Diagnosis of Small Airway Disease

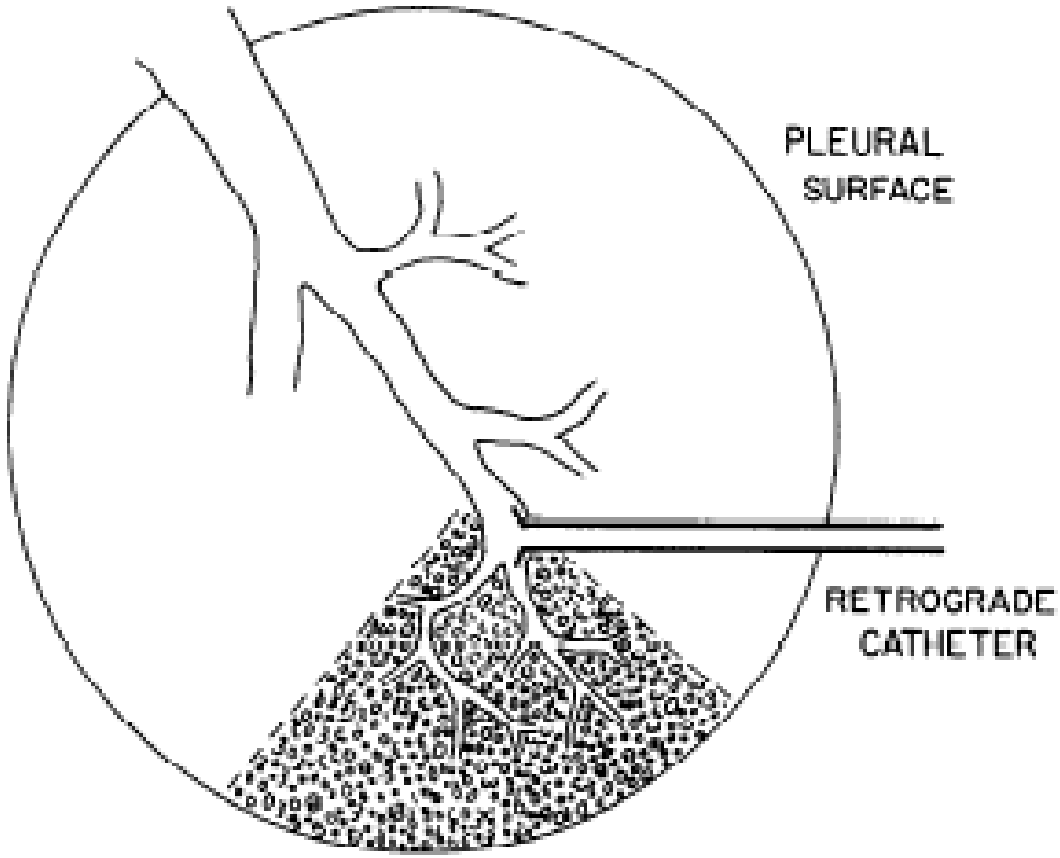
Jong Geol Jang, MD

Assistant Professor
Division of Pulmonary, Allergy, and Critical Care Medicine
Department of Internal Medicine
Yeungnam University Medical Center
Yeungnam University of Korea

Contents

Hogg et al. (1968)

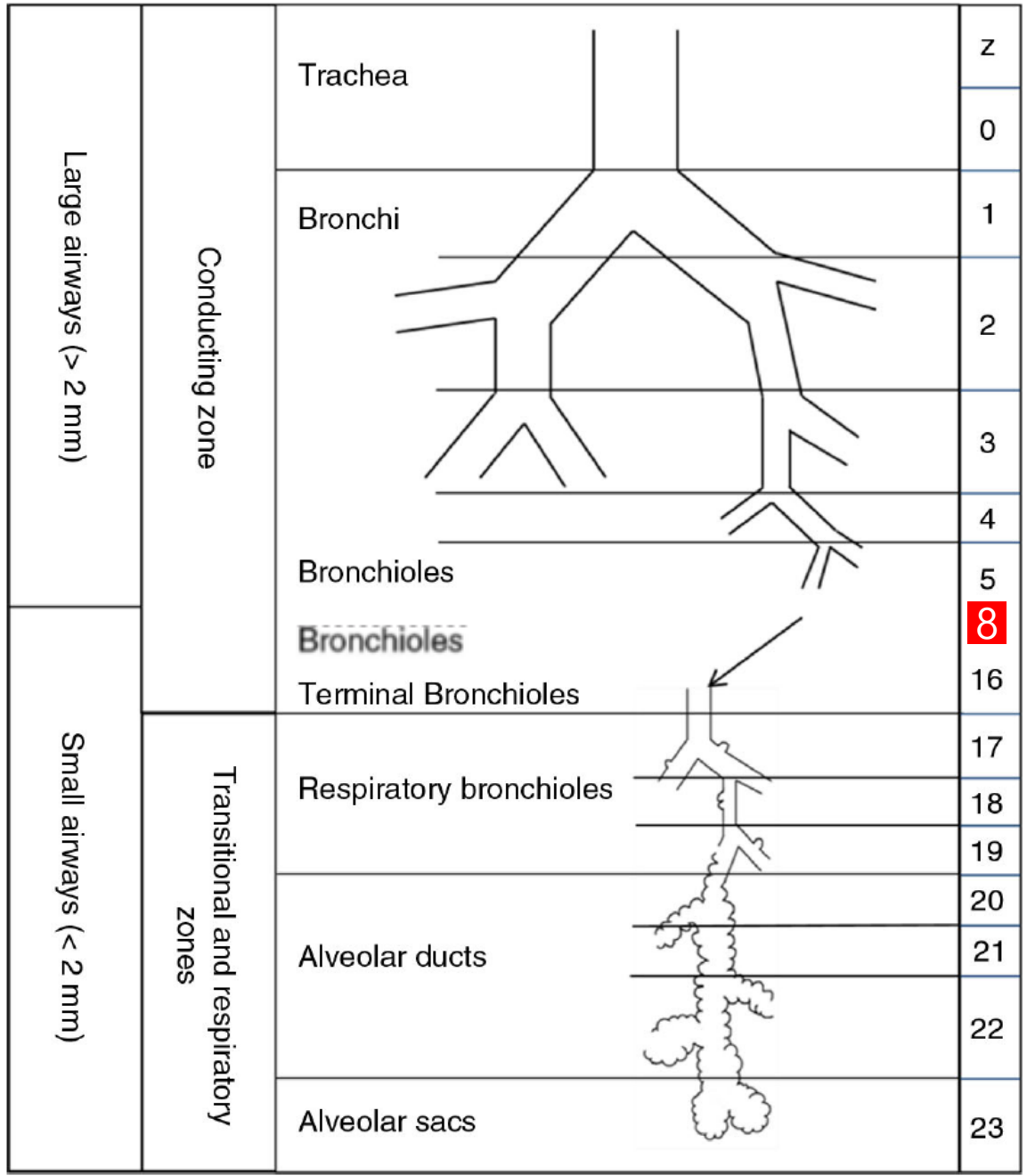
- introduce the term small airways
- major site of airway resistance in patients with emphysema



MACKLEM AND MEAD (1967)

MACKLEM, PETER T., AND JERE MEAD. Resistance of central and peripheral airways measured by a retrograde catheter. J. Appl. Physiol. 22(3): 395-401.
Pierachille Santus et al., The Relevance of Targeting Treatment to Small Airways in Asthma and COPD, Respir Care 2020;65(9):1392–1412

Airway generations



European Clinical Respiratory Journal 2014,

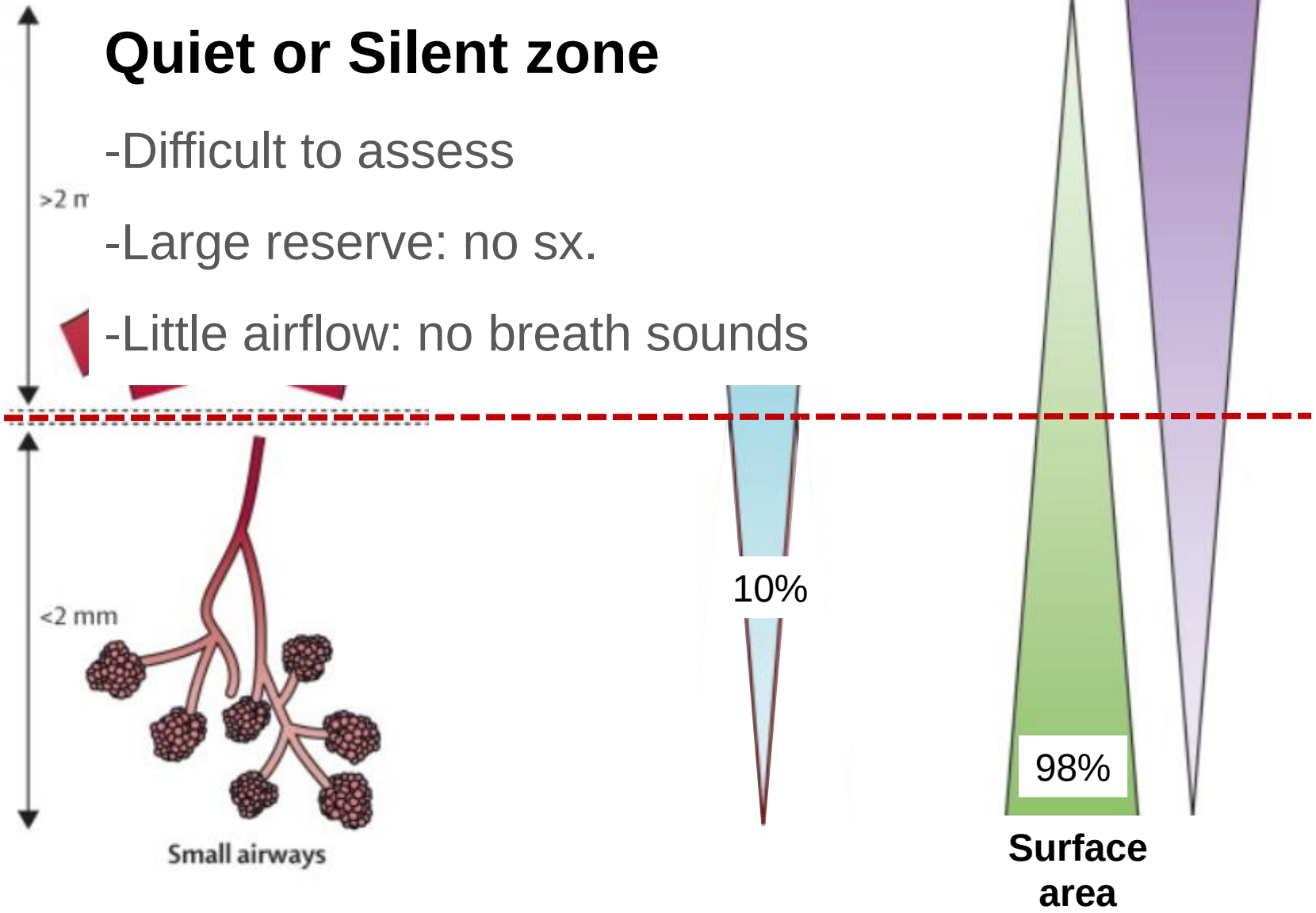
Small airway

Quiet or Silent zone

-Difficult to assess

-Large reserve: no sx.

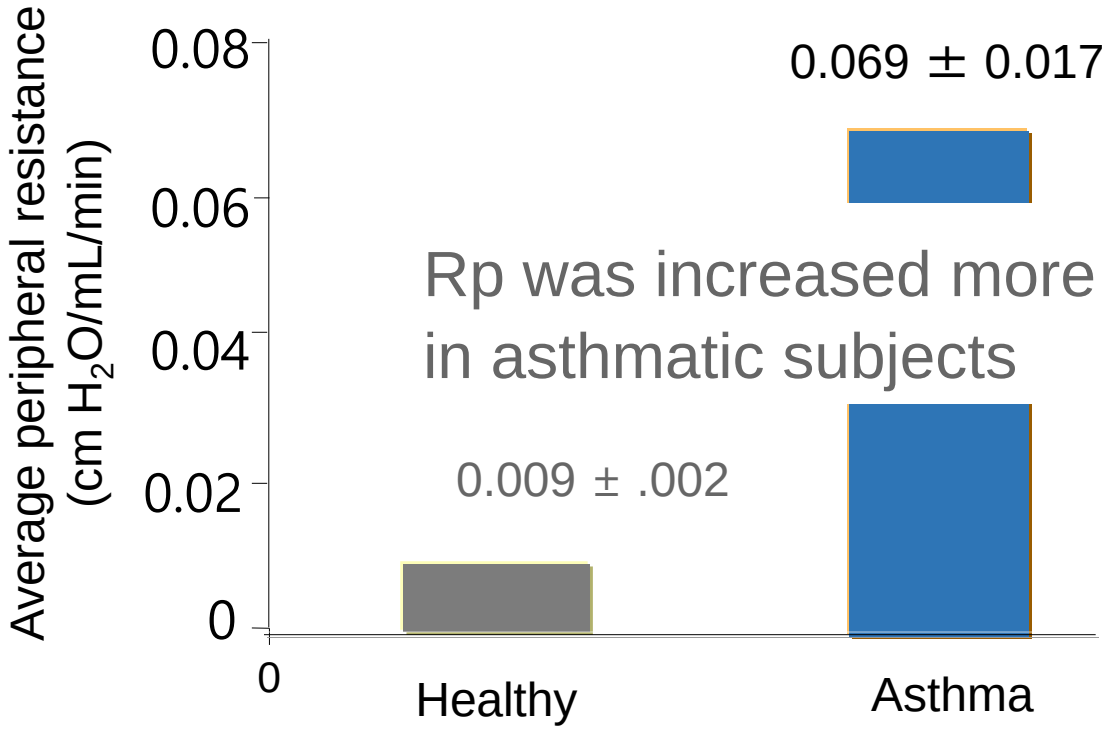
-Little airflow: no breath sounds



Lancet Respir Med 2014;2: 497-506

Contents

Peripheral Lung Resistance in Normal and Asthmatic Subjects

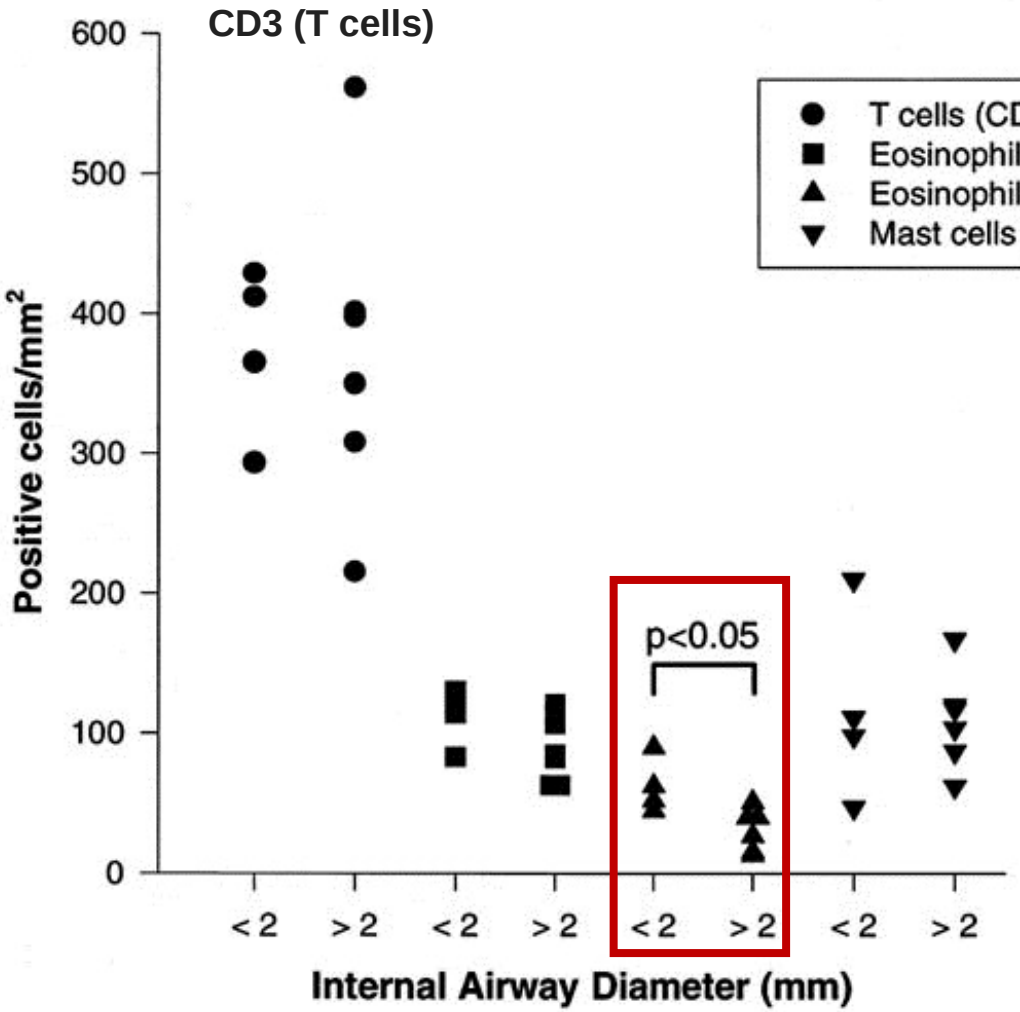


Rp was increased more than **seven-fold** in asthmatic subjects

Wagner EM, et al. Am Rev Respir Dis 1990

Inflammation of small airways in asthma

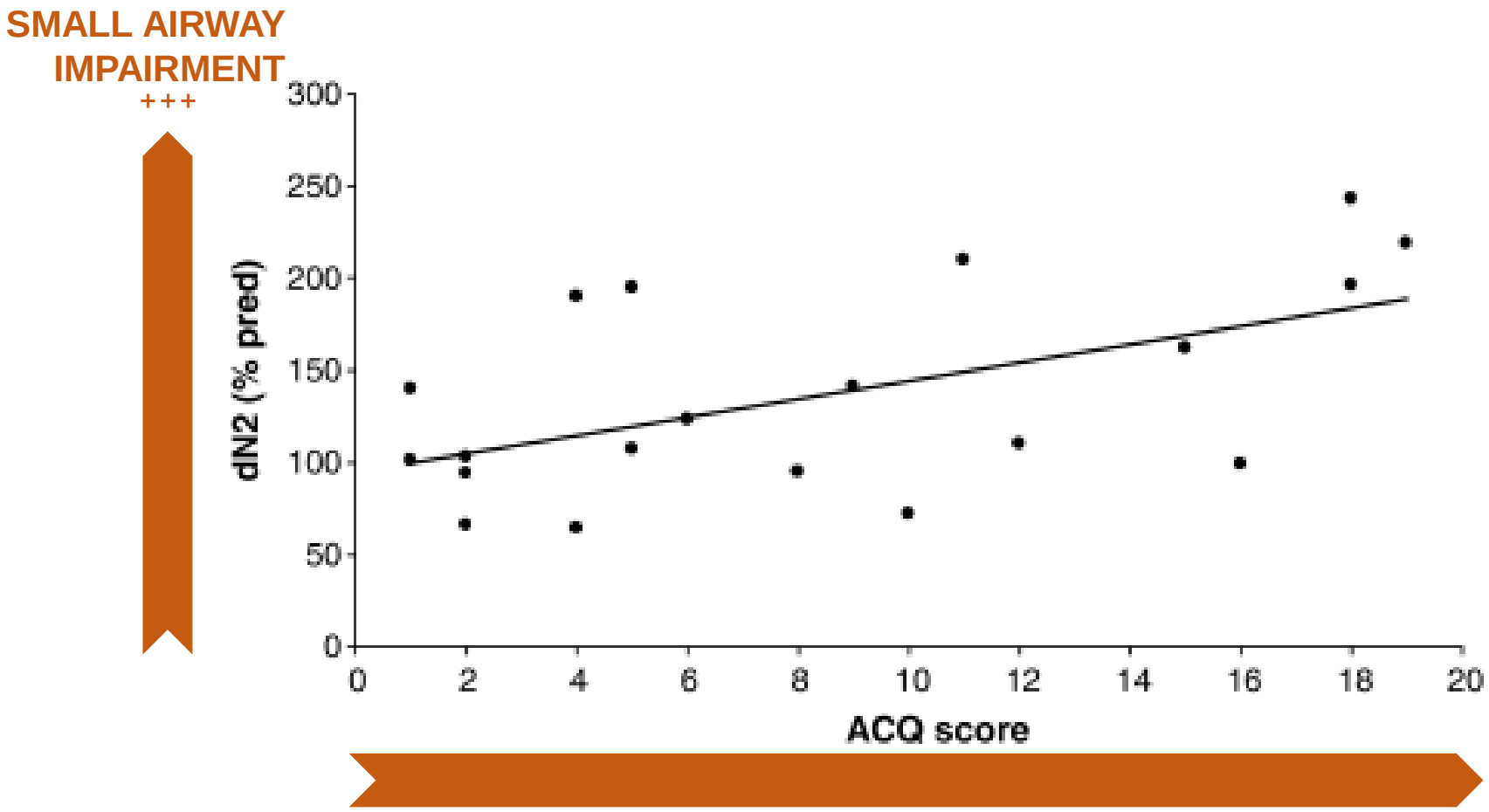
Qutayba Hamid, MD, PhD,[a] Yunling Song, MD,[a] Thomas C. Kotsimbos, MD,[a]
Eleanor Minshall, PhD,[a] Tony R. Bai, MD,[b] Richard G. Hegele, MD,[b] and
James C. Hogg, MD, PhD[b] *Montreal, Quebec, and Vancouver, British Columbia, Canada*



major basic protein (total eosinophils)
activated eosinophils

J Allergy Clin Immunol 1997;100:44-51

Small airway impairment and asthma control

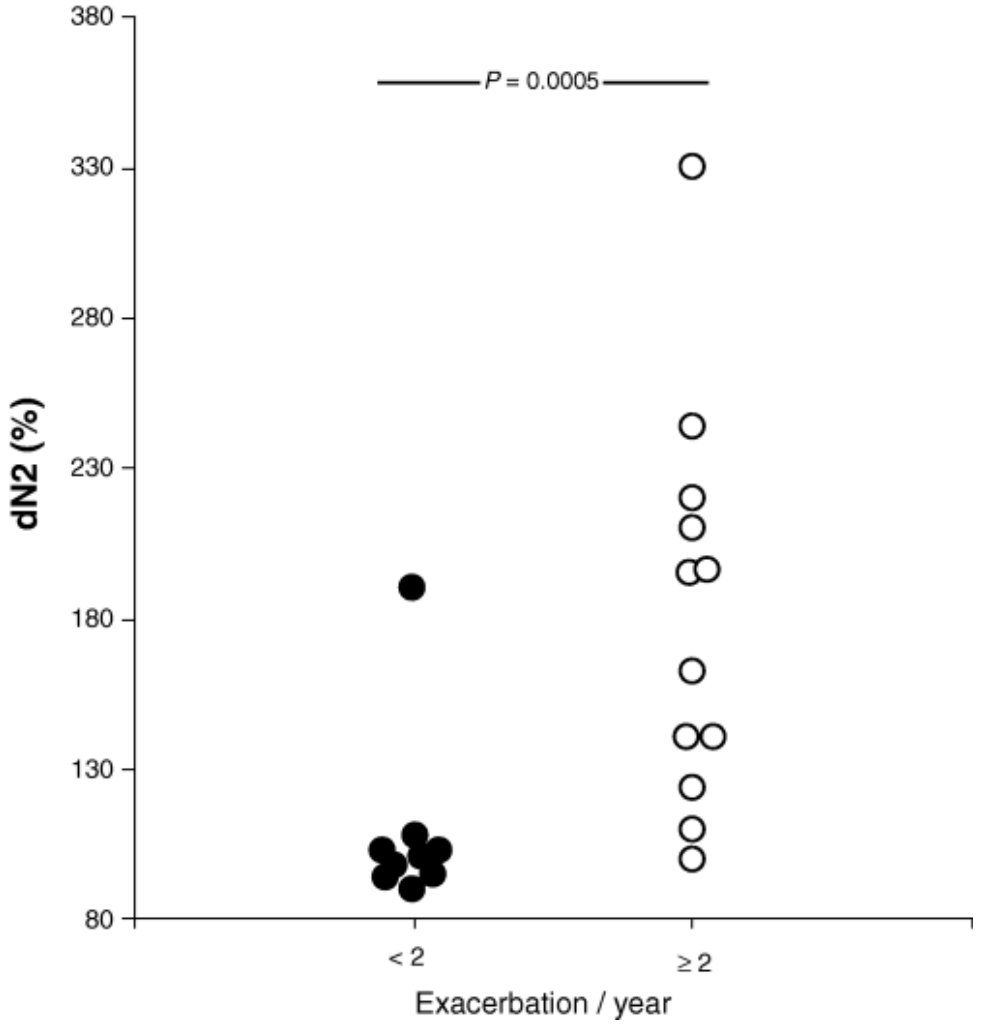


Allergy 2006: 61: 85–89

Small airway impairment and exacerbations

SMALL AIRWAY IMPAIRMENT

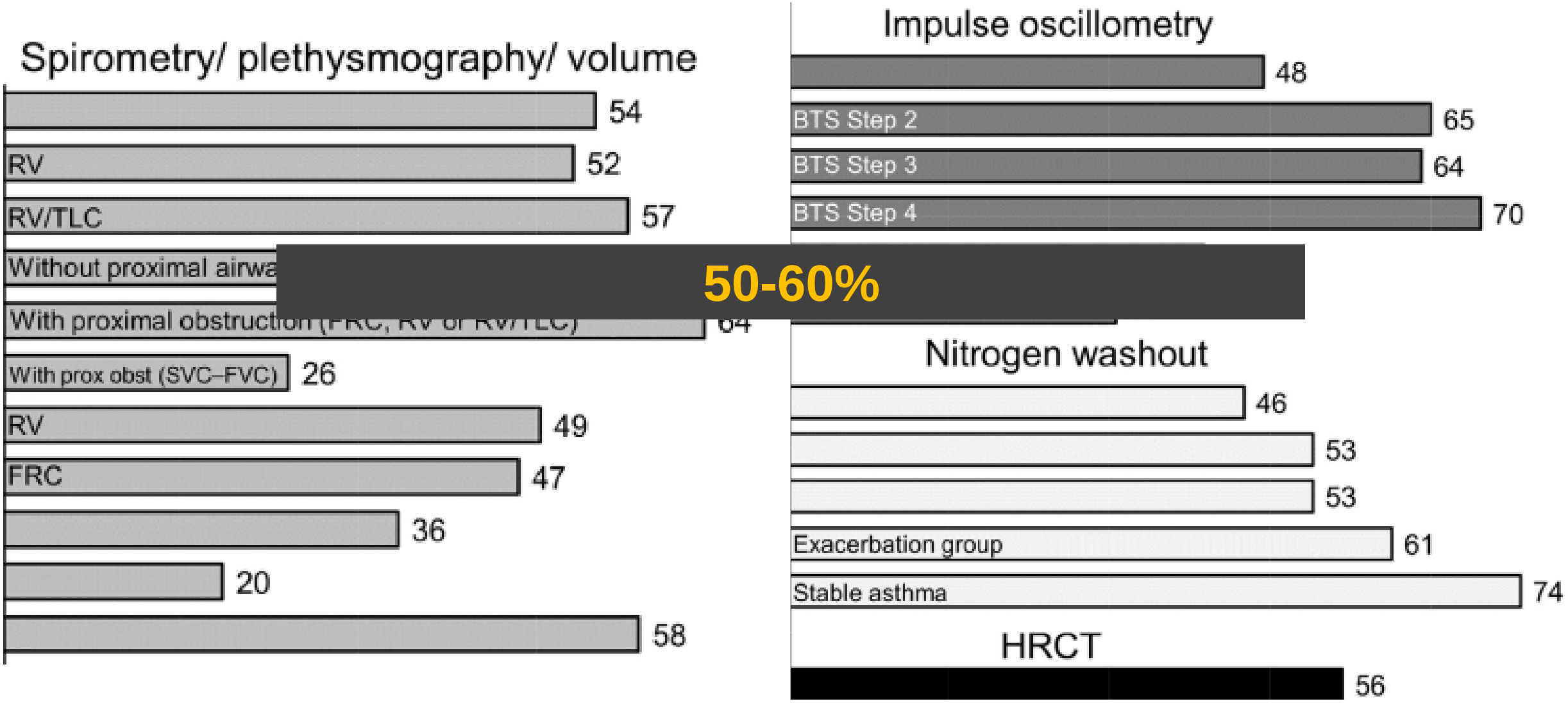
+++



Allergy 2006: 61: 85–89

Contents

Prevalence of SAD in patients with asthma

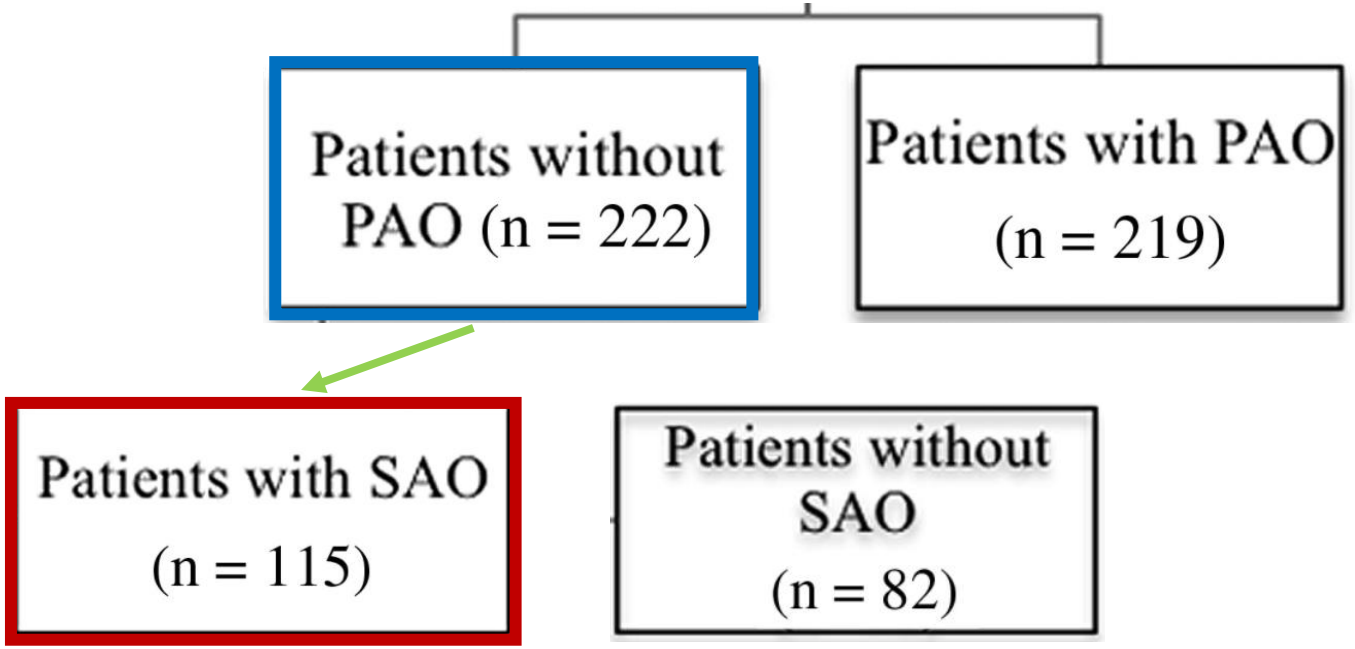


O.S. Usmani et al. / Respiratory Medicine 116 (2016) 19e27

Small airway impairment in moderate to severe asthmatics without significant proximal airway obstruction

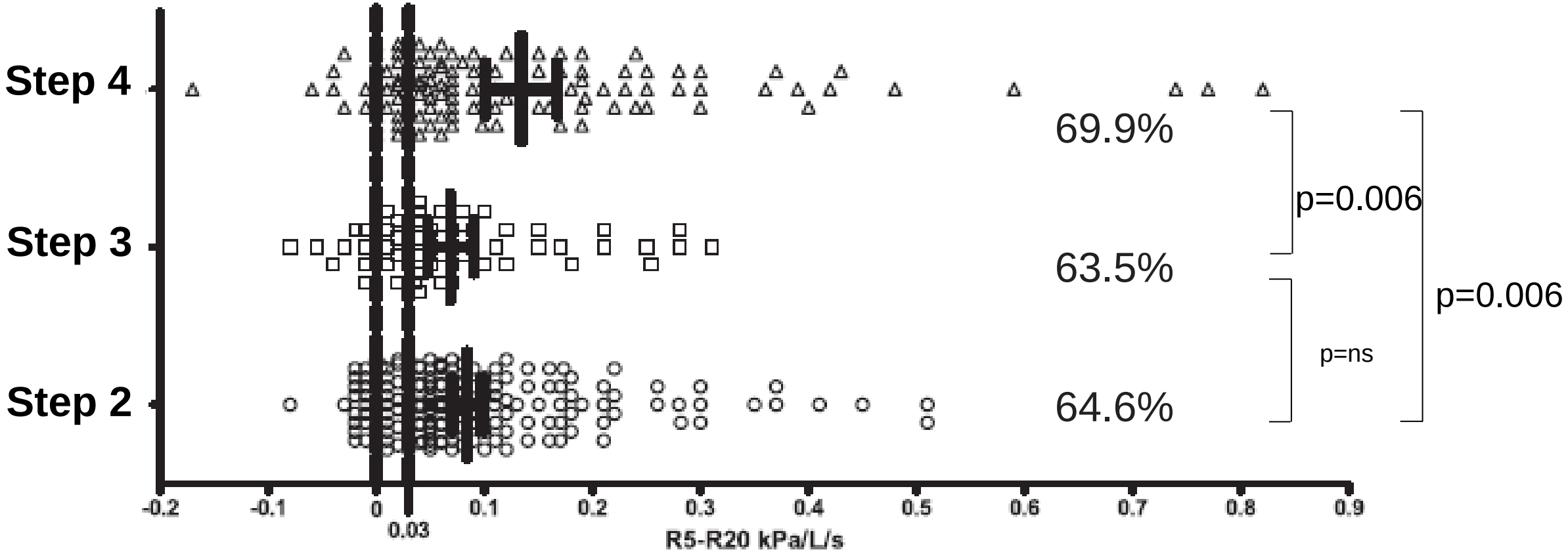
Patient with SAD without PAD

52%



Respiratory Medicine 116 (2016) 19e27
Respir. Med., 107 (2013), pp. 1667-1674

Are we overlooking persistent small airways dysfunction in community-managed asthma?



Ann Allergy Asthma Immunol. 2012 Sep;109(3):185-189

Contents

Diagnosis of SAD in Patient with Asthma

- **Clinical approach**
  - Clinical characteristics
  - Response to therapy
- **Invasive technique**
  - Surgical resection, TBLB, BAL
- **Non-invasive technique**
  - Physiology and Imgaing

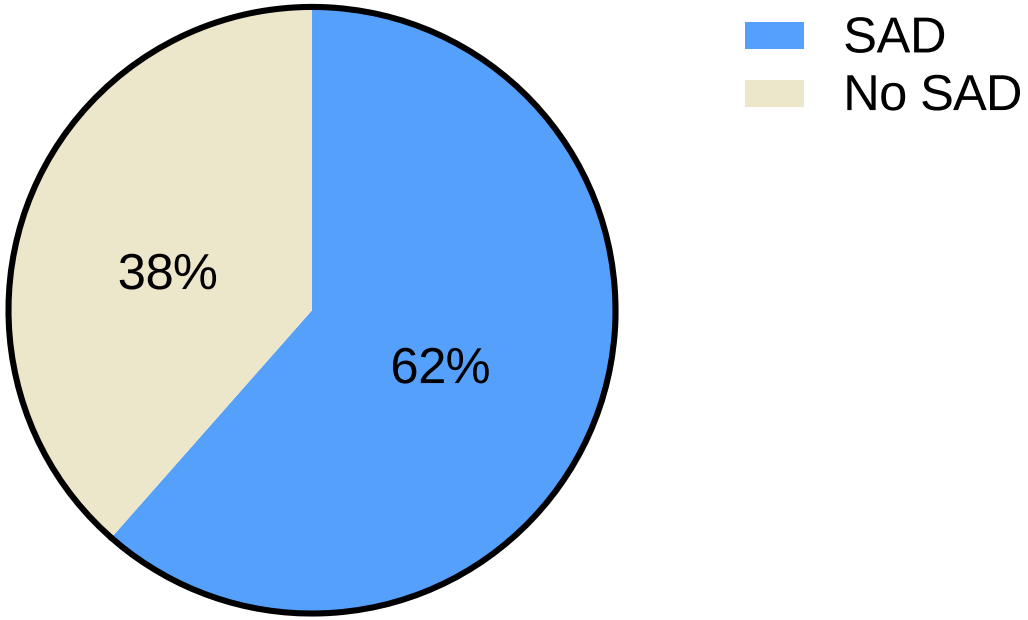
Diagnosis of SAD in Patient with Asthma

- **Clinical approach**
  - **Clinical characteristics**
  - Response to therapy
- **Invasive technique**
  - Surgical resection, TBLB, BAL
- **Non-invasive technique**
  - Physiology and Imgaing

Original Article

Clinical Characterization and Predictors of IOS-Defined Small-Airway Dysfunction in Asthma

Marcello Cottini, MD[a], Anita Licini[a], Carlo Lombardi, MD[b], and Alvise Berti, MD[c,d] *Bergamo, Brescia, and Trento, Italy; and Rochester, Mass*



Total=400

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84	1.23-2.78	.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07	2.57-6.54	<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80	2.89-8.29	<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61	0.40-0.93	.0217	—	—	—
Esoinophil count > 300 mm^3	2.62	1.62, 4.28	<.0001	—	—	—
Feno >25 ppb	2.94	1.93-4.50	<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59	1.05-2.42	.0273	—	—	—
FEV_1 < 80%	3.64	2.12-6.54	<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84	1.23-2.78	.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07	2.57-6.54	<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80	2.89-8.29	<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61	0.40-0.93	.0217	—	—	—
Esoinophil count > 300 mm^3	2.62	1.62, 4.28	<.0001	—	—	—
Feno >25 ppb	2.94	1.93-4.50	<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59	1.05-2.42	.0273	—	—	—
FEV_1 < 80%	3.64	2.12-6.54	<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.

6.39

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84			2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07			3.64	1.99-6.85	<.0001
Smoking, former or current	4.80	2.89-8.29	<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61	0.40-0.93	.0217	—	—	—
Esoinophil count > 300 mm^3	2.62	1.62, 4.28	<.0001	—	—	—
Feno >25 ppb	2.94	1.93-4.50	<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59	1.05-2.42	.0273	—	—	—
FEV_1 < 80%	3.64	2.12-6.54	<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.

Obese

3.64

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84		.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07		<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80		<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62	1.62, 4.28	<.0001	—	—	—
Feno >25 ppb	2.94	1.93-4.50	<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59	1.05-2.42	.0273	—	—	—
FEV_1 < 80%	3.64	2.12-6.54	<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32		—	—	—
Night awakenings due to asthma	8.24	5.09-13.74		3.34	3.34	35-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.

Obese

Night sx.

3.34

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 50 y	3.19	2.10-4.88		3.08	7-5.49	<.0001
Sex: female	1.84		.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07		<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80		<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62		<.0001	—	—	—
Feno >25 ppb	2.94		<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59	1.05-2.42	.0273	—	—	—
FEV_1 < 80%	3.64	2.12-6.54	<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

Age ≥ 50

3.08

EIA sx.

Obese

Night sx.

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84		.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07			3.64	1.99-6.85	<.0001
Smoking, former or current	4.80			3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62		<.0001	—	—	—
Feno >25 ppb	2.94		<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59		.0273	—	—	—
FEV_1 < 80%	3.64		<.0001	—	—	—
FEV_1/FVC < 70%	1.76	1.12-2.82	.0139	—	—	—
FEF_{25-75} < 60%	3.35	2.12-5.31	<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.
Obese
Night sx.
Age ≥ 50
Smoker
3.06

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 50 y	3.19	2.10-4.88		3.08	77-5.49	<.0001
Sex: female	1.84			2.27	29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07		<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80		<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62		<.0001	—	—	—
Feno >25 ppb	2.94		<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59		.0273	—	—	—
FEV_1 < 80%	3.64		<.0001	—	—	—
FEV_1/FVC < 70%	1.76		.0139	—	—	—
FEF_{25-75} < 60%	3.35		<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25	5.75-15.19	<.0001	—	—	—
Asthma exacerbations	6.32	3.88-10.65	<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

Female

2.27

EIA sx.

Obese

Night sx.

Age ≥ 50

Smoker

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84		.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07		<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80		<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62			—	—	—
Feno >25 ppb	2.94			2.05	14-3.70	.0164
Asthma duration > 15.0 y	1.59		.0273	—	—	—
FEV$_1$ < 80%	3.64		<.0001	—	—	—
FEV$_1$/FVC < 70%	1.76		.0139	—	—	—
FEF$_{25-75}$ < 60%	3.35		<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25		<.0001	—	—	—
Asthma exacerbations	6.32		<.0001	—	—	—
Emergency room visit	6.19	3.59-27.80	<.0001	—	—	—
Hospitalization	7.19	4.11-24.32	.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.
Obese
Night sx.
Age ≥ 50
Smoker
Female

FeNO>25

2.05

J Allergy Clin Immunol Pract 2020;8:997-1004

TABLE IV. Univariate and multivariate analysis of baseline predictors of SAD in our patient cohort with asthma

Univariable analysis				Multivariable analysis		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 50 y	3.19	2.10-4.88	<.0001	3.08	1.77-5.49	<.0001
Sex: female	1.84		.0031	2.27	1.29-4.06	.0046
Overweight, BMI > 25 kg/m^2	4.07		<.0001	3.64	1.99-6.85	<.0001
Smoking, former or current	4.80		<.0001	3.06	1.60-6.05	.0006
Presence of atopy	0.61		.0217	—	—	—
Esoinophil count > 300 mm^3	2.62		<.0001	—	—	—
Feno >25 ppb	2.94		<.0001	2.05	1.14-3.70	.0164
Asthma duration > 15.0 y	1.59		.0273	—	—	—
FEV_1 < 80%	3.64		<.0001	—	—	—
FEV_1/FVC < 70%	1.76		.0139	—	—	—
FEF_{25-75} < 60%	3.35		<.0001	—	—	—
Asthma control (UC and PC vs WC)	9.25		<.0001	—	—	—
Asthma exacerbations	6.32		<.0001	—	—	—
Emergency room visit	6.19		<.0001	—	—	—
Hospitalization	7.19		.0003	—	—	—
Night awakenings due to asthma	8.24	5.09-13.74	<.0001	3.34	1.85-6.17	<.0001
EIA symptoms	9.99	6.27-16.31	<.0001	6.39	3.65- 11.45	<.0001
High ICS dosage*	4.45	0.78-83.63	.1644	—	—	—
Extrafine ICS use	0.13	0.08-0.20	<.0001	—	—	—
Antileukotriene use	3.60	1.84-7.75	<.0001	—	—	—

EIA sx.
Obese
Night sx.
Age ≥ 50
Smoker
Female
FeNO>25

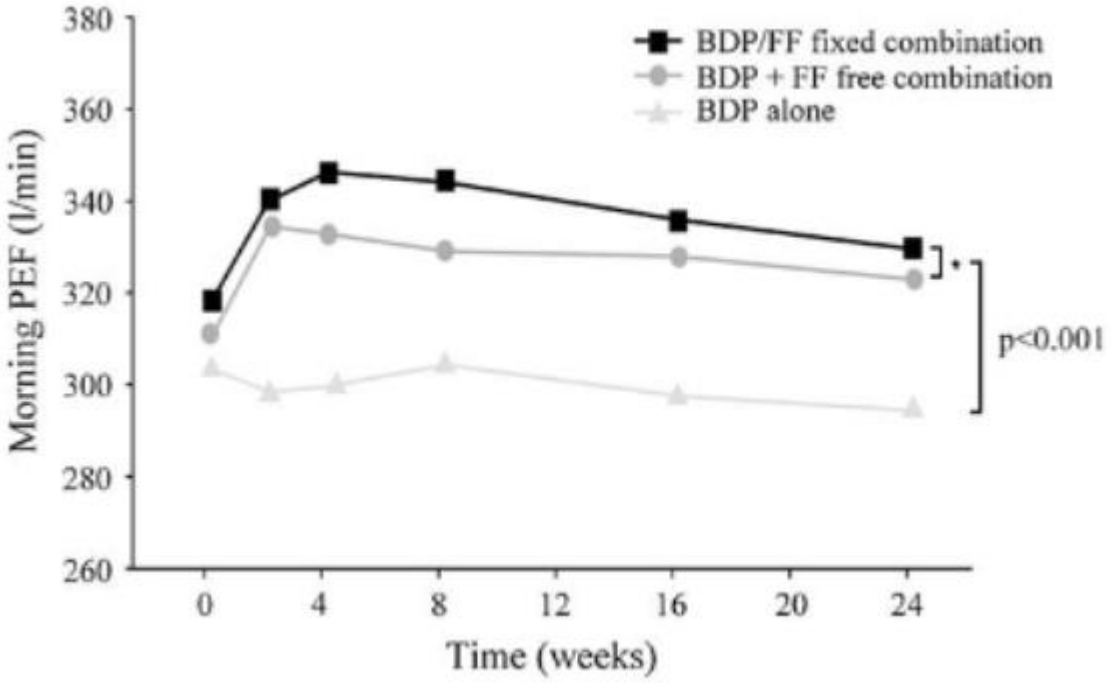
J Allergy Clin Immunol Pract 2020;8:997-1004

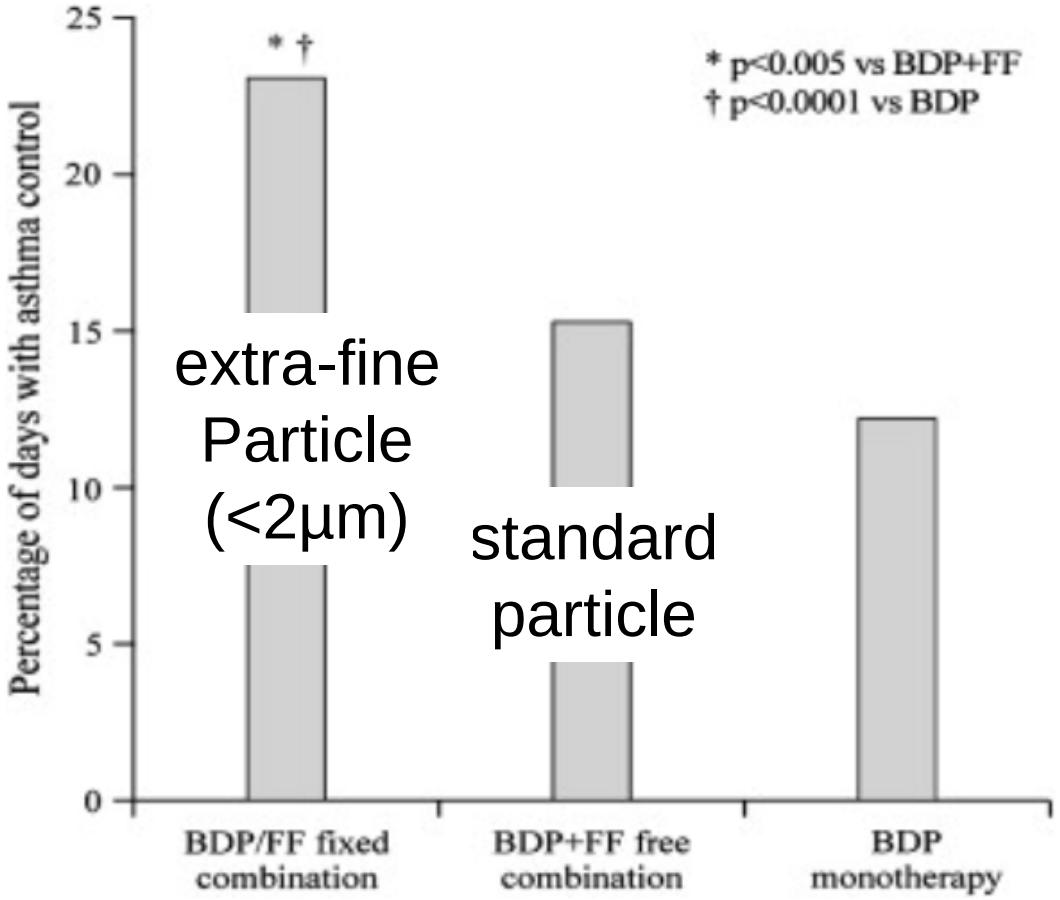
Diagnosis of SAD in Patient with Asthma

- **Clinical approach**
  - Clinical characteristics
  - **Response to therapy**
- **Invasive technique**
  - Surgical resection, TBLB, BAL
- **Non-invasive technique**
  - Physiology and Imgaing

Lung function and asthma control with beclomethasone and formoterol in a single inhaler

G. Huchon, H. Magnussen, A. Chuchalin, L. Dymek, F. Bonnet Gonod, J. Bousque





Assessment of SAD in Patient with Asthma

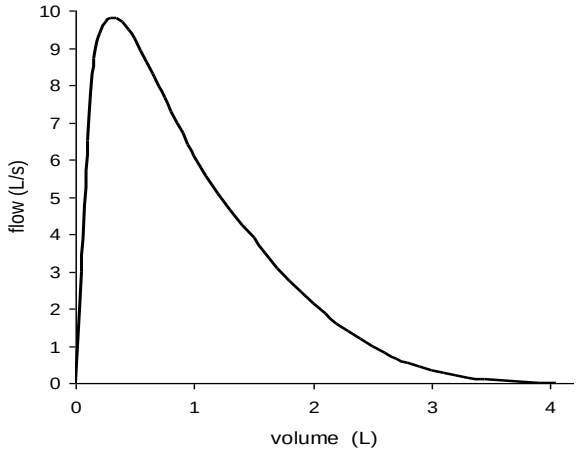
- **Clinical approach**
  - Clinical characteristics
  - Response to therapy
- **Invasive technique**
  - Surgical resection, TBLB, BAL
- **Non-invasive technique**
  - Physiology and Imgaing

Assessment of SAD in Patient with Asthma

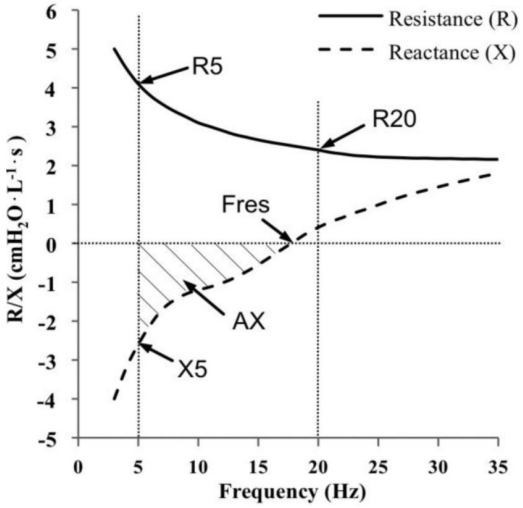
- **Clinical approach**
  - Clinical characteristics
  - Response to therapy
- **Invasive technique**
  - Surgical resection, TBLB, BAL
- **Non-invasive technique**
  - Physiology and Imgaing

Physiological assessment

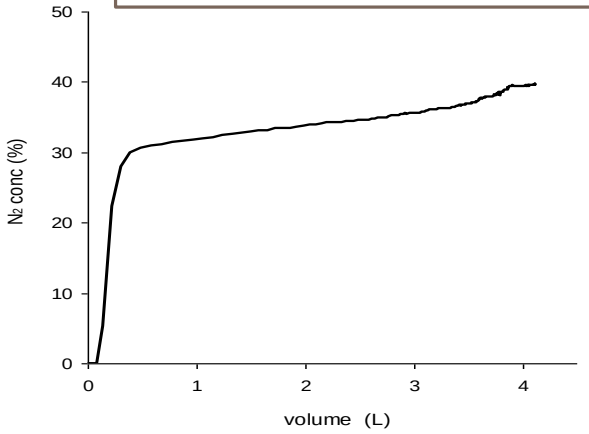
Spirometry



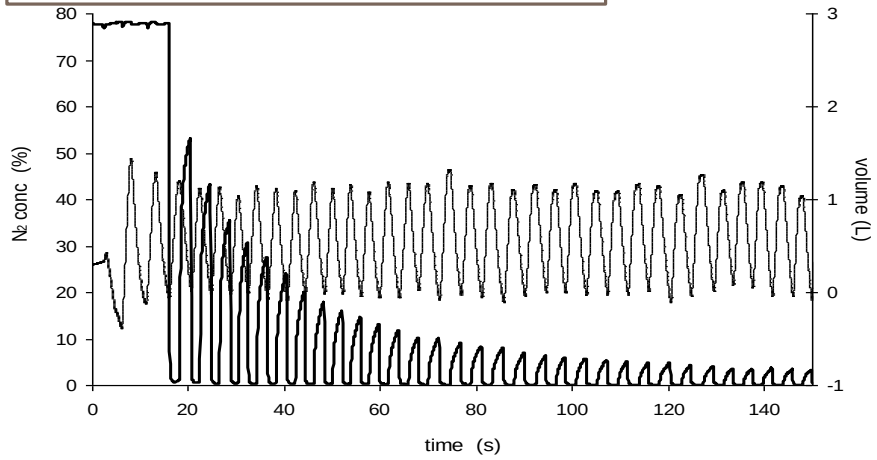
Impulse oscillometry(IOS)



Single breath washout



Multiple breath washout



Large Airway Function

FEV1

FEV1/FVC

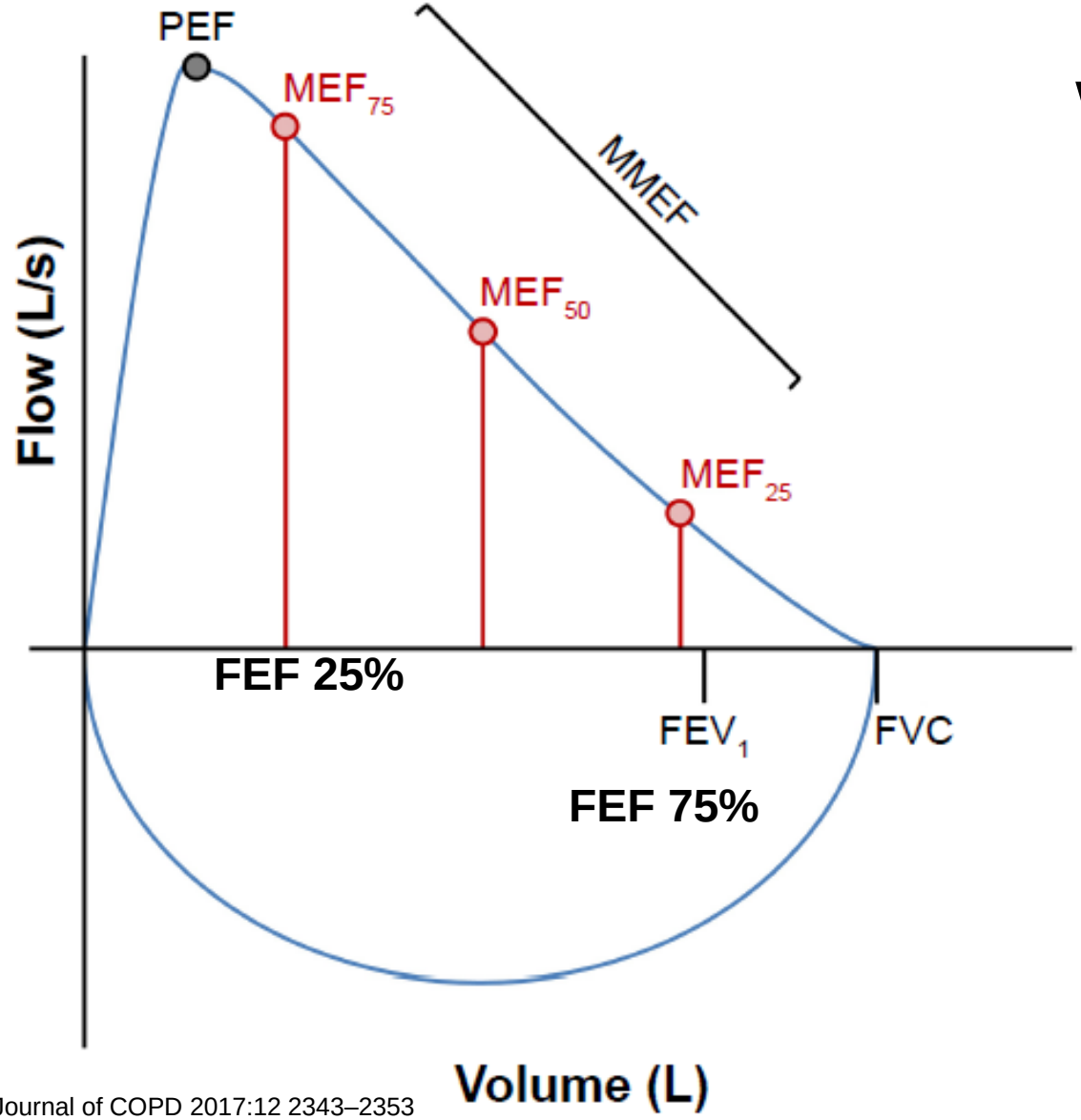
Small Airway Function

FEF 25-75%

FVC/SVC

FVC

FEF 25-75%



Well correlated with Clinical outcome

-disease severity

-control status

-airway hyperresponsiveness

Disadvantages

-Broad normal range

-Less reproducible than FEV_1

-Difficult to interpret if the FVC is reduced or increased

International Journal of COPD 2017:12 2343–2353

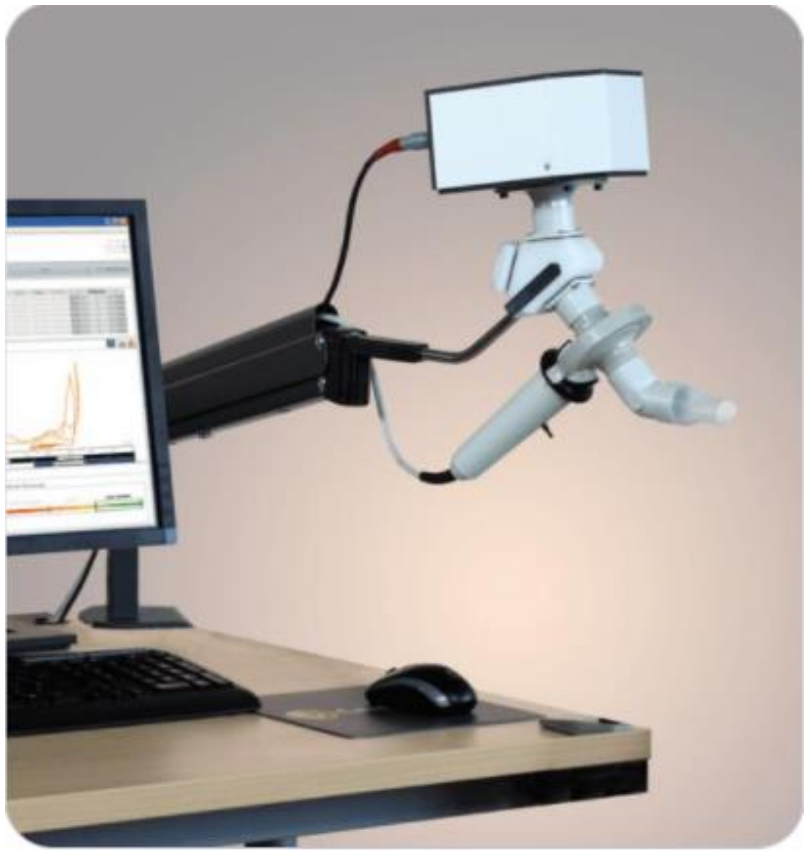
FVC/SVC

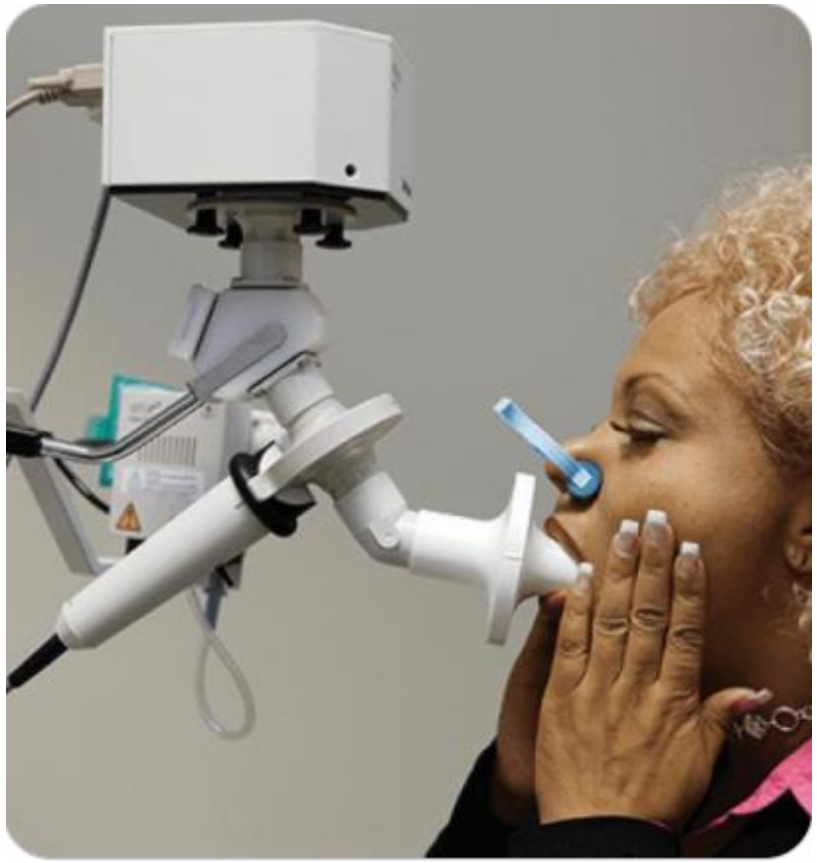
SUBJECT CATEGORY	GROUP	FVC	SVC
Normals	–	3.57 ± 0.82	3.50 ± 0.82
Asthmatics	Group 1 (n = 26)*	3.19 ± 0.77	3.22 ± 0.76
	Group 2 (n = 20)**	2.69 ± 0.81	2.81 ± 0.84
	Group 3 (n = 20)**	2.23 ± 0.46	2.40 ± 0.42

SUBJECT CATEGORY	GROUP	SVC–FVC	
Normals	–	–67	(–140–2)
Asthmatics	Group 1 (n = 26)	30	(–24–84)
	Group 2 (n = 20)	127	(55–198)
	Group 3 (n = 20)	163	(99–232)

Journal ot Asthma, 35141, 361-365

Impulse oscillometry: IOS



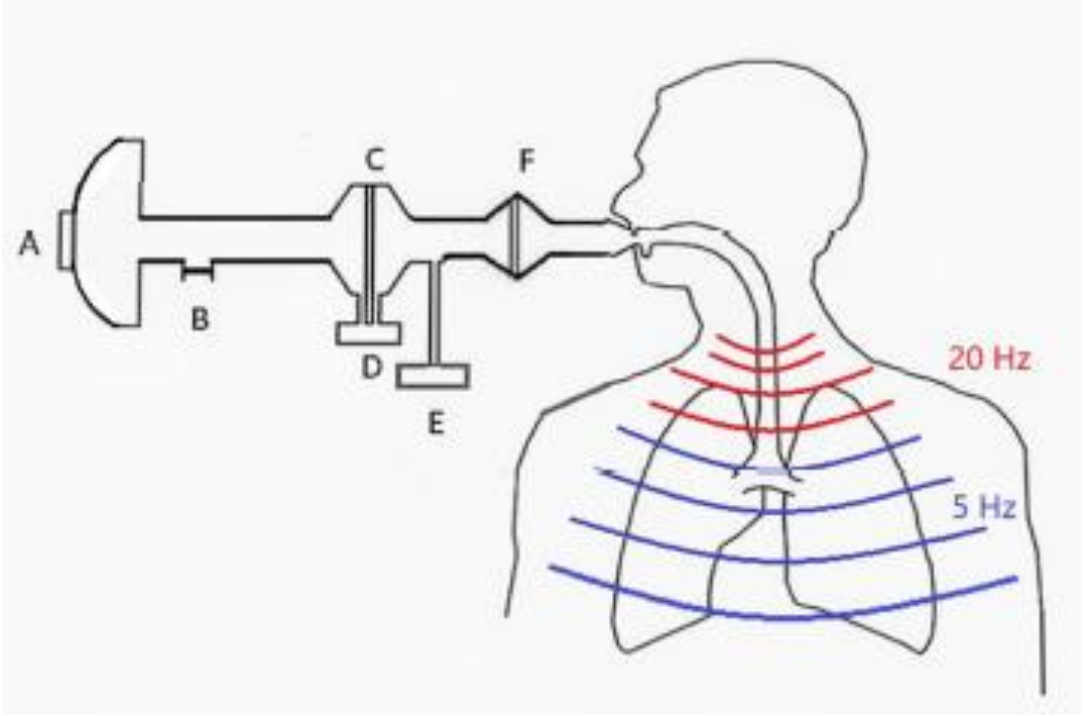


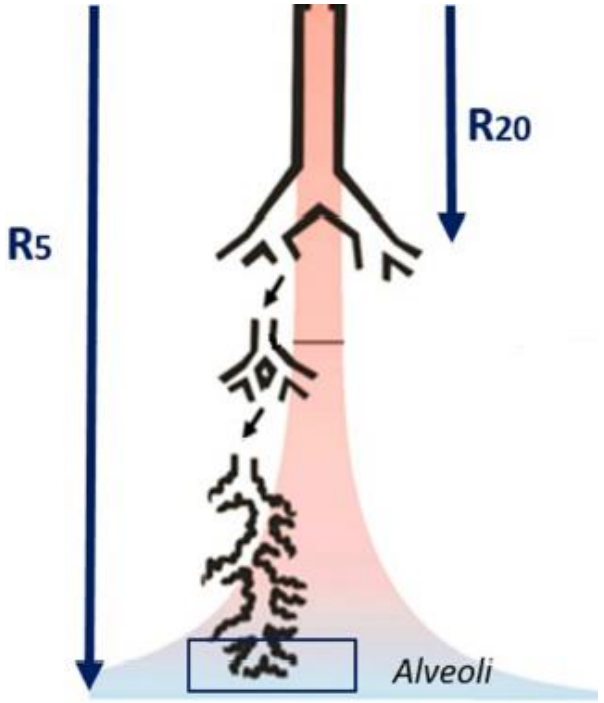
Impulse oscillometry: IOS

Impulse generator

5 - 20 Hz

Spectrum



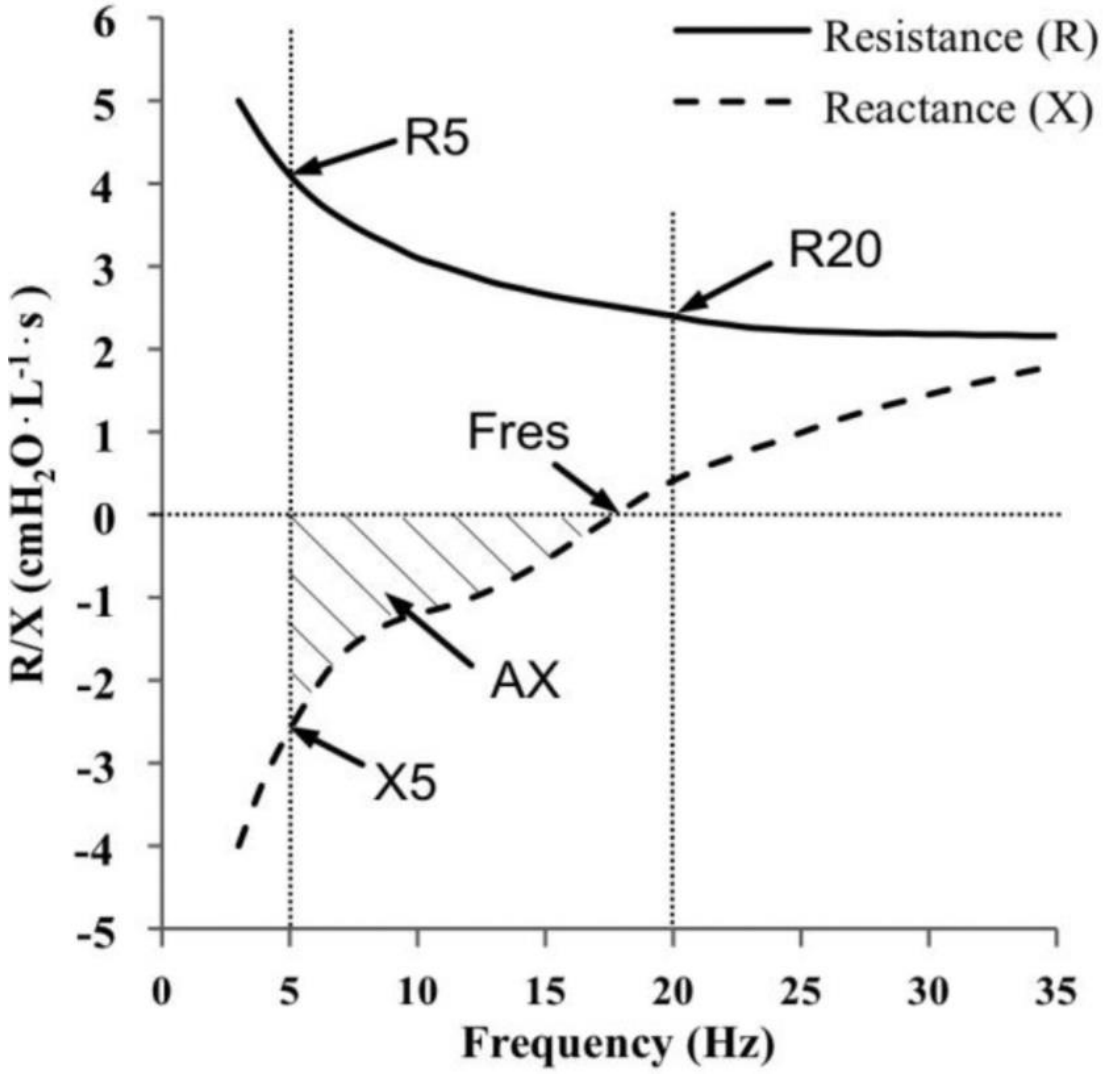


R5: total airway resistance

R20: central airway resistance

J Allergy Clin Immunol. 2012 Mar; 129(3): 671–678

IOS



Peripheral airway resistance;

R5-R20

X5

AX (reactance area under curve)

J Allergy Clin Immunol. 2012 Mar; 129(3): 671–678

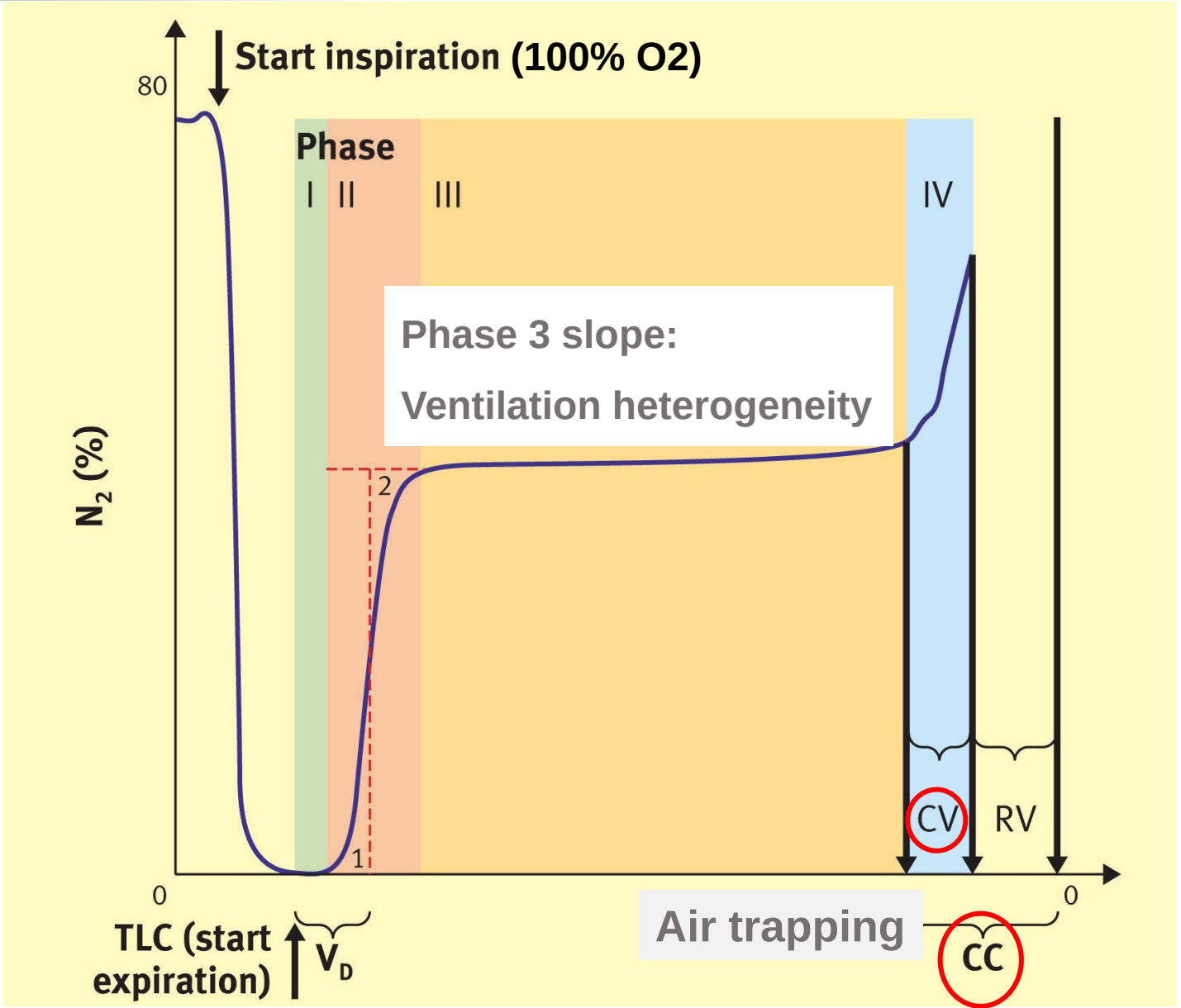
Single breath nitrogen washout test (SBNT)

Phase I: anatomical dead space

Phase II: bronchial phase

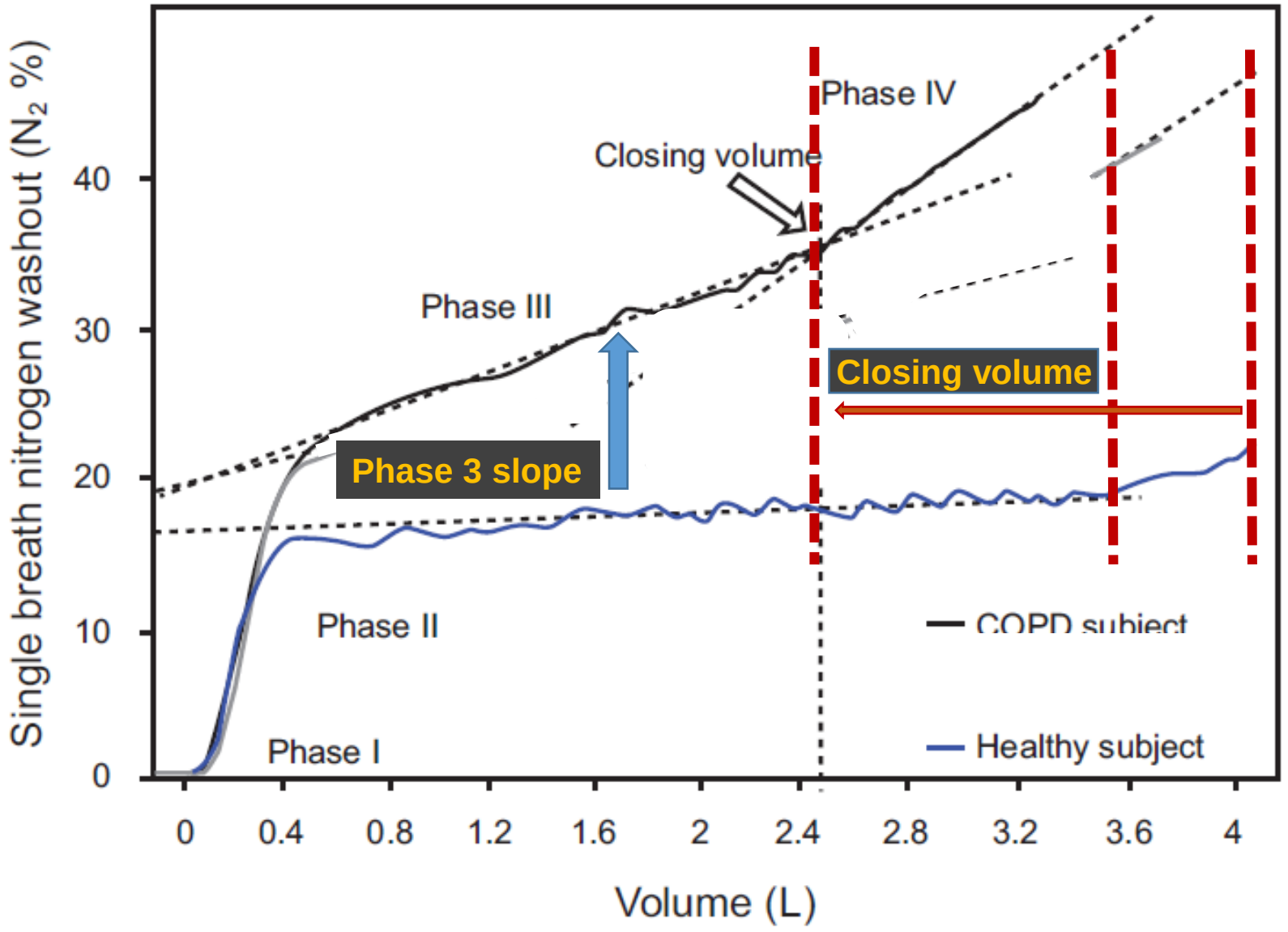
Phase III: alveolar phase

Phase IV: airway closure



Anaesthesia & Intensive Care Medicine 2011 12453-457

Single-breath nitrogen washout test in a healthy young subject and a subject with severe COPD



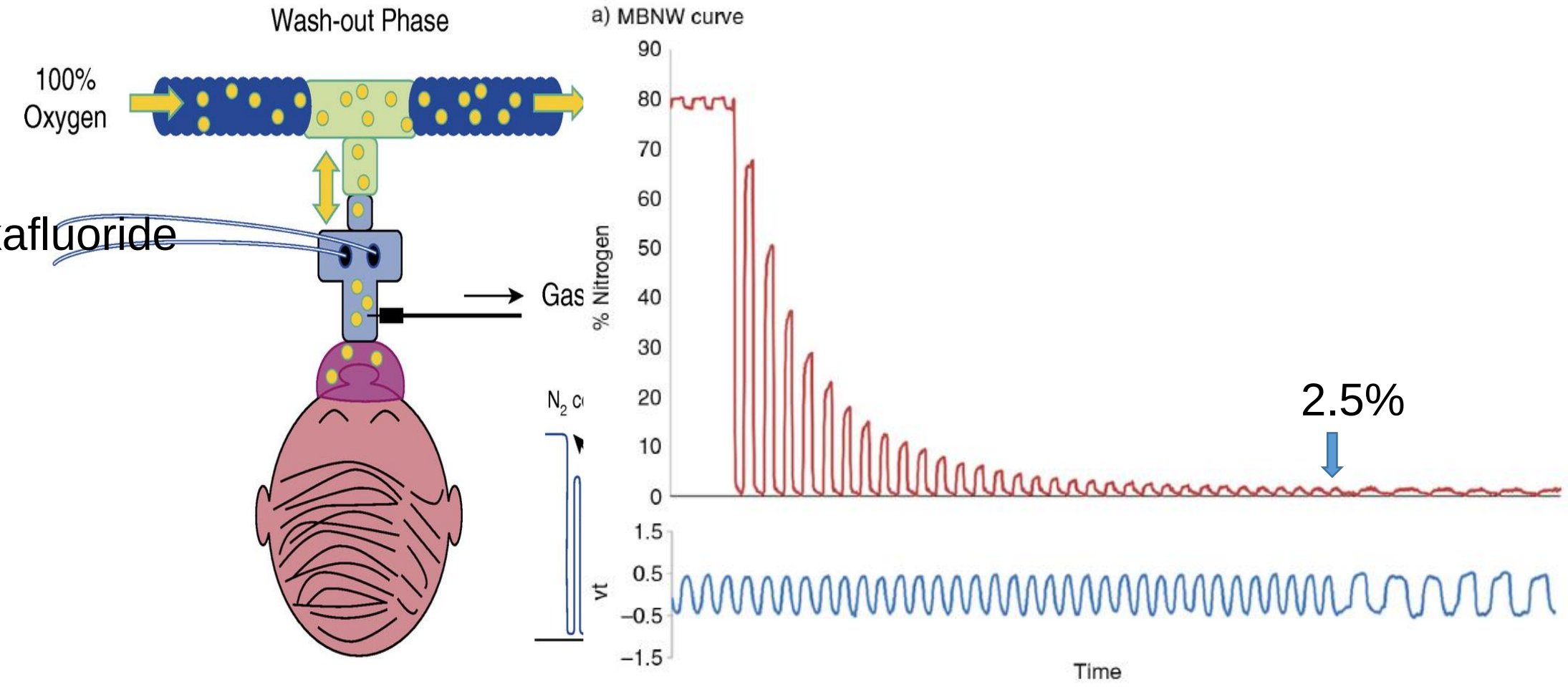
Respir Care 2020;65(9):1392–1412

Multiple breath washout test (MBW)

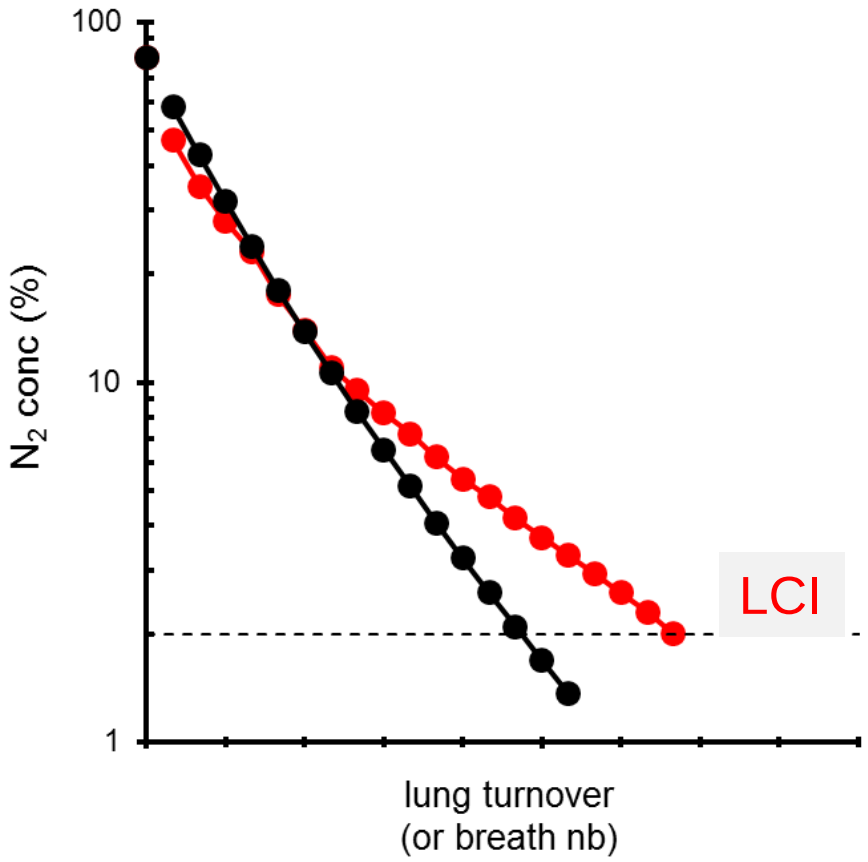
Inert Gas:

Nitrogen

Sulfar hexafluoride



Ann Am Thorac Soc. 2015 Jun; 12(6): 932–939
European Clinical Respiratory Journal 2014, 1: 25898



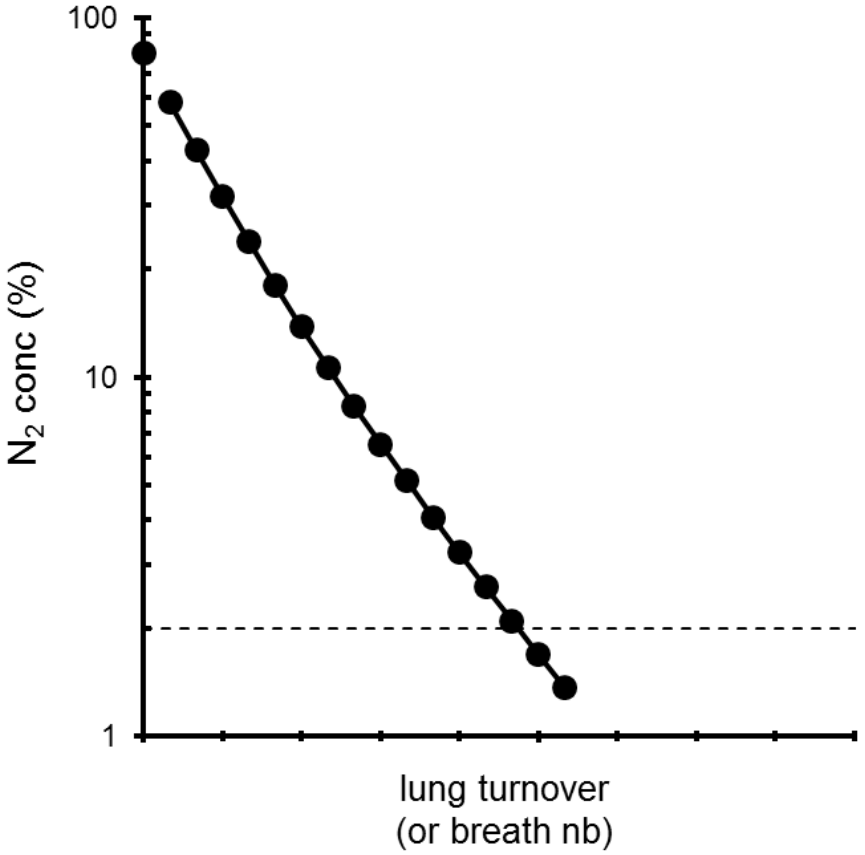
From breath-by-breath N2 :

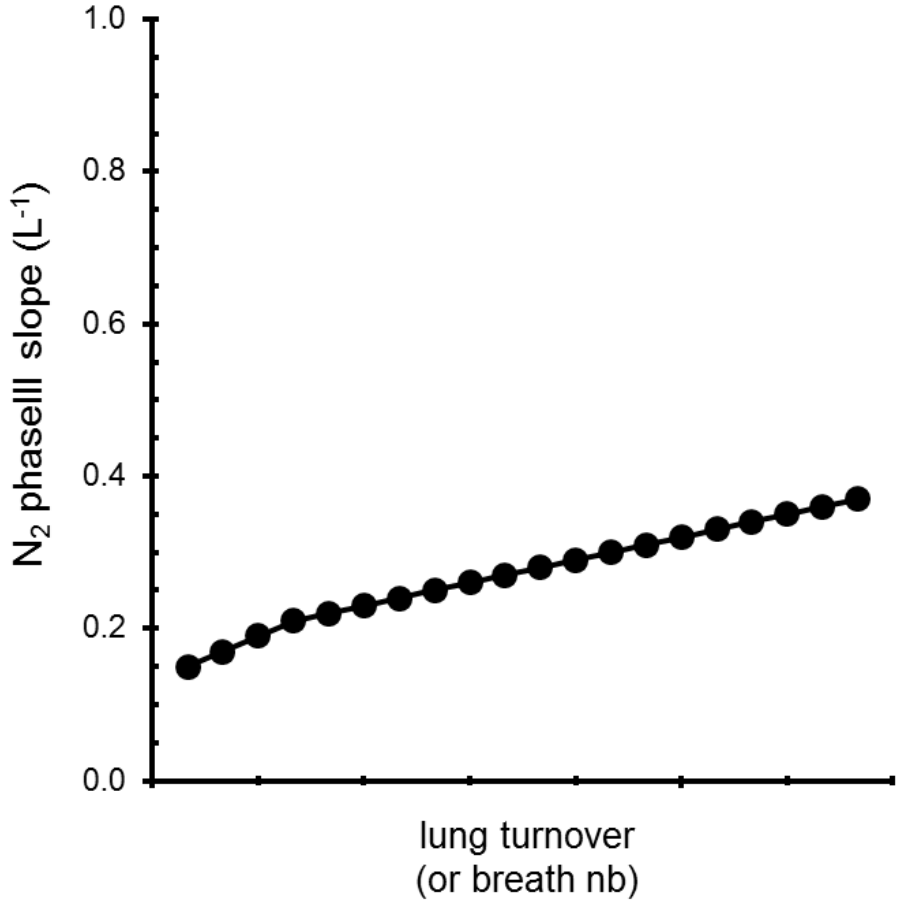
-FRC

-Lung clearance index

=cumulative expiratory volume/FRC

Adapted from slide presented by Professor Sylvia Verbanck





From breath-by-breath N2 :

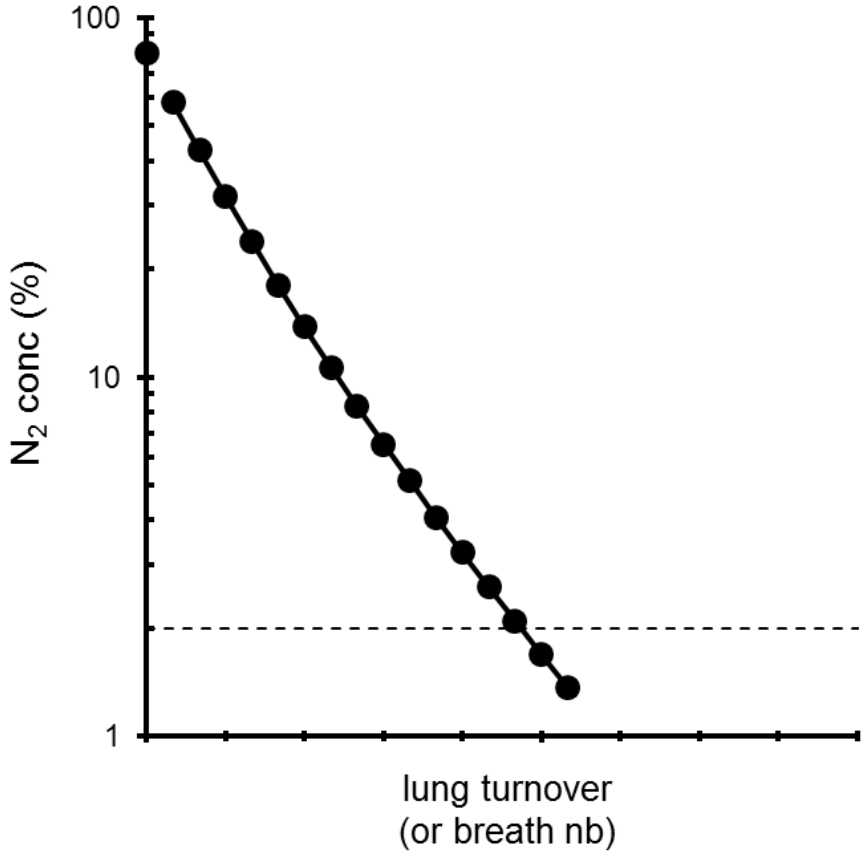
-FRC

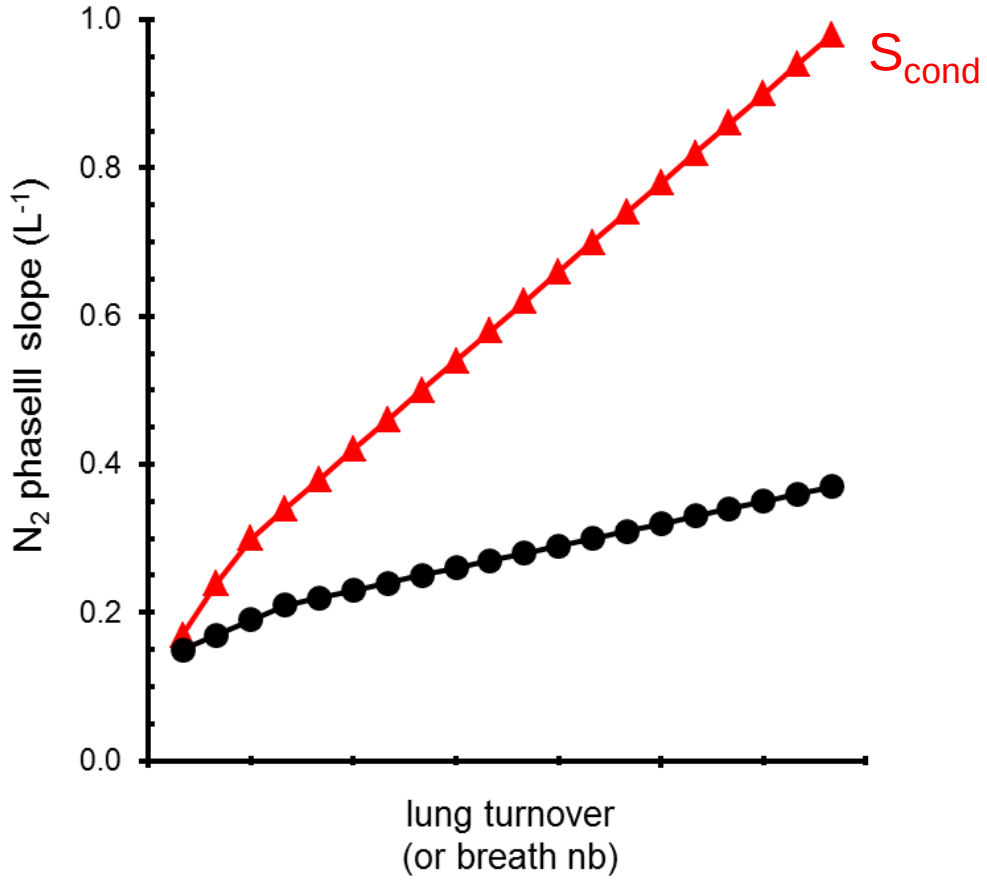
-Lung clearance index

=cumulative expiratory volume/FRC

From within breath N_2 phase III slope:

Adapted from slide presented by Professor Sylvia Verbanck





From breath-by-breath N2 :

-FRC

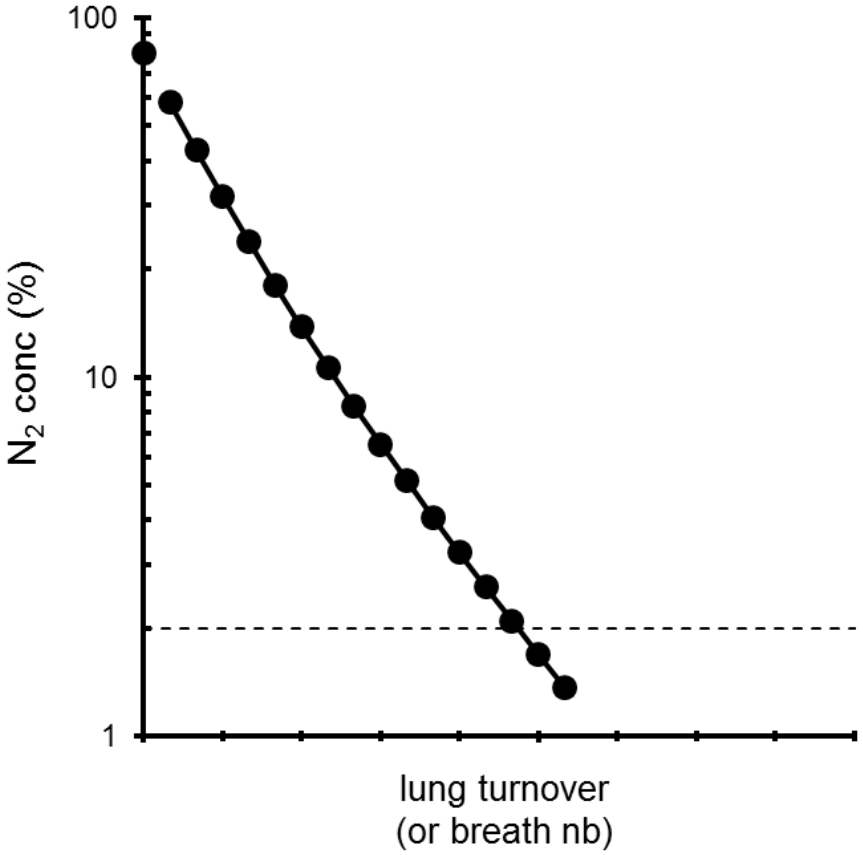
-Lung clearance index

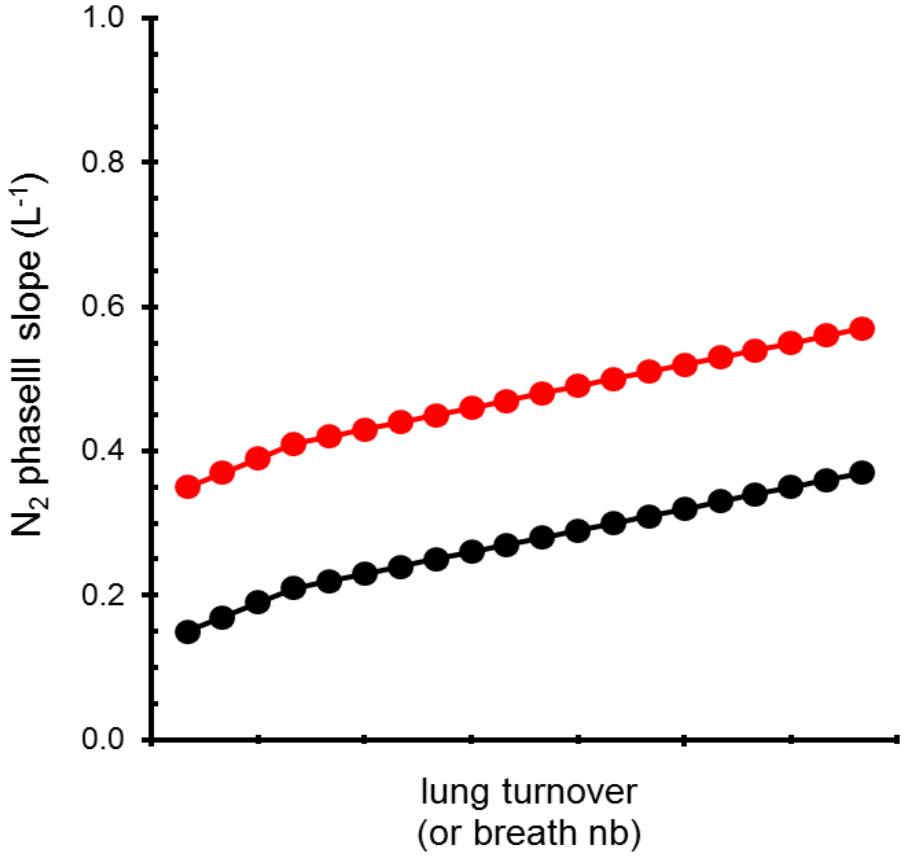
=cumulative expiratory volume/FRC

From within breath N_2 phase III slope

-Conductive index (Scond)

Adapted from slide presented by Professor Sylvia Verbanck





S_{acin}

From breath-by-breath N2 :

-FRC

-Lung clearance index

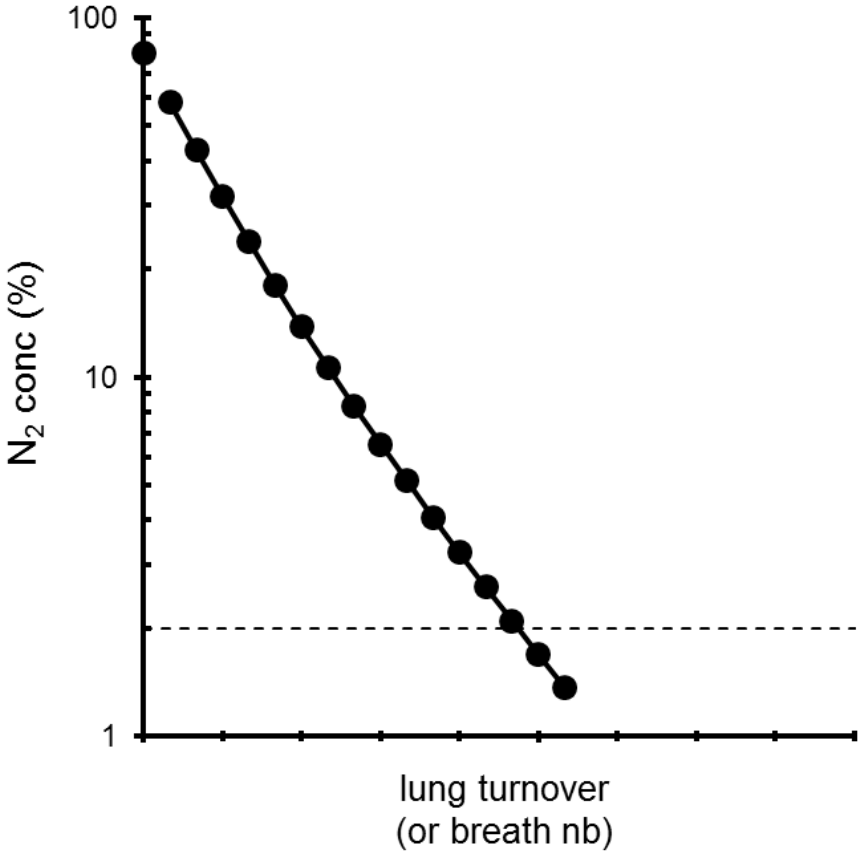
=cumulative expiratory volume/FRC

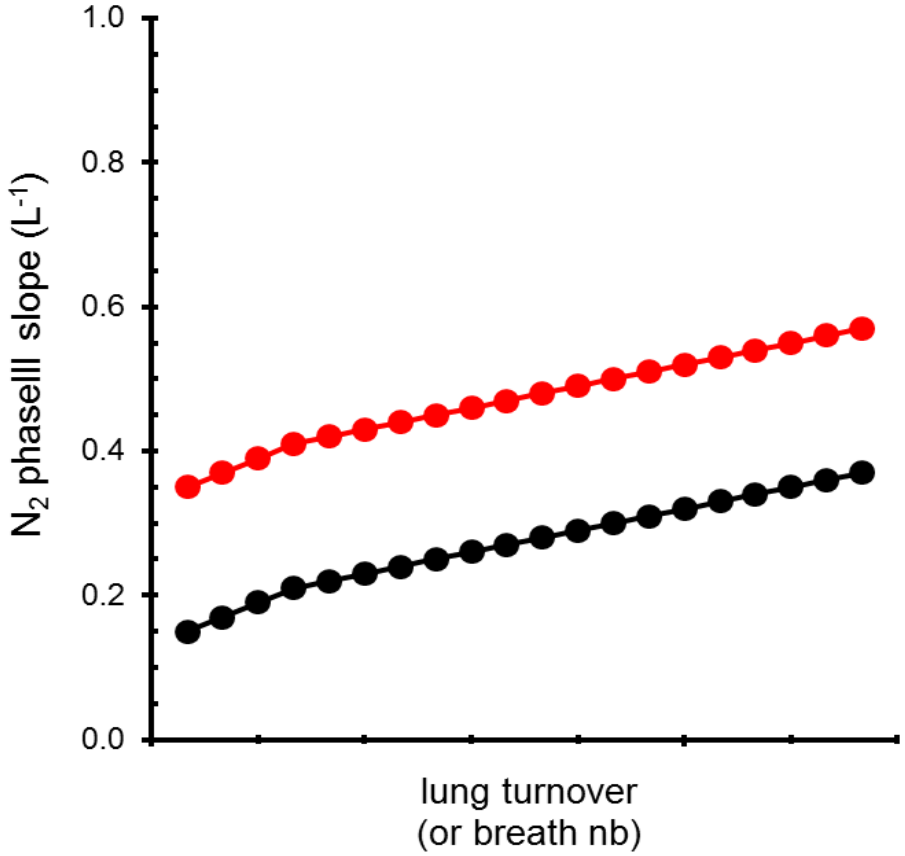
From within breath N_2 phase III slope

-Conductive index (Scond)

-Acinar index (Sacin)

Adapted from slide presented by Professor Sylvia Verbanck





S_{acin}

From breath-by-breath N2 :

-FRC

-Lung clearance index

=cumulative expiratory volume/FRC

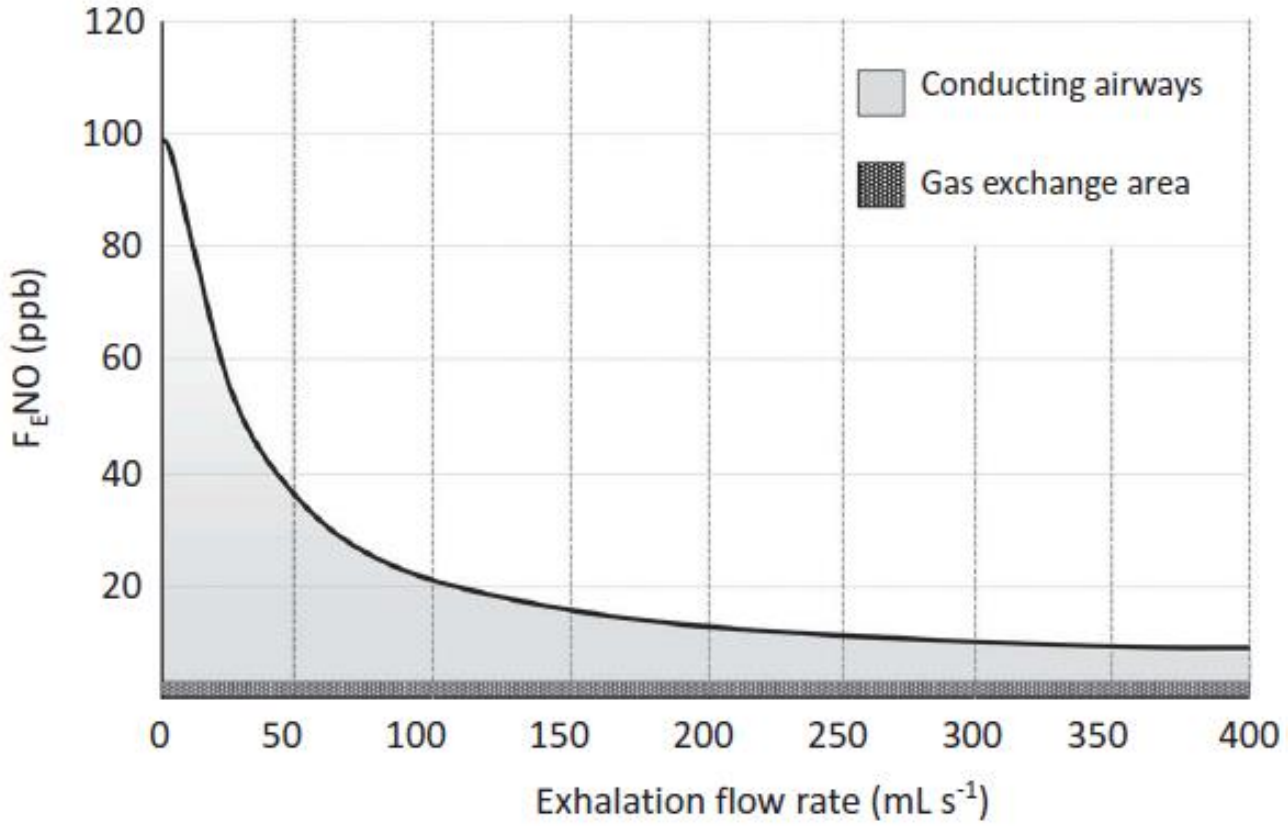
From within breath N_2 phase III slope

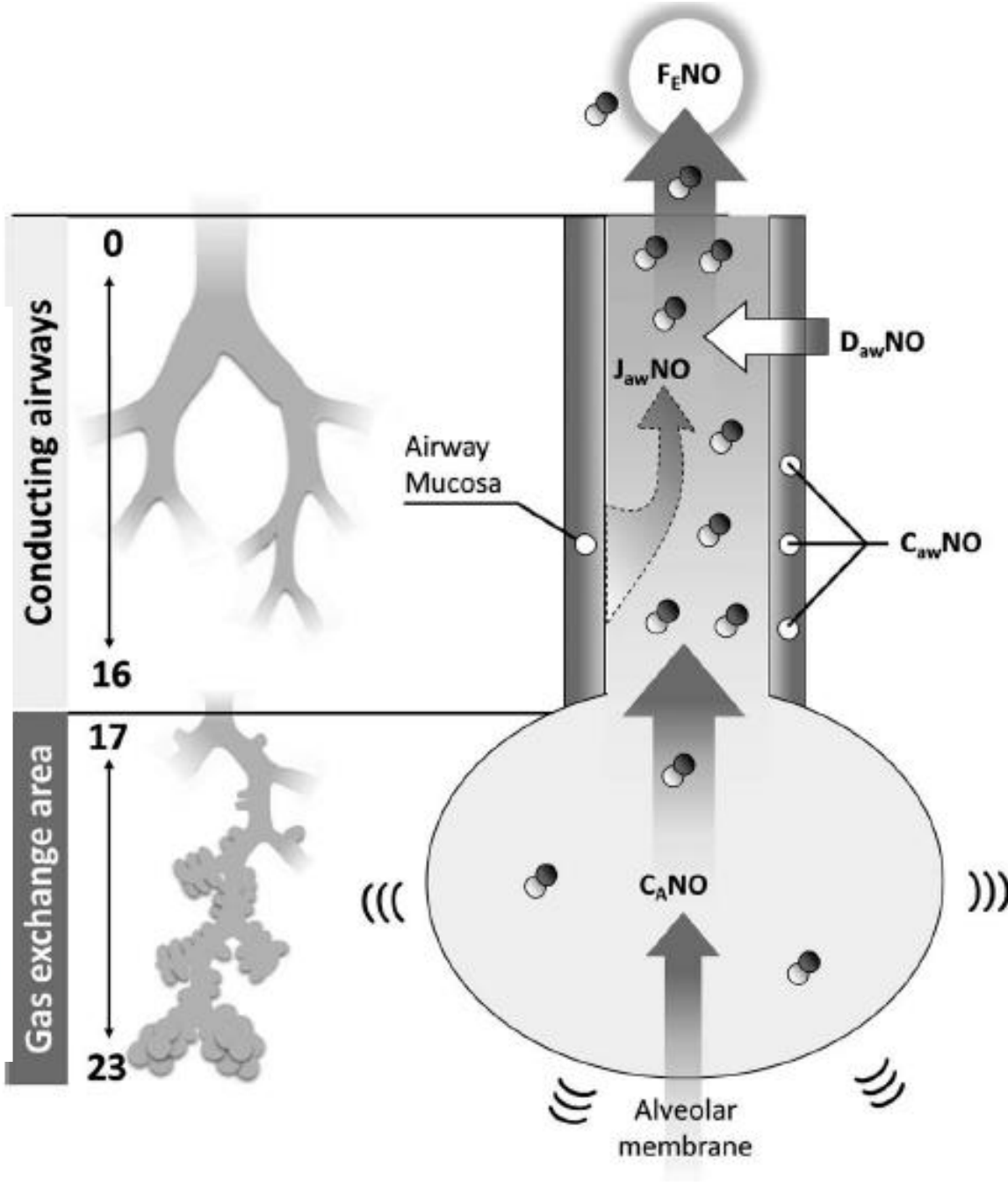
-Conductive index (Scond)

-Acinar index (Sacin)

Adapted from slide presented by Professor Sylvia Verbanck

Alveolar FeNO (C_ANO)





Respiratory Medicine, 11:2, 101-109

Exploring the relevance and extent of small airways dysfunction in asthma (ATLANTIS): baseline data from a prospective cohort study

*Dirkje S Postma, Chris Brightling, Simonetta Baldi, Maarten Van den Berge, Leonardo M Fabbri, Alessandra Gagnatelli, Alberto Papi, Thys Van der Molen, Klaus F Rabe, Salman Siddiqui, Dave Singh, Gabriele Nicolini, Monica Kraft, on behalf of the ATLANTIS study group**

ATLANTIS study

AssessmenT of smalL Airways involvemeNT In aSthma

Aim of ATLANTIS

To determine the role of small airways abnormalities in the clinical manifestations of asthma

To assess which combination of biomarkers, physiological tests, and imaging markers best measure the presence and extent of SAD in patients with asthma

Exploring the relevance and extent of small airways dysfunction in asthma (ATLANTIS): baseline data from a prospective cohort study

*Dirkje S Postma, Chris Brightling, Simonetta Baldi, Maarten Van den Berge, Leonardo M Fabbri, Alessandra Gagnatelli, Alberto Papi, Thys Van der Molen, Klaus F Rabe, Salman Siddiqui, Dave Singh, Gabriele Nicolini, Monica Kraft, on behalf of the ATLANTIS study group**

Includes people with asthma of all severities

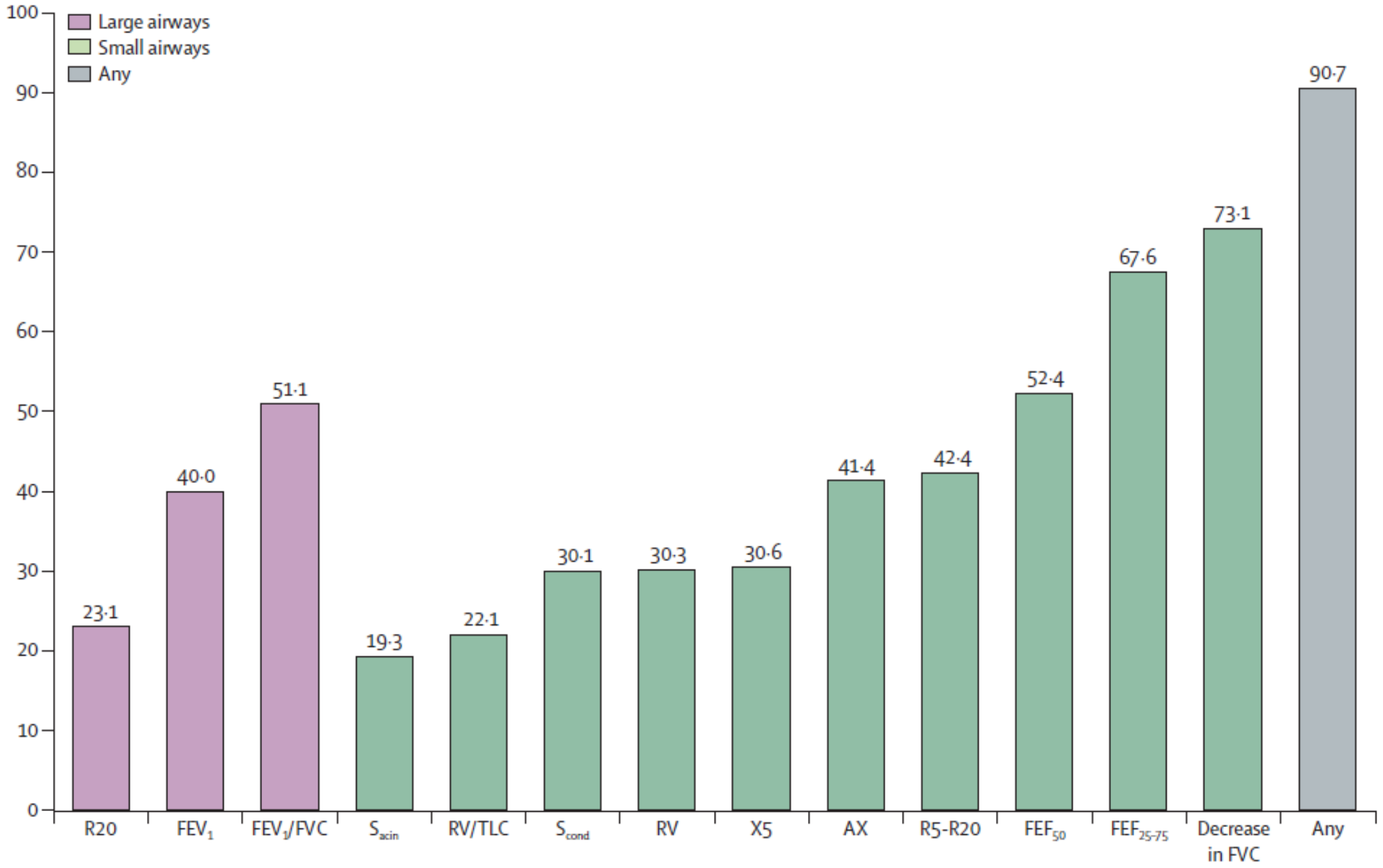
Includes control participants without airway disease

Multicentre, multinational, 1-year prospective cohort study

Includes smokers

Prevalence

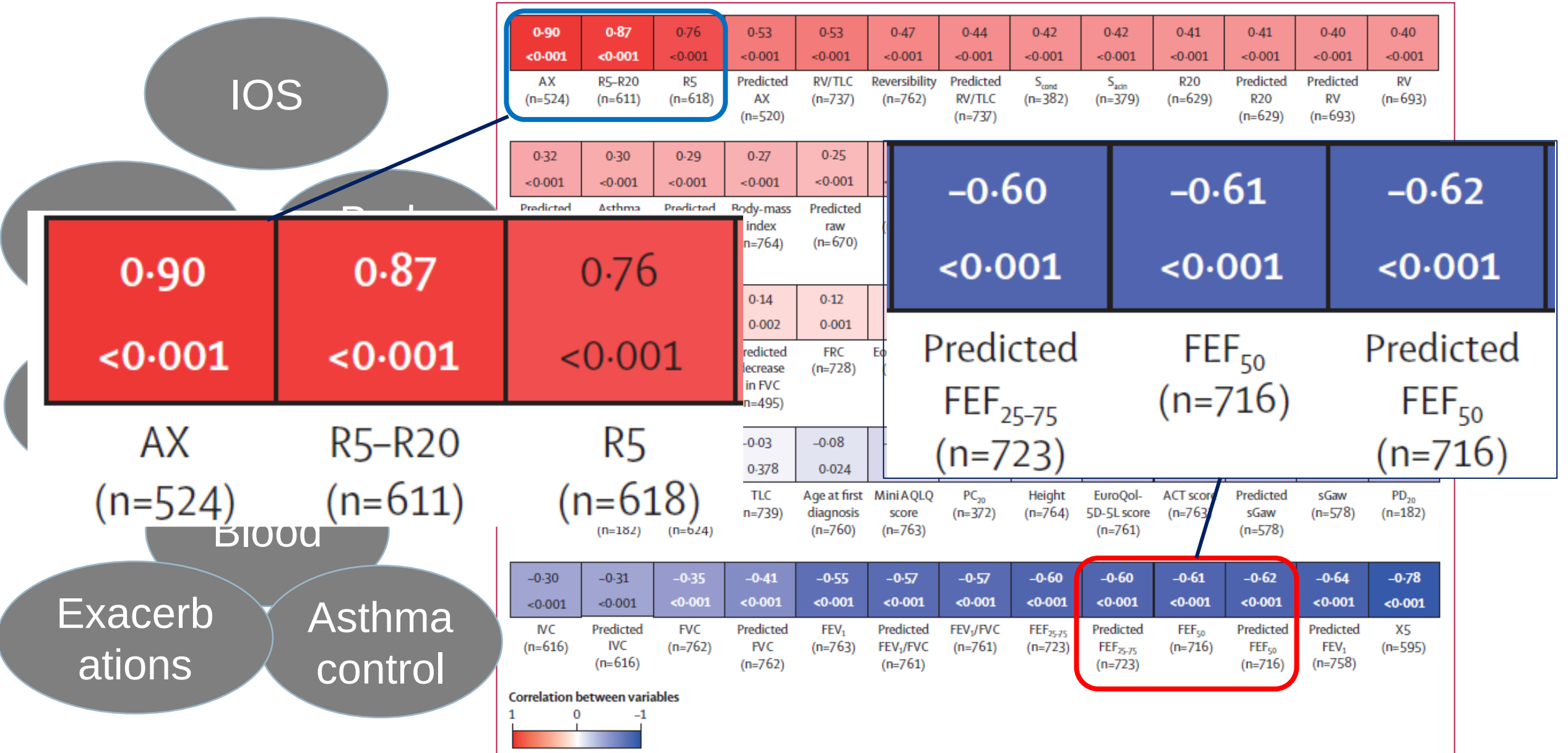
n=773

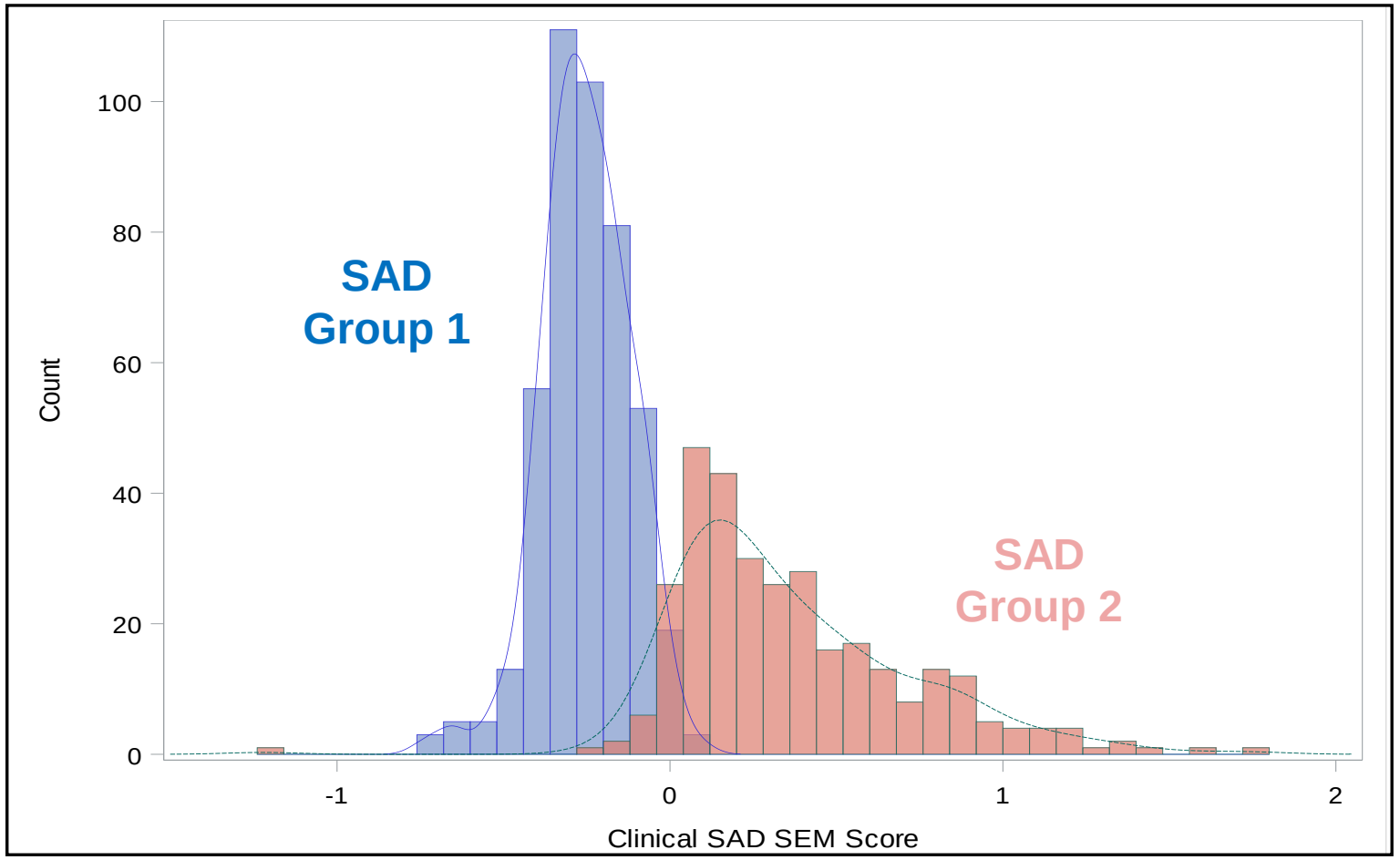


Prevalence by GINA severity

	GINA1 (n=135)	GINA2 (n=85)	GINA3 (n=207)	GINA4 (n=300)	GINA5 (n=46)
Spirometry	**17%**	**11%**	**27%**	**39%**	**6%**
FEF_{25-75}	41%	43%	51%	55%	80%
FEF_{50}	37%	49%	54%	55%	75%
Decrease in FVC	72%	68%	75%	73%	84%
Body plethysmography					
Residual volume/total lung capacity	14%	16%	19%	28%	31%
Functional residual capacity	16%	23%	19%	25%	27%
Impulse oscillometry					
R5–R20	30%	40%	37%	51%	71%
AX	32%	34%	35%	49%	68%
X5	23%	32%	29%	33%	53%
Multiple breath nitrogen washout					
S_{cond}	21%	20%	30%	33%	64%
S_{acin}	12%	18%	19%	21%	41%

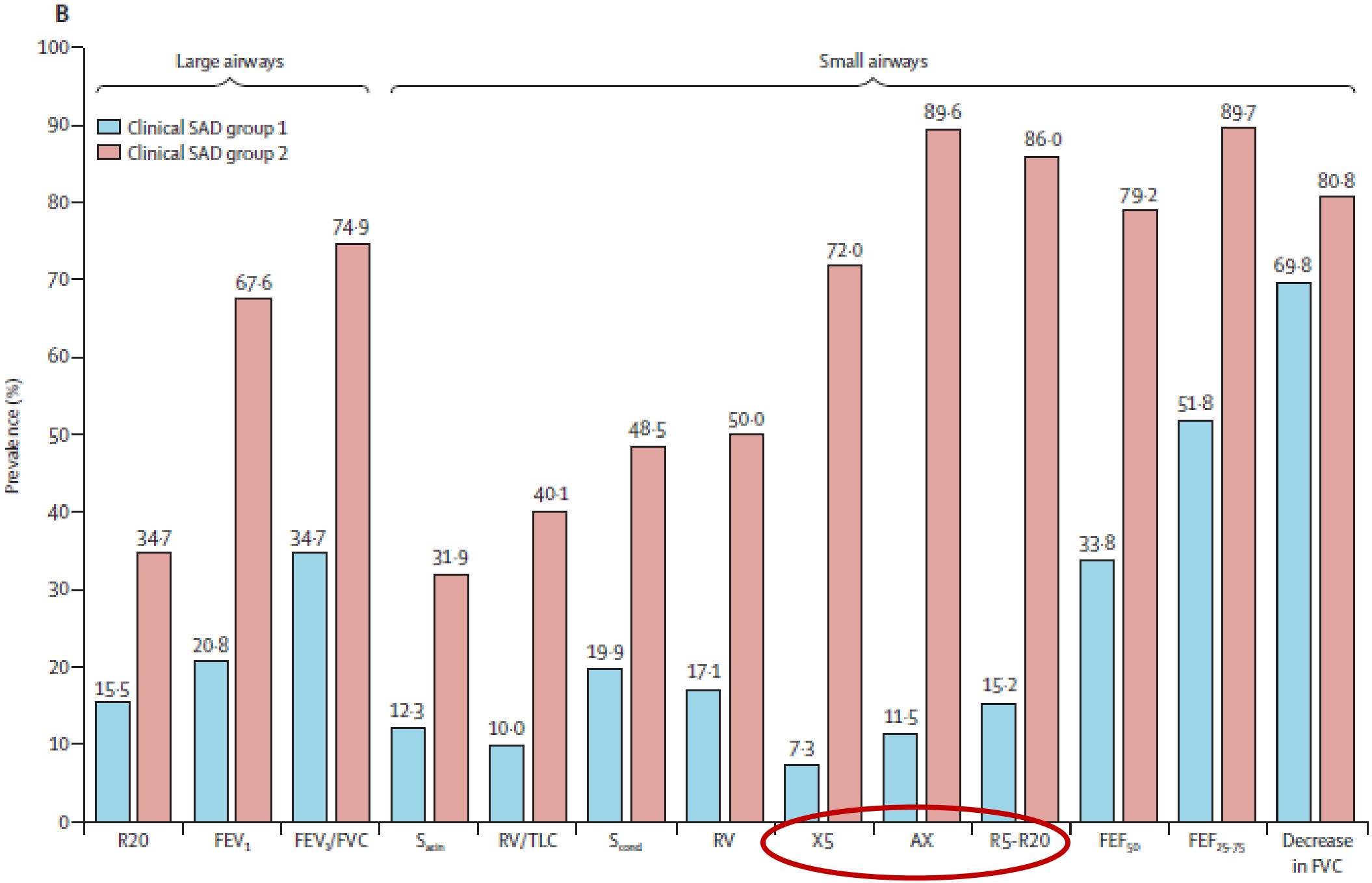
Correlations between the clinical SAD score of participants with asthma and all variables measured




SAD
Group 1
SAD
Group 2
Count
100
80
60
40
20
0
-1
0
1
2
Clinical SAD SEM Score

Asthma control was worse in clinical SAD group 2

Parameter	Group1 n=452	Group2 n=312	P
No. of asthma-specific emergency	0.06	0.15	0.023
No. unscheduled consultations	0.15	0.50	0.001
No. exacerbations	0.16	0.29	0.002
≥ 1 exacerbation, %	50	59	0.002
Duration of disease, years	11.61 (4.4;24.5)	21.51 (9.4;35.0)	<0.001
ACT total score	22 (19.0;24.0)	20 (17.0;23.0)	<0.001
ACT score ≤ 15, %	8.9	19.2	<0.001
ACQ-6 total mean score	0.66 (0.2;1.3)	1.00 (0.5;1.8)	<0.001
ACQ-6 score ≥ 1.25 ,%	27.4	40.4	<0.001
EQ-5D-5L: VAS score	83 (75.0;90.0)	80 (70.0;90.0)	<0.001


B
Large airways
Small airways
Clinical SAD group 1
Clinical SAD group 2
Prevalence (%)
100
90
80
70
60
50
40
30
20
10
0
15·5
34·7
20·8
67·6
34·7
74·9
12·3
31·9
10·0
40·1
19·9
48·5
17·1
50·0
7·3
72·0
11·5
89·6
15·2
86·0
33·8
79·2
51·8
89·7
69·8
80·8
R20
FEV1
FEV1/FVC
Sacin
RV/TLC
Scond
RV
X5
AX
R5-R20
FEF50
FEF25-75
Decrease in FVC

Summary

Summary

Small airway

<2mm, 8 generation

Silent zone: large surface area and little airflow

Summary

Small airway

<2mm, 8 generation

Silent zone: large surface area and low airflow

Role of small airway disease in asthma

airway resistance and inflammation ↑↑↑

asthma control ↓↓ and AE ↑↑

Summary

Small airway

<2mm, 8 generation

Silent zone: large surface area and low airflow

Role of small airway disease in asthma

Prevalence of small airway disease in asthma

about 50~60%

all asthma severity, more severe disease

Summary

Small airway

<2mm, 8 generation

Diagnosis of Small Airway disease

EIA, Obese, night sx., old age, smoker

Physiological test: IOS and Sprirometry

Summary

Small airway

<2mm, 8 generation

Silent zone: large surface area and low airflow

Role of small airway disease in asthma

airway resistance and inflammation ↑↑↑

asthma control ↓↓ and AE ↑↑

Prevalence of small airway disease in asthma

about 50~60%, all asthma severity, more severe disease

Diagnosis of Small airway disease

EIA, Obese, night sx., old age, smoker

Physiological test: IOS and Sprirometry

감사합니다.!!!