European Journal of Radiology 84 (2015) 2671–2678

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Expiratory air trapping during asthma exacerbation: Relationships with clinical indices and proximal airway morphology

Thitiporn Suwatanapongched[a,*], Chayanin Thongprasert[a], Siwaporn Lertpongpiroon[b,1], Dittapol Muntham[c,2], Sumalee Kiatboonsri[b]

[a] Division of Diagnostic Radiology, Department of Diagnostic and Therapeutic Radiology, Mahidol University, Bangkok, Thailand
[b] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mahidol University, Bangkok, Thailand
[c] Section of Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

ARTICLE INFO

Article history:
Received 5 June 2015
Received in revised form 21 August 2015
Accepted 8 September 2015

Keywords:
Asthma
Asthma exacerbation
CT
Air trapping
Bronchial collapse
Bronchial wall thickness

ABSTRACT

Objectives: To semi-quantitatively assess expiratory air trapping (AT_{exp}) and structural changes in the proximal airways in asthma during asthma exacerbation (AE) and to explore the relationships among AT_{exp}, clinical indices, and proximal airway changes.

Methods: Paired inspiratory-dynamic forced expiratory CT scans of 36 asthmatics (30 women, 6 men; mean age, 49.2 ± 18.9 years) performed during AE were retrospectively reviewed for the total AT_{exp} score (summed scores [extent grading (0–4) × pattern grading (1–4)] of the twelve lung zones), morphologic parameters and expiratory bronchial collapse (BC_{exp}) of the proximal airways. The relationships of the score with clinical indices and proximal airway morphology (normalized by body surface area [BSA]) were analyzed. A p value of <0.05 was considered statistically significant.

Results: The mean total AT_{exp} score was 110.1 ± 43.4 (range, 8–166). It was higher in the lower zones and in patients older than 60 years, having BMI of <27.5 kg/m^2, and peak expiratory flow rate (PEFR) of <60% predicted. Correlation existed between the score and age ($r = 0.331$), BMI ($r = -0.375$), BSA ($r = -0.442$), % predicted PEFR ($r = -0.332$), right upper lobe apical segmental bronchus (RB1)-wall area (WA)/BSA ($r = 0.467$), %RB1-WA ($r = 0.395$), and RB1-bronchial wall thickness (BWT)/BSA ($r = 0.378$). The score showed no correlation with BC_{exp} and other morphologic bronchial parameters. Area under receiver-operating-characteristic curve 0.724 (95% CI) showed that the score of 110 could discriminate patients with PEFR of <60% predicted from those with PEFR of ≥60% predicted.

Conclusion: During AE, there was a high prevalence of extensive AT_{exp} which was correlated with patient's age, BMI, BSA, AE severity and RB1 morphology but not correlated with BC_{exp}.

1. Introduction

Despite a deeper understanding and greater knowledge of the pathology and management of asthma, the disease remains inadequately controlled on currently available therapies in some patients [1]. Frequent asthma exacerbation (AE) accounts for high personal and social healthcare burdens and poses the risk of long-term respiratory impairment and disability. In recent decades, there is evidence supporting the contribution of small airway dysfunction (SAD) to pathophysiology and clinical manifestations of asthma [1–3]. SAD has been found to be associated with a particular and more severe phenotype of asthma. However, it remains unclear whether there is a link between AE severity and SAD. Novel asthma therapies targeting small airways might provide clinical benefit to asthmatics who have prevalent SAD during AE [1,2,4–7].

At present, assessment of SAD remains relatively challenging. Commonly employed spirometric tests, for example, generally reflect function of the large airways and loss of lung elastic recoil [1]. Impulse oscillometry (IOS) is gaining greater importance as a non-invasive test for assessment of both peripheral and proximal airway dysfunction in adult and pediatric asthma but only provides physiologic data [1]. Most approaches to biologic assessment of the small

---

* Corresponding author at: Division of Diagnostic Radiology, Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, 270 Rama VI Road, Toong Phayathai, Ratchathewi, Bangkok 10400, Thailand. Fax: +66 2201 1297.

E-mail addresses: ratrspoom@yahoo.com (T. Suwatanapongched), airtikky652@hotmail.com (C. Thongprasert), siwaporn083@gmail.com (S. Lertpongpiroon), dittapol.mun@gmail.com (D. Muntham), sml_kt2@yahoo.com (S. Kiatboonsri).

[1] Current address: Yala Hospital, Mueng Yala, Yala Province 95000, Thailand.

[2] Current address: Section for Mathematics, Faculty of Science and Technology, Rajamangala University of Technology Suvarnabhumi, Phranakhon Si Ayutthaya Province 13000,Thailand.

http://dx.doi.org/10.1016/j.ejrad.2015.09.008
0720-048X/

airways are still under investigation and are not easy to perform in routine clinical practice [1,6].

Evidence in recent decades suggest that CT scan has emerged as a useful non-invasive tool for assessment of SAD that is not readily captured by physiologic measures [2–4,6,8,9]. CT has also been used to define asthmatic phenotypes and to help identify a group of individuals who might be at risk of severe disease. The cardinal CT sign of peripheral or small airway obstruction is generally defined by the presence of expiratory air trapping (AT_{exp}), i.e., an abnormal retention of air in all or parts of the lungs at any stage of expiration [2,9,10]. On CT, AT_{exp} can be quantified by the visual score [11] or by the densitometric analysis [3,12]. Recently, computer-assisted 3-dimensional analysis of the bronchial tree structure has enabled the quantification of morphology of the proximal airways [1–4,8,13–15]. However, such dedicated software is currently unavailable in many countries, including Thailand, which limits their use from a research perspective. Quantitative CT assessment of airway abnormalities in asthmatics on the basis of visual estimation and manual measurement has been shown to be effective and has provided strong correlations between visually scored AT_{exp} and morphologic changes in the proximal airways with pulmonary function [9–11,16].

Although there is extensive research on CT assessment of airway abnormalities in asthma [1–4,8,13–15], CT data on SAD and morphologic changes in the proximal airways during AE are still limited. It is largely unknown in what proportion of asthmatics with AE will have AT_{exp} and whether AT_{exp} will be related to the structural changes in the proximal airways. Therefore, this study was undertaken to quantify the presence of AT_{exp} during AE and the structural changes in the proximal airways, e.g., expiratory collapse of the proximal bronchi (BC_{exp}), on the basis of paired inspiratory and dynamic forced expiratory CT scans. Our secondary aim was to assess the relationships among airway abnormalities and clinical indices. By measuring the amount of AT_{exp} and changes in the proximal airways, CT may help clarify the complexity of AE, identify the at-risk asthma phenotype, and evaluate the possibility of individualized therapeutic decision during AE [1–4].

2. Materials and methods

2.1. Patients studied

This retrospective study included 36 asthma patients (aged ≥18 years) presenting with AE between May 2012 and December 2012. All of them had been previously enrolled in a prospective study approved by the Local Ethic Committee on Human Rights related to research involving human subjects at our institution. All of the patients provided written informed consent for the aforementioned prospective study and for future retrospective studies. All the patients fulfilled diagnostic criteria of asthma published by Global Strategy for Asthma Management and Prevention, GINA 2012 update (Available from: http://www.ginasthma.org/) [17]. None of the female patients were pregnant (based on date of last menstrual period and a urine pregnancy test).

The patient's demographic data (sex, age, body height, body weight), smoking habit, status of asthma and severity of AE were reviewed. Peak expiratory flow rate (PEFR) was used as the primary determinant of AE severity, based on recommendations issued in GINA 2012 [17].

2.2. Chest CT examination

2.2.1. Scanning protocol

All CT scans were performed on a 64-detector CT scanner (Aquillion TM/CX, Toshiba Medical Systems, Japan) installed in our Emergency Department.

Prior to CT scanning, all the patients received bronchodilators for initial treatment for their AE until their clinical status was stable and they were able to lie supine. The patient was then transferred to the CT room and peak flow measurement was obtained approximately 5 min prior to the CT scanning using a Mini-Wright peak flow meter (Clement Clarke International Ltd., United Kingdom).

Each patient was taught how to perform full suspended inspiration (taking a deep breath and holding it throughout the scan) and how to perform forced dynamic expiration (taking a deep breath and blowing it out without holding throughout the scan).

Helical CT scanning was performed in the craniocaudal direction for both end-inspiratory and dynamic forced expiratory images from the lung apices to approximately 1 cm below the right hemidiaphragm dome. The craniocaudal scanning length varied depending on the patient's lung height. The images were acquired with 64 detectors × 0.5 mm collimation, a gantry rotation time of 0.5 s, and a pitch factor of 1.484 (helical pitch/number of slices scanned in a single rotation). End-inspiratory CT scan was obtained first using a tube voltage of 120 kVp and a tube current of 120–200 mA (adjusted to the patient's body mass index (BMI)). Dynamic forced expiratory CT scanning was subsequently obtained and was coordinated with the onset of the patient's expiratory effort, using a tube voltage of 120 kVp and a tube current of 30 or 40 mAs. Images were reconstructed by using low (FC08) and high (FC52) spatial frequency algorithms and Quantum Denoising Software with a section thickness of 2 mm. The iterative reconstruction algorithm was not used. Images were transferred to the picture archiving and communications system (Synapse version 4.2.300; Fujifilm Medical Systems, USA), based on DICOM conformance, and were viewed on a high-resolution LED monitor (Coronis Fusion 6MP LED (MDCC-6130), Barco limited, Hong Kong). Image interpretation was performed using window width of 1600 Hounsfield units (HU) and window level of -550 HU.

2.2.2. CT assessment

A chest radiologist with 17 years of experience in chest CT and a senior radiology resident, both of whom were blinded to other clinical data, separately reviewed all CT images in a randomized order to decrease the potential for bias. The final results reached by consensus were used for statistical analysis.

2.2.2.1. Visual assessment of expiratory air trapping (AT_{exp}). The dynamic forced expiratory and end-inspiratory CT images from each examination were compared for evidence of air trapping at the 6 following anatomic levels: level 1, the crossing left brachiocephalic vein; level 2, the mid aortic arch; level 3, the carina; level 4, 1 cm below the origin of the right bronchus intermedius; level 5, the right inferior pulmonary vein; and level 6, 1 cm below the right hemidiaphragm dome.

AT_{exp} was considered present when a lung region exhibited a less-than-normal increase in attenuation and a lack of change in volume during expiration when compared to the appearance of that lung region on the paired end-inspiratory CT images [18,19]. The extent and pattern of AT_{exp} were adapted from previous studies [10,18,19]. The extent of AT_{exp} (Fig. 1) was graded on a 5-point scale: 0, no visible AT_{exp}; I, 1–25%; II, 26–50%; III, 51–75%; and IV, 76–100% of the cross-sectional area of each lung zone [18,19]. The pattern of AT_{exp} in each lung zone (Fig. 1) was categorized as (1) small areas of air trapping corresponding to one or two adjacent secondary pulmonary lobules; (2) three or more areas of lobular air trapping; (3) subsegmental air trapping; and 4, diffuse air trapping (contiguous area of air trapping larger than subsegmental in distribution) [18,19].

We scored the extent and pattern of AT_{exp} in each of the 12 lung zones. The AT_{exp} score in each zone was subsequently derived by multiplying the extent grading with pattern grading in each lung