Original Article
Relationship of ghrelin, acid uric and proinflammatory adipocytokines in different degrees of obesity or diabetes

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Abstract: We compared and examined factors associated with ghrelin and uric acid in obese subjects (OB), obese plus type 2 diabetes mellitus (OBDM) and healthy controls (C). *Methods.* We analyzed blood count, renal function, liver enzymes, lipids, resistin, leptin, IL-6, uric acid and ghrelin in OB, OBDM and C. We included 76 subjects with different body mass index (BMI): 36 C (24 ± 3), 11 $OB_{<40}$ (30-39.9), 20 $OB_{>40}$ (40-60), and 9 OB_{DM} (45.9 ± 9). *Results.* Metabolic profile was as follows: HOMA-IR 4.7 ± 3 and 5 ± 3 vs 2 ± 1 (p < 0.01), resistin 8.7 ± 2 and 9.4 ± 2 vs 5.4 ± 2 ng/mL (p < 0.001), leptin 6.2 ± 3.9 and 5.3 ± 2 vs 3.6 ± 1.8 ng/mL (p = 0.001) and IL-6 197.5 ± 78.9 and 223.6 ± 115 vs 7.4 ± 8.3 pg/mL (p = 0.001) in OB and OB_{DM} vs C, respectively. Ghrelin was higher in $OB_{<40}$ compared to C (1780 ± 197 vs 1465 ± 12 pg/mL, p < 0.05), and lower in OB_{DM} (987.4 ± 114 pg/mL, p < 0.05). BMI showed a positive correlation with resistin (p < 0.001); leptin (p = 0.004), IL-6 (p = 0.001), uric acid (p = 0.0005) and negative with ghrelin (r = -0.431, p = 0.028). Resistin was directly correlated with leptin (p < 0.001) and inversely correlated with renal function (p = 0.03). *Conclusion.* Severe obesity and obesity-associated diabetes affected ghrelin and uric acid levels. This may well be associated with proinflammatory adipocytokines, insulin resistance, liver enzymes or renal function.

Keywords: Obesity, diabetes, ghrelin, uric acid, adipocytokines

Introduction

Medical complications of obesity and overweight are a public health problem in worldwide. Central obesity is mainly associated with insulin resistance, diabetes and high cardiovascular mortality. The prevalence of insulin resistance among families or ethnic groups depends on genetic and environmental factors and may be associated with conditions different from obesity [1, 2].

Obesity itself is a low-grade inflammation resulting from the unbalanced production of active molecules called adipocytokines. These adipocytokines, such as leptin, resistin, tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6), play an important role in the mechanisms of peripheral resistance to insulin action [3]. Adipocytokines act in an autocrine, paracrine

or endocrine form on glucose homeostasis, proteins, and on other cytokines that control immune functions [4]. In diabetic and obese patients, elevation of resistin is associated with insulin resistance, and it has been observed experimentally that this resistance is primarily in the liver [5].

Leptin produced from adipocytes and adenohypophysis as a signal of energy reserve for the hypothalamus regulates body mass by altering appetite and secretion of growth hormone [6]. Leptin, resistin and IL-6 are related to the activation of inflammatory processes, hypertriglyceridemia and hypercholesterolemia, which together promote endothelial dysfunction and atherosclerosis. Increased TNF-α in obesity contributes by interfering with the insulin receptor at the onset of insulin resistance [3]. Ghrelin is an orexigenic hormone produced by endo-

crine cells in fasted stomach and is a key factor in leptin-receptor function [7]. It inhibits vascular inflammation and participates in the regeneration of endothelial cells [8]. In healthy humans, ghrelin infusion in physiological doses decreases insulin secretion, but at higher doses results in reduced insulin sensitivity [9].

The aim of this study was to explore the relationship of proinflammatory adipocytokines with ghrelin and uric acid among subjects with different degrees of obesity including those who have developed diabetes.

Material and methods

Study design and participants

This was a case/control cross-sectional study including patients > 16 years of age. Consecutive new patients with BMI > 30 were included as cases. Patients with diabetes mellitus must have demonstrated adequate control without use of insulin. Nonobese controls were recruited from the blood bank. Their BMI was < 29 (WHO) and control subjects did not report any chronic degenerative disease. Groups were classified as obese subjects (OB), obese subjects plus type 2 diabetes mellitus (OBDM) and healthy controls (C).

Under fasting conditions, each subject had the following measurements taken: body weight, blood pressure, glucose, insulin, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. Insulin resistance index was calculated through surrogate marker HOMA-IR [10]. HDL-cholesterol < 40 mg/dL was considered abnormal and > 60 mg/dL was cardioprotective. Triglycerides > 150 mg/dL was considered hypertriglyceridemia. LDL-cholesterol was considered to be optimal if it was < 100 mg/dL as obtained from the ATP III criteria [11]. We also evaluated blood count, biochemical profile, liver enzymes and creatinine clearance. The study protocol complies with the Declaration of Helsinki as well as with local institutional guidelines and was approved by the local ethics committees. Written informed consent was obtained from all participants.

Material and methods

Assays. In order to obtain fasting plasma glucose (FPG) levels as well as lipid profiles and adipokine levels, venous blood samples were drawn after an 8- to 10-h overnight fast and were immediately stored at -70°C for subsequent assays. Based on the criteria of the American Diabetes Association (The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus), FPG < 100 mg/dL was considered as the normal reference value; therefore, isolated impaired fasting glucose (IFG) diagnosis was based on a FPG of 100 mg/dL or higher but < 126 mg/dL.

The glucose-oxidase method was employed to measure plasma glucose. Triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, glycated hemoglobin (HbA1c) and uric acid were assayed using a Technicon RA1000 analyzer (Bayer Diagnostics, Puteaux, France). Insulin was centrally assayed in serum by a specific radioimmunoassay (Linco Research Inc., St. Charles, MO, USA). Intra- and inter-assay coefficients of variation for all measurements were < 7%. Insulin resistance (IR) was estimated using the homeostasis model assessment index-insulin resistance (HOMA-IR). With the determination of insulin and glucose, it was possible to determine HOMA-IR using the following formula: [plasma insulin x plasma glucose/22.5] as a method for evaluating insulin resistance [10].

Measurements of adipokines and interleukins. Plasma ghrelin levels were measured by a specific radioimmunoassay (Linco Research Inc.). Plasma levels of resistin, leptin, TNF-α, IL-2, IL-6 and IL-10 were measured by enzyme-linked immunosorbent assay (ELISA) (R&D Systems, Minneapolis, MN, USA). Intra- and inter-assay coefficients of variation (< 10%) were obtained and values were expressed as ng/mL.

Statistical analysis

Data are presented as mean ± standard deviation (SD) from groups. Statistical difference was analyzed by analysis of variance (ANOVA). Plasma concentrations of adipocytokines, lipid profile, and biochemical profile and insulin resistance were analyzed by ANOVA followed by multiple comparisons test. We performed Pearson or Spearman correlation to test the relationship between the concentrations of the adipocytokines.

Table 1. Clinical features and biomarkers according to body mass index and presence or absence of T2DM

	Control n = 36	Obese n = 11 BMI < 40	Obese n = 20 BMI > 40	Obese without DM n = 31	Obese with DM n = 9
Age (years)	38 ± 11	41.5 ± 15	40.7 ± 10.4	40.7 ± 11	41.75 ± 15.27
Gender F/M	18/18	7/4	19/1	25/6	8/1
BMI kg/m^2	24 ± 4	33.75 ± 3.1	48.3 ± 7.5	43 ± 9.3	45.9 ± 9.5
SBP mmHg	111 ± 9	115.8 ± 9	122.9 ± 10.5	120.3 ± 10.3	122.5 ± 11.6
DBP mmHg	70 ± 6	77.9 ± 7.8	80 ± 5.5	79.38 ± 6	80 ± 7.56
Glucose mg/dL	89 ± 13	98.85 ± 8.7	93.8 ± 4.5	96.3 ± 3.7	114 ± 27.4*
HOMA-IR	2 ± 1.05	3.49 ± 3.1	5.4 ± 3.2	4.67 ± 3	6.1 ± 4.05**
Hb$_{A1c}$ (%)	4.2 ± 1.4	4.3 ± 2.7	5.96 ± 0.4	5.57 ± 2.3	5.98 ± 3.4
TC mg/dL	167 ± 8	192 ± 30.86	191.4 ± 30.7	189.2 ± 30.2	200 ± 31.3
HDL-C mg/dL	49 ± 7	38.5 ± 6.2	42.1 ± 10	41 ± 8.4	42.3 ± 13.5
LDL-C mg/dL	95 ± 7	115.4 ± 17.8	118.2 ± 22.8	116.1 ± 21.2	123.2 ± 23.5
Triglycerides mg/dL	120 ± 8	248.7 ± 105.4	178.1 ± 72	202.8 ± 91.4	168 ± 55.3
AST median (range) IU/L	19 (12-26)	20 (17-40)	21 (14-128)	21 (14-128)	22 (14-25)
ALT median (range) IU/L	20 (16-31)	30.5 (19-91)	21 (13-189)	25 (13-189)	23 (14-38)
GGT median (range) IU/L	21.5 (15-35)	29.5 (15-104)	28 (15-177)	28 (15-177)	38 (17-159)
Uric acid mg/dL	3.5 ± 1.1	5.3 ± 1.9	6.4 ± 1.3	6.34 ± 1.7	7 ± 2.3
Creatinine clearance ml/min/1.73 m^2	96.9 ± 29	100.5 ± 66	139.5 ± 47.9	129.8 ± 54.3	122 ± 43.8
Leptin ng/mL	3.6 ± 1.8	5.3 ± 3.02	6.3 ± 4	6.2 ± 4	5.3 ± 2.6
Resistin ng/mL	5.4 ± 2.2	8.7 ± 1.6	8.87 ± 2.3	8.66 ± 2.06	9.4 ± 2.5
IL-2 pg/mL	< 5	38.5± 13.1	48.1 ± 11.8	39.6± 18.9	81 ± 12.3**
IL-6 pg/mL	7.4 ± 8.3	177.2 ± 117.4	213.3 ± 80.76	197.5 ± 78.97	223.6 ± 115
IL-10 pg/mL	< 5	11.5 ± 8.5	25.39 ± 7.4	19.65 ± 6	36 ± 19
TNFα pg/mL	10 ± 4	63.5 ± 13.5**	8.24 ± 4.5	19.18 ± 14.8	14 ± 12
Ghrelin pg/mL	1465 ± 12	1780 ± 197**	1149 ± 89.03	1351 ± 116.9	987.4 ± 114*

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transaminase, DM, diabetes mellitus. *$p < 0.01$ (obese without DM vs. obese with DM). **$p < 0.05$ with respect to all groups (ANOVA, post-hoc Tukey).

Results

General description

We included 36 healthy, nonobese controls and 40 obese patients. Six males and 34 females were obese: grade I (8 subjects), grade II (3 subjects), and grade III (20 subjects) according to the 2004 WHO criteria. Nine patients were classified as OBDM and under dual therapy with oral hypoglycemic agents (sulfonylurea + metformin) and FPG between 70 and 130 mg/dl. Age was similar among groups (**Table 1**).

Characterization of patients

Biochemical characteristics of the obese group (BMI 43.9 ± 9.4) were as follows: HbA1c 5.5 ± 2.26, uric acid 6.3 ± 1.7 mg/dL, C-reactive protein (CRP) 4.8 ± 2.2 mg/L, erythrocyte sedimentation rate (ESR) 26 ± 11 mm/h, aspartate transaminase (AST) 26.4 ± 19 IU/L (range: 11-128), alanine transaminase (ALT) 36 ± 37.5 U/L (range: 14-91), gamma-glutamyl transaminase (GGT) 48 ± 45 IU/L (range 15-177), Hb 14.7 ± 1.25 g/dL, 7471 ± 1489 leukocytes/μL, and creatinine clearance 128 ± 51 mL/min. Comparative analysis is shown in **Table 1**.

To compare biochemical parameters, we divided the OB group into four subgroups: OB30-40 (BMI 30-39), OB40-50 (BMI 40-50), OB > 50 (BMI > 50) and OBDM (BMI > 30 plus type 2 diabetes mellitus, T2DM). Hypertriglyceridemia was found in 7/11 (63%) in OB30-40, 8/14 (57%) in OB40-50, 4/6 (67%) in OB > 50 and 6/9 (67%) in OBDM. Elevated LDL-cholesterol > 100 mg/dL was quantified in 5/11 (45%) in OB30-40, 11/14 (79%) in OB40-50, 5/6 (83%) in OB > 50 and 7/9 (78%) of OBDM. Overall, 71% of obese patients had LDL-cholesterol < 129 mg/dL. HDL-cholesterol < 40 mg/dL was

observed in 3/11 (27%) OB30-40, 6/14 (43%) OB40-50, 3/6 (50%) OB > 50 and 4/9 (45%) OBDM. Average group values are shown in **Table 1**.

Obese patients with HDL-cholesterol < 40 mg/dL were younger (35.2 ± 10.3 vs 45.9 ± 11.5 years, p = 0.01) and had higher creatinine clearance (145 ± 52 vs. 112 ± 44 ml/min/1.73 m^2, p = 0.041). Cardioprotective value of HDL-cholesterol > 60 mg/dL was found in only two patients in the OB40-50 group and one in the OBDM group.

Relationship among adipokines

Ghrelin was inversely correlated with fasting glucose concentrations (r = -0.4, p = 0.039) and BMI (r = -0.43, p = 0.028). Serum GGT was directly correlated with uric acid (r = 0.49, p = 0.01). Concentration of HDL-cholesterol remained inversely related to leukocytes/mm^3 (r = -0.42, p = 0.025) and creatinine clearance in 24-h urine (r = 0.42, p = 0.025).

In the OB group, BMI was positively correlated with resistin (r = 0.6, p < 0.001), leptin (r = 0.34, p = 0.004) and IL-6 (r = 0.4, p 0.001). HOMA-IR was > 3.2 in 3/11 (27%) OB30-40, 10/14 (71%) OB40-50, 4/6 (67%) OB > 50 and 8/9 (88%) in OBDM but showed no significant correlation with adipocytokines and serum lipids.

Resistin, leptin and IL-6 in OB, OBDM and C tend to increase with higher BMI (**Table 1**). There was no relationship among them except for resistin, which changes in direct correlation with leptin (r = 0.47, p < 0.001). The concentration of TNF-α was higher in non-morbidly obese than morbidly obese and healthy controls (**Table 1**). Ghrelin was inversely correlated with BMI (r = -0.431, p = 0.028). We found IL-2 and IL-10 elevated in obese patients relative to controls. IL-2 showed greater elevation in obese diabetic patients compared to non-diabetic obese patients (**Table 1**).

Creatinine clearance (ml/min/1.73 m^2) was < 70 in 9.4%, 70-120 in 37.5%, and > 120 (169 ± 28) in 21 (53%) of the obese patients studied. Patients with creatinine clearance > 120 ml/min/1.73 m^2 were younger than the group with normal creatinine clearance (37.7 ± 9.7 vs. 48.4 ± 10 years, p = 0.008) and four subjects

had T2DM. Renal hyperfiltration was associated with higher serum uric acid (6.98 ± 1.9 vs. 5.65 ± 1.16 mg/dL, p = 0.04), higher leukocytes (8060 ± 1499 vs. 6458 ± 1058/mm^3, p = 0.005) and lower concentrations of serum leptin (5.2 ± 3.3 vs. 8.4 ± 3.9 ng/mL, p = 0.042).

There were 30% of obese patients with elevated GGT (average 99.4 IU/L, range: 49-177 IU/L). This group of patients was younger than those without elevated GGT (35.6 ± 8.7 vs. 43.9 ± 11.8 years, p = 0.05) and was associated with increased uric acid (7.4 ± 2.4 vs. 6.0 ± 1.4 mg/dL, p = 0.046) and triglycerides (267 ± 83 vs. 172 ± 67 mg/dL, p = 0.048) but not with serum transaminases or adipocytokines.

In our study the proportion of males was lower than that of females. Males were younger and with lower body mass index. Biochemically, we found higher concentrations of ghrelin, uric acid, ALT and GGT. Males had lower total cholesterol, HDL-cholesterol and IL-6 than females (see **Table 2**).

Discussion

In this study we identified differences in the profile of adipocytokines, ghrelin and biochemical parameters in Mexican subjects with different degrees of obesity and obese subjects with T2DM. Leptin, resistin, IL-2, IL-6, and IL-10 increased with increasing BMI. These were even higher in the OBDM group. Leptin concentration was lower and uric acid was higher when creatinine clearance was > 120 mL/min. Ghrelin was higher in OB group with BMI < 40 than in controls, but decreased inversely related to BMI and tended to be even lower than controls when obesity was associated with diabetes. One third of patients who were generally younger had elevated serum GGT, uric acid and triglycerides, unrelated to BMI or adipocytokines. We found a gender difference in uric acid levels and ghrelin, with lower levels in females.

Increased glucose and surrogate marker of insulin resistance (HOMA-IR) predict a higher risk for diabetes and vascular disease. Associated vascular disease in these patients is due to decreased production of endothelial nitric oxide and increased systemic oxidative stress [12-14]. Obesity, however, is not synonymous with insulin resistance [10]. Although we

Table 2. Clinical features and biomarkers according to gender in Obeses

	Female $n = 34$	Male $n = 6$	p
Age (years)	41.8 ± 10.9	35.8 ± 15.8	0.07
BMI kg/m^2	45.4 ± 9.1	35.7 ± 6.3	0.01*
Ghrelin pg/mL	1190 ± 440	1737.6 ± 635	0.03*
Glucose mg/dL	102 ±18	96 ± 7	0.40
HbA$_{1c}$ (%)	5.76 ± 2.13	3.7 ± 3.27	0.39
Insulin μIU/mL	21 ± 14.6	19.1 ± 14.7	0.80
C peptide nmol/L	4.28 ± 1.4	3.94 ± 0.07	0.23
HOMA-IR	5 ± 3.3	4.5 ± 3.3	0.80
TG mg/dL	192.3 ± 74.9	219.8 ± 163.6	0.70
TC mg/dL	195.64 ± 29.4	158 ± 12.7	0.002*
LDL-C mg/dL	118.39 21.8	108.83 ± 19.4	0.50
HDL-C mg/dL	42.2 ± 9.2	31.1 ± 4.9	0.03*
Resistin ng/mL	8.76 2.2	9.48 1.3	0.39
Leptin ng/mL	6 ± 3.9	6 ± 2.5	0.99
IL-6 pg/ml	237.36 ± 397	18.7 ± 20.4	0.008*
Uric acid mg/dL	6 ± 1.3	9.5 ± 2.6	0.01*
Leukocytes/mm^3	7520.7 ± 1479.5	7000 ± 1833	0.67
Creatinine clearance ml/min/1.73 m^2	125.7 ± 52.9	148.3 ± 31.6	0.34
AST IU/L	23.4 ± 9.6	57.6 ± 60.9	0.43
ALT IU/L	30.3 ± 16.8	93.3 ± 83.8	0.06*
GGT IU/L	37.7 ± 28.2	168 ± 12.7	0.001*

Mann-Whitney U test was used to compare between groups. *Statistical difference. BMI, body mass index; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

found insulin resistance associated with increasing BMI, normal values were found in a low proportion of subjects. Previous studies found that ~11% of obese patients may be "metabolically healthy". The latter term refers to appropriate insulin sensitivity and normal lipid profile with no increase in cardiovascular risk [15].

Studies in obese patients have suggested that elevated IL-6 and TNF-α promote free fatty acid oxidation and inhibition of lipoprotein lipase in adipose tissue, causing insulin resistance [16]. In the present study we found that insulin resistance also increases the inflammatory profile derived from adipocytes. This increase was not in direct correlation; therefore, it is not possible to predict if the proportional increase in HOMA-IR will be the same in adipocytokines.

Elevation of triglycerides and reduction of HDL-cholesterol are frequently observed conditions in obese patients. According to the Adult Treatment Panel III (ATP III) classification, HDL < 40 mg/dL increases cardiovascular risk by reducing the antioxidant and anti-inflammatory action of these particles [11]. In our study, 69% of obese patients had HDL < 40 mg/dL. These patients were younger and had elevated creatinine clearance. It has previously been observed that HDL and apoA-I are inversely associated with renal creatinine clearance in obese and nonobese subjects without documented renal compromise. In this regard, the proximal renal tubules are capable of endocytosis of proteins associated with HDL-cholesterol, such as ApoA-I found in pre-β-HDL. Although the mechanism is unclear, increased creatinine clearance appears to be an independent indicator of cardiovascular risk associated with a pro-atherogenic lipid profile [17]. LDL-cholesterol presents an additional cardiovascular risk where 100-129 mg/dl is considered optimal according to the ATP III classification. High levels of LDL have been linked to atherogenesis and related proinflammatory cytokines such as IL-6 and resistin. We did not find this relationship in our study probably because only 29% of subjects had LDL > 129 mg/dL, with the highest value 165 mg/dL. We also found no correlation between LDL with BMI or HOMA-IR.

Leptin has been shown to be important in the regulation of food intake, body weight and energy expenditure by stimulating glucose uptake in muscle and stimulating lipolysis [7]. This exerts an insulin sensitivity effect, promoting oxidation of free fatty acids and reducing ectopic fat accumulation. Paradoxically, leptin in obesity is overproduced [18] and is regarded as leptin resistance. In obese subjects with insulin resistance, hyperleptinemia and hypertriglyceride-

mia are common and have been observed in our obese patients. In our patients there was no proportional relationship between leptin and triglycerides; however, we found a slight inverse correlation between triglycerides and the degree of obesity and BMI.

In our obese patients we found a positive correlation between leptin and resistin. The role of resistin in insulin resistance and obesity has been controversial. Initial models of hyperresistinemia showed that resistin can be neutralized with specific antibodies, improving insulin resistance. Obese humans have shown resistin overexpression in white adipose tissue, but not in correlation to increased body weight, adiposity and insulin resistance [19]. Moreover, resistin participates in vascular wall changes and development of atherosclerosis by stimulating the expression of endothelin-1 (ET-1) and adhesion molecules VCAM-1 and MCP-1 [20].

We found increased resistin in obesity in correlation with elevation of IL-6. A direct effect of IL-6 on insulin sensitivity has also been shown on the stimulation of hepatic triglyceride secretion and abnormal gluconeogenesis, induction of SOCS-3 protein (suppressor of cytokine signaling-3) in hepatocytes and inhibition of insulin-dependent receptor autophosphorylation [16]. A third of the IL-6 is derived from white adipose tissue and is higher according to increase of BMI [16, 21]. We found an association between IL-6 and insulin resistance. Likewise, it has been observed that IL-6, as well as other cytokines such as TNF-α, inhibits the action of nitric oxide and promotes increased production of reactive oxygen species, furthering atherosclerosis and endothelial dysfunction [22]. Also, some studies have explored the relationship between cardiovascular mortality and high levels of uric acid in possible response to chronic oxidative stress, principally in females [23]. Our population is probably different because males had higher uric acid than females. It is necessary to include more patients in order to analyze different gender risks.

Interestingly, our moderately obese patients showed an elevation in serum ghrelin. This decreased in patients with BMI > 40 and was lower in controls than in obese subjects with diabetes, in inverse correlation with leptin. Some studies found a negative relationship between ghrelin and adiposity. It has also previously been proposed that the lower level of ghrelin in obesity may be a secondary response to overeating as a conditioned response. Other studies support the concept that insulin is an inhibitor of ghrelin secretion. Thus, obesity-related hyperinsulinemia may, at least in part, be responsible for ghrelin suppression [24].

Regardless of the mechanism whereby ghrelin is decreased in patients with severe obesity and obese subjects with diabetes, the final result is an increased risk of endothelial dysfunction and atherosclerosis [25].

In summary, the inflammatory profile derived from adipose tissue is greater in obese subjects compared to non-obese subjects. This difference increases when obesity is combined with diabetes mellitus. Also, decrease in ghrelin concentrations and increase in uric acid levels may indicate significant vascular inflammation and dysfunction. Younger obese patients will also have elevated serum GGT and uric acid as additional independent predictors of metabolic risk for morbidity.

Disclosure of conflict of interest

None.

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