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Impact of vertical banded gastroplasty on body weight, insulin resistance, adipocytokine, inflammation and metabolic syndrome markers in morbidly obese patients

Wpływ pionowej plastyki żołądka na masę ciała, insulinooporność, adipocytokiny oraz na czynniki zapalne i wskaźniki zespołu metabolicznego u chorych z otyłością olbrzymią

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Abstract

Introduction: Diet, exercise, and pharmacological therapy have been shown to be unsatisfactory treatments for severe obesity in the long term. Bariatric surgery is the most effective means to achieve weight loss in morbidly obese subjects.
The aim of this study was to evaluate the action of a number of adipocytokines, as well as the metabolic syndrome parameters of obese patients, before and after vertical banded gastroplasty (VBG).
Material and methods: The test subjects comprised eight males and 20 females (total 28 patients) aged from 20 to 59 years (43.7 ± 10.0) with simple obesity and the presence of metabolic syndrome, both before and 3, 6, 12, and 24 months after bariatric surgery (six patients were also checked after 36 and 48 months).
Results: After surgical treatment (at 24 months), the values of body weight, BMI, waist circumference, blood pressure (RR-S, RR-D), HOMA-IR and blood concentrations of CRP, TG, IRI, AUC-IRI, and AUC-GLU gradually decreased. We did not observe any significant differences of fasting glucose, leptin, total cholesterol and LDL-cholesterol concentrations before or after surgery. The blood levels of HDL, adiponectin, resistin, and ghrelin gradually increased after treatment.
Conclusions: The significant decrease of body weight after vertical banded gastroplasty, as well as improvement of the main metabolic syndrome parameters and some adipocytokine blood levels, indicate the use of bariatric surgery as a valuable method of treating morbidly obese patients. **(Pol J Endocrinol 2011; 62 (2): 109–119)**

Key words: *morbid obesity, metabolic syndrome, bariatric surgery, adiponectin, leptin, resistin, ghrelin*

Streszczenie

Wstęp: Dieta, ćwiczenia fizyczne i zastosowanie leczenia farmakologicznego nie powodują długotrwałej redukcji masy ciała u pacjentów otyłych. Skuteczne w tym zakresie okazały się natomiast bariatryczne zabiegi operacyjne.
Celem pracy była ocena zmian w zakresie parametrów zespołu metabolicznego i stężenia niektórych adipocytokin u chorych ze znacznego stopnia otyłością leczonych za pomocą pionowej plastyki żołądka (VBG).
Materiał i metody: Dwudziestu ośmiu chorych (8 mężczyzn i 20 kobiet) w wieku 20–59 lat (43,7 ± 10,0) z otyłością prostą powikłaną zespołem metabolicznym badano przed i po 3, 6, 12 i 24 miesiącach (6 chorych oceniano także po 36 i 48 miesiącach) od operacji bariatrycznej.
Wyniki: Po leczeniu operacyjnym (po 24 miesiącach) zaobserwowano stopniowe zmniejszanie masy ciała, BMI, obwodu talii, skurczowego i rozkurczowego ciśnienia tętniczego (RR-S, RR-D), wartości wskaźnika insulinooporności (HOMA-IR) oraz stężeń we krwi: CRP, triglicerydów (TG), insuliny (IRI), glikemii (AUC-GLU) oraz mobilizacji wydzielania insuliny po glukozie (AUC-IRI). Nie stwierdzono zmian w zakresie stężeń glukozy (0′), leptyny, cholesterolu całkowitego i cholesterolu frakcji LDL. Natomiast po operacji stopniowo narastały stężenia: cholesterolu frakcji HDL, adiponektyny, rezystyny oraz greliny we krwi żylnej.
Wnioski: Po pionowej plastyce żołądka zaobserwowano znaczną redukcję masy ciała i poprawę w zakresie parametrów zespołu metabolicznego oraz profilu wydzielania niektórych adipocytokin. Uzyskane wyniki potwierdzają przydatność tego typu operacji bariatrycznej w leczeniu chorych z otyłością olbrzymią. **(Endokrynol Pol 2011; 62 (2): 109–119)**

Słowa kluczowe: *otyłość olbrzymia, zespół metaboliczny, operacje bariatryczne, adiponektyna, leptyna, rezystyna, grelina*

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Introduction

The prevalence of overweight and obesity has increased steadily in all Western countries, especially the United States [1–3]. Severe obesity is a risk factor for multiple serious health problems in adults, including heart disease, hardening of the arteries, high cholesterol, high blood pressure, certain types of cancer, stroke, diabetes, muscle and bone disorders and gall bladder disease [4].

Causes of obesity include the wide availability of unhealthy foods, increased consumption, changing eating habits, high-calorie beverages and lack of physical activity. In the USA, total healthcare costs attributable to obesity/overweight are predicted to double each decade, reaching $860.7–956.9 billion by 2030, accounting for 16–18% of total USA healthcare expenditure [3]. Overweight and obesity continue to climb steadily, not only in the United States but also to a lesser degree in Europe, among both adults and children, increasing the risk of a host of physical, psychosocial and economic problems.

In 2007–2008, the prevalence of obesity in the US was 32.2% among adult men and 35.5% among adult women [1, 2, 5]. More than half of the European population is overweight (body mass index (BMI) > 25 and < 30 kg/m^2) and up to 30% are obese (BMI ≥ 30 kg/m^2). Furthermore, 21% of the male and 22% of the female population of Poland is obese (Polish National Multicentre Health Survey WOBASZ study 2002–2005).

Obesity is closely associated not only with insulin resistance but also with elevated triglyceride levels, low HDL and high LDL cholesterol levels and elevated blood pressure; it produces a complex of medical conditions known as the *metabolic syndrome* [6, 7] leading to atherosclerosis. The development of the metabolic syndrome, involving a complex set of risk factors including glucose intolerance, hyperinsulinaemia, hypertension, and dyslipidaemia, dramatically heightens cardiovascular risk.

The National Cholesterol Educational Programme (Adult Treatment Panel III-ATP III) and other authors have suggested the use of the term *metabolic syndrome* to identify a common cluster of metabolic abnormalities, defined when at least three of five criteria are met:
— abdominal obesity (waist circumference, > 102 cm in men and > 88 cm in women)
— hypertriglyceridemia (≥ 150 mg/dL)
— low HDL (< 40 mg/dl in men and < 50 mg/dL in women)
— hypertension (≥ 130/85 mm Hg)
— elevated fasting glucose (≥ 110 mg/dL) [8–11].

According to International Diabetes Federation (IDF 2005) criteria, in order to be diagnosed as having metabolic syndrome, patients have to demonstrate abdominal obesity (waist circumference ≥ 94 cm in men and ≥ 80 cm in women) and fulfill at least two of four criteria:
— triglyceride concentration ≥ 150 mg/dL or treatment of hypertriglyceridemia
— concentration of cholesterol of HDL fraction < 40 mg/dL in men and < 50 mg/dL in women or dyslipidemia treatment
— systolic blood pressure (SBP) ≥ 130 mm Hg or diastolic blood pressure (DBP) ≥ 85 mm Hg or hypertension
— fasting glucose concentration in plasma ≥ 100 mg/dL or diagnosed type 2 diabetes.

Visceral fat accumulation in the abdomen is a potent modulator of insulin action on hepatic glucose production [12]. Human fat tissue is also able to produce several hormonal factors such as leptin, adiponectin and resistin, known as the adipocytokines or adipokines, which influence the development and severity of the clinical outcome of the metabolic syndrome [13, 14].

At present, bariatric surgery is the most effective method used to achieve long-term weight loss, the major goal in obesity treatment. It has been documented that post-surgical weight loss improves almost all obesity-related comorbidities [15–20].

The aim of our study was to evaluate a number of anthropometric parameters, some adipocytokines, ghrelin, insulin resistance markers, as well as the parameters of metabolic syndrome in morbidly obese patients for 3, 6, 12, 24, 36 and 48 months after vertical banded gastroplasty.

Material and methods

Eight males and twenty females (total 28 patients) aged from 20 to 59 years (43.7 ± 10.0) with simple obesity and the presence of metabolic syndrome (both by ATP III and IDF 2005 criteria) were studied both before and three, six, 12 and 24 months after bariatric surgery (six patients were also checked after 36 and 48 months).

Blood samples were drawn in the morning after an overnight fast, using EDTA as anticoagulant. Blood plasma leptin (DSL, USA kit; sensitivity-0.05 ng/mL; intra-assay precision — 3.0%, inter-assay precision — 3.4%), adiponectin (R & D Systems kit, USA; sensitivity — 0.25 ng/mL; intra-assay precision — 4.7%, inter-assay precision — 7.9%), resistin (R & D Systems kit, USA; sensitivity — 0.026 ng/mL; intra-assay precision — 5.3%, inter-assay precision — 8.2%) and serum ghrelin (DSL kit, USA; sensitivity — 0.09 ng/mL; intra-assay and inter-assay precision — < 10%) concentrations before and after treatment were evaluated by ELISA and plasma insulin (IRI) by MEIA (Abbott, Axsym System, USA; sensitivity < 1 μU/mL; intra-assay precision — 2.6%, inter-assay precision — 2.9%) methods.

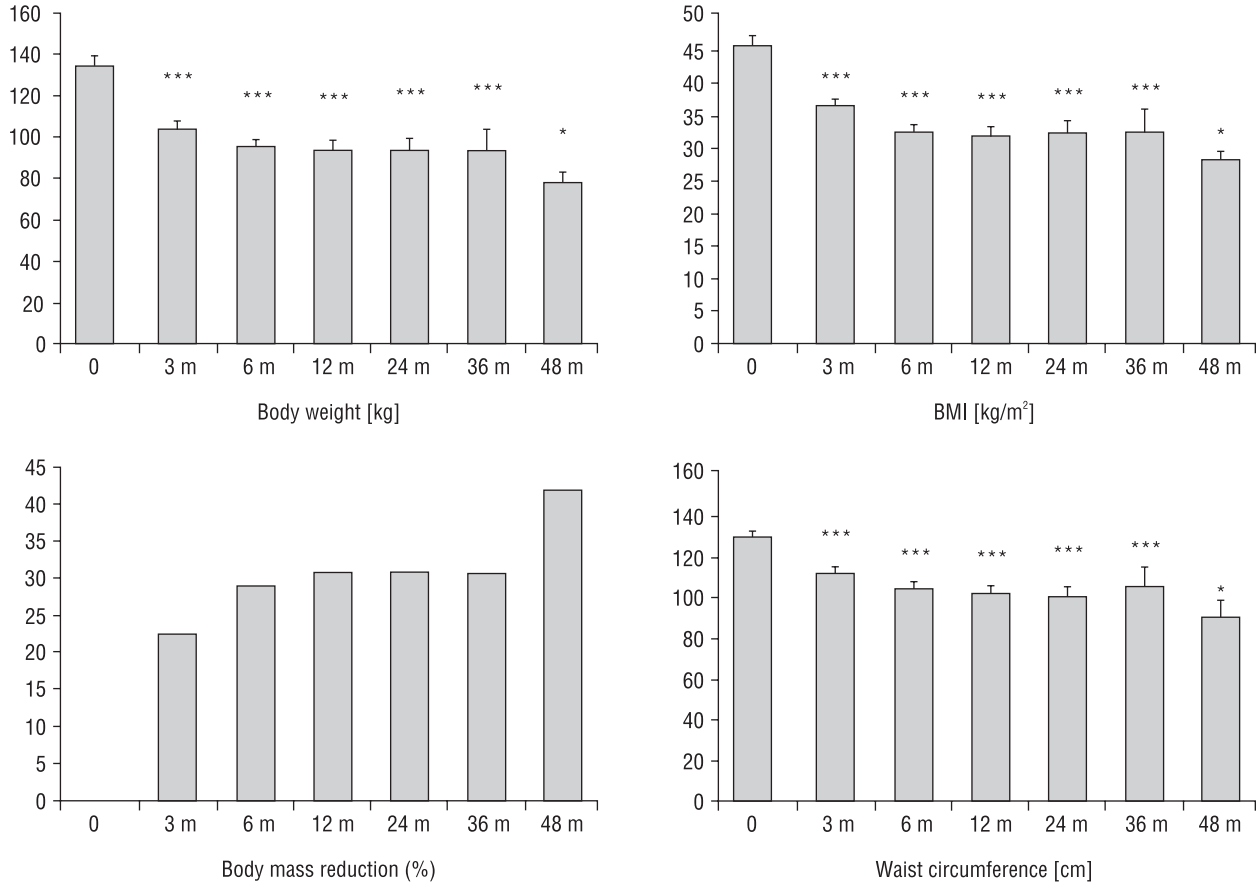

Figure 1. *Anthropometric data: body weight, BMI, body mass reduction (%), waist circumference of obese patients before and after surgery (m = months; x ± SEM; *p < 0.05; ***p < 0.001 vs. before surgery)*

Rycina 1. *Dane antropometryczne: masa ciała, BMI, stopień redukcji masy ciała (%), obwód talii u otyłych pacjentów przed i po leczeniu bariatrycznym (m = miesiące; x ± SEM; *p < 0,05; ***p < 0,001 v. przed operacją)*

Blood glucose, high-density lipoprotein (HDL), low--density lipoprotein (LDL), triglycerides, and high sensitivity C-reactive protein (CRP-using high sensitivity assay) were analysed. CRP and lipids were evaluated by COBAS INTEGRA Roche Diagnostics (Hitachi 912/ /917). Furthermore, systolic (RR-S) and diastolic (RR-D) blood pressure (patients were without any hypotensive medication) as well as the body mass index (BMI) were measured. Waist circumference and the homeostasis model assessment insulin resistance index [HOMA-IR = = fasting insulin (mIU/L) × × fasting glucose (mmol/L) 22.5] were calculated.

Statistical analysis

All comparisons were carried out using Statistica 8.0 software. The Student's paired t-test was used. The relationship between features was evaluated using the Pearson's correlation coefficient analysis. The values are presented as the mean ± SEM. A p value ≤ 0.05 or less was considered statistically significant.

The study was approved by the Local Ethics Committee of the Medical University of Lodz.

Results

After surgical treatment (at 24 months), the values of BMI, waist circumference, RR-S, RR-D, HOMA-IR and blood concentrations of CRP, TG, IRI, AUC-IRI, and AUC-GLU gradually decreased (Figs. 1– 4). We did not observe any significant differences of fasting glucose, leptin, total cholesterol and LDL-cholesterol concentrations before or after surgery. The blood levels of HDL, adiponectin, resistin, and ghrelin gradually increased after treatment (Fig. 5).

The positive and negative correlations between the parameters studied 3, 6, 12, and 24 months after VBG are given in Table I and Table II respectively.

Discussion

The evidence indicates that bariatric surgery is a more effective intervention for weight loss than non-surgical options. Diet, exercise, and pharmacological therapy have not been shown to be satisfactory methods in treat-

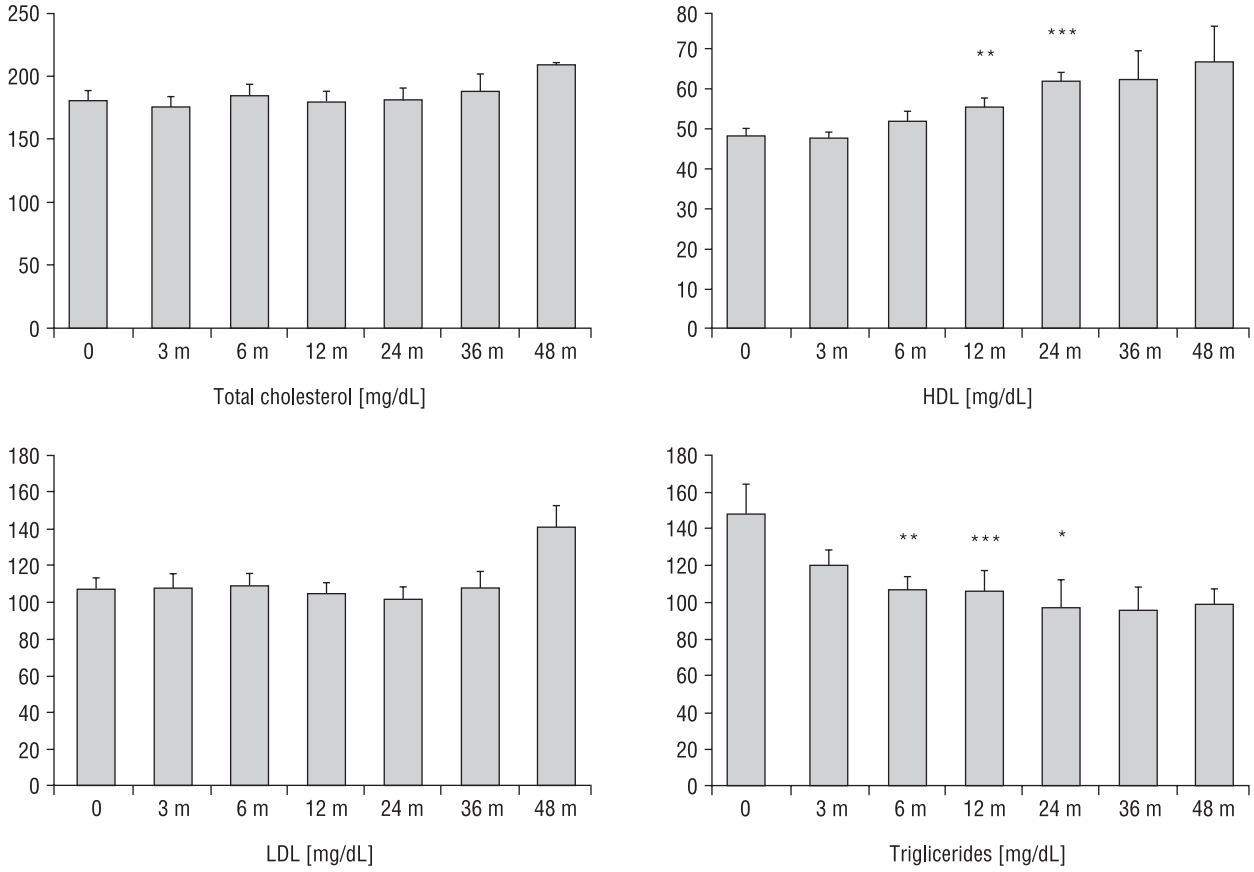

Figure 2. *Peripheral blood concentrations of total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density (LDL) cholesterol and triglycerides in obese patients before and after surgery (m = months; x ± SEM; *p < 0.05; **p < 0.01; ***p < 0.001 vs. before surgery)*

Rycina 2. *Stężenia: całkowitego cholesterolu, HDL-cholesterolu (HDL), LDL-cholesterolu (LDL) i triglicerydów w obwodowej krwi żylnej u otyłych pacjentów przed i po leczeniu bariatrycznym (m = miesiące; x ± SEM; *p < 0,05; **p < 0,01; ***p < 0,001 v. przed operacją)*

ing severe obesity in the long term [21, 22]. This, and the steep rise in the prevalence of severe obesity laparoscopic procedures, may explain the exponential increase in the number of bariatric surgeries performed in the USA from 13,365 in 1998 to 72,177 in 2002 [23], to 130,000 in 2005. An estimated 220,000 people underwent bariatric surgical procedures in the United States in 2008 (American Society for Bariatric Surgery 2009). The various types of bariatric procedures include Roux-en-Y gastric bypass (RYGB), gastric banding (GB), vertical banded gastroplasty (VBG), duodenal switch, biliopancreatic diversion, isolated intestinal bypass, and gastrectomy. Recently, RYGB and GB surgeries have been the most commonly performed (24) but vertical banded gastroplasty is the primary focus of this study. Gastric bypass (GBP) is more effective for weight loss than vertical banded gastroplasty (VBG) and adjustable gastric banding (AGB) [25].

According to a recent metaanalysis on bariatric surgery outcomes [26], patients who undergo bariatric surgeries lose up to 61.6% of their excess body weight, and a majority of patients with diabetes, hyperlipidaemia, hypertension, and obstructive sleep apnea experience complete resolution or improvement of these comorbidities. However, most of the studies included in the metaanalysis were uncontrolled case series, and patients were followed up for no more than two years. Emerging data, however, suggests some gradual weight regain and return of comorbidities in the long term [27]. Maximum weight losses in the surgical subgroups were observed by Sjostrom et al. [28] after one to two years: gastric bypass, 32%; vertical banded gastroplasty, 25%; and banding, 20%. After ten years, the weight losses from baseline were stabilised at 25%, 16%, and 14%, respectively.

In the present study, we examined the effect of weight loss surgery (VBG) on changes in body composition (BMI, waist circumference), metabolic, inflammation and adipokine markers over 24 months. These parameters were also checked at 36 and 48 months in six subjects who completed the study, to confirm whether the trends demonstrated by the obtained results are similar over a longer term.

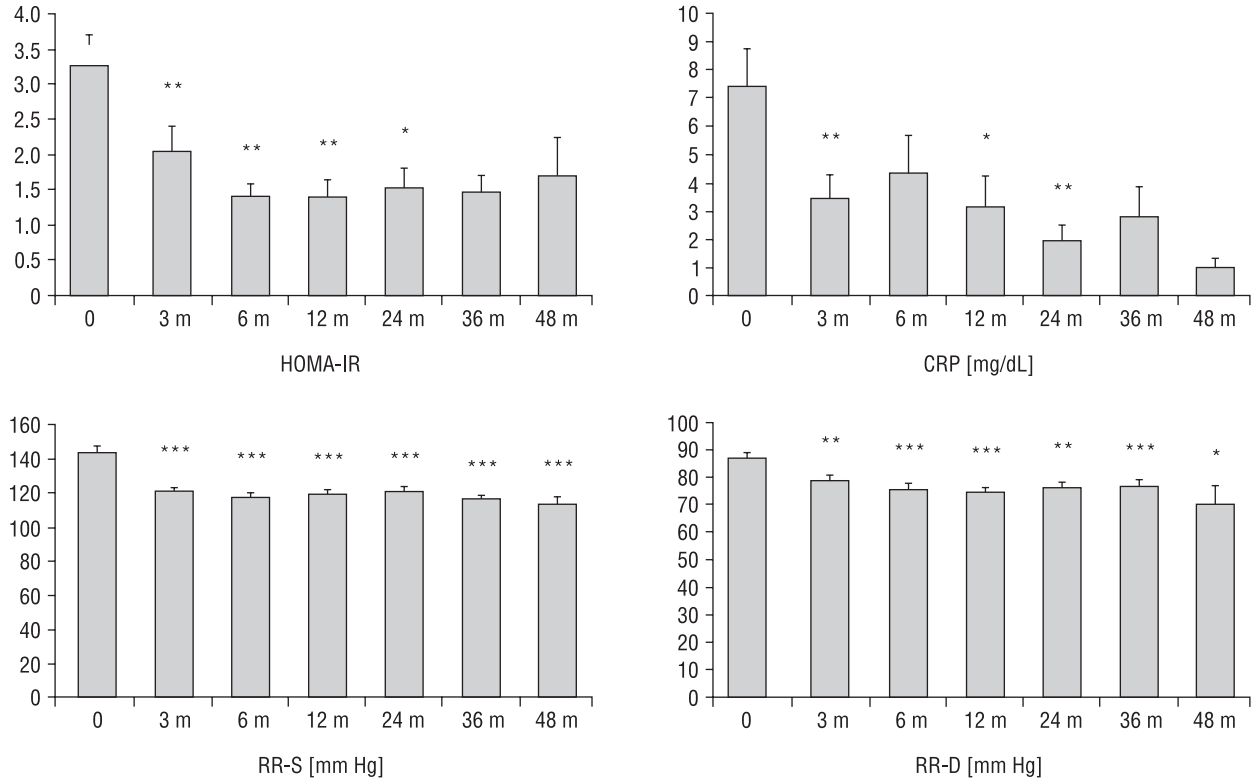

Figure 3. *Data concerning HOMA-IR, CRP, and systolic and diastolic blood pressure (RR-S, RR-D) in obese patients before and after surgery (m = months; x ± SEM; *p < 0.05; **p < 0.01; ***p < 0.001 vs. before surgery)*

Rycina 3. *Dane dotyczące wartości: HOMA-IR, CRP, skurczowego (RR-S) i rozkurczowego (RR-D) ciśnienia krwi u otyłych pacjentów przed i po leczeniu bariatrycznym (m = miesiące; x ± SEM; *p < 0,05; **p < 0,01; ***p < 0,001 v. przed operacją)*

The effectiveness of bariatric surgery has recently been studied in two meta-analyses [26, 29]. On average, surgical treatment of obesity results in 20–40 kg of weight loss (similar to our results) and a 10–15 kg/m^2 reduction in BMI [26, 29]. In the Swedish Obesity Study (SOS), the average ten-year weight loss was well over 19 kg [27]. This result was achieved despite the fact that vertical banded gastroplasty was the dominant procedure and only 5% of those who had a follow-up of ten years had a Roux-en-Y gastric bypass (which is superior to vertical banded gastroplasty regarding weight loss) [27]. After a period of 15 years, patients who had undergone laparoscopic gastric banding had lost 13±14% compared with the baseline weight. Corresponding weight losses 15 years after vertical banded gastroplasty and Roux-en-Y gastric bypass were 18 ± 11% and 27±12% respectively [28].

Few studies have compared weight loss between surgical procedures. In two randomised clinical trials collectively enrolling 231 patients, Roux-en-Y gastric bypass was compared with vertical banded gastroplasty [29–31]. Pooled results showed that at 12 and 36 months, patients assigned to Roux-en-Y gastric bypass lost substantially more weight than those assigned to vertical banded gastroplasty (42.43 kg versus 34.45 kg and 39.73 kg versus 30.65 kg at 12 and 36 months respectively) [29–31].

On the basis of these and other studies [32–34], it can be concluded that in regard to weight loss, Roux-en-Y gastric bypass is superior to vertical banded gastroplasty. Recently, laparoscopic adjustable gastric banding was compared to laparoscopic vertical banded gastroplasty in a randomized trial involving 100 patients [35]. In this study, excess weight loss was 58.9% three years after laparoscopic vertical banded gastroplasty and 39% three years after laparoscopic adjustable gastric banding [35].

Several studies using homeostatic model assessment have reported improvements in insulin sensitivity and β-cell function [36, 37]. These sets of data are substantiated by studies that have used euglycemic–hyperinsulinaemic clamp and i.v. glucose tolerance testing [38, 39]. Even normal weight individuals with increased amounts of abdominal adipose tissue can be metabolically obese, with insulin resistance and dyslipidaemia [40, 41].

Hypercholesterolaemia and hypertriglyceridaemia improve after surgical treatment of obesity, irrespective of the technique used [26]. Total and low density lipo-

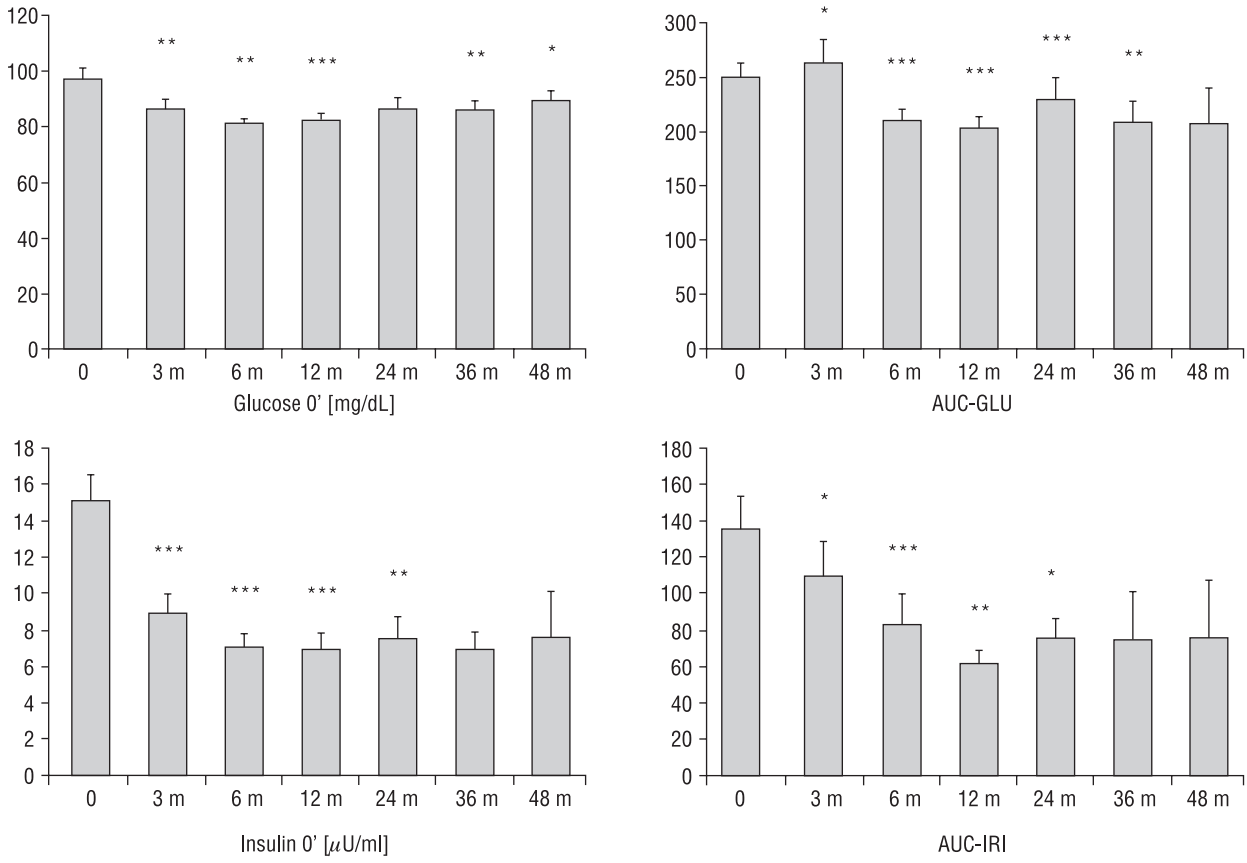

Figure 4. *Peripheral blood concentrations of glucose, insulin as well as glucose and insulin mobilisation after 75 g oral glucose (AUC-GLU, AUC-IRI) in obese patients before and after surgery (m = months; x ± SEM; *p < 0.05; **p < 0.01; ***p < 0.001 vs. before surgery)*

Rycina 4. *Stężenia: glukozy, insuliny oraz glikemii i insulinemii po podaniu 75 g glukozy doustnie (pole pod krzywą - AUC-GLU, AUC-IRI) w obwodowej krwi żylnej u otyłych pacjentów przed i po leczeniu bariatrycznym (m = miesiące; x ± SEM; *p < 0,05; **p < 0,01; ***p < 0,001 v. przed operacją)*

protein (LDL) cholesterol concentrations decreased with an average of 0.86 mmol/L (95% confidence interval (CI) 0.60–1.13 mmol/L) and 0.76 mmol/L (95% CI 0.46–1.06 mmol/L) respectively (26). While triglyceride concentrations decreased with an average of 0.90 mmol/L (95% CI 0.73–1.08 mmol/L), high density lipoprotein (HDL) cholesterol concentration showed no difference in a combined analysis of all surgical procedures (26). However, patients who underwent vertical banded gastroplasty (n = 253) or gastric banding (n = 623) showed an increase in concentration of HDL cholesterol of 0.13 mmol/L (95% CI 0.02–0.24 mmol/L) and 0.12 mmol/L (95% CI 0.04–0.20 mmol/L) respectively [26]. The study highlights another benefit concerned with surgery: a reduction of the prevalence of hypertension [26]. Of the surgically treated patients, 62% of those with hypertension recovered [26].

Leptin is the product of the obese (ob) gene and is generated predominantly in white adipose tissue [42]. It is involved in the maintenance of energy balance and body weight. In humans, peripheral blood leptin concentration is strongly correlated with the amount of body fat and body mass index [43]. The arcuate nucleus (ARC) of the hypothalamus serves as the leptin signalling centre. It is known that the insulin/leptin-arcuate nucleus of the hypothalamus axis regulates energy homeostasis through control of appetite and energy expenditure. Both hormones rise in direct proportion to adipose mass; they cross the blood-brain barrier and have receptors in the ARC [44]. The circulating leptin levels serve as a gauge of energy stores, thereby directing the regulation of energy homeostasis, neuroendocrine function, and metabolism. Persons with a congenital deficiency are obese, and treatment with leptin results in dramatic weight loss through decreased food intake and possible increased energy expenditure.

However, most obese persons are resistant to the weight-reducing effects of leptin [45]. Recent studies suggest that leptin is physiologically more important as an indicator of energy deficiency, rather than energy excess, and may mediate adaptation by driving increased food intake and directing neuroendocrine func-

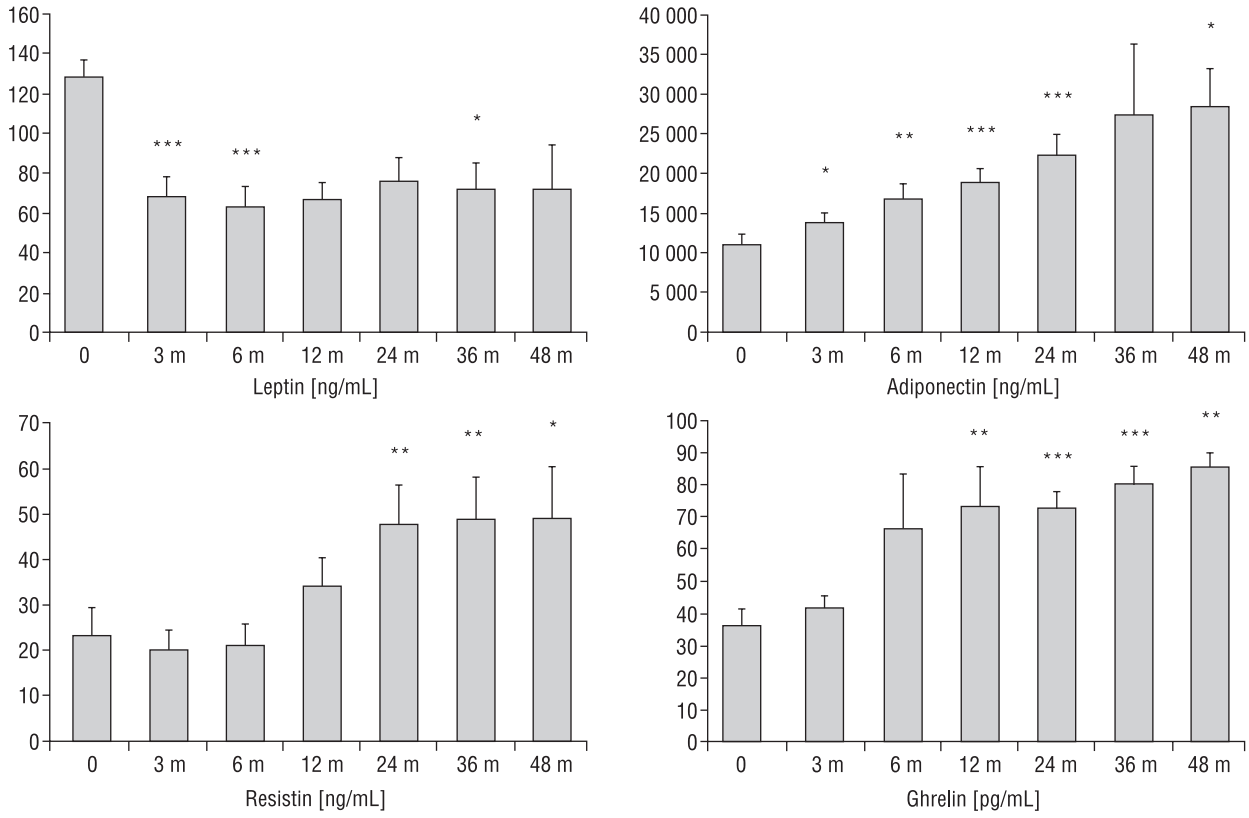

Figure 5. *Peripheral blood concentrations of leptin, adiponectin, resistin and ghrelin in obese patients before and after surgery (m = months; x ± SEM; *p < 0.05; **p < 0.01; ***p < 0.001 vs. before surgery)*

Rycina 5. *Stężenia: leptyny, adiponektyny, rezystyny i greliny w obwodowej krwi żylnej u otyłych pacjentów przed i po leczeniu bariatrycznym (m = miesiące; x ± SEM; *p < 0,05; **p < 0,01; ***p < 0,001 v. przed operacją)*

Table I. ***Positive correlations (months after surgery in brackets)***

Tabela I. ***Korelacje dodatnie pomiędzy badanymi parametrami (w nawiasach czas w miesiącach od operacji)***

Adiponectin	Ghrelin (6, 12); Total Cholesterol (0); HDL (0, 6, 12); LDL (0)
Resistin	Ghrelin (0, 24); RR S (24); RR D (0); Waist circumference (3, 24); BMI (3, 24); Triglycerides (24); CRP (24); Body mass (3, 24); Glucose AUC (12)
Leptin	RR S (12); RR D (12); Waist circumference (6, 24); BMI (0, 6, 12); HOMA-IR (12); Body mass (6, 12, 24); IRI 0′ (12, 24) IRI AUC (0)
Ghrelin	RR S (6, 24); RR D (24); HDL (6, 12); Triglycerides (0); CRP (3);
RR S	RR D (0, 3, 6, 12, 24); Glucose 0′ (0); Glucose AUC (0, 12)
RR D	Glucose AUC (0)
Waist circumference	BMI (0, 3, 6, 12, 24); LDL (24); Triglycerides (12, 24); HOMA-IR (6, 12, 24); Body mass (0, 3, 6, 12, 24); Glucose 0′ (6); IRI 0′ (6, 12, 24)
BMI	CRP (24); HOMA-IR (6, 12, 24); Body mass (0, 3, 6, 12, 24); IRI 0′ (6, 12, 24); IRI AUC (12)
Total cholesterol	HDL (0); LDL (0, 3, 6, 12, 24); Triglycerides (6, 24);
Triglycerides	HOMA-IR (3); Body mass (24;) Glucose 0′ (0, 3, 24); Glucose AUC (3, 6, 12, 24)
CRP	Body mass (24)
HOMA-IR	Body mass (6, 12, 24); Glucose 0′ (0, 3, 6, 12); Glucose AUC (0, 3, 6); IRI 0′ (0, 3, 6, 12, 24); IRI AUC (6, 24)
Body mass	Glucose 0′ (6, 12, 24); IRI 0′ (6, 12, 24);
Glucose 0′	Glucose AUC (0, 3, 6, 12, 24); IRI 0′ (0, 3, 12)
Glucose AUC	IRI 0′ (0, 3, 12); IRI AUC (24)

Table II. *Negative correlations (months after surgery in brackets)*
Tabela II. *Korelacje ujemne pomiędzy badanymi parametrami (w nawiasach czas w miesiącach od operacji)*

Adiponectin	Resistin (24); Waist circumference (6, 12, 24); BMI (6, 12, 24); Triglycerides (6); HOMA-IR (6); Body mass (12); Glucose AUC (6); IRI 0' (6, 12); IRI AUC (6, 12)
Leptin	Body mass reduction (12)
Ghrelin	HDL (24); Triglycerides (12);
Waist circumference	HDL (12, 24); IRI AUC (0)
BMI	HDL (12)
Total cholesterol	IRI AUC (3)
HDL	Triglycerides (6, 12, 24); HOMA-IR (6); Glucose AUC (12); IRI 0' (6); IRI AUC (12)
LDL	IRI AUC (3)
HOMA-IR	Body mass reduction (6, 12, 24);
Body mass	Glucose AUC (0); IRI AUC (0)

tion to convert energy, such as inducing hypothalamic hypogonadism to prevent fertilisation [45]. Current studies are investigating the role of leptin in weight-loss management because persons who have recently lost weight have relative leptin deficiency that may drive them to regain weight. Leptin deficiency is also evident in patients with diet- or exercise-induced hypothalamic amenorrhea and lipoatrophy [45].

According to a number of case studies, serum leptin levels decrease with weight loss after bariatric surgery [46–49]. The decrease in leptin peripheral blood concentration, as observed in our study, was beyond the expected value based on body composition [47, 50]. In a case-control study, serum leptin levels were lower in weight-stable RYGB patients 35 months after surgery, compared with BMI-matched controls [51]. Given the putative adipostatic role of leptin, it is possible that relative hypoleptinaemia may also play a role in weight regain.

Adiponectin (total and low molecular weight forms) is another adipocyte-derived cytokine that plays an important role in regulating energy homeostasis, protects the arterial wall against atherosclerosis and increases insulin sensitivity. Adiponectin is found in high concentrations in the peripheral circulation [52], and its circulating levels are diminished in obese patients and those with type 2 diabetes [53]. Moreover, adiponectin concentration is inversely associated with central or overall adiposity [54, 55] and is negatively associated with fasting insulin levels at baseline and may also participate in a regulation of lipid metabolism at baseline [56].

Resistin, a plasma protein, induces insulin resistance in rodents. Whereas rodent resistin is made in adipocytes, in humans its major source are the macrophages. Therefore resistin may be an inflammatory marker of atherosclerosis in humans [57–59].

For a long time it has been known that obesity is linked to insulin resistance. In recent years, many investigators have reported that adipocytes secrete a group of bioactive peptides called adipocytokines, which play a pivotal role in energy homeostasis by affecting insulin sensitivity, glucose and lipid metabolism, food intake and inflammation. Evidence from animal and human studies suggests that adiponectin plays an important role in insulin sensitivity [27, 28, 60–62] inflammation [63], atherogenesis [64, 65], lipid metabolism [27, 66], and thus influences hyperlipidaemia and cardiovascular disease [63]. The relationship between adiponectin and insulin sensitivity has been established in an animal model in which adiponectin administration reversed insulin resistance in lipoatrophic mice [26]. Moreover, the levels of adiponectin are lower in patients with type 2 diabetes or insulin resistance [65, 66] and higher in humans treated with thiazolidinediones [67, 68]. Adiponectin has recently been observed not to be a major determinant of weight loss-induced improvements in insulin sensitivity [56].

Although obesity may be linked to resistin, the role of resistin in humans is still controversial. Conflicting results of the associations between resistin and BMI and measures of insulin resistance have been reported. Recent results obtained by Owecki et al. [69] and Yuan et al. [70] did not reveal any relationship between resistin concentration and insulin resistance. Others proposed that resistin plays a role [71, 72] in obesity-mediated insulin resistance and is also a proinflammatory molecule [53, 73]. Therefore, it seems that resistin may be linked to inflammation and obesity and, indirectly, to insulin resistance [74]. Moreover, it has been shown that increasing levels of leptin, and decreasing levels of adiponectin, correlate [75]) with worsening insulin resistance in obese individuals. Furthermore, it has also been

shown that leptin levels decrease, and adiponectin levels rise, following bariatric surgery. These changes correlate with weight loss and improvement in insulin secretion [75].

Marker of chronic inflammation (CRP) decreased with time in our subjects treated by VBG, which may be partly related to a decrease in arterial hypertension [76] or a decrease of fat mass and increase of adiponectin levels [77].

The changes in energy intake, and perhaps even energy expenditure, seen after bariatric surgery may be affected by changes in gut and adipocyte hormones [19]. This 28-aminoacid peptide has been found to be essential for its effect on the appetite [78]. About two thirds of circulating ghrelin is thought to be produced by the stomach, but ghrelin-producing cells have also been found in the duodenum, ileum, caecum and colon. The primary regulator of plasma ghrelin levels is thought to be calorie intake [78]. There is a reversible suppression of ghrelin associated with obesity, such that ghrelin levels normalise after diet-induced weight loss or after bariatric surgery [78].

Gut hormones such as ghrelin, peptide YY (PYY), and glucagon-like-peptide (GLP)-1 have an important role in governing satiety [78]. Of these, ghrelin is an orexigenic peptide, secreted primarily by the enteroendocrine cells in the fundus of the stomach and acts through the hypothalamus [79–82]. Ghrelin is a natural ligand of the growth hormone secretagogue receptor, and has been demonstrated to enhance appetite, reduce fat utilisation and promote adiposity following central or peripheral administration to both rodents and humans [83]. Serum concentrations of ghrelin typically increase on fasting and decrease following food intake. Therefore, abnormal ghrelin regulation may influence the development of obesity.

Ghrelin levels have been found to increase after GB surgery [84, 85], although transiently in the case of one study [83], and suggest a role in weight regain after this procedure. Gastric secretion of ghrelin may be influenced by numerous factors, such as administration of glucose and insulin, activation of somatostatin receptors, the cholinergic system, GLP-1 (glucagon-like peptide 1), PYY (peptide YY), oxyntomodulin, thyroid hormones, and testosterone. Ghrelin levels are inversely related to BMI, with higher values observed in anorexia nervosa and cachexia, and lower levels in obesity. An exception to this rule is Prader-Willi syndrome, in which obesity is associated with increased ghrelin concentrations in serum. Changes in body weight are accompanied by changes in ghrelin levels, which increase with weight loss and decrease with weight gain [78]. Weight loss in RYGB surgery patients, however, is associated with a decrease in ghrelin levels, compared with weight loss after GB, biliopancreatic diversion, or conventional weight loss treatment [86–89], and has often been considered to contribute to the marked efficacy of the RYGB, compared with other procedures. This finding has, however, not been universally observed [90, 91]. The conflicting data may be due to the different surgical techniques that affect the functional integrity of the gastric fundus from which ghrelin is mostly secreted. Whether the changes in ghrelin levels in bariatric surgery patients are maintained in the long term should be evaluated. In patients in our study, the peripheral blood concentrations of ghrelin increased after VBG.

During VBG surgery, no part of the gastrointestinal tract acting as a source of adipocytokines was removed. The positive changes of almost all the post-surgery laboratory and clinical findings are probably related to the effect of a restriction of food intake. The positive or negative correlations revealed between insulin, HOMA-IR, leptin, adiponectin and anthropometric measurements after vertical banded gastroplasty suggest that a number of these factors are related to changes of body composition and metabolic function of patients receiving surgical treatment for severe obesity.

Conclusions

1. Vertical banded gastroplasty is still a valuable method of treating severe obesity leading to significant decrease of body weight and improvement of the main parameters of the metabolic syndrome in a few months after surgery.
2. A partial reverse in anthropometric parameters, as well as measures of insulin sensitivity, and adipokines at two (and four) years after bariatric surgery give very promising indications against atherosclerosis and other health risks.

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