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Trabajo Original

Obesidad y síndrome metabólico

Obesity, endothelial function and inflammation: the effects of weight loss after bariatric surgery

Obesidad, inflamación y función endotelial: efectos de la pérdida de peso tras cirugía bariatrica

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Abstract

Objective: Obesity is associated with a high risk for atherosclerotic cardiovascular disease. There is a causal association between obesity, inflammation, insulin resistance (IR) and endothelial dysfunction. The aim of this study was to evaluate changes in IR, proinflammatory state and markers of endothelial dysfunction in morbidly obese patients after weight loss following bariatric surgery.

Methods: In this study, we measured the levels of soluble intracellular adhesion molecule-1 (sICAM1), plasminogen activator inhibitor 1 (PAI-1), high-sensitivity C-reactive protein (hs-CRP), and interleukin-6 (IL-6) in 79 morbidly obese patients at baseline and 3, 6 and 12 months after gastric bypass. Also, we evaluated changes in IR.

Results: Twelve months after surgery, there was a significant decrease in plasma levels of sICAM1 ($p < 0.001$), PAI-1 ($p < 0.05$), hs-CRP ($p < 0.001$), IL-6 ($p < 0.001$) and homeostasis model assessment (HOMA) ($p < 0.001$) and a significant increase of McAuley index (McAuley) ($p < 0.001$). Baseline levels of hs-PCR were positively correlated with sICAM-1 ($r = 0.450$, $p < 0.01$) and IL-6 ($r = 0.451$, $p < 0.01$). Significant correlations were also found between the decrease of PAI-1 and the decrease of hs-PCR ($r = 0.425$, $p < 0.01$) and tryglicerides ($r = 0.351$, $p < 0.01$).

Conclusions: In patients with morbid obesity, substantial surgically induced weight loss is followed by a significant improvement in the endothelial function, inflammatory state and insulin sensitivity, that may reduce their cardiovascular risk. A relationship exists between improved inflammatory profile and endothelial function.

Key words:

Obesity. Bariatric surgery. Inflammation. Endothelial activation. Insulin resistance.

Resumen

Objetivo: la obesidad está asociada con un aumento del riesgo de enfermedad cardiovascular. Se ha propuesto una relación causal entre obesidad, inflamación, resistencia a la insulina, y disfunción endotelial. El objetivo de este estudio fue valorar marcadores de insulinorresistencia, inflamación y disfunción endotelial en pacientes con obesidad mórbida antes y después de la pérdida de peso por cirugía bariátrica.

Métodos: se midieron las concentraciones séricas de moléculas solubles de adhesión intercelular tipo 1 (sICAM-1), inhibidor del activador del plasminógeno tipo 1 (PAI-1), proteína C reactiva de alta sensibilidad (hs-PCR) e interleucina 6 (IL-6) en 79 pacientes con obesidad mórbida antes y a los 3, 6 y 12 meses de la realización de un by-pass gástrico. También se evaluaron índices de resistencia a la insulina.

Resultados: a los 12 meses de la cirugía disminuyeron los niveles de sICAM1 ($p < 0,001$), PAI-1 ($p < 0,05$), hs-CRP ($p < 0,001$), IL-6 ($p < 0,001$) y el índice homeostasis model assessment (HOMA) ($p < 0,001$) y aumentó el índice McAuley ($p < 0,001$). Los niveles basales de hs-PCR estaban correlacionados con los de sICAM-1 ($r = 0,450$, $p < 0,01$) y de IL-6 ($r = 0,451$, $p < 0,01$). También existía correlación entre el descenso de los niveles de PAI-1 y el descenso de hs-PCR ($r = 0,425$, $p < 0,01$) y triglicéridos ($r = 0,351$, $p < 0,01$).

Conclusiones: en pacientes con obesidad mórbida una importante pérdida de peso por cirugía bariátrica se acompaña de una mejora significativa de marcadores inflamatorios, de función endotelial e insulinorresistencia, lo que puede suponer una disminución del riesgo cardiovascular. Existe una relación entre mejora del perfil inflamatorio y función endotelial.

Palabras clave:

Obesidad. Cirugía bariátrica. Inflamación. Función endotelial. Resistencia a la insulina.

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INTRODUCTION

Obesity is a chronic pathology with high morbidity-mortality rates which is frequently associated with a high risk for atherosclerotic cardiovascular disease (1,2). A growing body of evidence suggests the role of low grade inflammation as a link between obesity, insulin resistance (IR) and endothelial dysfunction (3).

Endothelial dysfunction, a pathologic feature of obesity, is considered the earliest stage in the atherogenic process (4,5). Inflammation of the vascular wall is a crucial step in the pathophysiology of atherosclerosis, which causes endothelial cells increased secretion of different molecules. Disturbed endothelial function can be assessed by measuring the level of these molecules. The concentration of soluble intracellular adhesion molecule-1 (sICAM1) and plasminogen activator inhibitor 1 (PAI-1) have been shown to be the earliest markers of endothelial dysfunction (6,7) and there is evidence that these substances are increased in obese patients (8-21).

Previous studies have demonstrated that surgically induced weight loss is accompanied by an improvement of the endothelial function (18,19,21) and the proinflammatory state (18,21-31). However, few studies have studied endothelial function and proinflammatory state together, and have considered different time-points to determine postsurgical changes. We hypothesised that substantial weight loss would improve endothelial function and inflammatory state in both the short and the long term (one year).

This study was conducted to analyze the effects of weight loss after bariatric surgery on the plasma levels of sICAM 1, PAI-1, high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) and to evaluate changes in IR in obese human subjects. For comparison, healthy matched control subjects were also studied.

SUBJECTS AND METHODS

Seventy nine consecutive patients selected to undergo gastric bypass were investigated when they were referred to our nutrition outpatient department. The group comprised 46 women and 33 men, aged 38.5 ± 10.0 years with a mean body mass index (BMI) of 47.5 ± 7.0 kg/m^2 All the patients underwent gastric bypass using the method described by Capella (32). Exclusion criteria were age less than 18 years or more than 60 years, diabetes mellitus, pregnancy, coronary artery disease, peripheral vascular disease and current history of inflammatory, infectious or malignant disease. Twenty two patients were smokers. Eighteen subjects were hypertensive and nineteen were dyslipidemic. These comorbidities were controlled with drug treatment for 6 months before surgery.

Patients were evaluated before surgery and at 3, 6 and 12 months after the intervention.The study also included 40 healthy lean subjects. All participants gave written informed consent to their participation in this study, which was approved by the ethical committee of our hospital following the rules of the Declaration of Helsinki.

Out of the original cohort of seventy nine patients, seventy three completed the 1-year protocol. The reasons for patients leaving the study were lack of time, loss of interest or our inability to contact the participants. A sample of seventy nine subjects was estimated assuming an alpha risk of 0.05 ($\alpha < 0.05$) and a 20% risk beta ($\beta < 20\%$), and assuming a standard deviation (SD) of 7 and a rate monitoring loss of 10%. We decided to perform a per protocol analysis

CLINICAL AND ANTHROPOMETRICAL MEASUREMENTS

A general physical examination was performed by a physician. The systolic and diastolic blood pressure readings were recorded as the mean of two measurements taken with the subjects seated. Patients' weight, height, waist and hip circumferences were obtained; BMI was calculated as body weight divided by height squared (in kilograms per square meter) and waist-to-hip ratio was calculated as the ratio of waist and hip circumferences. Body fat was estimated by bioelectric impedance analysis (Model TBF-300, Tanita Corp., Tokyo, Japan).

ANALYTICAL METHODS

Venous blood samples were drawn from each subject before breakfast, between eight and nine o'clock, after overnight fast. Plasma glucose, insulin, cholesterol, triglycerides and high density lipoprotein cholesterol (HDL-C) were determined immediately after blood was drawn. The samples for, sICAM-1, hs-CRP, PAI-1 and IL-6 were stored at -80 °C until the analytical measurements were performed.

Serum levels of inflammation-related markers were measured by enzyme-linked immunosorbent assays (ELISA) using commercially available standard kits according to protocols described by the manufacturers. IL-6 and sICAM-1 were determined by ELISA from R&D Systems (Minneapolis, MN, USA), hs-CRP was measured by ELISA from DRG Diagnostics (Marburg, Germany), and PAI-1 was determined by ELISA. PeproTech (Rocky Hill, New Jersey). The concentrations of glucose, total cholesterol, HDL-C and triglycerides were determined using enzymatic methods (Advia 2500 autoanalyzer). Low density lipoprotein cholesterol (LDL-C) was calculated using the Freidewald equation (LDL-C = total cholesterol–HDL-C–triglycerides/5). Insulin concentration was measured by chemiluminescence (Advia Centaur). IR was assessed by indirect methods: the homeostasis model assessment (HOMA) = insulin (mUI/l) × [glucose(mmol/L)/22.5] and the McAuley index (McAuley) = exp [2.63 – 0.28 ln (insulin in mUI/L) – 0.31 ln (triglycerides in mmol/L)] (33).

STATISTICAL ANALYSIS

Data was expressed as the mean ± standard deviation (SD). Normality of distribution was verified with a Kolmogorov-Smirnov

test. Variables that were not normally distributed were log transformed. The differences between obese *vs.* lean groups were compared with an unpaired *t*-test. The differences between baseline, 3, 6 and 12 months after surgery measures were analyzed using repeated-measures multivariate analysis of variance adjusted for arterial hypertension, smoking and hyperlipidemia. Comparisons between preoperative baseline and postsurgery time points were obtained by using paired Student's t test, and the p values were Bonferroni corrected. The relations between continuous variables were assessed with nonparametric Spearman rank correlation. $p < 0.05$ was considered statistically significant. The data was analyzed with SPSS/PC, version 17.0 for Windows.

RESULTS

The average preoperative BMI was 47.5 ± 7.0 kg/m^2. BMI was dramatically reduced 12 months after surgery (30.1 ± 4.7 kg/m^2).

Table I shows the distribution of variables between the 73 obese patients and the 40 lean controls. The obese patients had higher concentrations of IL-6, hs-PCR, sICAM-1, PA1-1, triglycerides, LDL-C, glucose, insulin and HOMA and lower concentrations of HDL-C than the lean subjects.

Table II shows the anthropometric, clinical and metabolic characteristics of the obese patients before surgery and 3, 6 and 12 months after gastric bypass. Despite massive weight loss, only 8 patients attained the ideal body weight (BMI ≤ 25 kg/m^2), 36 patients attained BMI between 25 and 30 kg/m^2, and 29 persisted with BMI above 30 kg/m^2. Circulating glucose and insulin decreased progressively with time, which indicated an amelioration of insulin sensitivity, as further evidenced by the improvement of HOMA and McAuley values. Amelioration of glucose homeostasis was confirmed through a steady decrease of glycated hemoglobin. The reduction in total cholesterol, LDL-C and triglycerides was accompanied by an increase in HDL-C.

Table III shows the changes in plasma concentrations of circulating endothelial and inflammatory markers, before and after surgery, in morbidly obese patients. The circulating levels of all of them were markedly reduced at 12 months after bariatric surgery. At 3 months, only hs-CRP concentrations were significantly reduced, while at 6 months there was also a significant decrease of IL6, PAI-1 and sICAM-1 levels.

In the obese patients, the preoperative levels of hs-PCR were positively correlated with the levels of sICAM-1 ($r = 0.450$, $p < 0.01$) and IL-6 ($r = 0.451$, $p < 0.01$). Significant correlations were found between hs-PCR and IL-6 ($r = 0.330$, $p < 0.05$), PAI ($r = 0.310$,

Table I. Comparison of obese and lean groups

	Obese	Lean	p value
Age (years)	38.53 ± 10.00	38.63 ± 8.27	NS
Weight (kg)	129.78 ± 23.39	63.21 ± 10.67	< 0.001
BMI (kg/m^2)	47.56 ± 7.02	22.19 ± 1.93	< 0.001
WHR	0.92 ± 0.07	0.78 ± 0.07	< 0.001
FM (kg)	63.24 ± 13.94	14.52 ± 3.73	< 0.001
Systolic blood pressure (mmHg)	134.78 ± 20.61	113.52 ± 10.48	< 0.001
Diastolic blood pressure (mmHg)	82.22 ± 13.93	68.00 ± 8.03	< 0.001
Cholesterol (mmol/l)	5.01. ± 0.85	4.96 ± 0.74	NS
Triglycerides (mmol/l)	1.61 ± 0.84	0.70 ± 0.26	< 0.001
HDL-C (mmol/l)	1.34 ± 0.28	1.91 ± 0.45	< 0.001
LDL-C (mmol/l)	3.02 ± 0.72	2.73 ± 0.56	NS
Glucose (mmol/l)	5.66 ± 1.11	4.57 ± 0.35	< 0.001
Glycated hemoglobin (%)	5.82 ± 0.60	5.35 ± 0.30	< 0.001
Insulin (mUI/l)	22.10 ± 14.02	7.62 ± 4.57	< 0.001
HOMA-IR	5.86 ± 4.68	1.54 ± 0.94	< 0.001
McAuley-IR	5.46 ± 1.19	9.41 ± 1.76	< 0.001
IL-6 (pg/ml)	3.79 ± 1.97	0.93 ± 0.54	< 0.001
hs-CRP (mg/l)	24.34 ± 18.62	1.71 ± 1.17	< 0.001
PAI-1 (ng/ml)	60.13 ± 20.59	30.69 ± 14.17	< 0.001
sICAM-1 (ng/ml)	316.42 ± 74.69	181.80 ± 49.10	< 0.001

All data are presented as the mean ± SD. BMI: body mass index. WHR: waist to hip ratio. FM: fat mass. HDL-C: high density lipoprotein cholesterol. LDL-C: low density lipoprotein cholesterol. HOMA-IR: homeostasis model assessment of insulin resistance. McAuley-IR: McAuley index of insulin resistance. IL-6: interleukin 6. hs-CRP: high-sensitivity C-reactive protein. PAI-1: plasminogen activator inhibitor 1. sICAM1: soluble intracellular adhesion molecule-1.

Table II. Anthropometrical, body composition characteristics and biochemical parameters before and after bariatric surgery in obese subjects[1]

	Preoperative (baseline)	3 months	6 months	12 months	Overall p value[2]
Weight (kg)	129.78 ± 23.39	101.62 ± 16.82*	89.04 ± 15,30*	82.08 ± 15.94*	< 0.001
BMI (kg/m^2)	47.56 ± 7.02	37.06 ± 4.66*	32,45 ± 4.22*	30.17 ± 4.71*	< 0.001
WHR	0.92 ± 0.07	0.87 ± 0.07*	0.87 ± 0.13*	0.84 ± 0.06*	< 0.001
FM (kg)	63.24 ± 13.94	41.40 ± 9.36*	30.37 ± 8.28*	25.53 ± 10.18*	< 0.001
Systolic blood pressure (mmHg)	134.78 ± 20.61	119.57 ± 20.07*	119,08 ± 14,46*	119.80 ± 14.62*	< 0.001
Diastolic blood pressure (mmHg)	82.22 ± 13.93	74.66 ± 12.08*	72.60 ± 09.99*	71.92 ± 9.63*	< 0.001
Cholesterol (mmol/l)	5.01. ± 0.85	4.31 ± 0.67*	4.39 ± 0.72*	4.39 ± 0.67*	= 0.04
Triglycerides (mmol/l)	1.61 ± 0.84	1.30 ± 0.46*	1.08 ± 0.39*	0.92 ± 0.36*	< 0.001
HDL-C (mmol/l)	1.34 ± 0.28	1.21 ± 0.36	1.29 ± 0.28	1.49 ± 0.31	NS
LDL-C (mmol/l)	3.02 ± 0.72	2.58 ± 0.51*	2.66 ± 0.56*	2.50 ± 0.54*	= 0.02
Glucose (mmol/l)	5.66 ± 1.11	4.66 ± 1.11*	4.72 ± 0.44*	4.61 ± 0.39*	< 0.001
Glycated hemoglobin (%)	5.82 ± 0.60	5.50 ± 0.44*	5.44 ± 0.52*	5.26 ± 0.37*	< 0.001
Insulin (mUI/l)	22.10 ± 14.02	10.46 ± 6.93*	7.38 ± 3.36*	5.63 ± 2.53*	< 0.001
HOMA-IR	5.86 ± 4.68	2.36 ± 1.74*	1.51 ± 0.70*	1.15 ± 0.53*	< 0.001
McAuley-IR	5.46 ± 1.19	7.13 ± 1.42*	8.24 ± 1.67*	9.24 ± 1.66*	< 0.001

*[1]All data are presented as the mean ± S. BMI body mass index, WHR waist to hip ratio, FM fat mass, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, HOMA-IR homeostasis model assessment of insulin resistance, McAuley-IR McAuley index of insulin resistance. *Significantly different from baseline, p < 0.05. [2]Obtained by using repeated-measures multivariate analysis of variance. Comparisons between preoperative baseline and each time point after gastric surgery were obtained by paired Student's t test. p values were Bonferroni corrected.*

Table III. Proinflammatory cytokines, C-reactive protein and adiponectin before and after bariatric surgery in obese subjects[1]

	Preoperative (baseline)	3 months	6 months	12 months	Overall p value[2]
IL-6 (pg/ml)	3.79 ± 1.97	3.37 ± 1.46	2.31 ± 1.96*	1.62 ± 1.40*	< 0.001
hsCRP (mg/l)	24.34 ± 18.62	15.27 ± 9.05*	9.74 ± 6.79*	4.29 ± 3.14*	< 0.001
PAI-1 (ng/ml)	60.13 ± 20.59	54.36 ± 20.03	43.72 ± 19.26*	42.25 ± 19.70*	< 0.05
9999sICAM-1 (ng/ml)	316.42 ± 74.69	305.92 ± 86.84	270.13 ± 84.64*	247.19 ± 86.51*	< 0.001

*[1]All data are presented as the mean ± SD. IL-6 interleukin 6, hs-CRP high-sensitivity C-reactive protein, PAI-1 plasminogen activator inhibitor 1, sICAM1 soluble intracellular adhesion molecule-1.*Significantly different from baseline, p < 0.05. [2]Obtained by using repeated-measures multivariate analysis of variance. Comparisons between preoperative baseline and each time point after gastric surgery were obtained by paired Student's t test. p values were Bonferroni corrected.*

$p < 0.05$) and tryglicerides ($r = 0.379$, $p < 0.01$) at 12 months Significant correlations were also found between the decrease of PAI-1 and the decrease of hs-PCR ($r = 0.425$, $p < 0.01$) and tryglicerides ($r = 0.351$, $p < 0.01$) (data not listed in the tables).

DISCUSSION

The main findings of this study are that gastric bypass in severely obese patients, results in a marked weight loss and improved inflammatory profile, endothelial function and IR. This suggests that bariatric surgery may help obese subjects to reduce their cardiovascular risk.

Both obesity and atherosclerosis are considered states of chronic low-grade inflammation and-are associated with increased cardiovascular risk (34). The vascular inflammation is a central orchestrator of atherosclerotic lesion formation, progression, and eventual rupture (35). Adipose tissue contributes importantly to the inflammatory process in obese subjects in both vascular and nonvascular tissues (36).

The presence of low-grade inflammation in this study was assessed by measuring serum concentrations of hs-CRP and IL6.

Our investigation corroborates preliminary studies (18,21-31) as it shows that obesity is a state of chronic low-grade inflammation and the weight reduction resulting from bariatric surgery significantly improves the inflammatory state. This amelioration relies on the continuous reduction in hs-CRP and IL-6 concentrations, associated with a parallel decrease in BMI. The present study shows that hs-CRP levels decreased significantly at 3 months after bariatric surgery and IL6 levels decreased significantly at 6 months after surgery. C-reactive protein (CRP), an acute phase reactant, is secreted by the liver in response to IL-6 production in inflammatory conditions. Our data suggests that IL-6 might not be the sole determinant for elevated CRP levels in obesity, because 3 months after surgery hs-CRP levels decrease significantly despite of an only moderate decrease of IL-6 levels which were not statistically significant. Growing evidence suggests that macronutrient intake and obesity may activate inflammatory signaling pathways in cells (37-39). Glucose and fat intake have both been shown to induce inflammation, potentially through increases in oxidative stress (40). In clinical practice, it is well known that food intake is substantially modified after bariatric surgery, which initially leads to a lower consumption of sugars and fat.

This short term improvement in the hs-CRP levels could be explained by a shift in the energy balance and variations of macronutrients intake and suggests that these factors may affect the systemic inflammatory profile of obese subjects during the first months after surgery, while reduced adiposity might predominate in regulating long-term circulating cytokine concentrations (41-43).

Dysfunction of endothelial cells is probably the earliest event in the process of lesion formation, hence the concept that assessment of endothelial function may be a useful prognostic tool for cardiovascular disease. Endothelial cell activation leads to increased expression of inflammatory cytokines and adhesion molecules that trigger leukocyte homing, adhesion, and migration into the subendothelial space, which are processes fundamental to atherosclerotic lesion initiation. A broader appreciation of the numerous functions of the endothelium can be obtained by the study of the levels of some molecules of endothelial origin in circulating blood such as sICAM1 and PAI-1.

Inflammation is associated with endothelial dysfunction, an upregulation of proinflammatory cytokines leads to disturbances in the normal function of the vascular endothelium. Inflammation of the vascular wall causes endothelial cells to express a wide variety of endothelial adhesion molecules, including intracellular adhesion molecule-1. sICAM-1 can be regarded as a marker of both endothelial function and inflammation (11) that is associated with atherosclerotic progression (44) and its levels are increased in obesity (9,14-17,19). It has been suggested that sICAM-1 mediated endothelial dysfunction is stimulated by cytokines secreted by adipose tissue (45). IL-6 has an important roles here, leading to increased endothelial cell adhesiveness by upregulating E-selectin and intercellular adhesion molecule-1 (46,47). CRP displays a direct proinflammatory effect on endothelial cells, and stimulates diverse early atherosclerotic processes, including the expression of endothelial cell adhesion (48).

In the present study, sICAM-1 levels were increased in presurgery obese patients and significantly decreased 6 months after bariatric surgery. A correlation was observed between sICAM and IL-6 and hs-PCR levels. These results are of particular interest because they support the relationship between inflammation and endothelial activation, and are consistent with increased sICAM-1 levels associated with CRP and IL 6 in obese children (49).

PAI-1 is an adipocytokine that is expressed in adipose tissue and vascular endothelium (50). The procoagulant consequences of endothelial activation can be measured as an increase in the PAI-1 levels (7,51). In obesity, particularly in visceral obesity, PAI-1 expression has been reported to be upregulated, thereby increasing PAI-1 levels and this is responsible for the impaired fibrinolysis that accompanies obesity and presumably contributes to the increased cardiovascular risk in obese individuals (13). As adipocytes represent an important source of PAI-1 synthesis, changes in PAI-1 levels in obese patients after weight loss are commonly purported to mainly reflect fat loss. Other explanation for the association between the elevated PAI-1 levels and obesity would be that they both reflect a common causal mechanism outside the visceral fat compartment. Such mechanism could involve metabolic factors such as increased circulating free fatty acids or triglycerides. It has also been suggested that elevated PAI-1 levels could be implicated in metabolic disturbances (14,53).

In the current study, the plasma PAI-1 levels were increased in obese patients and decreased significantly with weight loss. Improvement of PAI-1 levels related with improvement of tryglicerides. These results support that hypertriglyceridemia may take part in the development of atherosclerosis in concert with the dysregulation of adipocyte-derived proteins such as PAI-1. In our study we have demonstrated a direct relationship between hs-CRP levels and PAI after weight reduction. This relation suggests that CRP may increase the expression and activity of PAI-1 and promote processes involved in the pathogenesis of atherothrombosis (54). Thus, CRP could be behind the postulated relationship of inflammation and endothelial activation with IR and adiposity (55).

The causes of endothelial dysfunction and low grade inflammation in obese subjects remain incompletely understood. There is no uniform mechanism by which weight loss leads to decrease endothelial activation and inflammation, although parallel mechanisms may operate in both processes. In this study we could demonstrate a direct relationship between weight loss and improvement in markers of endothelial activation and inflammation, although additional studies are required to identify the molecular and cellular actors involved in the down-regulation of systemic cytokines that occurs after surgically induced weight loss. Indeed, this study suggests that distinct mechanisms might be involved in the amelioration of systemic inflammatory response at early and late time points during the course of weight reduction in obese subjects.

Our study has several limitations. Firstly, our sample size was relatively small and consequently, its limited power may have obscured more subtle associations. Secondly, our cohort represents a real-life clinical scenario, and included smokers and patients with hypertension and hyperlipidemia. However,

even with a small cohort of patients with other comorbidities, we were able to determine a significant post-surgical decrease in molecular markers associated with atherosclerosis and its progression such as hs-CRP, IL-6, sICAM-1 and PAI-1 and an improvement of IR.

In summary, our data support the hypothesis that gastric bypass in severely obese patients may help reduce their cardiovascular risk, although additional studies are required to confirm that substantial surgically induced weight loss reduce cardiovascular morbidity and mortality.

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