Japanese Journal of Gastroenterology and Hepatology

Research Article

Spirometry Results of Reflux Esophagitis in Asthma Reflux Esophagitis in Asthma

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Received: 10 May 2020

Accepted: 04 June 2020

Published: 09 June 2020

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1. Abstract

1.1. Background: The symptoms of asthma and gastroesophageal reflux disease are similar making it difficult to distinguish. Diagnosing Gastroesophageal Reflux Disease (GERD) is complex, as it frequently presents with other pulmonary disease or conditions. Asthma has often been associated with gastroesophageal reflux disease. This study aimed at a better understanding of the association between the conditions. The purpose of this study is to compare spirometry results with endoscopic positive Erosive Reflux Disease group (ERD) and without GERD group who have asthma.

1.2. Methods: A total of 169 consecutive subjects (aged 20-90 years) underwent spirometry and upper endoscopy with asthma diagnosed first in pulmonology department and then looked for the presence of reflux esophagitis, or with reflux esophagitis identified first in gastroenterology department and then looked for the presence of asthma.

1.3. Results: A total number of 169 patients in asthma, with ERD group (n=100) and without GERD group (n=69) completed pulmonary function tests and esophagogastroduodenoscopy. In univatiate analysis, age (*P*=0.000), body mass index (BMI) (*P*=0.000), and pulmonary function tests (*P*=0.000) were significant in asthma with ERD group. The multivariate logistic regression analysis showed that asthmatic patients having ERD have 1.2 times the risk of poor pulmonary function (FEV1/FVC) (pooled odds ratio [OR] 1.215, 95% confidence interval [CI] 1.1-1.4) and 5.4 times the risk of obesity (BMI ≥25) (pooled odds ratio [OR] 5.381, 95% confidence interval [CI] 1.2-25.2).

1.4. Conclusions: This study highlights that the spirometry results severity is considerably higher ERD in asthma patients. Physicians should look out for reflux symptoms in asthma patients and consider evaluation with upper endoscopy when necessary. Likewise, asthmatics presenting with gastrointestinal symptoms may need consultation and evaluation for GERD.

2. Abbreviations: GERD: Gastroesophageal reflux disease; ERD: Erosive reflux disease; NERD: Non erosive reflux disease; BMI: Body mass index

3. Keywords: Spirometry; Gastroesophageal reflux disease; Reflux esophagitis; Asthma

4. Introduction

Gastroesophageal reflux disease (GERD) is a chronic functional disease with a worldwide increasing prevalence of 9-33% [1]. Gastroesophageal reflux disease (GERD) is caused by the reflux of gastric acid or food into the esophagus, which causes heartburn or reflux. It is one of the most common reasons for patients in gastroenterology clinics, and also decreased quality of life due to troublesome symptoms, increased the medical cost burden. The current paradigm of GERD diagnosis depends on the identification of esophageal mucosal lesions or annoying symptoms due to gastroesophageal reflux. GERD is classified into endoscopic positive Erosive Reflux Disease (ERD) and endoscopic negative non-erosive reflux disease (NERD) (2). The criteria, the putative standard

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for diagnosis GERD, take into account the frequency of GI symptoms and other factors esophagogastroduodenoscopy and Proton-Pump Inhibitor (PPI) therapy [2-4].

Asthma, another disease known to lower the quality of life, is usually associated with GI conditions such as GERD and eosinophilic esophagitis [5, 6]. The prevalence of GERD in asthma has been raising worldwide, 30-90% [7, 8]. The association between GERD and asthma was first identified in the 1960s (9); however, the question of how the two diseases are related is still controversial [10, 11].

The aim of this study was to investigate pulmonary function results in asthma with endoscopic positive erosive reflux disease in patients of pulmonology and gastroenterology department of internal medicine.

5. Material and Methods

5.1. Patients

The study included 169 patients consisted of both esophagogastroduodenoscopies (EGD) in gastroenterology clinic and pulmonary function tests in pulmonology clinics from January 2010 to December 2019 performed in a single tertiary hospital. Patients were divided into 2groups; the first group identified asthma and looked for the presence of Erosive Reflux Disease (ERD), the second included ERD and looked for the presence of asthma. Patient self-report symptom questionnaire and esophagogastroduodenoscopy were used for assessment of GERD. All patients were performed the following tests: chest X-rays or lung CT scan, body mass index (BMI), esophagogastroduodenoscopy. This study was retrospective observational design, waived written informed consent and approved by the Institutional Review Board (IRB No. B-2005-612-103).

5.2. Pulmonary Function Tests

Lung function was measured with a PC-based spirometry analyzer using a precalibrated MasterScreen Pneumo (Vyaire Medical, Mettawa, IL, US) according to the criteria of the American Thoracic Society and the European Respiratory Society for standardization [12]. The test was performed in a standing position by trained technicians. The information was examined and compared against criteria metrics for acceptability, reproducibility, and quality control. All of the lung functions were obtained and recorded; forced expiratory volume during the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio. All of these pulmonary functions are reported as percent predicted values.

The American thoracic society (ATS) describes asthma according to the following definition: "A condition with history of discrete attacks of wheezing, coughing or dyspnea and increase in forced expiratory volume in one-second (FEV_1) of 20% from baseline after bronchodilator administration or decrease in FEV_1 of 20% after methacholine bronchoprovocation." [13].

5.3. Gastroesophageal Reflux Disease: Endoscopic Positive ERD

Esophagogastroduodenoscopy was conducted on all study subjects by expert gastroenterologists (>10 years of endoscopic performance) certified by the Korean Society of Upper gastrointestinal endoscopy using conventional white light video scopy (GIF-H260 or GIF-H290; Olympus, Aizu, Japan). The grade of ERD seen on upper gastrointestinal endoscopy was classified from A to D according to the Los Angeles (LA) classification [14]. All endoscopic images of ERD were stored as pictures on the hospital network, namely PACS system and all gastroenterologists participated in the meeting who agreed the consensus of ERD findings.

6. Statistical Analysis

Data were analyzed using SPSS software (version 25.0, SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as mean ± standard deviation whereas the categorical variables, as absolute values and percentages. Medians and ranges are presented for continuous variables and percentages for categorical variables. Differences between variables were assessed by χ^2 tests. A logistic regression analysis was used to examine the relationships between asthma and various clinical factors, including lung function measures such as forced expiratory volume in 1 s (FEV1) and forced vital capacity (FCV). To estimate the odds ratios (OR) for age, gender, body mass index, FEV1, and FVC, these factors were regarded as continuous variables. A P value < 0.05 was considered to indicate statistical significance.

7. Results

7.1. Baseline Characteristics of the Asthmatic Subjects

The baseline clinical and demographic characteristics of the asthmatic subjects are presented in (Table 1). The subjects were categorized according to the presence of ERD based on endoscopic LA classifications and the mean age was 68.9 ± 13.2 years with ERD and 59.7 ± 16.3 years without GERD (P<0.001).

In the univariate analysis, gender did not differ ERD vs. control in asthmatic patients. Age, body mass index (BMI) were significantly higher in subjects with ERD (P<0.001). Pulmonary function test parameters, including FVC, FEV1, FEV1/FVC were significantly lower in subjects with ERD (P<0.001).

(Table 2) showed the ERD characteristics according to the pulmonary function tests by age and gender, based on endoscopic exams, by LA classification, 100 subjects were found to have ERD: 76 in LA-A, 24 in LA-B.

7.2. Associations of GERD in Asthmatics with the Components of Pulmonary Function Test

The results of the multivariate logistic regression analyses for pulmonary function and GERD in asthmatic patients are shown in (Table 3). After adjusting for age, high FVC, low FEV1 and high

FEV1/FVC were associated with a high risk of GERD in asthmatics (OR = 1.148, 95 % confidence interval [CI] 1.031–1.278, *P*=0.012, OR=0.877, 95 % CI 0.791–0.971, *P*=0.012, and OR = 1.215, 95 % CI 1.059–1.394, *P*=0.005, respectively).

Obesity (BMI ≥25) was significantly associated with a high risk of GERD in asthma subjects (OR = 5.381, 95 % CI 1.151-25.146, *P*=0.032).

Table 1: Demographics and baseline characteristics of Asthmatic subjects

variables	Control(n=69)	ERD (n=100)	*P* value
Age (years) (mean ± SD)	59.7 ± 16.3	68.9 ± 13.2	0
Male/Female, n, %	23/46	44/56	0.192
BMI (kg/m^2) (mean ± SD)			0
< 23, n, (%)	42	42	
23 ≤ < 25, n, (%)	16	33	
≥ 25, n, (%)	11	25	
Pulmonary Function Tests			0. 000
FVC(%) (mean ± SD)	92.9 ± 16.6	94.6 ± 13.5	
FEV1(%) (mean ± SD)	93.3 ± 20.4	93.3 ± 20.7	
FEV1/FVC (mean ± SD)	71.2 ± 11.8	73.4 ± 9.8	
BMI: body mass index FVC: functional vital capacity, FEV 1: forced expiratory volume in 1 s			

Table 2: ERD characteristics according to the pulmonary function tests by age and gender

Variables	LA-A	LA-B
	(n = 76)(%)	(n = 24)(%)
Gender		
Male	35 (45.0)	14 (66.7)
Female	41 (55.0)	10 (33.3)
Age (years)		
< 40	1 (1.7)	0
40-49	5 (5.0)	0
50-59	10 (11.7)	3 (11.1)
60-69	19 (26.7)	3 (11.1)
70-79	22 (28.3)	10 (44.4)
≥ 80	19 (26.6)	8 (33.3)
Pulmonary function test		
FVC(%)	92.4±17.6	97.9±8.8
FEV1(%)	93.3± 21.8	92.3 ± 23.3
FEV1/FVC	71.9 ± 11.0	66.2 ± 16.0
ERD: erosive reflux disease		

Table 3: Pulmonary function indices are predictors of ERD in Asthmatic people

		Adjusted Odds Ratio	95% Confidence Interval	*P* value
ERD	Age	1.03	0.947-1.122	0.488
	BMI< 23			
	23 ≤ < 25	3.286	0.756-14.280	0.112
	≥ 25	5.381	1.151-25.146	0.032*
	FVC	1.148	1.031-1.278	0.012*
	FEV1	0.877	0.791-0.971	0.012*
	FEV1/FVC	1.215	1.059-1.394	0.005*
*p<0.05 FVC: functional vital capacity, FEV 1: forced expiratory volume in 1 s				

8. Discussion

This present study demonstrated that low pulmonary function, which was represented by increased FVC or decreased FEV1 or increased FEV1/FVC, is associated with high risk of GERD in asthmatic patients. Until now, most studies have reported the relationships of GERD and respiratory disorders including asthma. However, recent studies have evaluated no relation with GERD and asthma, still controversial. Some studies suggest that GERD severity is associated with impairment of gas exchange (DLCO) and central airway affection (R20) on impulse oscillometry. This may be due to micro aspiration of gastric acid or fluid into the airways [15, 16].

Patients with GERD and coexisting asthma have been shown to have lower pulmonary functions. However, there have also been contradictory studies that showed no association between GERD and pulmonary conditions such as asthma, chronic bronchitis, chronic obstructive pulmonary disease or interstitial lung disease [17-20].

Estimates for the prevalence of GERD in asthma range from 47% to 53%, based on troublesome symptoms only or on pH monitoring and endoscopy, respectively [19, 21-24]. In controls, the prevalence of GERD in Korea is 7.1% [25]. The prevalence of asthma in Korea is estimated to be 3.9% [26]. In Korea, asthma morbidity and mortality in Korea are increasing and also the prevalence of GERD. Results of the large European Pro GERD study showed that 4.8% of GERD patients may have asthma [7]. A similar study in North America showed that asthma (9.3%) is the third most common extra-esophageal symptom of GERD [8]. In this study, gender was not related having GERD with asthma. However, univariate analysis showed that age, BMI were relatively associated with having GERD with asthma compared to without GERD in asthma. Some findings suggest that GERD is related to lung function [27, 28]. Schan et al. reported that intraesophageal acid infusions caused a decrease in peak expiratory flow rate without micro aspiration. The possible underlying mechanism is the broncho constriction mediated by vagal nerve after distal esophageal acid perfusion test in four groups: asthma with GERD group, asthma without GERD group, non-asthmatic GERD, and healthy group.

The current study does have strengths. This is the first study to diagnose by both departments of internal medicine specialist, in pulmonologists and gastroenterologists. The atypical symptoms of GERD are very difficult to diagnose by distinguishing themselves from asthma. In addition, all gastroscopies were performed by highly experienced endoscopists and obtained high-quality data. It does minimize the intra-observer variation. To complement the reproducibility of the lung function test data, well-trained one examiner performed. This study is a retrospective design with long period 10 years.

However, this study has some limitations. First, it was a cross-sectional, observational rather than a cohort study. Second, 24hr pH monitoring was performed to some subjects under gastroenterologist's decision. Despite these limitations,

the present study observed a relationship between lung function and GERD in asthma individuals.

9. Conclusions

In the present study, GERD showed a positive correlation with FEV1 and FVC in asthmatics, which is consistent with the findings of a previous experimental study. Pulmonary function tests are common, easy, and safe during routine medical health check-ups. When results on a pulmonary function test are lower than expected, pulmonary problem is first concerned. However, reductions in pulmonary function may reflect a GERD combined conditions in asthmatics. Our findings suggest that reduced pulmonary function could be used as a positive tool with which to predict the presence of GERD mixed in asthmatics.

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