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RESEARCH ARTICLE

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Metabolic syndrome rates in older patients with severe mental illness after five years of follow-up and the association with mortality

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Objectives: To establish the course of metabolic syndrome (MS) rates in older patients with severe mental illness (SMI) after 5-year follow-up and evaluate whether MS at baseline is associated with mortality or diabetes at follow-up.

Methods: Patients (>60 years of age) with SMI (N = 100) were included at a specialized mental health outpatient clinic. Metabolic parameters were collected from patients' medical files at baseline and after 5-year follow-up.

Results: Follow-up data were available of 98 patients (98%); nine patients had died. Parameters of MS were available of 76 patients; 34.2% were diagnosed with MS. This was not significantly different compared with baseline (46.1%). MS at baseline was not significantly associated with mortality or development of diabetes at follow-up.

Conclusions: In older patients with SMI, the rates of MS may reach a plateau. Screening for MS in older patients treated at a specialized mental health outpatient clinic may generate attention for their somatic health and treatment for the components of MS that may in turn have a positive effect on their outcome. However, further research with larger sample sizes is needed in order to confirm these findings.

KEYWORDS

elderly, metabolic screening, metabolic syndrome, mortality, severe mental illness

1 | INTRODUCTION

Patients with severe mental illness (SMI) like schizophrenia or bipolar disorder experience worse physical health and reduced life expectancy compared with the general population, predominantly due to the increased risk of cardiovascular disease such as stroke or myocardial infarction and diabetes.[1,2] To identify SMI patients with increased risk for cardiovascular disease and type 2 diabetes, screening for metabolic syndrome (MS) is advised.[3,4] MS is defined as a clustering of at least three of the five following criteria: abdominal obesity, high blood pressure, high fasting glucose, high serum triglycerides, and low high-density lipoprotein (HDL) levels.[5] High rates of MS have been shown in patients with SMI.[6-8]

Older patients with SMI are particularly prone to MS, diabetes, and cardiovascular disease, as both increased age and psychiatric history, including psychotropic drug use, are risk factors.[7,9]

Although MS has been studied extensively, few studies focused specifically on older SMI patients. Previously, we described the results of metabolic screening in 100 older patients with SMI.[10] We found that metabolic disturbances were often underdiagnosed in this population, but rates of MS were similar between patients and their healthy peers.

In order to gain more insight in metabolic disturbances in older patients, we repeated screening for MS in older patients with SMI after 5 years of follow-up. As MS rates are known to increase with age, we hypothesized that the MS rates would increase after 5 years. Furthermore, we expected that MS at baseline would be associated with an increased mortality and the development of diabetes in the subsequent 5 years.

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2 | METHODS

2.1 | Sample

Severe mental illness patients of the outpatient department for old age psychiatry of GGZ inGeest, Amsterdam, The Netherlands have been screened for MS as part of standard care since 2010. Included in the metabolic screening is blood pressure, waist circumference, fasting triglycerides, fasting HDL-cholesterol, and fasting glucose. In addition, current medication was noted. A detailed description of the study sample at baseline is given in Konz et al.[10] In this convenience sample, a total of 100 consecutive patients aged over 60 years and with a history of schizophrenia, schizoaffective disorder, or bipolar disorder type I and II retrieved from their medical records, with a completed metabolic screening, were included starting from January 2011 until January 2013. At baseline, the sample had a mean age of 69 years (SD 5.6), 65% were female, 91% were Caucasian, and 31% smoked. Fifty-two percent were diagnosed with bipolar disorder, and 48% with schizophrenia or other psychotic disorder; 30%, 15%, and 23% of the patients were treated for hypertension, diabetes, and dyslipidemia, respectively. First-generation antipsychotics were prescribed in 40% of the baseline sample; 21% received atypical antipsychotics. Respectively, 41% and 23% were using lithium and antidepressants.

2.2 | Follow-up data collection

For follow-up after 5 years, data were collected from patients' medical files between January 2016 and March 2017. The patients were screened for MS during that year, with lab testing completed within 2016. For patients without completed metabolic screening within 2016, lab testing was attempted to be obtained in early 2017. Patients no longer in care at this outpatient department were contacted with a letter by their treating psychiatrist asking for voluntary participation. If patients failed to respond, the treating psychiatrist contacted their general practitioner to inquire about their status (change of address, alive or deceased, cause of death). House visits were performed when metabolic screenings could not be achieved from patients' medical files, in order to retrieve a complete dataset. The study was approved by the Medical Ethics Committee of the VU University Medical Center, Amsterdam.

2.3 | Measures

Metabolic syndrome was defined in line with the National Cholesterol Education Program Adult Treatment Panel III criteria[5] as blood pressure: >130 mmHg systolic or >85 mmHg diastolic (or pharmacotherapy for hypertension); waist circumference: >102 cm for men and > 88 cm for women; fasting glucose: >6.1 mmol/L (or pharmacotherapy for hyperglycemia); HDL-cholesterol: <1.0 mmol/L for men and < 1.3 mmol/L for women (or pharmacotherapy for high cholesterol); fasting triglycerides: >1.7 mmol/L. For diagnosing MS, three or more individual components of MS are required. In case of missing values on separate metabolic parameters, we were able to calculate rates on MS in cases that three or more of the parameters were normal or abnormal, respectively.

Key points

- In older patients with SMI, the rates of MS did not significantly increase after 5 years.
- MS at baseline was not significantly associated with mortality or development of diabetes at follow-up.

Development of diabetes was presumed if antidiabetic medication was used at follow-up that was not being used at baseline, or if a diagnosis of diabetes was set by the general practitioner based on repeated blood glucose tests. Age, sex, ethnicity, and current smoking were assessed at baseline by interview.

2.4 | Statistical analysis

Descriptive statistics were used to describe patient characteristics, usage of psychotropic medication, and rates of MS, diabetes, and mortality at follow up. To verify whether the study did not suffer from selective drop-out, it was checked whether those with missing values at follow-up differed in socio-demographic characteristics and MS from the patients of whom follow-up data was available using chi-square analysis. Five year rates of MS were analyzed with the McNemar's test, which determines (if there are) differences on a dichotomous dependent variable between two related groups. Statistical output of McNemar test is limited to *P* value only. With a paired t test, the number of metabolic disturbances at baseline was compared with follow-up. A chi-square test was done to compare MS rates between patients using atypical or classical antipsychotics. Associations between metabolic disturbances at baseline and the outcome measures mortality (yes/no) and diabetes (yes/no) at 5-year follow-up were assessed with logistic regression analysis. All analyses were conducted using SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

3.1 | Follow-up

After 5 years, we were able to retrieve information on 98 patients (98%). Two patients were lost to follow-up due to migration. Nine patients died (causes of death: five cardiovascular disease, two pulmonary infection, two cancer); 63% of the initial cohort was still attending the outpatient clinic.

3.2 | Metabolic syndrome after five years

Metabolic parameters were available of 76 patients (76% of the initial cohort, 85.4% of the patients alive at follow-up). Besides the two patients that were lost to follow-up, one patient refused to participate, and 12 patients had missing values on the metabolic parameters prohibiting establishing MS status. There was no selective dropout;

patients with missing values prohibiting calculating MS at follow-up (n = 12) did not suffer from hypertension (χ^2 = 0.18, df = 1, P = .67), diabetes (χ^2 = 2.76, df = 1, P = .10), high triglycerides (χ^2 = 0.30, df = 1, P = .58), low HDL cholesterol (χ^2 = 0.40, df = 1, P = .53), or high waist circumference (χ^2 = 0.63, df = 1, P = .43) more often at baseline. Those with missing follow-up data also did not significantly differ from those who participated at follow-up on age, gender, or ethnicity.

At follow-up, 26 patients of the total group of 76 (34.2%) were diagnosed with MS as compared with 35 out of the 76 patients at baseline (46.1%); this difference was not statistically significant (exact McNemar P = .09, Table 1). In addition, the total number of disturbances at baseline (M = 2.21, SD = 1.31) was not significantly different from those at follow-up (M = 1.99, SD = 1.37); t (75) =1.52, P = 0.13), although rate of hypertension and low levels of HDL cholesterol increased significantly over a 5-year period (63.2% to 76.6%, P = .04 and 34.2% to 44.6%, P = .02, respectively).

At follow-up, we found that first-generation antipsychotics were prescribed in 14.5% of the patients, whereas 38.2% received atypical antipsychotics. The frequency of MS was not significantly higher for atypical antipsychotics (48.3%) than for classical antipsychotics (18.2%) (χ^2 = 3.01 df = 1, P = 0.09).

3.3 | Mortality and development of diabetes in relation to metabolic syndrome

Patients with MS at baseline had an almost three times higher risk of dying at follow-up in comparison to patients without MS. However, this was not statistically significant (odds ratio [OR] =2.97, 95% confidence interval [CI] = 0.50-17.70, P = .23). The number of metabolic disturbances at baseline was not significantly associated with mortality at follow-up (OR = 0.81, 95% CI = 0.45-1.45, P = .47). These analyses were controlled for age, gender, current smoking, use of psychotropic medication, and psychiatric diagnosis.

Furthermore, the rate for hyperglycemia (including fasting glucose >6.1 mmol/L, diagnosis of DM or pharmacotherapy for hyperglycemia) was not increased at 5-year follow-up (exact McNemar P = 1.00). MS at baseline was not associated with the development of diabetes, with only one new case using DM medication at follow-up that was not using this at baseline.

4 | DISCUSSION

In this follow-up study of a cohort of older outpatients with SMI, 9% of the patients had died after 5 years. There was no significant difference in MS rates or number of metabolic disturbances at 5-year follow up compared with baseline, although rate of hypertension and low levels of HDL cholesterol increased significantly over a 5-year period.

In our study, only nine patients had died in 5 years, which is lower than expected based on the literature.[11,12]

The odds of mortality at follow-up was 2.97 in patients with MS compared with patients without MS, but this was not statistically significant, possibly due to a lack of power due to the small sample size. Surprisingly, MS at baseline was not associated with development of diabetes at follow-up, with only one new case using DM medication at follow-up that was not using this at baseline.

In recent meta-analyses, the rates of MS were found to be 32.5% in patients with schizophrenia and 37.3% in patients with bipolar disorder.[7,9] Both studies found an increase of metabolic disturbances with ageing. The rate of MS in our study was higher (46.1% at baseline in the patients with follow-up and 34.2% after 5 years) but did not further increase like we expected. An explanation may be that screening for MS resulted in improved cardiovascular management for these patients, as indicated by the increased rates of patients treated for one or more of the parameters of MS at follow-up (64.5%) as compared with baseline (39.5%). This further emphasizes the importance of optimizing physical health, including annual somatic and metabolic screening and starting treatment accordingly, in patients with SMI.

TABLE 1 Sociodemographic characteristics, metabolic screening, and mortality at baseline and follow-up

	Baseline	Follow-up	P-Value[a]
Characteristics[b]			
Age, mean (SD), range in years	68 (5.4) 60-87		
Sex, % female	67.1		
Ethnicity, % Caucasian	89.5		
Smoking, % yes	32.9		
Diagnosis, bipolar disorder/schizophrenia	38/38		
Metabolic screening[b]			
Hypertension, n (%)	48/76 (63.2)	59/77 (76.6)	.04
Hyperglycemia, n (%)	23/76 (30.1)	24/75 (32.0)	1.00
Triglycerides, n (%)	18/76 (23.7)	23/73 (31.5)	.38
HDL cholesterol, n (%)	26/76 (34.2)	33/74 (44.6)	.02
High waist circumference, n (%)	50/76 (65.8)	20/49 (40.8)	.09
Metabolic syndrome, n (%)	35/76 (46.1)	26/76 (34.2)	.09
Mortality, n (%)[c]		9/98 (9.2)	

Notes

[a]Based on the McNemar's test.

[b]All analyses are done within the total follow-up sample of 76 persons; therefore, the baseline data can be somewhat different from the baseline article.

[c]Data on mortality were available for 98 patients.

Another explanation for the fact that there was no increase in MS rates after 5 years, is that with ageing the rate of MS may reach a plateau and that after age 60 MS as a construct to identify subjects at risk for developing diabetes and cardiovascular disease is of less value. Interestingly, the clinical value of MS remains subject to international debate,[13] as the criteria for MS supposedly do not offer more than the sum of parts.[14] Especially in healthy elderly, MS was found to be less sensitive at identifying individuals at risk for stroke[15] and vascular risk.[16]

The rate of hypertension and low levels of HDL cholesterol increased significantly over a 5-year period (63.2% to 76.6%, P = .04 and 34.2% to 44.6%, P = .02, respectively). This may partially be explained by natural course of blood pressure with ageing, as systolic blood pressure has been shown to increase (Franklin, et al 1997), and HDL cholesterol is known to decrease with ageing (Wilson, et al 1994).

First-generation and atypical antipsychotics differ in their propensity to induce metabolic disturbances. However, in our cohort at baseline, as well as at 5 years of follow-up, there was no significant difference in MS rates between atypical antipsychotics and classical antipsychotics. This lack of a statistically significant difference in MS rates between atypical and first-generation antipsychotics is most likely due to the lack of power in this cohort.

To the best of our knowledge, this is the first follow-up study on MS of an older psychiatric cohort. A major strength is that we were able to follow the initial cohort and collect mortality rates and MS parameters of the vast majority of patients (98% and 85%, respectively). However, this study sample was relatively small, possibly limiting our statistical power to find associations, and data on cardiovascular morbidity (events occurring during the follow-up period) were not available. Although there was no selective dropout, nor any difference between patients who died and lived at follow-up, selection bias may have been present at baseline in these community-dwelling older outpatient patients with SMI. Furthermore, it should be noted that this is a naturalistic follow-up study, and the prevalence rate of diabetes may be underestimated, due to the absence of systematic diagnostic testing in the study cohort.

This study stresses the importance of annual metabolic screening. Further longitudinal research is needed with larger sample sizes, and taking into account the cause of death, in order evaluate the correlation between MS and mortality and to draw more definite conclusions.

CONFLICT OF INTEREST

All contributing authors hereby certify to have no conflicts of interest, financial, or otherwise, in the manuscript.

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