

Original

# The Combination of Smoking and Overweight is Associated with Dyslipidemia Among Inpatients and Hypertension Among Outpatients with Schizophrenia

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## SUMMARY

**Objective** : As the physical health of patients with schizophrenia is relatively poor and their risk of premature death is considerably increased compared with the general population, we examined the association between lifestyle-related diseases and smoking, drinking, and overweight in inpatients and outpatients with schizophrenia.

**Methods** : The study design was cross-sectional. Subjects were 138 inpatients and 135 outpatients with schizophrenia from a psychiatric hospital in Japan. They were asked for information concerning smoking and alcohol use, and height and weight were measured to calculate body mass index. Data on hypertension, dyslipidemia, type 2 diabetes, cardiovascular diseases, and use of atypical antipsychotics were acquired from medical records.

**Results** : Inpatients were more likely to receive atypical antipsychotic medication and less likely to drink alcohol. The smoking prevalence was 38.4% (53.8% in men, 17.2% in women) in inpatients and 39.3% (56.3% in men, 20.3% in women) in outpatients. Multivariate odds ratio (OR) for hypertension was significantly higher among outpatients than inpatients. After adjustment for age, sex, and use of atypical antipsychotic medication, overweight smokers showed a significantly higher OR for dyslipidemia (3.17, 95% CI : 1.07-9.37) among inpatients, and a significantly higher OR for hypertension (3.15, 95% CI : 1.14-8.74) among outpatients. When the reference group is non-smokers with BMI below 25, smokers with BMI of 25 or more had a significant higher OR (3.38, 95% CI : 1.36-8.38) for dyslipidemia among patients with schizophrenia.

**Conclusion** : After adjustment for atypical antipsychotic medication use, the combination of smoking and overweight was significantly associated with the prevalence of dyslipidemia among inpatients and hypertension among outpatients with schizophrenia.

**Key Words** : Schizophrenia, hypertension, dyslipidemia, smoking, antipsychotics

## INTRODUCTION

Schizophrenia is considered to be a life-shortening illness<sup>1)</sup>. Several studies have shown that the physical health status of patients with schizophrenia is relatively poor and their risk of premature death because of

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lifestyle-related diseases is considerably higher than in the general population<sup>1-4</sup>. According to previous surveys, the prevalence of metabolic syndrome is higher among patients with severe mental illness than among the general population<sup>5,6</sup>. It is considered that their unhealthy lifestyle, such as an unhealthy diet, smoking, alcohol consumption, and obesity, is associated with the high prevalence of lifestyle-related diseases of this population. It has also been reported that atypical antipsychotic medications for patients with schizophrenia are associated with obesity and metabolic syndrome<sup>7,8</sup>. Mental illness is associated with both higher rates and higher levels of smoking<sup>2,9,10</sup>. Killian et al reported that risk of alcohol consumption and smoking were increased in patients with schizophrenia<sup>11</sup>.

In this study, we firstly compared the characteristics of lifestyle among inpatients with that among outpatients. Although smoking and overweight are well-established risk independent factors for lifestyle-related diseases, to our knowledge, few studies have investigated the combined risk of smoking and overweight for lifestyle-related diseases among psychiatric patients. Therefore, in this study, we examined the association between lifestyle-related diseases and smoking, and overweight in patients with schizophrenia. We hypothesize that patients with schizophrenia who smoke and are overweight have a high prevalence of lifestyle-related diseases.

## METHODS

This study was conducted within a cross-sectional survey of psychiatric inpatients and outpatients of a psychiatric hospital in Japan, from 2007 to 2008. After written informed consent was obtained from all participants who could understand the meaning of this survey, they were asked for information about smoking, alcohol use, habitual exercise, and intake of healthy foods. Data regarding the presence or absence of hypertension, dyslipidemia, type 2 diabetes, cardiovascular diseases, and the use of atypical antipsychotics were acquired from the participants' medical records. Participants' weight and height were measured, and body mass index (BMI) was calculated as weight/height<sup>2</sup> (kg/m<sup>2</sup>). A BMI of 25 or more was defined as excessive weight. This cross-sectional psychiatric survey was approved by the ethical review board of Dok-

kyo Medical University and a director of the psychiatric hospital where the survey was conducted.

The subjects of the present study were 138 inpatients (80 men, 58 women) and 135 outpatients (71 men, 64 women) with schizophrenia who had no missing values from the psychiatric hospital survey mentioned above. Thus, data regarding the presence or absence of hypertension, dyslipidemia, type 2 diabetes, and cardiovascular diseases, use of atypical antipsychotics and self-reported lifestyle behaviors were available for all subjects. Patients were diagnosed according to the International Classification of Disease (ICD)-10 criteria of the World Health Organization<sup>12</sup> with the use of structured clinical interviews by psychiatric specialists. Schizophrenia included schizotypal and delusional disorders (ICD F20-F29).

We examined the association between disease (such as hypertension, dyslipidemia, type 2 diabetes, and cardiovascular diseases) and lifestyle (such as smoking, BMI, smoking combined with excessive weight, and use of atypical antipsychotics). We did not analyze the data regarding habitual exercise and intake of healthy foods since these lifestyle-related factors, as well as alcohol consumption, differed greatly between inpatients and outpatients.

The characteristics of inpatients and outpatients were compared by chi-square, Fisher's exact, and t-tests. Then, multivariate odds ratios (ORs) among all patients for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases were calculated by binary logistic regression analysis. Each OR was calculated using binary logistic regression analysis among inpatients or outpatients adjusted by age, sex, and use of atypical antipsychotics. Statistical significance was defined as  $p < 0.05$ . All data were analyzed using the software Statistical Package for Social Sciences (SPSS, 16.0J for MAC).

## RESULTS

Table 1 shows the characteristics of inpatients and outpatients with schizophrenia. Inpatients were more likely to receive atypical antipsychotic medication ( $p < 0.001$ ). There were no significant differences in the prevalence of hypertension, dyslipidemia, type 2 diabetes, and cardiovascular diseases between inpatients and outpatients. The smoking prevalence of inpatients

**Table 1** Characteristics of inpatients and outpatients with schizophrenia

	Inpatients (n = 138)	Outpatients (n = 135)	<i>p</i> -value
Mean age (SD)	53.5 (12.8)	50.5 (13.2)	0.056
Mean BMI (SD)	23.86 (4.26)	24.85 (4.34)	0.059
Men	80 (58.0%)	71 (52.6%)	0.396
Hypertension	20 (14.5%)	31 (23.0%)	0.088
Dyslipidemia	19 (13.8%)	29 (21.5%)	0.112
Type 2 diabetes	24 (17.4%)	20 (14.8%)	0.623
Cardiovascular diseases	8 ( 5.8%)	3 ( 2.2%)	0.217
Smoking	53 (38.4%)	53 (39.3%)	0.902
BMI ≥25	55 (39.9%)	64 (47.4%)	0.224
Smoking with excessive weight	27 (20.0%)	28 (20.3%)	1.000
Drinking alcohol	2 ( 1.4%)	24 (17.8%)	<0.001***
Use of atypical antipsychotics	112 (81.2%)	81 (60.0%)	<0.001***

\*\*\*  $p < 0.001$ , by chi-square, Fisher's exact, or t-tests

**Table 2** Adjusted odds ratios for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among patients with schizophrenia by logistic regression analysis (n = 273)

	Hypertension	Type 2 diabetes	Dyslipidemia	Cardiovascular diseases
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Inpatients	1.00	1.00	1.00	1.00
Outpatients	2.01 (1.01-4.04) *	0.57 (0.19-1.67)	1.46 (0.74-2.89)	0.39 (0.09-1.68)
Smoking status	1.00	1.00	1.00	1.00
Non-smoker	1.77	1.03	1.25	2.05
Current smoker	(0.84-3.72)	(0.49-2.16)	(0.62-2.52)	(0.45-9.28)
BMI				
<25	1.00	1.00	1.00	1.00
≥25	1.17 (0.60-2.28)	1.56 (0.80-3.05)	2.32 (1.20-4.47) *	1.28 (0.34-4.82)
Atypical antipsychotics				
No	1.00	1.00	1.00	1.00
Yes	0.69 (0.23-1.40)	0.81 (0.39-1.70)	0.56 (0.27-1.14)	1.57 (0.35-7.02)

95% CI, 95% confidence interval ; OR : odds ratio adjusted for age, sex, smoking status, BMI, and use of atypical antipsychotics ; \*  $p < 0.05$ -by binary logistic regression

was 38.4% (53.8% in men, 17.2% in women) and that of outpatients was 39.3% (56.3% in men, 20.3% in women), showing no significant difference. As only two inpatients habitually consumed alcohol, there was a large significant difference between the proportion of drinkers among inpatients and outpatients. Over-

weight patients were more prevalent among outpatients (47.4%) than inpatients (39.9%), although this difference was not significant ( $p = 0.224$ ).

Table 2 shows multivariate ORs for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among all patients. Overweight inpatients had a

**Table 3** Adjusted odds ratios for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among inpatients with schizophrenia by logistic regression analysis (n = 138)

	Hypertension	Type 2 diabetes	Dyslipidemia	Cardiovascular diseases
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Smoking status				
Non-smoker	1.00	1.00	1.00	1.00
Current smoker	3.07 (0.86-11.30)	0.57 (0.19-1.67)	0.87 (0.29-2.58)	5.02 (0.78-32.2)
BMI				
<25	1.00	1.00	1.00	1.00
≥25	1.02 (0.35-2.95)	1.20 (0.48-3.00)	2.20 (0.82-5.95)	2.27 (0.54-10.41)
Smokers with BMI ≥25				
No	1.00	1.00	1.00	1.00
Yes	0.99 (0.24-4.10)	1.14 (0.36-3.58)	3.17 (1.07-9.37)*	5.50 (0.93-32.33)
Atypical antipsychotics				
No	1.00	1.00	1.00	1.00
Yes	0.77 (0.23-2.75)	1.70 (0.97-2.99)	0.73 (0.20-2.69)	3.15 (0.31-31.78)

95% CI, 95% confidence interval ; OR : odds ratio adjusted for age, sex, and use of atypical antipsychotics ; \* p<0.05-by binary logistic regression

significantly higher OR for dyslipidemia (2.32, 95% CI : 1.20-4.47). Outpatients had a significant higher OR (2.01, 95% CI : 1.01-4.04) for hypertension than inpatients. Among inpatients with schizophrenia, overweight smokers had a significantly higher OR for dyslipidemia (3.17, 95% CI : 1.07-9.37), as shown in Table 3. Moreover, overweight smokers had the highest adjusted OR for cardiovascular diseases (5.50, 95% CI : 0.93-32.33). Among outpatients with schizophrenia, overweight smokers had a significantly higher OR for hypertension (3.15, 95% CI : 1.14-8.74), as shown in Table 4. Additionally, outpatients receiving atypical antipsychotic medication had a significantly lower OR for type 2 diabetes (0.34, 95% CI : 0.13-0.99).

Adjusted odds ratios for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among all patients in relation to combination of smoking and overweight are shown in Table 5. The reference group is non-smokers with BMI below 25. Smokers with

BMI of 25 or more had a significantly higher OR (3.38, 95% CI : 1.36-8.38) compared with the reference group. The combination of smoking and overweight showed higher, but not significantly higher, ORs for hypertension, type 2 diabetes, or cardiovascular diseases compared with other groups.

## DISCUSSION

The results of our study show that the combination of smoking and overweight was significantly associated with prevalence of dyslipidemia among inpatients and prevalence of hypertension among outpatients with schizophrenia. The combination of smoking and overweight showed a strong association with prevalence of dyslipidemia. Akbartabartoori et al reported that the combination of smoking and overweight or obesity aggravated cardiovascular disease risk factors, particularly HDL-cholesterol and C-reactive protein<sup>13</sup>. To our knowledge, however, the present study is the

**Table 4** Adjusted odds ratios for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among outpatients (n = 135)

	Hypertension OR (95% CI)	Type 2 diabetes OR (95% CI)	Dyslipidemia OR (95% CI)	Cardiovascular diseases OR (95% CI)
Smoking status				
Non-smoker	1.00	1.00	1.00	1.00
Current smoker	1.60 (0.63-4.06)	1.65 (0.57-4.81)	1.66 (0.67-4.10)	—
BMI				
<25	1.00	1.00	1.00	1.00
≥25	1.02 (0.29-1.66)	2.00 (0.48-3.00)	2.32 (0.97-5.59)	0.33 (0.02-4.96)
Smokers with BMI ≥25				
No	1.00	1.00	1.00	1.00
Yes	3.15 (1.14-8.74) *	1.14 (0.36-3.58)	1.72 (0.65-4.59)	—
Atypical antipsychotics				
No	1.00	1.00	1.00	1.00
Yes	0.77 (0.23-1.57)	0.34 (0.13-0.99) *	0.42 (0.18-1.00)	0.43 (0.03-6.14)

95% CI, 95% confidence interval ; OR : odds ratio adjusted by age, sex, and use of atypical anti psychotics ; \* p<0.05 by binary logistic regression

first targeting patients with schizophrenia to show an association between lifestyle-related diseases and the combination of smoking and overweight.

The smoking prevalence was 38.4% (53.8% in men, 17.2% in women) in inpatients and 39.3% (56.3% in men, 20.3% in women) in outpatients in the present study, which was higher than the smoking prevalence among Japanese (39.4% in men, 11.0% in women) according to the Japanese National Health and Nutrition Survey in 2007<sup>14</sup>. In the United States, the prevalence of smoking among patients with schizophrenia was reported to be 68% , which was significantly higher than that of controls (35%)<sup>2</sup>, while a German study reported such prevalence among patients with schizophrenia at 68.8% and that of the general population at 32.2%<sup>11</sup>. Campo-Arias et al reported that the smoking prevalence among patients with schizophrenia was 26% (34.8% in men, 11.0% in women) and that smoking was associated with schizophrenia but not with mood disorders<sup>15</sup>.

Killian et al also reported that risk of alcohol consumption was increased among patients with schizophrenia and depression<sup>11</sup>, although patients with schizophrenia were less likely to drink alcohol in our study. As the inpatients of psychiatric hospitals are prohibited from drinking alcohol in Japan, this indicates that many outpatients continued with their cessation of alcohol consumption after hospitalization. The results of our study are in agreement with a report that patients with schizophrenia consume less alcohol but smoke more than the general population<sup>16</sup>.

Coodin reported that patients with schizophrenia had significantly higher BMI than the general population<sup>17</sup>. Obesity was more prevalent among individuals with mental illness than among the general population, and was associated with adverse health outcomes including diabetes and hypertension<sup>18</sup>. One of the risk factors for weight gain in patients with mental illness is the use of atypical antipsychotic medication<sup>19</sup>. Weight gain after taking antipsychotics was reported

**Table 5** Adjusted odds ratios for hypertension, type 2 diabetes, dyslipidemia, and cardiovascular diseases among inpatients and outpatients in relation to the combination of smoking and overweight (n=273)

	Hypertension	Type 2 diabetes	Dyslipidemia	Cardiovascular diseases
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Non-smoker with BMI < 25 (n = 102)	1.00	1.00	1.00	1.00
Smokers with BMI ≥ 25 (n = 52)	1.44 (0.49-4.24)	1.48 (0.44-5.02)	1.61 (0.51-5.14)	1.66 (0.11-24.82)
Non-smoker with BMI ≥ 25 (n = 64)	0.84 (0.35-2.05)	1.57 (0.66-3.75)	2.08 (0.86-5.03)	0.64 (0.10-4.14)
Smokers with BMI ≥ 25 (n = 55)	2.04 (0.77-5.40)	1.63 (0.64-4.19)	3.38 (1.36-8.38)*	2.99 (0.50-18.04)

95% CI, 95% confidence interval ; OR : odds ratio adjusted by age, sex, inpatients or outpatients, and use of atypical anti-psychotics ; \* p<0.05 by binary logistic regression

to be related to reduced levels of adiponectin<sup>7)</sup>. Therefore, the use of atypical antipsychotic medication was taken into consideration in the present study. However, in our study, use of atypical antipsychotic medication was a negative risk factor for lifestyle-related diseases, especially type 2 diabetes among outpatients. Because the side effects of atypical antipsychotics are well known, psychiatric doctors tend not to prescribe these agents to patients with type 2 diabetes. Clinicians should screen and monitor carefully for cardiometabolic side effects and risk factors for comorbid conditions<sup>8,20)</sup>.

The results of our study show that the combination of smoking and overweight was significantly associated with the prevalence of dyslipidemia among inpatients and the prevalence of hypertension among outpatients with schizophrenia. Therefore, it is important for psychiatric inpatients and outpatients to change to healthier behaviors to prevent lifestyle-related diseases. Thus, current smokers should be encouraged to participate in smoking cessation programs, and those who are overweight should be introduced to weight

loss programs.

Patients with schizophrenia who are diagnosed with and treated for lifestyle-related diseases have difficulty in changing unhealthy habits such as smoking and being overweight. However, weight management and lifestyle advice should be routinely offered to all patients with schizophrenia<sup>21)</sup>. Weiser et al suggested that a general strategy of health promotion for people with mental disorders should take into account behavioral, environmental, and iatrogenic health risks<sup>22)</sup>. Health promotion programs should be tailored to the needs and abilities of each psychiatric patient. Kitabayashi et al reported that 3 months after a trial of institutional smoking prohibition, the smoking rate decreased from 36.3% to 22.2%, but no significant increase in BMI was observed<sup>23)</sup>. Although institutional smoking prohibition is a good way to introduce a smoking cessation program into the health education provided by psychiatric hospitals, self-motivation to stop smoking is more important. Therefore, cessation advice and appropriate follow-up care should be provided to psychiatric patients<sup>24)</sup>.

As this study's design was cross-sectional and examined one point in time, the associations observed in this study do not indicate causality of lifestyle-related diseases. Thus, a further large-scale longitudinal study will be needed to explore the combined risk of smoking and overweight on lifestyle-related diseases among individuals with and without schizophrenia. Moreover, an intervention study involving health education to schizophrenic patients is warranted.

Nevertheless, this is the first study to show an association between lifestyle-related diseases and the combination of smoking and excessive weight among patients with schizophrenia. The results of our study suggested that the introduction of programs to stop smoking and lose weight is very important for patients with schizophrenia.

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