

Impact of post-laparoscopic sleeve gastrectomy weight loss on C-reactive protein, lipid profile and CA-125 in morbidly obese women

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Videosurgery Miniinv 2015; 10 (4): 521–526

DOI: 10.5114/wiitm.2015.56480

Abstract

Introduction: Obesity increases production of adipose tissue-derived proteins, such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6). Also there are elevated levels of C-reactive protein (CRP) and IL-6, CD8, and CD4, indicating chronic subclinical inflammation. Since obesity represents a serious risk factor in several metabolic diseases, identifying the status of carbohydrate antigen-125 (CA-125) would further link obesity and tumors.

Aim: To examine the effect of weight loss by laparoscopic sleeve gastrectomy (LSG) on plasma CRP, lipid profiles and CA-125 level in morbidly obese patients.

Material and methods: This prospective study was conducted in the Surgery Department, Fayoum University Hospital, between August 2013 and September 2015. To assess the effect of excess weight loss following this operation CRP, lipid profile and CA-125 were measured before and 12 months after the LSG operation for weight loss. The study included 30 cases of morbidly obese patients: 30 (100%) females aged 23–55 years who were considered clinically obese with a mean body mass index of 42.71 ± 4.3 (38–46) kg/m² and mean age of 40.3 ± 8.5 (23–55) years. The National Institute of Health (NIH) inclusion criteria for bariatric surgery were used.

Results: A mean weight loss of 29.30% decreased plasma CRP, triglycerides, total cholesterol and low-density lipoprotein cholesterol (LDL cholesterol), CA-125 level and increased high-density lipoprotein cholesterol (HDL cholesterol). The percentage weight loss was significantly associated with changes in plasma CRP, triglycerides, total cholesterol, total HDL cholesterol and CA-125.

Conclusions: Weight loss by LSG improves inflammation, dyslipidemia and CA-125 level.

Key words: morbid obesity, laparoscopic sleeve gastrectomy, lipid profile, C-reactive protein, carbohydrate antigen-125.

Introduction

Obesity is associated with an increased risk of dyslipidemia, coronary heart disease, hypertension, stroke, type 2 diabetes mellitus, and all-cause mortality [1, 2].

Obesity increases production of adipose tissue-derived proteins, such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) [3, 4].

Also there are elevated levels of C-reactive protein (CRP), IL-6, CD8, and CD4, indicating chronic subclinical inflammation, and incident cardiovascular disease, including myocardial infarction, stroke, and peripheral vascular disease [5–10].

There is debate about the effect of weight loss mortality and morbidity from cardiovascular disease in particular [11].

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The acute phase reactant CRP is a sensitive marker of inflammation, and several studies have demonstrated that elevated CRP levels are independently associated with an increased risk for cardiovascular disease morbidity and mortality as well as acute coronary events [12–16].

Since obesity represents a serious risk factor in several metabolic diseases, identifying the status of carbohydrate antigen-125 (CA-125) would further link obesity and tumors.

Aim

The aim of our study was to detect the effect of weight loss after the laparoscopic sleeve gastrectomy (LSG) operation on plasma CRP, lipid profile and CA-125 in morbidly obese female patients.

Material and methods

This prospective study was conducted in the Surgery Department, Fayoum University Hospital, between August 2013 and September 2015. To assess the effect of this operation on excess weight loss, CRP, lipid profile and CA-125 were measured before and 12 months after the LSG operation for weight loss. The study included 30 cases of morbidly obese patients: 30 (100%) women aged 23–55 years who were considered clinically obese with a mean body mass index (BMI) of 42.71 ± 4.3 (38–46) kg/m^2 , mean age 40.3 ± 8.5 (23–55) years. The National Institute of Health (NIH) inclusion criteria for bariatric surgery were used: patients with BMI $> 40 \text{ kg}/\text{m}^2$ or over $35 \text{ kg}/\text{m}^2$ with at least one comorbidity and this via LSG technique, and all of them had failed in trials of conservative management including dietary control and they are bulky eaters but not sweet eaters, also ASA (American Society of Anesthesiology patient classification) I and II. Laboratory investigations took the form of complete blood count (CBC), fasting blood sugar (FBS), renal functions, liver functions, coagulation profile, beside hormonal assay, to detect any endocrinal causes of obesity such as hypothyroidism.

We took plasma sample from all patients (prior to surgery and 12 months after surgery), by centrifugation of blood samples by 3000 rpm for 20 min. Plasma triglyceride levels, and total LDL and HDL cholesterol concentrations were measured enzymatically by colorimetric (enzymatic) end-point analysis. Plasma CRP levels were measured by means of a col-

orimetric competitive ELISA. Regarding CA-125, we used a two-step immunoassay for the quantitative determination of CA-125.

Pulmonary evaluation including chest X-ray and pulmonary function tests were carried out to detect if there were any tumors such as lung cancer. Cardiac assessment, ECG and echocardiography were done if needed. In addition, all patients underwent abdominopelvic ultrasound and computed tomography (CT) scan to detect any abdominopelvic diseases such as endometriosis or tumors such as pancreatic, liver tumors and to evaluate the presence or absence of cancer ovary, colon, and mammography for breast cancer.

Patients were then operated on after undergoing a 2-week low caloric (800–1000 kcal/day) preoperative diet. Informed consent was obtained from all patients. We included patients who were psychologically stable with no endocrinal causes of obesity and accepting surgery. We excluded patients who were pregnant or breast feeding females, psychologically unstable patients and any patient suffering from significant longstanding heart/lung disease or other severe systemic disease.

Surgical procedure

A nasogastric tube was inserted at the beginning to decompress the stomach. A window was dissected at the junction of the greater curvature and the greater omentum, around 10 cm from the pylorus. Division of the gastroepiploic, short gastric and posterior fundic vessels was done starting at 4 cm proximal to the pyloric ring all the way until the angle of His using the ultracision Harmonic scalpel (Harmonic; Ethicon Endosurgery, Cincinnati, OH, USA) (Photo 1).

Once the dissection part was over, a bougie was introduced orally by the anesthesiologist through the esophagus and inside the stomach; the bougie sizes used ranged from 32–46 Fr. The surgeon then guided it along the lesser curvature and into the pyloric channel and duodenal bulb.

Gastric transection began 4 to 6 cm proximal to the pylorus. A 60-mm, green or gold cartilage was placed across the antrum through the right midepigastric port and was fired. The second stapler was placed approximately 1 to 2 cm from the border of the lesser curvature in the direction of the gastroesophageal junction (Photo 2).

Sequential firings of the stapler along the border of the bougie on the lesser curvature completed the

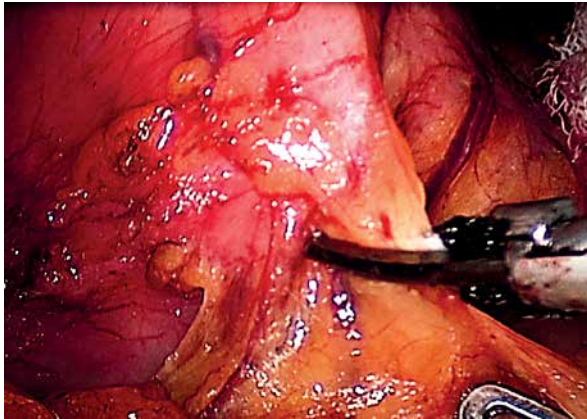


Photo 1. Devascularization of the stomach

gastric transection at the left crus. After completing the transection, the entire staple line was inspected carefully to make sure that the staples were well formed especially at the antrum where the stomach is thickest. A layer of Vicryl 3/0 can be applied (continuous or interrupted simple) at the junction staples line.

Statistical analysis

Differences between means and the effects of treatments were determined by one-way ANOVA using Tukey's test.

Results

The mean operative time was 60.8 ± 12.3 (60–100) min; there were no conversions. Postoperative complications were restricted to 2% in the form of nausea and vomiting and were treated conservatively, but there were no intraoperative complications.

Mean hospital stay was 2.2 ± 1.5 (range: 1–3) days, loss of weight was $29.30 \pm 2.2\%$, preoperative BMI was 42.71 ± 4.3 (range: 37–45) kg/m^2 while postoperatively it was 30.60 ± 1.2 (range: 24–33) kg/m^2 . The mean level of triglycerides was 204 ± 110 mg/dl preoperatively and 120 ± 45 mg/dl after the operation, $p = 0.0001$. So, there was a postoperative decrease in the level of triglycerides. Regarding total cholesterol, the mean level was 228 ± 50 and 170 ± 40 mg/dl pre- and postsurgically, respectively, $p < 0.001$. This in turn indicates that there was a postoperative decrease in the level of total cholesterol (Table I). The mean HDL cholesterol level was 48 ± 12 mg/dl preoperatively and increased to 58 ± 12 mg/dl postoperatively, $p < 0.5$. The mean LDL cholesterol level was 158 ± 34 mg/dl preoperatively and decreased

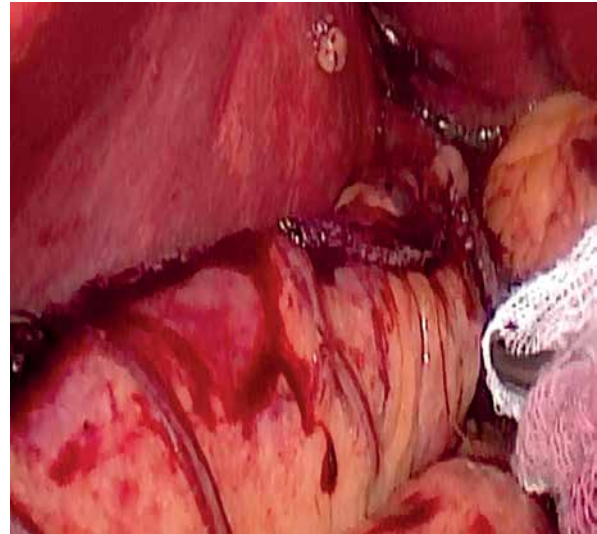


Photo 2. Gastrectomy by stapler 6 cm proximal to the pylorus LSG

to 91 ± 15 mg/dl postoperatively. Regarding CRP the mean level was 5.3 ± 1 U/ml preoperatively and decreased to 2.1 ± 2 U/ml postoperatively, $p < 0.05$. Regarding CA-125, the mean level was 10.80 ± 2 U/ml preoperatively and decreased to 6.6 ± 1 postoperatively, $p < 0.5$. All patients were free from ovarian cancer but 3 had a previous history of hysterectomy due to benign causes (large fibroid) and were over 50 years old (Table I).

Discussion

In our study, we investigated the effects of weight loss after LSG on plasma CRP levels in morbidly obese patients. Several studies have shown that obesity has been positively associated with plasma CRP, and adipose tissue has been proposed as a factor directly modulating CRP levels [17, 18]. In our study we found that losses of fat mass in obese women were associated with reductions in plasma CRP levels. Plasma CRP level is a sensitive marker of systemic inflammation [19] and it is related to cardiovascular disease through several pathways. C-reactive protein levels reflect inflammation of coronary vessels related to the formation and severity of the atherogenic plaque or inflammation related to myocardial ischemia or necrosis [20].

Also, it has been suggested that plasma CRP levels reflect the amount and activity of pro-inflammatory cytokines such as IL-1, tumor necrosis factor- α , and IL-6, which are implicated in the process of ath-

Table I. Patients characteristic

Parameter	Results		Value of <i>p</i>
Age [years]	40.3 ±8.5		
Gender: Female	30 (100%)		
BMI [kg/m ²]	(Preoperative) 42.71 ±4.3	(Postoperative) 30.60 ±1.2	
Weight loss [%]	29.30 ±2.2		
Operative time [min]	60.8 ±12.3		
Hospital stay [days]	2.2 ±1.5		
Triglycerides [mg/dl]	204 ±110	120 ±45	0.0001
Cholesterol [mg/dl]	228 ±50	170 ±40	< 0.001
HDL cholesterol [mg/dl]	48 ±12	58 ±12	< 0.5
LDL cholesterol [mg/dl]	158 ±34	91 ±15	NS
CRP [U/ml]	5.3 ±1	2.1 ±2	< 0.05
CA 125 [U/ml]	10.80 ±2	6.6 ±1	< 0.5

Data are expressed as mean values ± SD (standard deviation).

erosclerotic plaque formation and acute coronary syndromes [17, 18, 20, 21].

Interleukin-6 is secreted in several sites including activated macrophages and lymphocytes but also in adipose tissue. The contribution of adipose tissue to IL-6 secretion has been proposed to be the link between plasma CRP and adiposity, as CRP synthesis in the liver is largely under the control of IL-6 [21]. Thus, it is possible that this mechanism explains the higher CRP levels in obese patients and the reductions observed with weight loss in our study.

The beneficial effect of bariatric surgery on fasting plasma lipids is well recognized [22–25].

Benetti *et al.* reported a significant reduction in cholesterol levels after malabsorptive procedures (biliopancreatic diversion and biliointestinal bypass) but not after purely restrictive procedures (adjustable gastric banding), whereas triglycerides decreased similarly with the two types of surgery [26]. In our study, we found a significant postoperative decrease in the level of triglycerides ($p = 0.0001$). Regarding total cholesterol, there was a significant postoperative decrease postsurgically, $p < 0.001$. The mean HDL cholesterol showed a significant increase postoperatively ($p < 0.5$), and there was a decrease in LDL cholesterol postoperatively 1 year after surgery.

A raised total cholesterol level is often included as a comorbidity in morbid obesity. Recently, the Bariatric Analysis and Reporting Outcome System (BAROS)

has been proposed as a uniform way of assessing progress after bariatric surgery [27]. It lists high cholesterol as a major health comorbidity. The American Obesity Association defines a comorbidity as any condition associated with obesity that (a) usually worsens as the degree of obesity increases and (b) often improves as the condition is treated [27, 28].

Several previous articles reported that individuals with a BMI of 30 kg/m² or higher have a 23% higher risk of cancer than non-obese individuals [29]. Perfield *et al.* [30] reported abnormal expression of tumor progression locus 2 associated with metabolic complications in obesity. Several other studies have associated chronic inflammation and high free radical load in obesity to DNA damage and genomic instability, which may facilitate subsequent progression of cancer cells [31]. Erbağci *et al.* [32] reported that excess adipose tissue in obesity has a positive effect on the expression of CA-125. Bast *et al.* [33] also stressed that elevated levels of CA-125 are consistently detected in conditions such as endometriosis, epithelial ovarian cancer, as well as pancreatic, breast, colon and lung cancers. Disruption of the normal balance between cell proliferation, differentiation, and apoptosis in our obese subjects could therefore account for the significant expression of CA-125 observed in this study.

In our study, CA-125 level was influenced by age, hysterectomy, obesity, and there was a significant decrease in CA-125 level post weight loss ($p < 0.5$).

Conclusions

Weight loss by LSG improves inflammation, dyslipidemia and CA-125 level.

Conflict of interest

The authors declare no conflict of interest.

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Received: 26.08.2015, **accepted:** 17.11.2015.