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Original

Increased risk of early lung function alterations in people with psychosis: A cross-sectional case–control study

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ABSTRACT

Background: Tobacco smoking has been described as the main cause of chronic obstructive pulmonary disease (COPD) and this habit is clearly more frequent among individuals with psychosis than in the general population, with rates reaching up to 60%. However, little attention has been focused on the association of COPD and psychosis. We aimed to explore the risk of presenting early lung function alterations in a group of individuals with psychosis.
Methods: Following an observational cross-sectional design we studied a cohort of individuals with established psychosis ($N = 128$), and compared them with a sex, age, and smoking habit matched control group ($N = 79$). We evaluated respiratory symptoms by means of mMRC, CAT and Dyspnea-12 scales. And lung function through spirometry tests.
Results: Individuals with psychosis presented more respiratory symptoms than controls. Similarly, we observed significant differences in the lung function tests between these two groups, where individuals with psychosis presented worse results in most of the spirometry mean values (FEV_1 or forced expiratory volume in the first one second: 3.29 L vs. 3.75 L, $p < 0.001$; forced vital capacity or FVC: 4.25 L vs. 4.72 L, $p = 0.002$; and FEV_1/FVC ratio: 0.78 vs. 0.80, $p = 0.052$). Patients also presented worse values of lung diffusion, with lower diffusing capacity for carbon monoxide (DLCO) than controls (6.95 vs. 8.54 mmol/min/kPa, $p < 0.001$).
Conclusions: The individuals with psychosis in our study presented greater respiratory symptoms and poorer lung function measured through spirometry. These signs have been described as early signs of COPD.

Introduction

Much of the excess mortality observed in individuals with schizophrenia-spectrum is related to physical pathology[1] and to some extent to chronic respiratory disease.[2,3] The prevalence of severe respiratory co-morbidities, such as chronic pulmonary disease (COPD) is higher among individuals with chronic psychosis.[2,4,5]

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Tobacco smoking, which has been described as the main cause of COPD, is more frequent among individuals with psychosis, with rates reaching up to 60%.[6] Moreover, tobacco smoking is highly associated with cannabis use,[6] being the prevalence of cannabis smoking also higher among individuals with psychosis.[7,8] COPD is a highly prevalent lung disease, affecting 10–12% of adult population,[9] that is generally diagnosed in the late adulthood (above 40 s) after a chronic progression. Thus, the pathological mechanisms leading to COPD, not only tobacco exposure but also early social and life disadvantage, are present several years before its diagnosis.[10] And, unspecific lung function signs and respiratory symptoms could be early identified, even before an established diagnosis of COPD.[10] However, most of the studies on respiratory health and psychosis have been done on population-based registers of individuals with chronic psychosis, and no previous studies have tried to identify these early signs and symptoms preceding an established lung pathology.

The aim of the present study was to explore the early presence of lung function alterations and respiratory symptoms in a group of middle-age individuals with psychosis, and compare them with a control group without psychiatric disorders. Based on the evidence described we hypothesize that psychosis diagnosis will be associated with poorer lung function and greater severity of respiratory symptoms.

Material and methods

Study design

The study followed an observational cross-sectional design and was performed at the Departments of Psychiatry and Pneumology of the University Hospital Marqués de Valdecilla (Santander, Spain). All subjects provided written informed consent prior to their inclusion in the study, which was approved by the Biomedical Research Ethics Committee of Cantabria (ref.: 2017.239).

Subjects

The study is part of a larger prospective longitudinal research project on first episode non-affective psychosis, the PAFIP program.[8] Individuals with a confirmed diagnosis of schizophrenia-spectrum disorder (schizophrenia, schizophreniform, schizoaffective, psychosis not-otherwise specified, delusional, or brief psychotic disorders), of at least 10 years (8–12) of progression, were invited to participate in this study. A group of subjects without psychiatric illness was recruited as control group through public advertisements from the same catchment area. Individuals in the control group were matched to psychosis cases for age, sex, and tobacco use.

Respiratory and clinical evaluation

The clinical respiratory status was evaluated using the following validated scales. The *modified Medical Research Council* (*mMRC*) assesses the severity of breathlessness in patients with COPD. It is consistent with other measures of health status and predicts the decline of lung function and future mortality risk.[11] The established threshold for severe dyspnea (breathlessness) is a score of 2 or above. The *COPD Assessment Test* (*CAT*)[12] is a self-reported questionnaire developed to quantify the impact of COPD on health status, focusing on daily symptoms and activities. The threshold for COPD symptoms' severity (not only breathlessness) is a score of 10 or above.[11] Finally, the *Dyspnea-12* has a multidimensional approach to the assessment of dyspnea, including its sensory component and the affective response.[13]

Respiratory function was measured through spirometry tests, performed by specially trained nurses as recommended in international guidelines.[14] The main outcome variables were forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1). Spanish reference values were applied to compute the individual FEV_1 and FVC values as a percentage of those predicted for corresponding age, gender and height in healthy, non-smoking adults. Based on spirometry results, pulmonary obstruction was defined as a $FEV_1/FVC < 70\%$; and restriction as a $FVC < 80\%$ of the predicted value and a $FEV_1/FVC > 70\%$ to exclude obstruction. A bronchodilatation test was also carried out as part of the spirometry measurements, being positive if achieving an improvement of $FEV_1 > 12\%$ and 200 mL from basal (pre-bronchodilatation) test results.

Statistical analyses

Chi-square and ANOVA analyses were performed to compare qualitative and quantitative variables between the two groups. To clarify whether the lung function alterations were related to psychosis and other variables beyond tobacco exposure, we ran multiple linear regressions (FVC and FEV_1 as dependent variables) and multiple logistic regression ($DLCO < 80\%$ as dependent variable) where psychosis, female sex, age, tobacco lifetime habit ("current/ex-smokers" vs. "never-smoked"), number of tobacco pack-years, $mMRC \geq 2$, Dyspnea-12 scale, BMI, and benzodiazepines use, were the independent variables. We also carried out exploratory analyses comparing the lung function between patients and controls, that had never smoked. The Statistical Package for Social Science (SPSS) version 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. All statistical tests were two-tailed and significance was determined at the 0.05 level.

Results

Sociodemographic and clinical characteristics

Both groups were similar in the main sociodemographic variables, including age and sex, as well as regarding their smoking habits (see Supplementary material 1). In this sense, psychosis patients and controls presented a similar age of initial tobacco exposure (16.5 vs. 17.1 years, $p = 0.422$) and age of initial daily use (18.1 vs. 19.6 years, respectively; $p = 0.101$). Both groups had a similar age of tobacco use cessation (32.9 vs. 32.4 years, $p = 0.857$). We neither observed significant differences between groups regarding the rates of passive tobacco smoking (44.1% vs. 52.6%, $p = 0.293$). However, individuals with psychosis were heavier smokers than the control ones (19.4 vs. 12.1 cigarettes/day, $p < 0.001$; and, 21.2 vs. 14.1 pack-years of tobacco, $p = 0.005$). Both groups presented similar results regarding cannabis exposure, with no significant differences between groups (all $p > 0.05$) in their age of first exposure to cannabis (17.2 vs. 17.7 years), age of initial daily use (18.2 vs. 18.0 years), and number of joints per day (4.7 vs. 4.4 joints/day).

Respiratory symptoms' differences between psychosis patients and controls

Psychosis patients and controls reported similar severity of respiratory symptoms, with no significant differences between groups in mean mMRC scores (0.47 vs. 0.37, $p = 0.367$) (Table 1). However, a significantly greater proportion of individuals among the psychosis group presented a score above the dyspnea threshold ($mMRC \geq 2$) (8% vs. 0%, $p = 0.024$). Patients with psychosis also presented higher mean scores in the Dyspnea-12 scale than controls (4.5 vs. 2.0, $p = 0.001$). And although both groups presented similar

Table 1
Respiratory symptoms in patients and controls.

	Patients		Controls		Total			Statistics	
	N = 128		*N* = 79		*N* = 207				
	Mean *N*	SD %	Mean *N*	SD %	Mean *N*	SD %		Value	*p*
mMRC, n (%)									
0	76	63.3	48	63.2	124	63.3			
1	36	30.0	26	36.8	64	32.7			
2	7	5.8	0	0	7	3.6			
3	0	0	0	0	0	0			
4	1	0.8	0	0	1	0.5			
mMRC total score	0.45	0.68	0.37	0.49	0.42	0.61	X^2	0.819	0.367
mMRC ≥ 2	8	6.7	0	0	8	4.1	X^2	5.282	0.024
Dyspnea-12 (D-12) scale	4.5	5.5	2.0	3.4	3.5	4.9	*F*	12.525	0.001
D-12, physical subscale	3.3	3.4	1.7	2.4	2.6	3.1	*F*	12.472	0.001
D-12, affective subscale	1.3	2.5	0.4	1.3	0.9	2.2	*F*	8.488	0.004
CAT score, points									
Total	5.56	5.16	5.41	4.60	5.44	4.93	*F*	0.004	0.947
Cough	0.96	1.29	1.13	0.99	1.02	1.18	*F*	0.968	0.326
Phlegm	0.86	1.25	0.85	1.09	0.85	1.19	*F*	0.004	0.953
Chest tightness	0.35	0.79	0.37	0.79	0.36	0.79	*F*	0.022	0.882
Breathlessness	1.55	1.59	1.25	1.30	1.43	1.48	*F*	1.859	0.174
Limited activity	0.45	1.09	0.05	0.27	0.30	0.89	*F*	10.307	0.002
Confidence leaving home	0.13	0.59	0.01	0.11	0.09	0.47	*F*	3.189	0.076
Sleeplessness	0.26	0.19	0.64	1.07	0.41	0.93	*F*	8.488	0.004
Energy	1.00	1.38	1.15	1.26	1.06	1.33	*F*	0.620	0.432
CAT total score ≥ 10, n (%)	27	22.5	12	15.4	39	19.7	X^2	1.513	0.273
CAT total score ≥ 18, n (%)	6	5.0	1	1.3	7	3.5	X^2	1.916	0.249

Abbreviations = mMRC: modified Medical Research Council dyspnea scale; CAT: COPD Assessment Test.

mean CAT scores, we observed a non-significant greater proportion of individuals with psychosis reaching CAT threshold for severe COPD symptoms (i.e.: CAT score ≥ 10) (22.5% vs. 15.4%).

Lung function differences between individuals with psychosis and the control group

Individuals with psychosis presented a worse lung function, measured by spirometry, than controls (Table 2). The psychosis group presented lower FEV_1 (3.29 L vs. 3.75 L, $p < 0.001$), FVC (4.25 L vs. 4.72 L, $p = 0.002$), and FEV_1/FVC ratio (0.78 L vs. 0.80, $p = 0.052$) than the control group. Patients also presented significantly lower values of MEF50 and MMEF (3.77 L vs. 4.37 L, $p = 0.002$; and 2.98 L vs. 3.65 L, $p < 0.001$), and worse values of lung diffusion, with lower mean DLCO than controls (6.95 vs. 8.54 mmol/min/kPa, $p < 0.001$) leading to a greater proportion of individuals meeting criteria for poor DLCO (<80%) within the psychosis group (74.1% vs. 39.0%, $p < 0.001$).

Regression analyses and exploratory analyses

Regression analyses (Supplementary material 2) showed psychosis and female sex among the independent predictors of poorer lung function (lower FEV_1 and FVC, and DLCO < 80%). On the contrary, tobacco lifetime habit did not predict any of the lung function outcomes, and the number of tobacco pack-years correlated with lower FVC ($p = 0.027$) and FEV_1 ($p = 0.003$), but not with DLCO < 80% ($p = 0.128$). Benzodiazepines' use did not contribute to lower FVC and FEV_1 or DLCO < 80% (all $p > 0.05$).

Exploratory analyses comparing participants that had never smoked (30 psychosis patients vs. 23 controls) showed (Supplementary material 3) significant differences between groups, where individuals with psychosis presented lower FEV_1 (3.18 L vs. 3.93 L, $p = 0.001$), FVC (4.02 L vs. 4.88 L, $p = 0.002$), MEF50 (3.88 vs. 4.69, $p = 0.038$) and MMEF (3.07 L vs. 3.99, $p = 0.015$) than controls. The psychosis group also presented lower mean DLCO (7.47 vs. 8.76 mmol/min/kPa, $p = 0.068$) leading to a greater proportion of individuals with low (<80%) lung diffusion capacity (69.6% vs. 39.1%, $p = 0.038$).

Discussion

This study shows the greater risk, among individuals with psychosis, of presenting early lung function alterations and respiratory symptoms, that are known to precede chronic lung diseases.

Individual with psychosis in our study presented higher rates and severity of respiratory symptoms, with higher mean score in the Dyspnea-12 scale, and were more likely to score above the clinical severity thresholds of mMRC and CAT scales than the healthy controls. Similarly, Filik and colleagues[15] reported that those patients with schizophrenia presented higher rates of respiratory symptoms than those subjects from the general population.

In line with presenting more respiratory symptoms, psychosis patients showed a poorer lung function, with significantly reduced values for FEV_1 and FVC and a trend towards a lower FEV_1/FVC ratio, that control individuals. These results are in accordance with previous studies.[15–17] Filik and colleagues[15] found that 89.6% of patients with schizophrenia had a lung function lower than predicted for FEV_1, compared with 47% of the general population. Similarly, psychosis has been associated with presenting FEV_1 values lower than 80% of the expected rate.[18] Besides, a greater proportion of participants with psychosis (31.7–35.5%) had either restrictive or obstructive pulmonary impairments compared with the general population (16.3%),[16] in line with a 26% prevalence of restrictive lung dysfunction reported among patients with schizophrenia.[19]

We identified 13 cases (6.3%) of previously undiagnosed COPD. A recent study identified 24% of participants with psychosis meeting criteria for COPD.[18] This bigger rate of undiagnosed COPD in the latter study may be explained by the older mean age of their participants (49 vs. 42 years) compared to ours, since COPD prevalence

Table 2
Lung function measured through spirometry test in patients and controls.

	Patients		Controls		Total			Statistics	
	N = 128		*N* = 79		*N* = 207				
	Mean *N*	SD %	Mean *N*	SD %	Mean *N*	SD %		Value	*p*
FEV_1, L	3.29	0.86	3.75	0.79	3.47	0.86	*F*	14.463	<0.001
FEV_1, % pred.	96.16	15.83	102.92	13.54	98.81	15.30	*F*	9.799	0.002
FEV_1, % improvement	4.33	6.55	3.24	4.04	3.86	5.63	*F*	1.707	0.193
FVC, L	4.25	1.09	4.72	0.98	4.43	1.07	*F*	9.610	0.002
FVC, % pred.	102.57	15.81	105.11	12.45	103.56	14.61	*F*	1.463	0.228
FVC, % improvement	1.29	5.25	0.46	3.38	0.93	4.55	*F*	1.501	0.222
FEV1/FVC	0.78	0.07	0.80	0.06	0.78	0.07	*F*	3.749	0.054
MEF50, L	3.77	1.29	4.37	1.39	4.00	1.36	*F*	9.642	0.002
MEF50, % pred.	93.08	34.20	120.39	34.39	103.76	36.71	*F*	30.543	<0.001
MEF50, % improvement	14.77	19.22	10.71	12.85	13.02	16.85	*F*	2.631	0.107
MMEF, L	2.98	1.05	3.65	1.20	3.27	1.16	*F*	16.063	<0.001
MMEF, % pred.	79.74	26.24	100.49	28.95	88.65	29.23	*F*	25.793	<0.001
MMEF, % improvement	15.13	17.20	12.83	11.11	14.14	14.89	*F*	1.071	0.302
DLCO, mmol/min/kPa	6.95	2.21	8.54	2.36	7.62	2.40	*F*	21.789	<0.001
DLCO, % pred.	71.42	15.27	84.93	14.96	77.04	16.51	*F*	35.816	<0.001
DLCO < 80	80	74.1	30	39.0	110	59.5	X^2	22.992	<0.001
KCO	1.50	0.27	1.49	0.22	1.49	0.25	*F*	0.142	0.707
KCO, % pred.	92.49	17.68	91.27	14.11	91.98	16.26	*F*	0.251	0.617
KCO < 80	29	26.9	14	18.2	43	23.2	X^2	1.894	0.217

Abbreviations: FEV1, forced expiratory volume during the first second; FVC, forced vital capacity; MEF50, maximal expiratory flow at 50% of the forced vital capacity; MMEF, maximal mid-expiratory flow; DLCO, diffusing capacity for carbon monoxide; KCO, carbon monoxide transfer coefficient.

increases with age. Individuals with schizophrenia has increased risk of mortality from COPD at any age above 40 years,[20] with increasing risk across their lifespan. A high proportion of patients with schizophrenia with COPD registered as cause of death, had no previous diagnosis of COPD,[20] supporting the hypothesis that COPD is widely under-diagnosed in schizophrenia.[2,18] In addition, the risk for COPD may be present several years before the break-out of the psychosis. A recent study found that the individuals with schizophrenia had a higher risk of presenting COPD during the 1 year prior to their diagnosis of schizophrenia.[21] And, when compared to other physical co-morbidities in schizophrenia, COPD prevalence presented one of the biggest increase in the 5 years after the diagnosis of the psychotic disorder.[22]

Approximately 22.3% of the global population use tobacco, being the exposure to smoke the main cause of COPD. Tobacco smoking is highly associated with cannabis use,[6] and both of them have been associated with increased respiratory symptoms,[23] impaired lung function and higher COPD prevalence. Cannabis exposure increases COPD prevalence by 0.3% per additional joint-year, however, there is contrary evidence, with reports of short-term cannabis consumption producing bronchodilatation[24] and chronic use being associated with increased FVC.[25] Recently, it has been proposed that schizophrenia may entail by itself a risk for COPD, even beyond the effect of exposure to smoking. Smoking individuals with schizophrenia had a greater risk of COPD than those smoking individuals without schizophrenia,[26] partly due to different smoking patterns such as being heavier smokers or inhaling the smoke deeper than non-psychiatric subjects.[27,28] Similarly, the individuals with psychosis in our study were heavier smokers than those from the control group, with more cigarettes per day and more tobacco packs-year. Despite of this, regression analyses, and exploratory analyses considering only participants that had never smoked, indicated that the observed lung function alterations were not only related to the exposure to tobacco, but also to other factors, including the psychosis itself. In any case, it is necessary to put in place effective tobacco cessation programs for individuals with psychosis.[29,30]

Strengths and limitations

The study has several strengths, being the main one that it evaluates for the first time early alterations of lung function in individuals with psychosis, providing novel results, and performing a complete evaluation of respiratory health of the participants. The subjects included in this study were well-characterized, and controls were matched to psychosis patients by sex, age and smoking-status avoiding the possible confounding effect of these variables on lung function measurements. On the other hand, our study has some limitations. The results should be replicated in other settings and populations. Future prospective studies should be performed to evaluate whether these early alterations lead to COPD or other lung conditions in patients with psychosis.

Conclusions

Individuals with psychosis presented more frequently and more severe respiratory symptoms and a poorer lung function measured through spirometry. These signs and symptoms have been described as early signs preceding the later establishment of chronic lung disorders. Therefore, we can conclude that psychosis patients are at greater risk of presenting early stages of chronic pulmonary disorders.

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Conflict of interest

The authors report no conflicts of interest in their participation in this study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.sjpmh.2023.10.004.

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