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Pulmonary function in patients with eosinophilic chronic rhinosinusitis

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ABSTRACT

Objective: There is a close relationship between upper and lower respiratory tract diseases. Chronic rhinosinusitis patients frequently have lung diseases including asthma and chronic obstructive pulmonary disease. Eosinophilic chronic rhinosinusitis is considered a refractory and intractable subtype of chronic rhinosinusitis. However, there has been no report on pulmonary function in patients with eosinophilic chronic rhinosinusitis. The purpose of this study is to examine the pulmonary function in eosinophilic chronic rhinosinusitis patients and non-eosinophilic chronic rhinosinusitis patients, and evaluate clinical factors associated with the pulmonary function of these patients.

Methods: Pulmonary function was measured in 53 patients with eosinophilic chronic rhinosinusitis with asthma, 58 patients with eosinophilic chronic rhinosinusitis without asthma, and 30 patients with non-eosinophilic chronic rhinosinusitis. The diagnosis of chronic rhinosinusitis was based on the definition in the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2012. Eosinophilic chronic rhinosinusitis was diagnosed based on the Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis (JESREC) scoring system. The relationship between pulmonary function and clinical parameters was assessed. These parameters included radiographic severity of chronic rhinosinusitis, peripheral blood eosinophil percentage, serum total immunoglobulin E level, and eosinophilic infiltration in nasal polyps.

Results: The pulmonary function of the patients with eosinophilic chronic rhinosinusitis was significantly affected. The eosinophilic chronic rhinosinusitis patients had more peripheral airway obstruction as compared to the patients with non-eosinophilic chronic rhinosinusitis.

Conclusion: Our findings indicated latent obstructive lung function changes in the eosinophilic chronic rhinosinusitis patients. The patients with eosinophilic chronic rhinosinusitis should be carefully monitored in order to detect lung diseases.

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1. Introduction

The immuno-physiological characteristics of upper and lower airway diseases are similar, and both sites have similar anatomical structures. The presence of inflammatory upper

airway disease may influence the pathological condition of some lower airway diseases. Significant interaction between the upper and lower airways has been reported in numerous studies, and the concept of unified airways or one airway-one disease has been established [1].

Chronic rhinosinusitis (CRS) is one of the most common upper airway diseases, and is frequently found in patients with asthma and chronic obstructive pulmonary disease (COPD). CRS has been defined as a persistent inflammatory response involving the mucous membranes of the nasal cavity and paranasal sinuses. CRS can be classified into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [2]. A high recurrence rate of CRSwNP after endoscopic sinus surgery has been reported, and a histological study showed that two-thirds of nasal polyps in refractory CRSwNP is characterized by eosinophilic edema [3]. In recent years, refractory CRSwNP with eosinophilic infiltration has been denominated as eosinophilic CRS (E CRS) [4]. It is well known that E CRS frequently coexists with asthma, and E CRS can be regarded as asthma of the upper airway [5].

Because there has not been a universally accepted definition or diagnostic criterion for E CRS, a retrospective study of refractory CRS was conducted by 15 institutions participating in the Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis (JESREC) to diagnose and classify E CRS. They evaluated 1716 patients with refractory CRS, and proposed pre-operative diagnostic criteria for E CRS without the use of biopsy or operational specimens (Table 1). According to an algorithm, the CRS patients were first classified as E CRS or non-E CRS on the basis of the JESREC score; the cutoff value of the score was 11 points. They also counted the number of eosinophils in the mucosal tissues obtained from the nasal polyps or polypoid lesions of the ethmoid cavity during endoscopic sinus surgery, using a microscope at a high-powered field (HPF) (400 \times). Among the patients with a JESREC score of more than 11 points, the patients with 70 or more eosinophils/HPF in mucosa were definitely diagnosed as E CRS [6].

Recent studies showed that CRS patients have subclinical obstructive lung function changes relative to healthy controls [7,8]. Although E CRS patients with asthma have been expected to have obstructive lung function by airway remodeling, to the

best of our knowledge, there has been no study of pulmonary function in patients with E CRS without asthma diagnosed by the JESREC study criteria. This study aimed to examine the pulmonary function in E CRS patients with asthma, E CRS patients without asthma, and non-E CRS patients, and evaluate clinical factors associated with the pulmonary function of these patients.

2. Materials and methods

2.1. Subjects

A total of 141 CRSwNP patients who received endoscopic sinus surgery at ***** University or ***** Hospital were recruited. The diagnosis of CRS was based on the definition in the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2012 [2]. The patients were divided by the JESREC scoring system, and definitely diagnosed as E CRS by pathological examination (70 or more eosinophils/HPF). One hundred and eleven E CRS patients were divided into two groups (E CRS with asthma and E CRS without asthma). Comorbidity of asthma and aspirin-exacerbated respiratory disease was determined from medical records [9]. We diagnosed the CRSwNP patients who had bilateral nasal polyps and fewer than 70 eosinophils infiltrating a nasal polyp as non-E CRS [6]. Thus, three groups of participants were enrolled in this study: E CRS with asthma (n = 53), E CRS without asthma (n = 58), and non-E CRS without asthma (n = 30). The patients who received lung surgery or administration of an oral steroid and the patients with nasal neoplasm were excluded from this study.

The smoking status was examined, and the patients who had been smoking on preoperative inspection were defined as current smokers. The Brinkman index (number of cigarettes per day \times smoking years) was calculated for all smokers

Informed consent was obtained from all enrolled subjects. This study was conducted in compliance with the Helsinki Declaration of 1975, as revised in 2008, and was approved by the Institutional Review Board of Okayama University (approval number: RINRI-877) and Kagawa Rosai Hospital (approval number: RINRI-28-1).

2.2. Pulmonary function

A pulmonary function test was performed with the Chestac-9800 spirometer (Chest MI, Tokyo, Japan). The following parameters were measured: percentage of predicted vital capacity (%VC); ratio of predicted forced expiratory volume in 1 s to forced vital capacity (FEV₁%); percentage of predicted peak expiratory flow (%PEF); percentage of predicted mean forced expiratory flow between 25 and 75% of forced vital capacity (%FEF₂₅₋₇₅); percentage of predicted maximal expiratory flow rate at 50% of vital capacity (%V₅₀); percentage of predicted maximal expiratory flow rate at 25% of vital capacity (%V₂₅); and ratio of maximal expiratory flow rate at 50% of vital capacity to maximal expiratory flow rate at 25% of vital capacity (V₅₀/V₂₅).

Table 1

JESREC score criteria for the diagnosis of eosinophilic chronic rhinosinusitis.

Factor	Score
Disease side: both sides	3
Nasal polyp	2
CT shadow: ethmoid \geq maxillary	2
Eosinophils of peripheral blood	
Greater than 2% and less than or equal to 5%	4
Greater than 5% and less than or equal to 10%	8
Greater than 10%	10
Diagnosis	JESREC score
E CRS	\geq 11
Non-E CRS	\leq 10

E CRS: eosinophilic chronic rhinosinusitis.

JESREC: Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis.

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