Cardiometabolic Risk, Physical Activity and Psychiatric Status in Patients in Long Term Psychiatric Inpatient Departments

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Abstract

Purpose

People with severe mental illness (SMI) have markedly reduced life expectancy; cardiometabolic disease is a major cause. Hospital departments should provide optimal prevention of cardiometabolic risk by optimizing prevention and treatment. Characteristics of cardiometabolic risk and physical activity in inpatients are still not well known. We aimed to describe the status of cardiometabolic risk in inpatients with severe mental illness and identify associations with psychiatric status and treatment.

Methods

Cross sectional descriptive study of inpatients with SMI from long term psychosis treatment wards in South Eastern Norway. Comprehensive assessments were made of cardiometabolic risk parameters, physical activity, lifestyle habits, symptoms, life satisfaction and treatment. Associations and potential prognostic factors were analyzed using linear and logistic regression.

Results

A total of 83 of 114 patients consented to participation, but most individual datasets were incomplete. The average age was 40 (SD 11.7), and 57 (64 %) were male. Over half of the subjects had unhealthy eating habits. Obesity was found in 44 %, 23 % had elevated fasting triglycerides, 55 % had elevated blood pressure and 78% smoked daily. Low levels of physical activity were significantly associated with more symptoms (p=.041). A nominal increase in cardiometabolic risk was found for olanzapine and clozapine users.

Conclusion

Inpatients in long term psychosis treatment wards have alarmingly high cardiometabolic risk. Level of physical activity was associated with both psychiatric and somatic health. Focus on lifestyle and somatic health should be an integrated part of the treatment for hospitalized severely mentally ill patients.

Keywords: Cardiometabolic, mortality, inpatient, SMI, schizophrenia

Background

Severe mental illness (SMI) is associated with increased risk for metabolic syndrome, which is a group of risk factors that occur together and increase the risk for coronary artery disease, stroke, and type-2 diabetes (U.S. National Library of Medicine) and cancer (1-3). SMI includes schizophrenia spectrum disorders and other disorders with psychotic features (4). Schizophrenia is among the top 10 causes of reduced disability adjusted life years (DALYs) worldwide (5). Life expectancy for people with schizophrenia is 20 % shorter than for the general population, and cardiometabolic risk is a major contributor to this (3, 6-9).

Side effects of especially the 'second generation' antipsychotics are regarded as a cause for the increased risk for the metabolic syndrome (10, 11), but the overall effect of antipsychotics on mortality is debated (12). Some antipsychotics, as clozapine and olanzapine, have a stronger association with cardiometabolic risk than others (13-15). Low levels of physical activity and physical fitness reduce life expectancy and increase risk for cardiovascular disease and metabolic syndrome in the general population (16) as well as in schizophrenia (17, 18). Negative symptoms, including apathy, passivity and social withdrawal, are the most debilitating aspects of schizophrenia spectrum disorders. These symptoms, together with poor economy, are factors that could be associated with physical inactivity (19) and also an unhealthy diet (20). Tobacco smoking is highly prevalent (21, 22), and has well-known detrimental effects on health and mortality, also in schizophrenia (23, 24). Low D-vitamin levels are associated with both psychiatric illness and cardiovascular disease (25). The explanations for increased cardiovascular morbidity and mortality in SMI are multifactorial, and common genetic factors may also contribute to adverse medical conditions in schizophrenia (26). However, the specific factors underlying the increase in cardiometabolic disease risk are not fully understood (27).

Although the majority of people with SMI live most of their lives in private or communal homes, this patient group is still relatively often in need of hospitalization. The majority of patients who are admitted to compulsory mental health care in Norway are diagnosed with schizophrenia (28), and patients with schizophrenia occupies a substantial part of psychiatric inpatient care beds (29, 30). During hospital admissions activities are often restricted, thus, admissions of longer duration may have negative impact on physical activity behaviours (31, 32). The nature of an inpatient psychiatric setting have in fact been considered 'obesogenic' (33). Psychiatric forensic hospital wards will typically have special challenges in physical activity because of their focus on passive security. However, there are few studies of cardiometabolic health risk and important potential modifying factors, as e.g. physical activity levels, in patients with SMI in long term psychosis treatment wards (34). In the current study we focused on this vulnerable patient group. Patients with SMI are mainly receiving public health care, nevertheless, a substantial proportion of inpatients with SMI in Norway are cared for by private institutions receiving public reimbursement.

The current study aimed at answering the following questions: 1) What is the cardiometabolic risk status and level of physical activity among patients in public and private long-term inpatient psychosis care facilities in Norway; 2) What are the associations between cardiometabolic risk and physical activity, characteristics of treatment, symptoms and functioning?

Materials and Methods

Setting

The current study investigates the baseline data of included participants enrolled in an intervention project for physical activity enhancement carried out at two long term psychosis

inpatient departments at the Oslo University Hospital (OUH) and the private inpatient psychiatric care facility Skjelfoss Psychiatric Centre (SPC) - Lukas Foundation in Hobøl County south of Oslo. Before the intervention started, baseline data were recorded in the period from January -August 2013 at OUH, and from January – April 2014 at SPC. The total number of patients in treatment at these facilities was 116 (n=78 at OUH and n=38 at SPC). The participating departments provide psychiatric treatment for non-acute phase patients with SMI in need for 24-hour specialized care. The departments are locked-door and have the capacity to administer compulsory measures and restrictions. OUH serve specific catchment areas in and near Oslo and have in total 3 regular intermediate/long term wards and 3 high security/forensic wards. The SPC receives patients proportionately from catchment area based Hospitals in the South-East Health Region of Norway. Most of the patients are admitted after an initial stay at an acute ward, and some are judicially sentenced to psychiatric treatment after serious crimes of violence according to the Norwegian Mental Health Care Act.

The study was approved by the Regional Ethics committee in South-Eastern Norway, reference number 2012/2266.

Design

Inclusion criteria: Inpatients at long term psychosis wards at the psychiatric departments of OUH and SPC, aged between 18 – 65 years and with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, psychotic disorder NOS, bipolar I or bipolar disorder NOS. Exclusion criteria were severe cognitive deficits (IQ < 70), severe brain damage, BMI<17.5, inability to speak Scandinavian or English or inability to give informed consent. The study aimed at including most patients at all wards. Effort was made to have a continuous inclusion of consecutive patients unbiased of clinical status or other patient related factors. The project did not influence the natural flow of patients through the wards during the study period.

Diagnostic and Symptom Assessments

The participants were diagnosed with the Structural Clinical Interview for DSM-IV for axis I disorders (SCID-I)(35). The use of current psychopharmacological medication was recorded using information from medical charts. Height, weight and blood pressure (BP) were measured using standardized techniques. Waist circumference was measured with a horizontal tape measurement from the top of the iliac crest. The degree of psychotic symptoms were measured with The Positive and Negative Symptom Scale (PANSS)(36), depressive symptoms with the Montgomery Asberg Depression Rating Scale (MADRS) (37). Global symptoms and psychosocial functioning were measured by the Global Assessment of Functioning Scale (GAF), the scores were split into scales of symptoms (GAF-S) and functioning (GAF-F) to improve psychometric properties (38). Apathy was measured with the abridged clinical version of the Apathy Evaluation Scale (AES-C-Apathy) (39, 40). Self-esteem was assessed by the Rosenberg Self-Esteem Scale (41).

Diagnostics and symptom assessments were done by MDs and psychologists, who had participated in a training course in SCID and PANSS assessments and these attended regularly diagnostic consensus meetings led by clinically experienced specialists.

Due to variable staff resources for data gathering, datasets are not complete for a number of participants. Missing data were distributed differently among the participants, and the data gathering procedure was not considered to give bias in selection of the main outcome assessments.

Physical Health and Diet

Level of physical activity was assessed by interviewing about hours of daily physical activity, and at least 30 minutes daily physical activity was recorded (according to international guidelines for physical activity (42)). We used the questions (questions 32-36) of physical

activity in The Nord-Trøndelag Health Study (HUNT) questionnaire which cover frequency, duration and time in inactivity (43, 44), see presentation of categories of the HUNT-questions in Table 1. Quality of regular daily diet was assessed by the clinicians according to national dietary guidelines as "healthy" or "unhealthy".

Somatic risk factors were assessed according to established guidelines (45). S-glucose, glycosylated hemoglobin (HbA1C) and fasting plasma lipids (total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglycerides) were measured using the regular hospital laboratories.

All assessments of the individual patients were carried out in the course of few days; the exception being hours of daily physical activity and height, which was recorded up to 3 months before the other assessments. The weight (and BMI) presented in this study was recorded at both time intervals. Due to a more complete dataset of weight (and BMI) at the earliest assessments (N=53), these values are presented in table 1. In all other parts of this study, the assessments done at the same time points as the other assessments (N=34) were used.

Statistics

We performed visual analyses of the distributions of missing variables in the dataset. We did not perform apriori subsample analyses, but included the maximum available sample for each analysis. There were unsystematic distributions of missing values across variables and participants. All analyses were done using the IBM Statistical Package for the Social Sciences (SPSS) version 24.0 (IBM, Armonk, NY, USA). Continuous variables were tested for normality by comparing means and medians, and by analyzing normality plots. Group comparisons for continuous normally distributed variables were evaluated with independent sample *t*-tests, group comparisons for non-normally distributed variables were evaluated with

Mann-Whitney U-tests and group comparisons for dichotomous data were evaluated with chi-squared tests or Fischer's exact tests.

We made a dichotomous variable of physically activity of 30 minutes per day, where those who met this criterion were labeled physically active, and the rest were inactive. To evaluate the significant relationships found in group comparisons or bivariate analyses between physical activity and symptom and functioning variables, linear and logistic regressions were performed. Independent variables were chosen based on their potential role as a confounder of the relationship. This variable set thus included sex, age and diagnostic group or use of antipsychotic medication according to association with the dependent variable. Several variables of potential interest were not associated with the dependent variables and were thus not included in further analyses. In the regression analyses we used an approach were the independent variables were entered hierarchically in several blocks; with sex and age in the first step, use of antipsychotics and/or diagnostic group in the second step and physical activity in the last step. Results are presented as β-coefficients or odds ratios (OR) with 95 % confidence intervals (CI). The assumption of a linear regression was evaluated based on examinations of residual plots for each analysis. The logistic regressions were assessed using the Hosmer-Lemeshow goodness of fit test. Due to non-linearity of the MADRS-variable, a median split was performed to create a dichotomous variable to perform a logistic regression. The significance level was set to 0.05.

Results

Of a total of 114 eligible patients, 83 patients (73 %) signed informed consent to participate. We have no records of reasons why patients refused to participate. Demographics and clinical characteristics are shown in Table 1 [Table 1 near here]. Clinical somatic risk markers for cardiometabolic disease and activity levels are shown in Table 2 [Table 2 near here]. Biochemical cardiometabolic risk markers are shown in Table 3. No mean or median values

were outside their respective reference areas. Individual extreme values outside the reference area were found in most tests with especially high proportions of pathological values for triglycerides, D-vitamin and C-reactive protein. In the subsample of 48 with valid lipid measures, 15 (31.3 %) had an abnormal lipid profile [Table 3 near here]. According to the diagnostic criteria for the metabolic syndrome (International Diabetes Federation criteria 2006) (46), 29 patients of 34 (85,3 %) met the criteria for central obesity, and 22 participants out of 26 (84,6 %, with sufficiently complete datasets for evaluating the criteria), had metabolic syndrome.

Use of clozapine, olanzapine or depot injectable antipsychotics showed a nominal increase for both BMI and waist circumference, and for levels of HbA1C, insulin and C-reactive protein as well as a decrease in D-vitamin levels. For blood lipids, there were no clear trends (Table 4) [Table 4 near here]. There were no significant associations between type of hospital or hospital wards and risk markers for cardiometabolic disease after controlling for treatment characteristics.

Bivariate analyses showed significant correlations between weekly hours of physical activity (amount of physical activity) and 25-OH-vitamin D levels. In linear regression analyses with 25-OH-vitamin D as dependent variable, there was a significant effect of weekly hours of physical activity entered as last variable after correction for sex, age and use of antipsychotics (Adjusted R^2=.514, β =.941, 95% CI 6.5-31.2, P = .009). There were no associations with amount of physical activity and life satisfaction.

Daily physical activity was assessed in subsample of n= 31-48 with valid measures (Table 5). Patients with daily physical activity had lower levels of depression than those without daily activity (Table 5). A logistic regression for the dichotomous MADRS-variable found the association with high level of depression to be significantly associated with low frequency of

physical activity, also after correcting for sex, age and use of antipsychotics (OR=.18, 95% CI: .03 to .93, P=.041). The findings of lower levels of apathy and self-esteem were not significant after correcting for the same factors in linear regressions [Table 5 near here].

There were significant associations between BMI and several biochemical markers of cardiometabolic risk in linear regression analyses after controlling for sex, age and use of antipsychotics. HbA1C: Adjusted R^2=.49, β =.5539, 95% CI: 2.3 to 12.6, P = .007. Total cholesterol: Adjusted R^2=.43, β = .62, 95% CI: 2.0 to 9.2 P = 0.005. HDL-cholesterol: Adjusted R^2=.34, β =-4.93, 95% CI: -22.7 to -1.5, P = .028. LDL Cholesterol: Adjusted R^2=.52, β = .722, 95% CI: 3.4 to 10.4, P = 0.001.

Discussion

The current study documents highly elevated levels of the two main cardiometabolic risk factors obesity and tobacco use in this population of psychiatric inpatients with long duration of illness. Nearly half were obese; this is over twice the prevalence in the corresponding general population (47). The proportion of daily smokers was six times higher than in the general population (48). An increase in risk factors was present in a substantial number of blood tests. Further, daily physical activity levels were low and over half of the subjects had unhealthy eating habits.

The cardiovascular risk levels described in the current study are comparable to the highest risk levels reported in a major meta-analysis of 77 international studies of schizophrenia spectrum patients published before mid-2011 (34), in this meta-analysis about half of the patients were inpatients. A recent English study however, with 450 randomly selected patients with established (multi-episode) psychosis in both urban and rural community mental health teams, showed cardiometabolic risk levels similar to the current study (49). In a recent Danish clinical trial of 214 predominantly outpatients using clozapine or olanzapine,

cardiometabolic risk levels were slightly higher or similar to the current study (50). Symptom severity was comparatively high in the present study group, and a significant majority used antipsychotics. There were conspicuous patterns of a higher risk on several cardiometabolic risk factors in subgroups using antipsychotics, which did not reach individual statistical significance, but could represent factual trends. Together these findings may be taken as an indication that other conditions as e.g. medication are more important in explaining cardiometabolic risk than length of admission or inpatient or outpatient status. The lack of significant findings on associations with medication prevents us however from further speculations on the role of antipsychotics.

We found an association between lower frequency of physical activity and more symptoms of depression also after correction for possible confounders. Lack of initiative and psychomotor slowing are part of the depressive syndrome and could intuitively explain why depressive patients could be more prone to passivity and physical inactivity. Treatment strategies targeting depression or apathy might represent possible "points of attack" when addressing sedentary behavior in this patient group. However, we cannot rule out a reverse causation were less activity might lead to more depressivity. A recent Dutch study with continuous monitoring of physical activity using accelerometers, found an association between physical activity and quality of life, with the stronger association in the patients with the lowest activity levels, possibly suggesting an effect of mobilizing from sedentary behavior (51).

We also found significant associations between BMI and important biochemical cardiometabolic risk markers, after controlling for possible confounders, including use of antipsychotics. These associations are known from the general population, but here we show them to be present independently of use of antipsychotics in a psychiatric inpatient population.

In the small subsample with assessment of D-vitamin levels we found an association between frequency of physical activity and D-vitamin levels, showing daily activity to explain almost 50 % of the variation in vitamin-D levels. As lower physical activity might correlate strongly with less exposure to sunlight, this association also seems clinically meaningful, adding to the total risk burden of low activity levels.

We did not find any association with sex and cardiometabolic risk. This is contrary to other studies, which have found a higher prevalence in females (52, 53). The finding of higher levels of triglycerides in the non-smoking participants was unexpected, as there is an established association between smoking and a disadvantageous lipid profile (54). As smoking is known to induce CYP1A2 activity which, in turn, reduces serum levels of olanzapine and clozapine (55), a reduced effect of medication on lipids may be part of the explanation.

We did not find any significant differences between the public services at a university hospital and the private services at a smaller institution in cardiometabolic risk characteristics. As the private services typically serve as discharge units for the public hospital departments, it is plausible to interpret this as an indication that the patient population is very similar and that eventual differences between services in the medical care will take longer to cause effects.

Limitations and Strengths

This naturalistic study has limitations. The sample size is small and there are missing data for several of the assessments in the subgroup analyses. This gives a risk for type II errors and also limitations in the validity of results for the adjusted linear regressions. Although there were no indications of systematic bias of the missing variables, the findings from smaller subsamples must be interpreted with caution. Another limitation is the primary recruitment. Although clinicians were urged to invite all patients to participate in the study, we did not

obtain 100 % participation, and there is a risk for selective recruitment of better functioning or more cooperating patients. However there were no reports of such factual selection bias and the mean values of the symptom and functioning scores are in line with what could be expected in this patient population and higher than in the referred studies. As the study was cross-sectional, data cannot be used to draw conclusions about causal relationships. Information on physical activity was based on self-report, which may have low reliability. Dosage of medication was not reported and we did not check compliance with serum levels.

The study also has strengths. Studies on patients in long term inpatient treatment are few. The naturalistic design with consecutive inclusion of patients enables a description of status in long-term psychosis departments with participation of the majority of real-time unselected inpatients. This gives a high degree of representativity and provides clinically relevant information in a vulnerable group of patients.

Conclusion

The present study documents high cardiometabolic risk in this group of long-term hospitalized patients. Low level of physical activity was associated with both important metabolic risk factors and depressivity, opening potentials for improving care. Inpatient hospital departments care for the most severely ill for prolonged periods of time, and they have a substantial responsibility for prevention of cardiometabolic illness. More longitudinal and interventional studies are needed to identify cause-effect relationships and identifying the best prevention strategies for cardiometabolic disease and premature death in this vulnerable patient population.

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Disclosure of interest:

The authors report no conflicts of interest

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