler with green cartridge loads and subsequently firings with blue cartridges. All the firings were performed in close proximity with

Table 1: Anthropometric and biochemical parameters preoperatively and 1 month after LSG (75 patients)/ LOAGB (35 patients), 6 months after LSG (67 patients)/ LOAGB (28 patients), 12 months after LSG (67 patients)/LOAGB (26 patients).

	Preoperatively LSG Median (min-max) (82 patients)	Preoperatively LOAGB Median (min-max) (41 patients)	LSG 1 month Median (min-max) (75 patients)	LOAGB 1 month Median (min-max) (35 patients)	LSG 6 months Median (min-max) (67 patients)	LOAGB 6 months Median (min-max) (28 patients)	LSG 12 months Median (min-max) (67 patients)	LOAGB 12 months Median (min-max) (26 patients)
BMI (kg/m ²)	45.36 (37.3-67)	47 (38-72.9)	41.6 (29-63)*	43.4 (32-67)*	33.1 (18.7-55.7)*	34.3 (27.6-61)*	30 (19.3-52.7)*	29.9 (20-60)*
WAIST (cm)	135 (100-180)	134 (105-178)	124 (90-180)*	130 (98-165)*	107.5 (80-165)*	110 (65-154)*	99 (59-149)*	100 (64-150)*
HIP (cm)	139 (116-170)	143.5 (120-180)	134 (110-170)*	134 (106-168)*	118 (96-166)*	117 (102-163)*	107 (59-143)*	108 (96-160)*
CHOL (mg/dl)	185 (115-296)	186 (123-288)	154 (109-233)*	157.5 (95-229)*	175 (113-238)**	171 (111-226)**	171 (113-254)*	170 (112-220)*
HDL (mg/dl)	45 (23-103)	44.6 (17-78)	38 (22-64)*	35 (17-53)	45 (27-79)	46.5 (20-69)	56 (35-94)*	50 (20-69)**
LDL (mg/dl)	114 (50-211)	117 (57-210)	94.7 (53-163)*	98 (40-171)*	109 (60-164)	107 (38-162)**	102 (51-173)*	102 (25-148)*
TG (mg/dl)	116 (43-312)	105 (44-494)	102.5 (40-375)**	111 (75-200)	82.5 (40-201)*	93.5 (40-158)**	68 (39-144)*	71 (54-161)*
VLDL (mg/dl)	23.2 (8.6-62)	21 (9.4-99)	20.5 (8-75)**	22 (15.4-40)	16 (8-40)*	18.8 (8-32)**	13.7 (7.8-29)*	13.5 (11-34)*
ApoB (mg/dl)	96 (54-158)	103 (40-174)	89 (51-139)*	89 (42-150)**	86 (58-154)*	95 (34-140)	83.5 (53-152)*	89.5 (26-134)**
ApoA1 (mg/dl)	140 (80-202)	144 (93-270)	115 (82-182)*	111 (89-174)*	131 (82-183)*	133 (77-170)*	141 (89-198)	150.5 (82-170)
Lp(a) (mg/dl)	10.3 (0.4-213.5)	10.7 (3.1-129.9)	9.05 (0.6-133)*	8.1 (1-111)	9.7 (2.3-115.5)**	7 (1.2-154)	9.1 (1.5-105)**	6.7 (1.2-109)*
GH (ng/ml)	0.1 (0.01-3.98)	0.1 (0.01-2)	0.2 (0.03-2.9)**	0.35 (0.08-4)*	0.51 (0.09-8)*	0.9 (0.1-6.7)*	0.84 (0.1-9.3)*	0.7 (0.02-8)*
IGF-1 (ng/ml)	149 (45-368)	130 (38-313)	111 (27-261)*	95 (28-231)*	128 (40-640)*	108 (46-362)*	142 (63.5-391)*	138 (52-247)*
EWL%			19 (3.3-61)*	16.7 (1.8-27)*	52.7 (21-88)*	53.3 (22.8-87.8)*	70.8 (33-100)*	72.3 (24-93)*
BODY FAT%	48.9 (36.7-56.1)	48.7 (37.9-55.9)					37 (24-50)*	37.8 (17-50.5)*

p* ≤ 0.001, p** ≤ 0.05 after Wilcoxon Signed Rank test between preoperative and postoperative parameters

GH: Growth Hormone; IGF-1: Insulin-like Growth Factor-1; BMI: Body Mass Index; LSG: Laparoscopic Sleeve Gastrectomy; LOAGB: Laparoscopic One Anastomosis Gastric Bypass; EWL%: Excess Weight Loss percent; TC: Total Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; TG: Triglycerides; VLDL: Very Low Density Lipoprotein; ApoA1: Apolipoprotein A1; ApoB: Apolipoprotein B; Lp(a): Lipoprotein(a)

Table 2: Spearman's correlation coefficient between GH/IGF-1 and anthropometric/biochemical parameters preoperatively.

	BMI	Waist	Hip	CHOL	HDL	LDL	TG	VLDL	ApoA1	ApoB	Lp(a)	BODY FAT%
GH (123 patients)	-0.11	-0.12	-0.11	0.01	0.25*	-0.03	-0.18**	-0.18**	0.23*	-0.04	-0.1	0.18
GH(LSG)	-0.11	-0.07	-0.008	0.04	0.36*	-0.05	-0.22**	-0.24*	0.35*	-0.03	-0.12	0.12
GH(LOAGB)	-0.19	-0.27	-0.24	-0.03	0.02	0.04	-0.08	-0.05	-0.09	-0.03	-0.01	0.58*
IGF-1 (123 patients)	-0.34*	-0.23*	-0.25*	-0.08	-0.1	-0.03	-0.11	0.23	-0.18**	-0.12	-0.14	-0.24**
IGF-1(LSG)	-0.44*	-0.32*	-0.21	-0.1	-0.12	-0.08	-0.02	-0.04	-0.12	-0.15	0.19	-0.21
IGF-1 (LOAGB)	-0.14	0.002	-0.2	-0.02	-0.09	0.03	-0.33	-0.35*	-0.23	-0.09	0.02	-0.4

p* < 0.05, p** < 0.1 after Spearman's rank correlation coefficients

GH: Growth Hormone; IGF-1: Insulin-like Growth Factor-1; BMI: Body Mass Index; LSG: Laparoscopic Sleeve Gastrectomy; LOAGB: Laparoscopic One Anastomosis Gastric Bypass; EWL%: Excess Weight Loss percent; TC: Total Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; TG: Triglycerides; VLDL: Very Low Density Lipoprotein; ApoA1: Apolipoprotein A1; ApoB: Apolipoprotein B; Lp(a): Lipoprotein(a)

the bougie. After the operation, nasogastric tubes were placed, and methylene blue was instilled to ascertain the integrity of the stomach.

LOAGB The gastrectomy begins at the angular incisure of the stomach and continues towards the Gastroesophageal Junction (GEJ). A 34 Fr bougie is used for volumetric reasons. Special attention is paid during fundus incision so that the gastric pouch remains small enough for maximum weight control, but also to keep a safe distance from the GEJ (about 1 cm). For that reason the fat pad around GEJ is being mobilized and dissected until left crus is visible. If small hiatal hernia is recognized intraoperatively, retraction of the stomach in the abdominal cavity is performed without any other prophylactic measures (e.g. crural closure). We perform a hand-sewn end-to-side gastro-ileum anastomosis with a diameter of approximately 1.5 cm. The biliopancreatic limb measures 200 cm to 300 cm from Treitz ligament depending on patients' preoperative BMI-200 cm

for BMI=35-50 kg/m², 250 cm for BMI=50-60 kg/m² and 300 cm for BMI>60 kg/m². The afferent part of the biliopancreatic limb is being suspended on the side of the stomach. This enables the bile and the pancreatic juices to flow towards the efferent limb. An intraoperative methylene blue test for identification of possible anastomotic leak is performed to all patients. Nasogastric tube and drains are not routinely used.

Statistical analysis

Quantitative variables are presented as median (min, max), while qualitative variables are presented as absolute and relative (%) frequencies. Spearman's correlation coefficient was used to investigate linear relationship between quantitative variables. To detect differences in the median values of a quantitative variable at different time points, we used Wilcoxon' signed-rank test. A p-value <0.05 was considered statistically significant.

Table 3: Spearman's correlation coefficient between the variations of GH/IGF-1 and the variations of anthropometric/ biochemical parameters 1, 6 and 12 months after LSG (1) and LOAGB (2).

	δGH(1)	δIGF1(1)	δGH(6)	δIGF1(6)	δGH(12)	IGF1(12)
δBMI(1)	0.05	-0.10	0.03	-0.05	0.11	-0.05
δBMI(2)	0.10	0.02	-0.01	0.13	0.20	-0.09
δWaist(1)	-0.04	-0.06	0.04	0.02	0.07	-0.08
δWaist(2)	-0.02	-0.19	-0.20	-0.32	0.18	-0.11
δHip(1)	-0.02	-0.02	0.18	0.04	-0.02	-0.01
δHip(2)	-0.42*	-0.19	-0.27	-0.12	0.11	-0.18
δCHOL(1)	0.11	-0.01	0.10	-0.04	-0.004	0.02
δCHOL(2)	-0.05	-0.20	-0.43*	-0.13	0.23	-0.18
δHDL(1)	0.35	-0.19	0.13	0.06	-0.03	0.06
δHDL(2)	-0.02	0.01	-0.16	0.002	0.34	-0.06
δLDL(1)	0.11	0.09	0.11	-0.01	0.06	-0.01
δLDL(2)	0.05	-0.10	-0.28	-0.11	0.06	0.11
δTG(1)	-0.08	0.03	-0.04	-0.11	-0.06	0.12
δTG(2)	-0.13	-0.12	-0.14	0.03	-0.17	-0.03
δVLDL(1)	-0.08	-0.003	0.02	-0.20	-0.04	0.08
δVLDL(2)	-0.06	-0.02	-0.20	0.09	-0.11	-0.18
δApoA1(1)	0.22	0.07	0.06	0.12	0.01	0.01
δApoA1(2)	-0.03	-0.34	-0.23	0.02	0.37**	-0.57
δApoB(1)	0.06	-0.16	0.21**	-0.05	0.10	-0.08
δApoB(2)	-0.36**	-0.18	-0.28	-0.04	-0.10	-0.13
δLp(a)(1)	-0.11	0.14	-0.06	0.09	-0.10	0.15
δLp(a)(2)	-0.10	0.09	-0.12	0.35	-0.53*	0.46*
δEWL%(1)	-0.05	-0.22	-0.18	-0.05	-0.05	-0.14
δEWL%(2)	0.02	-0.01	0.51*	-0.04	0.09	0.25

p<0.05 , p**<0.1 after Spearman's rank correlation coefficients
 GH: Growth Hormone; IGF-1: Insulin-like Growth Factor-1; BMI: Body Mass Index; LSG: Laparoscopic Sleeve Gastrectomy; LOAGB: Laparoscopic One Anastomosis Gastric Bypass; EWL%: Excess Weight Loss percent; TC: Total Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; TG: Triglycerides; VLDL: Very Low Density Lipoprotein; ApoA1: Apolipoprotein A1; ApoB: Apolipoprotein B; Lp(a): Lipoprotein(a)

All statistical analyses were performed in IBM SPSS v.25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Results

123 morbidly obese non diabetic patients were enrolled in the study. 82 patients underwent LSG and 41 performed LOAGB.

The median BMI preoperatively was 45.36 kg/m² for LSG group and 47 kg/m² for LOAGB with a median GH levels 0.1 ng/ml (Table 1). Preoperative GH levels were positively correlated with HDL and ApoA1 levels and negatively correlated with TG and VLDL in the LSG group (Table 2). Respectively, IGF-1 levels were negatively correlated with anthropometric features and Body Fat% (Table 2).

One month after LSG, 75 patients recruited had a median BMI 41.6 kg/m² (p<0.001) and 35 patients that underwent LOAGB 43.4 kg/m² (p<0.001) respectively (Table 1). Independently of the surgery performed, there is a remarkable increase in GH levels followed by a significant decrease in anthropometric (BMI, Waist and Hip circumference) and lipidemic variables (Table 1). In the LOAGB

Table 4: Spearman's correlation coefficient between the preoperative levels of anthropometric/ biochemical parameters and changes in EWL% (pre-and 1 year postoperatively).

	GH	IGF-1	TG	VLDL	ApoB
δEWL%LSG	0.04	0.43*	0.28*	0.29*	0.08
δEWL%LOAGB	-0.28	0.39**	-0.05	-0.04	0.17

p<0.05 , p**<0.1 after Spearman's rank correlation coefficients
 GH: Growth Hormone; IGF-1: Insulin-like Growth Factor-1; LSG: Laparoscopic Sleeve Gastrectomy; LOAGB: Laparoscopic One Anastomosis Gastric Bypass; EWL%: Excess Weight Loss percent; TG: Triglycerides; VLDL: Very Low Density Lipoprotein; ApoB: Apolipoprotein B

group, the increase in GH levels was correlated with a significant decrease in hip circumference and ApoB levels (Table 3).

Six months after LSG, 67 patients recruited had a median BMI 33.1 kg/m² (p<0.001) with an EWL% 52.7% (p<0.001) and 28 patients that underwent LOAGB 34.3 kg/m² (p<0.001) with an EWL% 53.3 (p<0.001) respectively (Table 1). Six months after bariatric surgery, the increase in GH/IGF-1 levels continued, followed by a decrease in anthropometric and metabolic parameters except from HDL and ApoA1 which had begun to increase (Table 1). Additionally, in patients that underwent LSG, the increase in GH levels was correlated with a significant decrease in ApoB levels and in those that underwent LOAGB, GH variations were positively correlated with EWL% and negatively correlated with CHOL levels (Table 3).

One year after bariatric surgery, in 93 patients recruited, the median BMI was 30 kg/m² (p<0.001) with an EWL% 70.8 (p<0.001) after LSG and 29.9 kg/m² (p<0.001) with an EWL% 72.3 (p<0.001) after LOAGB respectively (Table 1). There was a remarkable increase in GH/IGF-1 concentrations (p<0.001), independently of the surgery performed. Additionally, all anthropometric and lipidemic parameters were decreased significantly, except from HDL and ApoA1 which were increased compared to preoperative levels (Table 1). Even if EWL% was similar between the two bariatric surgeries, only after LOAGB the increase in GH was correlated negatively with Lp(a) levels and positively with ApoA1 levels (Table 3).

Greater EWL% was noticed between patients with higher IGF-1, TG and VLDL levels preoperatively in the LSG group (Table 4). In the LOAGB group, lipid parameters preoperatively do not seem to predict the variation of EWL% postoperatively as IGF-1 levels does (Table 4).

Discussion

The suppression of somatotrophic axis in obesity is known for more than 25 years [17]. In obese individuals there is a 25% daily reduction of GH production because of the reduction in secretory daily bursts and its concomitant increased clearance [4,5,17].

The prevalent theory in order to explain the low GH levels in obesity includes perturbation of GHRH, Somatostatin and insulin pathways (Figure 1) [2,5]. The hyperinsulinemia and the high circulating Free Fatty Acids (FFA) produced mainly by the visceral adipose tissue, reduce IGF-Binding Protein-1 (IGF-BP-1) production by the liver and consequently are responsible for the decreased GH secretion from the pituitary, contributing to an increase of Somatostatin from the hypothalamus at the same time (Figure 1) [2,13]. Consequently, low GH secretion reflects low production of IGF-1 from the liver [6]. Thus, FFA, insulin and GH/IGF-1 axis are controlled by a negative feedback loop which depends on body composition and in particular visceral adiposity (Figure 1) [2,5,13].

Galli et al. [18], have reported that after a restrictive bariatric technique, the extent of IGF-1 deficiency is proportional to the increased preoperative BMI and the raise in IGF-1 levels postoperatively is proportional to the extent of weight reduction [18]. Savastano et al. [19], have concluded that the efficacy of a restrictive bariatric surgery in the reduction of fat mass depends on the integrity of somatotrophic axis preoperatively [19]. This is in concordance with our study in which patients with higher IGF-1 and increased adiposity, mirrored by higher TG and VLDL levels preoperatively, had a greater EWL% after LSG (Table 4).

Another important finding of this study is that higher IGF-1 levels preoperatively predict a higher EWL% especially after a malabsorptive surgery like LOAGB, but are significantly correlated with EWL% after LSG too (Table 4). Mittempergher et al. [13], have obtained the same results after proving that GH/IGF-1, IGF-BP-1 and IGF-Binding Protein-3 (IGF-BP-3) levels increased one year after malabsorptive bariatric procedures [13].

Our results could be considered particularly encouraging for patients with increased cardiovascular risk factors. In this study, morbidly obese non diabetic patients obtained a statistically significant reduction in Lp(a) levels, a lipoprotein considered as an important cardiovascular risk factor, for which, there is no other therapeutic treatment till now [20].

In this study, there is also a remarkable reduction in LDL and in ApoB levels; one year postoperatively (Table 2). The latter molecule seems to represent the most atherogenic lipoprotein because it is the precursor of all the others [10]. Additionally, these precursor particles are considered the strongest predictors of myocardial infarction [21,22]. A remarkable reduction in other atherogenic parameters such as TG and VLDL has also been proven in the present study (Table 1). Particularly in patients who underwent LOAGB, from the first month postoperatively, there is a negative correlation between GH and ApoB levels (Table 3). GH represents a potent lipolytic hormone and seems that the reduction of potent lipoproteins such as ApoB depends on the respective GH levels (Table 3). It is interesting that this correlation is noticed only after LOAGB surgery even if there is a smaller number of patients who underwent this procedure. This issue may be explained by the fact that LOAGB is a mixed-type bariatric procedure in which not only the synthesis but also the absorption of cholesterol is reduced [23].

Cardioprotective molecules such as HDL were increased one year postoperatively and its precursor ApoA1 was correlated with GH levels (Table 3). Doğan S et al. [24], noted a decrease in HDL levels during the early postoperative period up until 3 months after LSG, followed by an increase 3 to 6 months postoperatively (24), as it is also proved in our study (Table 2). This issue may be explained by the increased peripheral insulin sensitivity observed a few months after a restrictive surgical procedure such as LSG [25].

One limitation of our study could be considered the absence of GH's provocative tests. This decision was determined by the reduced validity and reproducibility of these provocative tests on obese individuals [26]. In respect of the current guidelines, only individuals with evidence of hypothalamic/pituitary disease should be tested for GH deficiency [26]. Consequently, we decided to measure GH levels in fasting morning samples in 123 morbidly obese non diabetic patients. Another limitation of this study could be considered the smaller number of patients who underwent LOAGB (41 patients)

compared to those who underwent LSG (82 patients). Besides the smaller number of patients in the LOAGB group, their results are remarkably interesting.

Conclusion

LOAGB seems to earn ground continuously in the treatment of morbid obesity [27,28]. It is a long-term effective bariatric surgical technique with encouraging results in the field of obesity in order to resolve obesity's comorbidities as confirmed by our study [28-30].

As far as we know, until now, there is no other clinical study that compares anthropometric and metabolic parameters with somatotrophic (GH/IGF-1) axis variations between these two newly evolved bariatric surgeries (LSG/LOAGB) for the treatment of obesity. They seem to reduce precursor atherogenic molecules such as ApoB and therefore decrease TG, LDL and Lp(a) and increase the concentrations of cardioprotective factors such as ApoA1. To this day, no other therapeutic approaches have been able to efficiently control Lp(a) levels [20]. In conclusion, LSG and LOAGB could be proposed as another effective treatment in these patients as the beneficial actions of weight loss in relation to the increase in GH levels ameliorates their metabolic profile and reduces cardiovascular risk factors.

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