

## Comparison of metabolic parameters and Framingham cardiovascular risk scores before and after in-hospital treatment with antipsychotics

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### Summary

**Background.** The objective of this naturalistic study was to evaluate changes in the prevalence of metabolic syndrome (MetS) and Framingham cardiovascular risk scores in adult with schizophrenia after in-hospital treatment with antipsychotics.

**Methods.** For 58 patients (36 women and 22 men) the following data was acquired on admission and at discharge: body height and weight, waist circumference, cigarette smoking, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides (TGA), fasting plasma glucose (FPG), blood pressure, concomitant use of antidiabetic, antihypertensive and antihyperlipidemic medications.

**Results.** Mean TGA levels increased significantly (140.32 mg/dL vs. 180.17 mg/dL), other parameters did not change. MetS prevalence on admission and at discharge did not differ significantly, irrespective of definition used (IDF: 50.00% vs. 60.34%; ATPIII: 39.66% vs. 43.10%; ATPIII A: 46.55% vs. 51.72%). Two cardiovascular risk scores were reduced at discharge: stroke, 10-year (4.10% vs. 3.46%) and hypertension, 4-year (22.18% vs. 16.58%). Other Framingham risk scores did not change. Very high prevalence of abnormal body weight (up to 65%), abdominal obesity (63% in men and 89% in women), hypertension (>50%) and lipid abnormalities (31-64%) was found.

**Conclusions.** We have found a very high rate of MetS in patients treated with antipsychotics. No metabolic parameters improved after hospital stay, while some worsened. This did not, however, result in increased risk of cardiovascular events. Abnormal body weight and lipid abnormalities were very common in our study population. Our results indicate that metabolic parameters should be monitored regularly, particularly in outpatient settings, and appropriate treatment should be introduced as soon as any significant changes are found.

schizophrenia / antipsychotics / metabolic syndrome / cardiovascular risk

### INTRODUCTION

Metabolic syndrome (MetS) is a complex clinical condition. It is a cluster of disorders comprising central (abdominal) obesity, dyslipidemia, hypertension and abnormal blood glucose lev-

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**Acknowledgments.** The study was supported by the Medical University of Lodz, grant No. 502-03/8-040-01/502-64-023.

No competing financial interests exist.

els. Various criteria are used to diagnose MetS. International Diabetes Federation (IDF) criteria are the most widely used in European studies [1]. These are slightly more restrictive than American ATPIII criteria [2]. The presence of MetS increases the risk of death due to cardiovascular diseases [3]. Current researches indicate that MetS prevalence may be higher in patients treated with antipsychotics comparing to general population [4] and therefore patients with psychiatric disorders may have increased mortality resulting from increased risk of cardiovas-

cular events (e.g. myocardial infarction, sudden cardiac death and stroke) [5]. This applies not only to antipsychotics, but also to mood stabilizers [6] and antidepressants [7]. Treatment-induced metabolic disorders may account for dramatically increased mortality of schizophrenia patients [8]. However, large Finnish study shows lower mortality compared with no antipsychotic use [9].

Framingham cardiovascular (CVD) risk scores allow to estimate risk score profiles of various cardiovascular disease outcomes in different time horizons: coronary heart disease, type 2 diabetes, general cardiovascular disease and hypertension. Studies indicate increased 10-year coronary heart disease risk in schizophrenia [10]. Middle-aged and older patients with psychotic symptoms (and thus taking antipsychotics) have increased 10-year risk of coronary heart disease (up to 79% in case of schizophrenia) [11].

The objective of this naturalistic study was to assess if there are changes in metabolic parameters, the prevalence of metabolic syndrome (MetS) or cardiovascular risk after in-hospital treatment with antipsychotics. Subjects with schizophrenia usually have low level of physical activity [12], have poor diet [13] and lack medical support [14].

## SUBJECTS AND METHODS

Data for 58 European Caucasian adult in-hospital patients with paranoid schizophrenia (men,  $n = 22$ ; women,  $n = 36$ ) was included into the study. The only inclusion criteria was current in-hospital antipsychotic treatment with at least one antipsychotic, irrespective of treatment type and previous treatment duration. The following data were collected on admission and at discharge: body height and weight, waist circumference, cigarette smoking, lipid panel and fasting plasma glucose levels, systolic and diastolic blood pressure. Antipsychotic treatment (class - first or second generation, drug name and daily dose) and treatment of comorbidities (diabetes, arterial hypertension and hyperlipidemia) were also registered. For antipsychotic treatment we collected data for all antipsychotics administered for at least one week during current hospital stay.

The blood samples for the chemistry panel that included fasting plasma glucose and lipid panel (total, HDL, and LDL cholesterol as well as triglycerides) were collected between 7 am and 8 am, after ensuring at least 8 h of overnight fasting. The samples were immediately transferred to the central laboratory where they were analyzed. Plasma glucose and serum lipids were estimated using a Dirui CS-400 Auto-Chemistry Analyzer (Dirui, China).

Height was measured with a wall-mounted height measure to the nearest 1 cm. Weight was measured with a spring balance that was kept on a firm horizontal surface. Subjects wore light clothing, stood upright without shoes and weight was recorded to the nearest 0.5 kg. Body mass index (BMI) was calculated as body weight in kilogram divided by the height in meter squared ( $\text{kg}/\text{m}^2$ ). Waist circumference was measured using a non-stretchable fiber measuring tape. Waist circumference was measured at a level midway between the lowest rib and the iliac crest.

MetS and its components were defined according to the National Cholesterol Education Program criteria (NCEP, Adult Treatment Protocol, ATPIII), adapted ATP-III criteria (ATPIII A) and International Diabetes Federation (IDF) criteria. These criteria are defined in Table 1 – *next page*.

For IDF criteria, if body-mass index (BMI) was over  $30 \text{ kg}/\text{m}^2$ , central obesity was assumed irrespective of waist circumference [1].

Impaired fasting glucose was defined as fasting plasma glucose level 100-125 mg/dL based on American Diabetes Association guidelines, new onset of type 2 diabetes was defined as fasting plasma glucose level  $>125 \text{ mg}/\text{dL}$ . Normal weight, overweight and obesity were defined as  $\text{BMI} <25 \text{ kg}/\text{m}^2$ ,  $25\text{-}30 \text{ kg}/\text{m}^2$  and  $\geq 30 \text{ kg}/\text{m}^2$ , respectively. Raised triglycerides (TGA) level  $\geq 150 \text{ mg}/\text{dL}$  and/or total cholesterol (TC)  $\geq 200 \text{ mg}/\text{dL}$  and/or reduced HDL cholesterol level  $<40 \text{ mg}/\text{dL}$  for men and  $<50 \text{ mg}/\text{dL}$  for women and/or raised LDL cholesterol level  $\geq 135 \text{ mg}/\text{dL}$  were interpreted as hyperlipidemia. Castelli atherogenic indices (AI) allow to evaluate atherosclerosis risk [15].  $\text{AI}_{\text{LDL}/\text{HDL}}$  is the ratio of LDL cholesterol to HDL cholesterol and  $\text{AI}_{\text{TC}/\text{HDL}}$  is the ratio of TC to HDL cholesterol. Low risk values are:  $\text{AI}_{\text{LDL}/\text{HDL}} \leq 3.3$  for men and  $\leq 2.9$  for women;  $\text{AI}_{\text{TC}/\text{HDL}} \leq 5.1$  for men and  $<4.4$  for women.

**Table 1.** Definitions of the metabolic syndrome

Criteria	ATP-III*	ATP-III A*	IDF†
Central obesity (waist circumference)	men >102 cm women >88 cm	men >102 cm women >88 cm	men ≥94 cm women ≥80 cm
Raised blood pressure or specific treatment	≥130/≥85 mm Hg or specific treatment	≥130/≥85 mm Hg or specific treatment	≥130/≥85 mm Hg or treatment of previously diagnosed hypertension
Reduced HDL level	men <40 mg/dL women <50 mg/dL	men <40 mg/dL women <50 mg/dL	men <40 mg/dL women <50 mg/dL or specific treatment
Raised TGA level	≥150 mg/dL	≥150 mg/dL	≥150 mg/dL or specific treatment
Raised FPG level or specific treatment	≥110 mg/dL or specific treatment	≥100 mg/dL or specific treatment	≥100 mg/dL or previously diagnosed type 2 diabetes
* MetS if 3 of 5 criteria are met.			
† MetS if central obesity (obligatory) and additional 2 criteria are met.			
HDL = high density lipoproteins; TGA = triglycerides; FPG = fasting plasma glucose.			

Framingham cardiovascular risk scores were calculated using current Framingham Heart Study algorithms (<http://www.framingham-heartstudy.org/risk/index.html>) using variables including LDL level, HDL level, blood pressure, diabetes and smoking status. The following scores were calculated: coronary heart disease, 2-year risk [16]; coronary heart disease, 10-year risk [17]; type 2 diabetes, 8-year risk [18]; general cardiovascular disease (coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure), 10-year risk [19]; hard coronary heart disease (myocardial infarction or coronary death), 10-year risk; recurring coronary heart disease (mostly hospitalized events consisting of myocardial infarction, coronary insufficiency, angina pectoris, and sudden and non-sudden coronary death), 2-year risk [16]; stroke, 10-year risk [20]; and arterial hypertension, 4-year risk. Next, the risk points were converted to corresponding percentage of risk [21].

Statistical procedures were performed with STATA 13.1 for OS X (StataCorp, College Station, Texas, USA). Simple descriptive statistics (means, standard deviations and 95% confidence interval) were generated for all continuous variables. For discrete variables number of patients and percentages are given. Shapiro-Wilk and Brown-Forsythe tests were used to test normality and equality of variances, respectively. The

difference between initial and final variables was analyzed by paired Student's t-test or Wilcoxon signed-rank test (for non-parametric analysis). The difference between two group proportions was analyzed by chi-square ( $X^2$ ) test. The difference between pre- and post-hospitalization proportions was analyzed by McNemar chi-square ( $X^2$ ) test (exact McNemar significance probability is given). The significant level was set at  $p < 0.05$ .

*The study protocol was approved by the local Bioethics Committee. There was no financial involvement from the industry.*

## RESULTS

Detailed demographic and clinical details (based on discharge values) of the study subjects are shown in Table 2 – *next page*. There were three subjects (5.2%) with the first episode of psychosis, other patients were taking antipsychotics for at least 4 months prior the study. During current hospital stay more than 90% of patients were taking second generation antipsychotics, among which olanzapine, quetiapine, clozapine, risperidone and aripiprazole were the most common. In case of depot-risperidone, its dose was converted to daily dose by dividing it by 14. Ten patients were also taking valproate (mean daily dose  $1030.00 \pm 454.73$  mg), four – lithium carbonate ( $937.50 \pm 388.64$  mg/day), five

**Table 2.** Demographic and clinical details.

	All (N = 58)	Men (n = 22)	Women (n = 36)	P†
Age	38.48±1.67 [35.13-41.83]	34.82±2.60 [29.41-40.23]	40.72±2.12 [36.42-45.02]	0.043 t = 1.74
Tobacco smoking	24 (41.38)	9 (40.91)	15 (41.67)	NS
Hospital stay (days)	54.95±2.96 [49.02-60.87]	50.77±5.64 [39.04-62.50]	57.57±3.25 [50.97-64.18]	NS
Treatment duration (months)	144.40±16.36 [111.63-177.16]	142.45±26.20 [87.97-196.94]	145.58±21.23 [102.49-188.68]	NS
Hyperprolactinemia	5 (8.62)	2 (9.09)	3 (8.33)	NS
Patients taking FGAs	14 (24.14)	8 (36.36)	6 (16.67)	NS
Patients taking SGAs	53 (91.38)	19 (86.36)	34 (94.44)	NS
Number of APs				
1	11 (18.97)	4 (18.18)	7 (19.44)	NS
>1	47 (81.03)	18 (81.82)	29 (80.56)	
APs, dose (mg/day) (no. of subjects)				
Quetiapine	591.91±25.91 [539.19-644.63] (34)	631.82±31.82 [560.92-702.71] (11)	572.83±34.89 [500.46-645.19] (23)	NS
Aripiprazole	27.5±1.71 [23.88-31.12] (18)	26.79±3.21 [18.92-34.65] (7)	27.95±2.04 [23.40-32.51] (11)	NS
Olanzapine	15.83±6.45 [12.26-19.41] (15)	17.50±8.22 [8.88-26.12] (6)	14.72±5.22 [10.71-18.73] (9)	NS
Clozapine	323.33±145.92 [242.53-404.14] (15)	450.00±150.00 [77.38-822.62] (3)	291.67±132.43 [207.52-375.81] (12)	NS
Risperidone*	3.29±1.84 [1.97-4.61] (10)	4.23±3.29 [-3.94-12.39] (3)	2.88±0.94 [2.02-3.75] (7)	NS
Antihypertensive treatment	10 (17.24)	4 (18.18)	6 (16.67)	NS
Dyslipidemia treatment	9 (15.52)	4 (18.18)	5 (13.89)	NS
Antidiabetic treatment	4 (6.90)	0	4 (11.11)	NS
Normal body weight	20 (34.48)	6 (27.27)	14 (38.89)	NS
Overweight	16 (27.59)	6 (27.27)	10 (27.78)	NS
Obesity	22 (37.93)	10 (45.45)	12 (33.33)	NS
Abdominal obesity‡	46 (79.31)	14 (63.64)	32 (88.89)	0.021, X <sup>2</sup> = 5.31
Data given as mean±standard deviation [95% Confidence Interval] for continuous variables or n (%) for discrete variables. †Men vs. women. * Including depot risperidone. ‡IDF-defined. APs = antipsychotics; FGAs = first generation antipsychotics; SGAs = second generation antipsychotics; NS = not significant.				

– carbamazepine ( $780.00 \pm 268.32$  mg/day) and 8 patients were taking selective serotonin reuptake inhibitors (SSRI). Women were significantly older ( $t = 1.74$ ,  $p = 0.043$ ). IDF-defined (criteria for European population) abdominal obesity was more common in women ( $X^2 = 5.31$ ,  $p = 0.021$ ). No other differences between men and women were found for subject characteristics. Table 3.

**Table 3.** Prevalence of metabolic syndrome and its components.

	On admission	At discharge	P
MetS ATPIII	23 (39.66)	25 (43.10)	NS
MetS ATPIII A	27 (46.55)	30 (51.72)	NS
MetS IDF	29 (50.00)	35 (60.34)	NS
Central obesity			
ATPIII / ATPIII A	34 (58.62)	34 (58.62)	NS
IDF	44 (75.86)	46 (79.31)	NS
Raised blood pressure	36 (62.07)	31 (53.45)	NS
Reduced HDL cholesterol			
ATPIII / ATPIII A	37 (63.79)	32 (55.17)	NS
IDF	37 (63.79)	32 (55.17)	NS
Raised TGA			
ATPIII / ATPIII A	18 (31.03)	30 (51.72)	<0.001, $X^2 = 12.0$
IDF	24 (41.38)	34 (58.62)	0.002, $X^2 = 10.0$
Raised FPG			
ATPIII	6 (10.34)	10 (17.24)	NS
ATPIII A / IDF	15 (25.86)	22 (37.93)	NS
All data given as n (%). MetS = metabolic syndrome; TGA = triglycerides; FPG = fasting plasma glucose; NS = not significant.			

Table 3 shows detailed data on the prevalence of MetS and its components. While MetS ATPIII, ATPIII A and IDF prevalence increased by 3.44%, 5.17% and 10.34%, respectively, there was no significant increase of MetS prevalence, irrespective of definition used. The prevalence of raised TGA increased significantly, while other variables did not differ between admission and discharge. No differences in sex, duration of schizophrenia, age or tobacco smoking between groups with or without MetS were found. Mean duration of hospital stay of subjects with MetS ATPIII A was significantly shorter comparing to subjects without MetS ( $50.09 \pm 19.42$  vs.  $62.13 \pm 24.74$  days;  $t = 2.05$ ,  $p = 0.002$ ), no such differences were found for IDF- or ATPIII-defined MetS. More subjects with MetS ATPIII were taking fewer

SGA during hospital treatment comparing to non-MetS ATPIII ( $X^2 = 11.82$ ,  $p = 0.037$ ). Again, there were no differences for other MetS definitions.

The analysis of changes in metabolic parameters (see Table 4 – next page) revealed that there were no improvements of these parameters. Triglyceride levels were significantly higher at discharge ( $z = -4.51$ ;  $P < 0.0001$ ). Mean total cholesterol on admission (210.2 mg/dL) and at discharge (208.5 mg/dL), as well as mean TGA at discharge (180.2 mg/dL) levels were above upper limit of normal ranges. The majority (39 of 48, i.e. 81.2%) of patients with any type of lipid abnormalities received no treatment for dyslipidemia. Although  $AI_{TC/HDL}$  exceeded the low risk range, there was no change from admission to discharge. Six patients (10.34%) gained  $\geq 7\%$  of body weight. Overweight and obesity were found in 27.59% and 37.93% of the patients, respectively. Mean BMI ( $28.5$  kg/m<sup>2</sup>) and waist circumference (96.5 cm) were above cut-off points for overweight and IDF-defined abdominal obesity, both on admission and at discharge.

Table 5 – next page – shows calculated Framingham CVD risk scores for various CVD events. Despite observed changes in metabolic parameters, we have observed a significant reduction in stroke ( $z = 2.02$ ,  $p = 0.043$ ) and hypertension ( $z = 2.02$ ,  $p = 0.043$ ) risk scores.

## DISCUSSION

Studies of general population demonstrated that the overall prevalence of MetS in European countries varies from 5.9% in men and 2.1% in women (France) [22], through 15.7% in men and 14.2% in women (Finland) [23] and 16.2% in men and 20.9% in women (Poland) [24] to 11.0% in men and 23.1% in women (Russia) [25]. American study found that MetS was present in 23.4% of women and 24% of men [26]. The prevalence of MetS increases with age and can reach up to

**Table 4.** Changes in metabolic parameters

	On admission	At discharge	P
Body weight (kg)	82.43±21.65 [76.69-88.17]	82.38±20.94 [76.82-87.93]	NS
BMI (kg/m <sup>2</sup> )	28.49±6.38 [26.80-30.18]	28.47±6.06 [26.86-30.07]	NS
Waist circumference (cm)	96.54±15.91 [92.32-100.76]	96.46±15.55 [92.33-100.58]	NS
Total cholesterol (mg/dL)	210.17±48.32 [197.35-223.00]	208.46±40.85 [197.62-219.29]	NS
HDL cholesterol (mg/dL)	44.09±13.22 [40.58-47.60]	44.40±13.41 [40.85-47.96]	NS
LDL cholesterol (mg/dL)	136.39±41.63 [125.34-147.43]	128.33±35.99 [118.78-137.88]	NS
TGA (mg/dL)	140.32±81.82 [118.60-162.03]	180.17±93.36 [155.40-204.95]	<0.0001 z = -4.51
AI <sub>LDL/HDL</sub>	3.38±1.51 [2.98-3.78]	3.19±1.41 [2.81-3.56]	NS
AI <sub>TC/HDL</sub>	3.19±1.41 [2.81-3.56]	5.14±1.91 [4.63-5.65]	NS
FPG (mg/dL)	95.77±23.73 [89.47-102.07]	96.81±14.16 [93.05-100.56]	NS
Systolic blood pressure (mm Hg)	127.40±18.56 [122.48-132.33]	120.67±15.24 [116.62-124.71]	NS
Diastolic blood pressure (mm Hg)	83.79±13.91 [80.10-87.48]	80.51±8.25 [78.32-82.70]	NS
Hyperglycemia	14 (24.14)	20 (34.48)	NS
Impaired FPG	3 (5.17)	8 (13.79)	NS
Type 2 diabetes	5 (8.62)	5 (8.62)	NS

Data given as mean±standard deviation [95% Confidence Interval] for continuous variables or n (%) for discrete variables.

47.2% in the 80-89 years of age group in men and 64.4% for women in the corresponding age groups [27]. Large meta-analysis (n = 25,692) revealed that the overall rate of MetS in schizophrenia and related disorders is 32.5% [28]. De Hert et al. reported MetS prevalence in patients with schizophrenia treated with antipsychotics of 28.4% (ATPIII), 32.3% (ATPIII A) and 36% (IDF) [4]. Therefore, the rate of MetS at discharge observed in our study is a lot higher than reported in other European studies. Our results are close to those observed in Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study (ATPIII: 40.9%; ATPIII A: 42.7%) [29]. Our study on the prevalence of MetS in adults

schizophrenics taking antipsychotics re-confirms high prevalence of MetS in this population, reaching as much as twice (or even thrice) the prevalence of the general population.

We have also demonstrated the prevalence of individual MetS components to be higher than in other studies. De Hert et al. found abdominal obesity, raised blood pressure, reduced HDL, raised TGA and raised FPG in 62.1%, 48.8%, 29.8%, 42.3% and 25.3% of patients, respectively [4]. The corresponding rates (IDF criteria) in our study are: 75.9%, 62.1%, 63.8%, 41.4% and 25.9% on admission and 79.3%, 53.4%, 55.2%, 58.6% and 37.9% at discharge. Our results are also higher than reported by Sicras-Mainar et al. (ATPIII A): abdominal obesity (defined as BMI >28.8 kg/m<sup>2</sup>) 17.8%, raised blood pressure 24.3%, reduced HDL 29.3%, raised TGA 11.2% and raised FPG 9.7% [30].

Increased TGA levels could be associated with changes in antipsychotic treatment and/or life-style changes during hospital stay (diet, physical activity, cigarette smoking). Increase of MetS prevalence and TGA levels may be explained by several factors. First of all, hospital stay may have caused changes in subjects' life style (diet, tobacco smoking, physical activity). However, we believe that hospital diet and physical activity (due to participating in group activities, e.g. occupational therapy) should not be worse comparing to their equivalents in the out-of-hospital setting. Most subjects were taking antipsychotics of well-established detrimental effect on body weight and other metabolic parameters (olanzapine, clozapine, quetiapine, risperidone). Effect of individual antipsychotics cannot be assessed at the moment due to limited size of each drug subgroup. Moreover, the majority of subjects were on polypharmacy. Another important issue is that appropriate hypolipemic treatment was almost non-existent (the most probable reason is that it was ignored by psychiatrists), which could also lead to lipid abnormalities. Most probably, a multifactorial mechanism is involved.

**Table 5.** Framingham cardiovascular risk scores

	On admission	At discharge	P
Coronary Heart Disease 2-year risk (%)	0.88±1.31 [0.53-1.22]	0.79±1.39 [0.43-1.16]	NS
Coronary Heart Disease 10-year risk (%)	7.19±8.45 [4.97-9.41]	6.07±6.43 [4.38-7.76]	NS
Type 2 diabetes 8-year risk (%)	6.52±7.50 [4.54-8.49]	7.55±8.36 [5.35-9.75]	NS
General Cardiovascular Disease 10-year risk (%)†	8.00±9.24 [5.55-10.45]	6.60±7.26 [4.67-8.53]	NS
Hard Coronary Heart Disease 10-year risk (%)‡	5.60±7.64 [3.59-7.61]	4.41±5.90 [2.86-5.96]	NS
Recurring Coronary Heart Disease 2-year risk (%)§	4.10±2.87 [3.35-4.86]	4.15±2.95 [3.38-4.93]	NS
Stroke 10-year risk (%)	4.10±3.43 [3.20-5.01]	3.46±2.19 [2.89-4.04]	0.043 z = 2.02
Hypertension 4-year risk (%)	22.18±18.04 [17.44-26.92]	16.58±13.18 [13.11-20.05]	0.043 z = 2.02

All data given as mean±SD [95% Confidence Interval]. NS = non-significant. †Coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure. ‡ Myocardial infarction or coronary death. § Mostly hospitalized events consisting of myocardial infarction, coronary insufficiency, angina pectoris, and sudden and non-sudden coronary death.

Despite observed metabolic alteration, the risk of cardiovascular events was **not increased** during this short-term treatment observation. We observed reduced 10-year risk of stroke and 4-year risk of hypertension. Risk factors for stroke score include age, systolic blood pressure and antihypertensive treatment, antidiabetic treatment and tobacco smoke. For hypertension score these are: blood pressure, sex, BMI, tobacco smoke. The reduction of these scores may be explained by small (non-significant) reduction of BMI, systolic and diastolic blood pressure values at discharge. It should be noted that these two scores were analyzed using lower-power non-parametric Wilcoxon signed-rank test and that P values were of low significance. Since none of the CVD risk factors improved significantly during hospital stay, we might assume that all CVD risk scores remain unaltered. It should be also noted that calculated risk scores are relatively low. While being non-significant, the reduction in blood pressure may be responsible for the decrease in the risk scores for stroke and hypertension. This

emphasizes the importance of proper hypertension treatment and management in patients with mental disorders.

Our results indicate one more important finding that it is important to monitor metabolic parameters during out-hospital treatment with antipsychotics. While a detrimental effect of this type of drugs are well established, they may remain undetected during the first weeks of treatment. This would indicate that during a relatively short period of time (mean hospital stay was approximately 8 weeks) severe metabolic alterations may not occur, but they develop during the next weeks or months.

In our study population mean values of BMI and waist circumference exceeded upper normal limits (as defined by WHO and IDF). We also found that mean total cholesterol levels were above upper limit of normal range (ULN), while mean TGA levels were above ULN at discharge. Mean value of atherogenic

indices  $AI_{LDL/HDL}$  and  $AI_{TC/HDL}$  were above respective ULN. Moreover, a very high (up to 89%) prevalence of increased body weight, abdominal obesity (which was significantly more frequent in women) and hyperlipidemia was found in patients taking antipsychotics. This confirms that physical health condition of people taking antipsychotics (regardless they have metabolic syndrome or not) is **very poor** [31]. Since increased mortality and morbidity is potentially preventable by improving medical treatment, our finding that the majority (more than 80%) of patients with hyperlipidemia did not receive specific treatment is alarming.

Although the prevalence of cigarette smoking among schizophrenics can be up to 90% [32], our result (41.38%) is almost twice as high as in the general population [33]. Since there is a well known adverse effect of smoking on LDL and HDL cholesterol, and triglycerides in a hypercholesterolemic population, regardless of age [34], this indicates an area for possible improvement.

Every research has its limitations, and so has this one. Our sample size is relatively small and so is the time interval between the two observations (the period of follow-up was only about 8 weeks). This unlikely to have a significant impact on the Framingham risk scores. Therefore, detailed analysis of some factors (e.g. individual antipsychotics) was not possible. Second, due to a naturalistic study design, a sufficient control for the effect of different pharmacological treatments is limited. The majority of subjects were on polypharmacy, so it was difficult to analysis and discuss. Moreover, it results in heterogeneity of the study group (e.g. in terms of treatment duration, types and doses of antipsychotics). Since patients were recruited only in one site, this could have also affected our results. Data on physical activity and diet were not available for analysis. **We cannot analyzed data regarding the duration of the mental disorder the subjects were diagnosed.** Also, we did not use rating scales to demonstrate the symptomatology and the severity of the schizophrenia.

## CONCLUSIONS

Between admission and discharge, the prevalence of MetS did not increase. Very high rate of MetS in patients treated with antipsychotics that we found in this study (up to 60.34%) exceeds MetS prevalence in general population. Significantly more subjects had raised triglycerides levels at discharge. Other MetS components did not improve. Most patients had at least one component of MetS. Abdominal obesity, raised TGA, reduced HDL cholesterol and raised blood pressure were the most frequent MetS components. No metabolic parameters improved after hospital stay, while triglyceride levels and the number of subjects with hyperglycemia increased significantly during in-hospital treatment. The risk of cardiovascular events did not increase. Framingham risk scores for stroke and hypertension were significantly lower at discharge, yet this could be an artifact. The majority of our subjects were overweight or obese, had abdominal obesity and lipid abnormalities. A very important clinical finding was that the majority of patients with hyperlipidemia had no antihyperlipidemic treatment introduced. The prevalence

of tobacco use is still too high. **Metabolic parameters should be monitored, particularly in outpatient settings, on a regular basis using available algorithms.**

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