Metabolic syndrome in acute psychiatric inpatients: clinical correlates

Sindrome metabolica in pazienti ricoverati in S.P.D.C.: correlati clinici

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Summary

Objectives

Compared to the general population, patients with major mental disorders have a higher prevalence of metabolic syndrome (MetS), which is known to increase cardiovascular risk and mortality. Many factors contribute to development and maintenance of metabolic disturbances in psychiatric patients. Nevertheless, gaps remain in relevant aspects, encouraging further studies in specific subgroups to evaluate the impact of each variable in developing MetS. Our aim is to identify the clinical and sociodemographic features consistently associated with the occurrence of MetS in a sample of inpatients affected by severe and acute mental illness.

Methods

Our study had a naturalistic design and involved inpatients consecutively admitted to the Psychiatric Unit of 'S Luigi Gonzaga Hospital' of Orbassano from December 2013 to September 2014. At study entry, general sociodemographic and clinical information was collected for each subject, including lifestyles and comorbidity for cardiovascular diseases and diabetes. Through index visit and routine blood exam, all metabolic parameters were assessed to define the presence of MetS according to NCEP ATP III modified criteria. Sociodemographic and clinical correlates of MetS were then investigated.

Results

One hundred twenty-five patients were enrolled. Of these, 37 (29.6%) had schizophrenia spectrum and other psychotic disorders, 47 (37.6%) had bipolar and related disorders, 28 (22.4%) had depressive disorders and 13 (10.4%) had personality disorders.
MetS was present in 35.2% of the sample. Low HDL-C levels were the most frequently endorsed criterion, present in 57.6% of subjects. Abdominal obesity, high triglycerides, hypertension and fasting hyperglycaemia were observed in 51.2%, 30.4%, 28.8% and 20% of patients, respectively. Patients who fulfilled MetS definition were more often characterised by current atypical antipsychotic treatment, current alcohol abuse, current psychiatric comorbidity with substance related disorders and longer duration of illness. After performing regression analysis, only current atypical antipsychotic treatment was significantly associated to MetS.

Conclusions

Our study confirms the increased risk of MetS in patients treated with atypical antipsychotics. No other clinical or sociodemographic variables were associated with MetS. These findings suggest a shared susceptibility to antipsychotic-related metabolic dysregulation that is not primarily related to psychiatric diagnosis or concomitant to other psychiatric treatment.

Key words

Metabolic syndrome • Atypical antipsychotics • Inpatients • Schizophrenia • Bipolar disorder

Introduction

Patients with major mental disorders are subject to premature death from all causes compared to the general population [1]. Among causes of death, cardiovascular (CV) disease is responsible for as much as 50% of excess mortality. The association between CV risk and major mental disorders such as bipolar disorder and schizophrenia is well established and comparable [2-4]. Furthermore, individuals with unipolar major depression have levels of CV risk that are at least as high as those in patients who suffer from bipolar disorder [5 6].
There are many reasons why patients with mood and psychotic disorders have elevated CV risk, but one source of CV risk, which is overrepresented in this population, is the cluster of findings that define metabolic syndrome (MetS) [7-10].
More specifically, MetS occurs in nearly one-third of patients with schizophrenia [11 12], while 37.3% of patients with bipolar disorder develop MetS, which is nearly twice the rate in the general population [13 14].
Many factors contribute to development and maintenance of MetS in psychiatric patients including poor lifestyle choices, such as excessive caloric and cholesterol intake, cigarette smoking and physical inactivity [15 16]. Moreover, major psychiatric disorders have been related to genetic liability and lifelong use of medications such as antipsy-

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chotics or mood stabilisers that have been associated with weight gain, dyslipidaemia and development of diabetes. Longitudinal follow-up studies to estimate changes in MetS rates among patients with schizophrenia and bipolar disorder suggest that the prevalence of MetS usually increases over time, in parallel with duration of illness and treatment [17-19]. A recent study from our research group showed that MetS rapidly increases from 28.6 to 44.3% over 2 years follow-up in a sample of patients with bipolar disorder treated as usual; moreover, patients developing MetS over time were taking antipsychotics at baseline, most of which were atypical antipsychotics, confirming the increased risk associated with this class of medications [20]. In addition to duration of illness, gender should be another clinical parameter that needs to be highlighted in evaluating the risk profile of MetS. Few studies have reported higher rates of MetS in males with bipolar disorder, with a prevalence of around 32% in men and 22% in women [21]. On the other hand, a high prevalence of MetS was noted in women (52%) compared to men (36%) with schizophrenia [8].

While considerable debate exists regarding the causes of the high prevalence of metabolic disturbances in patients with severe mental illness, gaps remain in relevant aspects, encouraging further studies in specific subgroups of psychiatric patients to evaluate the impact of each variable in developing MetS. Our aim is to identify the clinical and sociodemographic features consistently associated with the occurrence of MetS across different diagnostic groups in a sample of patients affected by severe and acute mental illnesses.

Materials and Methods

The study had a naturalistic design and involved inpatients consecutively admitted to the Psychiatric Inpatient Unit of the San Luigi Gonzaga Hospital, Orbassano (University of Turin, Italy) from December 2013 to September 2014.

Subjects

All patients consecutively admitted to the inpatient unit were considered for the present study. Patients with a main diagnosis of schizophrenia spectrum and other psychotic disorders, bipolar and related disorders, depressive disorders or personality disorders (DSM-5) [22] were asked to participate. The aims of the study and study procedures were thoroughly explained to potential participants who gave oral consent before participation. Exclusion criteria included age < 18 years, severe and unstable general medical conditions, any of the remaining main psychiatric diagnoses (e.g. substance related disorders, neurodevelopmental disorders, neurocognitive disorders), pregnancy or having just given birth and refusal to give consent prior to participating in the study.

Assessments and procedures

At study entry, general sociodemographic and clinical information was collected for each subject. Lifestyles were also investigated in the study sample: information about exposure to cigarette smoking, duration of alcohol and drug consumption and physical activity was obtained by directly interviewing patients. A score was assigned to the intensity of physical activity: absent, mild (< 4 h/week), moderate (4 h/week) and intense (> 4 h/week, regular) [23]. Comorbidity and family history for diabetes or cardiovascular diseases and current treatments for hypertension, diabetes or dyslipidaemia were assessed by looking at medical reports and by directly interviewing patients. At index visit, weight, height, waist circumference and blood pressure were measured. Weight was measured with the participant undressed and fasting height was measured barefoot. Waist circumference, measuring central adiposity, was measured midway between the inferior margin of the ribs and the superior border of the iliac crest, at minimal respiration. Two blood pressure measurements were obtained by using a mercury sphygmomanometer: the first with the subject in a supine position and the second with the subject in a seated position at least 2 min after the first measurement. The mean blood pressure of the two measurements was used. All the procedures were performed by the attending physician in the hospital setting.

A blood draw for routine blood exam was performed upon hospital admission, as part of routine clinical management. At the time when blood was drawn, patients were fasting for the previous 10 h; patients who did not fast were rescheduled. Blood exams included assessment of the following: glucose, total cholesterol, triglycerides, LDL and HDL-C. Patients were stated to have MetS if they endorsed at least three of the following five criteria, according to NCEP ATP III modified criteria:

- abdominal obesity: waist circumference ≥ 102 cm in men and ≥ 88 cm in women;
- hypertriglyceridaemia: ≥ 150 mg/dl or on being lipid-lowering medication;
- low HDL-C: < 40 mg/dl in men and < 50 mg/dl in women or being on triglyceride-lowering medication;
- high blood pressure: systolic pressure ≥ 130 mmHg or diastolic pressure ≥ 85 mmHg or on antihypertensive medication;
- high fasting glucose: ≥ 100 mg/dl or being on glucose-lowering medication.

Statistical analysis

Characteristics of subjects were summarised as mean and S.D. for continuous variables and frequency and percentage for categorical variables. We examined sociodemographic and clinical correlates of MetS using a chi-square test in the case of categorical variables, performing the

Yates correction in the case of a 2×2 table and independent-samples t tests in the case of continuous variables. In order to control for confounding factors, we entered the significant independent variables in a stepwise logistic regression analysis (LogReg) with MetS as the dependent variable.

Results

One hundred twenty-five patients were recruited in the study. The mean (±S.D.) age of the sample was 44.94 (±13.51) years; 48% of patients were females; 29.6% had schizophrenia spectrum and other psychotic disorders, 37.6% had bipolar and related disorders, 22.4% had depressive disorders and 10.4% had personality disorders.

Sociodemographic and clinical characteristics are shown in Table I.

Of the 125 patients, MetS was present in 35.2% of the sample. Low HDL-C levels were the most frequently endorsed criterion, present in 57.6% of subjects. Abdominal obesity was the second most frequent metabolic abnormality, affecting 51.2% of participants. High triglycerides, hypertension and fasting hyperglycaemia were observed in 30.4%, 28.8% and 20% of the sample, respectively (Table II).

We divided the sample in two groups according to the presence (n = 44) or the absence (n = 81) of MetS criteria. As shown in Figure 1, patients with a main diagnosis of schizophrenia spectrum and other psychotic disorders and bipolar and related disorders showed a higher rate of MetS, respectively 34.1% and 29.5%. MetS was observed in 25% of individuals affected by depressive disorders, while 11.4% of patients with a main diagnosis of personality disorders met MetS criteria. These differences were not statistically significant.

The other sociodemographic and clinical features of the

TABLE I.
Baseline sociodemographic and clinical characteristics of the sample. *Caratteristiche socio-demografiche e cliniche del campione*.

Characteristics	Value
Sex, *n* (%)	
Male	65 (52.0)
Female	60 (48.0)
Age (years), mean (±SD)	44.94 (±13.51)
Marital status, *n* (%)	
Never married	64 (51.2)
Married	39 (31.2)
Separated or divorced	16 (12.8)
Widowed	6 (4.8)
Education level (years), mean (±SD)	9.94 (±3.60)
Occupational status, *n* (%)	
Employed full-time	34 (27.2)
Employed part-time	10 (8)
House-wife	6 (4.8)
Student	4 (3.2)
Unemployed	53 (42.4)
Retired	18 (14.4)
Main diagnosis (DSM V), *n* (%)	
Schizophrenia spectrum	37 (29.6)
Bipolar and related disorders	47 (37.6)
Depressive disorders	28 (22.4)
Personality disorders	13 (10.4)

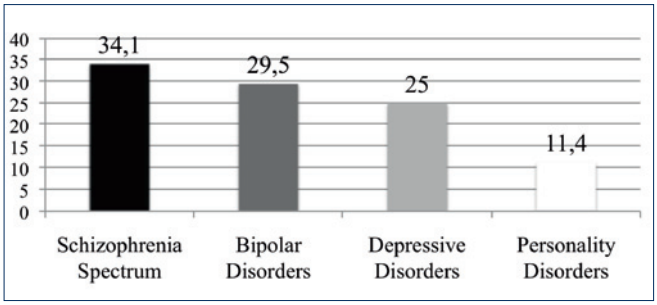

FIGURE 1.
Prevalence of MetS (NCEP ATP III modified criteria) in the main different diagnoses of the sample. *Prevalenza della sindrome metabolica nelle differenti diagnosi principali del campione*.

TABLE II.
Prevalence of MetS (NCEP ATP III modified criteria) and its components. *Prevalenza della sindrome metabolica e delle sue componenti nel campione*.

Criteria	*n* (%)
Abdominal obesity: > 102 cm (men) or > 88 cm (women)	64 (51.2)
Hypertriglyceridaemia: ≥ 150 mg/dl or being on triglyceride-lowering medication	38 (30.4)
Low HDL-C: < 40 mg/dl (men) or < 50 mg/dl (women) or being on lipid-lowering medication	72 (57.6)
High blood pressure: ≥ 130 mm systolic or ≥ 85 mm diastolic or being on antihypertensive medication	36 (28.8)
High fasting glucose: ≥ 100 mg/dl or being on glucose-lowering medication	25 (20)
MetS (three or more criteria)	44 (35.2)

TABLE III.
Comparison between patients with MetS (n = 44) and without MetS (n = 81): sociodemographic and clinical characteristics.
Confronto tra pazienti con MetS (n = 44) e senza MetS (n = 81): caratteristiche socio-demografiche e cliniche.

	MetS	No MetS	p
Sex, *n* (%)			0.458
Male	56.8	49.4	
Female	43.2	50.6	
Age (years), mean (±SD)	47.09	43.78	0.192
Positive family history for psychiatric disorders, *n* (%)	34.1	41.8	0.445
Positive family history for bipolar disorder, *n* (%)	9.1	7.6	0.744
Positive family history for CV disease, *n* (%)	45.2	38.5	0.560
Positive family history for diabetes, *n* (%)	19.0	15.4	0.616
Educational level (years), mean (±SD)	9.52	10.16	0.346
Occupational status, *n* (%)			0.810
Employed full-time	27.3	27.2	
Employed part-time	6.8	8.6	
House-wife	4.5	4.9	
Student	0	4.9	
Unemployed	47.7	39.5	
Retired	13.6	14.8	
			0.701
White collar	73.3	80.8	
Blue collar	26.7	19.2	
Marital status, *n* (%)			0.786
Never married	52.3	50.6	
Married	29.5	32.1	
Divorced	6.8	2.5	
Separated	6.8	9.9	
Widowed	4.5	4.9	
Locality, *n* (%)			0.158
Urban	2.3	9.9	
Rural	97.7	90.1	
Living arrangement, *n* (%)			1.000
Family of origin	38.6	38.3	
Own family	50.0	50.6	
Therapeutic facility	9.1	9.9	
Homeless	2.3	1.2	
Current smoking, *n* (%)	54.5	59.3	0.705
Lifetime smoking, *n* (%)	59.1	61.7	0.849
Current alcohol abuse, *n* (%)	18.2	4.9	**0.025**
Lifetime alcohol abuse, *n* (%)	22.7	12.3	0.200
Current substance abuse, *n* (%)	11.4	8.6	0.752
Lifetime substance abuse, *n* (%)	20.5	21.0	1.000
Main diagnosis (DSM V), *n* (%)			0.583
Schizophrenia Spectrum	27.7	72.3	
Bipolar and related disorders	40.5	59.5	
Depressive disorders	39.3	60.7	
Personality disorders	38.5	61.5	

(continues)

Table III - Follows

	MetS	No MetS	p
Current psychiatric comorbidity, *n* (%)			
Neurodevelopmental disorders	0	2.5	0.540
Anxiety disorders	0	1.2	1.000
Obsessive compulsive and related disorders	2.3	0	0.352
Somatic symptom and related disorders	4.5	1.2	0.283
Feeding and eating disorders	0	1.2	1.000
Substance related disorders	11.4	1.2	**0.020**
Neurocognitive disorders	2.3	0	0.352
Personality disorders	13.6	17.3	0.799
Lifetime psychiatric comorbidity, *n* (%)	34.1	27.2	0.421
Neurodevelopmental disorders	0	2.5	0.540
Depressive disorders	2.3	0	0.352
Anxiety disorders	0	1.2	1.000
Obsessive compulsive and related disorders	2.3	0	0.352
Somatic symptom and related disorders	4.5	1.2	0.283
Feeding and eating disorders	0	1.2	1.000
Substance related disorders	18.2	7.4	0.081
Neurocognitive disorders	2.3	0	0.352
Personality disorders	18.2	18.5	1.000
Age of onset (years), mean (±SD)	31.03	31.70	0.804
Duration of illness (years), mean (±SD)	16.31	11.47	**0.034**
Lifetime aggressiveness, *n* (%)	56.8	46.9	0.350
Lifetime suicide attempted, *n* (%)	40.9	34.6	0.561
Involuntary treatment, *n* (%)	9.1	8.6	1.000
Duration of involuntary treatment (years), mean (±SD)	7.00	10.33	0.104
Duration of hospitalisation (years), mean (±SD)	15.56	15.23	0.866
Seasonal admission, *n* (%)			0.209
Autumn	56.8	40.7	
Winter	22.7	40.7	
Spring	6.8	7.4	
Summer	13.6	11.1	
Hospital discharge, *n* (%)			0.283
Ordinary	95.5	98.8	
Patient request	4.5	1.2	
Current typical antipsychotic treatment, *n* (%)	20.5	9.9	0.110
Current atypical antipsychotic treatment, *n* (%)	59.1	39.5	**0.041**
Current treatment with mood stabilizers, *n* (%)	34.1	27.2	0.421
Current treatment with antidepressants, *n* (%)	38.6	39.5	1.000
Current treatment with anxiolytics, *n* (%)	52.5	50.6	1.000
Lifetime psychiatric treatment, *n* (%)	95.3	86.4	0.216
Lifetime treatment with antipsychotics, *n* (%)	75.6	62.0	0.157
Lifetime treatment with mood stabilisers, *n* (%)	56.4	39.7	0.115
Lifetime treatment with antidepressants, *n* (%)	63.4	58.2	0.695
Lifetime treatment with anxiolytics, *n* (%)	88.1	72.2	0.065
Physical activity			0.069
Absent	100	86.4	
Mild (< 4 hours/week)	0	7.4	
Moderate (4 hours/week)	0	1.2	
Intense (> 4 hours/week)	0	4.9	

two subgroups (with MetS and without MetS) are summarised in Table III.

Patients who fulfilled MetS definition were more often characterised by current atypical antipsychotic treatment (59.1% *vs* 39.5%; p = 0.041), current alcohol abuse (18.2% *vs* 4.9%; p = 0.025), current psychiatric comorbidity with substance related disorders (11.4% *vs* 1.2%; p = 0.020) and longer duration of illness (16.31 years *vs* 11.47 years; p = 0.034).

Next, a LogReg analysis was conducted to assess the relationship between the above-mentioned variables and the occurrence of MetS. The following explanatory variables were included in the analysis as independent variables: current atypical antipsychotic treatment, current alcohol abuse, current psychiatric comorbidity with substance related disorders and duration of illness. The only variable significantly associated with the presence of MetS was current atypical antipsychotic treatment (p = 0.005).

Discussion and conclusions

MetS increases the risk for cardiovascular diseases, insulin resistance and diabetes mellitus, and can lead to increased morbidity and mortality, in addition to impairing patient adherence to medication[24]. These are the reasons why, in recent years, MetS has emerged as a significant problem in both psychiatry and public health. There is thus a need to detect high-risk groups for developing MetS that should especially be screened and treated.

This study investigated the sociodemographic and clinical correlates of MetS in a sample of inpatients with major psychiatric disorder. More specifically, we highlighted whether the risk profile is the same depending on diagnostic subgroup, since several original reports as well as reviews did not provide unequivocal evidence. Moreover, we explored whether MetS rates differ depending on individual variables such as age, gender, duration of illness and treatment settings in order to guide clinicians in monitoring and treatment decisions.

The sample comprised 125 consecutively recruited hospitalised patients with a main diagnosis of schizophrenia spectrum and other psychotic disorders (34.1%), bipolar and related disorders (29.5%), depressive disorders (25%) or personality disorders (11.4%).

In our sample, the overall prevalence of MetS was 35.2%. This result is similar to that reported among patients affected by schizophrenia spectrum disorders [12 25-27] and mood disorders [13 28 29]. Nevertheless, this is higher than the prevalence of MetS (23.7%) found among hospitalised psychiatric patients by Centorrino and colleagues [30]. This could be due to a younger average age of the study subjects (35.7± 13.0 years) than in sample (44.94 ± 13.51 years).

We did not observe a specific psychiatric disorder significantly associated with MetS. This finding is in line with previous studies evaluating inpatients affected by psychotic and mood disorders [30 31] and with a recent meta-analysis in which no difference was seen in MetS in studies directly comparing schizophrenia and bipolar disorder, or in those directly comparing bipolar disorder to major depressive disorder [32].

Furthermore, we found no significant differences in the prevalence of MetS between men and women. Several studies are consistent with our results, indicating that both sexes deserve the same attention [9 13]. However, other studies have reported higher rates of MetS in females, especially with schizophrenia [8] and recurrent major depressive disorder [33], while higher MetS rates were found in young males with bipolar disorder [21]. Nevertheless, in the bipolar disorder population, the majority of studies have reported no differences between sex or do not report on it specifically [9].

We found that 59.1% of patients in the MetS subgroup were taking atypical antipsychotics (SGAs) compared with 39.5% in the subgroup of patients without MetS. This difference was statistically significant and confirmed by LogReg analysis (p = 0.005). The lower proportion of MetS (30%) found by Centorrino and colleagues in a sample of antipsychotic-exposed hospitalised patients is probably due to the younger mean age of subjects; nonetheless, patients taking antipsychotics presented MetS more frequently than those who had never taken antipsychotics [30]. The association between SGAs and MetS is confirmed by several studies in patients with different diagnoses. In particular, Correll and colleagues found that inpatients with bipolar disorder and schizophrenia who are treated with SGAs have similarly high rates of MetS [31].

It must be emphasised that in our study only current use of atypical antipsychotics was significantly associated with MetS. This is a relevant finding, although current treatment with SGAs could underlie previous antipsychotic treatments that are not always easy to retrace, especially for length and dosage. However, our results showed that exposure to atypical antipsychotics, even for a brief period of time, can lead to the development or worsening of metabolic dysregulations that can consequently give rise to MetS.

Published data examining changes in weight during short-term antipsychotic treatment (4-12 weeks) of schizophrenia revealed that increases in weight and body mass index in subjects who received risperidone, amisulpride or olanzapine were clinically and statistically significantly greater than in those who received placebo [34]. Considering glucose tolerance, Sacher et al. investigated the acute effects of oral administration of olanzapine and ziprasidone in healthy volunteers and observed a significant decrease (p < 0.001) in whole body insulin sensitivity after oral intake of olanzapine (10 mg/day) for 10 days [35].

In conclusion, our study confirms the association between

treatment with SGAs and increased risk of MetS among psychiatric patients independently of the diagnosis and other clinical features. Our findings are in agreement with those reported in a recent meta-analysis, although our study was conducted in an Italian sample of acute inpatients [32]. These conclusions suggest a shared susceptibility to antipsychotic-related metabolic dysregulations that is not primarily related to psychiatric diagnosis or concomitant to other psychiatric treatment.

The limitations of the present study include its observational nature and the relatively small sample size, especially regarding individuals primarily affected by personality disorders. Therefore, our conclusions are to be considered as suggestive. However, the alarmingly high frequency of MetS in all diagnostic subgroups and its relevant association with current atypical antipsychotic treatment warrant further analyses of risk factors in patients with major mental disorders in order to administer safer and better-tolerated treatments, giving particular attention when using atypical antipsychotics that are known for their metabolic side effects, and preventive programs targeting general health among psychiatric patients.

Conflict of interests

None.

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