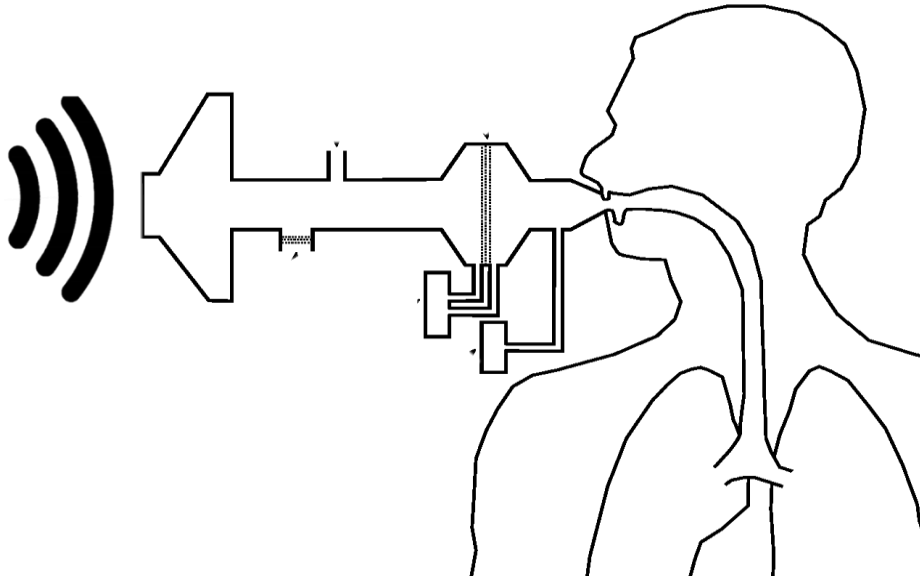
2019台灣胸腔暨重症加護醫學會
2019 Taiwan Society of Pulmonary and Critical Care Medicine

Small Airway Dysfunction by Impulse Oscillometry in Symptomatic Patients with Preserved Pulmonary Function

VGHTPE Hwa-Yen Chiu, MD



Symptomatic Patients with Preserved Pulmonary Function

SYMPTOMS

cough

sputum

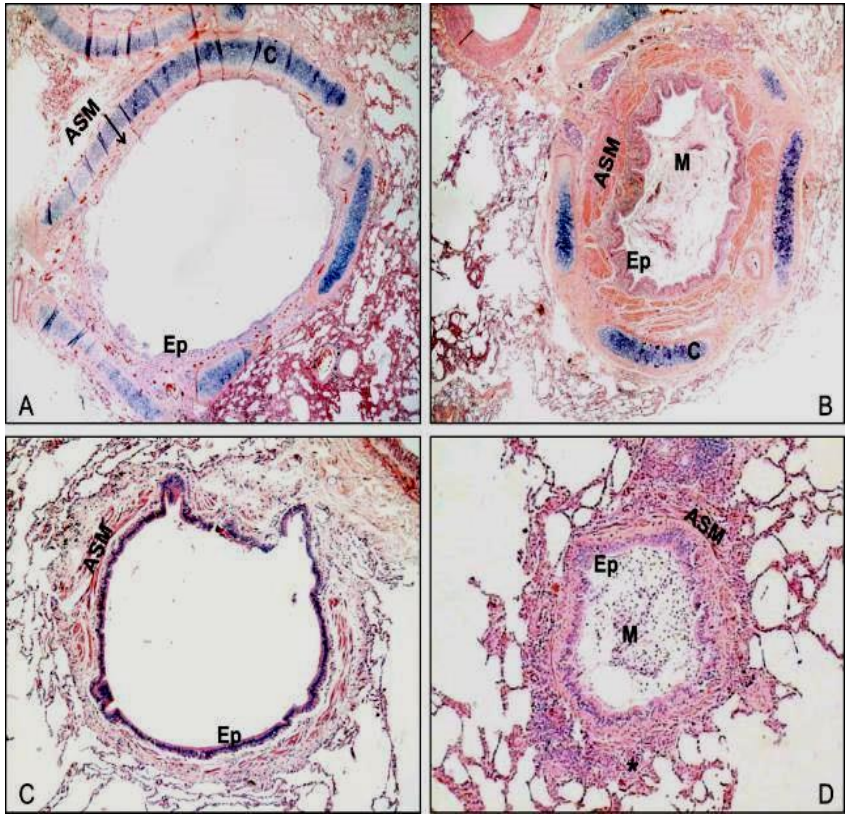
dyspnea

Small airway involvement in BOTH Asthma and COPD

Normal Asthma

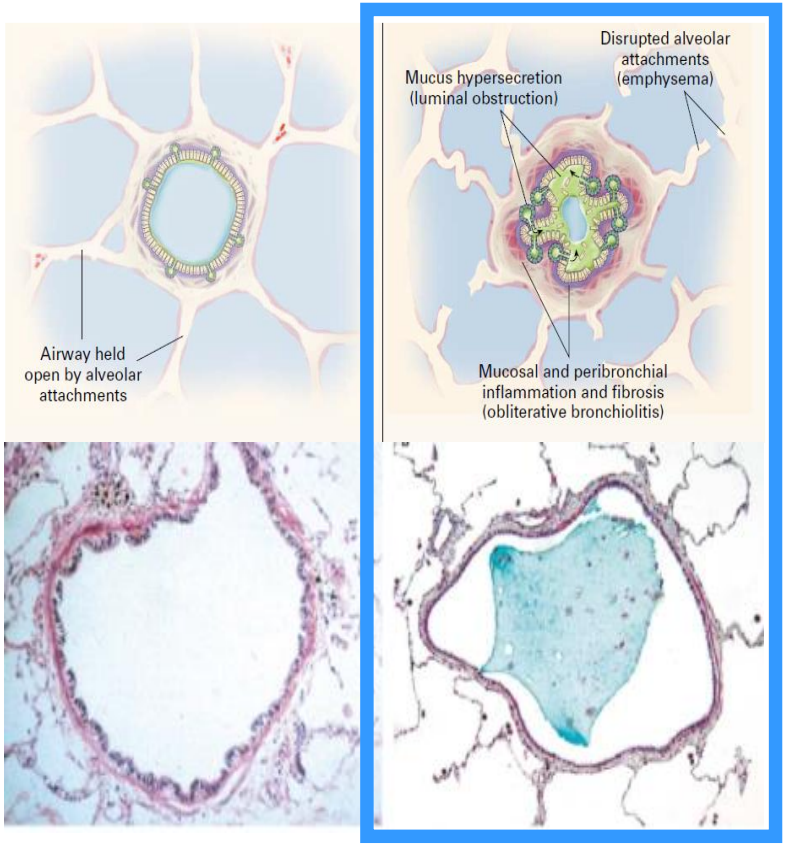
Central

Peripheral



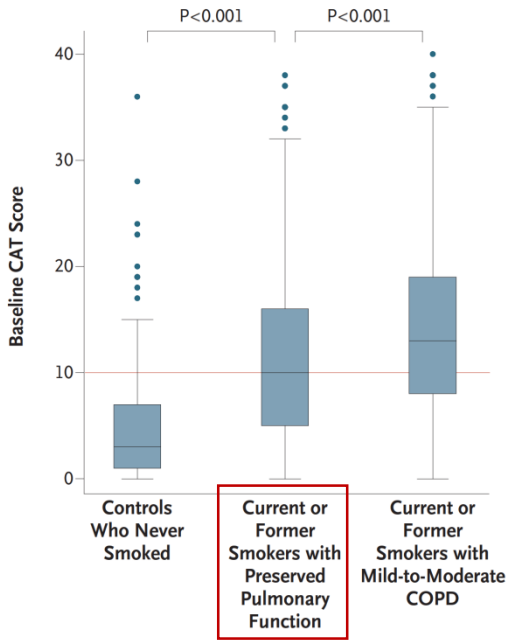
Mauad et al. J Allergy Clin Immunol 2007
Tulic & Hamid, CHEST 2003; 123:348s-355s

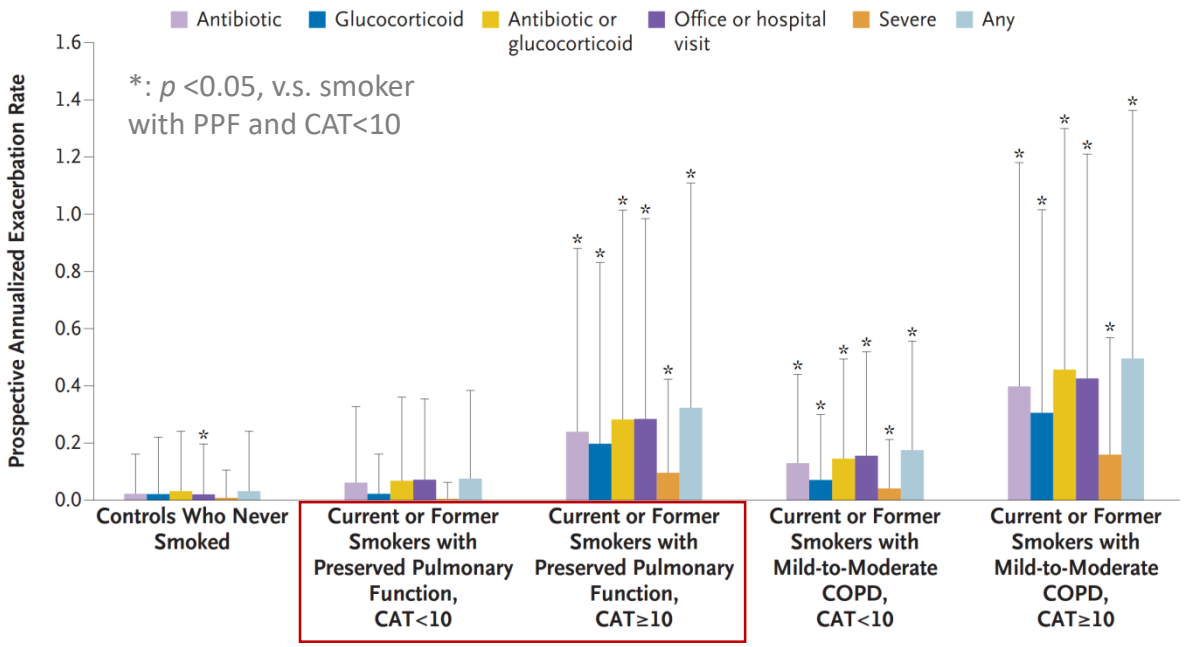
Normal **COPD**



Barnes, NEJM 2000; 343:269-280
Hogg, Lancet 2004; 364:709-721

Symptomatic Smokers with Preserved Pulmonary Function





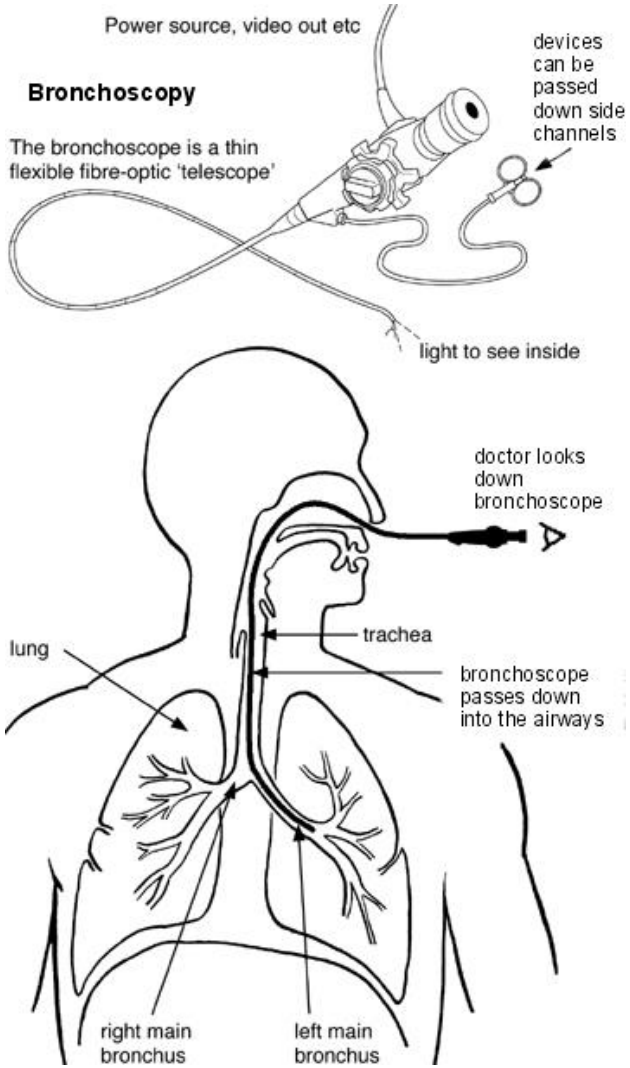
- More respiratory symptoms (50%)
- More respiratory exacerbations
- Greater limitation of activity,
- Slightly lower FEV1, FVC, and IC

- Greater airway-wall thickening without emphysema on HRCT
- 42% used BDs and 23% used ICS (off-labeled use)

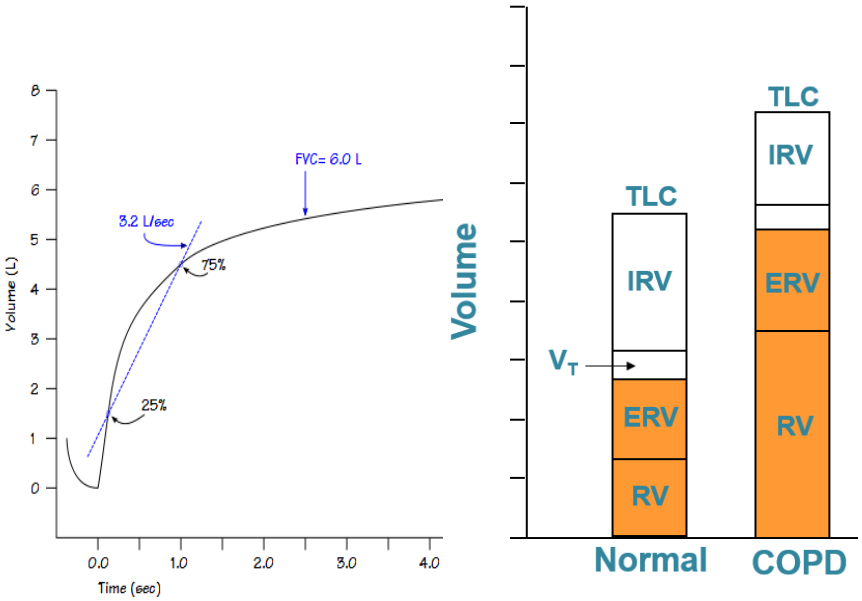
CAT: COPD assessment test; FEV1: forced expiratory volume at 1st second
FVC: forced vital capacity; IC: inspiratory capacity; HRCT: high resolution computer tomography; BDs : bronchodilators; ICS: inhaled corticosteroid

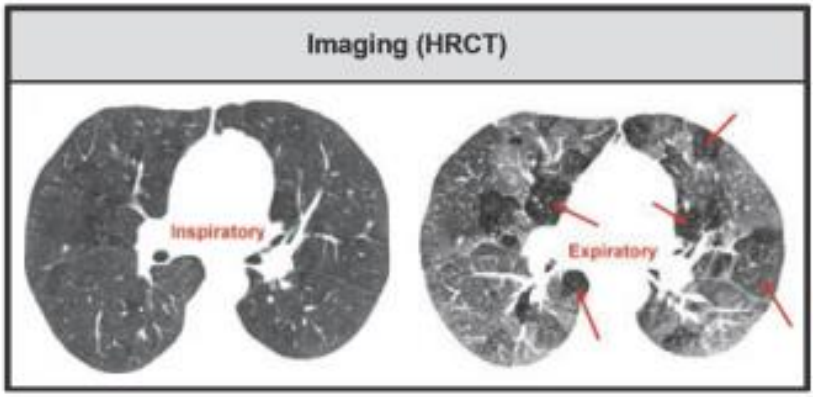
Woodruff PG et al, N Engl J Med. 2016 May 12;374(19):1811-21

Measurements of Small Airway Dysfunction



Wagner EM, Am Rev Respir Dis. 1990 Mar;141(3):584-8

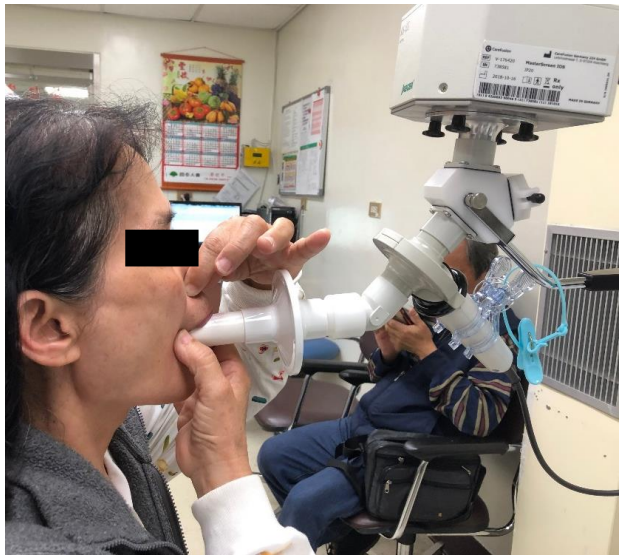




Cottini et al. Asthma Research and Practice (2015) 1:13

Kraft et al, Chest 2006 and AJRCCM 2001

Impulse Oscillometry System (IOS)



- Much greater sensitivity to detect **peripheral airways** obstruction
- Patient needs to perform **simple tidal breathing** maneuvers
  - Children and elderly
  - Patient with MV
  - Patient during sleep

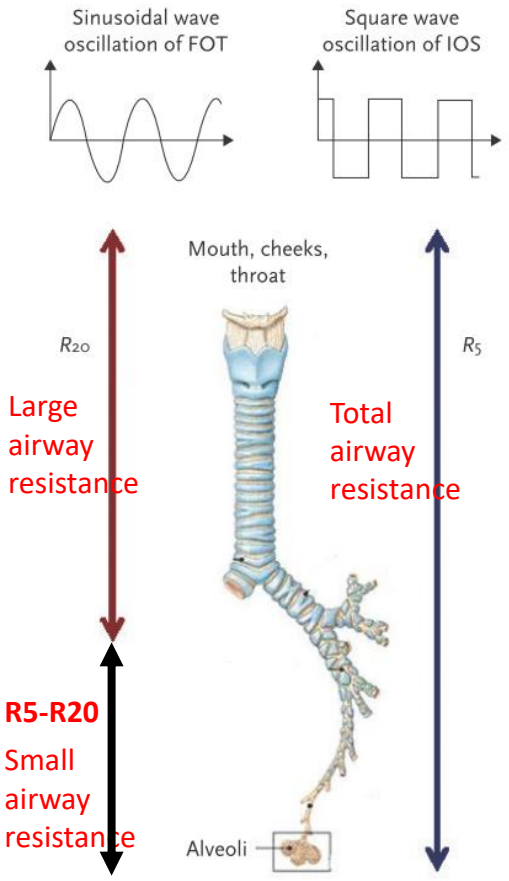


Figure 1
Type of sound waves in FOT and IOS and distances travelled by sound waves of different frequencies.

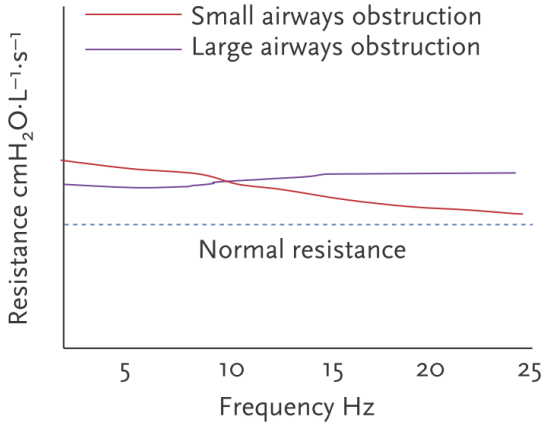


Figure 2
Respiratory resistance versus frequency.

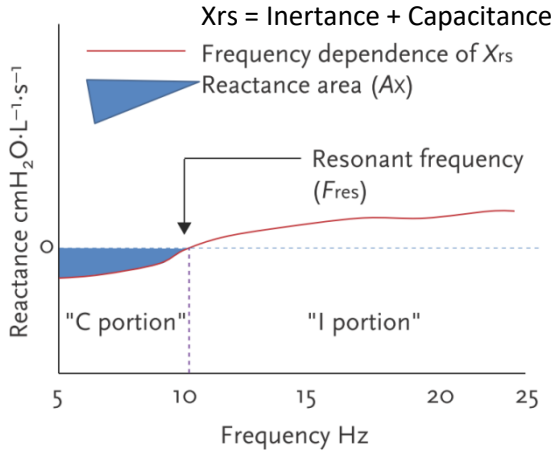
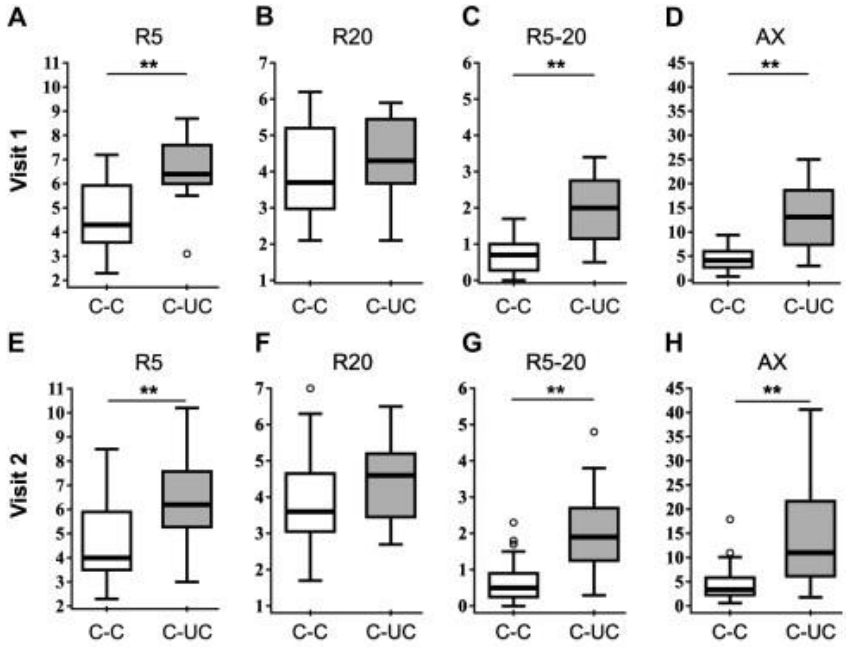


Figure 3
Reactance values in a healthy subject showing the "C" (compliance) and "I" (inertance) portions of reactance, area of reactance (Ax) and resonant frequency (Fres).

Breathe (Sheff). 2015 Mar;11(1):57-65.

Application of IOS/FOT

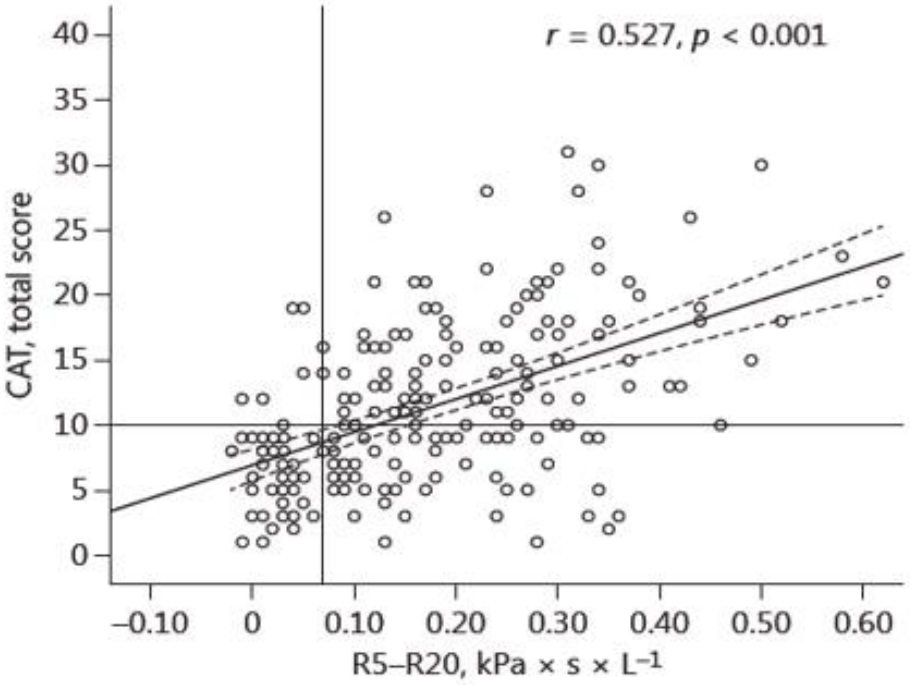
IOS parameters and asthma control



J Allergy Clin Immunol. 2013 Mar;131(3):718-23.

R5-R20 v.s. SGRQ

R5-R20 v.s. CAT score



N= 202

Haruna et al. BMC Pulmonary Medicine 2010
Crisafulli E. et al., Respiration. 2017;93(1):32-41.

Enrollment

From March 1, 2017 to July 31, 2017

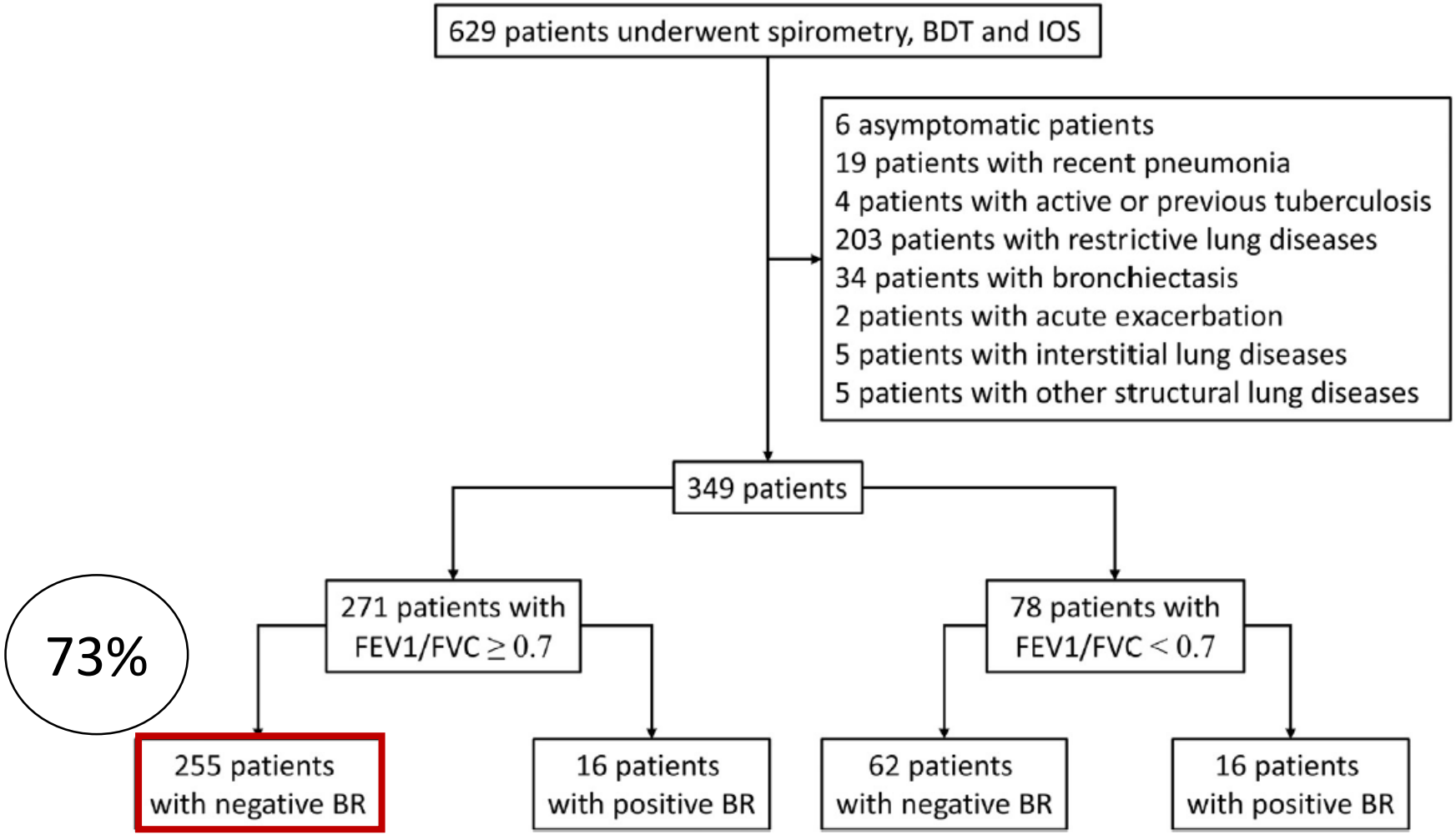


FIGURE 1. Enrollment of study population. *BDT*, Bronchodilator test.

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Demographics

Characteristic	Nonobstructive group ($FEV_1/FVC \geq 0.7$)		Obstructive group ($FEV_1/FVC < 0.7$)		*P* value
	BR (−) (N = 255)	BR (+) (N = 16)	BR (−) (N = 62)	BR (+) (N = 16)	
Age (y)	56 (41-64)	59 (51-70)	67 (62-75)	63 (56-80)	<.01
Height (cm)	165 (158-170)	160 (157-167)	162 (157-167)	164 (159-173)	.19
Weight (kg)	65 (56-75)	68 (57-77)	63 (57-70)	62 (54-78)	.62
BMI (kg/m^2)	24.3 (21.7-26.8)	25.8 (23.1-28.1)	24 (21.9-26.1)	22.8 (20.7-26.4)	.30
Sex: male, n (%)	133 (52.2)	7 (43.8)	44 (71.0)	11 (68.8)	.03
Smoking, n (%)	87 (34.1)	4 (25)	32 (51.6)	9 (56.3)	.02
Symptoms, n (%)					
Wheeze	34 (13.3)	0 (0)	3 (4.8)	3 (18.8)	.10
Cough	180 (70.6)	12 (75)	42 (67.7)	10 (62.5)	.85
Sputum	120 (47.1)	8 (50)	36 (58.1)	7 (43.8)	.46
Dyspnea	119 (46.7)	5 (31.3)	42 (67.7)	9 (56.3)	.01
Pulmonary function test					
FEV_1/FVC	0.82 (0.78-0.86)	0.77 (0.72-0.78)	0.63 (0.56-0.66)	0.58 (0.52-0.65)	<.01
FEV_1 (L/s)	2.70 (2.16-3.22)	1.95 (1.76-2.35)	1.84 (1.54-2.13)	1.70 (1.3-2.08)	<.01
FEV_1 (% predicted)	99.87 ± 12.36	86.86 ± 14.26	80.12 ± 14.4	72.82 ± 16.97	<.01
FVC (L/s)	3.30 (2.68-3.95)	2.66 (2.25-3.15)	3.11 (2.54-3.58)	2.97 (2.67-3.47)	<.01
FVC (% predicted)	96.1 (88-104.2)	86.4 (82.6-91.5)	97.1 (90.6-107.9)	89.6 (84.6-101.2)	<.01
PEF (% predicted)	90.6 ± 17.78	75.53 ± 12.53	64.93 ± 17.72	55.31 ± 10.55	<.01
$FEF_{25\%-75\%}$ (% predicted)	82.09 ± 25.65	59.34 ± 28.39	29.89 ± 9.3	30.69 ± 13.68	<.01
$FEF_{50\%}$ (% predicted)	96.54 ± 30.17	66.83 ± 25.14	35.62 ± 12.03	34.39 ± 17.43	<.01
IOS					
R_5 [kPa/(L/s)]	0.36 (0.3-0.45)	0.36 (0.32-0.5)	0.41 (0.34-0.53)	0.41 (0.34-0.52)	.03
$R_5 - R_{20}$ [kPa/(L/s)]	0.07 (0.04-0.11)	0.07 (0.02-0.14)	0.11 (0.08-0.17)	0.14 (0.1-0.18)	<.01
X_5 [kPa/(L/s)]	−0.1 (−0.13 to −0.07)	−0.11 (−0.16 to −0.05)	−0.15 (−0.21 to −0.11)	−0.19 (−0.22 to −0.15)	<.01
F_{res} (Hz)	14.17 (10.66-16.72)	15.87 (11.72-18.19)	17.35 (15.46-21.06)	18.17 (17.08-21.39)	<.01
AX (kPa/L)	0.4 (0.2-0.7)	0.56 (0.23-1.29)	0.9 (0.54-1.66)	1.15 (0.94-1.83)	<.01
$FEF_{25\%-75\%}$ <65% predicted, n (%)	64 (25.1)	10 (62.5)	62 (100)	16 (100)	<.01

BMI, Body mass index; $FEF_{50\%}$, forced expiratory flow at expiration of 50% of FVC; *PEF*, peak expiratory flow.

The data are described using mean (SD) for normally distributed variables and median (interquartile range) for nonnormally distributed variables. *P* value is for 1-way ANOVA for 4 groups.

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Characteristics of healthy controls and symptomatic patients (N =43)

Characteristic	Healthy controls (N = 43)	Symptomatic patients with PPF and SAD (N = 43)	*P* value
Age (y)	55 (42-63)	5 7 (46-66)	0.47
Sex: male, n (%)	21 (48.84)	21 (48.84)	1
Height (cm)	165 (159-172)	164 (156-170)	0.39
Smoking, n (%)	0 (0.00)	10 (23.26)	<0.01
FEV_1 (% predicted)	101.24 (94.12-108.52)	86.89 (82.05-92.25)	<0.01
FVC (% predicted)	101.14 (89.56-107.99)	92.94 (85.16-101.23)	0.02
$FEF_{25\%-75\%}$ (% predicted)	83.47 (72.65-100.07)	53.55 (45.71-59.26)	<0.01
$R_5 - R_{20}$ [kPa/(L/s)]	0.07 (0.04-0.09)	0.09 (0.05-0.15)	0.03
X_5 [kPa/(L/s)]	−0.09 (−0.13 to −0.07)	−0.11 (−0.14 to −0.08)	0.11
F_{res} (Hz)	13.14 (10.53-14.9)	15.33 (13.36-18.92)	<0.01
AX (kPa/L)	0.34 (0.16-0.57)	0.49 (0.28-1.05)	<0.01

The data are described using mean (SD) for normally distributed variables and median (interquartile range) for nonnormally distributed variables.
*Matched by age and sex.

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Correlation between spirometry and IOS parameters in patients with PPF (N=255)

	FEV_1 (%pred)		FVC (%pred)		PEF (%pred)		$FEF_{25-75\%}$ (%pred)		$FEF_{75\%}$ (%pred)		$FEF_{50\%}$ (%pred)		$FEF_{25\%}$ (%pred)	
	r	p value	r	p value	r	p value	r	p value	r	p value	r	p value	r	p value
R5-R20	-.14*	.03	-.21**	<.01	-.11	.10	-.13*	.04	.26**	<.01	-.15*	.01	-.18**	<.01
X5	.13*	.03	.11	.07	.11	.09	.15*	.02	-.14*	.03	.09	.15	.08	.22
Fres	-.22**	<.01	-.27**	<.01	-.11	.11	-.21**	<.01	.06	.34	-.20**	<.01	-.17**	<.01
AX	-.16**	<.01	-.22**	.<01	-.14*	.04	-.18**	<.01	.22**	<.01	-.16*	.01	-.17**	<.01

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Cutoff values of SAD-related IOS parameters in patients with pPFT (N=255)

	Cutoff value	Sen (%)	Spe (%)	LR(+)	LR(-)	AUC	Youden index	p value
R5-R20	>0.07	62.5	59.7	1.55	0.63	0.62	0.22	<0.01
X5	<-0.12	46.9	77.5	2.08	0.69	0.64	0.24	<0.01
Fres	>14.14	75.0	57.9	1.78	0.43	0.69	0.33	<0.01
AX	>0.44	65.6	61.9	1.72	0.56	0.67	0.28	<0.01

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Incidence of SAD

-- defined by $FEF_{25-75\%}$ and IOS parameters

	$FEV_1/FVC \geq 0.7$		$FEV_1/FVC < 0.7$	
	BDR(-) (N=255)	BDR(+) (N=16)	BDR(-) (N=62)	BDR(+) (N=16)
$FEF_{25-75\%}$<65%pred, N (%)	64(25.1)	10(62.5)	62(100)	16(100)
R5-R20>0.07, N (%)	127(49.8)	7(43.8)	50(80.6)	14(87.5)
X5<-0.12, N (%)	74(29.0)	7(43.8)	39(62.9)	14(87.5)
Fres >14.14Hz, N (%)	128(50.2)	11(68.8)	54(87.1)	15(93.8)
AX >0.44, N (%)	111(43.5)	10(62.5)	51(82.3)	15(93.8)

50.2% patients with PPF
had SAD defined by Fres>14.14Hz

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

The Journal of Allergy and Clinical Immunology:
In Practice

Original Article

Small Airway Dysfunction by Impulse Oscillometry in Symptomatic Patients with Preserved Pulmonary Function

Hwa-Yen Chiu, MD[a,*], Yi-Han Hsiao, MD[a,b,c,*], Kang-Cheng Su, MD[a,b,c], Yu-Chin Lee, MD[c,d], Hsin-Kuo Ko, MD[a,b,c], and Diahn-Warng Perng, MD, PhD[a,c] *Taipei and New Taipei City, Taiwan*

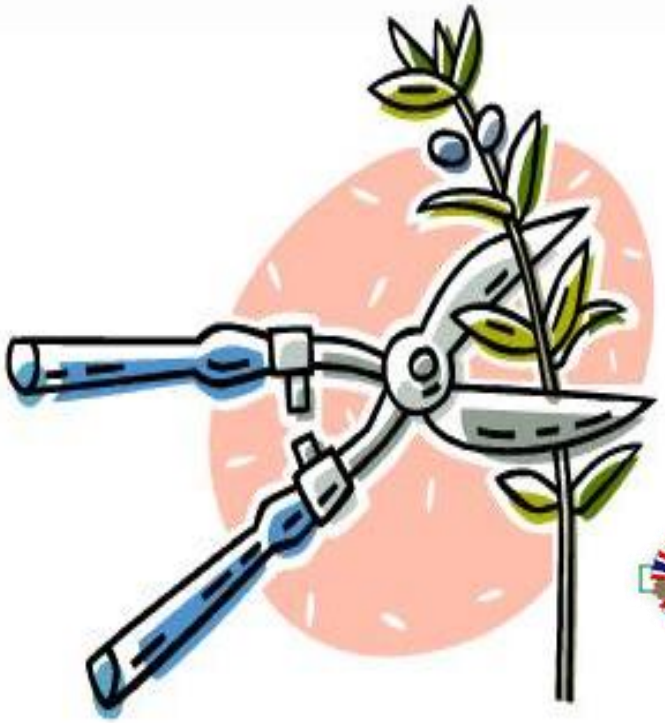
What is already known about this topic? Compared with forced expiratory flow between 25% and 75%, impulse oscillometry (IOS) is an effort-independent utility to detect small airway dysfunction.

What does this article add to our knowledge? This study provides reference values of IOS parameters, and the IOS parameter resonant frequency is more sensitive than forced expiratory flow between 25% and 75% to detect small airway dysfunction.

How does this study impact current management guidelines? Patients with respiratory symptoms and preserved pulmonary function may have small airway dysfunction that can be diagnosed with IOS in addition to spirometry.

107-V-B-038

Thanks for your attention



Parameter	SAD (−)	SAD (+)	*P* value
$FEF_{25\%-75\%} < 65\%$ predicted	191	64	
Wheeze, n (%)	23 (12.0)	11 (17.2)	.30
Cough, n (%)	136 (71.2)	44 (68.8)	.71
Sputum, n (%)	88 (46.1)	32 (50)	.59
Dyspnea, n (%)	86 (45.0)	33 (51.6)	.36
$FEF_{50\%} < 60\%$ predicted	226	29	
Wheeze, n (%)	28 (12.4)	6 (20.7)	.22
Cough, n (%)	160 (70.8)	20 (69.0)	.84
Sputum, n (%)	103 (45.6)	17 (58.6)	.19
Dyspnea, n (%)	103 (45.6)	16 (55.2)	.33
$R_5 - R_{20} > 0.07$ [kPa/(L/s)]	128	127	
Wheeze, n (%)	11 (8.6)	23 (18.1)	.03
Cough, n (%)	86 (67.2)	94 (74.0)	.23
Sputum, n (%)	51 (39.8)	69 (54.3)	.02
Dyspnea, n (%)	55 (43.0)	64 (50.4)	.24
$X_5 < -0.12$ [kPa/(L/s)]	181	74	
Wheeze, n (%)	17 (9.4)	17 (23)	<.01
Cough, n (%)	124 (68.5)	56 (75.7)	.25
Sputum, n (%)	77 (42.5)	43 (58.1)	.02
Dyspnea, n (%)	83 (45.9)	36 (48.6)	.69
$F_{res} > 14.14$ Hz	126	128	
Wheeze, n (%)	7 (5.6)	27 (21.1)	<.01
Cough, n (%)	87 (69)	93 (72.7)	.53
Sputum, n (%)	51 (40.5)	69 (53.9)	.03
Dyspnea, n (%)	54 (42.9)	65 (50.8)	.21
AX > 0.44 kPa/L	142	111	
Wheeze, n (%)	13 (9.2)	21 (18.9)	.02
Cough, n (%)	101 (71.1)	78 (70.3)	.88
Sputum, n (%)	59 (41.5)	61 (55)	.03
Dyspnea, n (%)	63 (44.4)	56 (50.5)	.34

Respiratory symptoms and SAD detected by different parameters in patients with PPF

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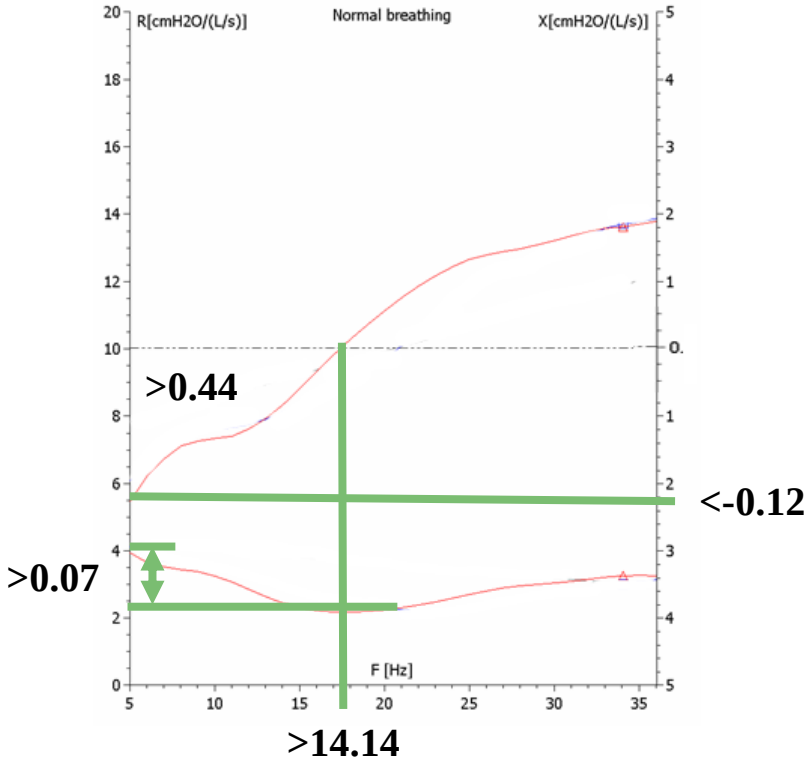
Reference value for symptomatic patients with PPF

	Cutoff value
R5-R20(kPa L(-1)s)	>0.07
X5(kPa L(-1)s)	<-0.12
Fres(Hz)	>14.14
AX(kPa L(-1))	>0.44



HY Chiu, YH Hsiao and DW Perng,
Thematic Poster Session, B64-9831, Monday May 21, ATS 2018, San Diego

Clinical diagnoses

TABLE E3. Clinical diagnoses of the participants

	Nonobstructive group ($FEV_1/FVC \geq 0.7$)		Obstructive group ($FEV_1/FVC < 0.7$)	
Diagnosis	**BR (−) (N = 255)**	**BR (+) (N = 16)**	**BR (−) (N = 62)**	**BR (+) (N = 16)**
Allergy history, n (%)	39 (15.3)	6 (35.7)	8 (12.9)	2 (12.5)
Allergic rhinitis, n (%)	108 (42.4)	7 (43.8)	21 (33.9)	8 (50)
Clinical diagnosis, n (%)				
Bronchitis	104 (40.8)	3 (18.8)	2 (3.2)	1 (6.3)
Asthma	122 (47.8)	10 (62.4)	28 (45.2)	6 (37.4)
COPD		3 (18.8)	27 (43.5)	4 (25)
ACO			5 (8.1)	5 (31.3)
Other diagnosis	29 (11.4)	0	5 (8.1)	5 (31.3)

ACO, Asthma-COPD overlap.

Other diagnoses include allergic rhinitis, gastroesophageal reflux disease, and upper respiratory tract infection.

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

TABLE E1. Between-group analysis with Scheffe method in patients without BR

Characteristic	Nonobstructive group (N = 255)	Obstructive group (N = 62)	*P* value
Age (y)	53 ± 16.1	68.2 ± 9.7	<.01
Height (cm)	163.9 ± 8.9	161.8 ± 8	.40
Weight (kg)	67 ± 13.7	64.1 ± 11.4	.47
BMI (kg/m^2)	24.9 ± 4.3	24.4 ± 3.7	.81
Sex: male, n (%)	133 (52.2)	44 (71)	.01
Smoking, n (%)	87 (34.1)	32 (51.6)	.01
Symptoms, n (%)			
Wheeze	34 (13.3)	3 (4.8)	.06
Cough	180 (70.6)	42 (67.7)	.66
Sputum	120 (47.1)	36 (58.1)	.12
Dyspnea	119 (46.7)	42 (67.7)	<.01
Chest tightness	91 (35.7)	17 (27.4)	.22
Pulmonary function test			
FEV_1/FVC	0.82 ± 0.06	0.6 ± 0.09	<.01
FEV_1, % predicticted	99.87 ± 12.36	80.12 ± 14.4	<.01
FVC, % predicted	97.13 ± 11.06	99.5 ± 12.08	.53
PEF, % predicted	90.6 ± 17.78	64.93 ± 17.72	<.01
$FEF_{25\%-75\%}$, % predicted	82.09 ± 25.65	29.89 ± 9.3	<.01
$FEF_{50\%}$, % predicted	96.54 ± 30.17	35.62 ± 12.03	<.01
$R_5 - R_{20}$ [kPa/(L/s)]	0.08 ± 0.07	0.14 ± 0.11	<.01
X_5 [kPa/(L/s)]	−0.1 ± 0.06	−0.18 ± 0.13	<.01
F_{res} (Hz)	14.59 ± 5.66	18.53 ± 5.41	<.01
AX (kPa/L)	0.56 ± 0.54	1.32 ± 1.24	<.01

BMI, Body mass index; *$FEF_{50\%}$*, forced expiratory flow at expiration of 50% of FVC; *PEF*, peak expiratory flow.
The data are described using mean (SD) for normally distributed variables and median (interquartile range) for nonnormally distributed variables.

TABLE E2. Between-group analysis with Scheffe method in patients without airflow limitation

Characteristic	BR (−) (N = 255)	BR (+) (N = 16)	*P* value
Age (y)	53 ± 16.1	57.6 ± 19.1	0.72
Height (cm)	163.9 ± 8.9	161.7 ± 7.3	0.80
Weight (kg)	67 ± 13.7	66.9 ± 10.4	1.00
BMI (kg/m^2)	24.9 ± 4.3	25.5 ± 3.4	0.94
Sex: male, n (%)	133 (52.2)	7 (43.8)	0.51
Smoking, n (%)	87 (34.1)	4 (25)	0.45
Symptoms, n (%)			
Wheeze	34 (13.3)	0 (0)	0.12
Cough	180 (70.6)	12 (75)	0.71
Sputum	120 (47.1)	8 (50)	0.82
Dyspnea	119 (46.7)	5 (31.3)	0.23
Chest tightness	91 (35.7)	4 (25)	0.39
Pulmonary function test			
FEV_1/FVC	0.82 ± 0.06	0.77 ± 0.06	0.05
FEV_1, % predicted	99.87 ± 12.36	86.86 ± 14.26	<0.01
FVC, % predicted	97.13 ± 11.06	87.74 ± 6.22	0.02
PEF, % predicted	90.6 ± 17.78	75.53 ± 12.53	0.01
$FEF_{25\%-75\%}$, % predicted	82.09 ± 25.65	59.34 ± 28.39	<0.01
$FEF_{50\%}$, % predicted	96.54 ± 30.17	66.83 ± 25.14	<0.01
$R_5 - R_{20}$ [kPa/(L/s)]	0.08 ± 0.07	0.09 ± 0.08	0.99
X_5 [kPa/(L/s)]	−0.1 ± 0.06	−0.11 ± 0.07	0.95
F_{res} (Hz)	14.59 ± 5.66	15.05 ± 4.72	0.99
AX (kPa/L)	0.56 ± 0.54	0.73 ± 0.61	0.85

BMI, Body mass index; $FEF_{50\%}$, forced expiratory flow at expiration of 50% of FVC; *PEF*, peak expiratory flow.
The data are described using mean (SD) for normally distributed variables and median (interquartile range) for nonnormally distributed variables.

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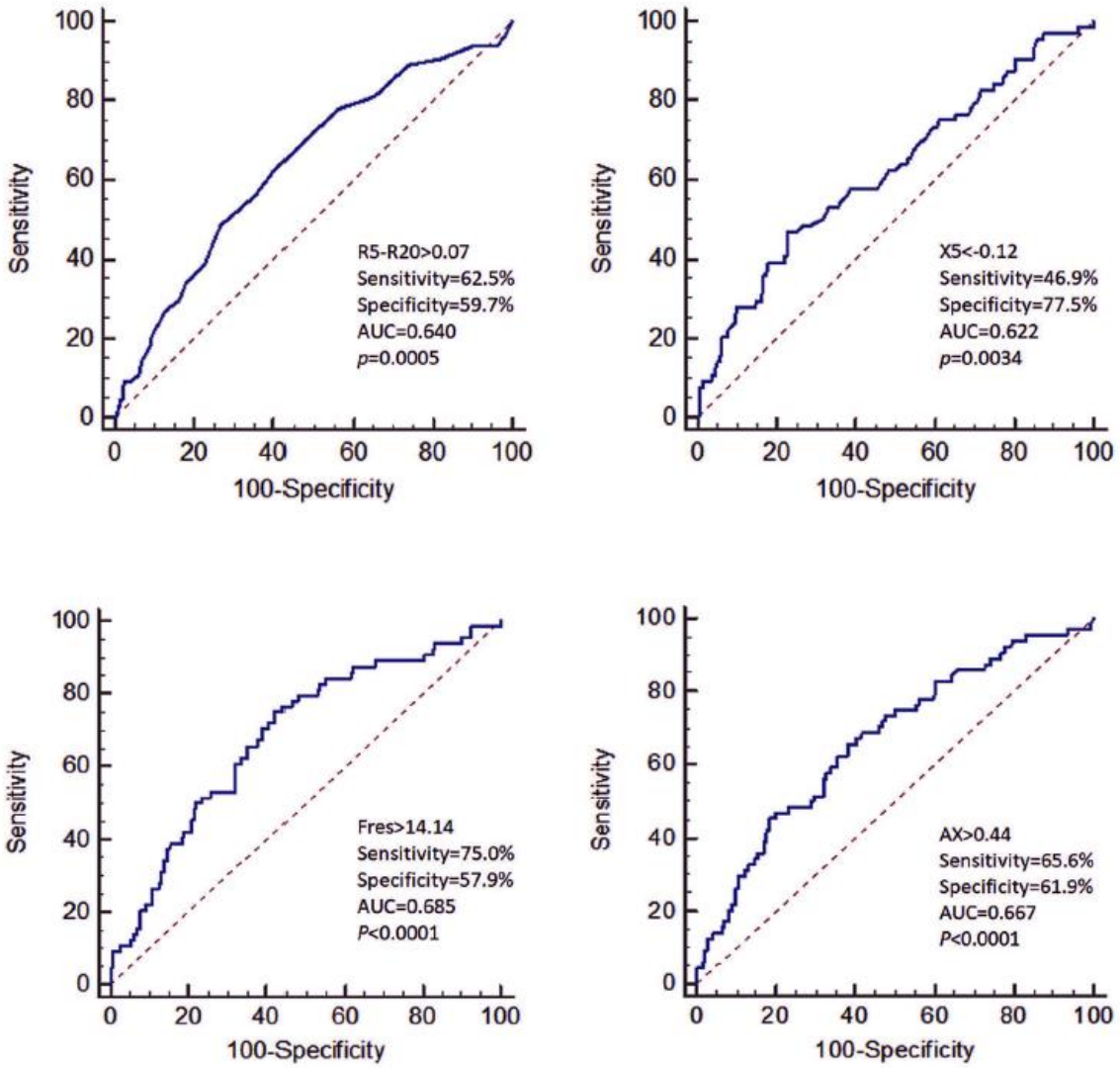

FIGURE E1. Small airway dysfunction defined by $FEF_{25-75\%} < 65\%$ predicted detected by impulse oscillometry (IOS) parameters. *AUC*, Area under curve.

Chiu et al, J Allergy Clin Immunol Pract. 2019 Jul 10.

Conclusion

- Reference values of IOS parameters
- F_{res} is more sensitive than $FEF_{25\%-75\%}$ to detect SAD
- Patients with respiratory symptoms and PPF may have SAD, which can be diagnosed with IOS in addition to spirometry.

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