ORIGINAL PAPERS

Estimation of Cardiovascular Risk by Framingham Score in a Cross-sectional Sample of Schizophrenia Inpatients

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Abstract

The lifespan of schizophrenia (SCZ) patients is considered 25 years shorter compared to the general population, primarily due to cardiovascular (CV) disease. This study aims to assess the CV profile of the SCZ inpatients from Psychiatry Clinic I and II of Cluj-Napoca between 2018-2019. **Methods:** The following indicators were documented from interview and laboratory data: arterial hypertension (AHT), smoking, dyslipidemia, obesity, metabolic syndrome (MS), medication adherence (MA), Framingham score (FS), and CV diagnosis (CVd). The sample was separated into two groups based on FS and CV diagnosis: high-risk/CVd and medium/low-risk. **Results:** 50 SCZ patients were included in the study. 58% had AHT and 10% were prediagnosed, 90% had lipids perturbations of which 26.7% were prediagnosed, 66 % met the criteria for MS from which one prediagnosis, 12% had a CVd and the average FS was 12.7% corresponding to intermediate risk category. MA subjects had a lower risk to be in the high-risk/CVd group (OR=1/0.22, p=0.02) and no association was found for the gender-CV risk categories (p=0.08). **Conclusion:** 1. The known CV risk factors are underdiagnosed in SCZ patients 2. SCZ might attenuate the gender CV risk stratification; and 3. MA might decrease the CV risk in SCZ.

Keywords: schizophrenia, cardiovascular, Framingham score, comorbidities, metabolic syndrome.

Rezumat

Speranța de viață a pacienților cu schizofrenie (SCZ) este cu 25 de ani mai mică decât a populației generale, îndeosebi din cauza patologiei cardiovasculare (CV). Scopul studiului este de a evalua profiul CV al pacienților cu SCZ spitalizați în Clinicile de Psihiatrie I și II din Cluj-Napoca între 2018-2019. **Metode:** Indicatorii următori au fost obținuți pe baza unui interviu și a datelor de laborator: hipertensiunea arterială (HTA), fumatul, dislipidemia, obezitatea, sindromul metabolic (SM), aderența la tratament (AT), scorul Framingham (SF) și diagnosticele CV (dCV). Eșantionul a fost împărțit în două grupuri după SF și dCV: risc mare/dCV și risc mediu/mic. **Rezultate:** 50 de pacienți cu SCZ au fost incluși în studiu. 58% au avut HTA, dintre care 10% au fost prediagnosticați, 90% au avut minim un tip de dislipidemie, dintre care 26.7% prediagnosticați, 66% au îndeplinit criteriile de SM și un singur prediagnostic, 12% au avut dCV și media SF a fost 12.7% corespunzătoare categoriei de risc intermediar. Pacienții cu AT au avut o șansă mai mică de a fi în grupul CV de risc mare/dCV (OR=1/0.22, p=0.02) și nicio asociere nu s-a putut stabili între sex și categoriile de risc CV (p=0.08). **Concluzii:** 1. Factorii de risc CV sunt subdiagnosticați la pacienții cu schizofrenie; 2. Schizofrenia atenuează stratificarea de risc CV între sexe și 3. AT ar putea reduce riscul CV în schizofrenie.

Cuvinte cheie: schizofrenie, cardiovascular, scor Framingham, comorbidități, sindrom metabolic

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INTRODUCTION

Schizophrenia is considered one of the main causes of long-term worldwide disability[1,2], as beyond the primary deficit, it is associated with multiple morbidities and premature mortality[3]. Mounting evidence indicates that among patients with SCZ death occurs 25 years earlier than in the general population[3], and a substantial role in generating this gap might be played by cardiovascular disease[4–6].

One matter that draws attention is the discrepancy between the high prevalence of post-mortem CV pathology and the lifetime CV diagnoses in SCZ[5], which suggests that SCZ patients suffering from CV disease often go unnoticed. Numerous explanations have been submitted, from the low addressability of these patients to non-psychiatric medical services[6] and the non-detection of CV risk factors[7] to the lack of improvement of the therapeutic conduct for these patients compared to the rest of the population[5,8]. In one way or another, the underdiagnosis of CV pathology in schizophrenia is certain. Nevertheless, despite this presumed underdiagnosis, epidemiological indicators remain impressive: CV diagnoses prevalence is about threefold higher in patients with schizophrenia than in the general population and myocardial infarction occurs 5 times more frequently in young patients diagnosed with schizophrenia[10]. In addition to the diagnosis of heart disease, well-known CV risk factors such as smoking and metabolic syndrome, are endemic in SCZ, with prevalence values of over 70% for smoking[11] and 32-68% for metabolic syndrome[12]. Thus, the bridge of co-morbidity between mental disorder and cardiovascular disease is expressed both by shortening the lifespan of patients and by the cumulation of CV risk factors, which some authors do not longer consider independent entities, but rather a set of risks immanent to schizophrenia[3] as a systemic disorder[13].

This study aims to evaluate the CV comorbidities of patients diagnosed with schizophrenia at the Psychiatric Clinics I and II of Cluj-Napoca. Three major objectives were pursued: 1. A separate assessment of the known CV risk factors such as smoking, hypertension, dyslipidemia, obesity, and metabolic syndrome; 2. The prevalence of actual diagnoses of CV disease and calculation of CV risk categories according to the Framingham equation and 3. The assessment of some clinical factors relevant to schizophrenia patients such as treatment adherence, family history of cardio-metabolic perturbations, and their importance as risk or protection factors against CV disease.

MATERIALS AND METHODS

Materials

The present study was designed as cross-sectional and included subjects admitted to the Psychiatric Clinics I and II of Cluj-Napoca between August 2018 and March 2019. The following inclusion criteria were applied: diagnosis of schizophrenia according to ICD-10; at least 18 years old. The exclusion criteria consisted of indecision on the definite diagnosis of schizophrenia and the unavailability of necessary data to assess the CV risk (lipid profile, blood glucose) in the medical file of inpatients.

The obtained data were classified into three major classes: demographic data- age, gender, background, civil and socio-economic status; clinical data-the age of SCZ onset, the number of admissions in the last 8 years, the family history of CV diagnoses or CV risk disorders, smoking, psychotropic and cardiotropic medication, medication adherence (MA), the existence of a diagnosis of CV disease in the history of patients or CV risk factors, body mass index (BMI) and blood pressure (BP) values; laboratory data: lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides) and glucose profile (fasting blood glucose-BG);

Methods

Clinical and laboratory data were used to identify the following indicators:

- Risk factors for the development of CV pathology: **smoking**; **hypertension** - affirmative for the value of systolic blood pressure (SBP) higher than or equal to 140 mm Hg and/or the value of diastolic blood pressure (DBP) higher than or equal to 90 mm Hg (according to ESC 2018), taken from the patients hospitalization record; the specifier of diagnosed arterial hypertension (AHT) is added if it is among the other diagnoses of patients in their medical record; **dyslipidemia** – affirmative in the presence of at least one disturbance of the lipid profile, defined by: total cholesterol levels higher than/equal to 190 mg/dL, of LDL-cholesterol of at least 115 mg/dL, of HDL-cholesterol less than 40 mg/dL in men and below 50mg/dL in women and values higher than/equal to 150 mg/dL of serum triglycerides, or as mere diagnosis of dyslipidemia in the patient re-

cord; **obesity** – defined by a BMI higher than/equal to 30kg/m^2 or as diagnosis in the patient record; **metabolic syndrome**, already diagnosed or defined by the presence of at least 3 of the following changes: 1.SBP higher than/equal to 130 mm Hg and/or DBP higher than/equal to 85 mm Hg; 2. the triglyceride levels equal to/higher than 150 mg/dL; 3. HDL-cholesterol below 40 mg/dl for men and below 50 mg/dl for women; 4. BG levels of at least 110 mg/dL and 5. Abdominal obesity/BMI greater than 30 kg/m^2; **diabetes and impaired glucose tolerance** – either prediagnosed or established by fasting BG levels of at least 126 mg/dL for diabetes and values of 100-125 mg/dL for pre-diabetes

- Particular factors of SCZ patients: **Psychotropic medication**: the antipsychotics and the type of antipsychotic-typical or atypical were included; **cardiotropic medication**: all medications prescribed for cardio-metabolic diseases (anti-hypertensive, beta-blockers, statins, etc.) were included; **medication adherence**: the data were taken from the history sheet and interview; **the number of admissions** to the Psychiatric Clinic in the last 8 years: all the admissions for each patient from the point where the record was kept through the Computerized System Atlas MED were counted;
- Diagnosis of CV disease and calculation of risk categories according to the Framingham score (FS): **diagnosis of cardiovascular disease**: any diagnosis of a disorder of the circulatory system has been recorded, according to the ICD-10 (rheumatic cardiopathy, ischemic heart disease, pulmonary heart disease, cerebrovascular diseases, diseases of the arteries and veins, heart failure, etc.) apart from the aforementioned CV risk factors; **Framingham cardiovascular risk categories**: the FS estimates the individual risk for a full-blown CV pathology in the next 10 years and requires the following data for the score calculation: gender, age, smoking, SBP, total cholesterol and HDL-cholesterol levels, diabetes, and antihypertensive treatment. After the score, the risk is layered into three categories: a. **High risk**: for a score ≥ 20%; b. **Intermediate risk**: for a score between 10% and 19%; c. **Low risk**: a score of less than 10%

Patients already diagnosed with CV disease were excluded from the FS calculation. Finally, the subjects were regrouped into two separate main CV categories/groups based on the FS categories and CV diagnoses: 1. present CV disease/high-risk subjects and 2. Intermediate/low-risk subjects.

STATISTICAL ANALYSIS

The data was processed within the IBM SPSS Statistics 24 program. Descriptive data analysis was performed (mean, maximum, minimum, amplitude, and standard deviation for continuous data and frequency analysis for categorical data). Chi-square and T-tests were performed to verify the association between specific variables after testing for the normality of data.

RESULTS

Demographic data: The group consists of 50 inpatients, of which 24 (48%) were males and 26 (52%) females. The average age of participants was 45.08 years, with the minimum corresponding to the age of 23 years and the maximum age of 77 years. Most patients were between 45 and 49 years of age (32%) as seen in Fig. 1. Most of the participants (26%) came from urban areas; more than two-thirds (70%) were medically or else retired and only 9 (18%) were employed. Most patients (68%) were unmarried.

Clinical data: The average age of SCZ onset was 27.4 years, with a minimum of 16 years and a maximum of 45 years. The average number of admissions in the last 7 years was 6.86 admissions, with most patients having less than 5 admissions during this period. A family history of heart disease or CV risk was recorded in 31 of the participants (62%).

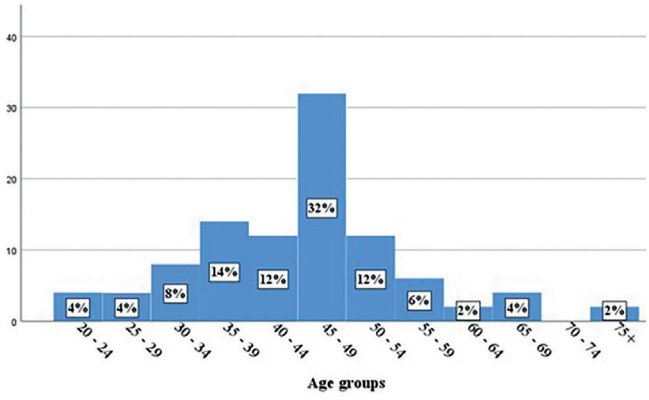

Figure 1. Age group histogram: The sample was organized in 5-year age groups. The most numerous cluster was the 45-49 age group that represent one third of the entire sample.

CV risk factors:
Smoking was found in 34 patients (68%).
In terms of BP values, the average SBP was 131 mm Hg and DBP 86.1 mm Hg. 29 patients (58%) had BP values above the normal range, of which 10 (34.5%) had the diagnosis of predetermined AHT. Only 14 (48.3%) of 29 hypertensive subjects received long-term antihypertensive treatment.

At least one lipid profile disorder was detected in 45 of the patients (90%): 40% had total cholesterol above the normal range. The average total cholesterol levels were 178.68 mg/dl; 40% had increased LDL-cholesterol levels and the average levels were 104.96 mg/dL; 70% had hypo-HDL-cholesterol levels and the average levels were 40.3 mg/dL. 40% had hypertriglyceridemia and the average levels were 173.88 mg/dL. Only 12 (26.7%) of dyslipidemia subjects (90%) had a predetermined diagnosis and only 2 (4.5%) followed treatment with statins.

The average levels of the measured fasting BG were 91.6 mg/dl, with extreme values between 52 mg/dl and 281 mg/dl; 3 patients (6%) had the diagnosis of diabetes type 2, and 9 (18%) had an alteration of glucose tolerance (pre-diabetes).

The average BMI value was 28.6 kg/m^2 with extreme values between 18.4 kg/m^2 and 41.5 kg/m^2. 18 patients (36%) had obesity, of which only 10 (55.6%) were prediagnosed.

Metabolic syndrome was detected in 33 of the patients (66%), of which only 1 patient was prediagnosed.

CV pathology: only 6 patients (12%) had diagnoses of cardiovascular disease. The average Framingham score was 12.7%, corresponding to the intermediate risk category, and the extreme values were 0.06% and 75.57%. The risk categories were distributed as shown in Fig. 2.

Antipsychotic medication consisted mostly of atypical antipsychotics and in a few cases (12%) in combination with typical antipsychotics or only typical antipsychotics. As can be seen in Fig.3, the most used therapeutic scheme during the study was risperidone (28%), followed by olanzapine (18%), and quetiapine (10%). In terms of MA, 29 (58%) of patients declared themselves adherents to antipsychotic treatment.

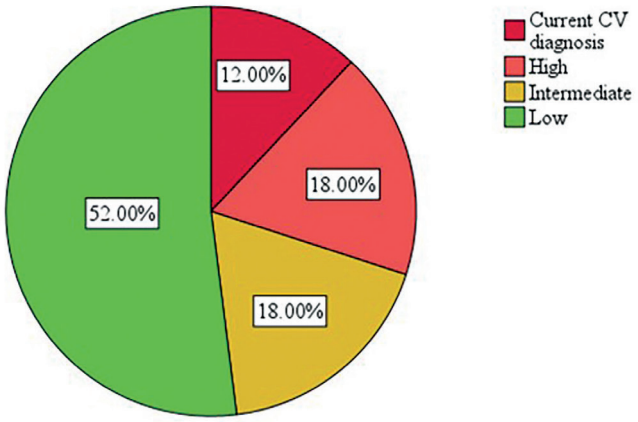

Figure 2. Framingham Score distribution within the sample group

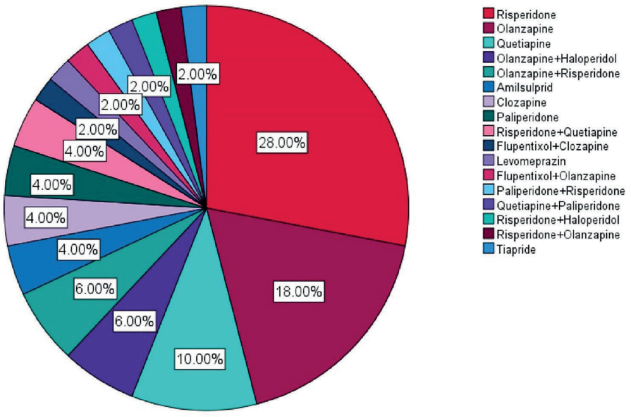

Figure 3. The main antipsychotic treatment distribution within the sample group

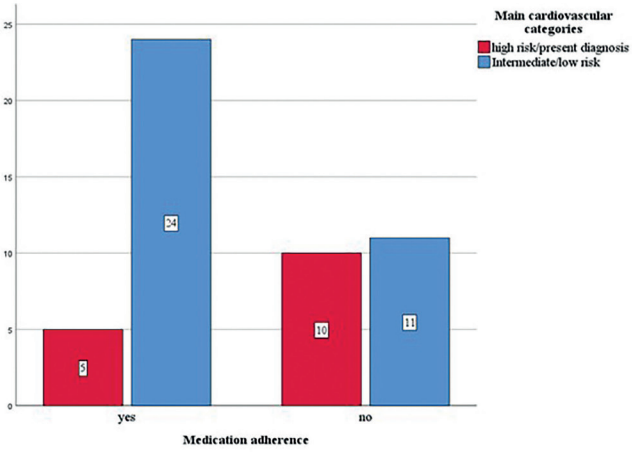

Figure 4. The cardiovascular categories grouped by medication adherence (MA) groups: Subjects in the yes MA groups has a lower chance of being in the high risk/present CV disease category (red) the the non-MA subjecs

The descriptive data are summarized in Table Nr. 1.

	N	%	
Gender			
▪ **male**	24	48	
▪ **female**	26	52	
Residence (urban)	37	74	
Social status (active)	9	18	
CV risk factors			
Smoking (yes)	34	68	
AHT (total yes)	29	58	
▪ **preD**	10	20	
Dyslipidemia (total yes)	44	88	
▪ **preD**	12	24	
Obesity (total yes)	18	36	
▪ **preD**	11	22	
MS (total yes)	33	66	
▪ **preD**	1	2	
Diabetes (yes)	3	6	
Prediabetes (yes)	9	18	
CV diagnosis (yes)	6	12	
CV categories			
▪ **high/very risk**	15	30	
▪ **low/medium risk**	35	70	
Antipsychotics			
▪ **atypical**	44	88	
Medication adherence (yes)	29	58	
	N	**Mean**	**± SD**
Age (years)	50	45.08	10.79
Onset age (years)	50	27.40	5.70
Admissions (number)	50	6.44	4.94
SBP	50	131.00	16.75
DBP	50	86.10	10.463
Cholesterol (mg/dL)	50	178.68	40.765
LDL-C (mg/dL)	50	104.96	36.254
HDL-C (mg/dL)	50	40.30	11.638
TGL (mg/dL)	50	173.88	142.308
Gly (mg/dL)	50	91.60	31.96
BMI (kg/m²)	50	28.556	5.57
FS	50	12.702	13.30

Table 1. Summary of the descriptive data
Abbreviations: CV=cardiovascular; AHT=arterial hypertension; preD=prediagnosed; MS=metabolic syndrome; SBP=systolic blood pressure; DBP=diastolic blood pressure; LDL-C=LDL-cholesterol; HDL-C=HDL-Cholesterol; TGL=triglycerides; Gly=glycemia; BMI=body mass index; FS=Framingham score

TESTS

Three Chi-squared tests and two t-tests for independent samples were performed:

In the case of the first test, we examined the association between CV family history and the main CV categories, where the two variables were found dependent (p=0.003; X^2=8.93, and OR= 14.82). Therefore, participants with CV family history had 14.8 higher odds ratio than the others of being in a high risk/present CV disease group.

In the case of the second Chi-squared test, an association between MA and CV categories was examined. We found the two variables dependent, where MA-yes group had an odds ratio equal to 0.22 of being in a high CV risk status/ present CV disease (p=0.02; X^2 of 5.32; OR=0.22). This association suggests that subjects adherent to antipsychotic treatment had a 4.55 times lower (1/0.22) chance of being in a high CV risk status or already diagnosed CV disease group.

A t-test for independent samples was also performed to compare the average scores of FS grouped by MA categories. When the hypothesis was unidirectional, that the MA „yes" group had a smaller FS mean score, the test was statistically significant (one-sided p=0.037), but when bidirectional, that the two groups had merely unequal means, the test found no significant difference (two-sided p=0.075).

	MA	***N***	**Mean**	**Std. Deviation**	**Std. Error Mean**
FS	yes	26	9.7377	7.33913	1.43932
	no	18	16.9989	18.32756	4.31985

Table 2. The mean values of Framingham scores (FS) grouped by Medication adherence (MA)

In the case of the third Chi-squared test, a possible association between gender and CV categories was tested. The null hypothesis of independence between the two variables (p=0.08, X^2=2.9) was accepted, which indicated no significant association between gender and CV categories.

The second t-test was performed to compare the means of FS and the other CV risk factors grouped by gender. No significant difference was found between the gender CV indicators, apart from one single variable (total cholesterol), as shown in Table nr. 4.

	Gender	*N*	Mean	Std. Deviation	Std. Error Mean
FS (%)	M	19	**13.1674**	10.09977	2.31705
	F	25	**12.3592**	15.51144	3.10229
SBP mm Hg	M	24	**131.46**	15.427	3.149
	F	26	**130.58**	18.184	3.566
DBP mm Hg	M	24	**88.33**	9.402	1.919
	F	26	**84.04**	11.137	2.184
Chol-T mg/dL	M	24	**166.29**	39.062	7.974
	F	26	**190.12**	39.624	7.771
LDL-C mg/dL	M	24	**92.83**	34.042	6.949
	F	26	**116.15**	35.193	6.902
HDL-C mg/dL	M	24	**37.04**	10.310	2.105
	F	26	**43.31**	12.168	2.386
TGL mg/dL	M	24	**196.08**	182.074	37.166
	F	26	**153.38**	91.018	17.850
BMI Kg/m2	M	24	**29.033**	3.4739	.7091
	F	26	**28.117**	7.0258	1.3779

Table 3. Average score of CV risk indicators grouped by gender: Abbreviations: FS=Framingham score; SBP=systolic blood pressure; DBP=diastolic blood pressure; LDL-C=LDL-cholesterol; HDL-C=HDL-Cholesterol; TGL=triglycerides; BMI=body mass index;

DISCUSSION

The current study aimed to assess the CV risk factors and disease prevalence within a sample of SCZ inpatients, and to identify associations between the CV risk indicators and independent clinical factors of SCZ patients such as adherence to antipsychotic treatment.

The risk factors assessed here were those conditions considered CV premorbidities such as smoking, high blood pressure, dyslipidemia, obesity, and metabolic syndrome, for which the results of the current study indicate high prevalence among the participants.

More than two-thirds of subjects declared themselves smokers (68%), a prevalence corresponding to data from the literature, according to which more than 70% of individuals diagnosed with schizophrenia are regular smokers[11]. Smoking is an undoubted risk factor for the development of a CV pathology or a major cardiac event, and recent studies have shown in this regard that smoking patients with SCZ have a 12 times higher risk of cardiogenic death than other non-smoking patients[14]. On the other hand, the prevalence of smokers in the general population in Romania was estimated at 27%[15], a difference that indicates a considerable concentration of smokers among SCZ patients.

More than 50% of the study participants had BP values above the limit, with an average SBP value of 131 mm Hg, below the Romanian average of 142 mm Hg[16]. This difference can also be explained by the hypotensive effects of antipsychotic agents, without which the BP values could have been higher[17]. Lipid metabolism disorders had an impressive prevalence: at least one type of dyslipidemia was identified in 90% of subjects. Also, the prevalence of obesity was 36%. Several studies have associated lipid profile disturbances and weight gain in patients with schizophrenia with second-generation antipsychotics[18,19], but some authors are claiming that at least the hypertriglyceridemia could be intrinsically

				Significance				95% Confidence Interval of the Difference	
		t	df	One-Sided p	Two-Sided p	Mean Difference	Std. Error Difference	Lower	Upper
FM	Equal variances assumed	.197	42	.422	**.845**	.80817	4.09699	-7.45989	9.07623
	Equal variances not assumed	.209	41.165	.418	**.836**	.80817	3.87207	-7.01068	8.62701
SBP	Equal variances assumed	.184	48	.427	**.855**	.881	4.789	-8.748	10.511
	Equal variances not assumed	.185	47.678	.427	**.854**	.881	4.758	-8.686	10.449
DBP	Equal variances assumed	1.467	48	.074	**.149**	4.295	2.928	-1.591	10.181
	Equal variances not assumed	1.477	47.639	.073	**.146**	4.295	2.908	-1.552	10.142
Chol-T	Equal variances assumed	-2.139	48	.019	**.038**	-23.824	11.140	-46.223	-1.424
	Equal variances not assumed	-2.140	47.782	.019	**.038**	-23.824	11.134	-46.213	-1.435
LDL-C	Equal variances assumed	-2.378	48	.011	**.021**	-23.321	9.807	-43.039	-3.602
	Equal variances not assumed	-2.381	47.887	.011	**.021**	-23.321	9.794	-43.014	-3.627
HDL-C	Equal variances assumed	-1.956	48	.028	**.056**	-6.266	3.203	-12.707	.174
	Equal variances not assumed	-1.969	47.668	.027	**.055**	-6.266	3.182	-12.665	.133
TGL	Equal variances assumed	1.061	48	.147	**.294**	42.699	40.231	-38.191	123.589
	Equal variances not assumed	1.036	33.209	.154	**.308**	42.699	41.230	-41.164	126.562
BMI	Equal variances assumed	.577	48	.283	**.567**	.9164	1.5885	-2.2776	4.1103
	Equal variances not assumed	.591	37.163	.279	**.558**	.9164	1.5496	-2.2230	4.0558

Table 4. Results of T-test for independant samples for the mean values of CV indicators grouped by gender
Abbreviations: FS=Framingham score; SBP=systolic blood pressure; DBP=diastolic blood pressure; Chol-T=total cholesterol; LDL-C=LDL-cholesterol; HDL-C=HDL-Cholesterol; TGL=triglycerides; BMI=body mass index;

linked to the pathobiology of schizophrenia, independent of medication[20,21]. MS was identified in 66% of the study participants, which is in concordance with the literature, where the prevalence of MS among SCZ multiepisodic patients has values ranging from 46% to 69%[12,22–24]. The risk of CV disease, CV fatality, or stroke is considered to be 2 times higher in the presence of MS[25], and in SCZ the emergence of MS has been linked both to external factors such as cumulation of unhealthy habits or antipsychotic medication[18] and to genetic diathesis[26].

The underdiagnosis and consequently the under-treatment of these CV premorbidities were constant, so that: only 34.5% of the total hypertensive patients had a prediagnosis of AHT and less than half of them received or maintained an anti-hypertensive treatment; 26.7% of the dyslipidemia patients were prediagnosed and less than 5% took any cholesterol-lowering medication, 55.6% of the subjects found to have obesity were diagnosed, and only one patient of the patients meeting the MS criteria had a prediagnosis. In support of these results, several studies have reported underdetection and deficiency of care for CV risk factors, such as AHT or dyslipidemia in patients with schizophrenia[5,7,27].

Patients with a diagnosis of CV disease accounted for only 12% of the group. A sub-detection gap can also be suspected in this case, given that 18% of the other participants without any diagnosis had Framingham high-risk scores of developing CV disease in the next

10 years (over 20%). In support of this underdiagnosis hypothesis, a recent study concluded that patients with schizophrenia are 66% more likely not to be properly diagnosed before dying of a CV cause[28]. The Framingham average score was 12,7%, with means of 13,17% for men and 12,4% for women, a score considered intermediate and similar to the results of other studies[24]. Two tests were performed to compare the CV risk status among the participants based on gender: a Chi-squared test examining the two main CV risk categories and gender, and a t-test comparing the means of FS grouped by gender. Both failed to find any significant association between the CV risk and gender, nor a difference in Framingham score between male and female subjects. This nondiscriminative distribution of the CV risk indicators among the participants indicates a cancellation of the protective effect of the female gender against CV risk in the case of SCZ.

All participants were being treated with second-generation antipsychotics, and less than one-third also received typical antipsychotics. The most commonly prescribed were risperidone, olanzapine, and quetiapine. It is considered that both types of antipsychotics can prolong the QT interval, thus increasing the risk of ventricular arrhythmia[29] and risperidone and olanzapine were, in particular, associated with a high risk of developing metabolic syndrome[12]. Patients adherent to antipsychotic medication accounted for more than half of the sample. Although antipsychotic medication has been associated with several cardiometabolic perturbations, our Chi-squared and t-test analyses found that patients who declared MA had a 4.55 times lower odds ratio for being in a high CV risk/present diagnosis group than the non-MA subjects, which suggests a possible protective role of the antipsychotic treatment against the CV burden. This paradoxical protection can be explained by the overall improvement of cognitive functions under antipsychotic medication and by increasing awareness of the disease and its consequences, including non-psychiatric comorbidities, and better involvement in the healthcare system[5,30,31]. In addition, mounting evidence highlights the anti-inflammatory effects of antipsychotics[32], which could also explain their protective role against developing a cardiovascular disease.

The prevalence of cardiometabolic disorders in the family history of the participants was 62%, and the odds ratio of these subjects being in a high CV risk/present disease group was 14.8 times higher than that of subjects with no CV family history. Observations in the literature about the high prevalence of cardiometabolic perturbations among unaffected relatives of SCZ patients point to the possibility of a common family diathesis for higher CV risk and psychosis[33]. Vulnerability is believed to be given by both genetic liability and external factors and epigenetic interactions. As regards the genetic factors, increasing data support the existence of certain common loci associated with both SCZ and CV risk factors, which might explain the high prevalence of CV conditions in individuals with SCZ and their primary relatives[21]. Another study identified a major dysfunction of the autonomic system in first-degree relatives of SCZ patients, which might suggest a specific pattern of CV pathogenesis in SCZ[34]. External factors refer to those environmental adversities shared by patients and their relatives such as unhealthy lifestyles, or poor economic status, which could compromise access to healthcare facilities[33]. Such a salient concentration of cardiometabolic conditions in the family of SCZ patients best reflects the multiple facets of the conjunction between cardiovascular disease and psychosis, as well as the multiple links of a long pathogenetic chain, from genetics to the environmental factors.

The present study has several limitations: first, there was not a control group for an accurate comparison, therefore we used data from the most proximate literature (national and regional statistics of CV risk factors and disease); second, the sample might not be representative enough for the entire picture of CV comorbidity in schizophrenia, as only the inpatients admitted in the acute regime were included, with the omission of long-term units inpatients or of stabilized outpatients; third, certain categories of data such as family history and the medication adherence could not be fully objectified and documented from the patient file, with the risk of a lack of accuracy; and forth, the real cardiovascular risk of the participants could be underestimated, given the larger proportion of young patients.

CONCLUSION

Three main conclusions can be drawn on the basis of the present cross-sectional study: 1. Patients diagnosed with schizophrenia have a high prevalence of known cardiovascular risk factors (dyslipidemia, smoking, metabolic syndrome, hypertension) which are underdetected; 2. The protective role of female gender against the CV disease might be attenuated in schizophrenia, and

3. Adherence to antipsychotic treatment might be a protective factor for schizophrenia patients against cardiovascular risk.

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Funding Body
This research received no specific grant from any funding agency, commercial or not-for-profit sectors.