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METABOLIC SYNDROME AND CARDIOMETABOLIC RISK AMONG PATIENTS WITH SEVERE MENTAL ILLNESS FROM AN ITALIAN COMMUNITY MENTAL HEALTH SERVICE

Abstract

Objectives: The study aimed to investigate the cardiometabolic health in a sample of patients with severe mental illness from an Italian Community Mental Service.

Material: Of 77 patients enrolled, 46.5% smoked cigarettes, 58.1% of patients were overweight, 17% had hypertension. Diabetes, high levels of fasting triglyceride and low levels of fasting HDL-C were present in 5.1%, 47.5% and 40.0% of subjects respectively. 31.4% of patients had Metabolic Syndrome.

Results: A significant correlation between the length of antipsychotic exposure and BMI, waist circumference, LDL-C and fasting glucose was found only in the subsample of subjects with less than 15 years of illness.

Conclusions: Our results highlight the need to implement appropriate cardiovascular risk assessment and prevention in Mental Health Services.

Key words: Metabolic Syndrome, Severe Mental Illness, Community Mental Health, Cardiovascular Risk

Introduction

People with Severe Mental Illness (SMI) show a greater cardiometabolic risk than the general population, resulting in in a 2-3 fold increased mortality, primarily from cardiovascular disease (CVD), and up to 20% reduction in life expectancy in this population [1]. Poor diet, sedentary lifestyle, smoking and the antipsychotic agents prescribed to treat mental health conditions are among the causes of this elevated risk for CVD.

Many of CVD-related risk factors are modifiable by changing unhealthy lifestyles and, when indicated, by referring for treatment. Nevertheless, people with SMI may often choose to avoid health services and the Community Mental Health team may represent the only health professionals who have contacts with them [2]. Despite the development of guidelines recommending an active role of psychiatrists in the management of CVD-related risk factors, Mental Health Services do not appear to be implementing appropriate screening of cardiovascular risk factors within current systems. So that, the physical health management of the severe mentally ill population remains inadequate [3]. On the other hand, little is known about the trajectory of cardiometabolic risk as patients progress through their illness and the few data available are mostly limited to samples assessed in controlled trials or in academic settings.

The present study aims to investigate the cardiometabolic health of

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patients with SMI enrolled in a Community Mental Service in northern Italy. Specifically, the presence of Metabolic Syndrome (MetS) and individual cardiometabolic risk factors will be evaluated in relation to sex, illness duration, and antipsychotic treatment duration.

Methods

Subjects were recruited in two outpatient centers of the Community Mental Health Service of the Azienda Ospedaliera Fatebenefratelli e Oftalmico in Milan (Italy) between may 2007 and april 2008.
Inclusion criteria were: a) being aged 18 to 75 years; b) being diagnosed as having schizophrenia, schizoaffective disorder, delusional disorder, psychotic disorder not otherwise specified, or bipolar disorder. The following were exclusion criteria: a) being diagnosed as having substance-induced psychotic disorder, or psychotic disorder due to a general medical condition; b) having current neurological disorders affecting diagnosis or prognosis. Any treatment received prior to and after study assessment was based on the community clinician's choice. After receiving a complete description of the study and providing written informed consent, eligible subjects were administered the Structured Clinical Interview for DSM- IV Axis I Disorders (SCID-I) to ascertain the inclusion diagnoses. Informations about demographic variables, prescribed medication, illness duration, were also collected. Moreover, patients underwent assessments of height, weight, waist circumference, and systolic and diastolic blood pressure as well as fasting phlebotomy for levels of glucose, hemoglobin A1c (HbA_{1c}), and lipids.
In proceeding with guidelines of the National Cholesterol Education Program-Third Adult Treatment Panel [4], MetS was defined as the presence of at least three of the five criteria including: 1) abdominal obesity (waist circumference > 102 cm for men and > 88 cm for women); 2) hypertriglyceridemia (≥ 1.7 mmol/l or 150 mg/dl); 3) low high-density lipoprotein cholesterol (HDL-C) (Men: < 1.03 mmol/l or 40 mg/dl; Women: < 1.29 mmol/l or 50 mg/dl); 4) raised blood pressure (≥ 130/≥ 85 mmHg); 5) impaired fasting glucose (≥ 5.6 mmol/l or 100 mg/dl).

Statistics

Beyond descriptive analysis of the entire sample, categorical and continuous cardiovascular variables were compared by sex using χ^2 test and t test respectively. Several Pearson's tests were carried out to evaluate correlations between illness and treatment duration and cardiometabolic parameters, both in the overall sample and in the two sub-sample of subjects with more/less of 15 years of illness. Analyses were performed using SPSS Statistical Package version 20.0 [5].

Results

The study sample included 77 patients. The mean (SD) age of patients was 45.3 (12.2) years; 46.5% of patients were male. Diagnoses included schizophrenia (37.6%), schizoaffective disorder (18.2%), bipolar disorder (15.3%), and psychotic disorder not otherwise specified or delusional disorder (28.2%). 96.5% were currently receiving antipsychotics, of which 90.7% were second-generation antipsychotics. The mean (SD) illness duration was 15.5 years (12.5), while the mean (SD) total life-time antipsychotic treatment was 7.8 years (9.3).
33.7 of subjects were taking only antipsychotic treatment. Other psychotropic medications consisted mainly of antidepressants (18.6%), benzodiazepines (16.3%) and mood stabilizers (14.0%).
Demographic and clinical characteristics of study sample dichotomized by sex are described in Table I. No differences were found for age, occupational status, education nor for inclusion diagnosis or pharmacological treatment.

Coronary Heart Disease (CHD) risk factors

Among all patients, 46.5% smoked cigarettes, with no significant differences between males and females. The mean (SD) BMI was 27.3 (6.1). Overall, 58.1% of patients were overweight. Females did not differ from males with regard to weight status, waist circumference or BMI (Table I). Among the patients, 17% had hypertension. Females did not differ from males with regard to systolic and diastolic blood pressure. Impaired fasting glucose levels were present in 11.7% of patients and diabetes in 5.2%. No differences in fasting glucose and HbA1c were found between males and females. Fasting triglyceride levels over 150 mg/dl were present in 45.7% of subjects. Overall, 40.0% of subjects had low levels of fasting HDL-C (less than 40 mg/dl for males and 50 mg/dl for females). As expected, males had lower HDL-C ($p < .001$) than females. 31.4% of patients had MetS. Males and females did not show differences in the

Table I. Socio-demographic and clinical characteristics of sample by gender..

	Male (n = 37)	Female (n = 40)	Chi2/T	p
Age	43.9 (11.9)	45.5 (14.2)	-.570	.570
Education (years)	12.7 (3.5)	13 (3.8)	.354	.724
Occupied	12 (33.3)	21 (53.8)	3.197	.103
Diagnosis (77 valid)				
Schizophrenia	16 (43.2)	15 (37.5)	.264	.389
Bipolar Disorder	6 (16.2)	5 (12.5)	.217	.750
Delusional/Psychotic NOS	10 (27.0)	11 (27.5)	.002	1
Schizoaffective Disorder	5 (13.5)	9 (22.5)	1.043	.382
Treatment				
BDZ	6 (16.2)	6 (14.6)	.037	1
Antidepressants	4 (10.8)	11 826.8)	3.213	.090
Mood Stabilizers	4 (10.8)	6 (14.6)	.254	.740
BMI	28.2 (5.7)	26.6 (6.4)	-1.195	.236
Smoking	23 (57.5)	17 (39.5)	2.679	.126
Overweight	24 (70.6)	23 (60.5)	.802	.460
Waist circumference	99.2 (14.5)	94.1 (13.4)	-1.511	.135
Exercise	19 (51.4)	17 (45.9)	.216	.816
Blood pressure • Systolic • Diastolic	 128.3 (18.6) 80.0 (9.5)	 120.5 (11.4) 79.5 (9.2)	 1.661 .185	 .106 .854
Lipid metabolism • Total cholesterol • HDL-C • LDL-C • Triglycerides	 208.4 (46.8) 45.7 (14.2) 120.2 (34.4) 198.4 (138.6)	 214.8 (49.5) 58.8 (15.6) 123.8 (37.3) 150.0 (140.2)	 .590 3.803 .414 -1.530	 .557 **.000** .678 .130
Carbohidrate metabolism • Fasting glucose • HbA_{1c}	 102.2 (37.3) 5.87 (2.1)	 93.6 (14.0) 5.39 (0.8)	 -1.315 -1.350	 .195 .181
MetS • Fasting glucose ≥ 100 mg/dl • HDL-C < 40 mg/dl/< 50 mg/dl • Waist circumference • Blood pressure ≥ 130/85 mmHg • Fasting triglycerides ≥ 150 mg/dl	8 (21.6) 6 (16.2) 18 (48.6) 19 (51.4) 5 (13.5) 19 (51.4)	14 (35.0) 3 (7.5) 10 (25.0) 10 (25.0) 7 (17.5) 13 (32.5)	1.957 1.415 3.996 3.270 .935 2.812	1 .299 .058 .084 .497 .110
Illness duration	14.7 (9.5)	16.2 (14.8)	-.493	.624
Overall antipsychotic exposition	7.4 (9.0)	8.1 (9.6)	-.172	.864

Cardiometabolic risk status by gender in the overall sample.

frequency of MetS nor in the frequency of individual MetS criteria.

Illness and treatment duration

Correlations between mean continuos cardiometabolic parameters and, respectively, duration of psychiatric illness and antipsychotic treatment exposure were not significant in the overall sample, nor in the subsample of subjects with duration of illness greater than 15 years (data not shown). In the subsample of subjects with less than 15 years of illness, significant correlations were found between the length of antipsychotic exposure and BMI (r = .391; p = .024), waist circumference (r = .481; p = .005), LDL cholesterol (r = .519; p = .007) and fasting glucose (r = .418; p = .019) (Table II).

Discussion

In agreement with previous data, our sample of 77 patients with SMI, with an average of 15.5 years of

Table II. correlation between duration of psychosys and cardiometabolic risk.

	Total Psychiatric Illness Duration			Cumulative Antipsychotic Treatment Duration		
	N	pearson	p	N	pearson	p
BMI	37	.317	.067	36	.391	.024
Waist circumference	37	.396	.025	36	.481	.005
Blood pressure						
Systolic	37	-.005	.984	36	.044	.862
Diastolic	37	.122	.630	36	.153	.545
Lipid metabolism						
Total cholesterol	37	.165	.366	36	.279	.129
HDL	37	-.292	.117	36	-.160	.408
LDL	37	.364	.062	36	.519	**.007**
Triglycerides	37	.074	.686	36	.024	.898
Carbohidrate metabolism						
Fasting glucose	37	.314	.080	36	.418	**.019**
HbA_{1c}	37	.060	.747	37	.126	.505

Correlations between Mean continuos Cardiometabolic Health Parameters and duration of Psychiatric illness and antipsychotic treatment among subjects with less than 15 years of illness duration.

mental illness duration and a 7.8 years of lifetime antipsychotic exposure, showed a pattern of increased smoking, overweight and MetS compared with the general Italian population [6-8].

Overall, almost half of the patients smoked tobacco (compared with a 21% rate in general population) [9] and way more than half were overweight. Rates of hypertension (17%), and diabetes (5.2%) were similar to those found in community samples, while the above 30% prevalence of MetS was dramatically higher compared to the general population. Our results are comparable with data deriving from other Italian clinical samples. Carrà et al. [10] found a 26% prevalence of MetS among individuals with SMI admitted to a University Hospital for inpatient treatment while Salvi et al. [11] found a prevalence of MetS as high as 25.3% among in- and outpatients with Bipolar Disorder referring to a University Psychiatric Clinic. Moreover, in the latter study high triglycerides, low HDL-C levels and high fasting glucose levels were observed in 34.7%, 32.3% and 11% of subjects, respectively. In a later study, the same research group found that MetS was present in about 21% of in- and outpatients with OCD [12] and was associated with greater duration of antypsychotic exposure.

Despite our results are quite consistent with previous studies, we are reporting the higher prevalence of MetS. A possible explanation might be that our sample included a big proportion of subjects with Schizophrenia spectrum or other psychotic disorders, that are arguably more disruptive of healthy lifestyles and/or socioeconomic status. In fact, body-composition alterations and other MetS components are likely to be mediated by the adoption of unhealthy lifestyles, such as poor diet, smoking and lack of exercise, related to these psychiatric conditions. On the other hand, the great prevalence in metabolic syndrome and overweight found in our sample might also be related to the exposure to antipsychotic agents. Salvi and colleagues [11], for example, reported that only 37% of subjects included were taking antipsychotics, compared with the 97% of our sample. However, our results are in keeping with a recent metanalysis of studies from different countries, reporting an overall rate of MetS among schizophrenic subjects of 32.5% [13].

Interestingly, while in the overall sample no correlations were found between individual cardiovascular risk factors and total duration of illness or overall exposition to antipsychotic treatment, body composition–related risk markers were significantly associated with longer total lifetime antipsychotic treatment duration and, to a lesser extent, to psychiatric illness duration in the subsample of patients with less than 15 years of illness. Similarly metabolic risk markers such as fasting LDL-C and fasting glucose were significantly associated with the overall mean treatment duration only in the subsample with shorter illness duration. Our findings confirm that antipsychotic drugs may closely impact weight-related risk factors during the first years of exposure, but also broad the putative critical period of 1-5 years after illness onset suggested by previous studies [14 15]. From this perspective, early stages of illness appear crucial both for

Table III. CVD risk assessment and management and members of the Community Mental Health team involved.

CVD risk assesment (baseline, 6 months and yearly thereafter)		CVD risk management	
Family history	**Nurse**	**Exercise classes**	**Occupational therapists**
BMI	Nurse	Diet and lifestyle advice	Nurse
Blood Pressure	Nurse	Smoking cessation	Psychiatric rehabilitation team
Fasting Glucose and Lipid Profile	Nurse	Liaison (dietist, cardiologist, diabetologist)	Psychiatrist

the choice of one antipsychotic over another and for implementing prevention programs and timely interventions on cardiovascular risk of subjects with SMI. However, we cannot exclude that other covariates, such as familiar risk or antipsychotic dose, might also play a role in the risk of developing MetS.

The extent to which SMI, antipsychotic medications and unhealthy life-styles, including poor access to health services, individually contribute to cardiometabolic risk and to the development of MetS is still under debate [16 17]. Taken together, our findings are consistent with the hypothesis that the higher cardiometabolic risk of individuals with SMI depends on mental illness and consequent unhealthy lifestyle but also correlates with antipsychotic medications, especially in the first years of illness.

While interpreting our findings, several important limitations have to be acknowledged. First, the small study sample did not allow us to draw definitive conclusions. Moreover, the cross-sectional design of the study prevented us to clarify the exact temporal sequence between the onset of MetS (and individual cardiometabolic risk factors) and antipsychotic treatment initiation. Further, several confounding factors, such as different antipsychotic medications, familiar predisposition, socio-economic variables, might arguably have affected our results. On the other hand, our study has the strength of providing data collected under real life practice circumstances about cardiovascular health of severely ill patients. From this perspective, it is noteworthy that we included patients with no limitations with regard to illness duration or concurrent medical conditions, that are likely to be among exclusion criteria of most clinical trials.

Despite the above limitations, our study confirms the high cardiometabolic risk of individuals with SMI referred to an Italian Community Mental Health Service, showing an important relationship between this risk and early phases of antipsychotic treatment. Results from this study provide a framework for appropriate CVD risk assessment and management, that could be implemented in the Community Mental Health Service by adapting the existing manpower resources (Table III) and that will ultimately contribute to improve clinical outcomes related to CVD in persons with SMI.

Take home messages for psychiatric care

- Related risk markers were significantly associated with longer total lifetime antipsychotic treatment duration and, to a lesser extent, to psychiatric illness duration
- Antipsychotic drugs may closely impact weight-related risk factors during the first years of exposure, but also broad the putative critical period of 1-5 years after illness onset
- Appropriate CVD risk assessment and management, that could be implemented in the Community Mental Health Service by adapting the existing manpower resources

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