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Trabajo Original

Obesidad y síndrome metabólico

Effects of depressive symptoms on clinical outcomes, inflammatory markers and quality of life after a significant weight loss in a bariatric surgery sample

Efectos de los síntomas depresivos sobre los parámetros clínicos, marcadores inflamatorios y calidad de vida en una muestra bariátrica tras una pérdida de peso significativa

Joana Nicolau[1], Rafael Simó[2], Pilar Sanchís[1], Luisa Ayala[1], Regina Fortuny[3], Rosmeri Rivera[1] and Lluís Masmiquel[1]

[1]Endocrinology and Nutrition Department. Hospital Son Llàtzer. Palma de Mallorca, Spain. University Institute of Health Sciences Research (IUNICS) and Health Research Institute of Palma (IdISPa). Palma de Mallorca, Spain. [2]Diabetes and Metabolism Research Unit. Vall d'Hebron Research Institute and Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), ISCIII. Spain. [3]Hormonal Laboratory Department. Hospital Son Llàtzer. Palma de Mallorca, Spain

Abstract

Introduction: Obesity is linked to a low-grade chronic systemic inflammation that improves after weight loss. Depressive disorder has been suggested to be associated with systemic inflammation up regulation.

Objective: We aimed to explore whether, after a significant weight loss, the presence of depressive symptoms was associated with differences in terms of inflammatory markers and quality of life.

Methods: Sixty patients (78.3%♀, age 46.4 ± 9.9) who underwent bariatric surgery, with a minimum follow up of 18 months, were evaluated. For the screening of depression, the Beck Depression Inventory (BDI) was administered.

Results: Ten subjects (16.6%) had a positive screening for depressive disorder. The percentage of patients with weight regain was greater among subjects with symptoms of depression (70% *vs.* 32%; p = 0.024), although no differences were seen regarding BMI prior to surgery and current BMI. Acute phase reactants were higher among subjects with symptoms of depression: platelets (319 ± 15 x 10^12/L *vs.* 232 ± 47 x 10 ^ 12/L; p = 0.001), erythrocyte sedimentation rate (24.7 ± 11.3 mm *vs.* 17 ± 10 mm; p = 0.03), fibrinogen (486 ± 107 mg/dL *vs.* 406 ± 66 mg/dL; p = 0.003), ferritin (106 ± 180 ng/ml *vs.* 34 ± 44 ng/ml; p = 0.014) and ultrasensitive C-reactive protein (0.96 ± 1.84 mg/dL *vs.* 0.24 ± 0.26 mg/dL; p = 0.008). All domains of quality of life were significantly lower in the depressive group.

Conclusions: Despite a significant weight loss, inflammatory markers are greater and quality of life lower when associated with depressive symptoms.

Key words:

Obesity. Depression. Bariatric surgery. Acute phase reactants. Quality of life.

Resumen

Introducción: la obesidad se asocia a una inflamación crónica de bajo grado que mejora tras la pérdida de peso. El trastorno depresivo también se ha asociado a una inflamación sistémica.

Objetivo: determinar si, tras una pérdida de peso significativa, la presencia de síntomas depresivos se asocia a diferencias en los marcadores inflamatorios y la calidad de vida.

Métodos: sesenta pacientes (78,3% ♀, edad 46,4 ± 9.9) sometidos a cirugía bariátrica, con un seguimiento mínimo de 18 meses, fueron evaluados. Se autoadministró el test de depresión de Beck (BDI) para el *screening* de depresión.

Resultados: diez sujetos (16,6%) tenían un *screening* positivo para depresión. El porcentaje de pacientes que ganaron peso fue superior en el grupo de pacientes con síntomas depresivos (70% *vs.* 32%; p = 0,024), aunque no se evidenciaron diferencias en cuanto al IMC antes de la cirugía ni al IMC actual. Los reactantes de fase aguda fueron mayores entre los sujetos con síntomas depresivos: plaquetas (319 ± 15 x 10^12/l *vs.* 232 ± 47 x 10^12/l; p = 0,001), velocidad de sedimentación globular (24,7 ± 11,3 mm *vs.* 17 ± 10 mm; p = 0,03), fibrinógeno (486 ± 107 mg/dl *vs.* 406 ± 66 mg/dl; p = 0,003), ferritina (106 ± 180 ng/ml *vs.* 34 ± 44 ng/ml; p = 0,014) y proteína C reactiva (0,96 ± 1,84 mg/dl *vs.* 0,24 ± 0,26 mg/dl; p = 0,008). Todas las esferas de la calidad de vida fueron significativamente inferiores en el grupo con test positivo para depresión.

Conclusiones: a pesar de una pérdida de peso significativa, los marcadores inflamatorios son superiores y la calidad de vida es menor cuando existen síntomas depresivos concomitantes.

Palabras clave:

Obesidad. Depresión. Cirugía bariátrica. Reactantes de fase aguda. Calidad de vida.

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Correspondence:

Joana Nicolau. Endocrinology and Nutrition Department. Hospital Son Llàtzer. Ctra. Manacor, km 4. 07198 Palma de Mallorca, Spain
e-mail: jnicolauramis@gmail.com

INTRODUCTION

Obesity is becoming a major health problem in developed countries. In fact, the most recent reports from the World Health Organization (WHO) estimate that up to 30% of adults in European Union countries are obese (1). Health problems associated with obesity include not only metabolic and cardiovascular diseases, but also psychological comorbidity (2-4). A particular feature of obesity is a low-grade and chronic systemic inflammation, characterized by increased plasma levels of acute phase proteins, such as C-reactive protein (CRP) and ferritin (5,6).

On the other hand, depressive disorder affects 340 million people worldwide. In Europe, it is estimated that around 7% of the adult population suffers from depression (7). The incidence of depression is much higher among persons with obesity, with epidemiological studies indicating prevalence rates ranging from 5 to 23% (8,9) and these percentages are even greater, up to 31.5%, among obese patients seeking bariatric surgery (10,11). In the same way, depression has been suggested to be associated with systemic inflammation up regulation (12). Along with this, studies previously published suggest a bi-directional relationship between these two common disorders, and evidence supports a role for low-grade inflammation in the pathophysiology of each disorder individually (13,14).

At present, bariatric surgery (BS) is considered the most effective treatment for severe obesity as it offers positive effects both on weight and on related comorbidities, including an improvement of the above mentioned low grade inflammatory state, measured through a reduction in the plasmatic concentration of inflammatory markers. Surgery also improves the psychological well-being of obese patients (15). Moreover, improvement in quality of life (QoL) has become recognized as a major outcome measurement for BS. In fact, the presence of significant depressive symptoms could be responsible for a lack of improvement of health-related QoL after BS (16). The hypothesis that psychological factors may contribute to the outcomes of BS is widely accepted among physicians treating these types of patients.

Our study aimed to explore whether, after a significant weight loss in a bariatric sample, the presence of depressive symptoms was associated with differences in terms of weight loss, metabolic parameters, inflammatory markers, satisfaction with surgery and quality of life compared with individuals without significant depressive symptoms.

MATERIALS AND METHODS

SUBJECTS

Patients having bariatric surgery at least 18 months prior to participation in the study were consecutively invited to participate until a total of sixty subjects were included. The study was approved by the Ethics Committee of the hospital. Written informed consent was obtained from all patients prior to study participation. Exclusion criteria were the same as individuals included in our bariatric surgery protocol, AIDS, an active neoplasm and any medical or psychiatric disease that could interfere with the outcomes of the surgical procedure. An extra exclusion criterion was active antidepressant therapy at the time of the evaluation.

ASSESSMENT OF DEPRESSIVE DISORDER

To rule out depressive syndrome, all participating patients rated the presence and severity of depressive symptoms by using the Spanish version of the Beck Depression Inventory (BDI), a 21-item questionnaire that assesses mood over the previous month. Total scores range from 0 to 63, with higher scores indicating greater symptoms of depression. A score in BDI $\geq$ 16 was considered as positive for significant depression (17).

ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE

In order to assess QoL in these subjects, we used the SF-36 Health Survey Spanish version. The SF-36 is a 36-item health questionnaire that yields an overall profile of functional health scores, as well as two summary variables: the physical component score and the mental component score, which are calculated to reflect quality of life related to physical and mental functioning, respectively. "Perception of health" was also included in this questionnaire. "Perception of health" refers to the way how the subject perceives their global health status, both physically and mentally, using a ten-point scale (0-10, "very bad" to "perfect") (18).

ASSESSMENT OF DIETARY HABITS AND COMPLICATIONS AFTER BARIATRIC SURGERY

To determine the proportion of macronutrients as well as the energy intake, a weekly dietary survey, including one weekend, was completed by all participants. A semi-structured interview regarding food intolerances was also performed by a trained nutritionist. A pattern of "grazing" was also assessed in this group of patients by interview. The definition of grazing was based on that reported by Saunders. Grazing was defined by the continuous consumption of smaller amounts of food continuously over an extended period of time which the subjects did not consider to be healthy for them (19). Common problems after BS, such as constipation, irregular menses, dumping syndrome, nausea or vomiting, dizziness, hair loss, nail frailty and early fullness were also registered.

HEIGHT AND WEIGHT

Height and weight were measured while each participant was wearing indoor clothing without shoes. Body mass index (BMI) was

calculated as weight divided by height squared. Weight regain was defined as an increase of more than 10% of the minimum body weight achieved.

METABOLIC AND INFLAMMATORY PROFILE

Blood samples were drawn for the following analyses: blood count, coagulation, fasting glucose, glycated hemoglobin (HbA1c), total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, apolipoproteins, ionograme, plasma creatinine, hepatic profile, albumin, prealbumin, 25OH vitamin D, Vitamins A, E, B1, B12, C and folic acid, zinc and selenium, serum cortisol, leptin, insulin, and thyroid profile. Inflammatory markers used for assessing changes in the low-grade inflammatory state were: C-reactive protein, homocysteine, ferritin, erythrocyte sedimentation rate, fibrinogen and platelet count. First morning void urine samples were collected to determine random albumin-to-creatinine ratio. All measurements were made at 8:00 am after an overnight fast (at least 8 hours fasting).

OTHER ASSESSMENTS

Initial weight and BMI were obtained from computerized medical history. Comorbidities related to obesity prior to surgery, such as diabetes, hypertension, dyslipidemia, sleep apnea syndrome, hyperuricemia, as well as presurgical psychiatric conditions were also recorded.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean ± standard deviation and/or median (interquartile range); and categorical variables were expressed as frequency (percentage). Differences between groups were compared using independent t-tests for continuous variables normally distributed; Mann-Whitney U-tests for continuous variables not normally distributed and chi-square or Fisher's exact tests for categorical variables. Forward and backward linear regressions were used to explore which variables were associated to screening positive for depression (BDI). A p-value < 0.05 on the two-tail was considered to indicate statistical significance. Data were analyzed using SPSS v.16 statistical software (SPSS Inc., Chicago, IL, USA).

RESULTS

All sixty participants had undergone a laparoscopic Roux-en-Y gastric bypass. Forty-seven participants (78%) were female. The mean age of the patients was 46.4 ± 9.9 years and the mean follow-up after bariatric surgery was 46.48 ±18.1 months. The mean pre-surgical BMI was 48.4 ± 7.5 kg/m^2 and, at the time of the evaluation, the mean BMI had decreased to 33.7 ± 6.2 kg/m^2. Forty-seven out of sixty (78%) patients were married. In terms of employment status, 48% of the total sample had a stable job and the remaining 52% were unemployed or retired. Only five participants (8%) had a university degree.

At the time of the evaluation, ten subjects (17%) had a positive screening for depressive disorder after administering the BDI, and the fifty remaining individuals (83%) had a score with the BDI considered as normal.

Although there were no differences among individuals with criteria for depression compared with subjects with a normal BDI score in initial BMI (48.1 ± 7.2 kg/m^2 *vs.* 48.4 ± 7.6 kg/m^2; p = 0.9) or BMI at the time of the evaluation (34.6 ± 9.5 kg/m^2 *vs.* 33.5 ± 5.4 kg/m^2; p = 0.6), the percentage of patients with weight regain was greater among subjects with symptoms of depression compared with subjects without significant depressive symptoms (70% *vs.* 32%; p = 0.024). However, waist circumference was comparable between the two groups (107 ± 13 cm *vs.* 107 ± 13 cm; p = 0.9). Furthermore, the group with positive screening for depression was less satisfied with current weight compared with individuals without depression, measured by the difference between current and desired weight (22 ± 25 kg *vs.* 12 ± 12 kg; p = 0.041). Moreover, we found that, among patients with depression, the desired weight was significantly lower compared to individuals without this psychiatric condition (62 ± 23 kg *vs.* 80 ± 12 kg; p = 0.001).

In addition, no differences were seen in terms of comorbidities related to obesity, such as type 2 diabetes, hypertension, dyslipidemia, sleep obstructive apnea or hyperuricemia between the two groups.

Non-specific systemic inflammatory markers were all significantly higher among subjects with positive screening for depression compared to normal individuals: platelet count (319 ± 15 x 10 ^ 12/L *vs.* 232 ± 47 x 10 ^ 12/L; p = 0.001), erythrocyte sedimentation rate (25 ± 11 mm *vs.* 17 ± 10 mm; p = 0.03), fibrinogen (486 ± 107 mg/dL *vs.* 406 ± 66 mg/dL; p = 0.003), ferritin (106 ± 180 ng/ml *vs.* 34 ± 44 ng/ml; p = 0.014) and ultrasensitive C-reactive protein (0.96 ± 1.84 mg/dl *vs.* 0.24 ± 0.26 mg/dL; p = 0.008). Also, plasmatic basal glucose was greater among subjects with criteria for depression compared to patients without this comorbidity (112 ± 43 mg/dL *vs.* 89 ± 17 mg/dL; p = 0.007). Subjects with criteria for depression had lower vitamin D levels compared with individuals with a normal BDI (18 ± 12 ng/mL *vs.* 26 ± 10 ng/mL; p = 0.024).

The percentage of subjects in the pathological group who reported less than 150 minutes of aerobic exercise per week was greater than the number reported in the group without criteria for depression (70% *vs.* 38%; p = 0.038).

Although no differences were found between the two groups when assessing dietary habits, both groups reporting similar percentages of the different macronutrients in their diet and a similar percentage of calories obtained from alcohol consumption, patients with depression complained more frequently about steatorrhea than the other subjects (30% *vs.* 6%; p = 0.021). No differences in other complications directly related to bariatric surgery, such as dumping syndrome, hair loss, amenorrhea or nail frailty were observed between the two groups.

We observed more difficulties in following the standardized visits according to our hospital's protocol among subjects with a

Table I. Comparison of clinical characteristics and lifestyle habits among subjects with criteria for depression and individuals without it

	Screening negative for depression (n = 50)	Screening positive for depression (n = 10)	p-value
	n (%)	n (%)	
Gender (female)	38 (76%)	9 (90%)	NS
Dumping syndrome	10 (20%)	4 (40%)	NS
Steatorrhea	3 (6%)	3 (30%)	0.021
Exercise	19 (38%)	7 (70%)	0.038

	Mean ± SD	Median (Q1-Q3)	Mean ± SD	Median (Q1-Q3)	
Age (years)	45.5 ± 9.4	46.0 (39.0-53.0)	50.7 ± 11.5	53.0 (40.0-58.5)	NS
Time since BS (months)	45 ± 19	38 (16-67)	53 ± 14	6 (28-76)	NS
Initial BMI (kg/m^2)	48.4 ± 7.6	46.8 (43.5-52.2)	48.1 ± 7.2	48.1 (45.5-1.0)	NS
Current BMI (kg/m^2)	33.3 ± 5.4	32.5 (30.4-34.9)	34.6 ± 9.5	35.9 (29.7-39.6)	NS
Desired weight (kg)	80 ± 12	77 (70-85)	63 ± 23	69 (65-78)	0.001
Weight regain (%)	32 ± 48	0 (0-100)	70 ± 50	100 (0-100)	0.024
Total kilocalories per day	1,350 ± 322	1,394 (1,150 -1,564)	1,273 ± 311	1,153 (1,006-1,464)	NS

Table II. Comparison of biochemical characteristics among the group with criteria for depression and the group with no criteria for depression

	Screening negative for depression (n = 50)		Screening positive for depression (n = 10)		p-value
	Mean ± SD	Median (Q1-Q3)	Mean ± SD	Median (Q1-Q3)	
Platelets (x10^12/L)	232 ± 47	230 (191-259)	319 ± 15	322 (206-449)	0.001
Erythrocyte sedimentation rate	17 ± 10	16 (9-21)	25 ± 11	25 (20-34)	0.03
Fibrinogen (mg/dL)	406 ± 66	404 (356-458)	486 ± 107	524 (401-567)	0.003
Ultrasensitive CRP (mg/dL)	0.24 ± 0.26	0.11 (0.07-0.27)	0.96 ± 1.84	0.25 (0.07-1.33)	0.008
Ferritin (ng/mL)	34 ± 44	15 (7-49)	106 ± 180	19 (6-82)	0.014
Plasma glucose (mg/dL)	89 ± 17	85 (81-92)	112 ± 43	97 (84-111)	0.007
HbA1c (%)	5.58 ± 0.90	5.40 (5.20-5.60)	5.70 ± 0.91	5.40 (5.00-6.00)	NS
Prealbumin (mg/dL)	22.5 ± 4.9	22.0 (19.9-25.3)	18.2 ± 4.7	18.4 (17.7-20.1)	NS
Total cholesterol (mg/dL)	172 ± 30	173 (149-190)	183 ± 41	186 (156-214)	NS
Triglycerides (mg/dL)	100 ± 49	89 (66-121)	118 ± 37	104 (83-139)	NS
Calcium (mg/dL)	9.10 ± 0.45	9.00 (8.80-9.40)	9.09 ± 0.35	9.20 (8.80-9.30)	NS
25OHVitD (ng/mL)	25.7 ± 9.5	23.4 (19.0-33.0)	17.8 ± 12.2	15.0 (5.9-29.0)	0.024
Iron (ug/dL)	74 ± 32	71 (49-104)	74 ± 50	4 (36-101)	NS
Folate (ng/mL)	32.5 ± 76.8	9.1 (5.4-16.2)	11.5 ± 8.1	8.9 (5.2-14.3)	NS
Cianocobalamin(pg/mL)	293 ± 187	274 (180-354)	281 ± 131	284 (174-379)	NS
Leptin (ng/mL)	39 ± 21	37 (26-48)	47 ± 33	36 (26-83)	NS
TSH (mcU/mL)	2.4 ± 1.4	2.0 (1.5-3.0)	2.5 ± 1.6	2.4 (1.4-3.7)	NS
Cortisol (mcg/dL)	17.2 ± 6.3	15.7 (13.4-20.8)	16.7 ± 4.8	16.9 (13.3-19.6)	NS

Table III. Comparison of psychological characteristics and quality of life among subjects with criteria for depression and individuals without it

	Screening negative for depression (n = 50)	Screening positive for depression (n = 10)	p-value
Presurgycal psychiatric comorbidities (%)	27 (54%)	9 (90%)	0.034
% subjects with non adherence to protocol	13 (26%)	7 (70%)	0.009
General health	73 ± 20	45 ± 24	< 0.0001
Physical functioning	91 ± 11	71 ± 30	< 0.0001
Role-physical	89 ± 29	61 ± 45	0.014
Role-emotional	86 ± 24	38 ± 46	< 0.0001
Social functioning	88 ± 18	40 ± 26	< 0.0001
Mental health	64 ± 20	27 ± 4	< 0.0001
Bodily pain	70 ± 24	64 ± 27	NS
Vitality	69 ± 19	37 ± 29	< 0.0001
Perception of health	7.4 ± 1.4	4.5 ± 2.4	< 0.0001

positive screening for depression compared to individuals without significant depressive symptoms (70% *vs.* 25%; p = 0.009).

Prior to surgery, individuals with positive screening for depressive syndrome were more commonly found to have a personal history of some psychiatric disorder (90% *vs.* 54%; p = 0.034), with depression being the most prevalent (n = 5).

On the other hand, when assessing health-related QoL in this group of patients with probable depression, significant differences in both the physical component score and the mental component score were found. General health (46 ± 24 *vs.* 73 ± 20; p < 0.0001), physical functioning (71 ± 30 *vs.* 91 ± 11; p < 0.0001), role physical (61 ± 45 *vs.* 89 ± 29; p = 0.014) for the physical component, and role emotional (38 ± 46 *vs.* 86 ± 24; p < 0.0001), social functioning (40 ± 26 *vs.* 88 ± 18; p < 0.0001), vitality (37 ± 29 *vs.* 69 ± 19; p < 0.0001) and mental health (27 ± 15 *vs.* 64 ± 20; p < 0.0001) for the mental domain. However, bodily pain was comparable between the two groups. Perception of health was lower among individuals with depression compared to subjects without depressive symptoms (4.5 ± 2.4 *vs.* 7.4 ± 1.4; p < 0.0001).

Table IV summarizes the results of the multivariate linear regression analysis of variables associated to Beck Depression Inventory (BDI) adjusted for age. As can be seen, among all the studied variables, general health and inflammatory markers were those with independent and strong association with depression. General health score was negatively correlated to BDI while platelets and ultrasensitive C-reactive protein presented positive correlations.

Table IV. Multivariate linear regression analysis of factors associated to depression (Beck depression inventory)

	β	Std. error	p-value
General Health SF12	-0,408	0,038	< 0,001
Platelets (10^12/L)	0,359	0,010	< 0,001
Ultrasensitive C-reactive protein (mg/dL)	0,279	1,023	0,006
Age (years)	0,037	0,080	0,689

R value of the model is 0,746.

DISCUSSION

Our study showed that the frequency of significant depressive symptoms after bariatric surgery was 17%. Also, the percentage of subjects with significant weight regain was higher among individuals with a positive screening for depression. Moreover, this group of patients was less satisfied with results related to bariatric surgery, in terms of desired weight, and also their quality of life was significantly worse. Furthermore, after a significant weight loss, subjects with a positive screening for depression had greater acute phase reactants compared with subjects without symptoms of depression. As expected, these subjects also had poorer lifestyle habits. Also, subjects with significant symptoms of depression had lower vitamin D levels compared with individuals with a normal BDI.

It is well established that depression is a major comorbidity among obese people, especially in patients seeking bariatric surgery, with weight loss reducing depressive symptoms significantly (20,21). Studies previously published indicate that levels of depressive symptoms increase proportionally as BMI increases (10,22). It is well known that after weight loss, either with bariatric surgery or any other type of intervention, depressive symptoms improve (23,24). The BDI is the most widely used scale to

measure symptoms of depression, and it has been validated as a screening tool for obese people. However, the use of BDI in medical populations has resulted in some difficulty when trying to establish a proper cut off, due to the overlap between symptoms of depression and physical symptoms of obesity. Therefore, a cut off of 16, instead of 12, has been proposed to be an accurate indicator of clinical depression among obese individuals (17). However, limited data exist regarding the prevalence of depression after bariatric surgery. Furthermore, even though depressive symptoms usually improve immediately after surgery, but they can reoccur after weight loss has reached a plateau. In fact, de Zwaan et al. demonstrated that depressive symptoms improve 6-12 months after surgery in a sample with preoperative depressive disorder, but these symptoms tended to reappear 24-36 months after surgery, and were associated with less weight loss (25). The frequency of significant depressive symptoms in our sample (16.6%) was comparable to the prevalence reported by de Zwaan et al. (14.3%) (25). Although none of the patients included was taking antidepressant therapy, our data show that a substantial number of subjects had symptoms of depression up to 18 months after bariatric surgery and, therefore, they would benefit from medical attention in order to improve clinical outcomes. Only two of our patients developed a non-preexistent depressive disorder (data not shown). Moreover, the rates of depression after bariatric surgery are higher than in the obese general population (7.6%) (26).

In our study, the proportion of subjects with weight regain was higher in the group with symptoms of depression. As mentioned above, depression has been linked to poorer weight loss after bariatric surgery (25,27).

Subjects with depressive symptoms did less physical activity. Poorer lifestyle habits could contribute to making weight maintenance difficult. In fact, overeating, alcohol intake, unhealthy diet preferences or insufficient exercise may be patterns adopted by people with a depressive disorder (28,29).

When comparing QoL, the group with significant depressive symptoms had worse health related QoL (HRQoL) compared to individuals without depression. It is well- known that bariatric surgery offers beneficial effects on the medical conditions associated with obesity. In fact, HRQoL is directly related to the degree of weight loss (16,30). Conversely, subjects who do not lose weight as expected or experience weight regain do not maintain their improvements in HRQoL (31,32). It has been suggested that the occurrence of depression as a comorbidity could predict an attenuation in improvement of HRQoL after BS (32).

We also found that individuals with criteria for depression had lower vitamin D levels. Because vitamin D receptor is found in areas of the brain that are involved in the pathophysiology of depression (33), the role of this vitamin as a therapeutic agent in depression is being investigated. A systematic review from observational studies concluded that vitamin D deficiency is positively associated with depression in adults (34). However, many randomized controlled trials (RCT) of vitamin D supplementation in depression have been reported with inconsistent findings. Recently, a systematic review and meta-analysis of RCT concluded that there is still insufficient evidence to support the efficacy of vitamin D supplementation in depression symptoms (35).

We also found that patients with a positive screening for depression had higher levels of low-grade chronic inflammation as measured by different inflammatory markers, such as CRP, ferritin of fibrinogen, even after a significant weight loss and despite the absence of differences in weight at the time of the evaluation. It is well recognized that a central feature of obesity is a chronic, low-grade inflammation promoted by adipocytes that are able to secrete acute phase reactants and inflammatory cytokines (5,36). On the other hand, depression has also been linked to systemic inflammation upregulation. Different hypotheses have been proposed to explain the physiopathology of this association. Traditionally, depression has been explained by the monoamine model, which attributes depressive symptoms to alterations in the metabolism or activity of serotonin, noradrenaline and dopamine. The inflammatory hypothesis of depression suggests that depressive symptoms may be a consequence of activation of various aspects of the immune system both peripherally and centrally. Another possible explanation is that cytokines cross the blood-brain barrier and activate microglia to produce cytokines centrally in order to interact with several brain mechanisms to induce depressive behaviors. One of the latest and also most widely accepted mechanisms for explaining depression is that cytokine-induced hyperactivity of the adrenal axis has the potential to contribute to depressive symptoms (12). Recently, it has been shown that obesity is associated with an increase in depressive symptoms which might be explained by obesity-related elevations in the inflammatory marker CRP (36). Taking all together, there is no doubt about the bi-directional relationship between obesity and depressive disorder: In other words, depression predicts obesity and obesity is a risk factor for depression. However, the depressogenic effect of obesity is not sufficient to explain such associations, due to the fact that, as we observed, after a significant weight loss and without differences in BMI at the time of the evaluation, symptoms of depression are associated with higher acute phase reactants which could explain our results. On the other hand, subjects with depressive symptoms did less exercise. The inactive skeletal muscle becomes an additional source of pro-inflammatory cytokines, which contributes to enhancing the systemic inflammatory status (37).

The current study was limited in several aspects. It was conducted on cross-sectional data, making it impossible to infer the depressive symptoms which preceded the presence of inflammation, as both depression and acute phase reactants were assessed at the same point. Also, depressive disorder was not assessed using a structured clinical interview. It is important, therefore, to conduct longitudinal studies prior to making the suggestion that depression might play a causal role in the maintenance of a low-grade inflammatory state among obese individuals after a significant weight loss has been achieved with bariatric surgery. Moreover, further studies are needed to determine which inflammatory markers could predict significant depressive symptoms among obese people.

In conclusion, in a bariatric surgery sample, when weight loss has reached a plateau, the presence of depressive symptoms was associated with higher levels of acute phase reactants and poorer health related quality of life.

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