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Metabolic syndrome and health-related quality of life in patients with schizophrenia

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The association of metabolic syndrome (MetS) with health-related quality of life (HRQol) in schizophrenia is poorly documented. The relationship between MetS, HRQol and global functioning were examined. For this goal, 76 individuals with schizophrenia and schizoaffective disorder (DSM-IV criteria) were interviewed to obtain sociodemographic data, lifestyle habits, psychopathology (PANSS scale), global functioning (GAF scale), sef-reported quality of life (EQ-5D scale) and the anthropometric measures and blood test results. MetS was defined by the NCEP (2005) criteria. The prevalence of MetS was 36.8%. MetS was directly associated with personal background of dyslipidaemia and diabetes mellitus. Subjects with MetS had greater weight, BMI, waist, blood pressure, triglycerides, fasting glucose and a lower HDL-cholesterol. The MetS is also associated with age, inactive employment status and better self-care. The EQ VAS (visual analogue scale) of EQ-5D shows that subjects with MetS who practice physical activity indicates a better subjctive perception of health, which remarks the necessity of improving healthy lifestyle and an interdisciplinary treatment of the MetS. There is no association between global functioning and HRQol. This is the first study which investigates the relationship between MetS, HRQol and GAF in individuals with schizophrenia in the European context.

Keywords: Schizophrenia, Metabolic syndrome, Quality of life/health-related quality of life

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Síndrome metabólico y calidad de vida relacionada con la salud en pacientes con esquizofrenia

La asociación entre el síndrome metabólico (SMet) y la calidad de vida relacionada con salud (CVRS) en individuos con esquizofrenia está poco documentada. Los objetivos fueron estudiar la relación entre SMet, CVRS y funcionamiento global. Fueron evaluados 76 individuos con esquizofrenia y trastorno esquizoafectivo (según criterios DSM-IV) y se registraron también sus características sociodemográficas, estilo de vida, sintomatología psicótica (PANSS), funcionamiento global (GAF), escala de CVRS subjetiva (EQ-5D), medidas antropométricas y análisis de sangre. El SMet fue evaluado según criterios del NCEP (2005). La prevalencia del SMet es de un 36,8%. Se evidenció una asociación directa entre SMet y antecedentes personales de dislipemia y de diabetes mellitus. Los sujetos con SMet presentan mayor peso, IMC, PAb, PA, Triglicéridos y glucosa y menor tasa de HDL-colesterol. También la presencia de SMet está asociada con la edad, con la inactividad laboral y con un mejor "autocuidado". La EQ VAS (escala análogo-visual) de la EQ-5D muestra que los sujetos con SMet que practican actividad física refieren una mejor autopercepción de salud, lo que refuerza la importancia de promover hábitos saludables y el tratamiento del SMet desde una perspectiva interdisciplinar. No se ha encontrado asociación entre el funcionamiento global y la CVRS. Este es el primer estudio que investiga la asociación entre SMet, CVRS y GAF en sujetos con esquizofrenia en el contexto europeo.

Palabras-clave: Esquizofrenia, Síndrome metabólico, Calidad de vida/calidad de vida relacionada con la salud

INTRODUCTION

Schizophrenia is a neurodevelopmental disorder as well as one of the most incapacitating diseases existing. In spite of advances, currently patients with schizophrenia continue to have lower life expectancy than the general population. This is mainly due to the presence of metabolic and cardiovascular risk factors related with the disease per se, style of life and antipsychotic treatment. The scientific literature has corroborated the association between schizophrenia and metabolic alterations for decades.[1,2] However, the growing epidemiological, clinical and therapeutic interest regarding MetS is because the risk

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Table 1 Prevalence of MetS in different populations with schizophrenia /SA

Authors/ Site	Sample*	N	Mean age	Prevalence (%)
Heiskanen et al. (2003) Finland	S/A	35	44.5	37.1
Straker et al. (2003) USA	S/H	94	39.6	28.7
Littrell et al. (2003) USA/ Taiwan	S+SA/OP+H	USA: 98 OP Taiwan: 27 H	41.8 42.0	51.0 22.2
Cohn et al. (2004) Canada	S+SA - 2/3OP	240	43.3	44.7
Kato et al. (2004) USA	S/A	48	ND	63.0
Basu et al. (2004) USA	SA/OP	33	44.5	42.4
Pandina et al. (2004) USA	S/A	121	41.1	53.7
McEvoy et al. (2005) USA	S/A	1460	40.6	40.9
Saari et al. (2005) Finland	S/A	31	ND	19.4
Cañas et al. (2006) Spain	S/H	733	38.0	19
Correll et al. (2006) USA	S/H	367	42.9	37.3
De Hert et al. (2006) USA	S/A	430	36.5	28.4
Hägg et al. (2006) Sweden	S/A	269	46	34.6
Bobes et al. (2007) Spain	S/A	1452	40.7	24.6
Sánchez-Araña et al. (2007) Spain	S+SA / H	136	39.1	36
Huang et al. (2009) Taiwan	S+SA / H	650	45.8	34.9

*Schizophrenia, SA=Schizoaffective D, S + SA =Mixed Sample; OP = Outpatient, H = Hospital, OP+H=Mixed Sample. Adapted from McEvoy et al. (2005) and Bobes et al. (2007)

factors that compose occur simultaneously and each one of them contributes individually to cardiovascular risk both in the general population[3] and in individuals receiving atypical antipsychotic treatment.[1,2]

The MetS study has intensified since it points to a clinical entity that functions as a risk factor of cardiovascular disease and the search for one of its components increases attention towards the other factors. In the schizophrenia population, presence of MetS is associated to greater prevalence of psychotic and depressive symptoms with worse perception of physical health.[4-5] The "Spanish consensus on physical health of patients with schizophrenia" concluded, after reviewing the literature published in the Medline data base until the year 2006, that MetS is 2-4 times more prevalent in this population. Prevalence would be related with age, gender and race. Besides, there seems to be a relation between MetS and the number of antipsychotics administered (polytherapy) without relating it to a specific psychopharmaceutical.[6]

On the other hand, studies with patients recently diagnosed of schizophrenia and not treated revealed that these subjects had 3 times more intraabdominal fat than those without this disease. This seems to be explained by the participation of the hypothalamic-pituitary-adrenal axis that regulates, among other functions, body metabolism and response to stress. Its unbalance seems to be associated to the development of schizophrenia.[7]

In Spain, the percentage of overweight and obese patients is 41.1% and 30.8%, respectively, according to the CLAMORS study[8] and it is estimated that the MetS incidence in the general Spanish population is 20.8% (males) and 30.9% (females).[1] In this context, the Spanish Society of Psychiatry, that of Diabetes, of Endocrinology and Nutrition and the Spanish Society for the Study of Obesity have established recommendations to evaluate metabolic and cardiovascular risk in patients with schizophrenia,[9] given the growing concern about the consequences of MetS.

It is known that the impact of schizophrenia on the quality of life (QoL) of the subject frequently entails worse functioning because of its chronic character, lack of fully efficacious treatment and its adverse effects. The complex relation is due to more specific factors of schizophrenia as the lack of disease awareness and social stigma. Presence of negative and affective symptoms negatively correlates with quality of life. Both QoL and, above all, health-related quality of life (HRQoL) are important to determine the

efficacy of the interventions, clinical decision making, understanding the causes and consequences of the differences on health, among other objectives. However, in the last 5 year, more than 17 articles that directly relate MetS and the quality of life have come to light in different countries, probably due to the difficulty of a quantitative/ qualitative estimation.

The Lapinlahti study[10] shows a positive relation between MetS and HRQoL in the general Finnish population. Some investigators consider that the presence of MetS is associated to a greater risk of psychiatric comorbidity, stress and worse QoL.[11-12] However, these studies did not analyze if QoL could be attributed to the MetS or to other components, for example, body mass index (BMI), an association found by Vancampfort et al.[13] in their study on MetS and HRQoL.

Corica and the investigators of the QUOVADIS study[14] concluded that psychological well-being is related with the HRQoL in obese patients in both the physical and mental domain of the SF-36, while the MetS is only related with the physical domain.

Huang et al.[15] studied the relation existing between depression, coronary disease, type 2 diabetes, MetS and QoL in 140 patients hospitalized in the General Hospital of Taiwan. They confirmed that QoL was worse in subjects who had criteria for MetS and individuals with diabetes and/or depression.

In the context of the studies on schizophrenia, MetS and QoL, the comparison between the subgroups with and without MetS provided by the CATIE[5] study points towards a still little developed line of research. The results of the CATIE confirm the relation between physical comorbidity and poor self-perception of physical health (data congruent with those found by Dixon et al.[4]). However, no association was found between MetS and severity of the symptoms or neurocognitive dysfunction.

In recent years, there have been many studies regarding the prevalence of MetS in schizophrenia in different contexts and with very unequal results (19.4-64%) (table 1). However, few worldwide studies have studied MetS and QoL in this specific population.

The principal objective of this study was to investigate the association between MetS and HRQoL in a sample of subjects with schizophrenia or schizoaffective disorder (SAD) seen in the Mental Health Center Nou Barris Nord (Barcelona/Catalonia/Spain). The secondary objectives were to calculate prevalence of MetS in the study sample, analyze level of functioning / discapacity and their relation with MetS in the sample studied, analyze level of functioning/ discapacity and their relation with HRQoL of the subjects.

MATERIAL AND METHODS

Subjects

The initial sample was made up of 81 subjects selected by consecutive case sampling who fulfilled criteria for the diagnosis of schizophrenia or schizoaffective disorder (SAD) between February 2008 and October 2009. Inclusion criteria were: patients of both genders, out-patient follow-up and in any evolutive phase of the disease, under treatment with antipsychotics for at least 12 weeks, consent signed by the patient or patient's legal representative, follow-up by nursing and having a recent blood test (less than 3 months). Exclusion criteria were: patients with incapacity to understand and fill out the health questionnaire formulated in Spanish and lack of informed consent. The final sample was made up of 76 subjects as blood tests were lacking for 5 individuals. The individuals who were not included in the analysis did not have differences in relation to the sample subjects.

Instruments

The subjects were evaluated using the SCID-I (Structured Clinical Interview for the DSM-IV- Axis I disorders).[16] They responded to a protocol that included sociodemographic characteristics, anthropometric measurements (weight, height, BMI, abdominal circumference and blood pressure), metabolic profile (HDL fraction of cholesterol, triglycerides and glucose), antipsychotic treatment (monotherapy- single antipsychotic (AP) drug or polytherapy - ≥ 2 APs), style of life (diet, physical exercise, substance abuse), presence of MetS, functioning and discapacity functioning scale (GAF), HRQoL scale (EQ-5D). **Perception of health** was assessed with the EuroQol **(EQ-5D)** validated by Badia et al.[17] for the Spanish population. The EQ-5D is a self-applied tool designed to assess health-related quality of life (HRQoL). It is divided into 2 parts. The first part evaluates 5 dimensions (mobility, personal care, usual activities, pain/malaise and anxiety/depression). It is scored on a 3 point scale. The second part is a visual analogue scale in form of "thermometer" (EQ-VAS, from worse to best imaginable state of health). It evaluates the global health state of the patient on the day of the interview. The EQ-5D has been shown to have validity in patients with schizophrenia. **Psychosocial functioning and level of symptoms** were evaluated using the Global Assessment of Functioning Scale GAF.[18] This scale was developed for clinical use and incorporated as Axis 5 in the DSM- versions III-R and IV. The scale has good psychometric properties and has been used in different psychiatry populations, independently of their diagnosis.

Design and procedure

This was an observational, analytic and cross-sectional study. Interviews were made by the psychiatrist and

reference nurse of the patient in individual sessions in the mental health center. The psychiatrists administered the protocol, diagnostic confirmation using the SCID-I and the request for the blood work. In turn, the nursing staff collected the anthropometric measures. The MetS diagnosis was evaluated using the modified NCEP-ATP-III criteria. The study complied with the basic ethical principles contained in the Declaration of Helsinki.

Data Analysis

First, the descriptive statistics of all the parameters were obtained. These included central tendency and dispersion measurements for the quantitative variables, absolute and relative frequencies for the categoric variables. The Student's T test was used for comparisons of means between continuous variables, the χ^2 test to study the association between nominal variables and the Mantel-Haenszel test for the ordinal ones. Logistic regression was used to evaluate the association of the MetS with the study variables, including, when necessary, adjustment due to confounding variables.

The EQ-5D dimensions were dichotomized into absent/present (value 1- absence and 2+3- presence of problem) and the amount of problems (dichotomized dimensions) were added up under the label of "total quality of life." When necessary, the data analyses were adjusted for age, gender, dyslipidemia, mono- or poly-treatment and physical activity. The five measurements were previously analyzed as potential modifier variables, except for dyslipidemia because its low prevalence (given by a limited N) provoked lack of convergence in the algorithm to estimate the logistic regression. Selection of these five potential confounders was done considering the theoretical criteria of the literature with the MetS. The SPSS 19 statistical program (SPSS Inc., Chicago, Illinois, USA) was used for all the statistical analysis.

RESULTS

Prevalence of MetS was 36.8% (95% CI:26.0-47.6%). From the sociodemographic point of view, statistically significant differences were observed between the subgroups with and without MetS. The MetS was directly associated to age (p=0.035) and inactive occupational status (situation of unemployment, retirement, work incapacity of any type) (p=0.042). Comparison of the subgroups in the group of sociodemographic variables and some clinical measurements is shown in table 2.

A positive relation was seen between MetS and history of dyslipidemia, diabetes and with greater weight, BMI, blood pressure, triglycerides, glucose and lower HDL, since they are diagnostic criteria of it. The clinical variables (GAF and PANSS) did not show significant differences (table 3).

Antipsychotic monotherapy is the most frequent practice (56.8%, 95% CI:46.0-67.6%). In the MetS subgroup, 39.3% were receiving antidepressant treatment, 67.9% with anxiolytics/hypnotics and 35.7% mood stabilizer drugs. A total of 21.4% were receiving treatment with anticholinergics and drugs for alcohol dependence (naltrexone and disulfiram).

Comparisons of the EQ-5D dimensions between the MetS subgroups did not show significant differences (table 4). However, the dimensions of "personal care" showed an OR of 3.96 (p=0.09) and that of "anxiety/depression" showed an OR of 0.47 (p=0.27). This suggests a tendency for the presence of MetS to be associated with better personal care and less anxiety/depression. The visual analogue scale of the EQ-5D (table 5) showed interactions between MetS and physical activity, in the sense that the subjects who have MetS and practice physical activity report better self-perception of health. No association was found between low scores on the GAF scale and worse HRQoL.

DISCUSSION

The results obtained showed a prevalence of MetS in accordance with the studies conducted in subjects with schizophrenia/ schizoaffective disorder (SAD). Heiskanen et al.,[19] Kato et al.[20] and Sánchez-Araña Moreno et al.[2] stressed the importance of the association between presence of MetS and greater abdominal circumference, systemic blood pressure, glucose, triglycerides and an association between presence of MetS and lower rates of Cholesterol-HDL. The need to investigate these clinical conditions in subjects with schizophrenia in order to find safer psychopharmacological treatments from the point of view of possible metabolic risk associated to antipsychotic treatment is established as a currently urgent objective. In this study, the positive relation between the previously mentioned variables is seen. However, it was not possible to know the proportion of subjects who met each diagnostic criteria for MetS because the diagnosis is made with at least three criteria and it was not possible to obtain all the necessary measurements in some subjects.

The direct association between MetS and age was found in several studies[1,2,21,22] as well as in the current one. The Kato et al.,[20] CATIE,[21] CLAMORS[8] and the Huang et al.[15] studies found an association between MetS and gender (women showed greater prevalence of MetS). However, in the remaining studies consulted and in our sample, no significant associations were found.

The association between work activity and presence of MetS has hardly been studied in the articles consulted. Sánchez-Araña Moreno et al.[2] did not find any significant association between being active or inactive in the labor market while Miettola et al.[10] found that MetS was associated

Table 2 Sociodemographic and clinical variables according to absence / presence of MetS

	MetS=No N (%)	MetS=Yes N (%)	$\chi^{2\,(A)}$	p
Gender				
Man	26 (54.2)	19 (67.9)	1.38	0.241
Woman	22 (45.8)	9 (32.1)		
Occupation Status				
Active	15 (31.3)	3 (10.7)	4.13	0.042
Inactive	33 (68.8)	25 (89.3)		
Civil Status				
Single	32 (66.7)	19 (67.9)	0.33	0.0848
Married	9 (18.8)	4 (14.3)		
Other (Separated/divorced/widow(er))	7 (14.6)	5 (17.9)		
Living condition				
Lives alone	7 (14.6)	1 (3.6)		
Lives with family of origin	26 (54.2)	16 (57.1)		
Lives with own family	11 (22.9)	6 (21.4)		
Lives with others	4 (8.3)	5 (17.9)		
Level of Studies				
Primary education	26 (54.2)	12 (42.9)	2.87	0.090
Secondary education	12 (25)	4 (14.3)		
Middle studies	8 (16.7)	9 (32.1)		
University studies	2 (4.2)	3 (10.7)		
Years since diagnosis				
Less than 5 years	8 (16.7)	3 (10.7)	0.59	0.443
5-10 years	9 (18.8)	5 (17.9)		
10-15 years	9 (18.8)	5 (17.9)		
More than 15 years	22 (45.8)	15 (53.6)		
Life Habits				
Smoking habit				
No	19 (39.6)	7 (25)	1.67	0.196
Yes	29 (60.4)	21 (75)		
Alcoholism				
No	36 (75)	21 (75)	0.00	1.000
Yes	12 (25)	7 (25)		
Other Substance/Drug abuse (B)				
No	33 (68.8)	23 (82.1)	1.64	0.201
Yes	15 (31.3)	5 (17.9)		
Diet				
Normal calorie				
No	12 (25.5)	10 (35.7)	0.88	0.349
Yes	35 (74.5)	18 (64.3)		
Normal sodium				
No	16 (34)	9 (34.6)	0.00	0.961
Yes	31 (66)	17 (65.4)		
With fiber				
No	21 (44.7)	10 (38.5)	0.27	0.607
Yes	26 (55.3)	16 (61.5)		
With saturated fat /cholesterol				
No	24 (51.1)	17 (63)	0.98	0.322
Yes	23 (48.9)	10 (37)		

Table 2 Continuation

	MetS=No N (%)	MetS=Yes N (%)	$\chi^{2\,(A)}$	p
Physical activity				
No	8 (16.7)	10 (35.7)	3.55	0.060
Yes	40 (83.3)	18 (64.3)		
Personal backgrounds				
Cardiovascular Disease				
No	44 (91.7)	21 (77.8)	2.89	0.089
Yes	4 (8.3)	6 (22.2)		
Dyslipidemia				
No	41 (85.4)	14 (51.9)	9.96	0.002
Yes	7 (14.6)	13 (48.1)		
Diabetes mellitus				
No	45 (93.8)	19 (70.4)	7.55	0.006
Yes	3 (6.3)	8 (29.6)		
Familial Backgrounds				
Cardiovascular Disease				
No	24 (53.3)	7 (30.4)	3.22	0.073
Yes	21 (46.7)	16 (69.6)		
Dyslipidemia				
No	25 (55.6)	15 (65.2)	0.59	0.444
Yes	20 (44.4)	8 (34.8)		
Diabetes mellitus				
No	33 (73.3)	14 (60.9)	1.11	0.293
Yes	12 (26.7)	9 (39.1)		
Psychopharmacological Treatment				
Antipsychotics (AP)				
Monotherapy	28 (58.3)	14 (50.0)	0.50	0.481
Polytherapy	20 (41.7)	14 (50.0)		
Antidepressants (AD)				
No	29 (60.4)	17 (60.7)	0.00	0.980
Yes	19 (39.6)	11 (39.3)		
Anxiolytics/Hypnotics (AN)				
No	21 (43.8)	9 (32.1)	0.98	0.318
Yes	27 (56.3)	19 (67.9)		
Mood Stabilizers (MS)				
No	34 (70.8)	18 (64.3)	0.35	0.554
Yes	14 (29.2)	10 (35.7)		
Others[(c)]				
No	40 (83.3)	22 (78.6)	0.27	0.605
Yes	8 (16.7)	6 (21.4)		

(A): χ^2 for nominal variables and Mantel-Haenszel for ordinal variables; (B): Caffeine, cannabis, cocaine, hypnotics; (C): Anticholinergics, pharmacotherapy for alcoholic dependence (naltrexone and disulfiram).

to lower HRQoL in unemployed or retired women, that is, occupationally inactive. In this current study, it has been seen that the percentage of inactive subjects in the MetS patient group is superior when compared with subjects without this clinical condition.

In the population study of Park et al.,[22] the "Korea National Health and Nutrition examination Survey 2005" found that the relation between MetS and HRQoL had differences in regards to gender. Women with more criteria for MetS had worse mobility (according to the EQ-5D) and

Table 3 Components of the MetS, GAF Scale and PANSS Scale according to absence/presence of MetS

	MetS=No		MetS=Yes				
	N	Mean (SD)	N	Mean (SD)	t	p	95% CI Difference
Age (years)	47	41.71 (10.15)	28	47.32 (12.15)	-2.15	0.035	-10.81 a -0.41
Weight (Kgs)	47	75.82 (14.05)	26	90.08 (16.79)	-3.87	<0.0005	-21.60 a -6.92
Height (cms)	47	167.55 (9.50)	26	167.38 (8.89)	0.07	0.941	-4.36 a 4.69
Body Mass Index (BMI) (Kg/m^2)	47	27.34 (4.93)	26	32.43 (5.99)	-3.91	<0.0005	-7.69 a -2.50
Abdominal circumference (cm)	47	97.85 (12.08)	25	110.56 (12.17)	-4.24	<0.0005	-18.68 a -6.73
Systolic Blood Pressure (SBP) (mmHg)	47	116.79 (11.44)	25	131.92 (16.63)	-4.07	<0.0005	-22.67 a -7.59
Diastolic Blood Pressure (DBP) (mmHg)	47	76.62 (9.61)	25	85.08 (11.17)	-3.36	0.001	-13.48 a -3.44
HDL-cholesterol (mg/dL)	35	49.46 (11.60)	23	39.86 (8.86)	3.37	0.001	3.89 a 15.30
Triglycerides (mg/dL)	38	105.16 (54.14)	28	234.68 (119.22)	-5.36	<0.0005	-178.60 a -80.44
Glycemia (mg/dL)	39	87.74 (10.33)	28	108.93 (31.04)	-3.48	0.002	-33.61 a -8.76
GAF	48	50.38 (14.57)	28	45.04 (12.15)	1.63	0.106	-1.17 a 11.85
PANSS +	48	11.85 (5.10)	28	12.21 (4.48)	-0.31	0.757	-2.68 a 1.96
PANSS -	48	17.17 (8.07)	28	19.79 (9.68)	-1.27	0.209	-6.74 a 1.50
General PANSS	48	32.00 (8.78)	28	33.64 (9.67)	-0.76	0.451	-5.96 a 2.67

worse self-perceived QoL (EQ-VAS), while men had worse self care on the EQ-5D. Men with high blood pressure and women with hypertension and abdominal obesity showed worse HRQoL. Sohn et al.,[23] using the data from the subsample of middle-aged individuals from the same Korean study, also found differences between genders in regards to the presence of MetS. In the current study, these results could not be compared given the small percentage of women in the sample analyzed.

In our sample, no association was found between psychoactive substance abuse and the presence of MetS. This result coincides with that obtained by Meyer et al.[5] and Sánchez-Araña Moreno et al.[2] However, 65.8% of the subjects had nicotine dependence and this confirms the high prevalence of smoking habit in this population.

In relation to psychopharmacological treatment, no associations were found between MetS and the different treatments divided by categories (antipsychotics, antidepressants, anxiolytics, mood stabilizers, others). However, some evidence has been found on the participation of some antipsychotics in the increase of risk of metabolic alterations which, added to not very healthy habits and genetic predisposition, ends up in the appearance of MetS.[21]

On the other hand, the relation between HRQoL and MetS in individuals with schizophrenia has not been previously studied within the Spanish setting: It has also been little studied in other populations. This is partly because QoL is an abstract and difficult to study construct. In this sense, the EQ-5D was chosen due to its validity in schizophrenia and its applicability in patients with different grades of clinical severity. However, it does not seem to be a good instrument

Table 4 Association between MetS and dimensions of the HRQoL- EQ-5D scale

EQ-5D Dimensions	N (% With problems)		Adjusted results (A)		
	MetS=No	MetS=Yes	OR	p	95% CI OR
Mobility	9 (18.0)	8 (28.6)	1.13	0.863	0.28 a 4.64
Personal Care	3 (6.3)	9 (32.1)	3.96	0.094	0.76 a 20.53
Daily Activities	16 (33.3)	11 (39.3)	1.06	0.921	0.34 a 3.32
Pain/Malaise	17 (35.4)	10 (35.7)	1.26	0.705	0.39 a 4.10
Anxiety/Depression	20 (41.7)	10 (35.7)	0.47	0.270	0.15 a 1.55

(A): Adjusted by gender, age, dyslipidemia, antipsychotic treatment and physical activity.

Table 5 Association between MetS and total score on the EQ-5D, EQ VAS and GAF

	Mean (SD)		Adjusted results(A)			
	MetS=No	MetS=Yes	Differ.	p	95% CI Differ.	
Total EQ-5D	6.50 (1.50)	7.04 (2.03)	0.15	0.755	-0.81 a 1.11	
Total EQ VAS	62.75 (19.99)	52.18 (18.90)	-24.0 -3.41	0.025 0.555	-44.94 a -3.14 -14.89 a 8.07	←Phys.Act. =No ←Phys.Act. =Yes
GAF	50.38 (14.57)	45.04 (12.15)	-3.67	0.355	-11.54 a 4.20	

(A): Adjusted by gender, age, dyslipidemia, antipsychotic treatment and physical activity.

to measure QoL related to MetS in subjects with schizophrenia because the responses are conditioned more by psychic limitations (psychiatric picture) than by physical ones (diabetes, hypertension, dyslipidemia or obesity).

Han et al.[24] used the EQ-5D and EQ-VAS and the "Korean Obesity-related QoL scale (KOQoL)," a specific scale for the Korean population with obesity. MetS was defined according to the criteria of the International Diabetes Federation (IDF) adapted for the population in question. Subjects with MetS had greater incapacity and therefore worse HRQoL compared to those who did not have MetS criteria. However, the specific scale for obesity (KOQoL) showed a stronger association than the generic one (EQ-5D). Development of a specific scale for HRQoL and the MetS in the schizophrenia population would be of great interest in public health.

In the CATIE[21] and PORT[4] study, an association was found between the individuals with physical disease and worse QoL, given by the physical components of the SF-12 (short version of the SF-36). In the current study, no correlation was seen between the presence of MetS and worse HRQoL. However, the "self-care" dimension of the EQ-5D showed that the subjects who have MetS would tend to have worse personal care. On the other hand, MetS subject and those who practice physical activity report better self-perception of general health (both physical and psychic). On the EQ-5D scale, this means a better HRQoL. Our conclusions are in the line with those of Liu et al.[25] They studied the effects of Tai Chi and Qigong on the indicators of MetS, on glucose control, on HRQoL (measured by SF-36) and on the mental health of adult individuals with high glucose rates. They found that the physical exercise program improved metabolic and psychological variables.

On the other hand, Frisman and Kristenson,[26] in a cross-sectional study in a Swedish sample, did not find differences in mental health and stress perceived on the SF-36 for individuals with and without MetS. Vancampfort et al.[13] also compared 60 patients with schizophrenia and their control group in order to study if lack of physical activity could contribute to deterioration of the HRQoL (analyzed according to the SF-36). Their data revealed that HRQoL (physical subscale) is related with BMI (and not with MetS *per se*) and with the lack of physical activity. However, the same predictors were not significant in relation to the mental subscale. The presence of MetS and incapacity to perform physical exercise did not justify the changes in HRQoL.

The results of the current study reinforce the need to promote sports practice in order to control weight gain, improve sleep habits, increase self-esteem, promote

psychological well-being and greater social interaction, in the long run. The need to incorporate physical activity into rehabilitation programs adapted to the context of each population where said activity is established is also seen.[1] The result from the "anxiety/depression" dimension of the EQ-5D indicates that individuals with MetS have fewer anxious/depressive symptoms. Although this association is not significant because of the reduced number of subjects, it could be explained by the influence of the individuals who practice a physical activity and who have MetS.

No association has been observed between the presence of MetS and low score on the GAF (that is, worse functioning /greater incapacity) or the association between worse GAF and worse HRQoL.

This study has some outstanding points. First, it is the first study to investigate the association between MetS, HRQoL and GAF in subjects with schizophrenia in the European context, according to the systematic review of the scientific literature. It stands out that only 17 articles have been published on this theme up to the review of this manuscript (June 2012). Second, it has a homogeneous sample in relation to the disease (the patients were diagnosed by the SCID-I), stage and in relation to the antipsychotic treatment (stability phase and antipsychotic treatment for more than 12 weeks). This point is important because there are differences in how the QoL interacts with the psychiatric symptoms in a sample was subjects having different diagnoses and two are in outpatient or hospital treatment. Third, the association between MetS and physical activity reinforces the importance of stressing healthy life habits and the need for interventions to promote customary physical activity.

However, the study also has some limitations. This is a cross-sectional study with limited sample from a public mental health center with all of the subjects receiving antipsychotic treatment. This affects the generalization of the results to subjects with schizophrenia in different contexts. Furthermore, the EQ-5D, although valid to study samples of subjects with schizophrenia, is not specific to measure HRQoL in a population with metabolic syndrome (there is still no scale for this purpose). MetS is an important public health problem, especially in this group of subjects because of the high morbidity -mortality in tailed and treatment with antipsychotics and schizophrenia per se. The use of multiple strategies in order to minimize metabolic risk and consequently to improved treatment adherence and quality of life of subjects with schizophrenia should be, if not the most important, one of the principal objectives of the individual therapeutic plan.

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