Sjukdom i små luftvägar vid svår KOL- finns det bättre metoder än spirometri?

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13931-14.03.2025

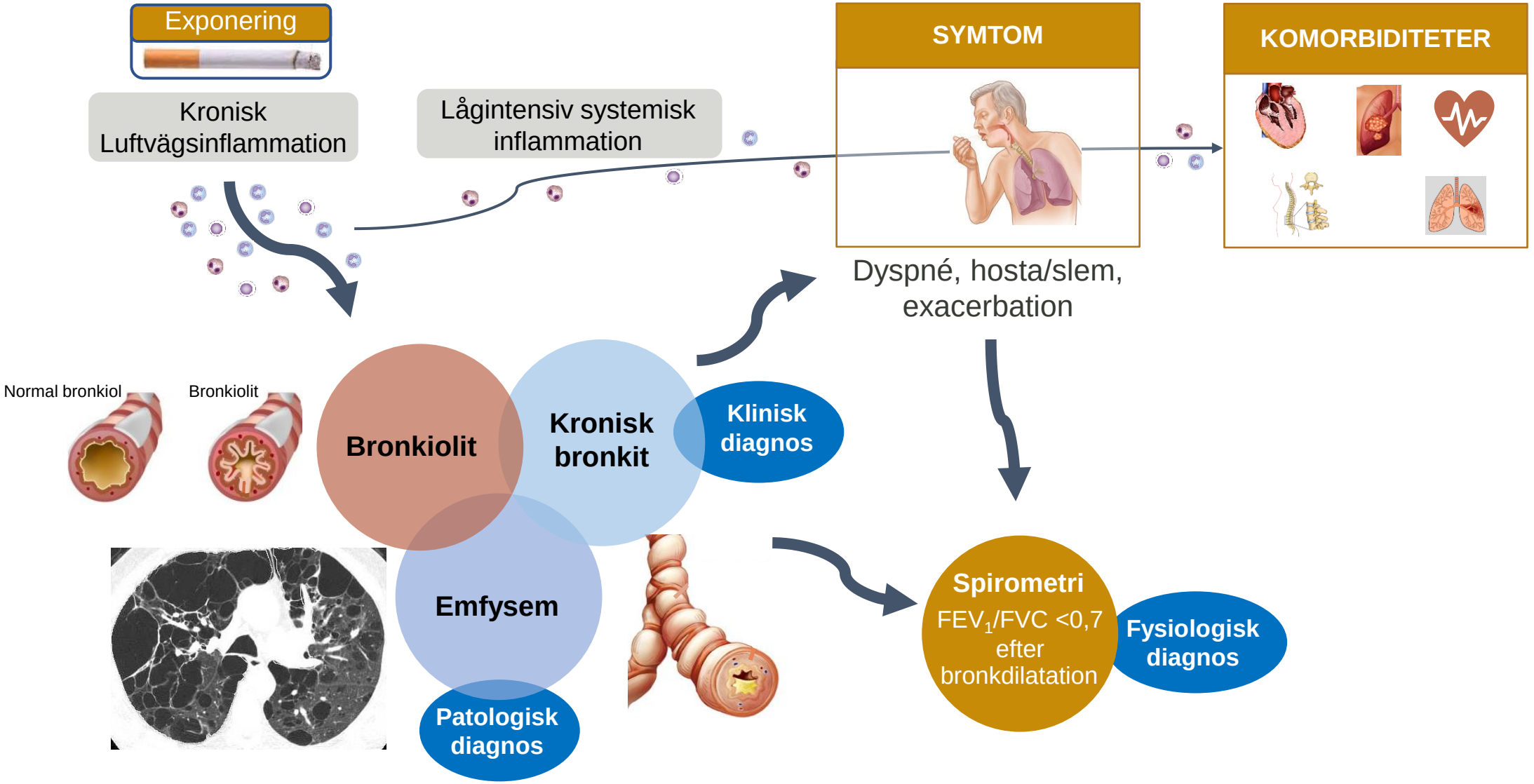
COI

- Advisory board/ speaker for AstraZeneca, GSK, Sanofi, Chiesi, ALK.

Översikt

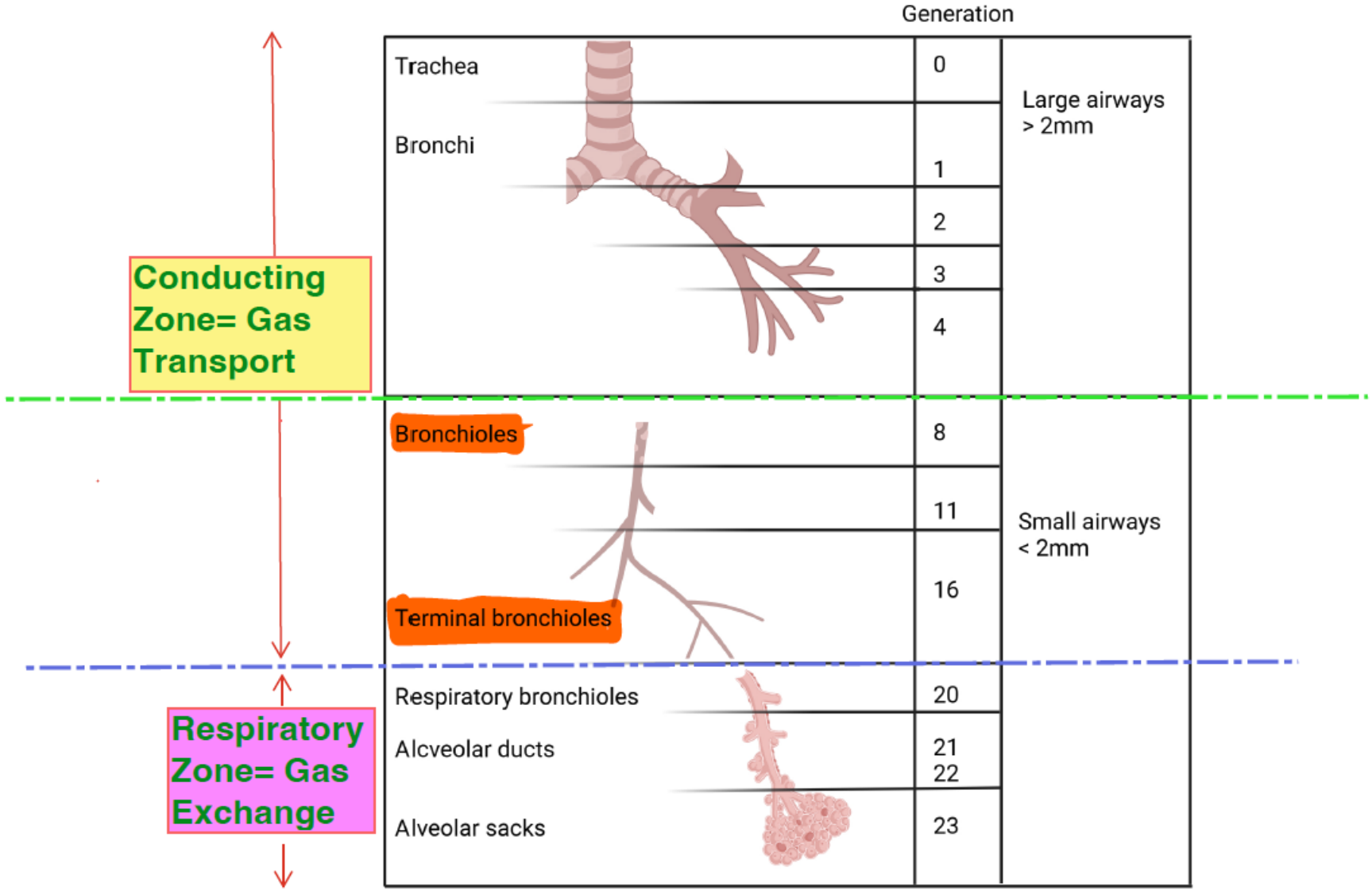
- Definitioner: KOL och små luftvägar
- Patologi i dem små luftvägarna vid KOL
- Impulsoscillometri (IOS) vid KOL
- Preliminära resultat från IOSCO studie

Vad är KOL? – *Patogenes och klinik*



Global Initiative for Chronic Obstructive Lung Disease (GOLD), Update 2023. Available at: www.Goldcopd.org

Stora vs små luftvägar: Definition



Små luftvägar och KOL

SITE AND NATURE OF AIRWAY OBSTRUCTION IN CHRONIC OBSTRUCTIVE LUNG DISEASE*

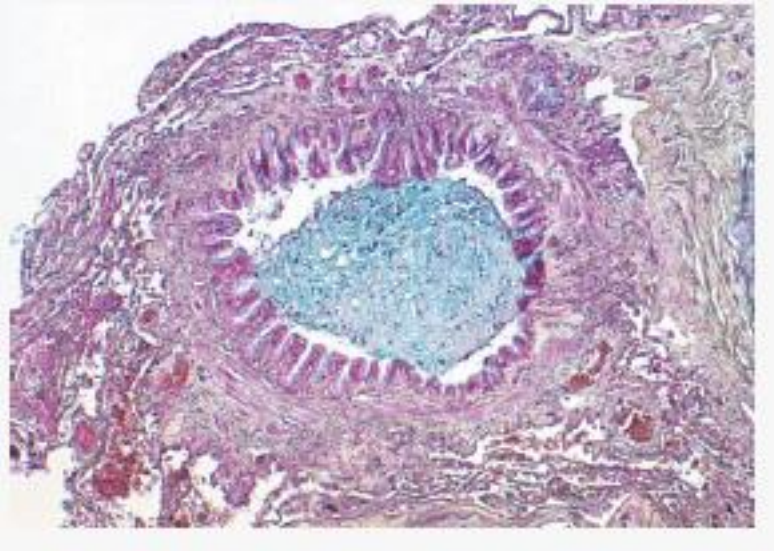
JAMES C. HOGG, M.D., M.SC., PETER T. MACKLEM, M.D., C.M., F.R.C.P. (C), AND W. M. THURLBECK, M.B., CH.B., M.C.PATH.

Abstract We have wedged a small catheter in airways 2 to 3 mm in diameter in excised human lungs to have measure airway resistance central (R_c) and peripheral (R_p) to this site. In five normal lungs, R_p accounted for only 25 per cent total airway resistance (R_l) and averaged 0.18 cm of water per liter per second. In seven patients with emphysema R_p was increased from four to 40 times. R_p was also increased in one case of bronchiectasis and another of bronchiolitis. In all, R_c scattered around the normal value. Bronchographic and histologic studies showed that R_p was increased because of mucus plugging, narrowing and obliteration of the small airways.

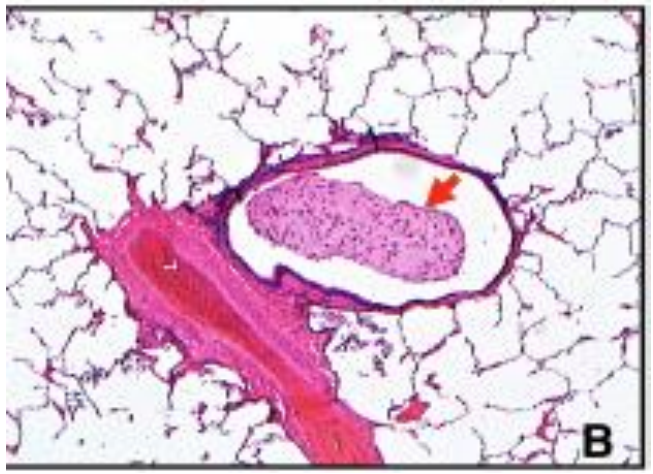
Disease of small airways may be common to various chronic obstructive lung diseases. Because R_p is normally so small, there may be considerable obstruction in peripheral airways that would affect ventilation distribution and gas exchange but would have little effect on function tests designed to reveal obstruction. When total airway resistance is elevated to a clinically detectable level by disease in the small airways, obstruction is much more severe than is generally recognized.

Hogg et al NEJM 1968

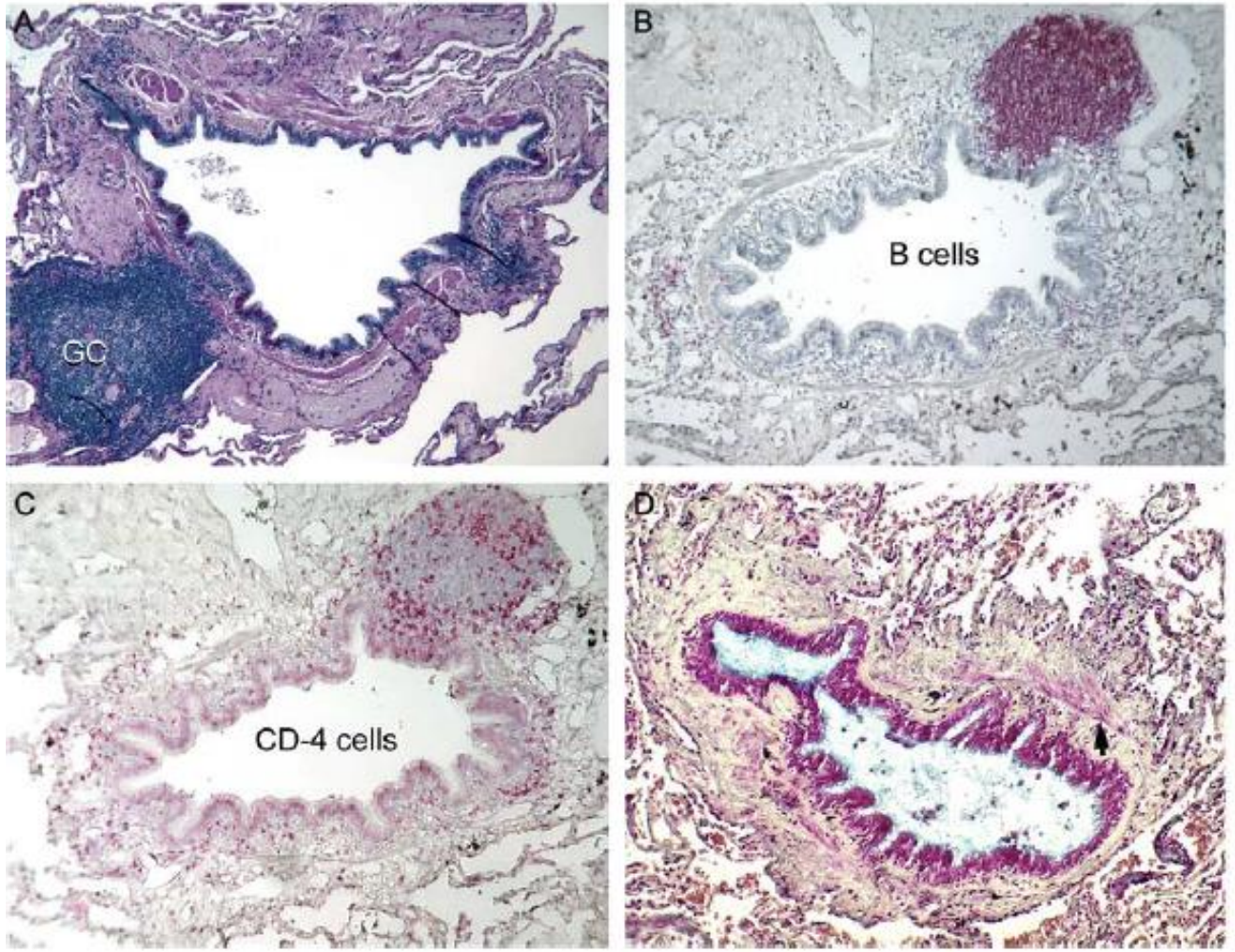
Patologi i dem små luftvägana vid KOL



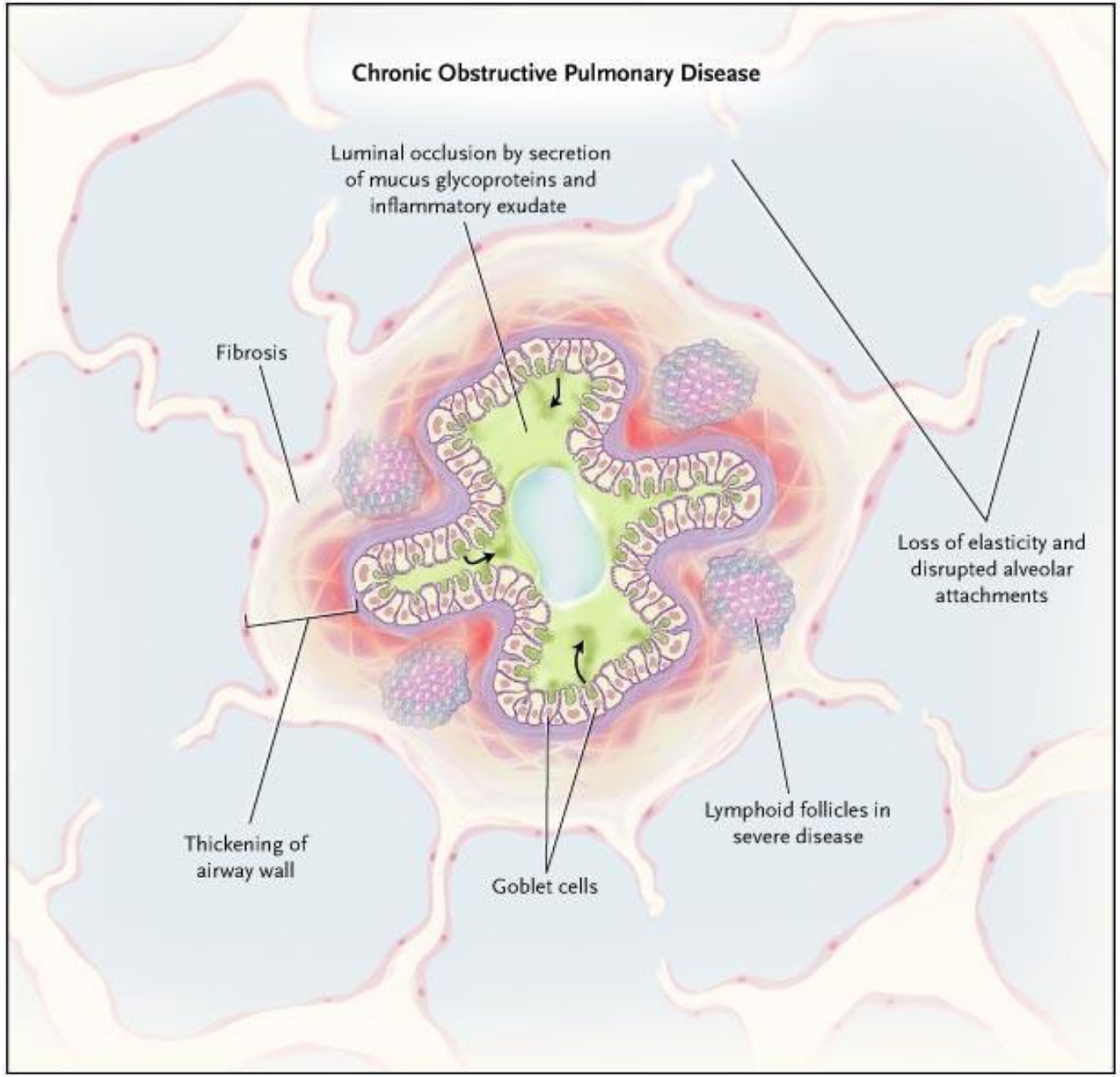
Hogg et al NEJM 2004



Higham et al Respir Res 2019



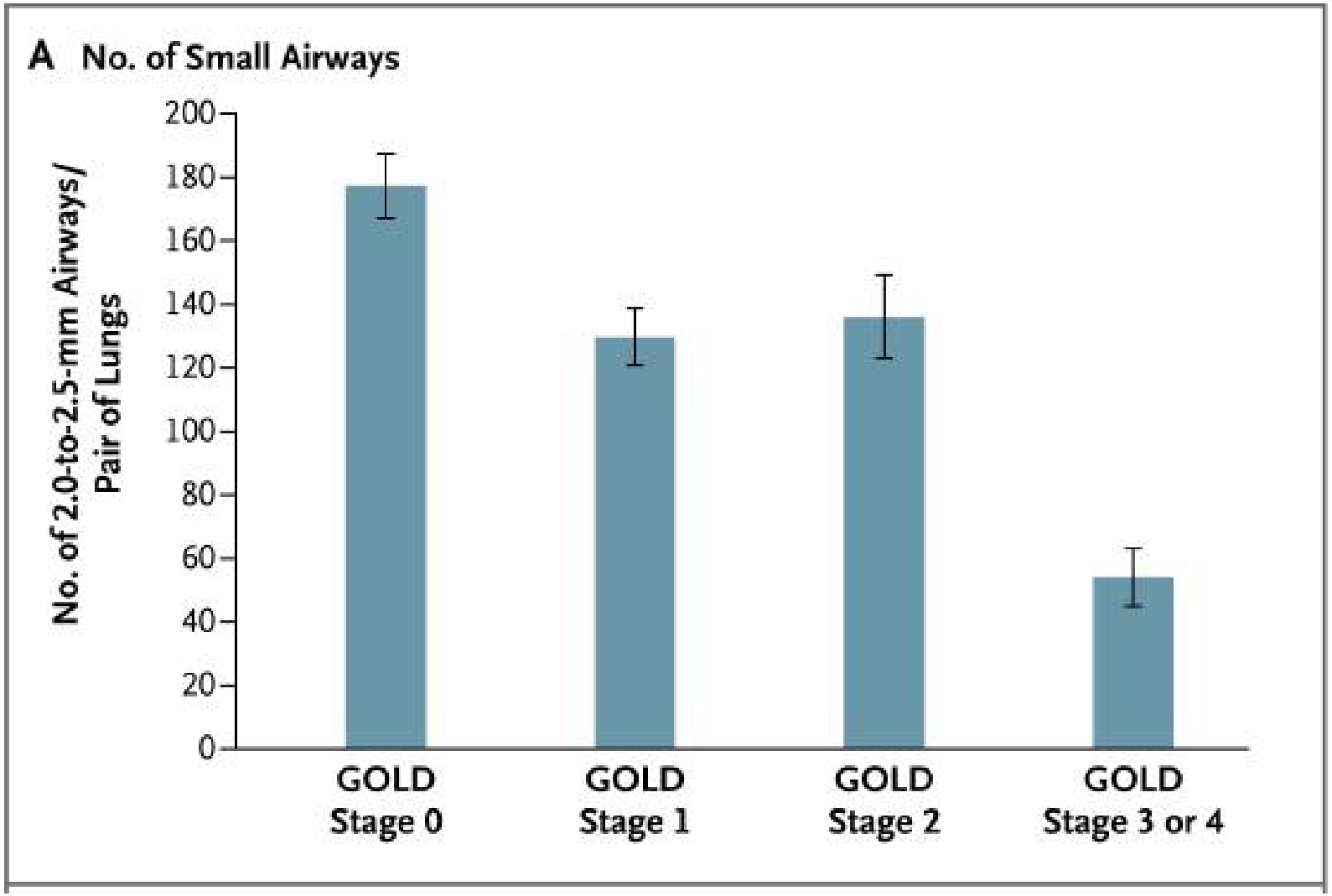
Hogg et al NEJM 2006



Small Airways Disease (SAD) vid KOL

Barnes PJ NEJM 2004

SAD och KOL stadium enligt GOLD

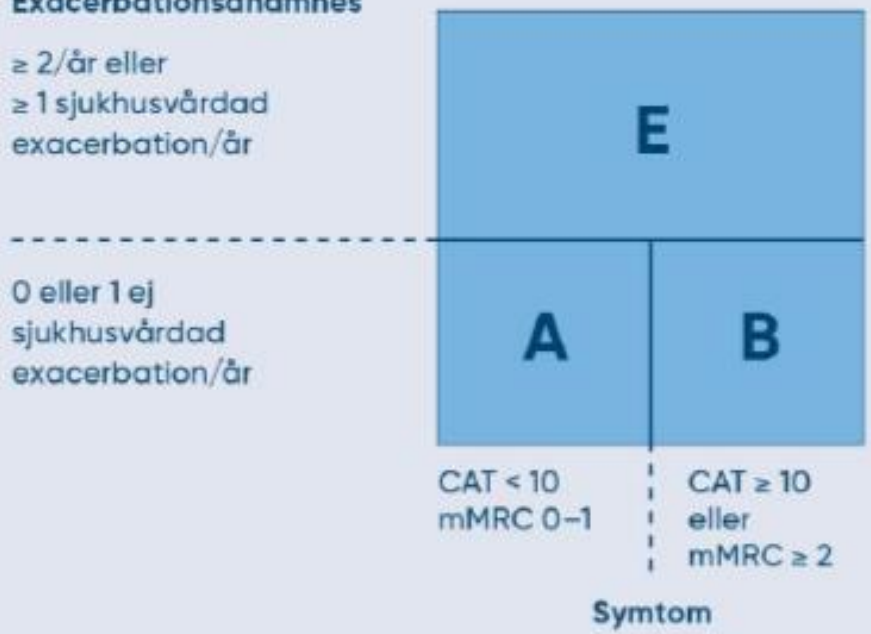


McDonough et al NEJM 2011

Gradering av sjukdomen

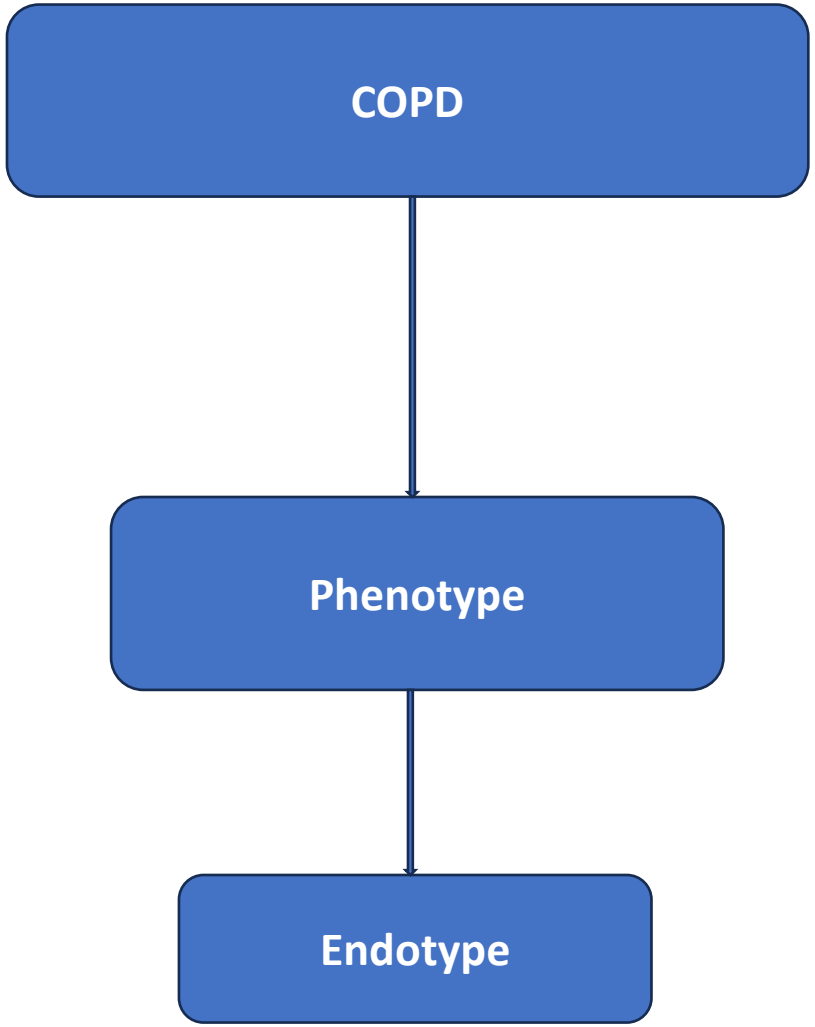
Diagnos bekräftad med spirometri efter bronkdilatation $FEV_1/FVC < 0,7$ → Lungfunktions-nedsättning GOLD 1–4 → Riskvärdering utifrån symtom och exacerbationer GOLD A, B och E

Gradering utifrån lungfunktionsförlust		FEV_1 (% förväntat efter bronkdilatation)
GOLD 1	Lindrig	≥ 80
GOLD 2	Måttlig	50–79
GOLD 3	Svår	30–49
GOLD 4	Mycket svår	< 30



Läkemedelsverket behandlingsrekommendation 2023

Phenotyping vs Endotyping



Grouping Based on:

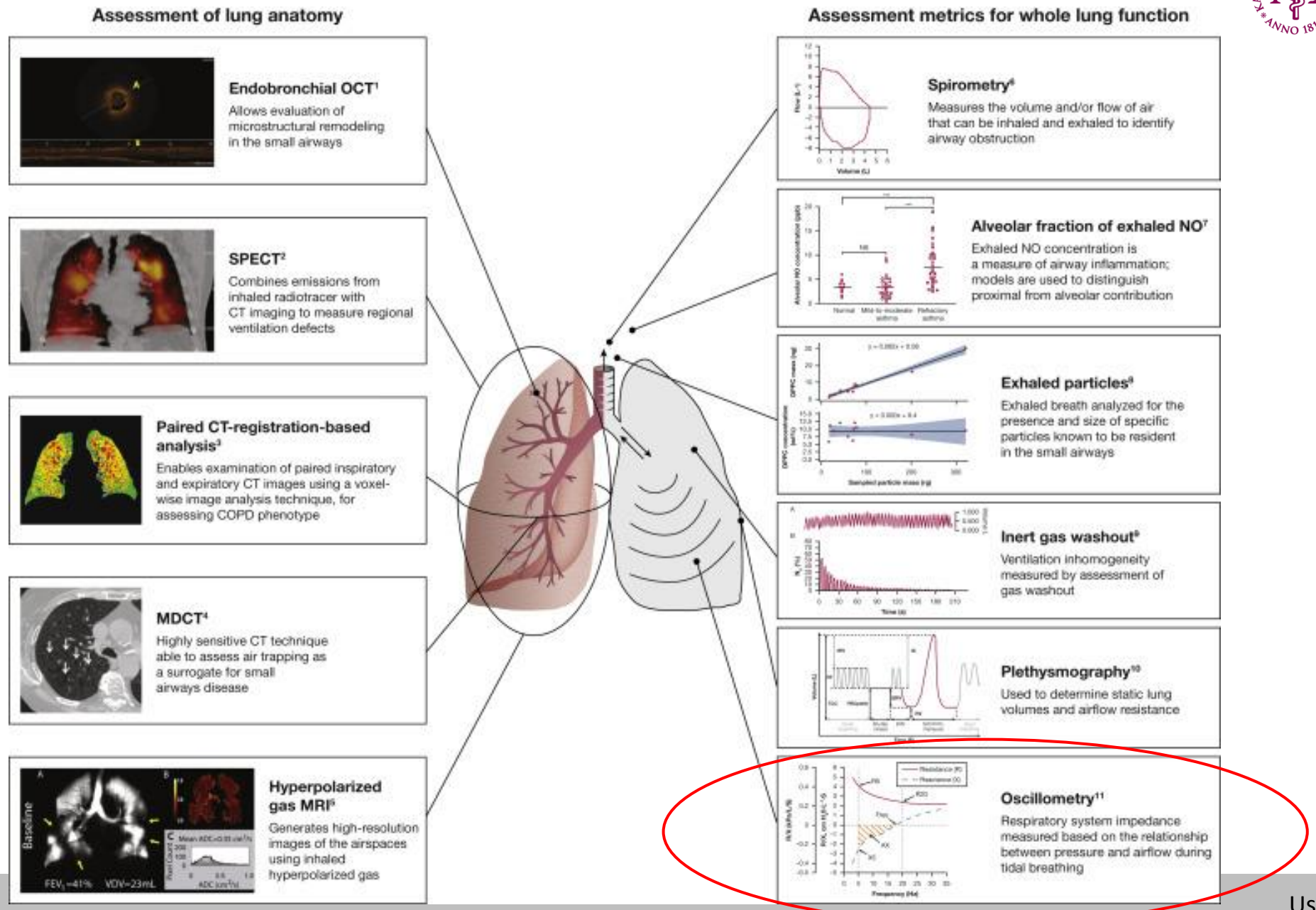
Observable characteristics

- Hyperinflation, chronic bronchitis, emphysema
- Exacerbations, symptoms, FEV_1
- Smoking status
- Hypoxemia or Hypercapnia
- Degree of SAD?

Distinct underlying biological mechanisms associated with outcome and/or are amenable to (existing) treatments

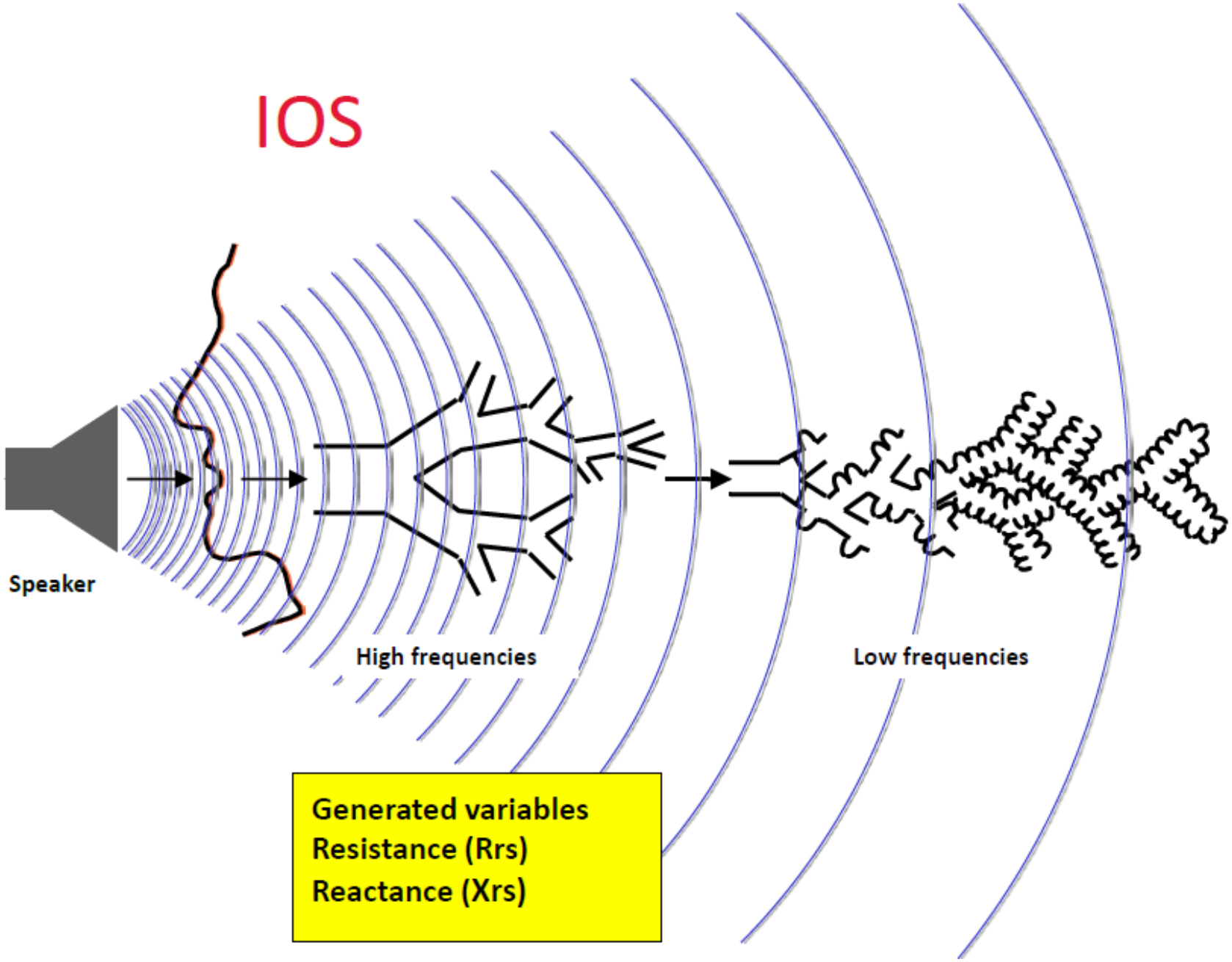
Hur kan vi upptäcka förändringar i dem små luftvägarna?

Metoder för att upptäcka SAD



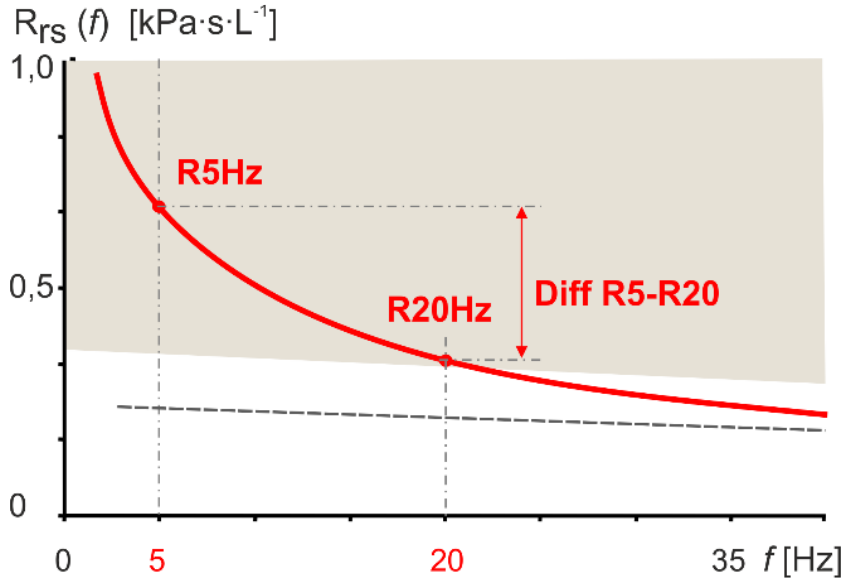
Usmani et al Chest 2021

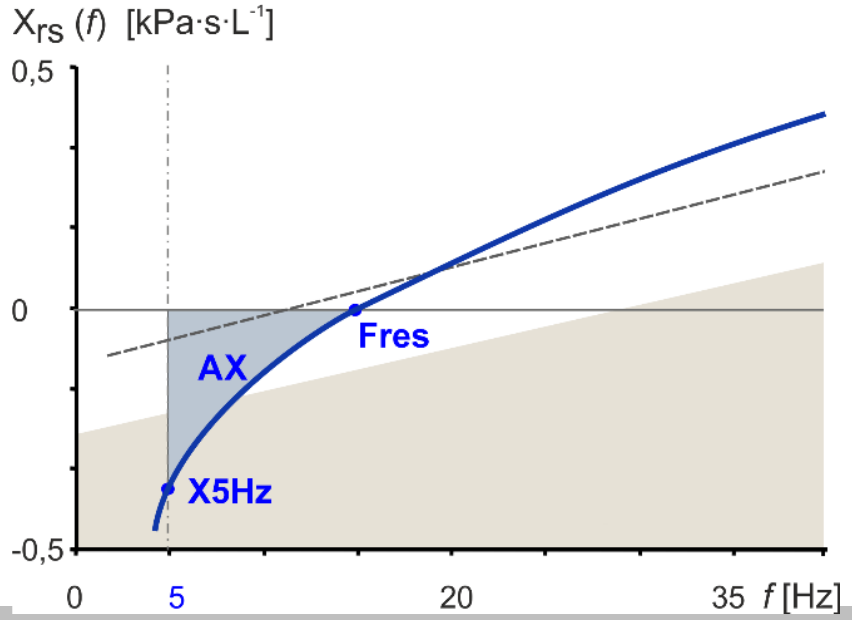
IOS



Generated variables
Resistance (Rrs)
Reactance (Xrs)

IOS – parameters





Normal lung function	
Respiratory resistance	R5Hz < 140% predicted
Lung reactance	(Predicted – X5Hz) < 0.15 kPa·s·L^{-1}

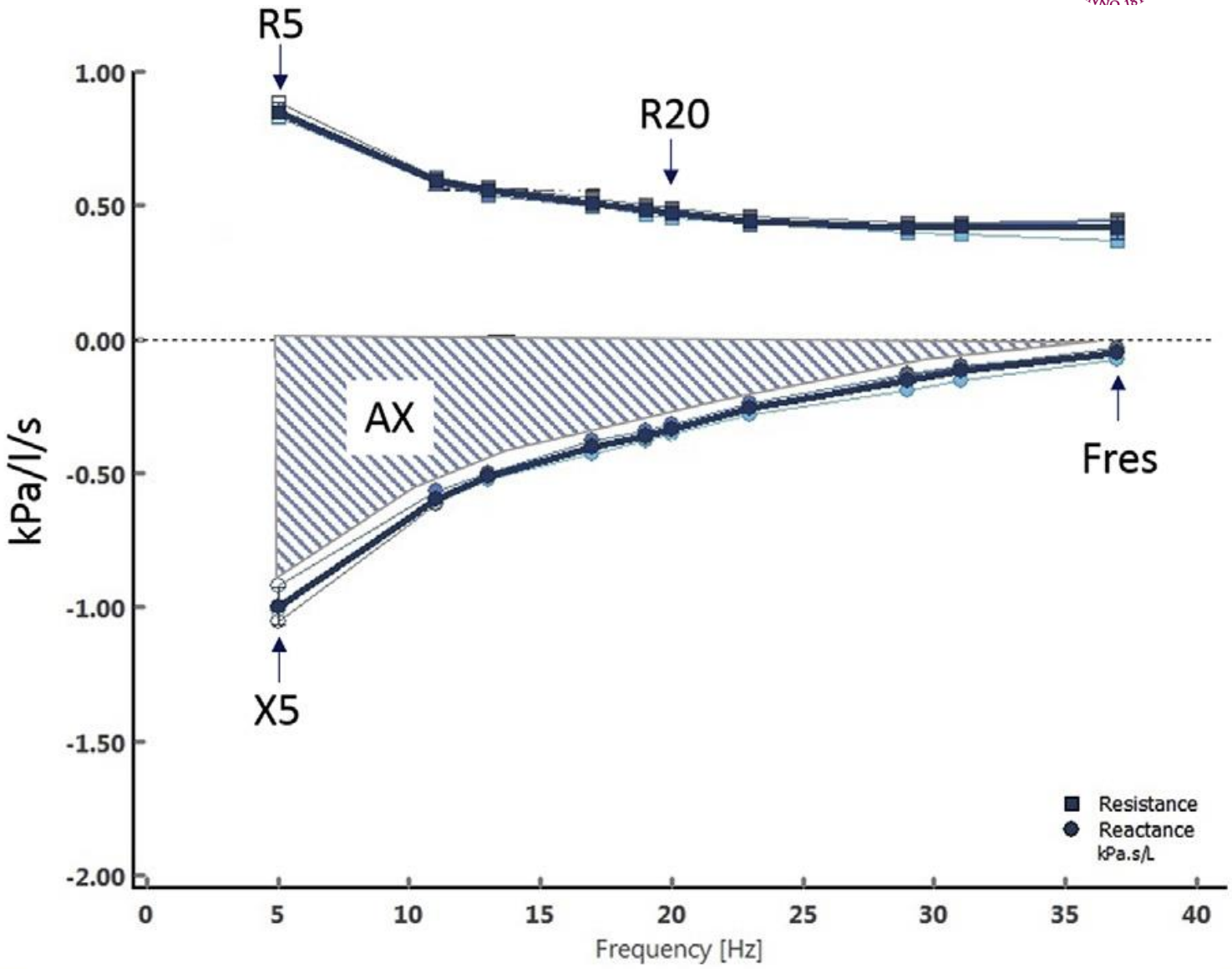
Abdo et al, ERJ 2023

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
M. ABDO ET AL.

Minimal clinically important difference for impulse oscillometry in adults with asthma

Mustafa Abdo[1], Anne-Marie Kirsten[2], Erika von Mutius[3,4], Matthias Kopp[5,6], Gesine Hansen[7], Klaus F. Rabe[1], Henrik Watz[2], Frederik Trinkmann[8,9,11] and Thomas Bahmer[10,11] on behalf of the ALLIANCE study group

IOS rapport hos patient med svår KOL



Lipworth et al Respiratory medicine 2018

IOS data från ECLIPSE studie

Table 2 Baseline IOS (impulse oscillometry) impedance parameters in ECLIPSE subjects.

	NSC[a] (n = 233)	CS (n = 322)	COPD (n = 2054)	GOLD 2 (n = 915)	GOLD 3 (n = 861)	GOLD 4 (n = 278)
R_5 (kPa/L/s)	0.33 (0.10)	0.31 (0.10)	0.49 (0.16)[b]	0.45 (0.14)	0.51 (0.16)[c]	0.55 (0.19)[d]
R_{20} (kPa/L/s)	0.26 (0.07)	0.25 (0.07)[e]	0.30 (0.08)[b]	0.29 (0.07)	0.31 (0.08)[c]	0.31 (0.09)[f]
$R_5 - R_{20}$ (kPa/L/s)	0.07 (0.05)	0.06 (0.05)	0.19 (0.10)[b]	0.15 (0.09)	0.20 (0.10)[c]	0.24 (0.12)[d]
X_5 (kPa/L/s)	−0.10 (0.06)	−0.09 (0.05)	−0.29 (0.17)[b]	−0.21 (0.13)	−0.32 (0.16)[c]	−0.44 (0.18)[d]
AX (Hz·kPa/L/s)	0.38 (0.40)	0.34 (0.35)	1.99 (1.46)[b]	1.37 (1.08)	2.25 (1.36)[c]	3.23 (1.79)[d]
F_{Res} (Hz)	12.4 (3.4)	12.1 (3.2)	20.7 (5.2)[b]	18.3 (4.3)	21.8 (4.7)[c]	25.3 (5.5)[d]

Data expressed as mean (SD) unless otherwise specified; Impedance parameters are post-bronchodilator. NSC = non-smoker controls; CS = control smokers; COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; $R_{5;}$ = respiratory resistance (R_{rs}) at 5 Hz; $R_{20;}$ = respiratory resistance (R_{rs}) at 20 Hz; $R_5 - R_{20}$ = difference in respiratory resistance at 5 Hz and 20 Hz; X_5 = reactance at 5 Hz; AX = integrated area of low-frequency reactance; F_{Res} = resonant frequency.

[a] 11 (5%) of NSC were former smokers.
[b] $p < 0.001$ compared with NSC and CS.
[c] $p \leq 0.001$ compared with GOLD 2.
[d] $p \leq 0.001$ compared with GOLD 2 and GOLD 3.
[e] $p = 0.041$ compared with NSC.
[f] $p = 0.002$ compared with GOLD 2. Comparisons between groups were adjusted for age and gender.

Har IOS ett kliniskt värde vid utredning av svår KOL ?

Karolinska Severe COPD Centre

First visit
COPD nurse
Specialist

Blood samples *
Spirometry with BD
Radiology
SO2/ABG
CAT/mMRC/1MSTS
Impulsoscillometry (IOS)
History
Inhalations technique
Treatment optimization
Written plan

CT scan
Bodybox/MBW
Physiotherapy
other referrals (dietician, smoking cessation)

Follow up visit
COPD nurse

CAT/mMRC/1MSTS
SO2/ABG
IOS
spirometry
inhalations technique

Follow up visit
Specialist

Blood samples
Written plan
Roflumilast
Macrolides
EBV treatment
Oxygen/NIV
Follow - up primary care or another specialist clinic

Registries:
Swedish National Airway Register

*blood samples: Alpha-1-antitrypsin, Hb, B-cells, CRP, SR, RFTs, NT-proBNP

First Visit

45 min visit - COPD nurse

- Blood pressure, pulse, SO2, ABG if < 92%
- Respiratory rate
- Spirometry with BD
- Impulsoscillometry (IOS)
- 1 min sit to stand test
- mMRC, CAT
- Height, weight, BMI, malnutrition risk
- Cough/mucous/chronic bronchitis medical history
- Exacerbations history
- Tobacco use
- Physical activity
- Vaccination history
- Inhalation technique

40 min visit - COPD specialist

- Medical history according to the KSKC checklist
- Therapy optimization
- Written therapy plan
- Referral to COPD physiotherapist
- Referral to dietician
- Referral for CT scan
- Referral for body-box
- Referral for smoke cessation

Sammanfattning

- SAD är en avgörande komponent i patologin vid KOL
- Patienter med svår KOL uppvisar tecken till avancerad SAD
- IOS är en effektiv och enkel metod att upptäcka SAD hos KOL patienter

Sammanfattning

- Svårighetsgraden av SAD, mätt med R5-R20 och AX, är positivt korrelerad med KOL-relaterade symtom bedömda med hjälp av CAT frågeformulär

- Både R5-R20 och AX är korrelerade med antalet KOL-exacerbationer under de 12 månaderna före rekryteringen.

- IOS har potential för mervärde vid prioritering/stratifiering av KOL patienter med svår sjukdom