The Use of Serum Uric Acid Concentration as an Indicator of Laparoscopic Sleeve Gastrectomy Success

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Laparoscopic sleeve gastrectomy (LSG) effectively reduces weight by restricting gastric capacity and altering gut hormones levels. We designed a prospective study to investigate the correlation of serum uric acid (SUA) concentration and weight loss. SUA and body mass index (BMI) were measured preoperatively and on first postoperative month and year in patients who underwent LSG in our department of bariatric surgery. Data on 55 patients were analyzed. Preoperative SUA concentration had a significant positive correlation with percentage of total weight loss (TWL) on first postoperative month ($P = 0.001$) and year ($P = 0.002$). SUA concentration on first postoperative month had a positive correlation with percentage of TWL on first postoperative year ($P = 0.004$). SUA concentration could be used as a predictor of LSG's success and could help in early detection of patients with rapid loss of weight, in order to prevent complications.

Key words: Bariatric surgery – Metabolic syndrome – Weight loss – Uric acid

Morbid obesity has reached epidemic proportions worldwide. In a recent epidemiological survey, the overall prevalence of obesity in Greece was estimated 22.5% (27.3% men and 25.7% women), while 35.2% of total population was found to be overweight (41.1% men and 29.9% women).¹ Recent studies suggest that morbid obesity represents an

important social and financial problem. Furthermore, morbid obesity is related with decreased overall survival, due to the related comorbidities, such as obstructive sleep apnea, hypoventilation syndrome, pulmonary hypertension, systemic hypertension, cholelithiasis, pancreatitis, fatty liver infiltration, cardiovascular disease, diabetes mellitus

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type 2, dyslipidemia, deep vein thrombosis, and pulmonary embolism and malignancies such as breast, colorectal, pancreatic, renal, and prostate cancer. Therefore, obesity poses a major problem for health care systems and treatment alternatives become very important in health care cost reduction and possibly in improvement of quality of life.

Laparoscopic sleeve gastrectomy (LSG) was used as a first step operation of biliopancreatic diversion in high risk or super obese patients.² Nowadays, LSG has proved its efficiency in weight loss and is used as a single bariatric operation. LSG achieves excess weight loss of 60 to 65% (in 3 years' follow up) and successful management of obesity comorbidities with resolution in about 45 to 95% of them.³ The mechanisms behind LSG weight-reducing actions are not yet fully elucidated. Reduction of the stomach capacity causing restriction in food intake is one of the most important mechanisms involved. Recent studies implicate that gut hormones and especially ghrelin may play a role in weight loss after LSG.⁴

Uric acid is the end product of purines (adenosine/guanosine) metabolism. Xanthine oxidase (XO) is the enzyme, responsible for the uric acid production. It converts hypoxanthine to xanthine and xanthine to uric acid (Fig. 1).⁵ Uric acid is produced mainly in the liver and intestine because of the high XO activity in those tissues. Serum uric acid (SUA) concentration is lower in women and children and increases with age. In postmenopausal women, SUA concentration is similar to this found in males. Normal values of SUA concentration are 3.5 to 7.2 mg/dL for adult men and 2.6 to 6.1 mg/dL for premenopausal women. It is obvious that concentration of SUA does not remain stable and it depends on genetic and environmental factors, the distortion of which can result to hyperuricemia.⁶ Uric acid excretion is conducted by the kidneys (75%) and the gastrointestinal tract (25%). In the kidneys, uric acid is filtered and secreted. However, a large amount of uric acid (90%) is usually reabsorbed and returns to blood.

Hyperuricemia is defined as the increase of SUA concentration over 7.0 mg/dL for men and 6.0 mg/dL for women. The value 7 mg/dL is of critical importance because solutions with greater uric anions concentration are oversaturated, leading to sedimentation of uric monosodium crystals. Hyperuricemia can be divided into primary and secondary. Primary hyperuricemia consists on hereditary metabolic abnormalities (e.g., enzyme deficiencies) that lead to overproduction or under excretion. On

Fig. 1 Correlation between preoperative BMI and preoperative SUA concentration ($P = 0.026$).

the other side, a variety of diseases can cause secondary hyperuricemia. However, many authors prefer to classify hyperuricemia according to the pathophysiological mechanism responsible for it (e.g., increased production, impaired excretion, or both).⁶

Patients and Methods

We designed a prospective study which lasted 1 year (September 2009–September 2010). The aim of our study was to investigate the correlation between SUA concentration and weight loss in obese patients who undergo LSG in our department of bariatric surgery. The study was motivated by an observation that patients with elevated preoperative SUA had higher percentage of total weight loss (TWL).

All patients were informed and asked to participate in our study. Patients who agreed to participate gave their signed consent.

During this time interval, 93 patients underwent LSG in our department. We included in our study patients aged older than 18 years old and with indications for bariatric surgery (body mass index [BMI] ≥ 40 kg/m² or ≥ 35 kg/m² with comorbidities). Exclusion criteria were renal impairment (elevated creatinine); medications (aspirin, diuretics of the loop, allopurinol, corticosteroids); postoperative surgical complications; myeloproliferating syndromes; and alcohol abuse. According to our

inclusion criteria, 55 patients were included in our study.

Preoperatively and on first postoperative month, we measured SUA concentration. We defined as abnormally elevated SUA concentration values over 7 mg/dL for men and 6 mg/dL for women. All participating patients underwent LSG.

For the laparoscopic sleeve gastrectomy the patient is placed in a reverse-Trendelenburg supine position. A 12-mm optical trocar is placed under direct vision approximately 15 cm below the xiphoid and 3 cm to the left of midline. Pneumoperitoneum is achieved by CO₂ insufflation. A 30-degree angled laparoscope is placed through the port into the peritoneal cavity and the remaining trocars—2 left upper quadrant trocars both 5 mm, and 2 right upper quadrant trocars, a 10 mm (lateral) and a 15 mm (medial) for use of the stapler and an extraction site for the resected stomach—are placed under direct vision. The liver is retracted anterosuperiorly. The pylorus of the stomach is then identified and the greater curve of the stomach elevated. An ultrasonic scalpel is then used to enter the greater sac via division of the greater omentum. The greater curvature of the stomach is then dissected free from the omentum and the short gastric blood vessels using the laparoscopic ultrasonic scalpel. The dissection is started 5 cm from the pylorus and proceeds to the angle of His. A 32-Fr bougie is then passed under direct vision through the esophagus, stomach, and into the first portion of the duodenum. The bougie is aligned along the lesser curvature of the stomach and used as a template to perform the vertical gastrectomy beginning 2 cm proximal to the pylorus and extending to the angle of His. An endoscopic linear cutting stapler is used to serially staple and transect the stomach staying just to the left and lateral to the bougie. The transected stomach, which includes the greater curvature, is completely freed and removed from the peritoneal cavity through the left 15-mm port incision. The stapler line along the remaining stomach is then tested for any leak with bleu de methylene solution intragastric infusion. The stapler line is concurrently evaluated for bleeding. A drain is left in the left upper quadrant along the sleeve gastrectomy staple line and a nasogastric tube for gastric content drainage is placed. Only the fascia of the left 15-mm port site is closed with an absorbable suture, to prevent bowel herniation.

Postoperatively patients remained nil per os for 24 hours. Then, if patient has no nausea, the nasogastric tube is removed and patients started

Table 1 Patients characteristics, BMI and SUA concentration preoperatively, on first postoperative month and on first postoperative year

Mean age, y (range)	38.5 (18–61)
Women, n (%)	31 (56.4)
Men, n (%)	24 (43.6)
Preoperative	
BMI, kg/m ² (range)	48.03 (35.29–78.6)
Mean SUA concentration, mg/dL (range)	6.35 (0.8–10.8)
First postoperative month	
BMI, kg/m ² (range)	41.48 (29.55–62.48)
Percentage of total weight loss (range)	12.13 (4.36–24)
Mean serum uric acid concentration mg/dL (range)	6.64 (3.2–13.2)
First postoperative year	
BMI, kg/m ² (range)	32.35 (21.74–51.93)
Total weight loss, % (range)	31.5 (10–53.89)

drinking liquids. All patients are discharged on the third postoperative day. Patients have follow-up appointments every 3 months for the first postoperative year and yearly thereafter.

Statistical software (SPSS version 19; SPSS Inc., Chicago, IL) was used for statistical analysis. Statistical significance was considered at $P < 0.05$.

Results

According to our criteria, 55 patients were included in our study, of whom 56.4% ($n = 31$) were women and 43.6% ($n = 24$) were men. All patients underwent LSG and had an uneventful postoperative period.

Table 1 summarizes the patients' characteristics and the pre- and postoperative SUA concentrations and BMI.

Patients' mean age was 38.58 years ($SE = 1.65$), patients' mean preoperative BMI was 48.03 kg/m² ($SE = 1.16$). BMI did not differ between sex (women: 47.97 and men: 48.12, $P = 0.948$) or age ($P = 0.564$).

Patients' mean preoperative SUA concentration was 6.35 mg/dL ($SE = 0.26$) with women having a lower mean preoperative SUA concentration (women: 5.66 mg/dL and men: 7.23 mg/dL, $P = 0.002$). Preoperative SUA concentration did not correlate with patients' age ($P = 0.791$). Abnormally elevated preoperative SUA concentration—as defined above—was found in 38.2% ($n = 21$) of the patients, of whom 52.4% ($n = 11$) were women. Preoperative abnormally elevated SUA concentration did not

Fig. 2 (a) Correlation between preoperative SUA concentration and percentage of TWL on first postoperative month ($P < 0.001$). (b) Correlation between preoperative SUA concentration and percentage of excess BMI loss on first postoperative month ($P = 0.007$).

differ between sex ($P = 0.778$), age ($P = 0.509$), or BMI ($P = 0.352$).

On the first postoperative month, the mean SUA concentration was 6.64 mg/dL (SE = 0.31). Women had lower mean SUA concentration compared with men (5.74 mg/dL versus 7.8 mg/dL, $P = 0.001$). Abnormally elevated SUA concentration was found in 47.3% ($n = 26$) of the patients on the first postoperative month, of whom 46.2% ($n = 12$) were women. Abnormally elevated SUA concentration on first postoperative month did not differ between sex ($P = 0.180$) or age ($P = 0.146$).

On the first postoperative month and on the first postoperative year, mean BMI were 41.48 kg/m² (SE = 1.06) and 32.35 kg/m² (SE = 1.23), respectively, the percentages of TWL were 12.13% (SE = 0.7) and

31.5% (SE = 1.67), respectively, and the percentages of excess BMI loss (EBMIL) were 28.44% and 68.08%, respectively.

Statistical analysis revealed that preoperative BMI and preoperative SUA concentration had a statistically significant positive correlation ($P = 0.026$; Fig. 1). Preoperative BMI did not correlate with percentage of TWL on first postoperative month ($P = 0.370$) or first postoperative year ($P = 0.765$). Age and sex also did not correlate with percentage of TWL on first postoperative month ($P = 0.934$ and $P = 0.052$, respectively) or first postoperative year ($P = 0.056$ and $P = 0.248$, respectively).

However, preoperative SUA concentration had a positive correlation with percentage of TWL and EBMIL during the first postoperative month ($P <$

Fig. 3 (a) Correlation between preoperative SUA concentration and percentage of TWL on first postoperative year ($P = 0.002$). (b) Correlation between preoperative SUA concentration and percentage of excess BMI loss on first postoperative year ($P = 0.022$).

Fig. 4 Comparison between patients with normal and elevated preoperative SUA concentration and the percentage of TWL on first postoperative month ($P = 0.001$).

0.001 and $P = 0.007$, respectively; Figs. 2a, 2b) and during the first postoperative year ($P = 0.002$ and $P = 0.022$, respectively; Figs. 3a, 3b). SUA concentration on the first postoperative month had also a positive correlation with percentage of TWL during the first postoperative year ($P = 0.004$).

Patients ($n = 22$) with abnormally elevated preoperative SUA concentration had a higher percentage of TWL and EBMIL on the first postoperative month than patients ($n = 33$) with normal preoperative SUA concentration (14.58% versus 10.68%, $P = 0.001$ and 32% versus 25.27%, $P = 0.018$; Fig. 4).

Finally, SUA concentration on the first postoperative month was also found to have a positive correlation with percentage of TWL on the first postoperative year ($P = 0.004$). Indeed, patients with abnormally elevated SUA concentration on the first postoperative month had statistically significant higher percentage of TWL compared with patients with normal SUA concentration (35.43% versus 28.01%, $P = 0.016$; Fig. 5).

Multivariate regression analysis adjusted for age, sex, and preoperative BMI revealed that preoperative SUA is an independent prognostic factor for postoperative weight loss as it positively correlates with the percentage of TWL on the first postoperative month (B coefficient [B] = 1.288, $P < 0.001$) and the first postoperative year ($B = 3.989$, $P < 0.001$). In addition, multivariate regression analysis adjusted for age, sex, and preoperative BMI revealed that SUA on the first postoperative month is an independent prognostic factor for postoperative

Fig. 5 Comparison between patients with normal and elevated SUA concentration on first postoperative month and the percentage of TWL on first postoperative year ($P = 0.016$).

weight loss as it positively correlates with the percentage of TWL on the first postoperative year ($B = 2.346$, $P = 0.017$).

Discussion

Metabolic syndrome is often related to obesity and is defined (according to National Cholesterol Education Program Adult Treatment Panel III⁷) as the presence of three or more of the following risk factors: (1) abdominal obesity: waist circumference for men >102 cm and for women >88 cm; (2) triglycerides: >150 mg/dL or drug treatment for elevated levels; (3) high density lipoprotein (HDL): men <40 mg/dL and women <50 mg/dL or drug treatment for reduced levels; (4) blood pressure: systolic ≥ 130 and/or diastolic ≥ 85 mmHg or drug treatment for hypertension; and (5) fasting glucose: >110 mg/dL or drug treatment for diabetes mellitus.

Hyperuricemia has been recognized as a common characteristic in patients with metabolic syndrome. It has been implied that insulin resistance causes impaired uric acid excretion and as a consequence, hyperuricemia, due to alterations in urine pH.⁸ In our study, we revealed a positive correlation between preoperative BMI and preoperative SUA concentration. Apart from metabolic syndrome, another possible cause for this correlation could be the dietary habits of obese patients (e.g., increased purines intake, increased sugar-sweetened soft drinks intake, fructose consumption).⁹

Preoperative BMI according to a recent review of the literature was not found to predict postoperative

weight loss.¹⁰ From 62 articles, only 16 revealed a positive association between preoperative BMI and postoperative weight loss, whereas 9 revealed no association and 37 revealed a negative association. In our study, preoperative BMI did not correlate with the percentage of TWL on the first postoperative month or on the first postoperative year.

However, the percentage of TWL on the first postoperative month has a strong positive correlation with preoperative SUA concentration and the percentage of TWL is statistically significantly higher in obese patients with elevated preoperative SUA. A literature search did not reveal any evidence on how preoperative SUA concentration correlates with postoperative weight loss.

Ghrelin, a recently discovered peptide produced by gastric cell lines, is considered to be the “hunger hormone.” A recent study revealed that ghrelin levels are inversely associated with SUA concentration in a nonobese population.¹¹ In patients with chronically increased levels of ghrelin—like obese patients—there may be a resistance developed to it over time. This might explain the fact that after LSG, which reduces the production of ghrelin, patients with preoperative elevated SUA, and thus lower levels of ghrelin, have greater weight loss.

We cannot oversee the fact that SUA is related with metabolic syndrome. The obese patients with elevated SUA may suffer from severe metabolic syndrome. No data exists on the hypothesis that obese patients with severe metabolic syndrome are able to lose weight faster than obese patients without metabolic syndrome. Maybe obese patients suffering from metabolic syndrome are more able to adjust their weight through faster changes in their metabolic rate.

Another possible explanation of our findings is that obese patients with elevated preoperative SUA concentrations consume special foods and have unhealthy dietary habits. LSG due to the gastric capacity restriction prevents these patients from consuming large quantities. The gut hormonal alterations of LSG may also play a role in the patients' dietary choices after the operation.

Severe and acute weight loss after bariatric surgery is not uncommon. Unhealthy nutritional habits and rapid weight loss can cause malnutrition (protein-calories malnutrition) and several deficiencies such as calcium, vitamin B12, iron, folate, thiamine and fat-soluble vitamins (vitamins A, D, K).^{12,13} Gallstones formation is another common complication of rapid weight loss.¹⁴

In order to prevent the above complications, a multidisciplinary approach is needed for patients who undergo bariatric operations, not only preoperatively but also postoperatively. Follow-up must be conducted by a team consisting of a surgeon, a dietitian, and a psychologist. It is of great importance to have prognostic tools that could predict patients in need of dietary supplements, in order to prevent complications of rapid weight loss.

Our study refers to a small group of patients who undergo LSG; however, it reveals that preoperative SUA concentration predicts the success of the operation by indicating patients who will have increased weight loss postoperatively. This finding implies that SUA concentration could possibly be used as a predictor of success of LSG. Further studies will be needed in order to clarify the relationship of uric acid and postoperative weight loss and to develop more accurate prognostic tools for the success of bariatric operations.

Conclusion

Our study reveals a correlation between SUA concentration and percentage of TWL after LSG, implicating that SUA concentration could be used as a predictor of success of LSG. Further studies will clarify the relationship of uric acid and postoperative weight loss towards the creation of more accurate prognostic tools.

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