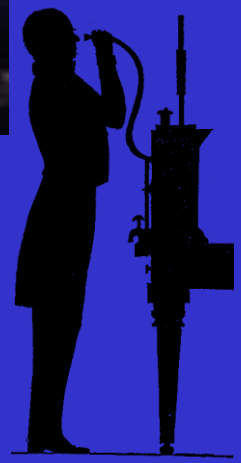
Η επίδραση της αναπνευστικής αποκατάστασης στον περιορισμό της ροής κατά την ήρεμο αναπνοή σε ασθενείς με ΧΑΠ

Ν Κουλούρης

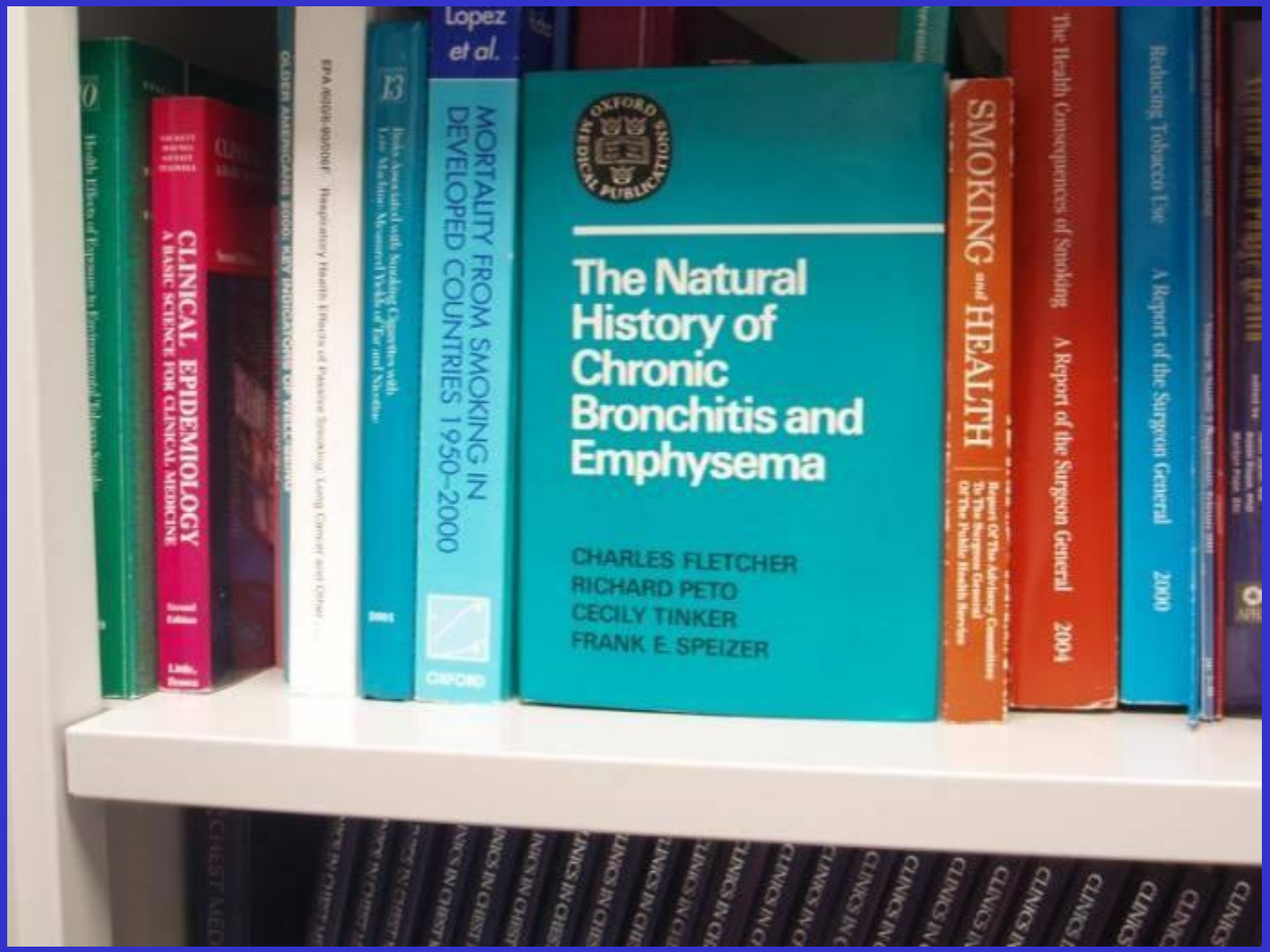
1st Department of Respiratory Medicine,
National & Kapodistrian University of Athens Medical School,
"Sotiria" Hospital for Diseases of the Chest,
Athens, Greece



210 εκατομμύρια ασθενείς παγκοσμίως

Μόνο οι μισοί διαγνωσμένοι

COPD Progression and Death



Fletcher et al, *The Natural History of Chronic Bronchitis and Emphysema*, 1976

3 εκατ. θάνατοι ετησίως

	Ετήσιο κόστος (€)	% επί του συνόλου
Άμεσο ιατρικό	**2,809.68**	**50%**
Κόστη παροξύνσεων	1,512.42	27%
Κόστη φάσης σταθεροποίησης	834.96	15%
Κόστη πρόσθετων πόρων	462.30	8%
Άμεσο μη ιατρικό	**1,374.30**	**25%**
Χρόνος ασθενών	211.00	4%
Χρόνος φροντιστών (από το οικογενειακό/ φιλικό περιβάλλον του ασθενή)	1,163.30	21%
Έμμεσο κόστος	**1,398.30**	**25%**
Συνολικό κόστος	**5,582.28**	**100%**

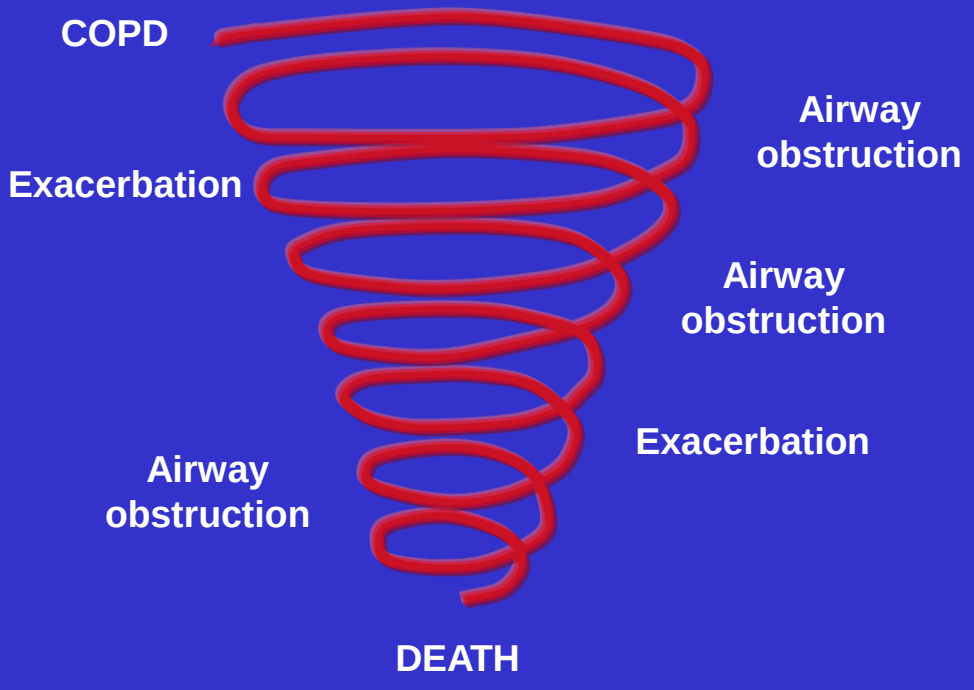
Σημείωση: Στο παραπάνω συνολικό κόστος δεν περιλαμβάνονται τα προνοιακά κόστη (επιδόματα και σύνταξη αναπηρίας)

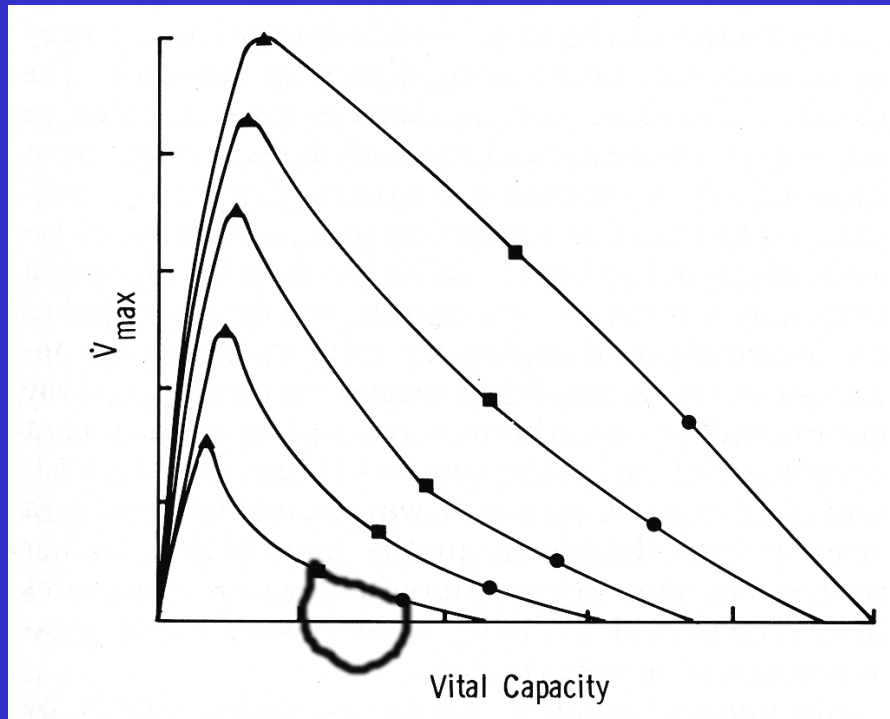
ΧΑΠ: Συχνό και σοβαρό νόσημα

Chronic airflow limitation indicates the reduction in maximum expiratory flow that progressively occurs in COPD and in other pulmonary diseases

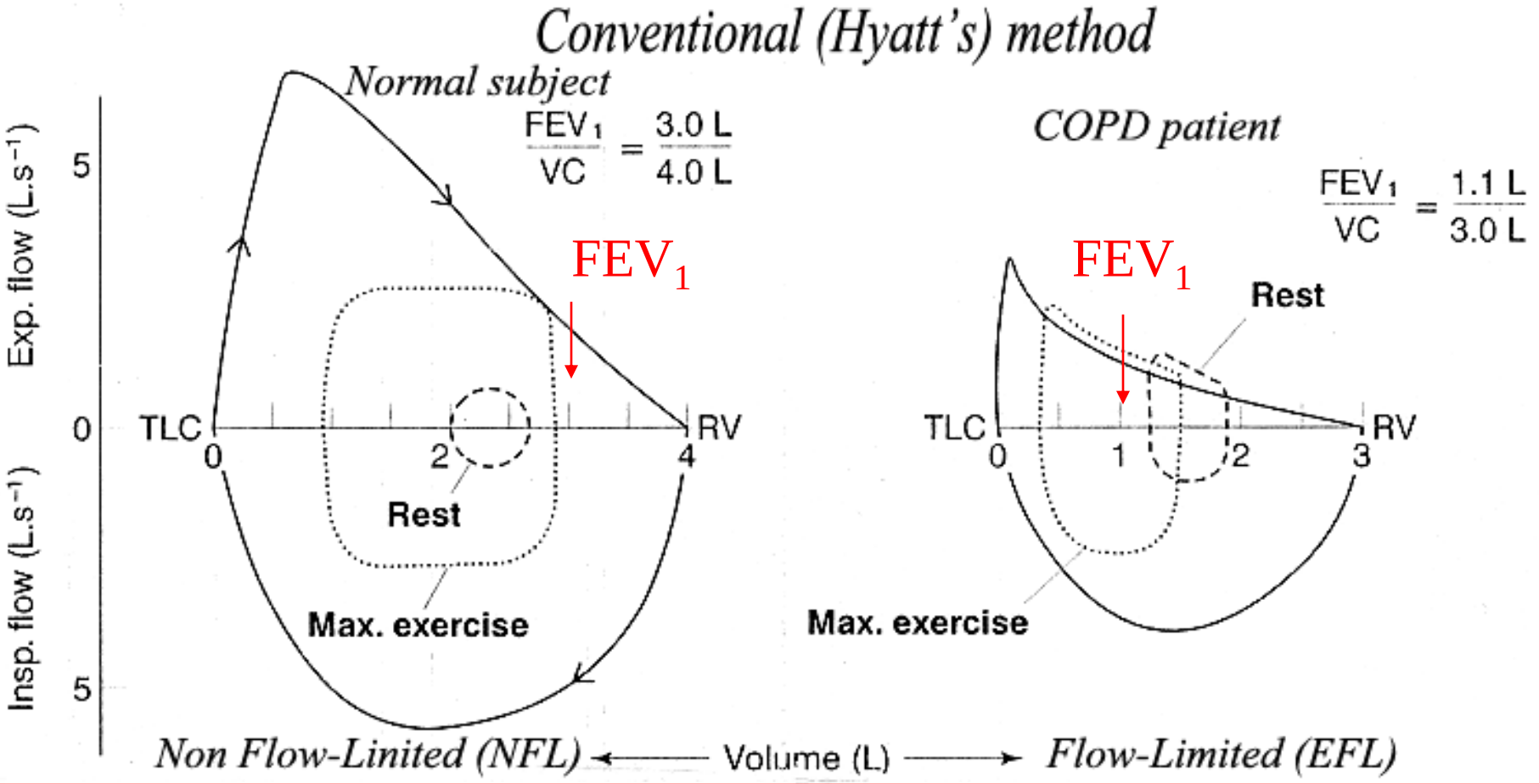
Expiratory flow limitation (EFL) indicates that maximal expiratory flow is achieved during tidal breathing and is characteristic of intra-thoracic airflow obstruction (dynamic airway compression)

Pride NB. In: Hughes & Pride (eds). Lung Function Tests. London WB Saunders, 1999





Conventional (Hyatt's) method of detecting Expiratory Flow Limitation



Pride NB. In: Hughes & Pride (eds). Lung Function Tests. London WB Saunders, 1999, p 21.

ΤΕΧΝΙΚΗ ΑΡΝΗΤΙΚΗΣ ΠΙΕΣΗΣ

Eur Respir J, 1995, 8, 306–313
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European Respiratory Journal
ISSN 0903 - 1936

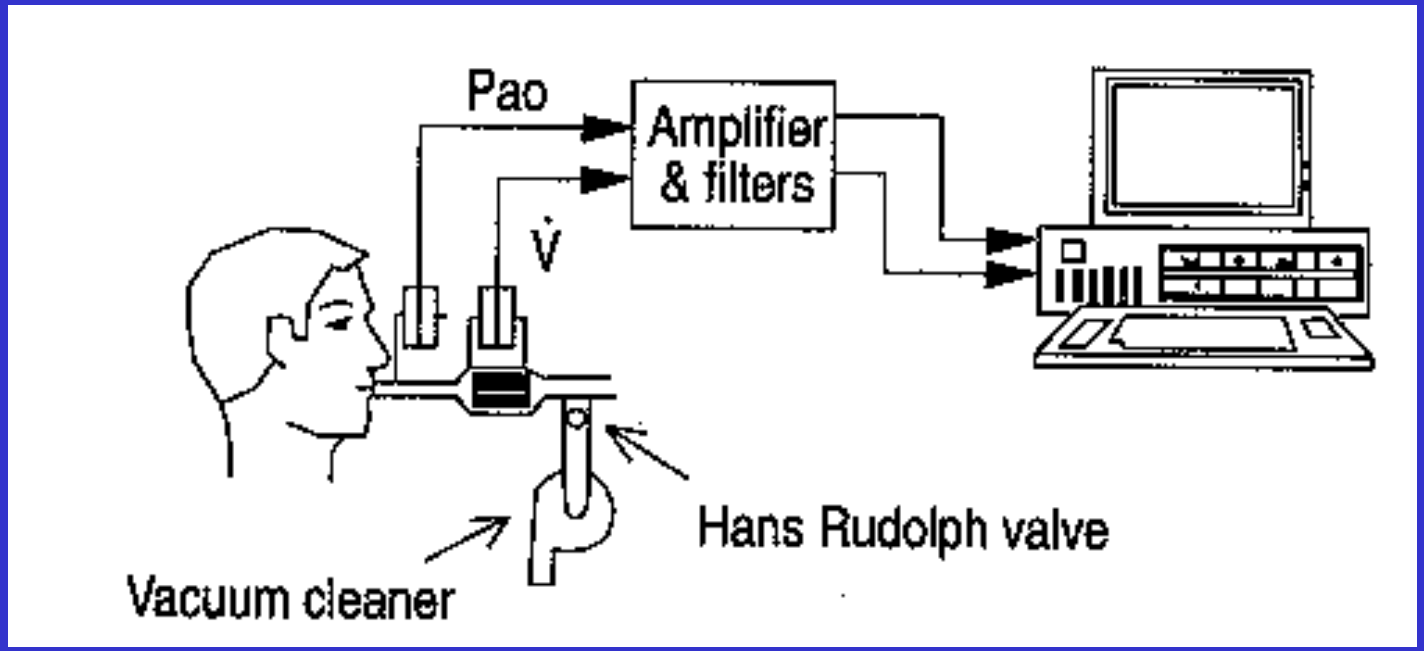
TECHNICAL NOTE

A simple method to detect expiratory flow limitation during spontaneous breathing

N.G. Koulouris*, P. Valta*, A. Lavoie*, C. Corbeil**, M. Chassé**, J. Braidy**, J. Milic-Emili*

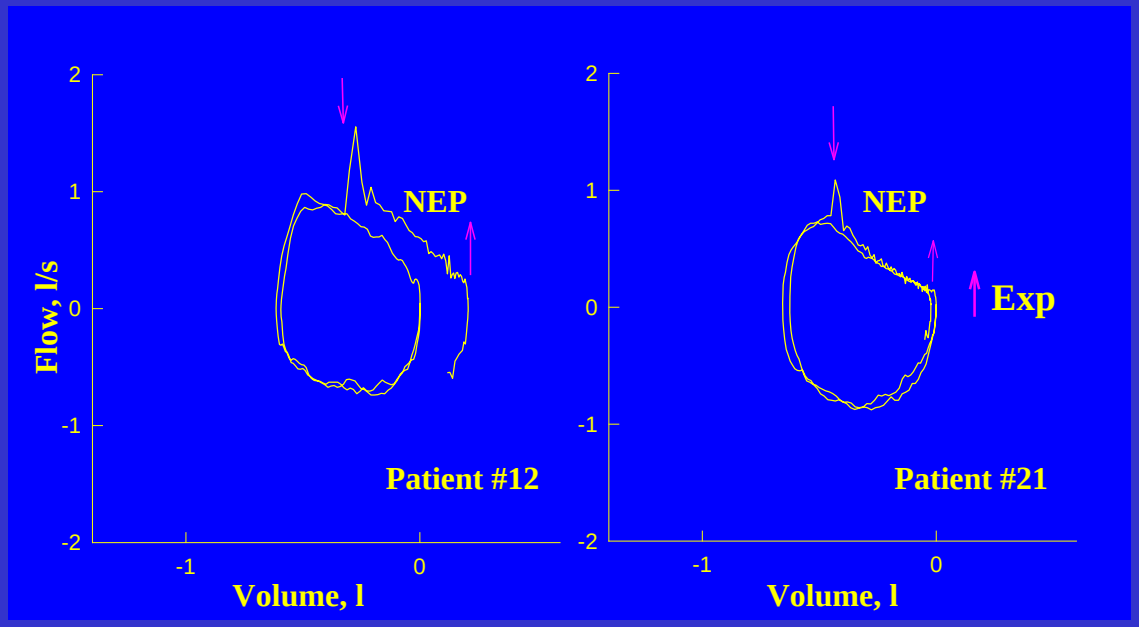
Negative Expiratory Pressure Technique (NEP)

Πειραματική Διάταξη Εφαρμογής της NEP



Koulouris et al, Eur Respir J 1995; 8: 306-13

Εναλλακτικά, για την ανίχνευση του φαινόμενου του "περιορισμού της ροής κατά την ήρεμη εκπνοή" προτείνουμε την μέθοδο της αρνητικής πίεσης ή άλλως NEP (Negative Expiratory Pressure) η οποία είναι απαλλαγμένη από αυτά τα θεωρητικά προβλήματα, δεν απαιτεί πληθυσμογράφο, είναι απλή και μη επεμβατική.



Koulouris et al, Eur Respir J 2003; 21: 743-8

Εάν σε σύγκριση με την κοντρόλ, η δεύτερη εκπνοή δεν εμφανίζει καθόλου ή εμφανίζει μερική αύξηση της εκπνευστικής ροής αυτό σημαίνει "δυναμική σύμπτωση αεραγωγών" και "περιορισμό της ροής". Αντίθετα, αν η εκπνευστική ροή της κοντρόλ εκπνοής και της αμέσως επομένης δεν συμπίπτουν καθόλου ο ασθενής δεν έχει "δυναμική σύμπτωση αεραγωγών". Η τεχνική (NEP) είναι απλή, ταχεία και αξιόπιστη στην ανίχνευση του φαινομένου της "δυναμικής σύγκλεισης των αεραγωγών" ή άλλως του «περιορισμού της ροής κατά την ήρεμη αναπνοή» σε καθιστή και ύπτια θέση.

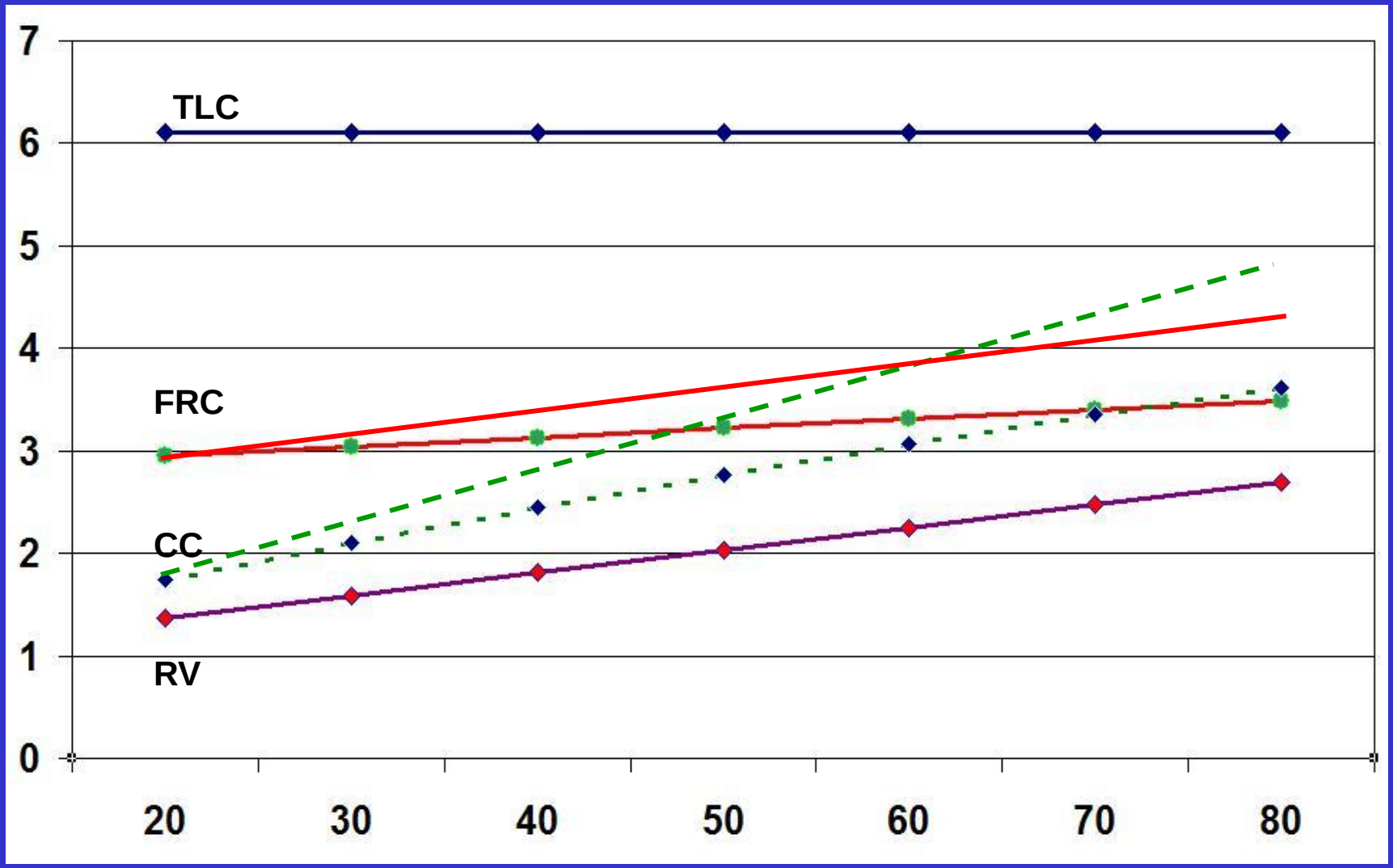
Significance of expiratory flow limitation during tidal breathing

1. Promotes lung damage
2. Promotes dynamic hyperinflation

Significance of expiratory flow limitation during tidal breathing

1. Promotes lung damage
2. Promotes dynamic hyperinflation

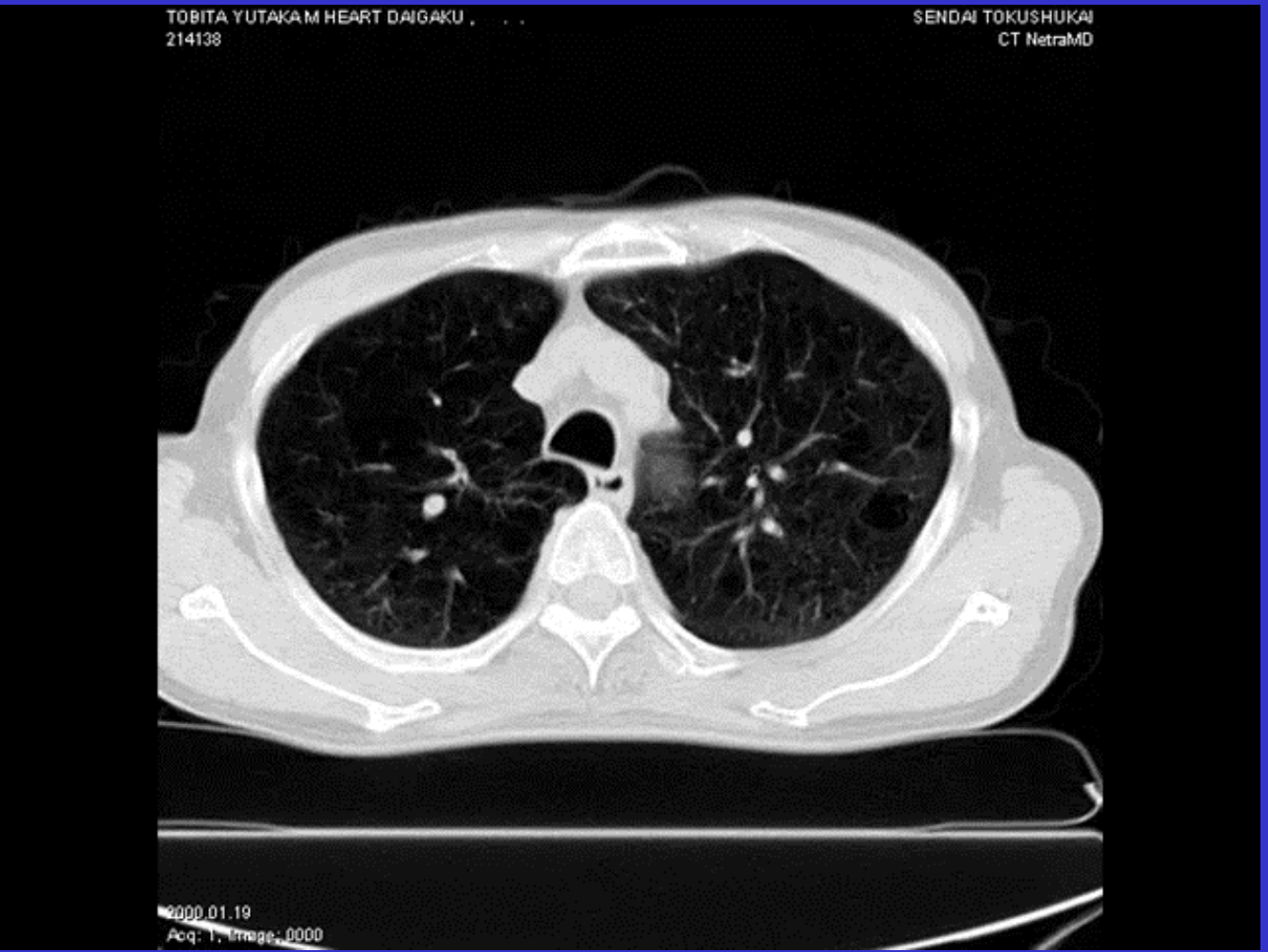
Male, 170 cm high



The NEW ENGLAND JOURNAL of MEDICINE

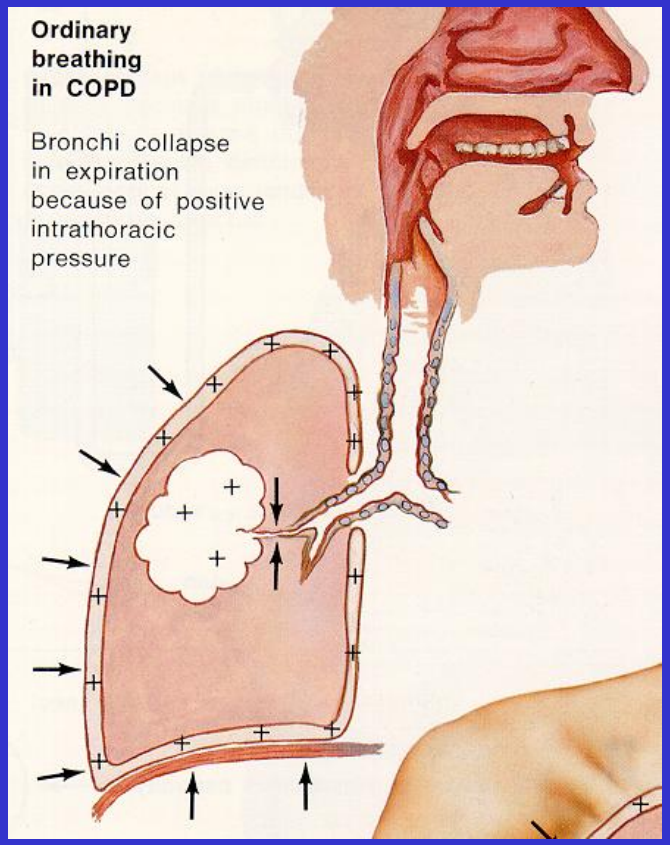
IMAGES IN CLINICAL MEDICINE

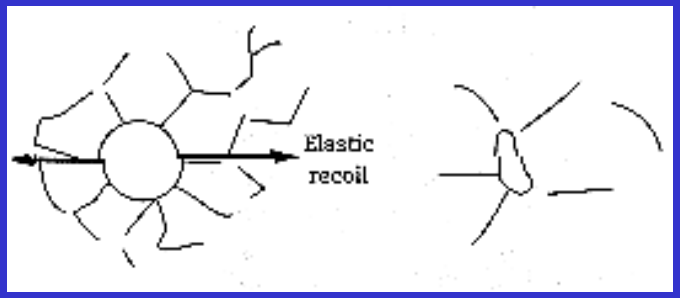
Dynamic Airway Narrowing



Hajime Kurosawa, M.D.
Masahiro Kohzuki, M.D.

Tohoku University Graduate
School of Medicine
Sendai 980-8574, Japan





Dynamic compression of the airways or flow-limitation during tidal expiration (EFL) is a factor that causes peripheral airway and parenchymal injury.

- necrosis and sloughing of bronchiolar epithelia
- rupture the alveolar-bronchiolar attachments,
- increased number of polymorphonuclear leukocytes (presence of parenchymal inflammation).

D'Angelo et al. Low volume ventilation induces peripheral airways injury and increased airway resistance in normal open chest rabbits. J Appl Physiol 2002; 92: 949-956.

D'Angelo et al. The fall in exhaled nitric oxide with ventilation at low lung volumes in rabbits. An index of small airway injury. Respir Physiol Neurobiol 2008; 160: 215-223

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Significance of expiratory flow limitation during tidal breathing

1. Promotes lung damage
2. Promotes dynamic hyperinflation

Hyperinflation

Old concept but with new implications for lung pathophysiology

Hyperinflation in COPD is not a new idea. In 1837, the Irish physician William Stokes, whose name is given to Stokes–Adams attack and Cheyne–Stokes respiration, published a textbook entitled “A Treatise on the Diagnosis and Treatment of Diseases of the Chest”

Stokes W. A treatise on the diagnosis and treatment of diseases of the chest. Part 1. Diseases of the lung and windpipe. London: The New Sydenham Society; 1837. pp. 168–169.

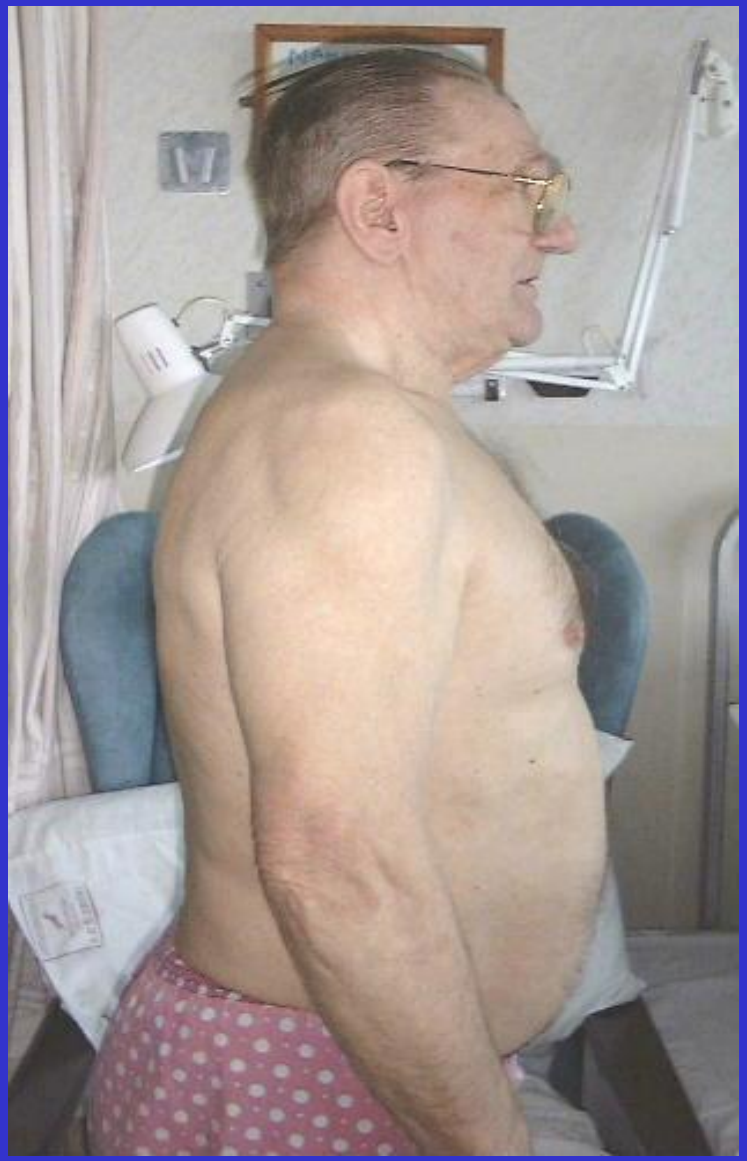
HYPERINFLATION

Dyspnoea

Decreased Exercise Capacity

Main Symptoms of COPD Patients

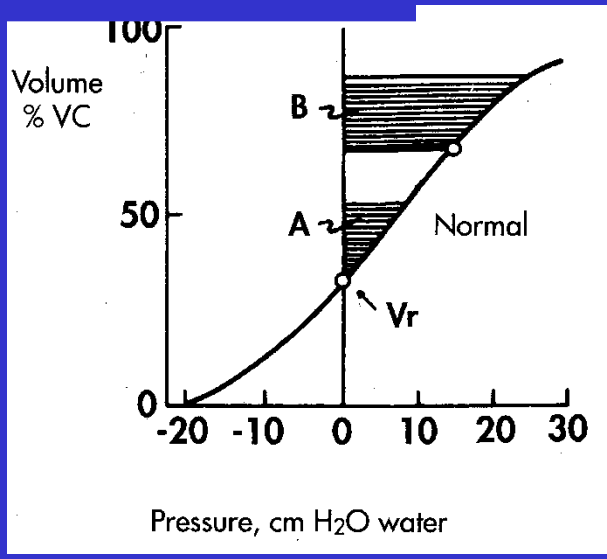
Hyperinflation

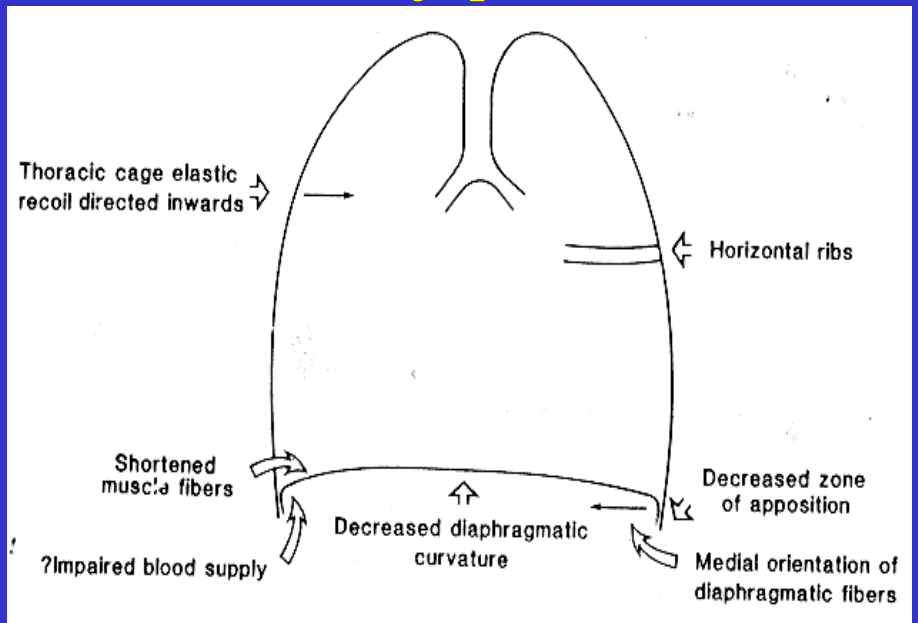


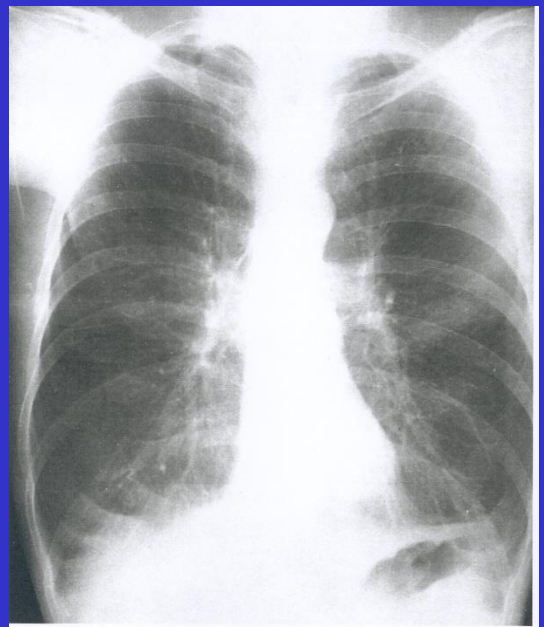
- *Increase in antero-posterior diameter (barrel-chest)*
- *Movements of the chest wall are symmetrically reduced, especially during expiration.*
- *Hyperresonant percussion note*
- *Reduced vesicular sounds*

Significance of expiratory flow limitation during tidal breathing

1. Promotes lung damage
2. Promotes dynamic hyperinflation
   - Impairs inspiratory muscle function
   - Increases work of breathing
   - Promotes PEEPi
   - Adversely affects haemodynamics
   - Contributes to dyspnoea



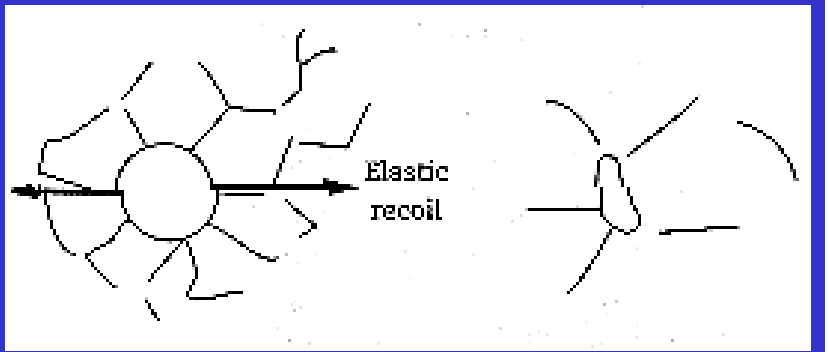


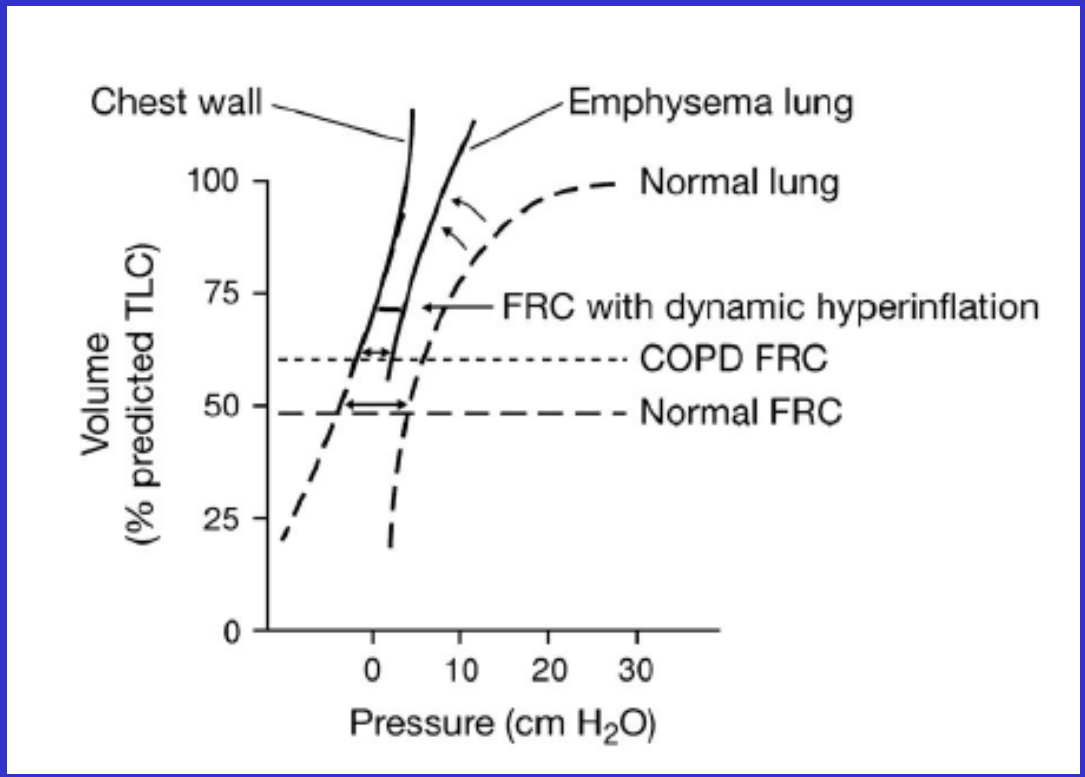


HYPERINFLATION

***Hyperinflation** of the lung is defined in various ways, but is commonly considered to be an elevation above normal of the resting FRC or EELV or Vr (relaxation volume). **Static Hyperinflation** results from destruction of elastic tissue associated with emphysema, which alters lung recoil (It is usually a modest contributor of total hyperinflation).*

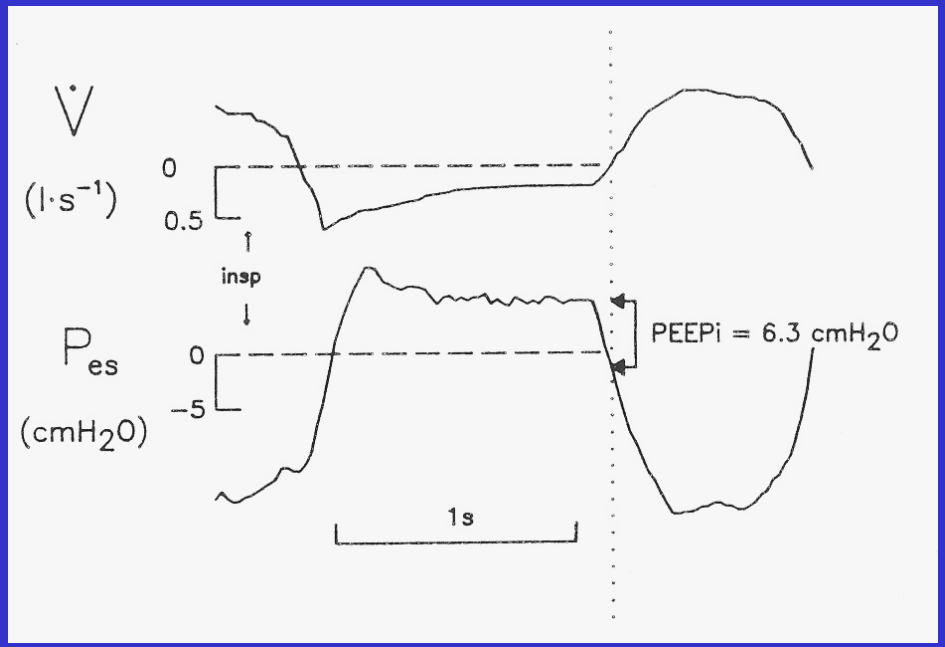
Ferguson GT. Proc Am Thorac Soc 2006; 3: 176-179

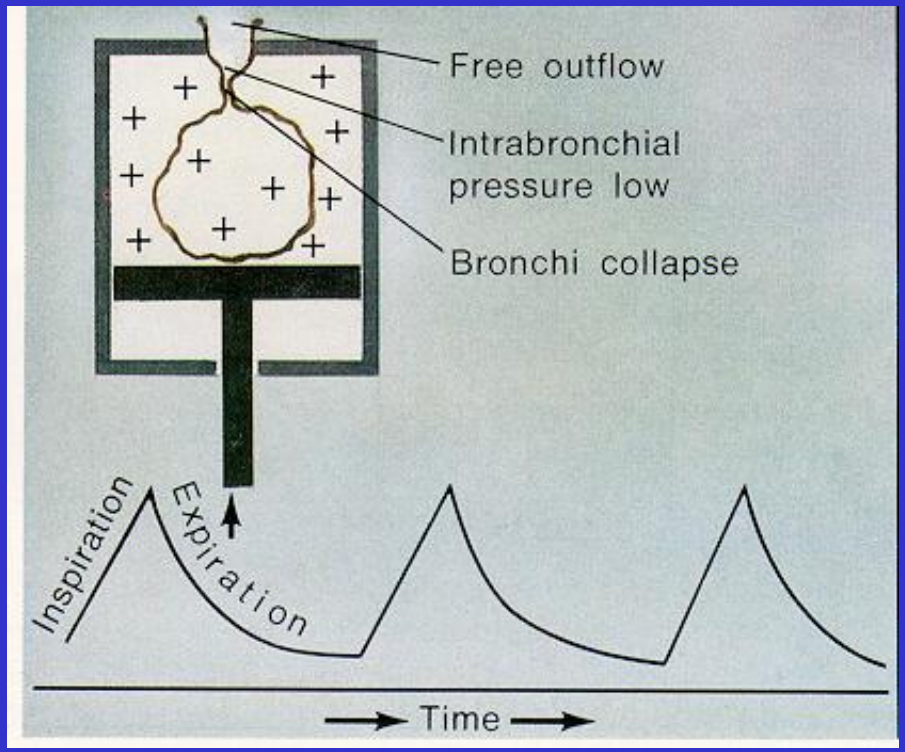




Dynamic hyperinflation occurs when patients commence inhalation before full exhalation has been achieved.

Haluszka et al. Am Rev Respir Dis 1990; 141: 1194-1197

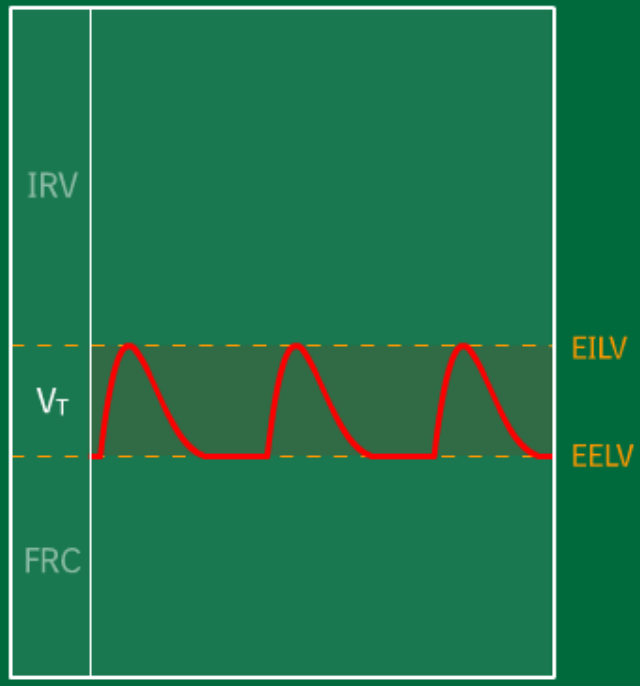


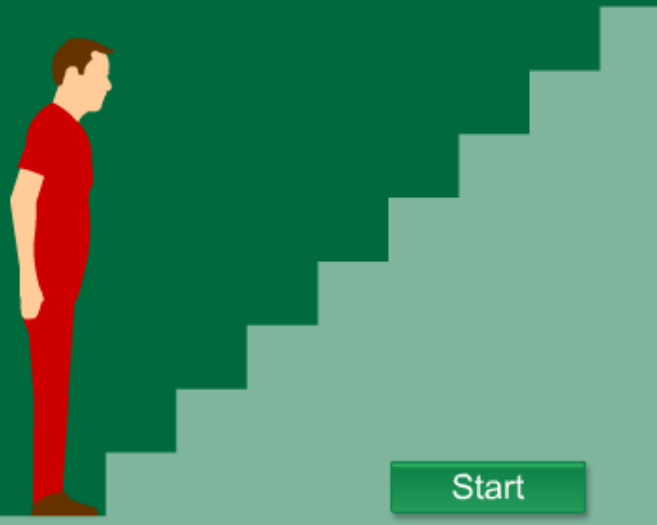


Dynamic Compression of the Airways≈Hyperinflation≈Peepi

Pathophysiology of COPD

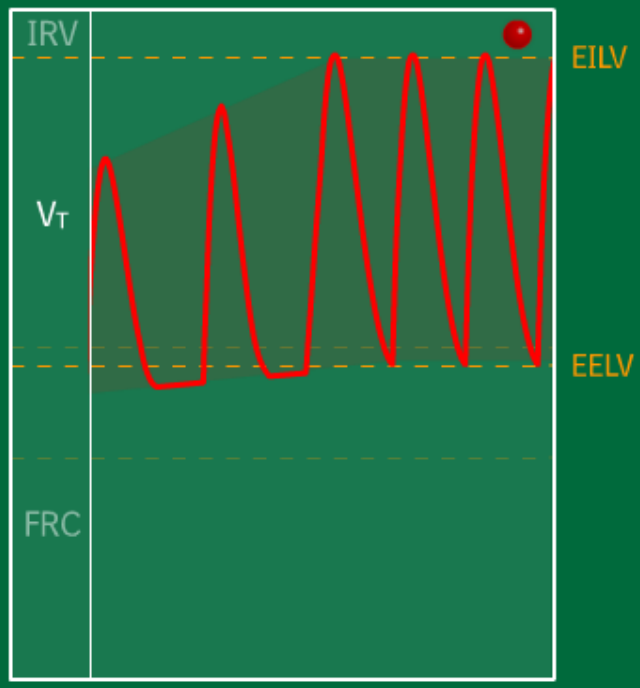
Breathing at Rest in COPD Patients





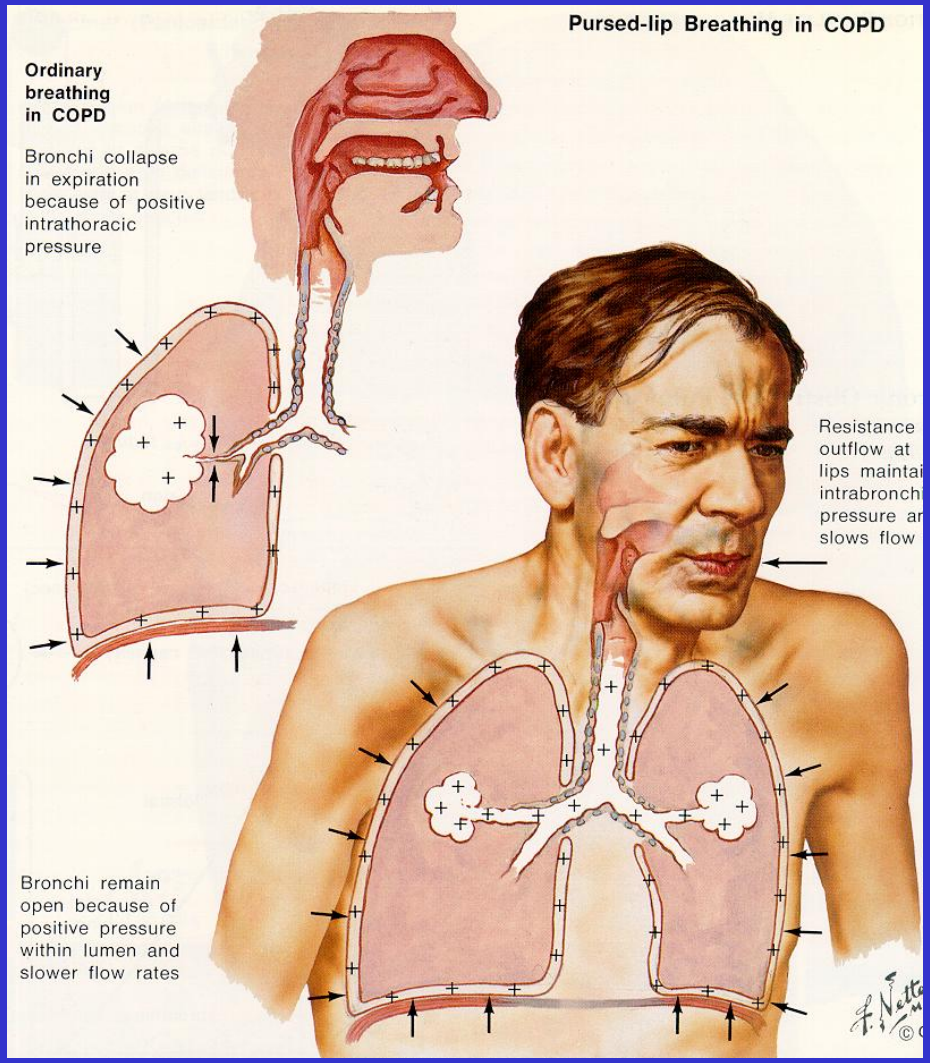
Start

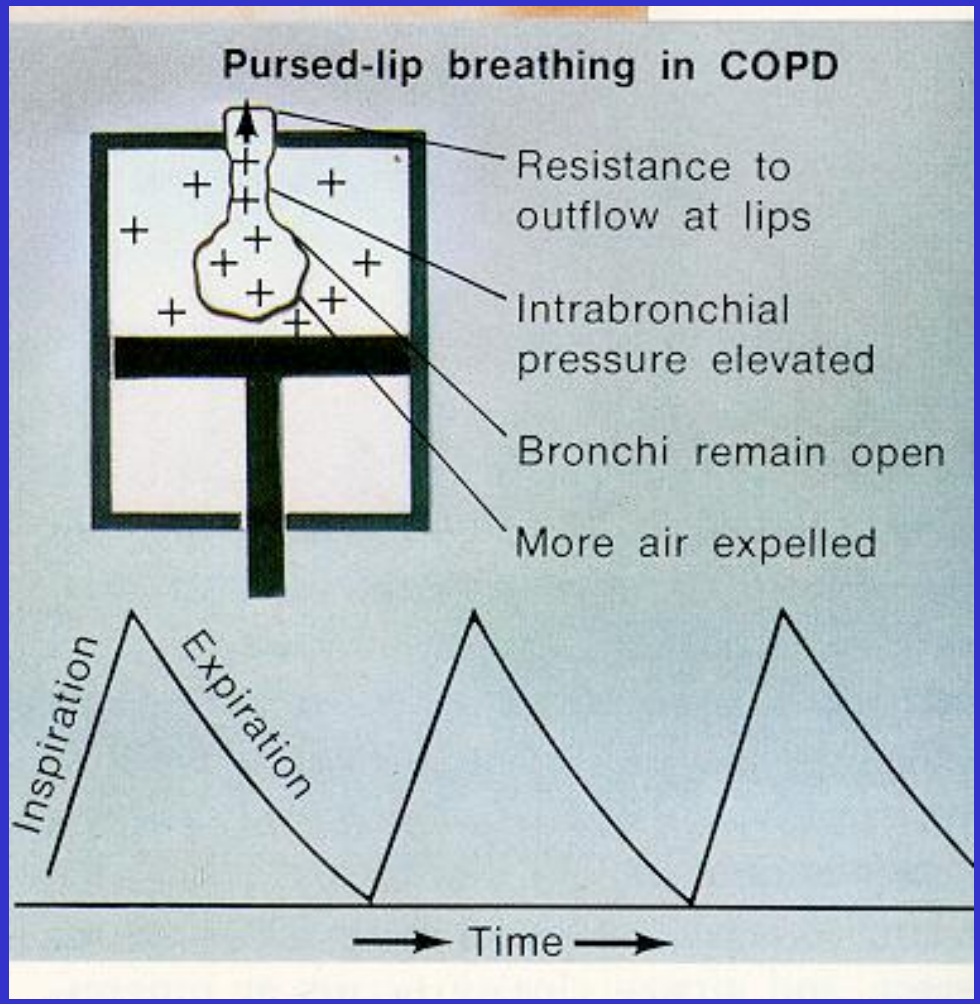
Breathing During Exercise in COPD Patients



Increased breathing rate

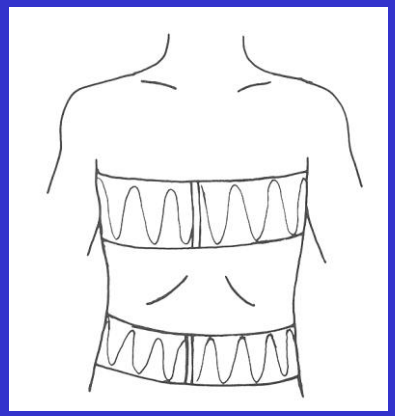
Pursed-lip breathing in COPD





Measurement of Hyperinflation II

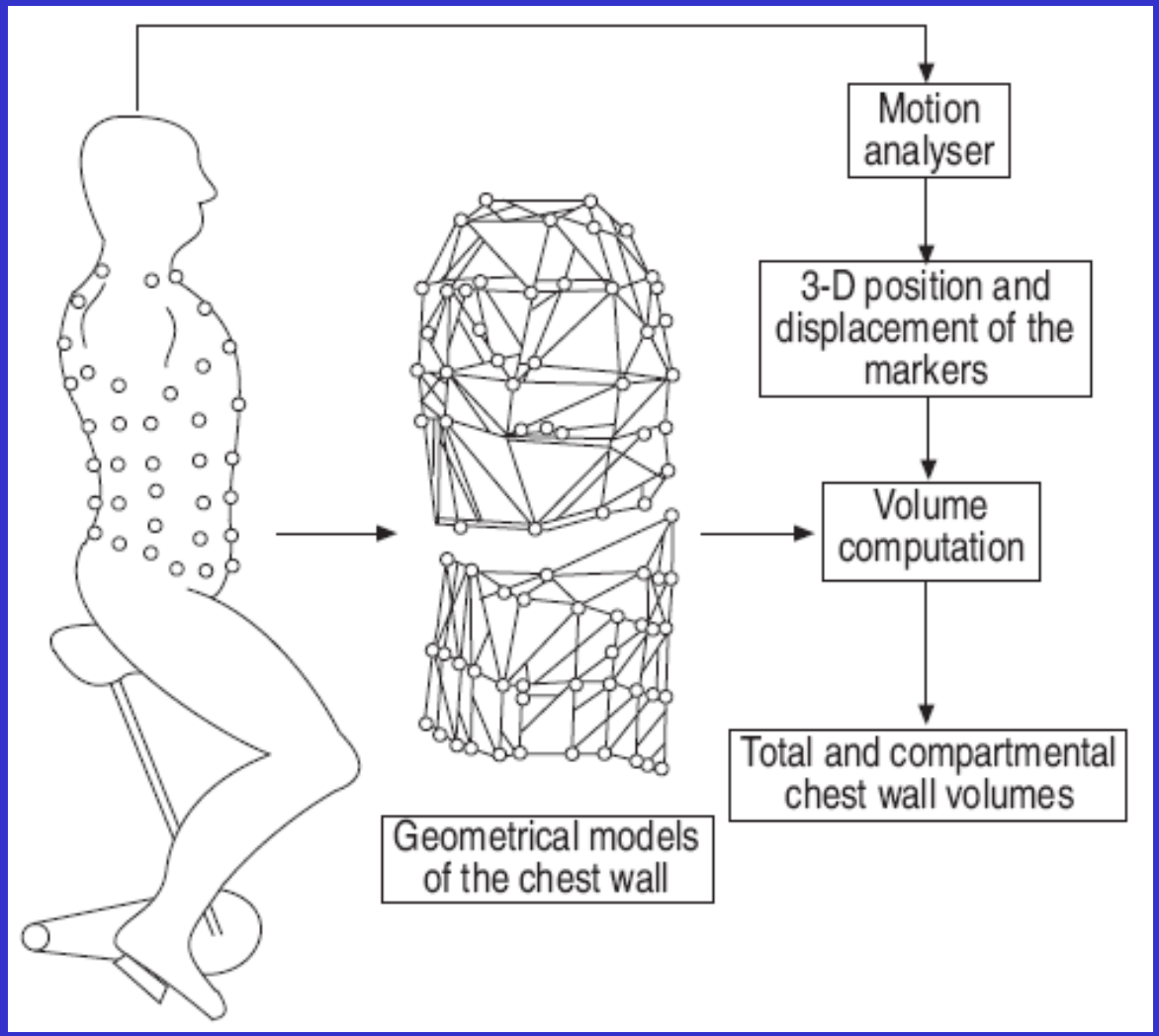
Magnetometers



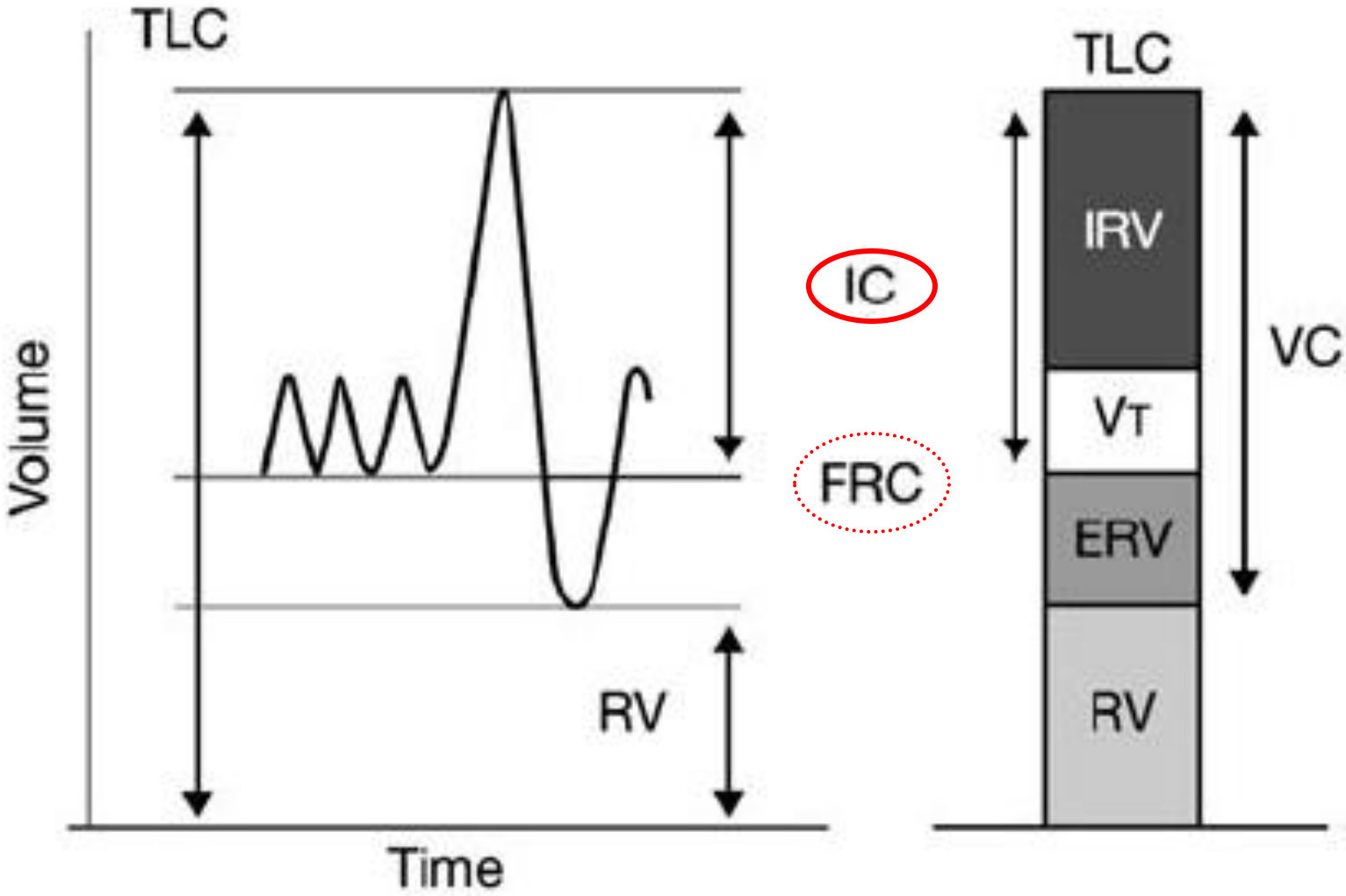
Inductive Plethysmography (RIP)

Optoelectronic Plethysmography (OEP)

Dellaca et al, Crit Care Med 2001; 29: 1807-1811



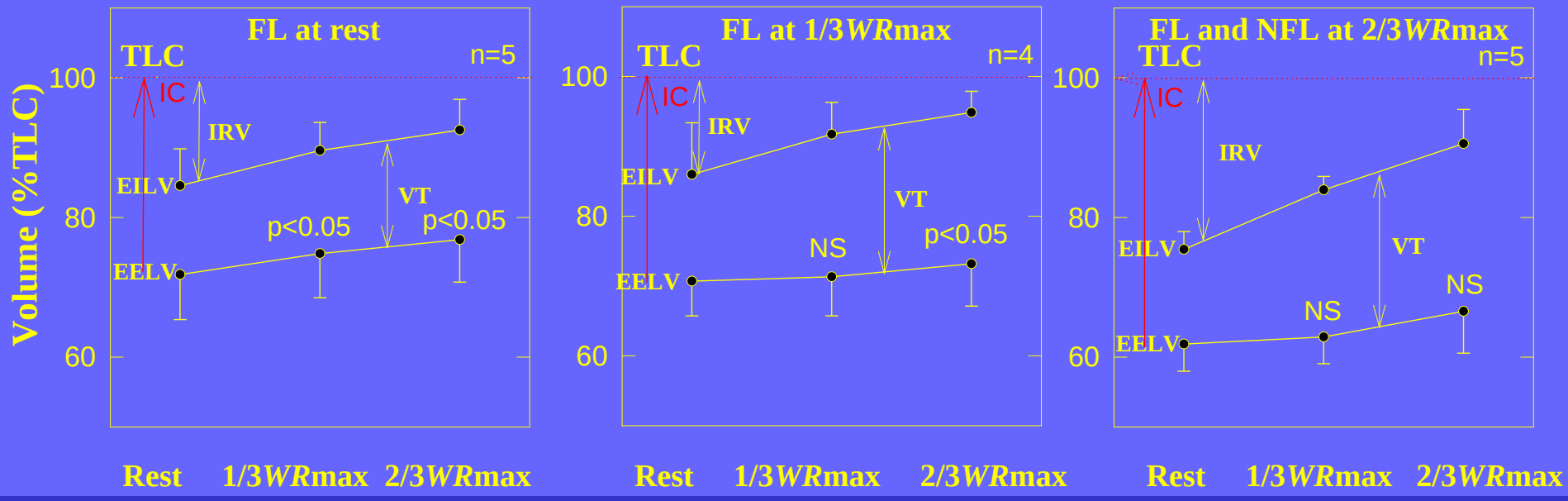
Measurement of Hyperinflation I



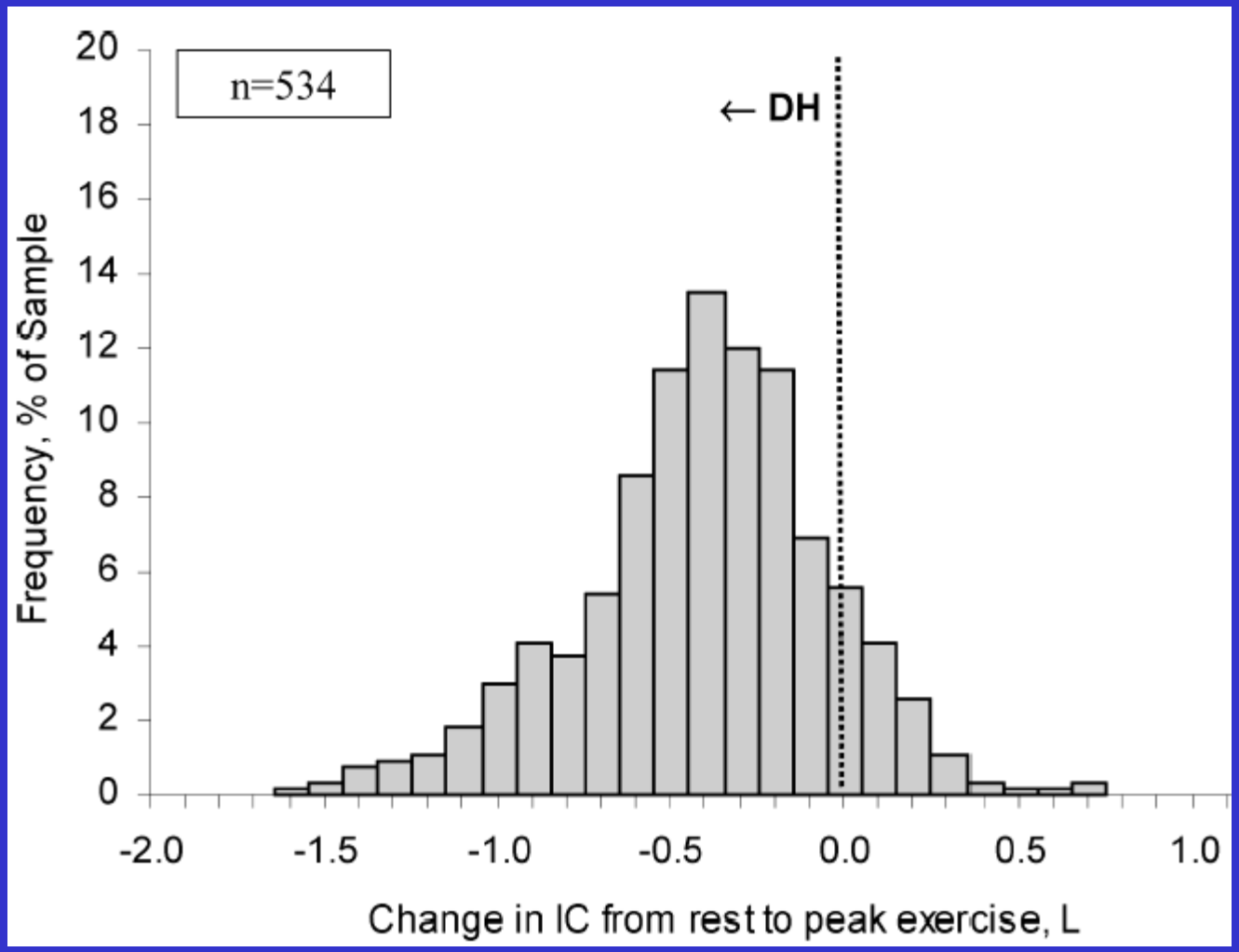
Ferguson GT. Proc Am Thorac Soc 2006; 3: 176-179

Exercise in COPD

Association of EFL with dynamic hyperinflation



Koulouris et al, JAP 1997; 82: 723-31



O'Donnell DE & Laveneziana P. COPD: Journal of Chronic Obstructive Pulmonary Disease 2006; 3: 219-232.

Significance of measuring IC at rest for COPD patients

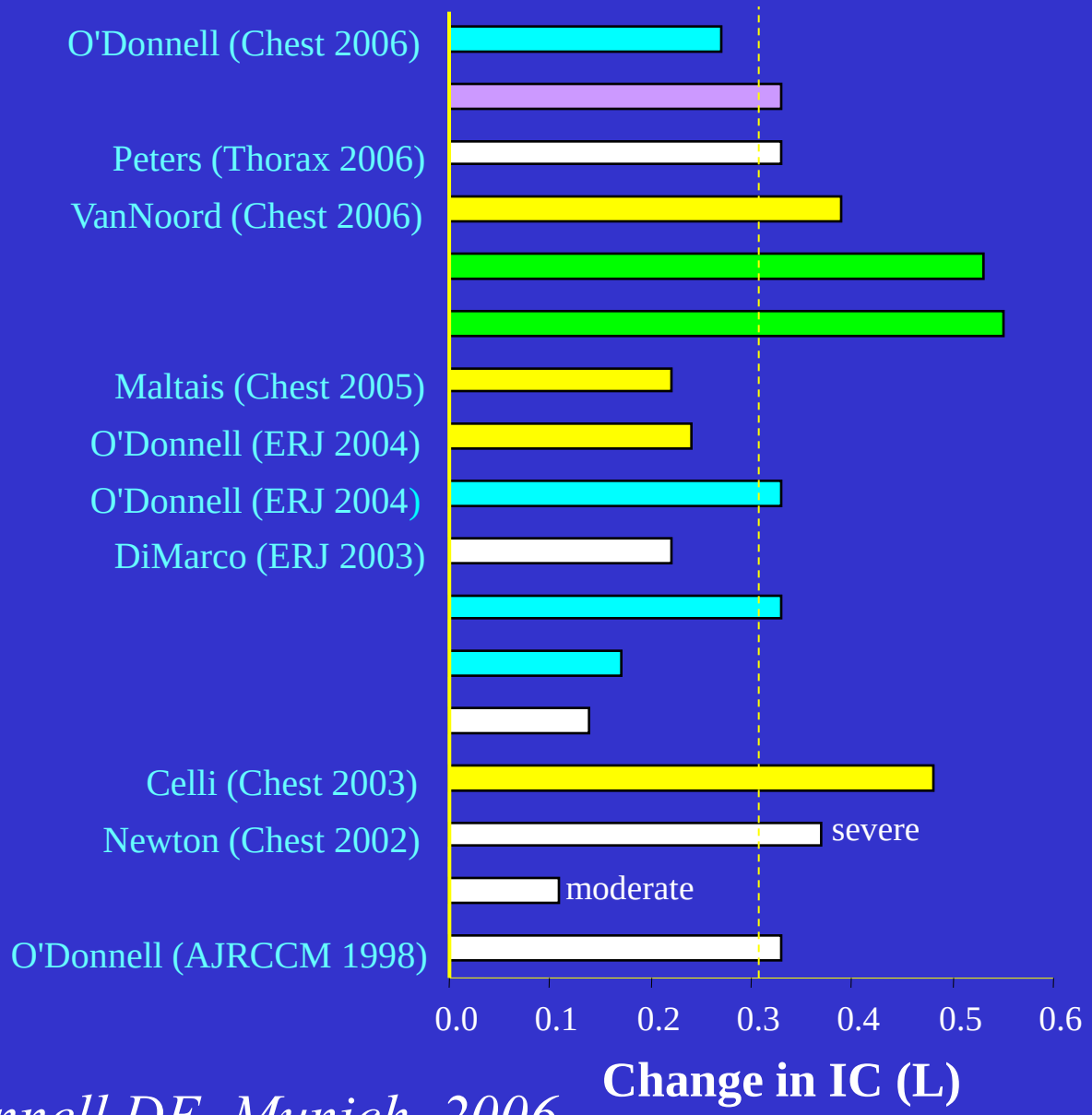
Hyperinflation appears to be the main determinant of exercise capacity and the magnitude of resting IC (a well recognized marker of Hyperinflation), the best clinical predictor.

Treatment of Hyperinflation I

Dynamic hyperinflation is a temporary and reversible increase in EELV, therefore it is amenable to therapeutic interventions.

Up to date, bronchodilators are the main pharmacological means for improving dynamic hyperinflation.

Bronchodilator-Induced Changes in IC



SABD

LABA

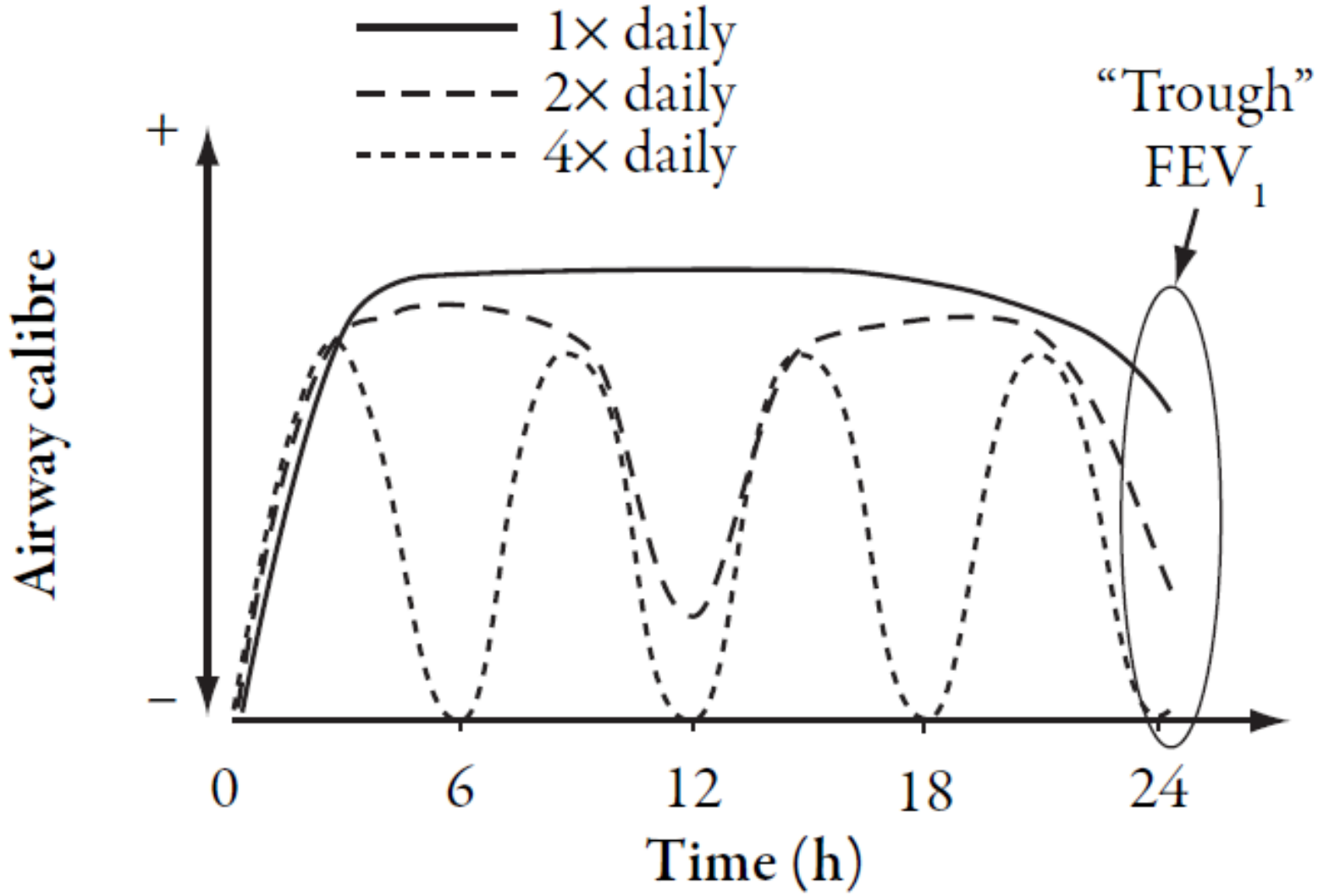
LABA+ICS

tiotropium

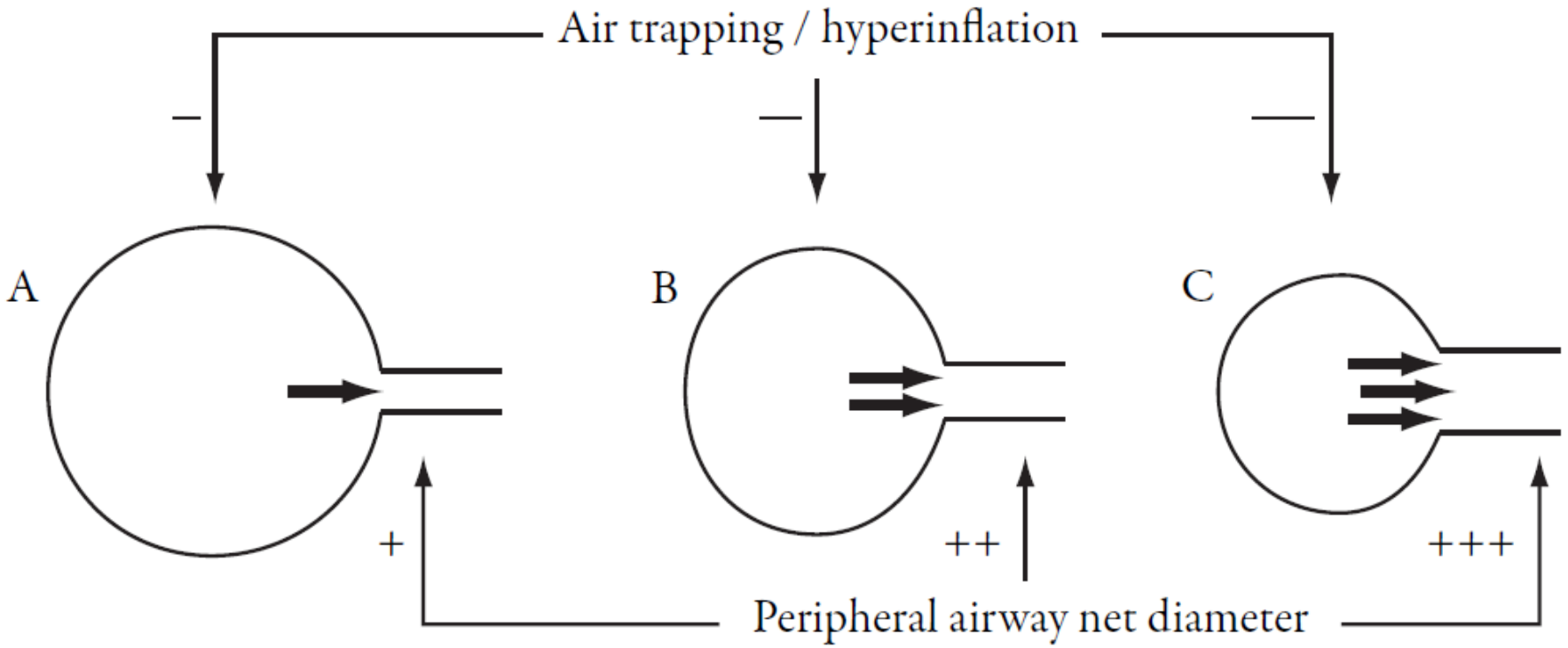
tio+LABA

O'Donnell DE, Munich, 2006

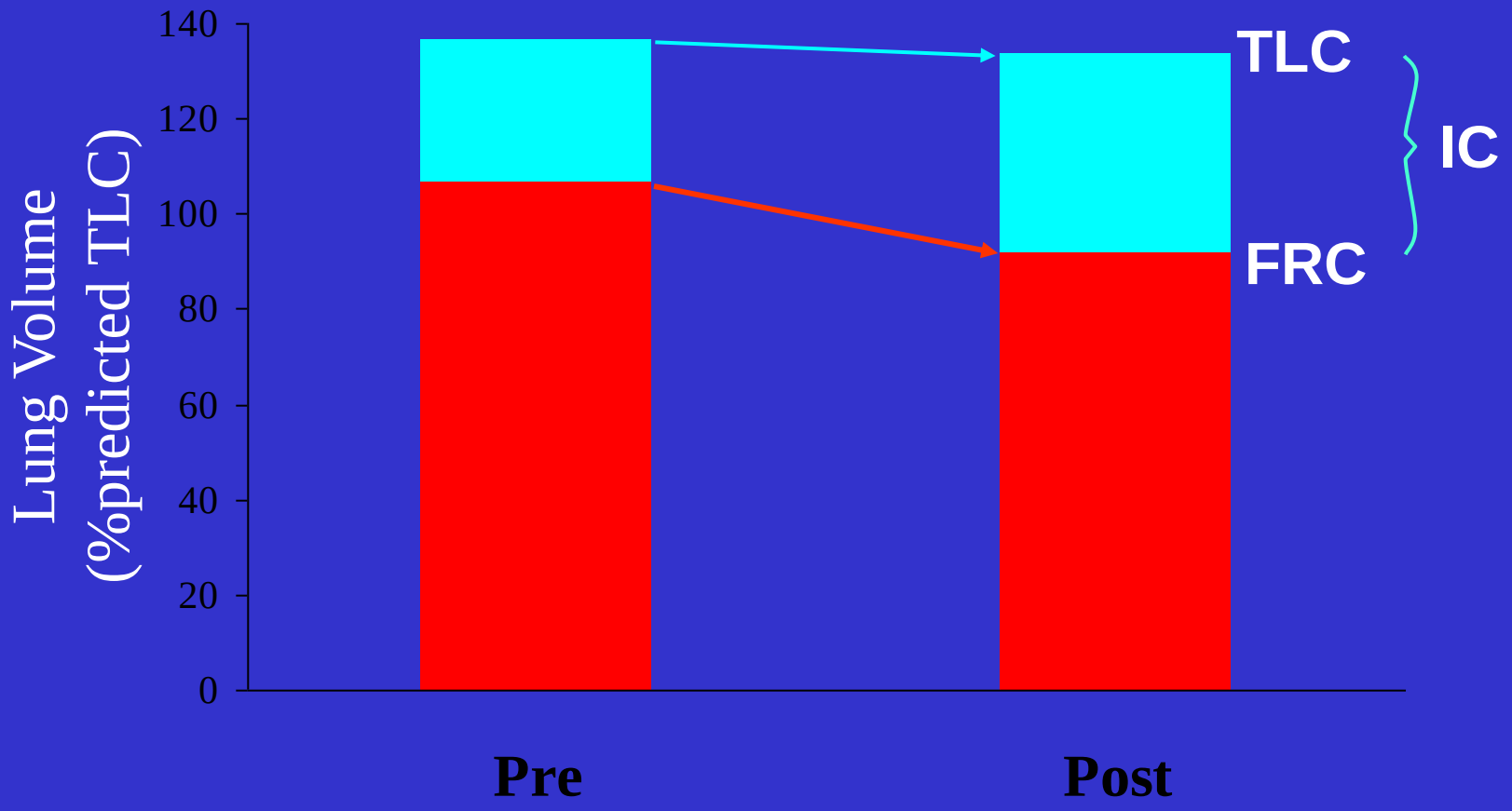
“Pharmacological stenting”



“Pharmacological lung volume reduction”



Pharmacological Volume Reduction by DEFLATORS



Adv Ther (2010) 27(3):150-159.
DOI 10.1007/s12325-010-0017-6

REVIEW

Other treatments of Hyperinflation

Table 2 Effects of other interventions on hyperinflation, exercise endurance, and dyspnea in patients with chronic obstructive pulmonary disease

Intervention	Study	Year	N	Baseline FEV_1 (%)	Change in Static IC* (mL)	Increase in Dynamic IC† (mL)	Increase in Exercise Endurance	Change in Dyspnea	*P* Value
Oxygen	Somfay et al[27]	2001	10	31	−31	330‡	618 sec‡	↓	<0.05 vs. room air
Exercise training	Porszasz et al[28]	2005	24	36	NM	133	696 sec	NM	<0.05 vs. before training
LVR surgery	Fishman et al[29]	2003	608	27	NM	NM	Improved >10 W§	NM	<0.02 vs. no surgery
	Appleton et al[30]	2003	29	28	NM	NM	126 m (survivor group)	↓	<0.01 vs. baseline (dyspnea only)
	Miller et al[31]	2005	93	15–40	NM	NM	45 m	NM	<0.05 vs. baseline
Heliox breathing	Palange et al[18]	2004	12	37‖	−80 (NS)	200	288 sec	↓	<0.001 vs. air
	Pecchiari et al[32]	2004	22	41–61	+20	NM	NM	NM	NS
Bronchoscopic LVR	Hopkinson et al[33]	2005	19	28	NM	170	131 sec	↓	0.03 vs. no surgery for endurance only

FEV_1 = forced expiratory volume in 1 second; heliox = helium-oxygen; IC = inspiratory capacity; LVR = lung volume reduction; NM = not measured; NS = not significant; ↓ = decrease.

*IC measured during body plethysmography as total lung capacity minus functional residual capacity.

†IC measured at isotime during constant load submaximal exercise.

‡Measured with 50% inspired oxygen concentration.

§On incremental exercise testing.

‖Calculated on the basis of predicted value.

Cooper Ch B. AMJ 2006; 119: S21-S31

Many studies have shown that Pulmonary Rehabilitation (PR) reduces dyspnea on exertion,increases exercise capacity and improves health-related quality oflife (QOL) in COPD patients. Symptomatic individuals with COPD who have lesser degrees of airflow limitation who participate in pulmonary rehabilitation programs derive similar improvements in symptoms, exercise tolerance, and quality of life as do those with more severe disease. However, little is known on the effect of a PR program in EFL and NFL patients, who substantially differ in terms of COPD severity and hence exercise capacity and dyspnea.

Aim of the study

Therefore, the aim of this study was to investigate the effectiveness of a PR program on EFL status and DH in stable COPD patients both at rest and during exercise.

Respiratory Physiology & Neurobiology 238 (2017) 47–54

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

Effect of pulmonary rehabilitation on tidal expiratory flow limitation at rest and during exercise in COPD patients

Elpida P. Theodorakopoulou[a,b], Sofia-Antiopi Gennimata[a], Maria Harikiopoulou[b], Georgios Kaltsakas[a], Anastasios Palamidas[a], Antonia Koutsoukou[a], Charis Roussos[a], Epameinondas N. Kosmas[b], Petros Bakakos[a], Nickolaos G. Koulouris[a,*]

[a] *Pulmonary Rehabilitation Unit, 1st Department of Respiratory Medicine, National & Kapodistrian University of Athens Medical School, "Sotiria" Hospital for Chest Diseases, Athens, Greece*

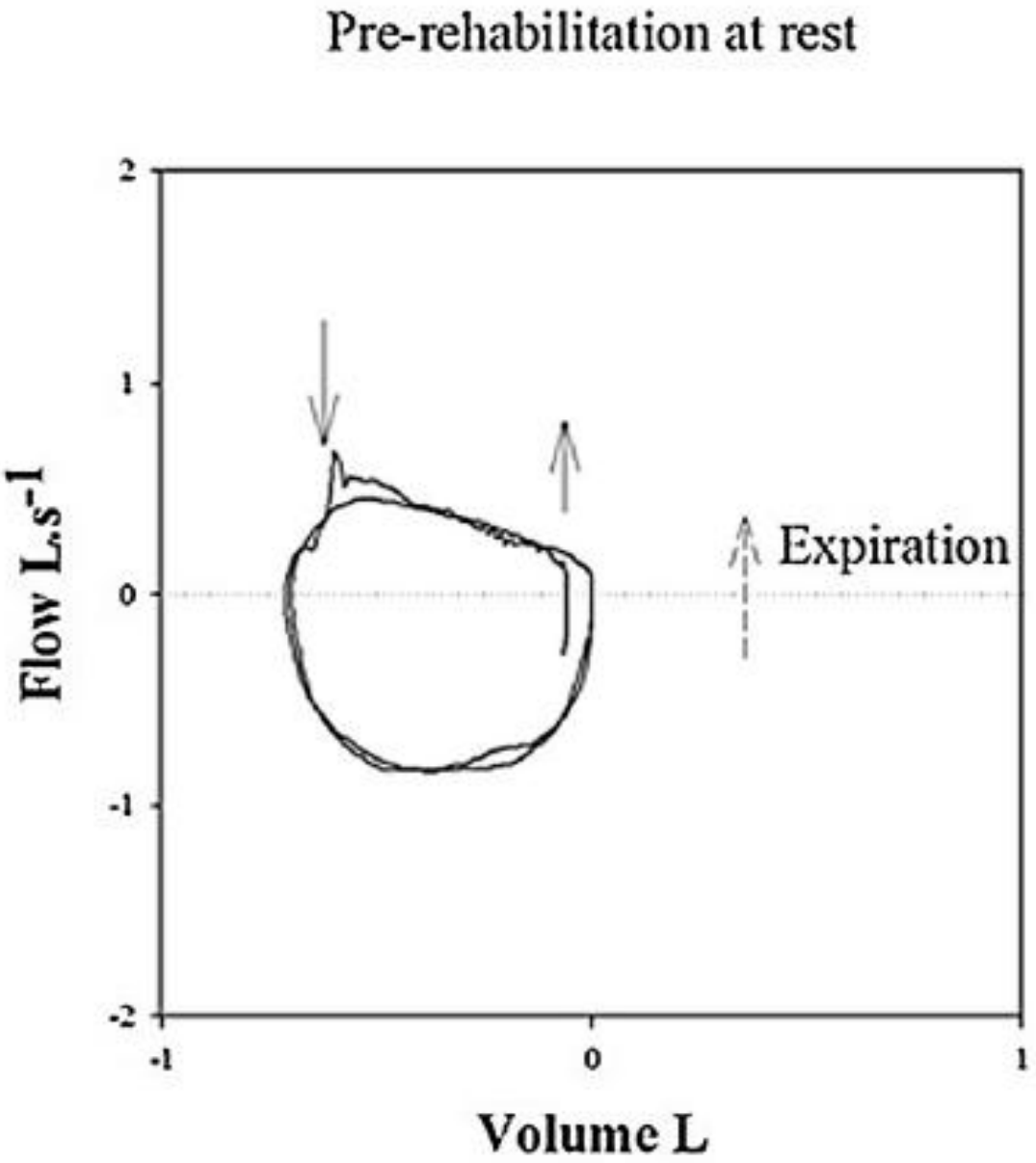
[b] *Pulmonary Rehabilitation Center, 3rd Department of Pulmonary Medicine, "Sotiria" Hospital for Chest Diseases, Athens, Greece*

Table 1
Anthropometric and lung function data of NFL and EFL patients.

	All patients	NFL patients	EFL patients
n	42	26	16
Gender	M:36, F:6	M:24, F:2	M:12, F:4
Age, yrs	65 ± 8	66 ± 8	62 ± 8
Ht, cm	167 ± 7	168 ± 7	166 ± 6
BMI, kg/m^2	28 ± 5	29 ± 5	28 ± 4
FVC, %pred	89 ± 23	93 ± 23	82 ± 21
FEV_1, %pred	50 ± 25	56 ± 27	35 ± 10
FEV_1/FVC, %	43 ± 15	49 ± 15	34 ± 7

Values are means ± SD; n: number of subjects; M: male; F: female; BMI: body mass index, Ht: height; FVC: forced vital capacity; FEV_1: forced expiratory volume in the 1 s.

METHODS


Pre-rehabilitation at rest
Expiration
Flow L.s-1
Volume L
2
1
0
-1
-2
-1
0
1

All patients followed a PR program for a period of 12–15 weeks, 2 sessions per week, each session lasting 120 min. The minimum and maximum number of sessions per patient ranged from 24 to 30, with an average of 27 per patient.

The quality of life was evaluated by the Saint-George's Respiratory Questionnaire (SGRQ) before and after PR completion.

Chronic dyspnea was rated according to the Modified Medical Research Council (mMRC) dyspnea scale.

Expiratory flow-limitation (EFL) was assessed using the negative expiratory pressure (NEP) technique described in detail by Koulouris (Koulouris et al., 1995)

Exercise tests

- Before starting the PR program all subjects underwent a maximal incremental symptom-limited exercise test on an electrically braked bicycle ergometer connected to an automated exercise system (P.K.Morgan, Kent, UK).
- The following ventilatory variables were recorded breath-by-breath through a pneumotachograph: minute ventilation (VE), tidal volume(VT), inspiratory time (TI), expiratory time (TE), respiratory drive (VT/TI), and breathing frequency (f).Immediately before and after the PR program, each subject was studied sitting on the cyclo-ergometer in steady state conditions at rest and at 30%, 60%, 90% of their WR max.
- In each experimental condition, EFL and operational lung volumes were evaluated by NEP application and measurements of inspiratory capacity (IC).
- Within the first week of admission to the PR program a 6 MW test was performed. The 6MWT was repeated at the end of rehabilitation program

Results

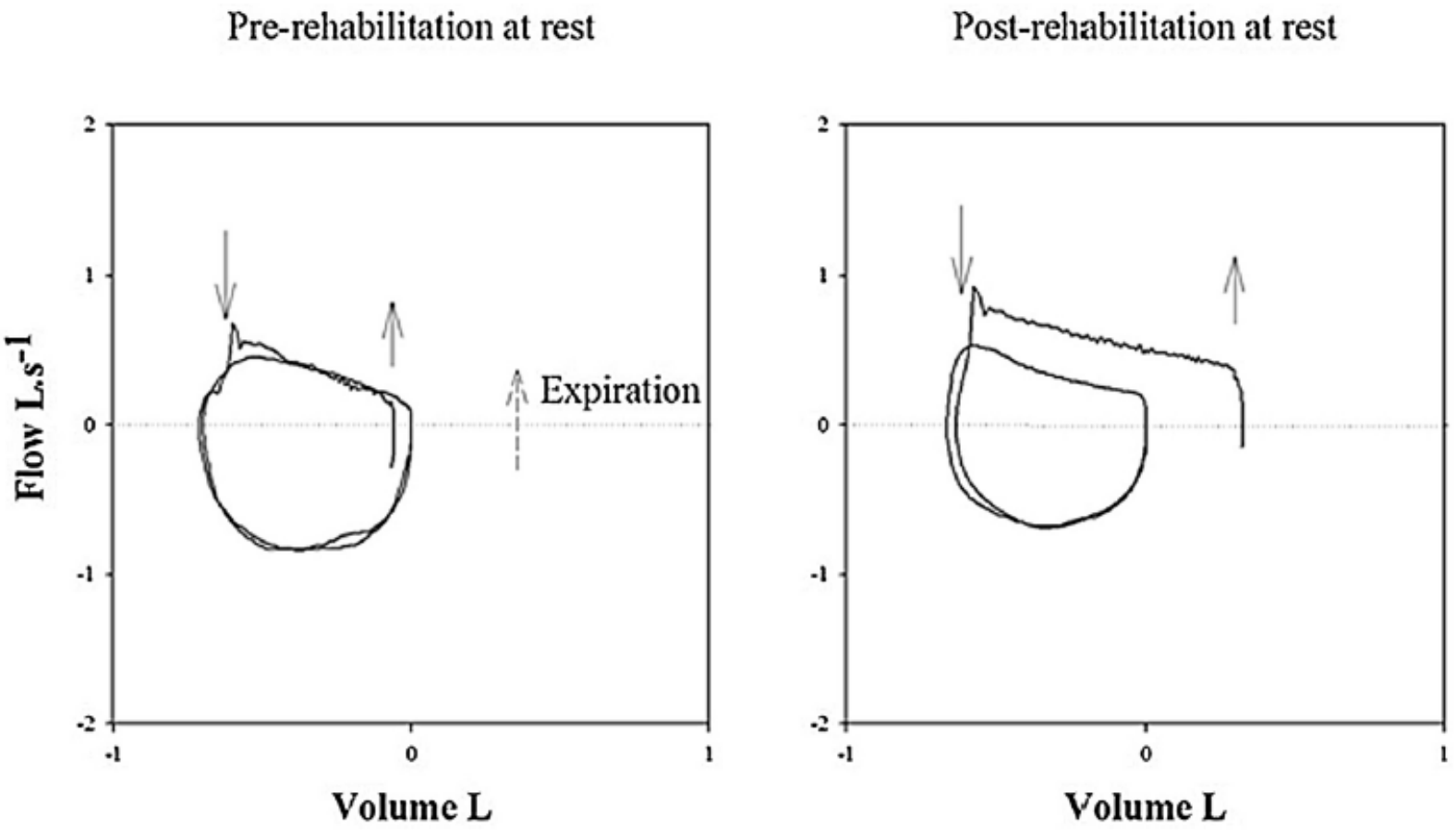


Fig. 1. A typical COPD patient, who was EFL at rest before the commencement of the PR program (left). The same COPD patient became NFL immediately after the completion of the PR program (right). Solid arrows indicate application (↓) and removal (↑) of negative pressure.

Table 2

Lung function data and patient-centered outcomes data between EFL and NFL patients pre- and post-PR.

Parameters	Patients	Pre PR	Post PR	paired *t*-test	% Change
FRC, %pred	All (n = 42)	122 ± 31	118 ± 29	NS	
	EFL (n = 16)	136 ± 36	117 ± 20	P = 0.02	
	NFL (n = 26)	113 ± 23	118 ± 34	NS	
	t-test	p = 0.013	NS		
IC, %pred	All (n = 42)	88 ± 28	91 ± 23	NS	
	EFL (n = 16)	73 ± 16	83 ± 19	P = 0.008	
	NFL (n = 26)	97 ± 30	96 ± 24	NS	
	t-test	p = 0.008	NS		
mMRC	All (n = 42)	2.3 ± 1	1.7 ± 1	P < 0.001	26%
	EFL (n = 16)	2.6 ± 1	2.1 ± 1	P = 0.014	17%
	NFL (n = 26)	2.0 ± 1	1.5 ± 1	P < 0.001	25%
6MWT, m	All (n = 42)	292 ± 66	339 ± 54	P < 0.001	15%
	EFL (n = 16)	270 ± 68	327 ± 43	P < 0.001	21%
	NFL (n = 26)	306 ± 62	346 ± 60	P < 0.001	13%

Table 2
Lung function data and patient-centered outcomes data between EFL and NFL patients pre- and post-PR.

Parameters	Patients	Pre PR	Post PR	paired *t*-test	% Change
WR max, watts	All (n = 42)	78 ± 26	87 ± 28	P < 0.001	10%
	EFL (n = 16)	69 ± 19	81 ± 22	P < 0.001	17%
	NFL (n = 26)	84 ± 29	91 ± 31	P = 0.03	8%
SGRQ	All (n = 42)	47 ± 14	34 ± 14	P < 0.001	28%
	EFL (n = 16)	56 ± 7	34 ± 7	P < 0.001	39%
	NFL (n = 26)	44 ± 16	33 ± 16	P < 0.001	25%
Borg scale – Dyspnea (90% WR max)	All (n = 42)	5.7 ± 3	3.7 ± 3.6	p < 0.001	35%
	EFL (n = 16)	6.1 ± 2	4.0 ± 2	p < 0.001	33%
	NFL (n = 26)	4.8 ± 3	2.8 ± 2	p < 0.001	42%
Borg scale – leg Fatigue (90% WR max)	All (n = 42)	4.9 ± 3	3.2 ± 2	p < 0.001	35%
	EFL (n = 16)	5.8 ± 2	2.9 ± 2	p < 0.001	50%
	NFL (n = 26)	4.3 ± 2	2.8 ± 2	p < 0.001	35%

Table 5

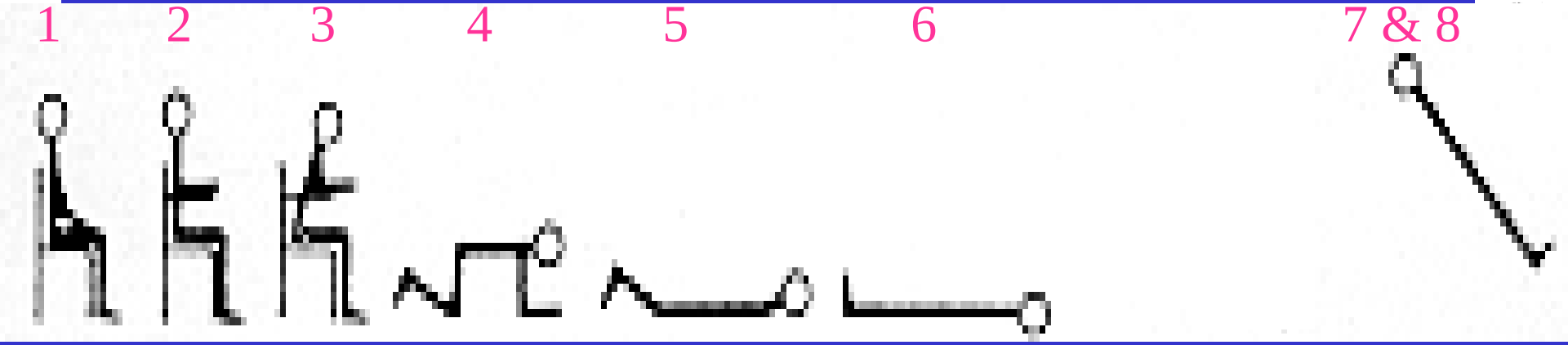
Changes in breathing pattern pre- and post-rehabilitation according to EFL or NFL status at rest and various stages of exercise.

		T_E-pre s	T_E-post s	P value	T_I-pre s	T_I-post s	P value	T_{TOT}-pre s	T_{TOT}-post s	P value	f-pre RR (br/min)	f-post RR (br/min)	P value
Rest	EFL → NFL (n = 6)	2.20 ± 0.4	2.71 ± 0.4	P = 0.03	1.29 ± 0.4	1.46 ± 0.3	P = 0.025	3.55 ± 0.6	4.24 ± 0.5	P = 0.021	17 ± 3	15 ± 2	P = 0.035
	NFL → NFL (n = 36)	2.27 ± 0.7	2.53 ± 0.8	P < 0.001	1.39 ± 0.3	1.51 ± 0.4	P = 0.043	3.66 ± 0.8	4.04 ± 1.0	P < 0.001	19 ± 5	17 ± 6	P = 0.007
30% WR max	EFL → NFL (n = 9)	1.28 ± 0.4	1.56 ± 0.4	P = 0.047	1.03 ± 0.4	1.29 ± 0.4	P = 0.002	2.32 ± 0.6	2.85 ± 0.5	P = 0.006	24 ± 4	22 ± 4	P = 0.03
	NFL → NFL (n = 33)	1.32 ± 0.5	1.54 ± 0.5	P < 0.001	1.19 ± 0.4	1.30 ± 0.5	P = 0.007	2.52 ± 0.8	2.92 ± 0.8	P < 0.001	25 ± 6	22 ± 6	P < 0.001
60% WR max	EFL → NFL (n = 12)	1.05 ± 0.5	1.21 ± 0.5	P = 0.02	0.94 ± 0.3	1.10 ± 0.3	P = 0.006	1.99 ± 0.7	2.29 ± 0.6	P < 0.001	29 ± 5	25 ± 5	P < 0.001
	NFL → NFL (n = 30)	1.11 ± 0.4	1.32 ± 0.4	P < 0.001	1.10 ± 0.3	1.25 ± 0.3	P < 0.001	2.24 ± 0.6	2.59 ± 0.6	P < 0.001	28 ± 7	25 ± 6	P < 0.001
90% WR max	EFL → NFL (n = 16)	0.85 ± 0.5	1.02 ± 0.4	P = 0.013	0.82 ± 0.2	1.01 ± 0.3	P < 0.001	1.66 ± 0.6	2.03 ± 0.6	P < 0.001	32 ± 4	28 ± 5	P = 0.002
	NFL → NFL (n = 26)	0.90 ± 0.4	1.16 ± 0.4	P < 0.001	1.04 ± 0.3	1.17 ± 0.3	P = 0.019	1.96 ± 0.6	2.31 ± 0.6	P < 0.001	30 ± 7	27 ± 6	P < 0.001

Values are means ± SD; n: number of subjects; NS: not statistically significant difference; EFL: expiratory flow limitation; NFL: non expiratory flow limitation; T_E: expiratory time; T_I: inspiratory time; T_{TOT}: total time; f: frequency; RR: respiratory rate; br/min: breath per minute; WR max: maximal work rate.

Conclusions

Before PR, 16 patients presented with EFL at rest and/or during exercise. After PR, EFL was abolished in 15 out of those 16 EFL patients who exhibited a significant increase in IC values. These were mainly accomplished through a modification of the breathing pattern. In the 26 NFL patients no increase was noted in their IC. However, both NFL and EFL COPD patients improved exercise capacity and patients centered outcomes undergoing the same PR program.



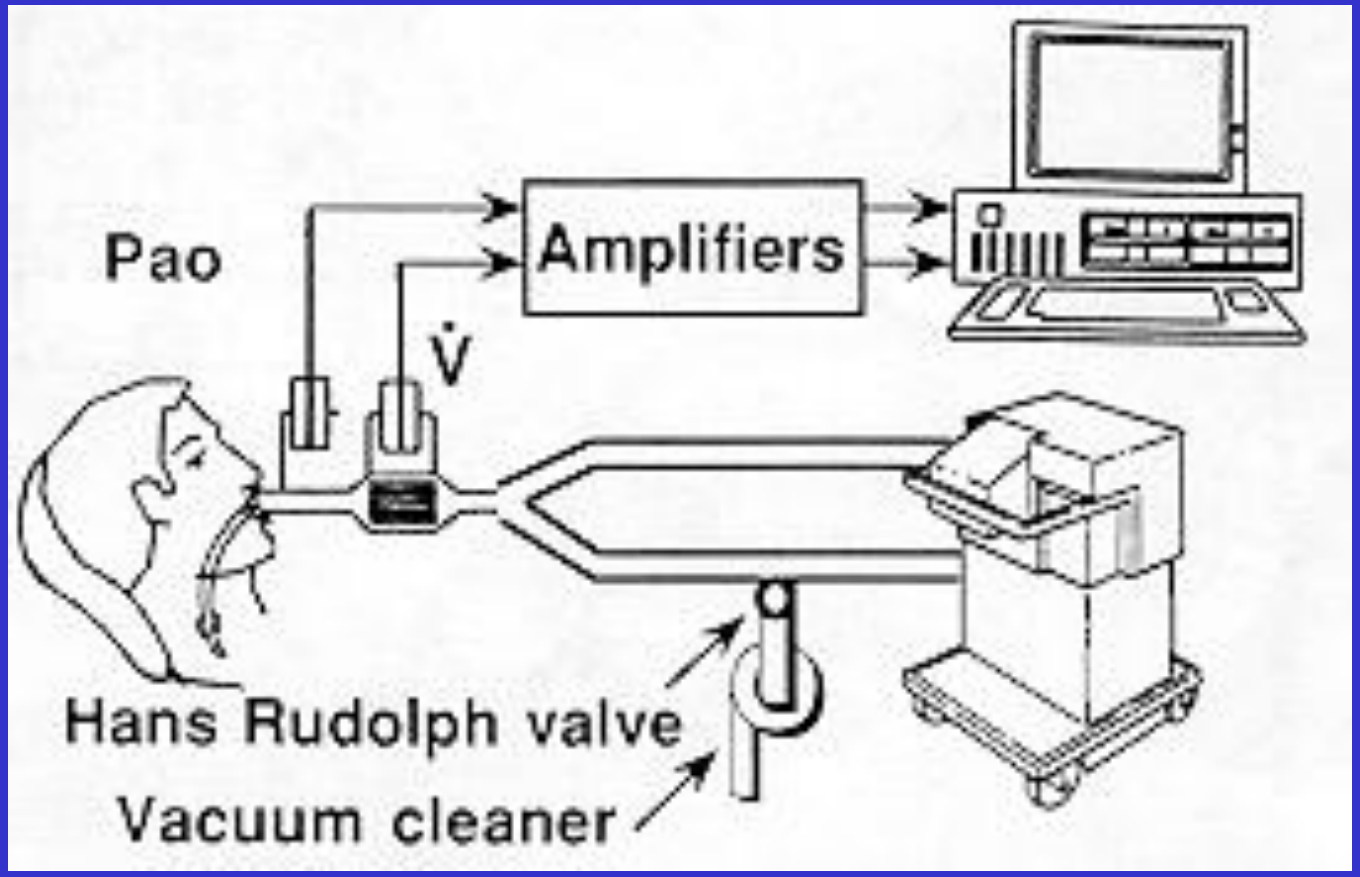
All patients were studied in eight different positions: *seated erect (pos.1), seated erect with arms supported (pos.2), seated leaning forward (pos.3), on hands and knees (pos.4), prone (pos.5), supine (pos.6), left (pos.7) and right lateral decubitus (pos.8).*

In 13 COPD patients was found that:

1. EFL is promoted not only in supine (9/13) but also in prone position (10/13)
2. EFL was abolished in hands and knees position in almost all COPD patients studied (8/9)
3. EFL was abolished in most patients (6/9) in both lateral decubitus posititions (can be easily adopted).

Dimitroulis et al, AJRCCM 2001; 163: A410 (Abstract)

During mechanical ventilation



Valta et al, AJRCCM 1994; 150: 1311-7
Armaganidis et al, Crit Care Med 2000; 28: 3837-42
Koutsoukou et al, AJRCCM 2000; 161: 1590-96
Koutsoukou et al Crit Care Med 2002; 30: 1941-49
Alvisi et al, CHEST 2003; 123: 1625-32

Conclusions

- Reducing hyperinflation in patients with COPD is a key mechanism for improving their dyspnoea, exercise tolerance and activity
- It is now possible to achieve sustained lung volume reduction not only by pharmacological means but with programs of Pulmonary Rehabilitation, which abolish almost completely the cause of hyperinflation in COPD patients, i.e., expiratory flow limitation by changing the pattern of breathing
- What remains to be clarified is whether the application of long term pharmacological lung volume reduction and other interventions will alter the natural history and mortality of this disease


Thank you!
Mykonos, Greece