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# Metabolic syndrome in patients who have been subjected to isolation security measures and treated with atypical antipsychotics

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**Summary**

**Aim.** The main aim of the study was to assess the incidence of metabolic syndrome and its individual components in patients subject to a confinement measure, treated with antipsychotics in mono – or polytherapy. Additional objectives included the analysis of associations between the occurrence of metabolic syndrome and patients' age, psychiatric diagnosis, overweight or obesity, and the presence of addictions to psychoactive substances.

**Method.** The study involved 61 patients of the Department of Forensic Psychiatry, including 9 women and 52 men, subject to a confinement measure from September 2019 to August 2021. All parameters of metabolic syndrome and BMI were measured twice, at the beginning of the stay at the Department and after six months of treatment with atypical antipsychotics. Appropriate statistical comparative analyses were then performed.

**Results.** There was no relationship between the occurrence of metabolic syndrome and the age of the subjects, medical diagnosis, addiction to psychoactive substances, including smoking. It has not been confirmed that the chronic use of atypical antipsychotics with parallel prophylactic and health-promoting effects in conditions of confinement leads to the development of metabolic syndrome and worsens its symptoms, apart from a marked increase in waist circumference and an increase in BMI.

**Conclusions.** Systematic measurements of BMI and waist circumference during treatment with atypical antipsychotics may be accurate tools in assessing the risk of metabolic syndrome. Long-term confinement hospitalizations should include psychoeducational interventions aimed at minimizing metabolic complications of pharmacotherapy.

**Key words:** metabolic syndrome, atypical antipsychotics, confinement measure

## Introduction

Metabolic syndrome is a constellation of interrelated symptoms [1], which increase the risk of developing atherosclerosis, cardiovascular diseases, pre-diabetes and diabetes [2]. Apart from cardiovascular and respiratory diseases, it is metabolic diseases that most often affect people with serious mental disorders [4–6]. Metabolic syndrome is also associated with increased mortality [7]. The prevalence of this syndrome in the world varies, from a dozen to about thirty percent in various populations [7]. In Poland, it affects about 20% of the adult population [8], and its frequency increases with age [3, 9]. In the case of elderly people taking antipsychotic drugs, this relationship does not necessarily have to occur, as these people are less sensitive to the metabolic complications of neuroleptic therapy [10]. Among psychiatric patients, the prevalence of metabolic syndrome ranges from 30 to 50% [11–13], so it is almost twice as high as in the general population [5].

For diagnostic purposes, the criteria of metabolic syndrome developed by the IDF (International Diabetes Federation) in 2005 can be used. Metabolic syndrome can be diagnosed with the presence of abdominal obesity (visceral, central) and 2 of the other 4 components, such as: (1) elevated triglycerides or treatment for triglyceridemia, (2) decreased HDL cholesterol level or treatment for this lipid disorder, (3) elevated blood pressure or treatment for hypertension, and (4) abnormal blood glucose fasting [10, 14, 15]. In 2009 IDF, AHA (American Heart Association) and NHLBI (National Heart, Lung, and Blood Institute) jointly presented new unified criteria for the diagnosis of metabolic syndrome [2, 16, 17]. The presence of any three of five criteria is required to diagnose the syndrome. The latest diagnostic concept from 2022 is based on, among others, the measurement of non-HDL cholesterol levels [18].

It has been noticed that the percentage of patients with metabolic syndrome is several times higher among overweight people and even higher in the obese group, therefore the body mass index (BMI) is used to monitor the condition of patients [19]. The basic component of metabolic syndrome is considered to be abdominal obesity, which can be diagnosed even with a normal BMI [20]. In the general population, apart from obesity, the most common components of the syndrome include hypertension (92%) and lowered HDL cholesterol level (70%) [21].

According to the research conducted by Wysokiński and Florkowski in 2009 [13], the most common elements of the syndrome in people taking antipsychotic drugs were: abdominal obesity (77%), hypertriglyceridemia (43%) and lowered HDL concentration (47%), while arterial hypertension (27%) and abnormal fasting glucose (20%) were less common. Obesity or overweight was found in 80% of the subjects. Another study by Wysokiński et al. from 2012 [22] confirms that in people taking atypical antipsychotics, the average values of BMI, waist circumference, HDL level, and triglyceride level exceeded the limits for the metabolic syndrome (elevated blood pressure and elevated glucose level were the least common).

According to available reports, there is no significant difference in the risk of metabolic complications when using classic and atypical drugs. Only the use of two different atypical drugs increases the incidence of metabolic syndrome [23]. Antipsychotics that

are considered the safest include amisulpride, aripiprazole and ziprasidone. Drugs that are associated with a moderate risk of metabolic disorders include quetiapine, risperidone and sertindole. The most adverse effect on the lipid profile, risk of diabetes and weight gain is expected with clozapine and olanzapine [24, 25]. In the case of the use of the last two drugs, the problem of weight gain affects more than 30% of patients, in the case of risperidone and quetiapine – 15–25%, and in the case of ziprasidone and aripiprazole – only 7–10%. There was no increase in body weight with sertindole [26–29]. The average weight gain in the first few months of taking antipsychotic drugs is estimated at 2–9 g, depending on the type of drug. However, there was no correlation between weight gain and the dose of the drug [30, 31]. In the case of taking clozapine or olanzapine, the annual weight gain is estimated at over 10 kg, with risperidone and quetiapine at 2–3 kg [32]. Taking aripiprazole and ziprasidone leads to weight gain of 1 kg. These drugs contribute to weight gain mainly in people with low (up to 23 kg/m$^2$) BMI [32, 33]. Other studies show that aripiprazole may even reduce body fat and indirectly reduce cardiometabolic risk [34]. In the group of patients treated with antipsychotics, arterial hypertension occurs in about 20% of the patients [35].

In some patients with schizophrenia or BPAD, insulin resistance is identified even before the implementation of antipsychotic treatment [32]. There is a hypothesis that these drugs do not cause diabetes but may contribute to its faster development [36, 37]. Some studies indicate that in terms of the risk of developing diabetes, atypical drugs differ only slightly from classic neuroleptics [38]. Other studies show that 58% of patients treated with atypical drugs develop diabetes, and in the case of patients treated with classic neuroleptics, this percentage is lower by 9% [36]. Diabetes in people taking atypical antipsychotics most often develops within the first three months of treatment. In about 25%, however, it is not accompanied by obesity or overweight [37]. Diabetes is observed in 12–36% of clozapine-treated patients and in 21–35% of olanzapine-treated patients [39, 40]. A lower risk of this complication is associated with treatment with quetiapine or risperidone [5, 41].

Among people taking atypical neuroleptics chronically, the incidence of dyslipidemia is almost 60% [42]. A significant increase in triglycerides and a decrease in HDL cholesterol levels are observed in patients treated with clozapine and olanzapine, while short-term and long-term therapies with ziprasidone and aripiprazole lead to normalization of the lipid profile [43]. Meyer [44] assessed the concentration of lipids after a year of using risperidone and olanzapine and showed a significant increase in triglycerides (by 104.8 mg/dl) in people treated with olanzapine and a significantly smaller increase (by 31.7 mg/dl) after risperidone. Moreover, olanzapine causes a greater reduction of the HDL fraction [12].

Somatic disorders in patients with schizophrenia may result not only from the effects of drugs, but also from the unfavorable course of the psychotic process itself, the presence of positive symptoms, negative symptoms, cognitive deficits, impulsivity, and emotional dysregulation [45]. Low level of health awareness [46] contributes to insufficient use of medical care and even its avoidance [4, 5]. People with serious mental disorders do not always follow a diet, reach for low-quality products or use psychoactive substances [47–49]. However, it has not been unequivocally confirmed

that cigarette smoking by schizophrenic patients taking antipsychotic drugs is directly related to abnormal values of metabolic parameters [13, 50].

## Objective of the study

The main aim of the study was to assess the incidence of metabolic syndrome and its individual components in patients subject to a court-ordered confinement measure, treated with antipsychotics in mono – or polytherapy. Other objectives included analysis of associations between the occurrence of metabolic syndrome and: (1) age of patients; (2) medical diagnosis; (3) overweight or obesity; (4) presence of drug and alcohol addictions; (5) smoking cigarettes.

The following hypotheses were put forward:

Hypothesis 1: Occurrence of metabolic syndrome is associated with older age, diagnosis of schizophrenia spectrum disorders, overweight and obesity, alcohol and drug addiction, and smoking.

Hypothesis 2: Chronic use of atypical antipsychotics is related to the development of metabolic syndrome as well as the intensification of its parameters in those patients who had this syndrome before long-term treatment.

## Material

The study included 61 patients of the Department of Forensic Psychiatry, including 9 women and 52 men, implementing a confinement measure in the period from September 2019 to August 2021. The diagnoses were established according to the diagnostic criteria of the ICD-10 classification. All subjects were treated with an atypical antipsychotic drug in mono – or polytherapy.

## Test methods

The following parameters were determined in patients: height, body weight, waist circumference. Height was measured using a height gauge with an accuracy of 1 cm. Body weight was measured using a spring scale set stably horizontally, with an accuracy of 1 kg. Waist circumference (half the distance between the lower rib and the iliac crest) was measured using a non-stretch measuring tape. Blood pressure was measured in patients in a sitting position before 8:00 am. Assessment of laboratory parameters (glucose, triglycerides, HDL fraction) was performed on the basis of biochemical analysis of venous blood taken from the basilic vein on an empty stomach before 8:00 am. Glucose concentration was determined by the reference enzymatic method with hexokinase, using the Roche CobasIntegra 400 plus analyzer and the Roche Glucose HK Gen.3 (GLUC3) reagent. The level of triglycerides was determined using the enzymatic colorimetric method using the CobasIntegra 400 plus analyzer by Roche and the Triglycerides (TRIGL) reagent by Roche. HDL-cholesterol fraction concentration was determined by homogenous colorimetric enzymatic method using Roche CobasIntegra 400 plus analyzer and HDL-Cholesterol Gen.4 (HDLC4) reagent by Roche.

On the basis of data from the literature on the subject [22, 26–28], which show that in people taking almost all atypical antipsychotics, abdominal obesity occurs in a very significant percentage (approx. 80%) and taking into account the limited number of patients examined, it was considered that in order to obtain more reliable assessments of the dynamics of the parameters of the metabolic syndrome (the effect of drugs), it would be optimal to use the diagnostic criteria of metabolic syndrome from 2005 and not the later ones, which would most likely emphasize the importance of abdominal obesity in the diagnosis of this somatic disorder. Therefore, the following threshold values for the components of the syndrome were adopted: abdominal obesity was defined as waist circumference for women ≥80 cm and for men ≥94 cm. The presence of at least 2 out of 4 other factors was necessary: (1) triglycerides ≥150 mg/dl (>1.7 mmol/L) or treatment for triglycerides, (2) HDL cholesterol levels <40 mg/dl (<1.0 mmol/l mg/dl) for men and <50 mg/dl (<1.3 mmol/l) for women or treatment for this lipid disorder, (3) elevated systolic (≥130 mmHg) or diastolic (≥ 85 mmHg) blood pressure or treatment of diagnosed hypertension, (4) impaired fasting glucose ≥100 mg/dl (≥5.6 mmol/l) or diagnosed type 2 diabetes [10, 13, 16]. Only three people were taking hypoglycemic drugs and also met the above-mentioned criteria.

Body mass index (BMI) was calculated as body weight in kilograms divided by the square of height in meters (kg/m$^2$), where: normal weight – BMI <25 kg/m$^2$, overweight – BMI 25–30 kg/m$^2$, obesity – MBI ≥30kg/m$^2$.

Measurements of all parameters were carried out twice: in the first period (from a few days to a month after admission to the Department) and in the second period (after six months of taking atypical antipsychotics).

## Statistical analyses

Statistical analyses were performed using the IBM SPSS Statistics 28 package. It was used to analyze basic descriptive statistics with the Shapiro-Wilk test, Student's *t*-test for dependent and independent samples, and cross-tab analysis with the chi-square test of independence. The significance level was $\alpha = 0.05$. In order to verify the assumption that atypical antipsychotics affect the parameters of the metabolic syndrome both in people who have been diagnosed with this syndrome and in those who, despite taking drugs, do not have such a diagnosis, a series of two-factor analyses of variance was performed in a mixed scheme 2 (metabolic syndrome: diagnosed vs. undiagnosed) x 2 (study date: I vs. II), where the dependent variables were: BMI, waist circumference, fasting blood glucose, triglycerides, HDL, SBP and DBP.

## Results

The study involved 9 women (15%) and 52 men (85%). Chart 1 presents the distribution of the following characteristics: height, body weight, waist circumference, BMI, systolic and diastolic BP, glycemia, triglycerides, and HDL fraction in two measurement dates.

Table 1. **Basic descriptive statistics of the examined variables together with the Shapiro-Wilk test (n = 61)**

| | M | Me | SD | SK | Kurt. | Min. | Max. | W | p |
|---|---|---|---|---|---|---|---|---|---|
| Height (cm) | 175.25 | 176.00 | 8.14 | 0.02 | 1.04 | 151.00 | 197.00 | 0.98 | 0.444 |
| Weight in 1st period (kg) | 86.31 | 84.00 | 16.14 | 0.49 | 0.07 | 58.00 | 135.00 | 0.97 | 0.147 |
| BMI in 1st period (kg/m$^2$) | 28.14 | 27.70 | 4.66 | 0.51 | -0.31 | 18.77 | 39.13 | 0.97 | 0.107 |
| Waist circumference in 1st period (cm) | 102.15 | 100.00 | 13.82 | -0.03 | -1.07 | 71.00 | 127.00 | 0.96 | 0.064 |
| SBP in 1st period (mmHg) | 118.92 | 118.00 | 16.97 | 1.86 | 7.06 | 96.00 | 199.00 | 0.87 | <0.001 |
| DBP in 1st period (mmHg) | 78.49 | 80.00 | 10.10 | -0.01 | -0.83 | 60.00 | 98.00 | 0.97 | 0.171 |
| Fasting blood glucose in 1st period (mg/dl) | 92.45 | 91.00 | 10.79 | 0.78 | 0.70 | 73.00 | 128.00 | 0.95 | 0.016 |
| Triglycerides in 1st period (mg/dl) | 152.36 | 134.00 | 75.70 | 0.89 | 0.08 | 56.00 | 348.00 | 0.91 | <0.001 |
| HDL 1st period (mg/dl) | 44.03 | 42.00 | 11.48 | 0.45 | -0.47 | 25.00 | 74.00 | 0.97 | 0.114 |
| Weight in 2nd period (kg) | 87.07 | 87.00 | 16.66 | 0.43 | -0.20 | 59.00 | 132.00 | 0.97 | 0.186 |
| BMI in 2nd period (kg/m2) | 28.57 | 28.44 | 5.09 | 0.69 | 0.52 | 20.41 | 44.25 | 0.96 | 0.030 |
| Waist circumference in 2nd period (cm) | 103.61 | 105.00 | 14.52 | 0.02 | -1.04 | 79.00 | 135.00 | 0.96 | 0.077 |
| SBP in 2nd period (mmHg) | 120.38 | 118.00 | 13.76 | 0.74 | 0.98 | 91.00 | 160.00 | 0.96 | 0.031 |
| DBP in 2nd period (mmHg) | 80.11 | 80.00 | 9.69 | 0.10 | -0.53 | 60.00 | 100.00 | 0.98 | 0.609 |
| Fasting blood glucose in 2nd period (mg/dl) | 94.13 | 91.50 | 11.11 | 0.47 | -0.58 | 76.00 | 120.00 | 0.96 | 0.032 |
| Triglycerides in 2nd period (mg/dl) | 164.62 | 139.00 | 82.30 | 0.97 | 0.52 | 36.00 | 393.00 | 0.91 | <0.001 |
| HDL in 2nd period (mg/dl) | 44.48 | 43.00 | 11.19 | 0.11 | -0.83 | 24.00 | 67.00 | 0.97 | 0.201 |

The result of the Shapiro-Wilk test in the case of some variables turned out to be statistically significant (their distributions significantly differed from the normal distribution). However, it should be noted that the skewness of the distribution of most variables did not exceed the conventional absolute value of 2, i.e., the distributions were asymmetric to a slight extent. In both study periods, the parameters whose average values exceeded the limit values for the metabolic syndrome included only waist circumference (mean 102 cm and 103 cm) and triglyceride levels (mean 152 mg/dl and 165 mg/dl). Other average values for the study group did not differ from the norm.

In the first period of the study, the criteria for metabolic syndrome were met in 25 patients (40%). Incorrect parameter values concerned: waist circumference – 25 people (100%), systolic BP – 7 people (28%), diastolic BP – 9 people (36%), blood glucose level – 9 people (36%), triglyceride level – 21 people (84%), HDL level – 20 people (80%).

In the second period, the metabolic syndrome was present in 29 patients (48%). In this group, incorrect parameter values concerned: waist circumference – 29 people (100%), systolic BP – 10 people (34%), diastolic BP – 14 people (48%), blood glucose level – 18 people (62%), triglyceride level – 24 people (83%), HDL level – 22 people (76%).

In the first term of the study, analyses were made on the occurrence of metabolic syndrome in relation to age, medical diagnosis, addictions, overweight and obesity, and smoking. In the second period, none of the patients used cigarettes (according to the regulations in force, smoking is prohibited in the ward with enhanced security).

The age of the patients ranged from 27 to 73 years (mean 49.5 years, standard deviation – 12.2 years). There were no statistically significant differences between the group with and without metabolic syndrome, which would be related to the age of the subjects ($t = -0.53$; $p = 0.599$, Cohen's $d = 0.14$).

Two diagnostic groups were distinguished: patients with schizophrenia spectrum disorders (schizophrenia, schizotypal disorders, schizoaffective disorders) and other diagnoses (BPAD, delusional disorders, organic delusional disorders, mental retardation, sexual preference disorders, organic mood disorders, exogenous psychotic disorders). The first group consisted of 47 people, of whom 20 (43%) had metabolic syndrome. The second group included 14 patients, including 5 (36%) with metabolic syndrome. There were no statistically significant differences between the two diagnostic groups due to the presence of metabolic syndrome (chi-square = 0.21; $p = 0.762$).

More than half of the respondents (35 people – 57%) were addicted to various psychoactive substances, of which 20 (57%) had not been diagnosed with metabolic syndrome, and 15 (43%) had its symptoms. Among the patients who did not show any addictions (26 people – 43%), the syndrome was present in 10 (39%). The diagnosis of metabolic syndrome was not found to depend on the coexistence of any of the addictions (chi-square = 0.12; $p = 0.796$).

18 patients (30%) had normal body weight, 23 (38%) were overweight and 20 (32%) were obese. In the first group, 16 people (89%) did not have metabolic syndrome. In the overweight group, 10 people (44%) had symptoms of the syndrome, and in the obese group, 13 people (65%) had the syndrome. A statistically significant rela-

tionship was found between BMI and the diagnosis of metabolic syndrome (chi-square = 11.47; $p = 0.003$). The exact distribution of values in this range is shown in Table 2.

Table 2. **Relationship between the diagnosis of metabolic syndrome and the BMI values of the subjects (n = 61)**

| | BMI <25 (kg/m$^2$) | | 25< BMI <30 (kg/m$^2$) | | BMI >30 (kg/m$^2$) | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | $\chi^2(2)$ | p |
| No diagnosis of MeS | 16 | 88.9% | 13 | 56.5% | 7 | 35.0% | 36 | 59.0% | 11.47 | 0.003 |
| MeS diagnosis | 2 | 11.1% | 10 | 43.5% | 13 | 65.0% | 25 | 41.0% | | |
| Total | 18 | 100% | 23 | 100% | 20 | 100% | 61 | 100% | | |

Before admission to the Department, 22 patients smoked cigarettes (36%), and half of them had metabolic syndrome (50%). Among non-smokers (39 people – 64%), this syndrome was present in 14 patients (36%). Metabolic syndrome was not associated with smoking (chi-square = 1.16; $p = 0.416$).

Of all the subjects, 23 people (38%) were identified in whom metabolic syndrome was diagnosed on both dates of the study. In 30 patients (49%), despite taking atypical antipsychotics, there was no basis for such a diagnosis. The average values of metabolic syndrome parameters and BMI for both groups in the 1$^{st}$ and 2$^{nd}$ period were compared, which is presented in Table 3.

Table 3. **Descriptive statistics of the tested effects of the analysis of variance on the effect of taking medications between the two study dates (n = 53)**

| | | | M | SD | N |
|---|---|---|---|---|---|
| BMI (kg/m$^2$) | Period I | No diagnosis of MeS | 25.73 | 3.84 | 30 |
| | | MeS diagnosis | 30.39 | 4.37 | 23 |
| | | Total | 27.75 | 4.66 | 53 |
| | Period II | No diagnosis of MeS | 25.71 | 4.05 | 30 |
| | | MeS diagnosis | 31.48 | 4.69 | 23 |
| | | Total | 28.22 | 5.18 | 53 |
| Waist circumference (cm) | Period I | No diagnosis of MeS | 93.67 | 11.47 | 30 |
| | | MeS diagnosis | 110.70 | 10.71 | 23 |
| | | Total | 101.06 | 13.95 | 53 |
| | Period II | No diagnosis of MeS | 94.63 | 12.23 | 30 |
| | | MeS diagnosis | 113.00 | 11.35 | 23 |
| | | Total | 102.60 | 14.91 | 53 |

*table continued on the next page*

| | | | | | |
|---|---|---|---|---|---|
| SBP (mmHg) | Period I | No diagnosis of MeS | 114.27 | 14.72 | 30 |
| | | MeS diagnosis | 121.91 | 11.35 | 23 |
| | | Total | 117.58 | 13.78 | 53 |
| | Period II | No diagnosis of MeS | 114.00 | 10.61 | 30 |
| | | MeS diagnosis | 124.91 | 13.52 | 23 |
| | | Total | 118.74 | 13.04 | 53 |
| DBP (mmHg) | Period I | No diagnosis of MeS | 73.50 | 9.69 | 30 |
| | | MeS diagnosis | 83.65 | 7.51 | 23 |
| | | Total | 77.91 | 10.10 | 53 |
| | Period II | No diagnosis of MeS | 76.07 | 8.82 | 30 |
| | | MeS diagnosis | 82.22 | 9.04 | 23 |
| | | Total | 78.74 | 9.35 | 53 |
| Fasting blood glucose (mg/dl) | Period I | No diagnosis of MeS | 87.37 | 7.65 | 30 |
| | | MeS diagnosis | 101.22 | 18.53 | 23 |
| | | Total | 93.38 | 15.03 | 53 |
| | Period II | No diagnosis of MeS | 87.57 | 6.80 | 30 |
| | | MeS diagnosis | 109.22 | 31.77 | 23 |
| | | Total | 96.96 | 23.88 | 53 |
| Triglycerides (mg/dl) | Period I | No diagnosis of MeS | 110.33 | 52.65 | 30 |
| | | MeS diagnosis | 213.61 | 68.67 | 23 |
| | | Total | 155.15 | 78.81 | 53 |
| | Period II | No diagnosis of MeS | 117.10 | 54.20 | 30 |
| | | MeS diagnosis | 224.52 | 74.83 | 23 |
| | | Total | 163.72 | 83.05 | 53 |
| HDL (mg/dl) | Period I | No diagnosis of MeS | 50.43 | 9.03 | 30 |
| | | MeS diagnosis | 36.61 | 11.17 | 23 |
| | | Total | 44.43 | 12.09 | 53 |
| | Period II | No diagnosis of MeS | 52.07 | 8.63 | 30 |
| | | MeS diagnosis | 35.91 | 8.08 | 23 |
| | | Total | 45.06 | 11.60 | 53 |

A statistically significant interaction effect was found for BMI measurement. In the subjects without metabolic syndrome, there was no increase in their BMI under the influence of the drugs they were taking. On the other hand, in the group of subjects diagnosed with metabolic syndrome, there was a statistically significant increase in their BMI under the influence of the drugs used ($p = 0.007$). This result is presented in Figure1.

A significant main effect was observed for the first and second measurement for people with metabolic syndrome when waist circumference was the dependent variable. In both periods, a statistically significant difference in waist circumference was found between the subjects with and without the syndrome. Subjects with a diagnosis of metabolic syndrome had significantly greater waist circumference in both study periods (both $p < 0.001$). There was also a statistically significant difference between the results in both periods, but only for subjects with metabolic syndrome (greater waist circumference in the second period: $p = 0.010$). Comparison of the values of the other analyzed parameters between the 1st and 2nd period of the study in the group with metabolic syndrome showed no statistically significant differentiation.

In the group of patients who were not diagnosed with metabolic syndrome during the entire period of pharmacotherapy, no statistically significant differences in the values of the syndrome parameters and BMI between the first and second measurement were confirmed. The subjects with the diagnosis of the syndrome had significantly higher systolic BP compared to the BP of people without this diagnosis, both in the first period of the study ($p = 0.044$) and in the second period ($p = 0.002$). The same pattern of results was observed for diastolic BP – in the first period, the subjects with metabolic syndrome had higher diastolic BP compared to the diastolic BP of the

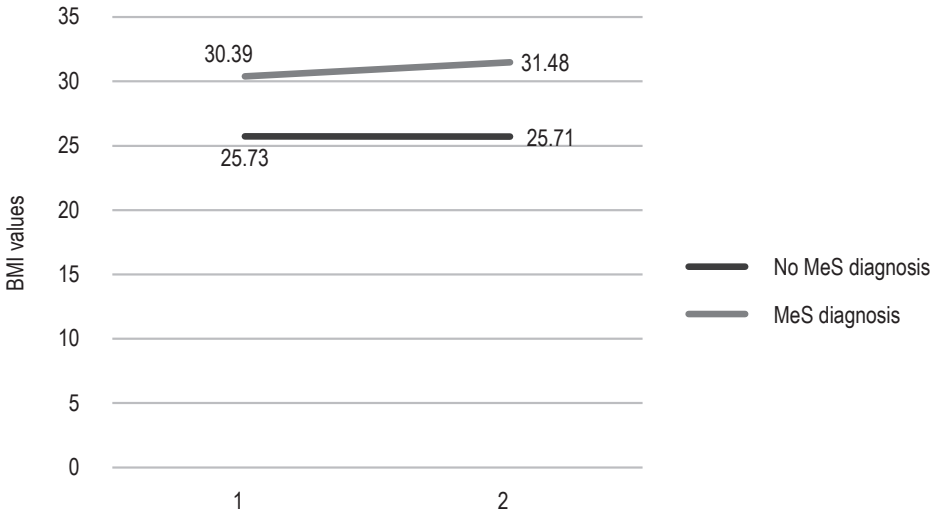


Figure 1. **Results for BMI depending on the date of the examination and metabolic syndrome vs. no metabolic syndrome**

subjects without the syndrome ($p < 0.001$), a similar situation occurred in the second term of research ($p = 0.016$).

There was also a main effect of metabolic syndrome on glycemia, triglyceride and HDL levels. Pairwise comparisons indicate that the subjects diagnosed with metabolic syndrome had higher levels of triglycerides and glycemia than the subjects without metabolic syndrome both in the first and second period of research (all $p < 0.001$). On the other hand, in terms of HDL, the subjects with metabolic syndrome had a significantly lower level of HDL compared to the subjects without the syndrome. These groups differed from each other both in the 1st and 2nd period of the study (both $p < 0.001$). The entire analysis is presented in Table 4.

Table 4. **The results of the 2x2 ANOVA analysis in a mixed design concerning the effect of taking drugs in two study periods and metabolic syndrome on metabolic syndrome parameters (n = 53)**

| | | SS | df | F | p | $\eta^2$ |
|---|---|---|---|---|---|---|
| BMI (kg/m$^2$) | Period | 7.52 | 1 | 4.40 | 0.041 | 0.08 |
| | Metabolic syndrome | 708.26 | 1 | 21.01 | <0.001 | 0.29 |
| | Period x metabolic syndrome | 8.01 | 1 | 4.69 | 0.035 | 0.08 |
| Waist circumference (cm) | Period | 69.65 | 1 | 8.13 | 0.006 | 0.14 |
| | Metabolic syndrome | 8155.36 | 1 | 31.81 | <0.001 | 0.38 |
| | Period x metabolic syndrome | 11.65 | 1 | 1.36 | 0.249 | 0.03 |
| SBP (mmHg) | Period | 48.63 | 1 | 0.37 | 0.546 | 0.01 |
| | Metabolic syndrome | 2242.19 | 1 | 11.82 | 0.001 | 0.19 |
| | Period x metabolic syndrome | 69.46 | 1 | 0.53 | 0.471 | 0.01 |
| DBP (mmHg) | Period | 8.34 | 1 | 0.19 | 0.666 | 0.00 |
| | Metabolic syndrome | 1730.11 | 1 | 15.33 | <0.001 | 0.23 |
| | Period x metabolic syndrome | 104.23 | 1 | 2.35 | 0.132 | 0.04 |
| Fasting blood glucose (mg/dl) | Period | 437.69 | 1 | 1.48 | 0.230 | 0.03 |
| | Metabolic syndrome | 8204.18 | 1 | 23.63 | <0.001 | 0.32 |
| | Period x metabolic syndrome | 396.03 | 1 | 1.34 | 0.253 | 0.03 |
| Triglycerides (mg/dl) | Period | 2034.67 | 1 | 1.10 | 0.299 | 0.02 |
| | Metabolic syndrome | 288975.05 | 1 | 49.42 | <0.001 | 0.49 |
| | Period x metabolic syndrome | 111.91 | 1 | 0.06 | 0.807 | 0.00 |
| HDL (mg/dl) | Period | 5.72 | 1 | 0.24 | 0.628 | 0.00 |
| | Metabolic syndrome | 5850.00 | 1 | 39.89 | <0.001 | 0.44 |
| | Period x metabolic syndrome | 35.31 | 1 | 1.47 | 0.231 | 0.03 |

Among the patients who took drugs in monotherapy in the first period of the study and had metabolic syndrome at that time, 16 patients (94%) had it not by accident also in the second period. The subjects without the diagnosis of the syndrome in the first period also did not have it in the second period in 74% (17 people) (chi-square = 18.28; $p$ <0.001). Almost 88% of the subjects (7 people) who were diagnosed with metabolic syndrome in the first period and were taking drugs as polytherapy at that time also had it in the second period. With this form of therapy, all those who did not have a diagnosis of metabolic syndrome in the first period did not have it in the second period (13 people) (chi-square = 17.06; $p$ <0.001). Among people taking drugs as monotherapy in the second period, those who were not diagnosed with metabolic syndrome, (68%, 13 people), also did not have it in the first period of the study. This diagnosis was confirmed in 14 patients (87.5%) in both study periods (chi-square = 11.09; $p$ = 0.002). All patients using polytherapy in the second period of the study in both periods had a diagnosis of metabolic syndrome and this relationship was statistically significant (chi-square = 26; $p$ <0.001).

In the second period of the study, 4 patients (7%) were taking clozapol and metabolic syndrome was present in 3 of them (75%) (chi-square = 1.29; $p$ = 0.338). In the group of patients taking olanzapine (34; 56%), metabolic syndrome was present in 15 (44%) patients (chi-square = 0.36; $p$ = 0.611). Twenty-two patients (36%) were treated with risperidone, and eight (36%) had the syndrome (chi-square = 1.72; $p$ = 0.286). Quetiapine was used by 12 people (20%), and two out of three had metabolic syndrome (chi-square = 2.19; $p$ = 0.200). Thirteen patients (21%) were taking aripiprazole and the syndrome was present in 30% of cases (chi-square = 1.86; $p$ = 0.219). There were no statistically significant relationships between the presence of metabolic syndrome and the use of individual antipsychotics.

## Discussion

The study of patients subject to a confinement measure was aimed at assessing the impact of atypical antipsychotics on their somatic condition. Statistical analyses comparing the values of parameters related to the metabolic syndrome during the six-month pharmacotherapy revealed that the distribution of some of them significantly differed from the normal distribution, but these values were asymmetric only to a slight extent. Only the waist circumference and the level of triglycerides clearly deviated from the norm, which can be explained by the fact that both of these parameters are the most common components of metabolic syndrome [13, 22].

Measurements during the first period of the study showed that metabolic syndrome was present in this group of patients with the frequency typical for people undergoing psychiatric treatment – 40% [5, 11–13], which is twice as high as in the Polish population [8]. It was not confirmed that the metabolic syndrome was related to the age of the subjects, which was probably due to the fact that the examined group consisted mainly of slightly elderly people (approx. 50 years old) and this group was rather homogeneous in terms of this variable.

The psychological and social burdens mentioned in the literature of the subject and the features of the psychotic process typical of patients with schizophrenia spec-

trum [45] suggested that the metabolic syndrome would be more common among this group of patients than in the case of other diagnoses. The study did not confirm this assumption, which should be associated with the fact that some patients, even before their stay at the Clinic, were subject to confinement measure, during which lifestyle risk factors of metabolic syndrome were probably minimized.

Addictions are treated as risk factors for various somatic diseases in the group of mentally disturbed people [49], which the current study in relation to metabolic syndrome has not confirmed. However, we cannot ignore the fact that the participants of the study were in long-period forced abstinence from psychoactive substances (stays in other psychiatric centers, confinement centers) even before its commencement. The frequency of co-occurrence of diagnoses of various types of addictions, which concerned more than half of the patients, turned out to be alarming. Conducting addiction therapy and maintaining abstinence from various psychoactive substances seems to be a very important protective element against somatic complications. It has also not been established that there is a relationship between cigarette smoking and occurrence of metabolic syndrome, which is consistent with the results of the 2009 study by Wysokiński and Florkowski [13].

The incidence of metabolic syndrome in the second period of the study increased by 8%, but it was still within the limits for patients taking atypical antipsychotics [5, 13]. In all subjects with metabolic syndrome, an abnormal waist circumference was observed on both examination dates, which resulted from the adopted diagnostic criteria [14]. The frequency distribution of the remaining parameters of the syndrome was the same in both periods. Hypertriglyceridemia was most frequently identified (almost the same level in both periods), slightly less often – a lowered HDL level (in the second period a decrease in frequency by 4%), less often – hyperglycemia (in the second period an increase of 26%), and the least frequent was elevated DBP (in the second period increase by 12%) and SBP (in the second period increase by 6%). The constellation of the components of metabolic syndrome differed from the data from the subject literature [22] only in terms of the frequency of hyperglycemia, which was probably due to the adopted diagnostic criteria of metabolic syndrome, which emphasize abdominal obesity, which is treated as one of the etiological factors of insulin resistance.

It was noteworthy that the incidence of individual parameters was significantly higher than those described in the literature (triglycerides, HDL, glycemia), which can be explained by the fact that all subjects were diagnosed with abdominal obesity, which contributes to the development of other somatic complications. It should be assumed that using the criteria from 2009 (three elements out of five), the percentage of individual components would be significantly lower.

During the six-month treatment with atypical neuroleptics, the metabolic syndrome persisted in every third of the subjects. At the same time, in almost half of the patients, despite systematic medication, the syndrome did not develop. Statistical analyses comparing the values of all syndrome criteria and BMI between these groups and between study periods showed a significant interaction effect in terms of BMI. In the group with the diagnosis of metabolic syndrome, a statistically significant relationship between

BMI and metabolic syndrome was demonstrated already during the first period. At the same time, a statistically significant increase in this parameter was observed under the influence of treatment. This suggests that regular assessment of this element is important not only in the process of diagnosing metabolic syndrome in people taking atypical antipsychotics, but also in monitoring its course. The importance of BMI for this group of patients was confirmed by the results of analyses from the first period of the study, when a significant relationship between overweight and obesity and metabolic syndrome was revealed (44% and 65%, respectively).

These results correlate with the analyses carried out in the group of subjects without a diagnosis of metabolic syndrome, who were subjected to half a year of pharmacotherapy – there was no significant increase in this indicator. It is worth noting that at the beginning of the study, normal body weight was statistically significantly associated with the absence of metabolic syndrome. The importance of BMI in the assessment of metabolic changes in patients treated with atypical neuroleptics is confirmed by numerous publications that clearly indicate the contribution of this category of drugs to overweight and obesity [23, 26, 28]. The study described here proves that BMI in the case of people treated with atypical neuroleptics can be a simple tool used for diagnostic purposes or for the prevention of metabolic syndrome. The analyses of waist circumference refer to the noted changes in BMI values. Only in the group of subjects diagnosed with metabolic syndrome, this parameter increased significantly over the course of six months of treatment. Therefore, it is not about any obesity or overweight, but about finding abdominal obesity among patients. Measurement of both of these elements when choosing an antipsychotic drug may prove to be accurate predictors of metabolic syndrome.

The comparison of the remaining parameters of metabolic syndrome (RR, glycemia, HDL, triglycerides) between the 1st and 2nd period of the study showed that there was no deterioration in the group with the syndrome. This should be explained not so much by the lack of impact of atypical antipsychotics on the somatic condition of patients, but by certain specific conditions of psychiatric hospitalization as a precautionary measure that minimize these negative effects. In general, long-period confinement makes it possible to at least partially eliminate those factors that are considered to contribute to the deterioration of the somatic condition and which are related to the course of mental disorders [45]. In confinement, patients are subject to controlled pharmacotherapy. They are provided with regular control of their somatic condition as well as appropriate care of various specialists [4, 5]. This group of psychiatric patients has the opportunity to use a long-term, properly balanced diet and physical activity adapted to their somatic conditions. These elements are considered to reduce the risk of metabolic and cardiovascular complications [47–49]. It seems that consistent psychoeducation, the aim of which is to develop health-promoting habits in patients (dietary recommendations, the importance of physical activity, care for mental and physical condition), is equally important. Wide-ranging interactions are therefore important in the prevention of somatic complications of pharmacotherapy [46, 47], which was reflected in the analyses of individual parameters among patients without metabolic syndrome. Despite the medications taken, their results did not deteriorate.

It can be assumed that appropriate hospitalization conditions may provide protection against the development of metabolic syndrome for a certain group of patients, but also protect people with metabolic syndrome against the aggravation of its symptoms.

The relatively consistent persistence of the symptoms of the syndrome in one group of patients and their absence in the other group, with similar conditions of hospital stay, may suggest that somatic complications of treatment with atypical neuroleptics may result from certain characteristics of patients – tendency to develop metabolic complications (regardless of mono – or polytherapy, the diagnosis of the syndrome persists in both periods in almost all subjects). The lack of statistically significant correlations between the use of individual atypical antipsychotics and the presence of metabolic syndrome suggests that there is practically no safe agent that would eliminate the risk of metabolic complications.

## Conclusions

1. There was no relationship between the occurrence of metabolic syndrome and the elderly age of the subjects, medical diagnosis, addiction to alcohol and drugs, and smoking.
2. It has not been confirmed that chronic use of atypical antipsychotics with simultaneous prophylactic and health-promoting effects under the conditions of a confinement measure leads to the development of metabolic syndrome and also causes the intensification of its symptoms, apart from a significant increase in waist circumference and BMI.
3. Systematic measurements of BMI and waist circumference during treatment with an atypical antipsychotic drug may be accurate tools in assessing the risk of metabolic syndrome.
4. Long-term hospitalizations as part of a confinement measure should include psychoeducational interventions aimed at minimizing metabolic complications of pharmacotherapy.

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