Laparoscopic Sleeve Gastrectomy Reduces the Predicted Coronary Heart Disease Risk and the Vascular Age in Obese Subjects

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Abstract

Background: Obesity is associated with high prevalence of coronary heart disease (CHD) and long term increased cardiovascular morbi-mortality. There are no data regarding the effect of laparoscopic sleeve gastrectomy (LSG) on long-term CHD - risk. It is known that “a man is as old as his arteries” and this concept is illustrated by Framingham coronary risk score, which can predict vascular age.

Purpose: To assess the 10-year CHD risk in patients with obesity, preoperatively, and 6 and 12 months after LSG.

Methods: 47 consecutive obese subjects (44.7% males, mean
Introduction

Global and national epidemiological data

Obesity is now considered a major clinical and epidemic problem, a world wide epidemic with a rapid increase in incidence.

The global prevalence of excessive weight has doubled in the last 30 years and is, in adults, at a level of approximately 33% for obesity and 50% for overweight and obesity. There are currently 200 million obese men registered in the world, 300 million obese women and 1.4 billion overweight subjects and there are regions where overweight and obese individuals account for over 65% of the population (U.S.). Equally worrying is the current number of obese adults and high prevalence of obesity among children - in 2010 more than 40 million children younger than 5 years were overweight (1,2).

In Romania, epidemiological studies conducted between 2000-2005 have shown an obesity prevalence in the general population of 28%, with a distribution of 26.3% in males and 35.1% in women; in patients with coronary heart disease, obesity had a higher prevalence: 31% - out of which 29% in men and 34% in women. Body mass index (BMI) in adults with average age of 25 years was 27.4 kg/m² (corresponding to overweight), and 30.6% of them had high cholesterol level and excess weight (overweight or obesity) (3,4).

A very recent population - based study (published in June 2013) described that, nowadays, in Romania, over 56% of men and over 46% of women are overweight and obese and 18% of the young subjects (15-24 years old) are overweight (5).

Obesity prognosis

The excess weight prognosis is extremely unfavourable: obesity is the fifth cause of death worldwide, giving 2.8 million deaths / year, with general mortality that increases by 30% with every BMI augmentation of 5 kg/m². Cardiovascular mortality is more pronouncedly increased by obesity: by 40% at every BMI augmentation of 5 kg/m² (6).

World Health Organization reports warn that 23% of the ischemic heart disease burden and 44% of the diabetes burden are attributable to overweight and obesity (7).

Metabolic and cardiovascular obesity disorders

Obesity potential "adverse effects" are related to: insulin resistance, high blood pressure, systemic proinflammatory and prothrombotic status, albuminuria and dyslipidemia (increased serum levels of total cholesterol, LDL-cholesterol, other forms of non-HDL cholesterol, triglycerides, apolipoprotein B, small dense LDL particles and decreased concentrations of HDL cholesterol and apolipoprotein A1) (8).

Major cardiovascular and cerebrovascular abnormalities seen in obesity are: endothelial dysfunction, increased sympathetic nervous system activity, abnormal left ventricular geometry, systolic and diastolic left ventricular dysfunction, heart failure, coronary artery disease, dilated left atrium, atrial fibrillation, stroke (8).

Cardiovascular risk assessment, Framingham score and vascular age

Cardiovascular disease is the most common cause of death in the general population and risk prediction formulas such as the Framingham Risk Score have been developed to easily identify patients at high risk that may require therapeutic interventions.

Using cardiovascular risk formulae at a population level to estimate and compare average cardiovascular risk among groups has been recently proposed as a way to facilitate surveillance of net cardiovascular risk and target public health interventions. Risk prediction formulas may help to compare interventions that cause effects of different magnitudes and directions in several cardiovascular risk factors, because these formulas assess the net change in risk using easily obtainable clinical variables (9).

The Framingham risk score estimates total CHD risk (risk of developing angina pectoris, myocardial infarction, or coronary disease death) over the course of 10 years. The predicted CHD Framingham riskdata are derived from 2,489
men and 2,856 women, all Caucasians, who were 30 to 74 years old at the time of their Framingham Heart Study examination in 1971 to 1974, with CHD ascertained at the 12-year follow-up (10).

Thomas Sydenham, a 17th century physician who has been called "the English Hippocrates", once said that "a man is as old as his arteries". The concept of vascular age underscores the crucial role blood vessels play in maintaining heart health.

Starting from Framingham risk score, one can estimate the vascular age. Such a calculation warns that the risk-factor burden is making people age faster. But, fortunately, it is assumed that, by reducing risk factors and the damage they inflict on arteries, it is possible to turn back the clock on vascular age.

**Bariatric surgery cardiovascular outcomes**

Bariatric surgery, a highly effective treatment for morbid obesity, induces a significant and long-lasting weight loss. Favourable cardiovascular outcomes after bariatric surgery are well documented in literature, but most published studies assessed cardiovascular changes after extensively used bariatric procedures, mainly Roux- en-Y gastric bypass (11). In a recently published meta-analysis over 16,867 bariatric procedures from the last 12 years, the cardiovascular risk profile improved, but only 0.2% of interventions were LSG (11).

LSG has recently been the target of much research in the bariatric community secondary to the observation that it may be effective as a stand-alone bariatric procedure with a superior safety profile (12).

**Methods**

47 consecutive obese subjects who consented to be included in this study were prospectively evaluated. They were scheduled for LSG in “Delta Hospital” (now called “Ponderas”) Bariatric and Metabolic Surgery Centre of Excellence, between January and May 2011.

Clinical examination and blood testing were performed in all subjects before intervention and 6 and 12 months after surgery. All patients were comprehensively evaluated by a multidisciplinary team before undergoing surgery, as well as postoperatively.

The study was approved by the ethics committee. Written informed consent was obtained from all patients.

**Anthropometric measurements**

BMI was calculated according to the formula: weight (kg)/squared height (m²).

The percentage of excess weight lost (EWL) was calculated according to the formula: \( \text{EWL} = \frac{(\text{initial weight-current weight}) \times 100}{\text{(initial weight-ideal weight)}} \)

**Laboratory tests**

Blood samples were obtained following the approved clinical protocol for bariatric surgery.

**Framingham risk score**

10-year CHD risk (risk of developing angina pectoris, myocardial infarction, or coronary disease death over the course of 10 years) was estimated in all patients using the 1998 gender-specific Framingham risk score (10).

The Framingham risk score was calculated using a software that included patient age, gender, serum total cholesterol, high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressure, systemic hypertension treatment, diabetes mellitus status and smoking status in the analysis.

Vascular age was derived from the Framingham score, by interpolation, by a computer program.

The predicted CHD Framingham risk was compared with the expected risk of the general population using published tables of CHD rates by age strata (10).

We used the Framingham score for evaluation, and not the European chart SCORE, because the latter, due to risk underestimation, is not recommended to be used in obese subjects, especially those with central obesity, in individuals with type 2 diabetes and in those with low HDL cholesterol or increased triglycerides (8).

**Surgical intervention**

All interventions were made by laparoscopic approach. The surgical technique of LSG was previously described (13,14). In all cases, LSG was intended as a definitive procedure.

**Statistical analysis**

Data are expressed as means ± standard deviation (SD) for continuous variables and as percentages for categorical variables. Findings at the pre- and post-operative examinations were compared by Student t-tests for paired data or chi square test, as appropriate.

The differences in the mean values between groups were compared using Mann-Whitney U or Wilcoxon test, as appropriate. The significance of association between variables was determined by Pearson and Spearman correlation.

A probability value of \( p < 0.05 \) was considered significant and two tailed \( p \) values were used for all statistics.

All data were analysed using SPSSv 17.0 for Windows (SPSS Inc.)

**Results**

The overall age of the study group was 39.8 ± 10.8 years, 41.6 ± 12.9 years for women (55.3%) and 37.5 ± 7 years for men (44.7%), all Caucasians.

Baseline and 6 and 12 months follow-up clinical, biological and CHD risk characteristics of the study group are shown in Table 1. None of the patients had history of previous coronary or peripheral vascular disease.
Weight loss

Obese subjects significantly lost weight early after LSG - at 6 and 12 months follow-up patients decreased their BMI by 12.4 kg/m², respectively by 15.2 kg/m² versus baseline (see Fig. 1).

Mean weight loss was 36.1 kg respectively, 44.1 kg. The waist circumference decreased also, with 27 cm, respectively 34.8 cm (see Fig. 1).

Mean EWL was 67.3±23.7% 6 months postoperatively and 78.3±23.4% at 12 months follow-up.

12 months EWL had a negative correlation with initial BMI (r = -0.56, p = 0.01) and with patient age (r = -0.46, p=0.01).

Changes in blood pressure values, glycemic status, lipid and smoking profile

Systemic hypertension prevalence was high preoperatively with respect to age: 46.8 % and decreased 6 months postoperatively to 10.6 % and to 8.5 % at 12 months follow-up.

Following surgery, systemic hypertension prevalence decreased 4.3 times at the 6 months visit and 7.3 times at the 12 months evaluation, both in terms of significantly lower blood pressure values and dramatic decrease in antihypertensive medication requirements. Most patients with hypertension were thusly categorized on the basis of medical treatment. Thus, besides systolic and diastolic blood pressure differences in absolute values (see Fig. 1), before surgery all hypertensive patients (22) were treated with mean 2.2 antihypertensive medication, while 6 and, respectively, 12 months postoperatively only 4 patients (8.5%), respectively 3 patients (6.4%), needed antihypertensive monotherapy.

Relative to baseline, diabetes mellitus prevalence was 4 times lower at 6 months follow-up and 5.3 times lower 6 months later.

At 6, respectively 12 months follow-up, patients demonstrated significant absolute and per cent decreases in: total cholesterol −40.4 mg/dl (−17.6%), respectively -56.8 mg/dl (−24.7%), LDL cholesterol: −33.6 mg/dl (−23.2%), respectively -41.3 mg/dl (−28.6%) and triglycerides: −71.9 mg/dl, (−40.1%), respectively - 82.4 mg/dl (−46%) and a significant increase in HDL cholesterol: +2.8 mg/dl (+6%), respectively +19.4 mg/dl (+41.6%) (see Fig. 1).

Smoking prevalence decreased 2.5 times at 6 months follow-up and 5 times one year after LSG.

Changes in 10 years coronary risk and vascular age

Mean baseline and 6 and 12 months postoperative 10-year Framingham CHD risk, for men and women, are shown in Fig. 2. The overall ranges and the medians are illustrated in Fig. 3.

Baseline 10-year Framingham CHD risk correlated with preoperative BMI (r=0.43, p=0.003) and the correlation between parameters maintained 12 months after LSG (r=0.35, p=0.017). A statistically significant decrease in predicted CHD risk was achieved after weight loss. Mean predicted 10-year CHD risks decreased 6 months, respectively, 12 months after surgery by 69 %, respectively 77% in men, 63 %, respectively 75 % in women, and 60%, respectively, 80% in all patients.

Obese subjects’ mean vascular age was, at baseline, 65.6 years, 25.8 years older than their mean chronological age (39.8 years). Preoperative chronological and vascular age distribution is illustrated by Fig. 4.

Vascular age decreased with 19.8 years at 6 month follow-up and with 24.9 years 12 months postoperatively, when a level similar to the chronological age (40.7 vs. 40.8 years, p=NS) was achieved. One year postoperatively, in men, vascular age was slightly above their chronological age.
(38.7 vs 38.5 years), respectively in women slightly below their chronological age (42.4 vs 42.6 years) (Fig. 5).

**Discussion**

This is an extensive report about clinical, metabolic and cardiovascular risk evolution after LSG.

The outcomes are favourable and concordant with previously reported data after a more aggressive, but extensively and traditionally used, bariatric intervention (gastric by-pass), without its risk of malabsorptive adverse effects.

We made the following observations: 1) weight decreased early (6 months) after weight loss surgery and continued its decline 12 months postoperatively, an EWL of 78% being
Changes in clinical data and metabolic profile

In this study, we reported a significant weight loss after laparoscopic sleeve gastrectomy, with a mean EWL of 67.3% at 6 months postoperatively and 78.3% at 12 months follow-up.

This is above the mean EWL of 60.4% (range 36 – 85%, n=1749 patients, mean follow-up 3-60 months) reported in a systematic review of the literature by Brethauer, in patients where LSG was intended as a definitive procedure, as it was the case in our patients (15).

For extensively used bariatric procedures, previously reported EWL at 6-months was 52.2% after gastric by-pass and 28.3% after gastric banding (16).

Previously reported EWL in one of the most comprehensive meta-analysis about bariatric surgery outcomes (at more than 2 years follow-up) was mean 65% for gastric by-pass and 69% for biliopancreatic diversion and 42% for laparoscopic gastric banding (17).

12 months after surgery EWL had a negative correlation with patients' age and with initial BMI, so young patients, with a shorter history of obesity, had the best response in losing weight. As expected, subjects with lower BMI achieved more rapidly a weight close to the ideal one.

Body weight decreased in parallel with waist circumference, so patients lost both total fat and abdominal fat, the latter known to be strongly associated with higher metabolic and cardio-vascular risk.

Diabetes prevalence had a marked decrease. This finding is concordant with the previously mentioned idea that, although type 2 diabetes has been the domain of physicians, surgeons may now be able to claim greater success in achieving improved metabolic control (18).

Smoking prevalence had also a marked decrease at 6 and 12 months follow-up, probably because bariatric patients are highly motivated subjects, who, when opting for LSG decide also to make serious lifestyle changes. Moreover, after bariatric surgery is the best moment for obese subjects to quit smoking, because they do not regain weight, a common experience in their history when trying smoking with drawal.

Thus, the so-called modifiable cardiovascular risk factors: systemic hypertension, diabetes mellitus, dyslipidemia, smoking were really and favourably modified in our studied group of obese subjects after LSG.

10-year Framingham CHD risk and vascular age evolution

Although weight is not included in the equation for calculating 10-year CHD risk, BMI and CHD Framingham risk proved a strong correlation, both preoperatively and 12 months after surgery.

Relative decreases in patient predicted 10-year CHD risk was 60% 6 months after LSG and 80% 12 months after surgery. On average, subjects moved from high to the low 10-year CHD risk category for age and gender, one year after bariatric surgery.

One year after LSG, mean vascular age decreased with 24.9 years one year after LSG.

These data suggest substantial and sustained weight loss after LSG may be a powerful intervention to decrease future rates of myocardial infarction and death in obese subjects.

To our knowledge, our study is the first to quantify a global decrease in CHD risk after substantial and sustained weight loss secondary to LSG. We found that weight loss was effective in decreasing the 10-year Framingham predicted CHD risk in obese subjects. Accordingly, this is the first study to suggest that LSG can achieve CHD risk levels similar to those expected for a low-risk population.

The lower CHD risk, as projected by the Framingham risk score, was driven by significant improvement in multiple risk factors after weight loss induced by LSG. Dyslipidemia, hypertension, and diabetes mellitus substantially improved or resolved after bariatric surgery.

Our findings are consistent with previous reports demonstrating a decrease in CHD risk and mortality after other types of bariatric interventions. Thus, Batsis et al. described a decrease in the 10-year risk for cardiovascular events (evaluated using NHANES risk models) from 37% at baseline to 18%, 3 years after Roux-en-Y gastric bypass, in 197 patients with Class II and Class III obesity (19).

Our results are also concordant with another study (20) that also demonstrated good results in improving the metabolic profile and decreasing coronary risk below the expected risk for age and gender (from 6 ± 5% and 4 ± 3% by Framingham score, at average 17 months follow-up) in 109 obese subjects, 75% women, mean age 46 years, after Roux-en-Y gastric bypass surgery.

Moreover, there is evidence that the good cardiovascular prognosis predicted by our study after LSG will be confirmed in the future. The proof is SOS (Swedish Obese Subjects) Study, which prospectively enrolled 2010 obese subjects who underwent other types of bariatric surgery than in the present study (19% gastric banding, 68% vertical banded gastroplasty and 13% gastric bypass) and 2037 matched conventionally treated obese control group, followed for an average of 10 years.
The SOS study revealed an adjusted mortality reduction of 30.7% at 10 years, the most common cause of death in obese subjects being myocardial infarction and cancer (21).

**Study limitations**

One of the study limitations is the follow-up period (one year), but it is a prospective study - it will be followed by other periodical evaluations. We acknowledge also that some changes in CHD risk may not be a direct, but a related result of bariatric surgery (e.g., decrease in smoking) and may reflect the effect of patient education, self-improvement, and overall betttercare than that of the general population. The Framingham Heart Study risk algorithm encompasses only coronary heart disease, and no other heart or vascular diseases (10).

**Conclusion**

Our study reveals that LSG is efficient not only in the reduction of obesity and its related comorbidities, but also in decreasing the long-term coronary event risk and, implicitly, in increasing life expectancy.

A longer follow-up and further studies are needed to elucidate the intrinsic cardiac and vascular pathophysiological mechanisms through which LSG bariatric surgery leads to improved long term cardiovascular prognosis.

**Abbreviations**

- **LSG**=laparoscopic sleeve gastrectomy
- **CHD**=coronary heart disease
- **BMI**=body mass index
- **HDL-cholesterol**=high density lipoprotein cholesterol
- **LDL-cholesterol**= low density lipoprotein cholesterol
- **vs.**=versus
- **SD**=standard deviation

**Statement of authorship**

Author contributions to the manuscript were as follows: MI designed the study, revised the literature, carried out the data analysis, performed the statistical analysis, coordinated and drafted the manuscript. CC participated in the coordination of this study and in the collection of data, obtained patients' informed consent and revised the manuscript critically for important intellectual content. MS participated in interpretation of data and revising the manuscript. CG participated in the coordination of this review and revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

**Conflict of interest statement**

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**References**