Allergology International 69 (2020) 626–627

Contents lists available at ScienceDirect

Allergology International

journal homepage: http://www.elsevier.com/locate/alit

Letter to the Editor

Annual changes in forced oscillation technique parameters correlate with FEV1 decline in patients with asthma, COPD, and asthma-COPD overlap

Dear Editor,

Evaluation of airflow limitation using spirometry is important for determining the disease severity and therapeutic effect in asthma and chronic obstructive pulmonary disease (COPD). Patients with asthma-COPD overlap (ACO) and late-onset asthma are susceptible to rapid deterioration of forced expiratory volume in 1 s (FEV_1), and have a very poor prognosis with respect to lung function decline, hospital admissions, and survival.[1] The distribution of airway stenosis and the physiological mechanism of airflow limitation may differ between patients with asthma and COPD. However, spirometry may not always distinguish the pathological and physiological mechanisms of airflow limitation in each disease.[2] Further, in advanced stages of COPD and ACO, spirometry, which requires forced expiration, places a burden on the patient. The forced oscillation technique (FOT) is a method for noninvasively measuring respiratory system resistance (Rrs) and reactance (Xrs) during tidal breathing. It provides information that cannot be obtained using spirometry.[3] Studies have also indicated the usefulness of the FOT for managing patients with obstructive lung diseases, including asthma, COPD, and ACO. We recently reported that the FOT may be useful for identifying ACO.[4] However, only a few studies have focused on the differences in the relationship between annual changes in FOT parameters and spirometry among patients with asthma,[5] COPD,[6] and ACO. Herein, we aimed to investigate the relationship between the annual changes in FOT parameters and those in FEV_1 in patients with asthma, COPD, and ACO.

This retrospective, observational study recruited adult patients with asthma or COPD from a previously published study.[7] The relevant ethics committee approved the study protocol (SGH 15-01-55). The patients with asthma and COPD fulfilled the definition of the Global Initiative for Asthma[8] and the Global Initiative for Chronic Obstructive Lung Disease guidelines,[9] respectively. ACO was diagnosed using our previously reported criteria at recruitment.[4] All patients underwent the FOT and spirometry on the same day, at least four times over 3 years (i.e., at least one time per year) before recruitment. The details are provided in the Supplementary Methods.

This study included 75 adult patients with ACO (n = 29), asthma (n = 23), and COPD (n = 23) (Supplementary Fig. 1). At recruitment, patients with COPD had lower FEV_1 and Xrs at 5 Hz (X5) and higher resonant frequency (Fres) and low-frequency reactance area (ALX) than did patients with asthma and ACO (Supplementary Table 1). The annual changes in FEV_1 and FOT are shown in Supplementary Table 2. The annual changes in X5, Fres, and ALX (in both whole-breath and Δ) were more significantly different in patients with COPD than in those with asthma and ACO. However, no significant intergroup differences were observed in the annual changes in FEV_1, Rrs at 5 Hz (R5), Rrs at 20 Hz (R20), and R5-20.

We evaluated the relationship between the annual changes in FOT parameters and FEV_1 using the Spearman rank correlation coefficient (Table 1). The annual changes in FOT parameters correlated with those in FEV_1 in each group; the changes in whole-breath correlated moderately and those in Δ correlated weakly. R5, R20, R5-20, Fres, and ALX showed a negative correlation and X5 showed a positive correlation with the annual changes in FEV_1. We also evaluated whether the annual changes in FOT parameters could predict rapid declines in FEV_1 (>30 mL/year) using the receiver operating characteristics (ROC) analysis. Twelve (52%) patients with asthma, 12 (52%) with COPD, and 11 (38%) with ACO showed rapid declines in FEV_1. These declines in FEV_1 could be predicted from the annual changes in FOT parameters, and all parameters exhibited high areas under the ROC curve (AUCs) (Table 2). Among the Rrs parameters, the annual change in R5 had the largest AUC in patients with asthma, COPD, and ACO. Among the Xrs parameters, the best predictor for rapid declines in FEV_1 was the annual change in ALX in patients with ACO and asthma, and the annual change in Fres in patients with COPD (Table 2).

We made two important clinical observations. First, the annual changes in FOT parameters correlated significantly with those in FEV_1 in patients with ACO and those with isolated asthma and COPD. Second, rapid declines in FEV_1 could be predicted by the annual changes in FOT parameters in patients with asthma, COPD, and ACO. Predicting the annual changes in FEV_1 using the FOT can reduce the invasiveness in assessing disease severity and treatment efficacy in daily clinical practice.

Recently, we showed that the changes in FEV_1 over 5 years were related to those in Xrs in COPD.[6] In this study, the annual changes in both Xrs and Rrs showed good correlations with those in FEV_1. This suggests that the annual changes in FEV_1 in COPD are closely related to the airway diameter represented by Rrs and elasticity or inertia of the thorax and lungs represented by Xrs. In patients with asthma, high correlation coefficients were observed between FEV_1 and R5, X5, and ALX. This result agreed with those of Kamada *et al.*[5] However, FOT parameters in asthma had weaker correlation coefficients than did those in COPD. The annual changes in FEV_1 in asthma may be due to the involvement of other pathophysiological factors that have a low correlation with FOT parameters. In ACO, the annual changes in FEV_1 correlated with those in both Rrs and Xrs parameters. Moreover, among FOT parameters, R5 had the highest

Peer review under responsibility of Japanese Society of Allergology.

https://doi.org/10.1016/j.alit.2020.03.013

Table 1
Correlations of annual changes in FOT parameters with annual change in FEV_1.

	ACO		Asthma		COPD	
	rho	P value	rho	P value	rho	P value
R5 (cmH_2O/L/s/y)						
Whole-breath	−0.619	<0.001	−0.506	0.015	−0.595	0.003
Δ	−0.034	0.861	−0.354	0.098	−0.565	0.006
R20 (cmH_2O/L/s/y)						
Whole-breath	−0.500	0.006	−0.478	0.022	−0.607	0.003
Δ	0.185	0.335	−0.221	0.309	−0.510	0.014
R5−R20 (cmH_2O/L/s/y)						
Whole-breath	−0.587	0.001	−0.353	0.099	−0.575	0.005
Δ	−0.198	0.303	−0.419	0.048	−0.380	0.074
X5 (cmH_2O/L/s/y)						
Whole-breath	0.435	0.019	0.526	0.011	0.697	<0.001
Δ	−0.468	0.011	−0.262	0.227	−0.498	0.017
Fres (Hz/y)						
Whole-breath	−0.483	0.009	−0.496	0.017	−0.681	<0.001
Δ	−0.132	0.495	−0.235	0.279	−0.383	0.072
ALX (cmH_2O/L/s × Hz/y)						
Whole-breath	−0.527	0.004	−0.537	0.009	−0.596	0.003
Δ	−0.408	0.029	−0.193	0.377	−0.544	0.008

ACO, asthma-COPD overlap; ALX, low-frequency reactance area; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; Fres, resonant frequency; rho, Spearman's rank correlation coefficient; R5 and R20, respiratory system resistance at 5 Hz and 20 Hz; X5, respiratory system reactance at 5 Hz.

Table 2
ROC curve analyses for rapid declines in FEV_1 (>30 mL/year).

	ACO		Asthma		COPD	
	AUC	(95% CI)	AUC	(95% CI)	AUC	(95% CI)
R5 (cmH_2O/L/s/y)						
Whole-breath	0.85	(0.69, 1.00)	0.76	(0.55, 0.96)	0.78	(0.59, 0.98)
Δ	0.61	(0.39, 0.82)	0.72	(0.49, 0.94)	0.86	(0.70, 1.00)
R20 (cmH_2O/L/s/y)						
Whole-breath	0.77	(0.59, 0.96)	0.70	(0.47, 0.92)	0.77	(0.58, 0.97)
Δ	0.54	(0.30, 0.78)	0.64	(0.40, 0.88)	0.77	(0.58, 0.97)
R5−R20 (cmH_2O/L/s/y)						
Whole-breath	0.82	(0.65, 1.00)	0.68	(0.44, 0.92)	0.77	(0.57, 0.97)
Δ	0.64	(0.42, 0.86)	0.76	(0.54, 0.98)	0.77	(0.56, 0.97)
X5 (cmH_2O/L/s/y)						
Whole-breath	0.75	(0.57, 0.93)	0.76	(0.56, 0.96)	0.81	(0.63, 0.99)
Δ	0.75	(0.57, 0.93)	0.68	(0.46, 0.91)	0.79	(0.59, 0.98)
Fres (Hz/y)						
Whole-breath	0.79	(0.62, 0.96)	0.71	(0.48, 0.94)	0.82	(0.64, 0.99)
Δ	0.64	(0.43, 0.85)	0.72	(0.50, 0.94)	0.77	(0.57, 0.98)
ALX (cmH_2O/L/s × Hz/y)						
Whole-breath	0.83	(0.68, 0.98)	0.81	(0.62, 1.00)	0.73	(0.52, 0.95)
Δ	0.75	(0.57, 0.93)	0.70	(0.49, 0.92)	0.80	(0.61, 0.98)

ACO, asthma-COPD overlap; ALX, low-frequency reactance area; AUC, area under the receiver operating characteristics curve; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; Fres, resonant frequency; R5 and R20, respiratory system resistance at 5 Hz and 20 Hz; X5, respiratory system reactance at 5 Hz.

correlation coefficient. This finding differed from that obtained for asthma and COPD. These results and our previous report[4] demonstrating the usefulness of the FOT for identifying ACO suggested that patients with ACO can be characterized using FOT parameters. Finally, FOT parameters could predict the rapid declines in FEV_1 in all three diseases, and the pathophysiological changes measured using the FOT in these three diseases may be similar.

The limitations of this retrospective study include a small sample size, uneven sample time interval, and variations in treatment even within the same disease group. Nevertheless, our findings suggest that the FOT, which is a noninvasive method, may help assess the treatment course in asthma, COPD, and ACO.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.alit.2020.03.013.

Conflict of interest

Toshihiro Shirai received honorarium from AstraZeneca. Other authors have no conflict of interest to declare.

Yuko Tanaka [a,b,*], Keita Hirai [c,d], Hiromasa Nakayasu [a], Kanami Tamura [a], Toshihiro Masuda [a], Shingo Takahashi [a], Hirofumi Watanabe [a,b], Yutaro Kishimoto [a], Kyouhei Ohishi [a], Mika Saigusa [a], Taisuke Akamatsu [a], Akito Yamamoto [a], Satoru Morita [a], Kazuhiro Asada [a], Toshihiro Shirai [a]

[a] *Department of Respiratory Medicine, Shizuoka General Hospital, Shizuoka, Japan*
[b] *Second Division, Department of Internal Medicine, Hamamatsu University School of Medicine, Japan*
[c] *Department of Clinical Pharmacology and Genetics, School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, Japan*
[d] *Laboratory of Clinical Pharmacogenomics, Shizuoka General Hospital, Shizuoka, Japan*

* Corresponding author. Second Division, Department of Internal Medicine, Hamamatsu University School of Medicine, 1-20-1 Handayama, Hamamatsu, 431-3192, Japan.
E-mail address: yukotana@hama-med.ac.jp (Y. Tanaka).

References

1. Lange P, Colak Y, Ingebrigtsen TS, Vestbo J, Marott JL. Long-term prognosis of asthma, chronic obstructive pulmonary disease, and asthma-chronic obstructive pulmonary disease overlap in the Copenhagen City Heart study: a prospective population-based analysis. *Lancet Respir Med* 2016;**4**:454–62.
2. Kanda S, Fujimoto K, Komatsu Y, Yasuo M, Hanaoka M, Kubo K. Evaluation of respiratory impedance in asthma and COPD by an impulse oscillation system. *Intern Med* 2010;**49**:23–30.
3. Shirai T, Kurosawa H. Clinical application of the forced oscillation technique. *Intern Med* 2016;**55**:559–66.
4. Shirai T, Hirai K, Gon Y, Maruoka S, Mizumura K, Hikichi M, et al. Forced oscillation technique may identify asthma-COPD overlap. *Allergol Int* 2019;**68**:385–7.
5. Kamada T, Kaneko M, Tomioka H. The relationship between respiratory system impedance and lung function in asthmatics: a prospective observational study. *Respir Physiol Neurobiol* 2017;**239**:41–5.
6. Akita T, Shirai T, Akamatsu T, Saigusa M, Yamamoto A, Shishido Y, et al. Long-term change in reactance by forced oscillation technique correlates with FEV1 decline in moderate COPD patients. *Eur Respir J* 2017;**49**:1601534.
7. Hirai K, Shirai T, Suzuki M, Akamatsu T, Suzuki T, Hayashi I, et al. A clustering approach to identify and characterize the asthma and chronic obstructive pulmonary disease overlap phenotype. *Clin Exp Allergy* 2017;**47**:1374–82.
8. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention 2018. Available from: www.ginasthma.org. [Accessed 23 December 2019]. Date last revised: March 29, 2018.
9. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Available from: www.goldcopd.org. [Accessed 23 December 2019]. Date last revised: November 20, 2017.

Received 10 January 2020
Received in revised form 4 March 2020
Accepted 20 March 2020
Available online 30 April 2020