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ORIGINAL ARTICLE

Metabolic syndrome, psychological status and quality of life in obesity: the QUOVADIS Study

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Objective: We aimed to investigate the association of the clinical variables of the metabolic syndrome (MS) and psychological parameters on health-related quality of life (HRQL) in obesity. In particular, our aim was to investigate the relative impact of physical symptoms, somatic diseases and psychological distress on both the physical and the mental domains of HRQL.
Design: Cross-sectional study.
Subjects: A cohort of 1822 obese outpatients seeking treatment in medical centers.
Measurements: HRQL was measured by the standardized summary scores for physical (PCS) and mental (MCS) components of the Short Form 36 Health Survey (SF-36). Patients were grouped according to tertiles of PCS and MCS. Metabolic and psychological profiles of PCS and MCS tertiles were compared by discriminant analysis.
Results: The profile of metabolic and psychological variables was tertile-specific in 62.4 and 68.3% of patients in the lowest and highest tertiles of PCS, respectively, while concordance was low in the mid-tertile (32.8%). Concordance was very high in the lowest (74.4%) and in the highest (75.5%) tertiles of MCS, and was fair in the mid-tertile (53.2%). The main correlates of PCS were obesity-specific and general psychological well-being, BMI, body uneasiness, binge eating, gender and psychiatric distress. Only hypertension and hyperglycemia qualified as correlates among the components of MS. The components of MS did not define MCS.
Conclusions: Psychological well-being is the most important correlate of HRQL in obesity, both in the physical and in the mental domains, whereas the features of MS correlate only to some extent with the physical domain of HRQL.
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Keywords: metabolic syndrome; well-being; psychological status; health-related quality of life; observational study

Introduction

Obesity is a complex, multifactorial disease,[1] having a significant impact on morbidity and mortality, as well as on psychosocial well-being and quality of life.[2] These features make the measurement of health-related quality of life (HRQL) a key issue in obesity studies.[2] HRQL progressively deteriorates across the whole spectrum of obesity classes among obese individuals, both seeking and not seeking medical treatment for weight loss.[3] The physical domain of HRQL is greatly affected by physical symptoms and somatic diseases[4,5] and pain is a leading symptom associated with poor HRQL.[6] Unexpectedly, also psychological distress[7] and binge eating[8] contribute to poor HRQL in obesity not only in the mental domain, but also in the physical domains. Therefore, an extensive assessment of both somatic and psychological variables is needed for a comprehensive profile of HRQL in obese subjects.

The metabolic syndrome (MS) is a cluster of inter-related risk factors for atherosclerosis and cardiovascular disease.[9,10] While acute cardiovascular events, such as myocardial infarction and stroke, have obvious consequences on the HRQL, the impact of MS on HRQL is less predictable and has not been clearly defined. Selected components of MS, such as abdominal obesity, hypertension and hyperglycemia,

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have been reported to impair HRQL in post-menopausal Ecuadorian women,[11] while insulin resistance was associated with poor HRQL in the physical domain, but not in the mental domain, in a large elderly population from the United Kingdom.[12]

The QUOVADIS program is an observational, multicentered study specifically aimed at measuring the burden of obesity and its complications on HRQL.[13] The study also collected extensive information on the individual components of MS as well as several data on psychological distress.[14] Thus, it represents a valuable opportunity to investigate the relationship between MS, psychological distress and HRQL in a large population sample of obese subjects seeking medical treatment. The aim of the present study was to verify the relative impact of the individual components of MS and of variables of psychological distress on both the physical and the mental domains of HRQL in obese outpatients.

Methods

Patients

The present report uses data from the QUOVADIS study, which has been described in detail elsewhere.[13,14] Briefly, during the years 1999–2000, 25 Italian centers with a specific interest in clinical obesity research consecutively enrolled treatment-seeking obese patients (BMI $>30\,kg/m^2$) into the study. The enrollment period was preceded by two meetings of the steering committee and by a general investigators' meeting to decide selection criteria and to agree on data collection and management of patients. All obese subjects seeking treatment were eligible for the study, provided that they were not on active treatment for obesity at the time of enrollment. All patients enrolled were in the age range between 20 and 65 years, and agreed to fill out a package of self-administered questionnaires.

Clinical data were collected by means of a structured questionnaire (Case Report Form) predefined at the time of the general investigators' meeting. Recorded data included information on civil and educational status, personal and family history of metabolic and cardiovascular diseases, and previous and current pharmacological treatment. To expedite handling of data, the study was totally web-based through an extranet system provided by CINECA (Casalecchio di Reno, Italy), using the Advanced Multicenter Research methodology developed by CINECA as a result of an extensive cooperation between clinicians, statisticians and experts in information technology. The management of all the data was performed by standard web browsers, and the quality level was guaranteed by upfront quality controls (on the client side) and consistency checks (on the server side). On enrollment, all subjects signed an informed consent to take part in the study, which was approved by the Ethical Committee of the coordinating center (Bologna; reference no. Sper65/99/U; 9 July 1999) and by the Institutional Review Boards of individual local centers.

Definition of the outcomes

The main outcome of the study was HRQL, as measured by the Short Form 36 Health Survey (SF-36) questionnaire.[15,16] SF-36 is a 36-item questionnaire measuring subjective health status in eight domains: physical functioning, role limitations (because of physical problems), bodily pain, general health, vitality, social functioning, role limitations (because of emotional problems) and mental health. The SF-36 questionnaire has been recently proved to maintain a robust internal structure also in obese outpatients.[17] The standardized summary scores for physical (PCS) and mental (MCS) components were computed as previously reported,[18] and separately used as outcome measures.

Measurements

Body weight was measured in light clothing and without shoes to the nearest 0.5 kg. Height was measured to the nearest 0.5 cm. BMI was calculated as weight (in kilograms) divided by squared height (in meters). Waist circumference was measured midway between the lower rib margin and the iliac crest. Diagnostic criteria for metabolic syndrome were those suggested by the US National Cholesterol Education Program—Adult Treatment Panel III (NCEP ATP-III): waist circumference >102 cm for men or >88 cm for women; plasma triglycerides $\geqslant 150$ mg/dl; high-density lipoprotein (HDL) cholesterol <40 mg/dl for men and <50 mg/dl for women; blood pressure $\geqslant 130/85$ mm Hg; fasting plasma glucose $\geqslant 110$ mg/dl.[10] Subjects treated for diabetes and hypertension were classified as positive, independent of glucose and blood pressure. Other variables specifically considered in the analysis were age, gender and education.

All patients underwent a comprehensive assessment exploring psychological well-being, including the following:

1. Obesity-Related Well-Being (ORWELL) 97:[19] an 18-item instrument exploring obesity-specific quality of life, and measuring intensity and subjective relevance of obesity-related physical and psychosocial distress. All items are computed in a single score.
2. Symptom Check List (SCL):[20] a 90-item instrument exploring psychiatric distress in 9 areas: somatization, obsessive-compulsive thoughts, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid conceiving and psychotic behavior. For the purpose of the present study, we used the global score (sum of the scores of the 90 items).
3. Psychological General Well-Being (PGWB) scale:[21] a 22-item instrument exploring subjective well-being in six affective states (anxiety, depressed mood, positive well-being, self-control, general health and vitality) and a general index used in the present study.
4. Binge Eating Scale (BES):[22] a 16-item tool measuring the severity of binge eating. It examines both behavioral manifestations (eating large amounts of food) and

feeling/cognition during a binge episode (loss of control, guilt and fear of being unable to stop eating).
5. Body Uneasiness Test (BUT):[23] a 71-item instrument specifically developed to evaluate concern for physical appearance, body image awareness and body parts that most severely contribute to body dissatisfaction. For the purpose of the present analysis, we used the scores of Part A, combined in a single global index (Global Severity Index).

All the scores obtained in the above tests were considered as potential correlates of HRQL and were tested in the analysis.

Statistical analyses

PCS and MCS scores were separately considered in the analysis. Patients were aggregated in tertiles of standardized scores, and the relationships between age, gender, education and MS risk factors with tertiles were initially evaluated by the χ^2 test for categorical variables and by the analysis of variance (ANOVA) one-way test for continuous variables. Two-tailed *P*-values less than 0.05 were considered statistically significant.

A discriminant analysis of metabolic and psychological profiles of tertiles was performed to identify tertile-specific patterns of study variables, that is, the most common combinations of metabolic and psychological variables within each tertile, and, then, to cross-tabulate individual patterns vs tertile-specific patterns. The higher the concordance between the actual tertile membership, resulting from tertile aggregation, and the predicted tertile membership, resulting from discriminant analysis, the greater the specificity of the metabolic and the psychological profiles of the corresponding tertile. We computed Wilk's λ coefficient to test the null hypothesis, that is, that groups did not differ in the means of the discriminating functions. Box's *M* coefficient was computed to assess the risk of misclassification by the discriminant function. We identified the items that were most useful for characterizing and discriminating tertiles on the basis of their standardized coefficients.[24] All analyses were performed using SPSS V10.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, 1944 obese patients were enrolled, but complete data for the present study were available in 1822 cases. The crude relationship between tertiles of PCS and study variables is reported in Table 1 (upper panel). Patients in the lowest tertile had the highest prevalence of women and the lowest educational level. Severe obesity was more prevalent among patients in the lower tertile of PCS, as were high blood pressure, hyperglycemia, hypertriglyceridemia and abdominal adiposity. Psychological and behavioral variables were more commonly altered among patients in the lowest PCS tertile. At variance, when tertiles of MCS were considered, only gender, psychological and behavioral variables were significantly associated with the outcome in univariate analysis (Table 1, lower panel).

The results of discriminant analyses are reported in Tables 2–4. The analyses identified two discriminant functions for both SF-36 components, and the former was highly significant (Table 2).

A good concordance between actual and predicted tertiles membership was observed in the lowest and the highest tertiles of PCS (Table 3, upper panel). Concordance between actual and predicted tertile membership was very high in the lowest and the highest tertile of MCS, and was fair in the mid-tertile (Table 3, lower panel). The highly significant Box's *M* coefficients indicated that the discriminant functions achieved a highly reliable definition of individual profiles of metabolic and psychological status. When psychological and behavioral variables were removed from the discriminant model, the classificatory capacity was significantly reduced, and only 48.8% of cases were correctly classified in the PCS analysis. The corresponding figure for MCS was 39.1%.

The contribution of individual study variables to the discriminant function 1 for PCS is reported in Table 4 (upper panel). ORWELL, PGWB and BMI were the main determinants of function 1 for the physical component, and also BUT, BES, gender and SCL contributed to define the clinical profile of the discriminant function. Among the individual components of MS, only blood pressure and plasma glucose qualified as significant correlates of PCS.

ORWELL and PGWB were the main determinants of discriminant function 1 for MCS, with a minor contribution of BUT, BES and gender (Table 4, lower panel), whereas the individual components of MS did not correlate significantly with MCS.

The results did not change significantly when we considered the contemporary presence of three or more components of MS instead of the single individual items. Indeed, the tertiles of PCS and MCS were correctly classified in 52.3 and 67.5% of cases, respectively. The presence of three or more components of MS was significantly correlated with PCS (standardized discriminant coefficient = 0.306), but not with MCS (standardized discriminant coefficient = 0.159).

Discussion

Our study shows that the presence of individual components of MS and poor HRQL parallel each other only to some extent. Although a higher prevalence of clinical variables constituting the MS characterized patients with a poorer HRQL in the physical domain, only BMI, blood pressure and fasting plasma glucose qualified as significant correlates of PCS in discriminant analysis, and none entered the discriminant analysis of MCS.

Table 1 Sociodemographic, clinical and psychological characteristics of patients divided according to the tertiles of the PCS (upper panel) or the MCS (lower panel)

	PCS tertiles			P
	<39.5 N = *608*	*39.5–49.5* N = *607*	*>49.5* N = *607*	
Age, years	45.1±11.0	44.2±11.1	44.9±10.8	0.300
Gender, females	524 (86.2)	478 (78.7)	418 (68.9)	0.001
Education				
Illiterate	12 (2.0)	10 (1.6)	9 (1.5)	0.001
Primary school	162 (26.6)	108 (17.8)	44 (7.2)	
Secondary school	226 (37.2)	195 (32.1)	182 (30.0)	
Commercial or vocational school	186 (30.6)	237 (39.0)	307 (50.6)	
Academic degree	22 (3.6)	57 (9.4)	65 (10.7)	
Body mass index, kg/m^2				
30–34.9	145 (23.8)	241 (39.7)	318 (52.4)	0.001
35–39.9	152 (25.0)	182 (30.0)	180 (29.7)	
40–44.9	176 (28.9)	117 (19.3)	67 (11.0)	
⩾45	135 (22.2)	67 (11.0)	42 (6.9)	
Blood pressure ⩾130/85 mm Hg	448 (73.7)	410 (67.5)	362 (59.6)	0.001
Waist circumference >102 cm for men or >88 cm for women	586 (96.4)	581 (95.7)	557 (91.8)	0.001
HDL cholesterol <40 mg/dl for men or <50 mg/dl for women	314 (51.6)	290 (47.8)	286 (47.1)	0.233
Triglycerides ⩾150 mg/dl	214 (35.2)	173 (28.5)	173 (28.5)	0.014
Fasting plasma glucose ⩾110 mg/dl	157 (25.8)	122 (20.1)	84 (13.8)	0.001
Metabolic syndrome (three or more criteria)	377 (62.0)	315 (51.9)	273 (45.0)	0.001
Obesity-related well-being	62.9±29.8	48.8±26.0	36.9±24.1	0.001
Symptom checklist	90.0±54.8	73.7±50.6	67.0±38	0.001
Psychological general well-being	60.9±17.5	67.8±18.1	77.4±16.2	0.001
Binge eating scale	17.1±9.9	14.6±8.9	12.6±8.9	0.001
Body uneasiness test	1.8±1.0	1.5±0.9	1.3±0.9	0.001
	MCS tertiles			
	<38.0 N = *618*	*38.0–50.0* N = *589*	*>50* N = *615*	P
Age, years±s.d.	45.0±10.7	44.7±10.8	44.4±11.3	0.575
Gender, females	524 (84.8)	461 (78.3)	435 (70.7)	0.001
Education				
Illiterate	11 (1.8)	9 (1.5)	11 (1.8)	0.293
Primary school	116 (18.8)	90 (15.3)	108 (17.6)	
Secondary school	203 (32.8)	189 (32.1)	211 (34.3)	
Commercial or vocational school	245 (39.6)	240 (40.7)	245 (39.8)	
Academic degree	43 (7.0)	61 (10.4)	40 (6.5)	
Body mass index, kg/m^2				
30–34.9	212 (34.3)	251 (42.6)	241 (39.2)	0.060
35–39.9	180 (29.1)	164 (27.8)	170 (27.6)	
40–44.9	140 (22.7)	106 (18.0)	114 (18.5)	
⩾45	86 (13.9)	68 (11.5)	90 (14.6)	
Blood pressure ⩾130/85 mm Hg	415 (67.2)	383 (65.0)	422 (68.6)	0.413
Waist circumference >102 cm for men or >88 cm for women	593 (96.0)	550 (93.4)	581 (94.5)	0.137
HDL cholesterol <40 mg/dl for men or <50 mg/dl for women	291 (47.1)	298 (50.6)	301 (48.9)	0.475
Triglycerides ⩾150 mg/dl	183 (29.6)	184 (31.2)	193 (31.4)	0.757
Fasting plasma glucose ⩾110 mg/dl	131 (21.2)	101 (17.1)	131 (21.3)	0.122
Metabolic syndrome (three or more criteria)	333 (53.9)	296 (50.3)	336 (54.6)	0.268
Obesity-related well-being	68.9±28.2	46.3±24.1	33.0±20.9	0.001
Symptom checklist	112.8±55.6	61.9±36.7	55.0±35.3	0.001
Psychological general well-being	51.5±14.3	70.2±11.9	84.5±11.3	0.001
Binge eating scale	19.5±9.8	14.4±8.5	10.3±7.4	0.001
Body uneasiness test	2.1±1.1	1.5±0.9	1.1±0.8	0.001

Abbreviations: HDL, high-density lipoprotein; MCS, mental component summary; PCS, physical component summary. Data are number of cases (percentage) or mean±s.d.

Table 2 Canonical discriminant functions

Function	*Eigenvalue*	*% of variance*	*Wilks's λ*	P
Components of metabolic syndrome vs PCS				
1	0.374	98.3	0.723	<0.001
2	0.007	1.7	0.994	0.613
Components of metabolic syndrome vs MCS				
1	1.241	98.7	0.439	<0.001
2	0.004	1.3	0.997	0.113

Abbreviations: MCS, mental component summary; PCS, physical component summary.

Table 3 Cross-tabulation of actual tertiles membership vs functional tertiles membership

Actual PCS tertiles membership	*Functional PCS tertiles membership*[a]		
	<39.5	*39.5–49.5*	*>49.5*
<39.5	62.4	20.9	16.7
39.5–49.5	30.9	32.8	36.3
>49.5	11.6	20.1	68.3
	Functional MCS tertiles membership[b]		
	<38.0	*38.0–50.0*	*>50.0*
<38.0	75.5	21.9	2.6
38.0–50	20.0	53.2	26.7
>50	2.8	22.7	74.4

Abbreviations: MCS, mental component summary; PCS, physical component summary. [a]Data are in percentages. Box's $M=1878.704$; $P<0.001$; 54.7% of original grouped cases correctly classified. [b]Data are in percentages. Box's $M=1820.720$; $P<0.001$; 67.8% of original grouped cases correctly classified.

Table 4 Variables significantly contributing to discriminant functions

	Function	
	1	2
Individual components of metabolic syndrome and clinical/psychological variables vs PCS		
Obesity-related well-being	0.667	—
Psychological general well-being	−0.624	—
Body mass index	0.515	—
Body uneasiness test	0.385	—
Binge eating scale	0.320	—
Gender	0.281	—
Symptom checklist	0.240	—
Blood pressure	0.188	—
Plasma glucose	0.180	—
Waist circumference	—	−0.424
Plasma triglycerides	—	0.372
Plasma HDL cholesterol	—	−0.211
Education	—	−0.199
Age	—	0.108
Individual components of metabolic syndrome and clinical/psychological variables vs MCS		
Psychological general well-being	0.964	—
Obesity-related well-being	−0.537	—
Body uneasiness test	−0.424	—
Binge eating scale	−0.376	—
Gender	−0.114	—
Education	—	−0.622
Body mass index	—	0.536
Symptom checklist	—	0.505
Plasma glucose	—	0.288
Waist circumference	—	0.233
Blood pressure	—	0.201
Plasma HDL cholesterol	—	−0.171
Plasma triglycerides	—	0.126
Age	—	0.101

Abbreviations: HDL, high-density lipoprotein; MCS, mental component summary; PCS, physical component summary.

The impact of BMI on physical domain of HRQL is well known.[4,5,17,25] Yancy *et al.*[4] showed that increasing BMI mainly affected the domains of physical activity and bodily pain, and, similarly, Doll *et al.*[5] reported that obesity had a particularly negative impact on physical well-being. BMI can significantly affect the internal structure of the SF-36 items exploring physical activity by affecting two main components, one related to vigorous activities and complex movements, and another related to all other physical activities.[17] This particular clustering of physical abilities with increasing BMI and poor HRQL in the physical domain may have important implications for the management of obese patients. Indeed, specific physical activity programs may be tailored to regain or maintain highly demanding physical functions or to approach wider defects of mild and moderate physical activities.[26] Furthermore, identifying patients with a greater impairment in mild and moderate physical activities could have some prognostic relevance, considering the importance of a regular physical exercise in the treatment of obesity and in weight loss maintenance.[27]

Conflicting results have been reported on the association between high blood pressure and HRQL, a few studies reporting a low influence,[28,29] others supporting a relevant effect on physical functioning.[30–32] Furthermore, the sole awareness of hypertension could contribute to worsen HRQL, and such a negative effect may be at least partially ascribed to the prescription of antihypertensive drugs.[28] On the contrary, the association between diabetes and poor HRQL is well known, with macrovascular complications, especially coronary heart disease, and non-vascular diseases as the strongest and the most commonly found predictors.[33] More recently, it has been demonstrated that also the early stage of the disease, that is impaired glucose tolerance, is associated with a reduced ability to perform physical activities.[34] Finally, diabetes has a greater impact on the scales of SF-36 measuring physical health as against the mental components, and the presence of coexisting hypertension in subjects with diabetes resulted in a further significant decrease of HRQL, with an additive effect.[35]

The most surprising finding of our study is the highly relevant role of measures of psychological well-being in

explaining PCS. Indeed, ORWELL and PGWB scores were the main correlate of PCS, and also BUT, BES and SCL contributed to define the discriminant function. Previous findings suggest that psychological disturbances can contribute significantly to poorly perceived health status. The presence of depressed mood and/or anxiety, which are the most common psychological disturbances observed in clinical samples of obese patients,[36] can increase subjective distress induced by disease-related physical symptoms and functional impairment.[19] It is worth noting that also binge eating behavior, as estimated by BES, contributes to define the clinical profile of obese patients with poor HRQL in the physical domain. Binge eating disorder is known to worsen HRQL measured by disease-specific questionnaires,[19,37] and it is possible that the association we observed between binge eating and PCS can be partly mediated by the higher BMI.[38]

Our results are partly in contrast with a previous survey in a small sample of obese patients undergoing bariatric surgery, where mental disorders appeared to affect psychosocial, but not physical, domains of SF-36.[39] However, the different sample size or type of referral could also account for this apparent discrepancy. Furthermore, the use of specific instruments for measuring psychological distress make our results more reliable than those obtained using only the formal diagnosis of mental disorders in previous studies. In general, these findings confirm how difficult it is to disentangle the effects of obesity on physical function from those on mental function in treatment-seeking patients,[17] reinforcing the need for a comprehensive approach.

Only gender and measures of psychological well-being qualified as significant correlates of MCS. This association could be related to the higher prevalence of psychological disorders among women,[19,40,41] or to a greater cultural drive for thinness of women in Western societies,[42] and confirms previous reports in clinic-based samples,[2,19,41,43] among patients with chronic disease[44] and in population studies.[45] Additionally, the lack of association between BMI and MCS tertiles suggests that the perception of the disease, more than its severity, could be important in determining psychological distress in obese outpatients.

This study has limitations too. First, waist circumference did not contribute to any discriminant function, in disagreement with recent findings in post-menopausal women.[11] Possibly, the high prevalence of abdominal adiposity in our study population did not allow a more precise evaluation of the relationship between abdominal adiposity and HRQL, and this issue deserves further investigation. Second, the results were obtained in a large outpatient population of obese individuals seeking medical treatment, and their external validity in the general population of obese patients and in different settings needs to be determined. Finally, the cross-sectional design did not allow us to investigate the directionality of the correlation between study variables and HRQL.

In conclusion, psychological well-being is the most important correlate of HRQL in obesity, both in the physical and in the mental domains, whereas the features of MS correlate only to some extent. Since HRQL is a primary treatment outcome in chronic diseases,[46] psychiatric and psychological support becomes mandatory in weight management programs. Only a multidisciplinary approach addressing both mental and somatic disorders is likely to reduce the burden of obesity in individual patients.

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