Impaired Pulmonary Function in Patients with Psoriasis

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Introduction

Psoriasis is a chronic, T-cell-mediated, inflammatory skin disease characterized by scaly erythematous plaques; the condition affects 1–3% of the population [1]. It has been suggested that psoriasis is associated with chronic obstructive pulmonary disease (COPD) [2, 3]. A population-based cohort study found that psoriasis patients were at a 2.35-fold higher risk of COPD than were controls after 18 months of follow-up [4]. A recent case-control study revealed that COPD is more prevalent in patients with psoriasis than in controls (5.7 vs. 3.6%) [5].

Details of the association between psoriasis and COPD remain unclear. Two principal suggestions have been made. First, a similar chronic inflammatory state may underlie both diseases. Th1 and Th17 cell-mediated immune responses increase the levels of certain cytokines including IL-1, IL-6, IL-8, and TNF-α. Increases in the levels of C-reactive protein (a systemic inflammatory biomarker) and pro-inflammatory cytokines are associated with COPD disease activity. An association of IL-17, which is involved in the Th17 response to psoriasis [6], with COPD has recently been shown. The sputum and bronchoalveolar lavage fluid of COPD patients exhibit increased expression of IL-17 and the other pro-inflammatory cytokines mentioned above [7–9]. The chemokine receptor CXCR2 (an inflammatory marker), which

Keywords
Psoriasis · Chronic obstructive pulmonary disease · Spirometry · Pulmonary function

Abstract

Background: Psoriasis is associated with chronic obstructive pulmonary disease. There is no study on the spirometric pulmonary function testing in patients with psoriasis. Objective: The aim of this study was to compare the spirometric parameters in patients with psoriasis and controls. Methods: Ninety-six patients with psoriasis and 60 sex- and age-matched control subjects were included in this study. Spirometric pulmonary function testing, including percent forced vital capacity (FVC%), percent forced expiratory volume in the 1st second (FEV1%), forced expiratory flow at 25–75% of FVC (FEF25–75%), and FEV1/FVC ratio, was performed in all study subjects. Results: The mean FEV1/FVC ratio and FEF25–75% were significantly lower in the psoriasis patients than in the controls (82.4 ± 6.3 vs. 90.7 ± 10.7, p < 0.001, and 86.7 ± 24.2 vs. 94.8 ± 23.0, p = 0.04, respectively). Both FEV1/FVC ratio and FEF25–75% were significantly associated with the presence of psoriasis (p < 0.001 and p = 0.029, respectively). Conclusion: Psoriasis patients had lower mean FEV1/FVC ratios and FEF25–75% compared with the control subjects. FEV1/FVC and FEF25–75% are independently associated with the presence of psoriasis.
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plays a major role in neutrophil accumulation and angiogenesis at sites of inflammation, is associated with both psoriasis and COPD [10, 11]. An aggravated inflammatory response may damage alveolar epithelial cells, triggering COPD [6–11].

Second, psoriasis and COPD share the same risk factors (smoking, metabolic syndrome and obesity), possibly contributing to an association between the 2 diseases [12]. The fraction of exhaled nitric oxide (FeNO) levels in COPD patients is affected by smoking and disease severity. FeNO elevation in psoriasis patients may increase the risk of COPD [6–11]. A recent study found that FeNO levels were elevated in patients with psoriasis, possibly reflecting subclinical airway inflammation. FeNO returned to normal levels after the psoriasis had been treated [14].

COPD is characterized by chronic inflammation causing airway obstruction and alveolar damage. Spirometry is accurate, reproducible, and reliable when used to diagnose and stage COPD, and it also plays a significant role in the diagnosis of early lung damage. Spirometry is widely used to screen asymptomatic individuals, especially those with lung disease risk factors [15].

This study is the first to determine spirometric parameters in psoriasis patients without evident COPD, compared with healthy controls.

Methods

For further details, see the supplementary materials (for all online suppl. material, see www.karger.com/doi/10.1159/000456032) [16, 17] (Fig. 1).

Results

The demographic and clinical features and spirometric measurements of all subjects are shown in Table 1. The current medications were topical steroids/calcipotriol (n = 48 patients), ultraviolet B treatment (n = 12), biologics (n = 9), methotrexate (n = 5), cyclosporine (n = 3), acitretin (n = 2), and psoralen plus ultraviolet A (n = 2); the remaining 15 patients did not receive treatment.

The mean forced expiratory volume in the 1st second/forced vital capacity (FEV1/FVC) ratio and forced expiratory flow at 25–75% of FVC (FEF25–75%) were significantly lower in psoriasis patients than in controls (82.4 ± 6.3 vs. 90.7 ± 10.7, p < 0.001, and 86.7 ± 24.2 vs. 94.8 ± 23.0, p = 0.040, respectively).

Fig. 1. Flowchart of the study.

Table 1. Demographic, clinical and spirometric features of the subjects

<table>
<thead>
<tr>
<th></th>
<th>Psoriasis patients (n = 96)</th>
<th>Controls (n = 60)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>42.8 ± 13.4</td>
<td>42.4 ± 12.5</td>
<td>ns^a</td>
</tr>
<tr>
<td>Male/female, n</td>
<td>60/36</td>
<td>35/25</td>
<td>ns^b</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>16.7 ± 9.3</td>
<td></td>
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<tr>
<td>PASI</td>
<td>9.5 ± 8.8</td>
<td></td>
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<tr>
<td>Ever smoker, n</td>
<td>51 (53.1)</td>
<td>15 (25)</td>
<td>0.001^b</td>
</tr>
<tr>
<td>Current smoker</td>
<td>40</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>11</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cigarette pack-years</td>
<td>17.7 ± 16.1</td>
<td>13.9 ± 17.8</td>
<td>ns^a</td>
</tr>
<tr>
<td>Intensity, cigarettes/day</td>
<td>17.3 ± 10.0</td>
<td>16.5 ± 12.3</td>
<td>ns^a</td>
</tr>
<tr>
<td>FBS, mg/dL</td>
<td>99.3 ± 15.6</td>
<td>97.4 ± 16.5</td>
<td>ns^a</td>
</tr>
<tr>
<td>Diabetes mellitus, n</td>
<td>4 (4.2)</td>
<td>2 (3.3)</td>
<td>ns^b</td>
</tr>
<tr>
<td>Hypertension, n</td>
<td>12 (12.5)</td>
<td>6 (10)</td>
<td>ns^b</td>
</tr>
<tr>
<td>BMI</td>
<td>28.2 ± 4.1</td>
<td>27.4 ± 4.0</td>
<td>ns^a</td>
</tr>
<tr>
<td>WHR, %</td>
<td>94.2 ± 7.8</td>
<td>93.1 ± 6.2</td>
<td>ns^a</td>
</tr>
<tr>
<td>FEV1, %</td>
<td>92.9 ± 11.6</td>
<td>93.5 ± 11.6</td>
<td>ns^a</td>
</tr>
<tr>
<td>FVC, %</td>
<td>94.9 ± 11.7</td>
<td>90.9 ± 12.7</td>
<td>ns^a</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>82.4 ± 6.3</td>
<td>90.7 ± 10.7</td>
<td>&lt;0.001^a</td>
</tr>
<tr>
<td>FEF25–75%, %</td>
<td>86.7 ± 24.2</td>
<td>94.8 ± 23.0</td>
<td>0.040^a</td>
</tr>
</tbody>
</table>

Figures in parentheses indicate percentages. ns, not significant; PASI, Psoriasis Area and Severity Index; FBS, fasting blood sugar; FEV1, forced expiratory volume in the 1st second; FVC, forced vital capacity; FEF25–75%, forced expiratory flow at 25–75% of FVC; BMI, body mass index; WHR, waist-to-hip ratio. ^a Student t test. ^b χ2 test.

On multiple linear regression analyses, both the FEV1/FVC ratio and FEF25–75% were significantly associated with the presence of psoriasis (p < 0.001, R2 = 0.195, adjusted R2 = 0.190, and p = 0.029, R2 = 0.083, adjusted R2 = 0.071, respectively). No clinical feature, smoking features (cigarette pack-years, smoking intensity [cigarette numbers per day], smoking status) or demographic da-
tum was associated with any spirometric parameter. Neither the type of current therapy nor any previous systemic medication was associated with any spirometric parameter.

On subgroup analysis by smoking status, the FEV$_1$/FVC ratio in non-smoking subjects was significantly lower in psoriasis patients than controls (83.6 ± 6.1 vs. 89.9 ± 9.1; p = 0.002). In smoking subjects, both the mean FEF$_{25-75}$% and the FEV$_1$/FVC ratio were significantly lower in psoriasis patients than controls (85.5 ± 26.6 vs. 102.1 ± 20.2, p = 0.029, and 81.4 ± 6.4 vs. 96.3 ± 13.4, p < 0.001, respectively).

In terms of spirometric findings, of the 96 patients with psoriasis, 3 had early obstructive disease, 2 mildly obstructive disease, 1 moderately obstructive disease, 1 mixed (obstructive and restrictive) disease and 3 restrictive lung disease. Thus, a total of 7 patients (7.3%) had COPD, and the remaining 86 were normal. Of the 60 controls, 2 had early obstructive disease, 1 mixed disease and 6 restrictive lung disease. Thus, a total of 3 (5%) had COPD, and the remaining 51 were normal. There was no significant difference in the COPD rate between the groups (p > 0.05).

**Discussion**

This study shows that spirometric findings including the FEV$_1$/FVC ratio and the mean FEF$_{25-75}$% are reduced in asymptomatic psoriasis patients with COPD, compared with controls. We also showed that both the FEV$_1$/FVC ratio and the FEF$_{25-75}$% are independently associated with psoriasis.

Several case-control and cross-sectional studies have suggested a clear association between psoriasis and COPD [4, 5]. One meta-analysis found that psoriasis patients were at a 1.45-fold increased risk of COPD [2]. Another meta-analysis showed that psoriasis patients were at a greater risk of developing COPD (OR = 1.90); this association was stronger in patients with severe psoriasis (OR = 2.15) [3]. These studies examined medical registry-based databases. Neither medical nor laboratory examinations were used to detect COPD. Also, the spirometric parameters of psoriasis patients without clinically evident COPD were not noted.

The FEV$_1$/FVC ratio is a reliable and important spirometric parameter used to identify both the presence and extent of airway disease [15]. The cut-off value used for COPD diagnosis is 0.70 [16, 17]. Abnormal FEV$_1$/FVC ratios compatible with COPD were evident in 7 (7.3%) of our psoriasis patients. However, the prevalence of COPD did not differ significantly between the groups. We suggest, however, that the significantly reduced FEV$_1$/FVC ratio in psoriasis patients may reflect a tendency toward COPD development in such patients.

COPD is an inflammatory airway disorder associated with airflow limitation in the bronchial tree. The reason why psoriasis patients are predisposed to COPD remains unclear. Several mechanisms have been suggested. Psoriasis and COPD are similar in that both are chronic inflammatory conditions. In both pathologies, T-cell-mediated immunity is elevated, and TNF-α and other pro-inflammatory cytokines including IL-1, IL-6, and IL-8 are secreted. T-cell cytokines including interferon-γ, IL-13, IL-17, and IL-23, chemokines, receptors, adhesion molecules, and proteases play roles in the pathogenesis of both diseases. IL-17 may induce expression of TNF-α, IL-1, and IL-8. IL-8 triggers neutrophil activation and migration of cells to the lung [6, 11]. Psoriasis-related comorbidities including smoking, diabetes mellitus, hypertension, and metabolic syndrome may contribute to COPD development [12]. In our current age- and sex-matched study, the groups were comparable in terms of anthropometric measurements, including body mass index and waist-to-hip ratio, and in terms of clinical features, including the rates of hypertension and diabetes mellitus. However, the number of smokers was significantly higher in the psoriasis group, in strong agreement with the literature [18]. On subgroup analysis, the FEV$_1$/FVC ratio was significantly lower in non-smoking psoriasis patients than in non-smoking controls.

Smoking is a major risk factor for COPD development [19]. In our current study, among the smokers, both the mean FEF$_{25-75}$% and FEV$_1$/FVC ratio were significantly lower in psoriasis patients than in controls. The FEF$_{25-75}$% is the mean forced expiratory airflow between 25 and 75% of the FVC [16, 17] and indicates obstruction of small airways (<2 mm in diameter) [20]. Our findings suggest that smoking may contribute to small airway obstruction in psoriasis patients. The significant relationship between psoriasis and the FEF$_{25-75}$% may also suggest that psoriasis is an independent risk factor for the development of small airway obstruction.

The systemic therapies used by psoriasis patients may affect both their metabolic status and COPD development. However, we found no significant association between the medications taken and spirometric parameters. We failed to detect any significant association between either the severity (the PASI score) or duration of psoriasis and any spirometric parameter.
In conclusion, we have shown that both the FEV$_1$/FVC ratio and FEF$_{25-75}$% are reduced in psoriasis patients. Both of these parameters were independently associated with the presence of psoriasis, which may be an independent risk factor for COPD development. Psoriasis patients should be screened for COPD using spirometry. Preventative approaches, including smoking cessation and therapies, are required to reduce the risk of COPD development in psoriasis patients.

**Ethics Statement**

The study protocol was approved by the ethics committee of our institution. All subjects gave written informed consent.

**Disclosure Statement**

The authors do not declare any conflict of interest.

**References**