Psychiatry and Behavioral Sciences 2019;9(3):85-93
https://doi.org/10.5455/PBS.20181106082036

ORIGINAL ARTICLE

The Effect of Positive Lifestyle on Reversal of Metabolic Syndrome in Patients with Schizophrenia Followed-up for Two Years

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ABSTRACT

Objective: The risk of metabolic impairment is higher in patients with schizophrenia due to long disease period, increasing age, unhealthy lifestyle, antipsychotic medication use, and genetic factors. Among these risk factors, unhealthy lifestyle and antipsychotic medication use are factors that can be changed by external interventions. Main objectives of our study were to retrospectively analyse the parameters of metabolic syndrome (MetS) in patients with schizophrenia whose metabolic parameters have been monitored for at least 2 years and whose medications and clinical conditions were stable, to detect new cases of MetS and cases with reversal of MetS, and to examine the factors that predict the incidence and reversal of MetS.

Methods: The sample group of the study comprised patients who were followed and monitored at the Psychotic Disorders Outpatient Clinic of Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery as outpatients between January 1st, 2014 and January 1st, 2017 and were admitted with schizophrenia diagnosis in accordance with the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). We present a retrospective analysis of longitudinal data addressing socio-demographic characteristics, metabolic parameters, positive lifestyle features in these patients. MetS was defined by the criteria defined by ATP-III A. The Positive and Negative Syndrome Scale, Schedule for Assessment of Insight, Clinical Global Impression Severity of Illness were also administered retrospectively. The interviews of the patients conducted in 2014 were regarded as the "first evaluation" and their interviews conducted 2 years after the first evaluation were regarded as the "final evaluation."

Results: Three hundred and fifty patients had a mean age of 42.6 were included in the study. The rate of MetS was 20% in the first evaluation and 25.4% in the final evaluation. Increase in the prevalence of MetS between the first and final evaluation was not significant. Two-year incidence were found as 13% with a rate of 30% for reversal of MetS. The logistic regression analysis revealed that the increase in age and less positive lifestyle had a significant predictive effect in incident cases and the only significant variable that predicted the reversal was the positive lifestyle.

Conclusions: In conclusion, the present study is important in terms of showing the variability of metabolic parameters of the patients with schizophrenia. Thus, the outcomes of interventions can be better understood by detecting new cases of MetS along with reversed cases. Finally, our study is important in terms of showing that positive lifestyle characteristics contribute to the reversal of MetS.

Keywords: Follow-up, lifestyle, metabolic syndrome, schizophrenia

INTRODUCTION

Metabolic syndrome (MetS) is a clinical condition characterized by impairment in certain metabolic parameters including increased central obesity, impaired lipid profile, increased blood pressure (BP), and increased fasting blood sugar (FBS) (1). The risk of metabolic impairment is found to be higher in patients with schizophrenia than in the normal population due to long disease period, increasing age, unhealthy lifestyle, antipsychotic medication use, genetic factors, and factors related to the psychotic process itself (2). Among these risk factors, unhealthy lifestyle and antipsychotic

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Received: November 06, 2018 **Accepted:** February 04, 2019

Citation: Baran Tatar Z. The Effect of Positive Lifestyle on Reversal of Metabolic Syndrome in Patients with Schizophrenia Followed-up for Two Years. Psychiatry and Behavioral Sciences 2019;9(3):85-93.
https://doi.org/10.5455/PBS.20181106082036

medication use are factors that can be changed by external intervention.

It was reported that second-generation antipsychotic (SGA) drugs, in particular, promoted the development of MetS, and among SGA drugs, olanzapine and clozapine were the most common medications that increase the prevalence of MetS (3,4). Clozapine is an antipsychotic drug, which is particularly preferred for the treatment of patients with schizophrenia refractory to treatment. In refractory cases with suspected metabolic disturbances, switching to a medication that does not cause metabolic disturbances may increase the risk of psychotic flare. In addition, an antipsychotic medication that does not cause metabolic disturbance may have already been attempted with no response. Therefore, medication change is not always possible despite the presence of metabolic abnormalities. Considering these factors, it may be beneficial to evaluate options other than medication change for patients who always use the same medication. At this point, changing the unhealthy lifestyle may become important. Negative lifestyle choices, such as a poor diet (5), lack of physical activity (6), are more commonly observed among patients with schizophrenia than among the normal population. It was found that diet characteristics (7) and low physical activity (8) in patients with schizophrenia are related to MetS and that regular physical activity decreases the risk of developing MetS in patients with schizophrenia (9). Hence, in cases where it is not possible to stop the medication, lifestyle changes can be beneficial in reversal of impaired metabolic parameters or prevention of the development of MetS.

One of the main objectives of our study was to retrospectively analyse the parameters of MetS in patients with schizophrenia whose metabolic parameters have been monitored for at least 2 years and whose medication and clinical condition were stable, to detect new cases of MetS and cases with reversal of MetS, and to evaluate the factors that predict the incidence and reversal of MetS. It is predicted that a group of patients who currently meet the MetS criteria would not be diagnosed with MetS at the end of 2 years and a positive lifestyle would be effective in reversal of MetS.

METHODS

Study Participants

The sample group of the study comprised patients who were followed and monitored at the Psychotic Disorders Outpatient Clinic of Bakirkoy Training and Research Hospital as outpatients between January 1st, 2014 and January 1st, 2017 and were admitted with schizophrenia diagnosis in accordance with the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (10). Informed consents were obtained after the procedure (s) were fully explained. We present a retrospective analysis of longitudinal data addressing metabolic parameters in these patients. Patients exhibiting the following clinical conditions and characteristics were excluded from the study: diagnosis other than schizophrenia, followed less than 2 years, antipsychotic drug change and/or hospitalization in the planned date range of the study, missed data of blood tests and scales, a history of significant neurological disorders, mental retardation, substance and/or alcohol abuse or addiction within the planned date range of the study. One hundred and eight of 557 patients were excluded from the study due to diagnosis of psychotic disorders other than schizophrenia (schizoaffective disorder, delusional disorder, psychotic disorder not otherwise specified). Ninety patients were excluded due to missing data. In conclusion; 350 of 557 patients were included in the study. Approval for the study protocol was obtained from Bakirkoy Training and Research Hospital Ethics Committee. (Confirmation number: 6.12.2016-590).

Measures

Sociodemographic Data Form

This form is a semi-structured form developed by researchers used to capture the socio-demographic features of the patients, duration of illness, the number of hospitalizations, smoking status, alcohol/substance use,

antipsyhotic drug therapy and other medication status and presence of favorable lifestyle.

The Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale (PANSS) comprises a 30-item rating scale and 3 subscales which rate positive, negative and general psychopathology (11). The validity and reliability study for Turkish adaptation of PANSS was performed by Kostakoglu et al. (12)

Schedule for Assessment of Insight (SAI)

The SAI was developed for the assessment of insight in psychotic patients (13). The validity and reliability study for the Turkish adaptation of the SAI was performed by Arslan et al. (14)

Clinical Global Impression Severity of Illness (CGI-S)

The CGI based upon observed and reported symptoms, behavior, and function in the past seven days (15).

Laboratory Analysis Methods

In our center, blood samples were regularly collected between 8.00–10.00 AM by the nurses every 6 months from patients who provided consent to blood withdrawal. Fasting blood sugar, high-density lipoprotein (HDL), and triglyceride (TG) levels were examined in the blood samples collected from the patients following an at least 8-hr fasting period. TG, HDL, and FBS values were measured on the LX20 auto analyzer (Manufacturer: BECKMAN COULTER). The external quality assurance of the laboratory has been performed by Bio-Rad EQAS programme (Diagnostics Group, 9500 Jeronimo Road, Irvine, California, 92618).

Procedures

Body weight was measured without shoes while wearing light clothing. Waist circumference was measured using a measuring tape from the midpoint between the lower edge of the costal margin and the upper margin of the iliac bone while the patient was standing up on a horizontal plane. Arterial BP was manually measured using a sphygmomanometer and a stethoscope while the patient was in seated position after at least 10 min of rest. When an irregularity in the metabolic parameters of a patient was detected, a consultation with an internist was requested and diet suggestions/reference to a dietician and suggestions of increasing physical activity were provided. According to the recommendations of the American College of Sports Medicine (16) and American Heart Association (17), patients who perform any type of exercises for at least 2.5 hr (150 min) per week were considered to have physical activity, and patients who avoided food with high sugar and fat content and with high saturated fat ratio and who preferred fruits/vegetables and high-fiber food such as whole wheat bread were considered to have good diet characteristics. In the last interview, it was noted that patients who performed regular physical exercise/had good diet characteristics for at least 1 year had positive lifestyles.

Metabolic syndrome was defined by fulfilling three or more of the five criteria according to the ATP-IIIA (18). For antipsychotic drugs chlorpromazine equivalents were calculated for each patient (19,20).

PANSS, SAI, and CGI-S were filled and recorded at each control visit. The interviews of the patients conducted in 2014 were regarded as the "first evaluation" and their interviews conducted 2 years after the first evaluation were regarded as the "final evaluation."

Statistical Analysis

The distributional characteristics of the variables were evaluated using the Kolmogorov-Smirnov Test. Parameters were assessed by non-parametric tests due to the fact that they did not show normal distribution. First, we compared patients with MetS with patients without MetS in terms of their demographic characteristics, drug use, scale values, smoking status, and positive lifestyle at last assessment. Chi-square (χ^2) test was used to compare categorical data, Mann-Whitney U test was used to evaluate numerical data. Secondly, patients were further divided into 4 subgroups those with MetS at last, not at initial assessment (new cases), those with Mets at initial, not at last assessment (reversed

cases), those without MetS at both assessments and those with MetS at both assessments and evaluated in terms of demographic characteristics, antipsychotic, and metabolic drug use, scale values, smoking status, and positive lifestyle. χ^2 test was used for the comparison of categorical data in this analysis and one way ANOVA test was used for continuous variables. McNemar's test was used for analysing MetS parameters differences in initial-last assessment for 3 groups: all patients, new cases, reversed cases.

The correlation coefficient (r) was calculated by dividing the Z value (determined by using the Mann-Whitney U test) with squared root of n value. A value of r=0.1 is considered as corresponding to a low-level effect size; a value of r=0.3 is considered as corresponding to a moderate level effect size; and a value of r=0.5 is considered as corresponding to a high-level effect size (21).

Prevalence of metabolic syndrome was calculated by dividing the number of patients with metabolic syndrome by the number of all patients. The incidence was calculated by the ratio of new cases to those who did not meet the Mets criteria at the initial assessment. The reversal was assessed by the ratio of patients who recovered from MetS to those who had metabolic syndrome at initial assessment.

Two different logistic regression analyses were conducted to determine the variables that predicted new and reversed cases. Age, sex, duration of illness, smoking, positive lifestyle, use of clozapine and olanzapine were variables included in the model.

The results were evaluated within a 95% confidence and by using a statistical significance level of $p<0.05$. Analysis of the data was done by Statistical Program for Social Sciences version 18 for Windows (IBM Corp., Armonk, NY)

RESULTS

Of the 557 patients who were monitored at our center, 350 were included in the study. Of the participating patients, 74.3% were male. The mean age was 42.64±9.82 years.

First, patients who were diagnosed with MetS in the final evaluation were compared with those who were not diagnosed with MetS with respect to sociodemographic characteristics, and clinical characteristics. The mean age was significantly higher in patients with MetS than in those without MetS (44.38±9.95 years vs. 42.05±9.72 years, U=9889.00, r=-0.111, p=0.036). The use of metabolic medications was higher in patients who were diagnosed with MetS (13.8% vs. 33.7%, p<0.001). Positive lifestyle was at a significantly higher rate in patients who were not diagnosed with MetS (11.2% vs. 24.1%, p=0.010). There was no significant difference between the two groups (patients without MetS vs. patients with MetS) in terms of gender (male; N=195, 74.7% vs. n=65, 73%); years of education (9.15±3.77 vs. 8.84±3.91); duration of illness (19.43±8.68 vs. 19.78±7.49); number of hospitalizations (n=3.55±4.01 vs 3.56±4.11); clozapine/olanzapine use (n=184, 70.5% vs. n=66, 74.2%); chlorpromazine equivalents (1007.50±566.75 vs 1042.26±606.06), other antipsychotics used (n=77, 29.5% vs. n=23, 23%), PANSS-positive symptom subscale (9.51±3.27 vs. 9.44±3.26), PANSS-negative symptom subscale (13.06±4.48 vs. 13.22±3.90), PANSS-general psychopathology subscale (24.43±6.76 vs. 25.40±7.66), PANSS- total (47.09±12.51 vs. 47.88±12.23), SAI (13.60±5.05 vs. 18.84±46.20), and CGI-S (2.15±0.95 vs.2.08±0.92) scores, and smoking status (n=134, 51.3% vs. n=50, 52.2%) (Table 1).

The patients were then divided into four subgroups as patients without MetS in both evaluations (n=239, 68.2%), patients with MetS in the first evaluation and without MetS in the final evaluation (reversed cases) (n=22, 6.3%), patients without MetS in the first evaluation and with MetS in the final evaluation (new cases) (n=38, 10.9%), and patients with MetS in both evaluations (n=51, 14.6%), and the parameters which were previously evaluated between the two groups were analysed among the subgroups. The incidence rate in 2 years was 13% and the reversal rate was 30%. The rate of metabolic drug use was significantly different between subgroups (χ^2=24.144, p=0.000). The rate of positive lifestyle was 36.4% in the reversed cases and 10.5% in the new cases and significantly different between subgroups (χ^2=8.888, p=0.031) (Table 2). There were no differences between

Table 1: Sociodemographic and clinical characteristics of patients with and without MetS at final assessment

Patient characteristics	Total (n=350)	Patients without MetS (n=261)	Patients with MetS (n=89)	z	Effect size (r)	P
Male	260 (74.3%)	195 (74.7%)	65 (73%)			0.427[a]
Female	90 (25.7%)	66 (25.3%)	24 (24%)			
Age (years±SD)	42.64 (±9.82)	42.05 (±9.72)	44.38 (±9.95)	-2.095	-0.111	0.036[b]*
Duration of education (years±SD)	9.07 (±3.81)	9.15 (±3.77)	8.84 (±3.91)	-0.920	-0.049	0.357[b]
Clozapine/Olanzapine	250 (71.5%)	184 (70.5%)	66 (74.2%)			0.303[a]
Metabolic drugs	66 (18.8%)	36 (13.8%)	30 (33.7%)			0.000[a]*
PANSS-positive symptom subscale (±SD)	9.49 (±3.26)	9.51(±3.27)	9.44 (±3.26)	-0.063	-0.003	0.950[b]
PANSS-negative symptom subscale (±SD)	13.10 (±4.34)	13.06(±4.48)	13.22 (±3.90)	-0.638	-0.034	0.523[b]
PANSS-general psychopathology subscale (±SD)	24.68 (±7.00)	24.43(±6.76)	25.40 (±7.66)	-0.870	-0.046	0.384[b]
PANSS-Total (±SD)	47.30 (±12.43)	47.09(±12.51)	47.88 (±12.23)	-0.536	-0.028	0.592[b]
SAI (±SD)	14.93 (±23.71)	13.60(±5.05)	18.84 (±46.20)	-0.390	-0.020	0.697[b]
CGI-S (±SD)	2.14 (±0.94)	2.15(±0.95)	2.08(±0,92)	-0.565	-0.030	0.572[b]
Smoking status	184 (52.6%)	134 (51.3%)	50 (52.2%)			0.253[a]
Positive lifestyle	73 (20.8%)	63 (24.1%)	10 (11.2%)			0.010[a]*

MetS: Metabolic syndrome; PANNS: The Positive and Negative Syndrome Scale; SAI: Schedule for Assessment of Insight; CGI-S: Clinical Global Impression Severity of Illness *p<0.05 **p<0.001; [a]Statistical significance of differences estimated with the Chi square (χ^2) test; [b]Statistical significance of differences estimated with the Mann-Whitney U

Table 2: Comparison of socio-demographic and clinical characteristics between subgroups

Patient characteristics	Patients without MetS at both assessments (n=239)	Reversed cases (n=22)	New cases (n=38)	Patients with MetS at both assessments (n=51)	χ^2 (1, 3)	F (3, 346)	p
Male	180 (75.3%)	15 (68.1%)	32 (84.2%)	33 (64.7%)	4.971		0.174[b]
Female	59 (24.7%)	7 (31.9%)	6 (15.8%)	18 (35.3%)			
Age (years±SD)	41.96±9.58	43.04±11.33	44.26±10.77	44.47±9.41		1.327	0.265[b]
Duration of education (years±SD)	9.11±3.70	9.50±4.57	9.84±3.92	8.09±3.77		1.743	0.158[b]
Metabolic drugs	33 (13.8%)	3 (13.6%)	8 (21.1%)	22 (43.1%)	24.144		0.000[a]*
Positive lifestyle	55 (23%)	8 (36.4%)	4 (10.5%)	6 (11.8%)	8.888		0.031[a]*

MetS: Metabolic syndrome; *p<0.05; [a]Statistical significance of differences estimated with the Chi square (χ^2) test; [b]Statistical significance of differences estimated with ANOVA (Analysis of variance)

the four subgroups in terms of age; years of education; duration of illness; number of hospitalizations; smoking status; antipsychotic medications used; chlorpromazine equivalents; PANSS, SAI, and CGI scores.

The rate of MetS was 20% in the first evaluation and 25.4% in the final evaluation. Increase in the prevalence of MetS between the first and final evaluation was not significant. Among the criteria of MetS, there was a significant increase in the prevalence of abdominal obesity and elevated FBS (Table 3).

The decreases in the prevalence rates of elevated FBG and hypertriglyceridemia, which are among the criteria for MetS, were significant among patients with reversed metabolic syndrome (Table 4). Among the new cases, there was a significant increase in the prevalence of elevated FBS and low HDL levels (Table 5). There was a significant increase in the prevalence of abdominal obesity among cases not having MetS in both evaluations; however, there was a significant increase in the prevalence of elevated FBS among patients having MetS in both evlauations.

Table 3: Comparison of the frequency of Mets parameters between first and last assessment in all patients

	First assessment n (%)	Last assessment n (%)	p[a]
Meeting ATP-IIIA criteria	73 (20.9)	89 (25.4)	0.052
Abdominal obesity (n)	108 (30.9)	136 (38.9)	0.000*
High Fasting glucose (≥100 mg/dl)	72 (20.6)	94 (26.9)	0.002*
Hypertansion (≥130/85 mmHg)	23 (6.6)	30 (8.6)	0.143
Hypertriglyceridemia (≥150 mg/dl)	165 (47.1)	174 (49.7)	0.349
Low HDL (E<40 mg/dl, K<50)	167 (47.7)	157 (44.9)	0.320

HDL: High Density Lipoprotein; [a]McNemar Test; *p<0.05

Table 4: Comparison of the frequency of Mets parameters between first and last assessment in all patients

	First assessment n (%)	Last assessment n (%)	p[a]
Abdominal obesity (n)	15 (68.2)	11 (50)	0.125
High Fasting glucose (≥100 mg/dl)	15 (68.2)	6 (27.3)	0.009*
Hypertansion (≥130/85 mmHg)	0	0	-
Hypertriglyceridemia (≥150 mg/dl)	19 (86.3)	10 (45.5)	0.016*
Low HDL (E<40 mg/dl, K<50)	19 (86.3)	13 (59.1)	0.109

HDL: High Density Lipoprotein; [a]McNemar test; *p<0.05

Table 5: Comparison of the frequency of Mets parameters between first and last evaluation in new cases (n=38)

	First assessment n (%)	Last assessment n (%)	p[a]
Abdominal obesity (n)	15 (39.5)	29 (51.7)	0.000*
High Fasting glucose (≥100 mg/dl)	11 (28.9)	22 (57.9)	0.003*
Hypertansion (≥130/85 mmHg)	2 (5.3)	7 (18.4)	0.063
Hypertriglyceridemia (≥150 mg/dl)	25 (65.8)	32 (84.2)	0.065
Low HDL (E<40 mg/dl, K<50)	22 (57.9)	33 (86.9)	0.003*

HDL: High Density Lipoprotein; [a]McNemar test; *p<.05

In logistic regression analysis, for incident cases Nagelkirk R^2 was 0.095 and, classification rate was 86.3. For reversed cases Nagelkirk R^2 was 0.276, and classification rate was 69.9. Also, it was detected that increasing age (OR: 1.06, 95% CI: 1.0-1.1, p=0.011) and low rate of positive lifestyle (OR:0.28, 95% CI: 0-0.9, p=0.035) had a significant effect on the emergence of new cases, and the only significant variable predicting reversal was a positive lifestyle (OR:6.49, 95% CI: 1.4-28.1, p=0.012).

DISCUSSION

Three hundred and fifty patients had a mean age of 42.6 were included in this study. At baseline, and at final evaluation, the rates of metabolic syndrome were 20% and 25.4%; respectively with no significant difference. The two year incidence of metabolic syndrome in this sample was 13% while rate of remission was 30% within the same period. In logistic regression, incident cases were predicted significantly by elevated age and reduced rates of positive lifestyle while remission was predicted by elevated rates of positive lifestyle.

The rates of MetS in the present study according to the ATP III-A criteria in patients with schizophrenia in the first and final evaluation were compared with those in patients with schizophrenia in other countries, were found to be lower than that in America (22), similar to the rates in other European countries (23), and lower than the rates reported in cross-sectional studies conducted in Turkey (24,25).

Although there was an increase in the prevalence of MetS within 2 years in our study, this increase was not significant. Majority of the follow-up studies have

reported an increase in incidence rates of MetS over time (4,26,27), but in contrary, there are also studies reporting a decrease in the incidence rate of MetS (35% vs 32%) (28).

When the results of the first and final evaluations were compared, there was a significant increase in the number of patients that met the criteria of abdominal obesity and elevated FBS. Follow-up studies on patients with schizophrenia have reported an increase in abdominal obesity and lipid disturbances (4). Abdominal fat was found to be the most common factor related to insulin resistance and MetS (29). Abdominal obesity is triggered by heavy consumption of high-calorie food and low physical activity. It was shown that correcting abdominal obesity, which shows the strongest relationship with MetS, also improves other parameters. A modest weight loss decreases TG, FBS, and insulin levels while increasing HDL levels (30).

In our study, there were cases who developed MetS and who underwent reversal of MetS within the 2-year follow-up. A prospective 1-year natural follow-up study on the Tai population reported an incidence rate of 20% (27), whereas a randomized and controlled study in which antipsychotic medications were compared to the incidence of MetS reported an incidence rate of 16% in patients receiving aripiprazole therapy and an incidence of 27% in patients receiving olanzapine therapy (26). Since the patients who were diagnosed with MetS at the beginning were not included in these studies, reversed cases were not evaluated. In another study conducted in the Netherlands examining the natural course of MetS among patients with schizophrenia being monitored for 1 year and thus including patients who had already been diagnosed with MetS, the incidence of MetS was reported to be 13% and the reversal rate was reported as 33% (28). Although it is difficult to compare the rates of new and reversed cases in a 2-year follow-up period with those in 1-year follow-up studies, it can be said that the incidence of MetS (13%) in our study was lower. These low rates can be related to the fact that metabolic parameters of patients with schizophrenia included in the study were closely monitored, and upon detection of a possible impairment, the patients were checked by an internist and referred to a dietician and they were advised to increase physical activity and maintain a balanced diet. It was found that increase or decrease in the physical activity level along with dietary measures produces changes in insulin activity (31) and regular exercises increase insulin sensitivity and decreases plasma TG levels, and cardiovascular morbidity and mortality (32). It was also shown that exercise protects from MetS and keeps existing MetS under control (33,34).

Therefore, the decrease of elevated blood sugar and TG levels among patients with reversal of MetS within 2 years and the increase in abdominal obesity, elevated FBG, and low HDL level among cases that developed MetS within 2 years may be related to lifestyle variables, such as changes in dietary habits and physical activity. In support of this hypothesis, the present study detected that positive lifestyle changes defined by balanced diet and/or regular physical activity were significantly more common in patients who did not have MetS than in those who had MetS in the final evaluation. In the examination of four subgroups, it was observed that positive lifestyle, in particular, was the highest among patients with reversal of MetS within 2 years and the lowest among patients who developed MetS within 2 years. Positive lifestyle being the only factor significantly predicting reversed cases in the logistic regression analysis indicates the importance of diet and physical activity. It was detected that patients with schizophrenia are indeed more sedentary (35,36), and regular physical activity protects patients with schizophrenia from MetS (9). It was found that this group of patients had poor dietary habits characterized by high intake of saturated fat and low intake of fiber and fruits (37) and it was suggested that diet characteristics are responsible for the increase in the prevalence of MetS (7).

It is known that antipsychotic medications affect the risk of developing MetS and that this risk is the highest with olanzapine (4,26) and clozapine (38). The patients included in the study had approximately 20 years of disease duration and had used many antipsychotic medications previously. Because most of them used clozapine, which is preferred as the last resort in patient's refractory to treatment, discontinuing or changing the drug because of metabolic disturbances is not always possible. There was no difference in the prevalence of

MetS between patients receiving clozapine/olanzapine therapy and those receiving other antipsychotic medications. Moreover, clozapine and olanzapine did not significantly predict reversed and new cases in the logistic regression analysis. Eskelinen et al. (9) reported that clozapine use increased MetS risk while medium level exercise decreased MetS risk and concluded that clinicians encouraging their patients for more exercise might have decreased the risk of developing MetS, Type 2 diabetes, and cardiovascular diseases.

There are some limitations of our study. First; since healthy lifestyle was based on patients' reports, a validated scale could be preferred to reach more valid results. The other limitations are the inability to evaluate medication adherence; unknown course of reversed cases; family history being unknown in terms of hypertension, dyslipidemia, and cardiovascular diseases; lack of controlling for dose changes; adjunct medications, and limited external validity.

In conclusion, the present study is important in terms of showing the variability of metabolic parameters of the patients with schizophrenia. Therefore, the outcomes of interventions can be better understood by detecting new cases of MetS along with reversed cases. Furthermore, this present study is important in terms of showing that positive lifestyle characteristics contribute to the reversal of MetS. Provision of mental health services in a dedicated center and close monitoring of metabolic parameters may allow early diagnosis and early intervention. If an abnormality is detected in the metabolic parameters of patients with chronic schizophrenia who are stable with the current antipsychotic medication, the clinicians make interventions toward supporting positive lifestyle, which, besides medication change, can be beneficial in reversal of metabolic disturbances.

Acknowledgements: This paper was presented as an oral presentation at the 10th International Congress on Psychopharmacology held on April 25-29, 2018, in Antalya, Turkey.

Ethics Committee Approval: Approval for the study protocol was obtained from Bakirkoy Training and Research Hospital Ethics Committee. The study is in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of in 2000.

Informed consent: Written informed consent was obtained from the patients after the procedure had been fully explained.

Conflict of Interest: There is no conflict of interest.

Financial Disclosure: There is no financial support.

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