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The Effect of Noninvasive Bariatric Surgery on the Levels of Certain Adipokines and Atherosclerosis Risk Factors in Patients with Metabolic Syndrome

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ABSTRACT

Objective: Besides glucose intolerance, dyslipidemia, and hypertension, visceral obesity is one of the most important atherogenic pathological factors in patients with metabolic syndrome (MetS). The aim of this study is to examine whether weight loss following BioEnterics Intragastric Balloon (BIB-system) therapy affects adipokine concentration and atherosclerosis risk factor profile in patients with MetS.

Methods: The study group comprised 30 patients (17 female, BMI = 38.5 ± 8.6 kg/m^2; 13 male, BMI = 43.3 ± 7 kg/m^2) with MetS qualified to BIB-system therapy. The control group included 18 age matched healthy volunteers (10 female, BMI = 23.3 ± 2.8 kg/m^2 and eight male, BMI = 27.3 ± 0.9 kg/m^2). Biochemical analyses of blood samples and anthropometric measurements were conducted, before and after six-month BIB system therapy.

Results: BIB therapy resulted in a significant drop in body weight, and body fat percentage, and in BMI, VAI, WHtR, BAI, TG, glucose, hsCRP, and leptin levels. In addition Tc/HDL, LDL/HDL, TG/HDL, and leptin/adiponectin ratios fell significantly, and adiponectin concentration increased. All anthropometric parameters apart from Tc and hsCRP, were significantly different post-therapy compared to healthy controls. The therapy induced downregulation of hsCRP which was positively correlated with the reduction in body weight, BMI and BAI. The decrease in leptin concentration correlated positively with the fall in total cholesterol and body weight. The fall in leptin/adiponectin ratio positively correlated with the downregulation of BAI and body fat.

Conclusion: BIB therapy appears to have beneficial effects on MetS. This is indicated by amelioration of the pro-inflammatory status related to obesity, demonstrated by an improved lipid profile significant downregulation of hsCRP concentration following therapy.

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BIB system; metabolic syndrome; atherosclerosis; risk factors; adipocytokines

Introduction

Obesity is a chronic disease defined as the increase in body weight resulting from excess adipose tissue accumulation. The highest risk of comorbidities is associated with the central (visceral) type obesity. The combination of central obesity with glucose intolerance, increased blood triglycerides, low HDL levels and hypertension has been defined the metabolic syndrome (MetS) (1). Patients with MetS present various symptoms including insulin resistance, hypertension and lipid abnormalities leading to cardiovascular diseases, heart failure and type 2 diabetes. Besides insulin resistance, one of the most important pathological factors which favors the development of atherosclerosis is visceral obesity (2). Adipose tissue is known to be a source of energy; however it also directly releases or indirectly stimulates the production of, a range of substances influencing various pathological states including elevated blood pressure (e.g., angiotensinogen), insulin resistance (e.g., leptin, resistin), a pro-inflammatory state (e.g., C-reactive protein, tumor necrosis factor-α, interleukin-6, monocyte chemotactic protein-1), or a pro-thrombotic state (e.g., fibrinogen, plasminogen activator inhibitor) (3). Free fatty acids (FFA) released from abdominal fat move directly to the liver, where they impair glucose tolerance affect lipid metabolism by increasing very-low and low-density lipoproteins (VLDL and LDL) production, and triglyceride (TG) concentration and reducing high density lipoprotein (HDL) level (4). The presence of these hallmarks of visceral obesity promote atherosclerosis and thus considerably elevate the risk of cardiovascular diseases in MetS patients.

Among MetS patients, considerable attention has been focused on the role of adipokines such as leptin and adiponectin in the regulation of metabolism and their association with atherosclerosis (5). These hormones govern energy consumption, food intake and thermogenesis. Leptin regulates appetite and body weight by means of satiety receptors and the hypothalamus, and it is believed that the increased appetite and weight observed in obese patients is linked to so-called "leptin resistance" (6). Insulin stimulates leptin synthesis and, conversely, leptin modulates insulin secretion. Numerous studies confirm that leptin plays a role in the chronic pro-inflammatory state observed in MetS and its complications such as atherosclerosis (7). This chronic low-grade inflammatory process deteriorates the microvasculature

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and arteries in patients with MetS and diabetes through its influence on the endothelium, resulting in a greater risk of atherogenesis and diabetic foot syndrome (8, 9). These states, chronic inflammation and atherogenesis, are regarded as the two most harmful consequence of the increased plasma leptin level observed in people with obesity (10). They are also strongly influenced by adiponectin: an adipokine that improves glucose metabolism and has anti-inflammatory and anti-atherogenic effects, and whose level in plasma is reduced in patients with obesity (11, 12). Hence, the leptin/adiponectin ratio is used as a predictor of atherosclerosis in obese, diabetic and MetS patients (13).

A long-term physical exercise program in patients with MetS significantly improves glycemic control, blood lipids profile and other cardiovascular risk factors (14); in addition, traditional approaches consisting of the combination of a weight-loss diet, active lifestyle, pharmacological therapies and behavioral therapy also demonstrate relatively low long-lasting efficacy against obesity. Therefore, there is growing interest in the use of bariatric surgery to treat morbid obesity by supporting long-term weight loss; the approach has been found to decrease overall mortality compared with matched controls and improve glucose tolerance, and hypertension (15, 16). However, these undeniably positive effects associated with bariatric surgery are tempered by a relatively high frequency of the complications varying from 2% to 5% of cases, depending on the procedure type (17). As a result, many patients who repeatedly attempt weight reduction without success choose to undergo noninvasive bariatric surgery using the BioEnterics Intragastric Balloon (BIB-system). The BIB System is designed to assist weight loss by partially filling the stomach with a balloon for at least six months, a procedure that induces satiety. Despite its low or moderate effectiveness (18, 19) most studies report BIB therapy to be associated with no or very rare severe complications compared to bariatric surgery (17, 20). Therefore, BIB therapy has been widely recognized as a relatively safe method of treatment of obese patients with severe comorbidities or a form of preoperative treatment of bariatric patients with morbid obesity.

The aim of this study was to examine whether weight loss, reflected in changes in anthropometric parameters after BIB System therapy affects adipokine concentration and atherosclerosis risk factor profile and improves the metabolic balance in patients with metabolic syndrome.

Materials and methods

Subjects

The study group comprised 30 patients selected from a group 90 patients with obesity (BMI $>$ 30 kg/m^2) who were qualified for noninvasive bariatric surgery with the BIB System. The 30 patients (17 female, aged 38.2 ± 13.7 and BMI $= 38.5 \pm 8.6$; 13 male, aged 44.2 ± 9.3 and BMI $= 43.3 \pm 7$) were classified with metabolic syndrome according to the generally-accepted criteria established by Adult Treatment Panel III report (ATP III) of the National Cholesterol Education Program (21). All demonstrated at least three of the five following medical conditions: abdominal obesity given as waist circumference; men $>$102 cm, women $>$88 cm, TG $\geq$ 150 mg/dl, HDL-cholesterol; men $<$40 mg/dl, women $<$50 mg/dl, blood pressure $\geq$ 130/$\geq$85 mm Hg, fasting glucose $\geq$110 mg/dl.

The control group included 18 healthy volunteers: 10 female, aged 39.1 ± 13, BMI $= 23.3 \pm 2.8$; 8 male, aged 38.1 ± 14.0, BMI $= 27.3 \pm 0.9$.

Study design

Anthropometric measurements including height, weight, waist, hip circumference were taken. Skin fold measurements was taken in four regions (ventral, anterior femoral, triceps, and above the pelvis) to estimate fat percentage. BMI was calculated as body weight (kg)/height (m)^2. Waist/hip (WHR), and waist/height (WHtR) rations were calculated. Body adiposity index (BAI) (22) was calculated according to the formula:

$$\mathrm{BAI} = \left[\text{hip circumference(cm)}/\text{height(m)}^{1,5}\right] - 18$$

Visceral adiposity index (VAI) was calculated according to the formulas (23):

$$\mathrm{VAI} = [\mathrm{WC}/39.68 + (1.88 \times \mathrm{BMI})] \times (\mathrm{TG}/1.03) \times (1.31/\mathrm{HDL}) \text{for male participants,}$$

$$\mathrm{VAI} = [\mathrm{WC}/36.58 + (1.89 \times \mathrm{BMI})] \times (\mathrm{TG}/0.81) \times (1.52/\mathrm{HDL}) \text{for female participants.}$$

Detection of biochemical parameters

Peripheral blood samples were drawn after at least 12 h overnight fasting on two occasions; before balloon implantation and on the day the balloon was removed (i.e., after six months).

Serum samples were obtained after 30 min centrifugation of blood samples at 2500 $\times$ g at room temperature. The obtained sera were divided into two samples: the first was directly used to determine biochemical parameter, while the second was stored at $-70\,^{\circ}$C for leptin, adiponectin, and hsCRP assessment.

Fasting serum total cholesterol (Tc), triglycerides (TG), and high-density lipoprotein cholesterol (HDL) levels were measured using an Alpha Diagnostics automatic analyzer (Warsaw, Poland). The serum levels of low-density lipoprotein (LDL) cholesterol were calculated using Friedewald's equation (24).

Serum leptin (Quantikine: Human Leptin Immunoassay, R&D Systems, Minneapolis, USA), adiponectin (human total adiponectin/Acrp30, Minneapolis, USA) levels were tested using commercial sandwich ELISA kits according to the manufacturer's instruction.

Tc/HDL, LDL/HDL, TG/HDL, and leptin/adiponectin (lep/adipo) rations were also calculated.

Serum high sensitive C reactive protein (hsCRP) concentrations were measured by immunoturbidimetry using an AU 680

Table 1. Anthropometric Parameters in Patients with Metabolic Syndrome Subjected to BIB Therapy and the Percentage Changes Associated with BIB.

Variable	Control group $N = 18$	Pre-BIB, $N = 30$ Med [25%;75%]	Post-BIB, $N = 30$ Med [25%;75%]	% changes Med [25%;75%]
Weight (kg)	68.9 [63.0;90.0]	113.5 [100.5;136] *$p < 0.00001$	100 [88;114] *$p < 0.0001$ **$p < 0.0001$	−13.6 [−16.7; −8.3]
BMI (kg/m^2)	26.2 [22.3;27.6]	38.9 [34.3;44.1] *$p < 0.000001$	34.5 [28.7;39.1] *$p < 0.00001$ **$p < 0.0001$	−11.9 [−17.9; −7.5]
Fat %	29.3 [26.0;32.8]	48.3 [41;55.9] *$p < 0.000001$	34.9 [29.3;37.1] *$p < 0.04$ **$p < 0.00001$	−29.9 [−37.7; −23.6]
WHR	0.83 [0.74;0.9]	0.9 [0.9;1.0] *$p < 0.003$	0.9 [0.86;1.0] *$p < 0.01$	−0.58 [−6.6; 0.0]
WHtR	0.5 [0.45;0.5]	0.69 [0.62;0.76] *$p < 0.0000001$	0.64 [0.56;0.67] *$p < 0.0000001$ **$p < 0.000001$	−11.4 [−15.9; −7.1]
VAI	0.67 [0.49;1.36]	2.83 [1.83;4.4] *$p < 0.000001$	1.8 [1.3;2.4] *$p < 0.00002$ **$p < 0.01$	−33.8 [−58.1; −8.6]
BAI	26.6 [23.9;29.8]	37.4 [33.8;42.8] *$p < 0.0000001$	32.1 [29.9;37.8] *$p < 0.00002$ **$p < 0.02$	−11.9 [−19.3; −10.2]

BMI, body mass index; WHR, waist-hip ratio; WHtR, waist-to-height ratio; VAI, visceral adiposity index; BAI, body adiposity index.
All variables are reported as median (Med), Q1 (25%), Q3 (75%).
*vs control.
**vs pre-BIB.

Clinical Chemistry Analyzer (Beckman Coulter, Pasadena, California, USA).

Statistics

The parameters tested before and after BIB and in the control group were expressed as medians and 25 and 75 percentiles of absolute values (IQR). The groups were compared using the Mann–Whitney *U*-test for unpaired data and Wilcoxon's test for paired data. Correlations between the studied parameters expressed as percentages of changes deriving from the therapy were analyzed using Spearman's test. Values of $p < 0.05$ were considered significant.

The study was approved by the Bioethics Committee of the Medical University of Lodz (no. RNN/20/11/KB).

Written informed consent was obtained from the participating subjects.

Results

Changes of anthropometric parameters associated with BIB are displayed in Table 1. BIB therapy, resulted in a significant drop in the body weight, BMI, VAI, WHtR, BAI and percentage of body fat. No change in WHR was observed.

Significant decreases were observed in body weight (13.6%; $p < 0.001$) and BMI (11.9%; $p < 0.0001$) resulting mainly from a marked drop of body fat percentage (29.9%; $p < 0.00001$). Among all the parameters measuring visceral type obesity, WHtR significantly ($p < 0.0000001$) fell after the BIB therapy. A similar, but less significant drop was observed in VAI ($p < 0.01$) and BAI ($p < 0.02$). No significant difference in WHR was observed.

All the anthropometric parameters after therapy remained significantly higher than those of healthy controls.

BIB implementation resulted in a significant down-regulation of TG, hsCRP, and leptin concentrations and Tc/HDL, LDL/HDL, leptin/adiponectin ratios. It was also associated with a marked rise of adiponectin concentration (Table 2). All biochemical parameters, both before and after the treatment, were significantly different than those of healthy controls, except Tc and hsCRP after treatment.

A significant drop of TG (36.3%; $p < 0.0001$) resulted in a marked decrease in TG/HDL ratio (−30.7%; $p < 0.0003$). The therapy induced a 22.8% increase of adiponectin and a 35.5% decrease of leptin concentration, resulting in a significant drop in the leptin/adiponectin ratio of 56.2%.

A significant decrease of hsCRP concentration was observed after the BIB therapy (by 40.9%); this appears to be a beneficial effect of the improved biochemical imbalance after surgery (Table 2).

A decrease was observed in the leptin or leptin/adiponectin ratio expressed as percentage reduction; this positively correlated with the percentage reduction associated with BIB therapy ($Rs = 0.77$, $p < 0.05$; $Rs = 0.68$, $p < 0.05$ respectively), BMI ($Rs = 0.38$, $p < 0.05$), BAI ($Rs = 0.48$, $p < 0.05$; $Rs = 0.56$, $p < 0.05$ respectively), body fat ($Rs = 0.67$, $p < 0.05$ vs leptin/adiponectin) and total cholesterol ($Rs = 0.38$, $p < 0.05$).

The reduction in hsCRP level positively correlated with the percentage reduction of body weight, BMI and BAI after treatment ($Rs = 0.57$, $p < 0.05$, $Rs = 0.66$, $p < 0.05$ and $Rs = 0.67$, $p < 0.05$, respectively), Table 3.

Discussion

Various types of bariatric surgery have been employed as therapy for obese patients, and these are well known to be effective at reducing weight and improving metabolic parameters (25, 26). Bariatric procedures, in addition to facilitating long-term loss of body weight, can also exert a beneficial influence on the value of various metabolic parameters

Table 2. Biochemical Parameters of Blood and Adipokine Concentration in Patients with Metabolic Syndrome Subjected to BIB Therapy and the Percentage Change Associated with BIB.

Variable	Control group $N = 18$	Pre-BIB, $N = 30$	Post-BIB, $N = 30$	% changes
	Med [25%;75%]	Med [25%;75%]	Med [25%;75%]	Med [25%;75%]
Tc (mg/dl)	179 [150;210]	196 [172;229]	179 [158;220]	−5.4 [−16.1;−5.6]
LDL (mg/dl)	95 [79;114]	133 [111;156]	111 [96;151]	−1.9 [−27;−13.8]
		*$p < 0.01$	*$p < 0.05$	
HDL (mg/dl)	66 [50;75]	41 [38;48]	45 [40;52]	+14.2 [+12.2;+31.7]
		*$p < 0.000003$	*$p < 0.0001$	
TG (mg/dl)	62 [50;120]	193 [121;246]	113 [92;161]	−36.3 [−54.8;−15.8]
		*$p < 0.00001$	*$p < 0.003$	
			**$p < 0.0001$	
Tc/HDL	2.95 [2.2;3.35]	4.85 [4.38;5.8]	3.8 [3.0;5.1]	−15.2 [−29.6;−9.4]
		*$p < 0.00003$	*$p < 0.001$	
			**$p < 0.03$	
LDL/HDL	1.7 [1.1;1.9]	3.32 [2.38;3.97]	2.6 [1.6;3.4]	−15.3 [−27.9;−14.5]
		*$p < 0.00001$	*$p < 0.0004$	
TG/HDL	0.89 [0.69;2.36]	4.37 [2.75;6.17]	2.45 [1.8;3.7]	−30.7 [−54.4;−14.2]
		*$p < 0.000002$	*$p < 0.0004$	
			**$p < 0.0003$	
Glucose (mg/dl)	80 [75;88]	110 [96;128]	91 [87;102]	−15.5 [−28;−3]
		*$p < 0.00001$	*$p < 0.0003$	
			**$p < 0.0001$	
Leptin (ng/ml)	3.9 [2.4;8.1]	38.3 [19.0;51.8]	22.7 [6.1;36.8]	−35.5 [−65.9;−22.6]
		*$p < 0.0001$	*$p < 0.002$	
			**$p < 0.04$	
Adiponectin (μg/ml)	10.9 [7.2;15.2]	4.7 [3.3;6.4]	6.0 [4.6;7.1]	+22.8 [+1.6;+53.1]
		*$p < 0.001$	*$p < 0.01$	
			**$p < 0.02$	
Lep/adipo (×1000)	0.44 [0.24;0.64]	6.1 [2.9;9.5]	2.4 [1.2;4.2]	−56.2 [−79.3;−42.1]
		*$p < 0.0001$	*$p < 0.001$	
			**$p < 0.01$	
hsCRP (mg/l)	0.9 [0.6;1.9]	3.3 [1.5;5.2]	1.85 [1.0;3.5]	−40.9 [−53.8;−23.3]
		*$p < 0.004$	**$p < 0.01$	

Tc, total cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglycerides; Tc/HDL, total cholesterol/high density lipoprotein ratio; LDL/HDL, low density lipoprotein/high density lipoprotein ratio; TG/HDL, triglycerides/high density lipoprotein ratio; Lep/adipo, leptin/adiponectin ratio.
All variables are expressed as medians (Med), Q1 (25%), Q3 (75%).
*vs control.
**vs pre-BIB.

Table 3. Correlations Between the Changes in Anthropometric Indices and Biochemical Parameters.

	Weight (kg)	BMI (kg/m^2)	% fat	Tc (mg/dl)	BAI
Leptin (ng/ml)	0.77	0.38	–	0.38	0.48
Leptin/adiponectin ratio (×1000)	0.68	–	0.67	–	0.56
hsCRP (mg/l)	0.57	0.66	–	–	0.67

Value of correlation coefficients (*Rs*) in Spearman's test ($p < 0.05$).

causing remission of MetS and its manifestations, such as atherosclerosis, diabetes mellitus and dyslipidemia (27).

Although bariatric operations are characterized by low hospital morbidity, they are still invasive and expensive procedures requiring a general anesthetic. For many obese patients who for various reasons are not ready to undergo bariatric surgery, the alternative is to implant a stomach balloon (BIB-system). However, little data exists on the effectiveness of intragastric balloon therapy in obese patients with MetS (18, 20): most studies focus on the usefulness of this method in reducing and maintaining weight, its safety, tolerance and the optimum way to prepare patients for bariatric surgery (28, 29).

Only few publications relate to the metabolic effect of BIB therapy with regard to lipid parameters, glucose, adipose-derived bioactive factors such as adipokines and inflammatory process indicators such as CRP. Our experiment not only examines the influence of BIB-system on the reduction of weight and body fat content described by anthropometric parameters but also examines its influence on the lipid and carbohydrate metabolism as well as the metabolic activity of adipose tissue.

Before treatment all study participants with MetS demonstrated significantly increased biochemical parameters in the blood; however, total cholesterol, HDL and adiponectin levels were significantly lower than healthy controls. As these parameters have been recognized as important atherosclerosis risk indices (8, 30), the improvement in these metabolic parameters observed in the present study, along with loss of body weight after BIB-system treatment, seems very promising. The loss of body weight was reflected in the reduction of anthropometric parameters (except WHR), which indicates that BIB treatment led to a reduction in percentage of body fat and adipose tissue content. Our results have been confirmed by other authors: Colquitt et al. report that any improvement of lipid parameters in patients undergoing any bariatric surgery depends on the lost mass of fat (31).

Weight reduction following the implantation of gastric balloon occurs as an effect of limiting food intake due to reduced stomach volume and delayed gastric emptying. A key role is also played by centrally-caused satiety resulting from the stomach walls being stretched, which stimulates the vagus nerve receptors and brain centers responsible for satiety, as well as changes in the activity of gastrointestinal hormones and neuropeptides, which affects appetite control (32). Weight loss resulting from a reduction in the total

amount of calories consumed results in the modification in the expression of adipogenic genes such as the PPAR receptor (Peroxisome proliferator-activated receptor) gene (33). Miyazaki et al. report that PPAR receptor agonists promote the transformation of preadipocytes into better functioning adipocytes in visceral and subcutaneous fat deposits (34) and promote the apoptosis of hypertrophic and dysfunctional adipocytes. This mechanism may play an essential role in improving metabolic processes in fat-related diseases like MetS. Another likely mechanism for the positive metabolic effect of a low-calorie diet includes its effects on the cannabioid receptor (CB)-1. Decreased adipogenesis associated with hypocaloric diets occurs as a result of the decreased appetite promoted by CB-1 receptor antagonists. Blocking the CB-1 receptor improves fat functions which is reflected in the improvement of glucose, TG, HDL and LDL metabolism (35).

BIB-system therapy induced amelioration of the pro-atherogenic indices despite the fact that only post-therapy hsCRP levels were similar to those observed in healthy controls. Knowing the consequences of increased concentrations of hsCRP, reflecting low- grade systemic inflammation, the observed significant down-regulation of hsCRP concentration, i.e., by 40.9% may have a very beneficial effect on the risk of atherosclerosis and on the biochemical imbalance noted in patients with obesity and metabolic syndrome (36, 37). It has been suggested that the low-grade inflammation observed in patients with MetS may significantly disturb atheroprotective activities of HDL (8). Therefore, although no significant increase in HDL concentration was observed in our patients after therapy, the removal of pro-inflammatory signals may nevertheless ameliorate the pro-atherogenic conditions. Moreover, the fact that the reduction of body weight, BMI and BAI observed in our patients following BIB therapy was positively correlated with downregulations of hsCRP confirms that the central obesity noted in the MetS patients had a pro-inflammatory effect (38, 39). Similar relations between the concentration of CRP and BMI have been described by Yatsuya (40).

Visceral obesity was the most common condition presented by our patients with MetS, being visible in 100% of cases; it is also a key feature of MetS besides hypertension, glucose intolerance, high triglyceride levels and low HDL (1). The key predisposing factor of MetS may well be obesity, as almost 50% of patients with Metabolically Healthy Obesity develop MetS in long-term follow-up and demonstrate a high risk of cardiovascular disease (41). The abnormal accumulation of the visceral adipose tissue has been suggested the primary causation of metabolic imbalance and is a primary target for research (42). Despite this, WHR, the simplest indicator of a central-type obesity, was significantly higher in patients before treatment compared to controls, and did not change after therapy; a very significant drop in VAI value was observed (by 33.8%), which suggests that was a decrease of visceral adipose tissue fraction has the most significant influence on lowering cardio metabolic risk in patients (23). This suggestion is supported by the marked drop of WHtR and BAI which have also been recognized as measures of the risk of heart attack or stroke (43). The therapy induced a reduction in most indicators of visceral obesity; this may have contributed to the metabolic improvement and changes in adipokine concentration noted in all our patients.

Our results demonstrate that noninvasive bariatric surgery (BIB-system) resulted in a significant weight and body fat loss reflected by an improvement in the majority of anthropometric parameters such as BMI, WHtR, VAI and BAI. Reduction of body weight was accompanied by amelioration in lipid parameters, glucose and various inflammatory markers as well as leptin and adiponectin levels. Similar results were obtained by other authors. Crea et al. described the effect of gastric balloon implantation on MetS parameters; during a one-year follow-up, they report a reduction in the incidence of type 2 diabetes, hypertriglyceridemia and hypercholesterolemia (19). In turn, Fuller et al. note 30% reduction in the incidence of MetS in obese patients three months after BIB-system implantation (44).

Increased plasma leptin level and leptin/adiponectin ratio, and decreased adiponectin levels, in obesity and related pathologies has been reported to promote both inflammation and atherogenesis (10). Elevated leptin concentration is considered a strong predictor of cardiovascular diseases, diabetes and MetS. There is considerable evidence that leptin accelerates atherogenesis by the stimulation of endothelial cells to generate reactive oxygen species (ROS), and synthesize and secrete monocyte chemoattractant protein-1 (MCP-1), and increase cholesterol uptake by macrophages (3, 45, 46). Inflammatory and infectious stimuli increase the plasma concentration of leptin parallel to the intensity of inflammation.

Although the importance of leptin as an independent MetS predictor is widely accepted, its relationship with other features of the metabolic syndrome remains ambiguous. Some studies show that leptin concentration shows strong correlations with waist circumference and abdominal obesity independent of BMI; however, as also indicated by our present findings, it has been found to demonstrate only a weak correlation with lipid profile (47). Our findings indicate only a weak correlation between changes in leptin and total cholesterol concentration after BIB-system procedure, but a very strong correlation between leptin and loss of weight. Yun et al., demonstrate that regardless of obese or non-obese weight status, the reduction of leptin levels may exert a protective effect against MetS, regardless of weight loss (48). Other studies describe a strong positive relationship between leptin concentration and obesity, hyperinsulinemia and insulin resistance, and only a small association with other MetS features (49).

Like leptin, adiponectin is an adipose-derived plasma protein; however, its biological effect is that opposite. Our research, and that of other authors, show that, unlike most adipose-derived factors, its decreased serum level in obese patients rises simultaneously with the loss of body weight and fat content. However, while adiponectin levels have been found to increase with the loss of body weight achieved by diet, bariatric surgery or, as in our experiments,

after BIB-system therapy, no such rise is associated with liposuction. This is probably a result of liposuction treatment removing only the subcutaneous fat tissue without reducing visceral tissue (50, 51). The decrease in leptin concentration and increase in adiponectin concentration observed in our patients after BIB surgery is reflected in the lept/adipo ratio.

To conclude, BIB therapy was found to be associated with a significant improvement in anthropometrical indices and biochemical parameters in patients, with no observed side effects. This finding supports the value of this kind of treatment in patients with MetS; nevertheless, little proven data exists regarding the long-term follow-up after the BIB-system therapy, and hence its long-lasting effects are uncertain (18, 19). As a minimally-invasive treatment of obesity, the BIB-system has been found to offer other beneficial effects on anthropometric parameters, glucose intolerance, metabolic disorder and certain hormone concentrations, and these are addressed in other research reports (52, 53).

Conclusions

BIB-system therapy appears to have a beneficial effect on obesity in patients with MetS. Its use also results in improvement of the lipid metabolism, leptin and adiponectin concentration and normalization of hsCRP, reflecting amelioration of the pro-inflammatory status related to obesity, these being consequences of the effect of central obesity on the metabolism.

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