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מרכז שניידר לרפואת ילדים בישראל
مركز شنايدر لطب الأطفال في اسرائيل
Schneider Children's Medical Center of Israel

The Role of CPET
(cardiopulmonary exercise testing)
in Assessing Lung Disease in CF

Dr. Meir Mei-Zahav
Kathy and Lee Graub CF Center
Schneider CMCI

Exercise in CF

You are probably quite sure that exercise:

- Improves aerobic fitness
- Lessen the decrease in pulmonary function
- Improves quality of life

Exercise in CF

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Physical exercise training for cystic fibrosis

Cochrane Database Syst Rev. 2015 Radtke T et al

OBJECTIVES:

- To determine the effects of physical exercise training on
  - aerobic exercise capacity
  - FEV1
  - QOL
  - other outcomes in cystic fibrosis
- 13/48 studies, 402 participants, met the inclusion criteria

Exercise in CF

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MAIN RESULTS:

- Limited evidence that aerobic or anaerobic physical exercise training has a positive effect on the outcome measures
  - Improvement in VO2 max (4/6 studies)
  - unclear effects on FEV1 (2/10 studies)
  - unclear effects QOL (2/5 studies)

AUTHORS' CONCLUSIONS:

- Evidence about the efficacy of physical exercise training in cystic fibrosis is limited

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Rationale

- Assessment of health status
- Assessing exercise associated side effects
- Assessing exercise intolerance etiology
- Tool to design individual exercise training

Rationale

- **Assessment of health status**
- Assessing exercise associated side effects
- Assessing exercise intolerance etiology
- Tool to design individual exercise training

Rationale

Assessment of health status

- Health status correlates better with exercise tolerance rather than resting measurements

  Joint ATS & ACCP statement on CPET

- Aerobic exercise capacity is associated with
  - Survival — Nixon NEJM 1992
  - CT changes
  - Future decline in FEV_1
  - Hospitalizations

Rationale

- Assessment of health status
- **Assessing exercise associated side effects**
- Assessing exercise intolerance etiology
- Tool to design individual exercise training

Rationale

Assessing exercise associated side effects:

- Hypoxemia
- Hypercarbia
- Cardiac arrhythmia

It would be imprudent to prescribe exercise without performing a test

Statement on exercise testing in CF- *Respiration 2015*

Rationale

- Assessment of health status
- Assessing exercise associated side effects
- **Assessing exercise intolerance etiology**
- Tool to design individual exercise training

Rationale

Assessing exercise intolerance etiology

- Exercise intolerance in CF may be due to:
  - Impaired lung function
  - Poor nutritional status
  - Low muscle power
  - Cardiac dysfunction
  - High level of inflammation
  - Low habitual activity

Rationale

- Assessment of health status
- Assessing exercise associated side effects
- Assessing exercise intolerance etiology
- **Tool to design individual exercise training**

Rationale

Tool to design individual exercise training

- 60-80% of peak Vo2
- 70-80% of maximal capacity
- 85% of anaerobic threshold
  - X5/week
  - 30min each
  - Gradually

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Can resting measures predict exercise capacity in cystic fibrosis?

- FEV1
- BMI
- LCI
- PsA
- Genotype

Methods

- Retrospective study
  - 17 CF centers, 14 countries
  - 726 CF patients

ECFS Exercise Working Group

T Radtke et al , AnnalsATS –in press

Study objectives

- To determine predictors of exercise capacity (VO_2peak) with a particular focus on CFTR genotype

T Radtke et al , AnnalsATS –in press

Mixed model

Parameters predicting Vo2 peak

	B-coefficients (95% CI's)	SE	P-value
VO_{2peak} (% predicted)			
Age	-0.14 (-0.32 to 0.04)	0.09	0.139
Sex	-1.29 (-3.46 to 0.88)	1.11	0.243
Pseudomonas aeruginosa	-1.93 (-4.44 to 0.58)	1.28	0.132
BMI z-score	**1.78 (0.78 to 2.77)**	**0.51**	**<0.001**
FEV_1 (% predicted)	**0.41 (0.35 to 0.47)**	**0.03**	**<0.001**
CFTR group	**-0.95 (-4.18 to 2.29)**	**1.65**	**0.567**

T Radtke et al , AnnalsATS –in press

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Lung clearance index (LCI) as a predictor of exercise limitation among CF patients

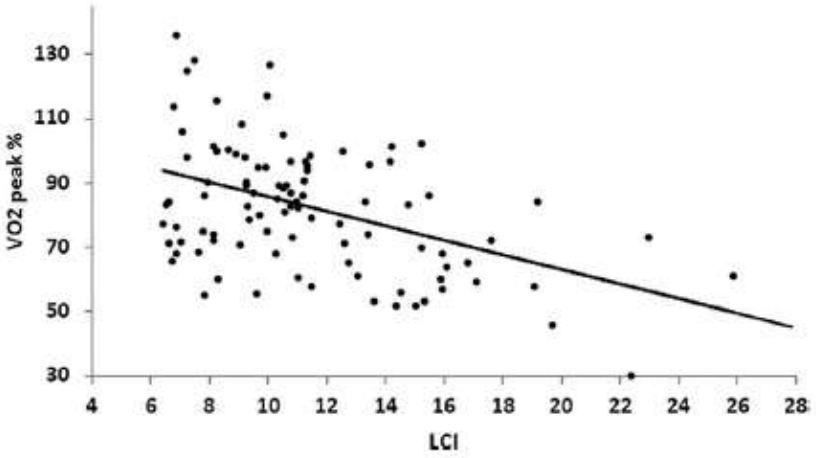

FIGURE 1 Correlation of LCI and VO_2peak. LCI was correlated with VOpeak % predicted ($P < 0.001$, r^2: 0.185)

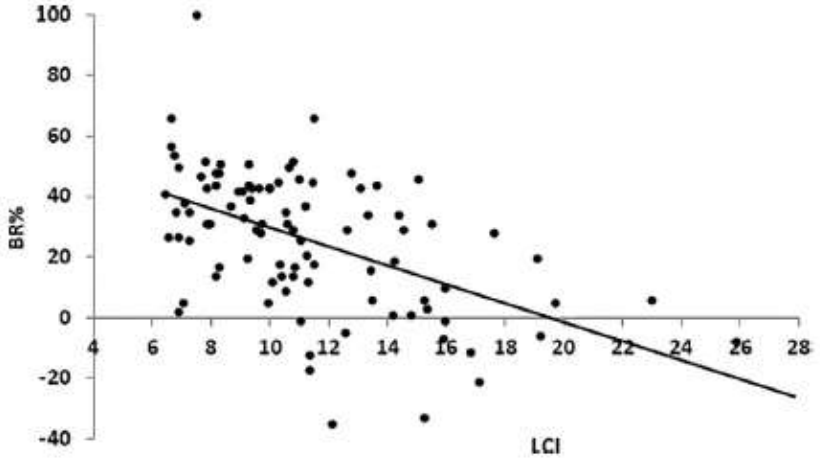

FIGURE 2 Correlation of LCI and breathing reserve % predicted (BR %). LCI was correlated with BR % predicted ($P < 0.001$, r^2: 0.272)

Pediatr Pulmonol 10.2017

Rationale

Assessment of health status

- Health status correlates better with exercise tolerance rather than resting measurements

Joint ATS & ACCP statement on CPET

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Assessment of health status

Which CPET parameters are important in assessing health status?

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THE PROGNOSTIC VALUE OF EXERCISE TESTING IN PATIENTS WITH CYSTIC FIBROSIS

PATRICIA A. NIXON, PH.D., DAVID M. ORENSTEIN, M.D., SHERYL F. KELSEY, PH.D., AND CARL F. DOERSHUK, M.D.

Conclusions. Higher levels of aerobic fitness in patients with cystic fibrosis are associated with a significantly lower risk of dying. Although better aerobic fitness may simply be a marker for less severe illness, measurement of $\dot{V}_{O_2\,peak}$ appears to be valuable for predicting prognosis.

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Are there better CPET parameters to assess lung disease severity?

Dynamic Hyperinflation

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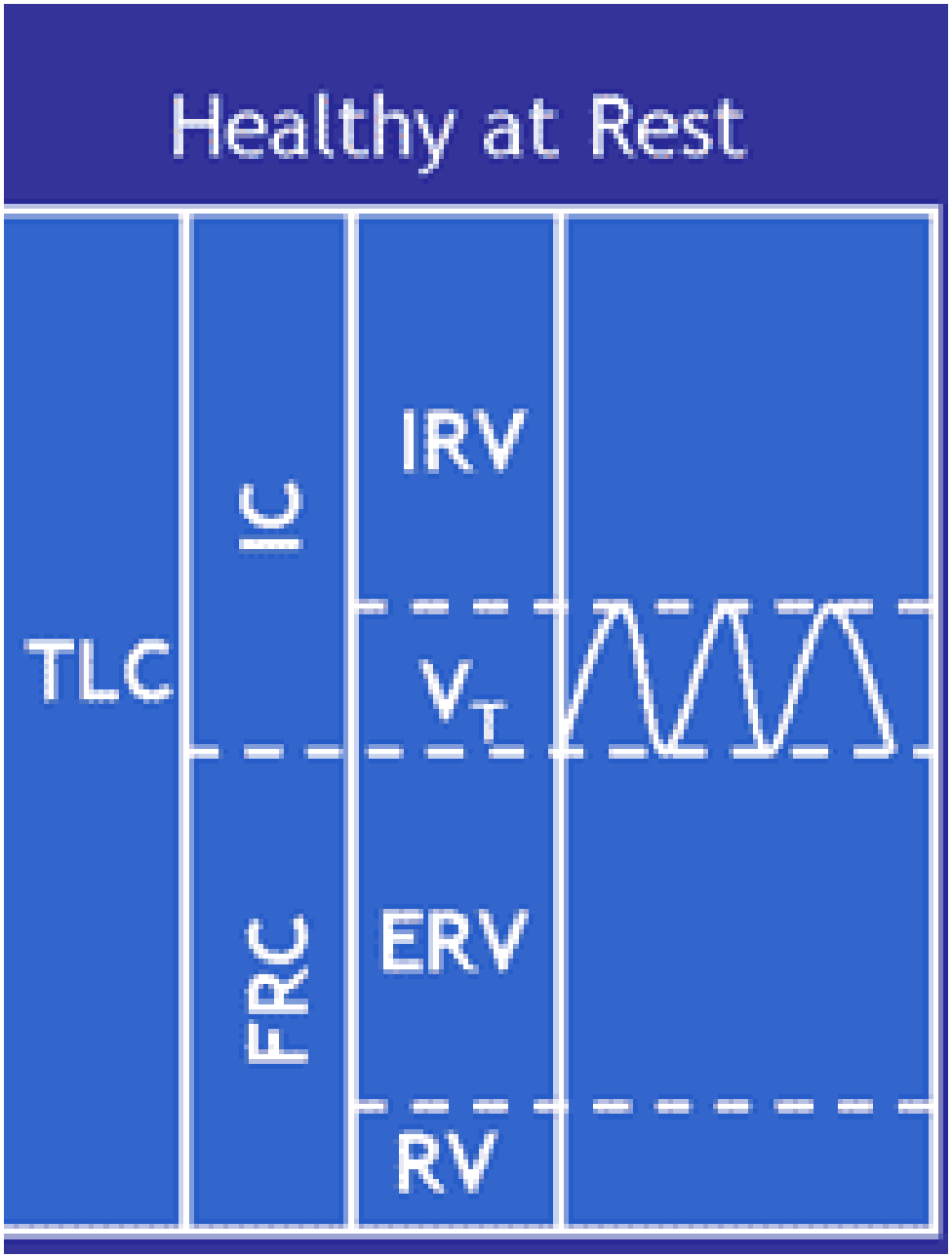
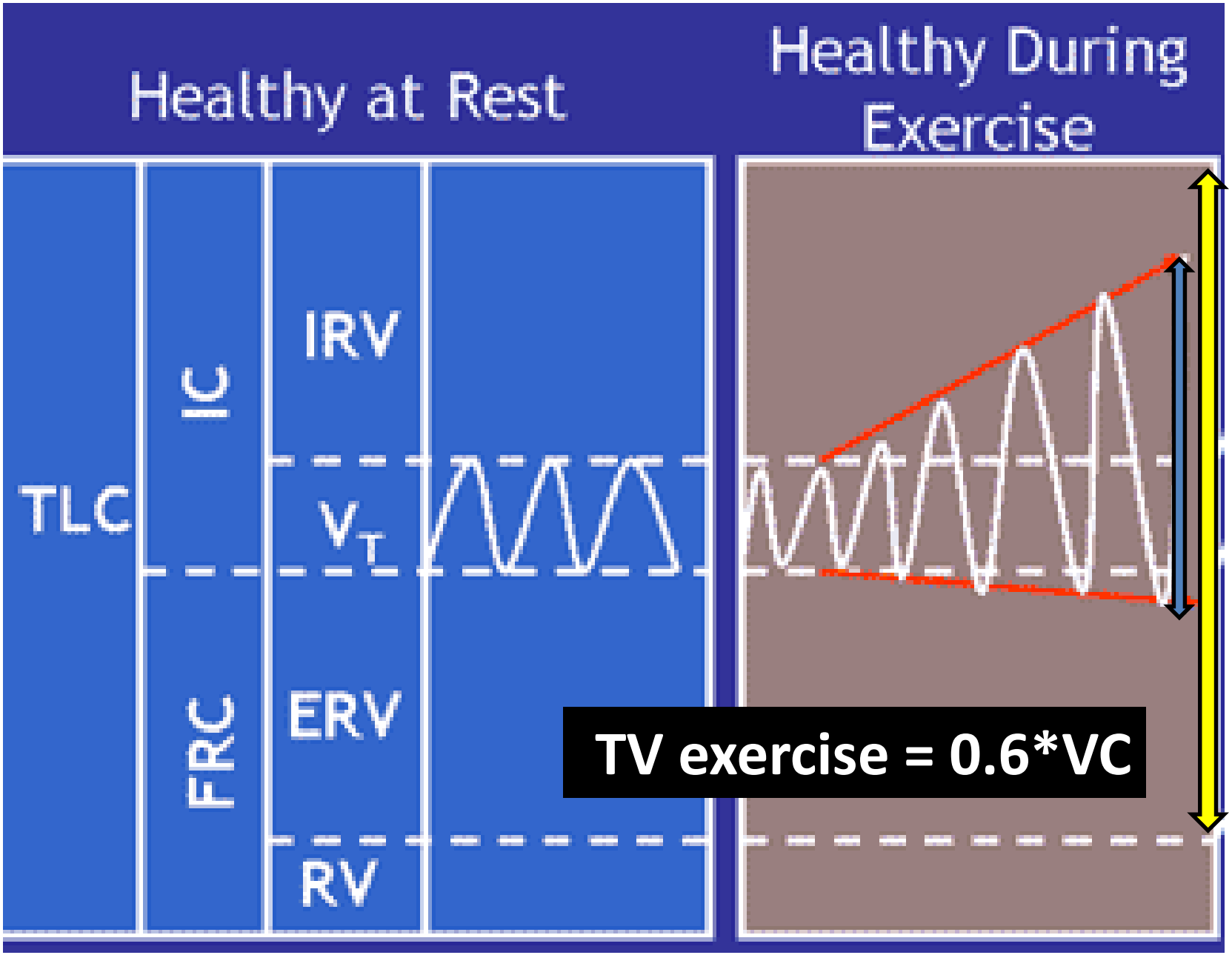
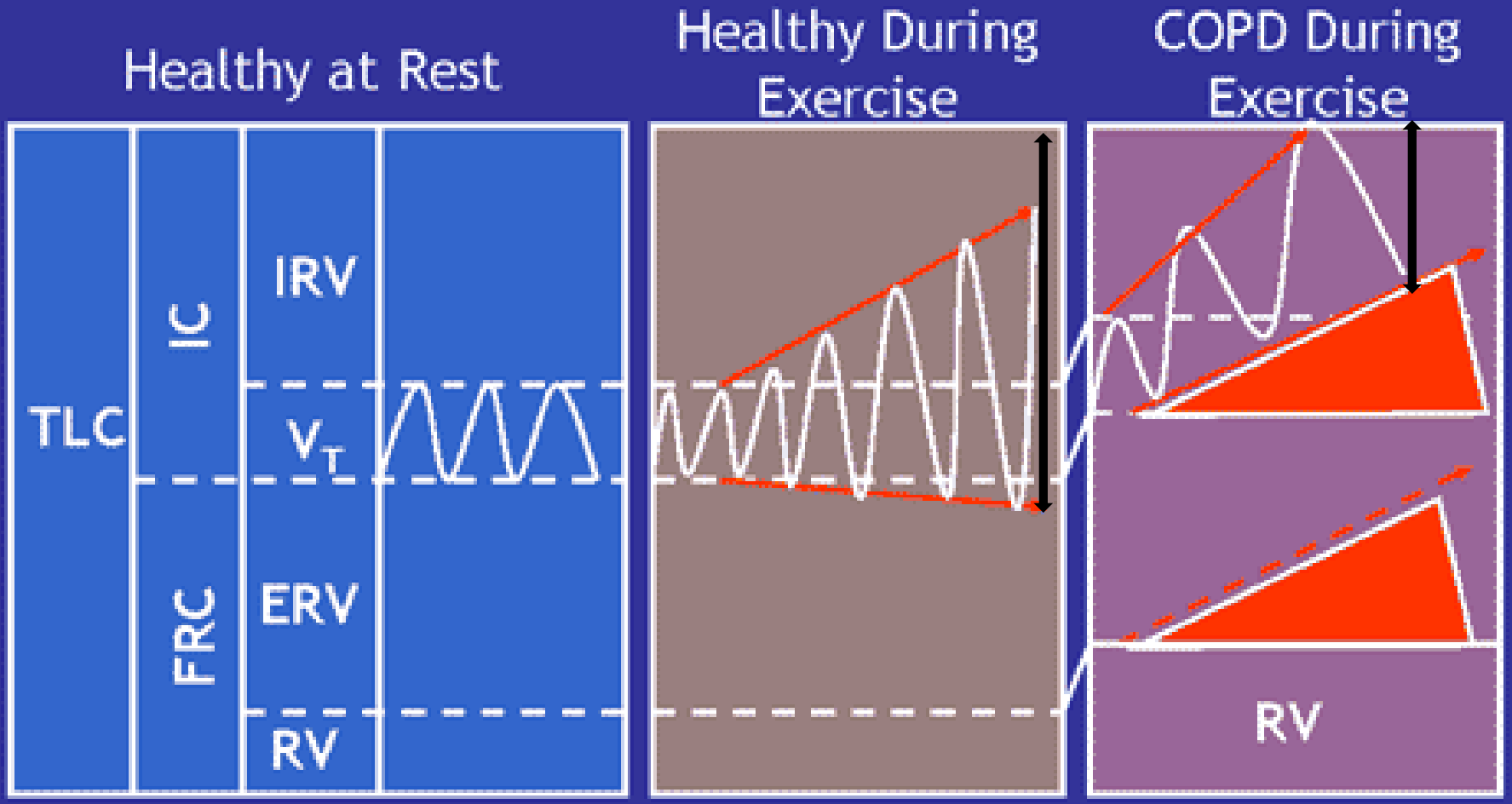

Healthy at Rest
TLC
IC
FRC
IRV
V_T
ERV
RV


Healthy at Rest
Healthy During Exercise
TLC
IC
FRC
IRV
V_T
ERV
RV
TV exercise = 0.6*VC

DYNAMIC HYPERINFLATION

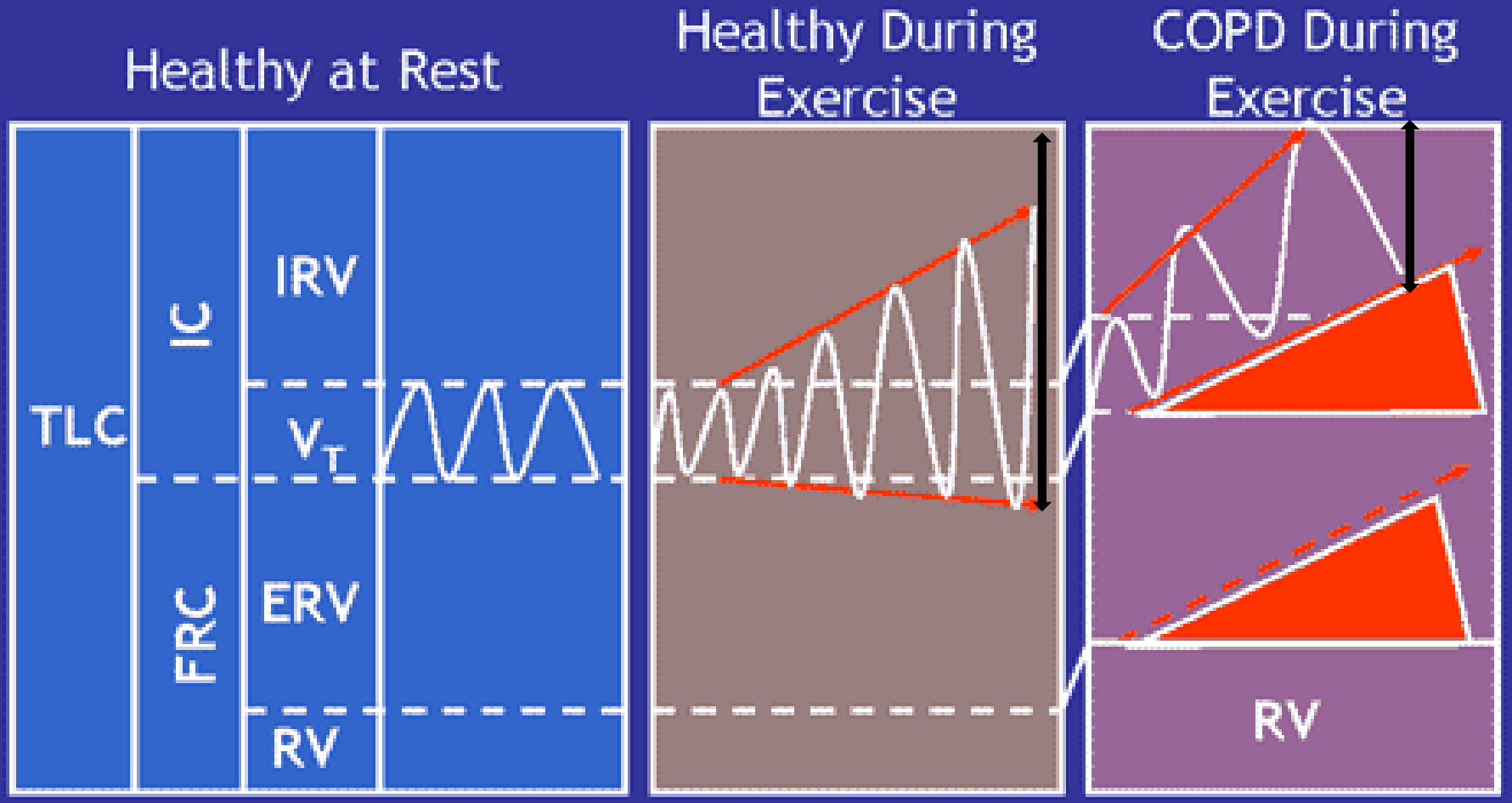
Tidal Volume During Exercise



Adapted from Denis O'Donnell, MD.

DYNAMIC HYPERINFLATION

Tidal Volume During Exercise

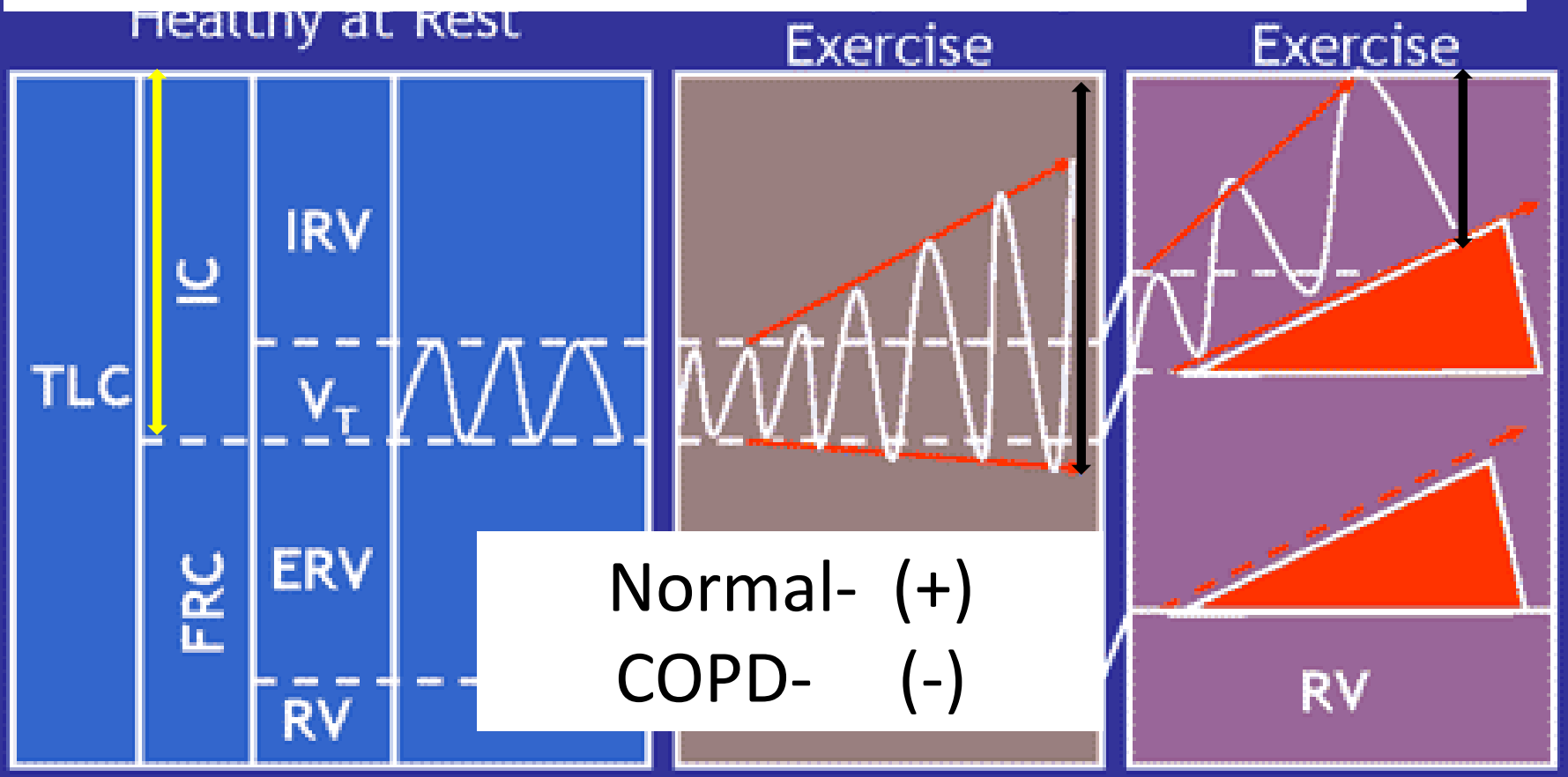


- **TV fails to increase**
- **IC exercise ↓**

Adapted from Denis O'Donnell, MD.

DYNAMIC HYPERINFLATION

DH = IC exercise-IC rest



Adapted from Denis O'Donnell, MD.

Dynamic Hyperinflation and Exercise Intolerance in Chronic Obstructive Pulmonary Disease

O'DONNELL et al AJRCCM 2001

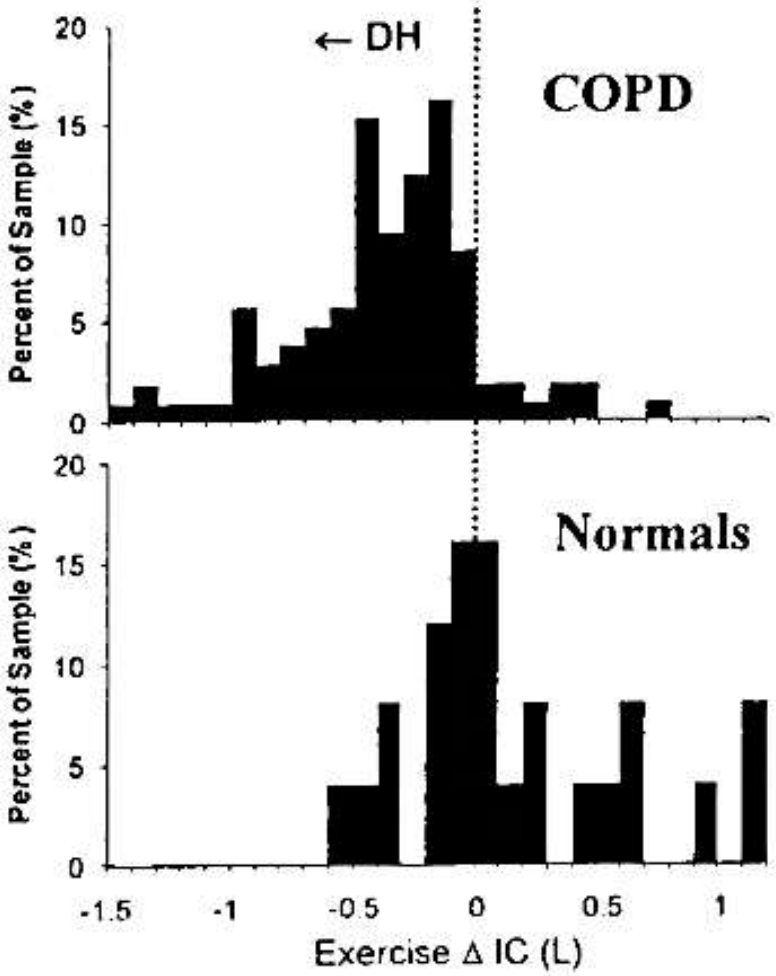
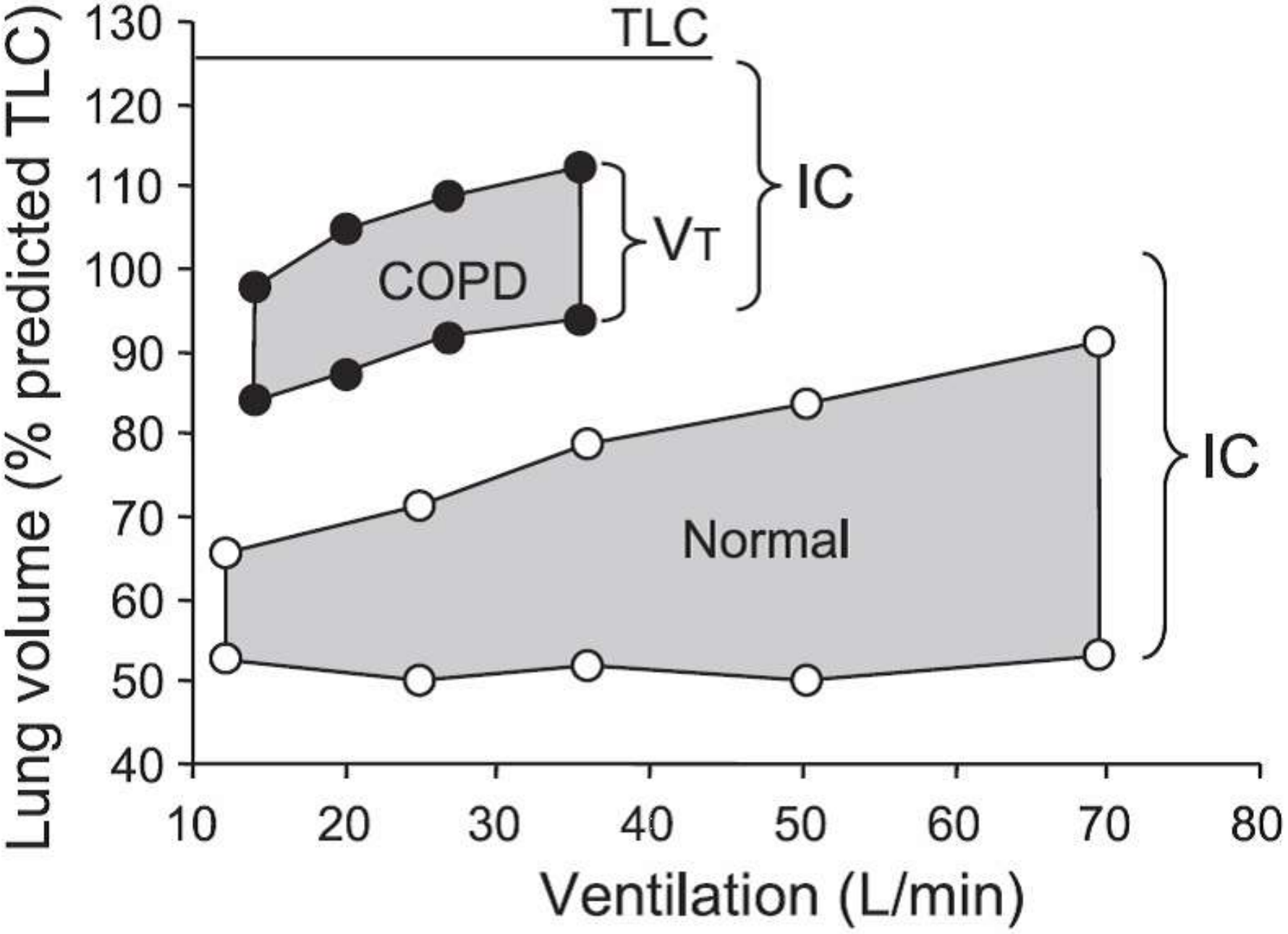


Figure 2. The distribution of the extent of change (Δ) in IC during exercise is shown in patients with COPD (n = 105) and in age-matched normal subjects (n = 25). A negative ΔIC reflects dynamic hyperinflation (DH) during exercise; each bar width corresponds to a ΔIC range of 0.10 L. In contrast to normal subjects, the majority of patients with COPD experienced significant DH during exercise despite reaching a


TLC
IC
V_T
COPD
Normal
IC
Lung volume (% predicted TLC)
Ventilation (L/min)
130
120
110
100
90
80
70
60
50
40
10
20
30
40
50
60
70
80

What about dynamic hyperinflation in CF?

Very little is known….

Original Article

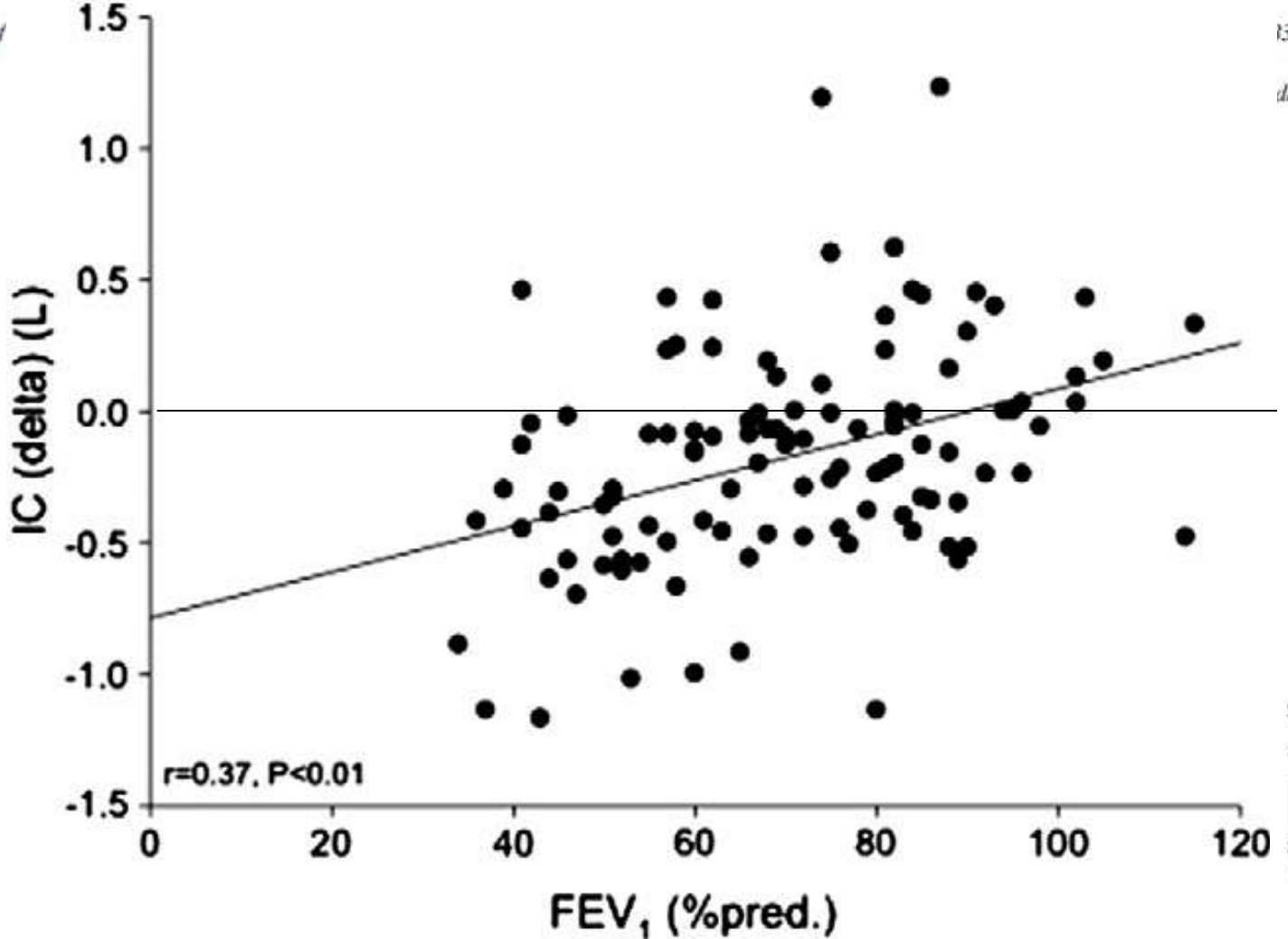
Prognostic relevance of dynamic hyperinflation during cardiopulmonary exercise testing in adult patients with cystic fibrosis

D. Stevens [a,b,*], A. Stephenson [b,c,d], M.E. Faughnan [b,c,d], E. Leek [b], E. Tullis [b,c,d]

[a] School of

3H 4R2, Canada

da



Journal of Cystic Fibrosis
www.elsevier.com/locate/jcf

2013

Results

Cardiopulmonary exercise testing parameters.

	Dynamic hyperinflation (n = 63)	Non-dynamic hyperinflation (n = 25)
$\dot{V}O_{2\ peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	28.7 ± 8.1	32.9 ± 6.1 *
$\dot{V}_{E\ peak}$ ($L \cdot min^{-1}$)	72.4 ± 20.5	83.4 ± 29.7 *
HR_{peak} ($b \cdot min^{-1}$)	176 ± 14	173 ± 16
WR_{peak} ($W \cdot min^{-1}$)	140 ± 49	177 ± 53 **
SpO_{2peak} (%)	93 ± 3	93 ± 3
$BorgSOB_{peak}$	7 ± 3	5 ± 2 *
$BorgLEG_{peak}$	7 ± 2	8 ± 3
$\dot{V}_E/\dot{V}CO_{2\,GET}$	33.2 ± 4.5	29.8 ± 3.9 **
$\dot{V}_{E\ peak}$/MVV	0.79 ± 0.22	0.67 ± 0.18 *
$V_{T\ peak}$ (L)	1.73 ± 0.56	2.20 ± 0.57 **
ICΔ (L)	−0.44 ± 0.26	+0.40 ± 0.28 **
EELVΔ (TLC-IC) (L)	+0.44 ± 0.26	−0.40 ± 0.28 **

Original Article

Prognostic relevance of dynamic hyperinflation during cardiopulmonary exercise testing in adult patients with cystic fibrosis

Results

- Dynamic hyperinflation did not predict FEV1 decline in 2 years

Original Article

Prognostic relevance of dynamic hyperinflation during cardiopulmonary exercise testing in adult patients with cystic fibrosis

Conclusions:

- Dynamic hyperinflation is associated with
  - Reduced lung functions
  - Exercise intolerance

- But has limited prognostic value

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CPET at Schneider CMCI

CPET at Schneider CMCI

- 50 CF patients performed 1-3 CPETS each in 6/12-9/17
- Tests of 6 patients were excluded – unacceptable

CPET at Schneider CMCI

Demographic data:

- 26 males
- Age – 24.6±6y (9-61y)
- 18 children

CPET at Schneider CMCI

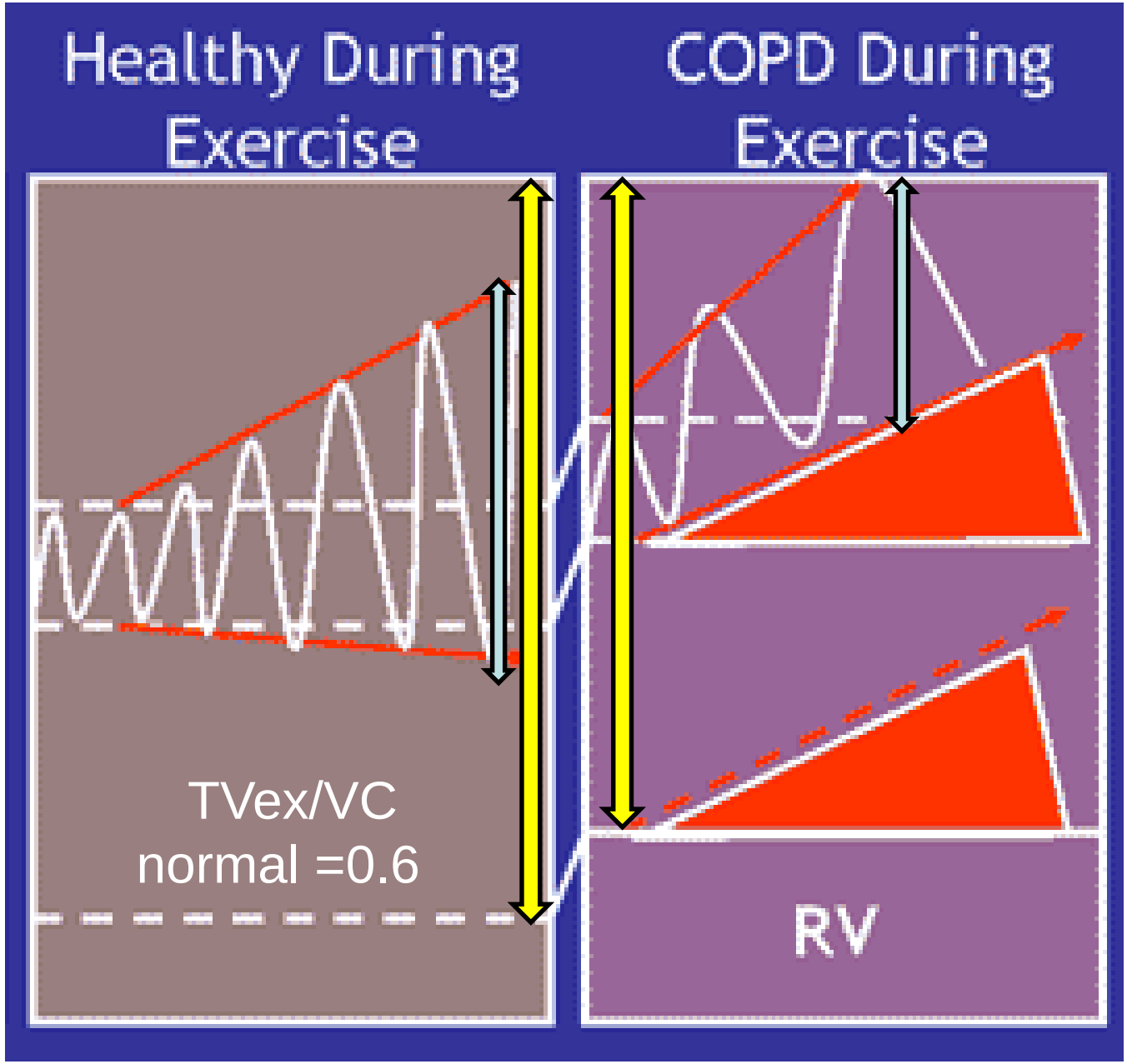
Resting PFTs:

	M (SD)%	Range %
FVC	90 (16)	49-139
FEV1	78 (18)	39-123
RV/TLC	33 (12)	18-58

CPET at Schneider CMCI

CPET results:

	M (SD)	Median (Range)	Normal range
VO2 peak % pred.	90 (16)	**76 (49-139)**	>82%
Max load -%	**74 (16)**	**73 (44-120)**	>93%
Breathing reserve %	**28 (17)**	**32 (0-62)**	>30%
Resp rate %	**128 (36)**	**139 (67-200)**	80-120%
TV/VC	**0.44 (0.08)**	**0.43 (0.26-0.63)**	>0.6


Healthy During Exercise
COPD During Exercise
TVex/VC
normal =0.6
RV

Dynamic Hyperinflation

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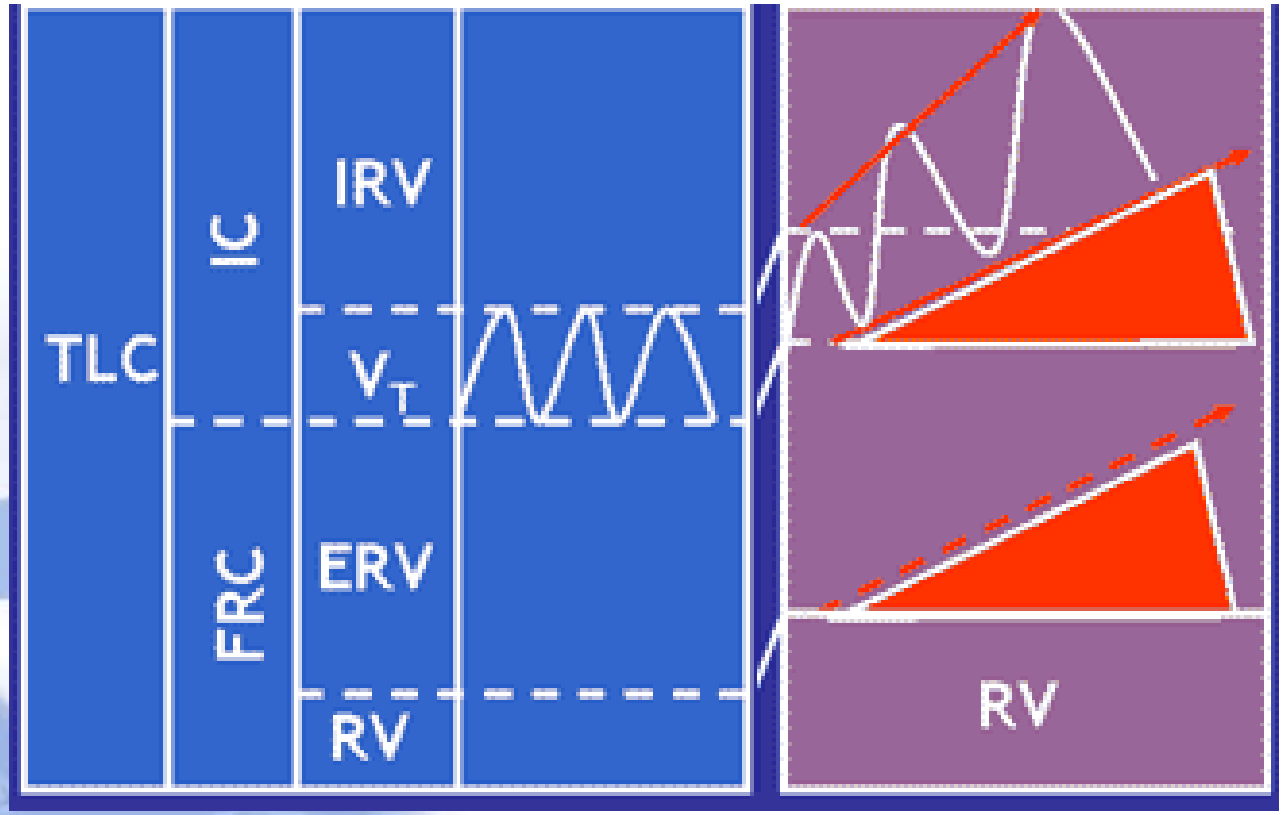
- Definition: decrease of >5% in IC



Dynamic Hyperinflation

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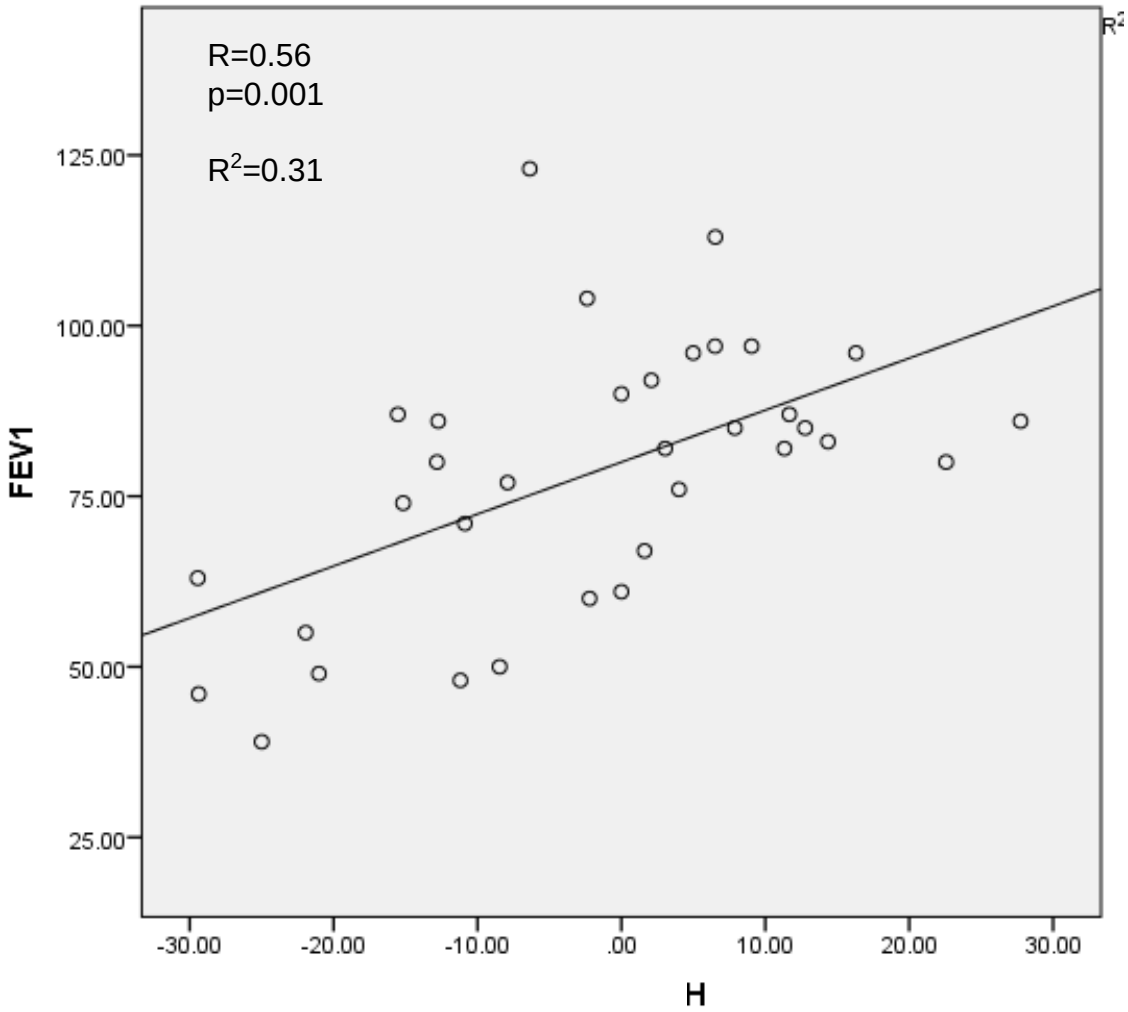
- Valid DH measurements were available in 31 patients

- 42% demonstrated DH:
  - ✓ Mean drop in IC-16%
  - ✓ Drop range – 6-29%

- 58% did not have DH
  - ✓ Mean change in IC- +7%
  - ✓ Range- -4-+23%

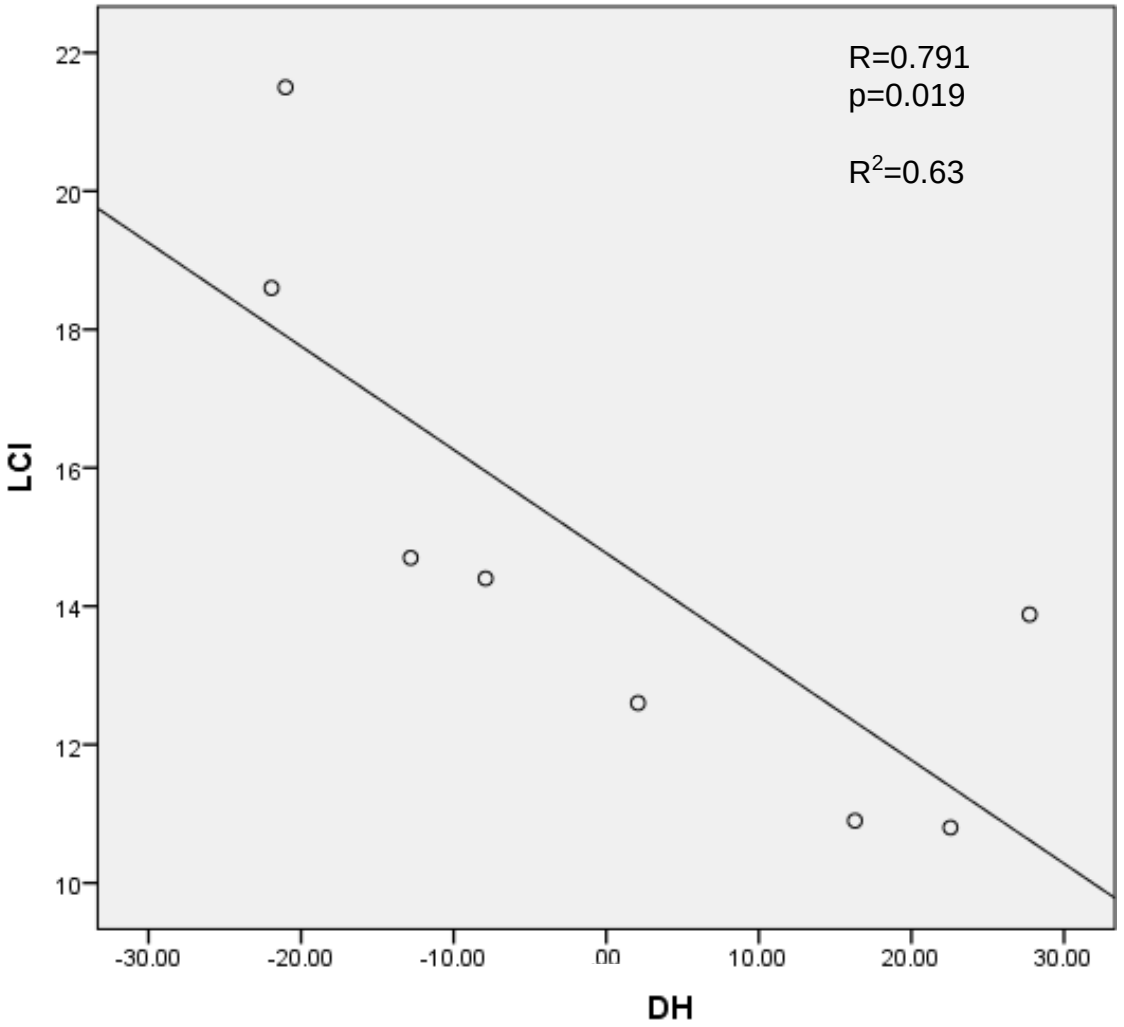
DH and FEV1

- Good correlation between DH and FEV1
- DH can predict FEV1-in 31%



DH and LCI

- **Excellent correlation between DH and LCI**
- **DH can predict LCI in 63%**



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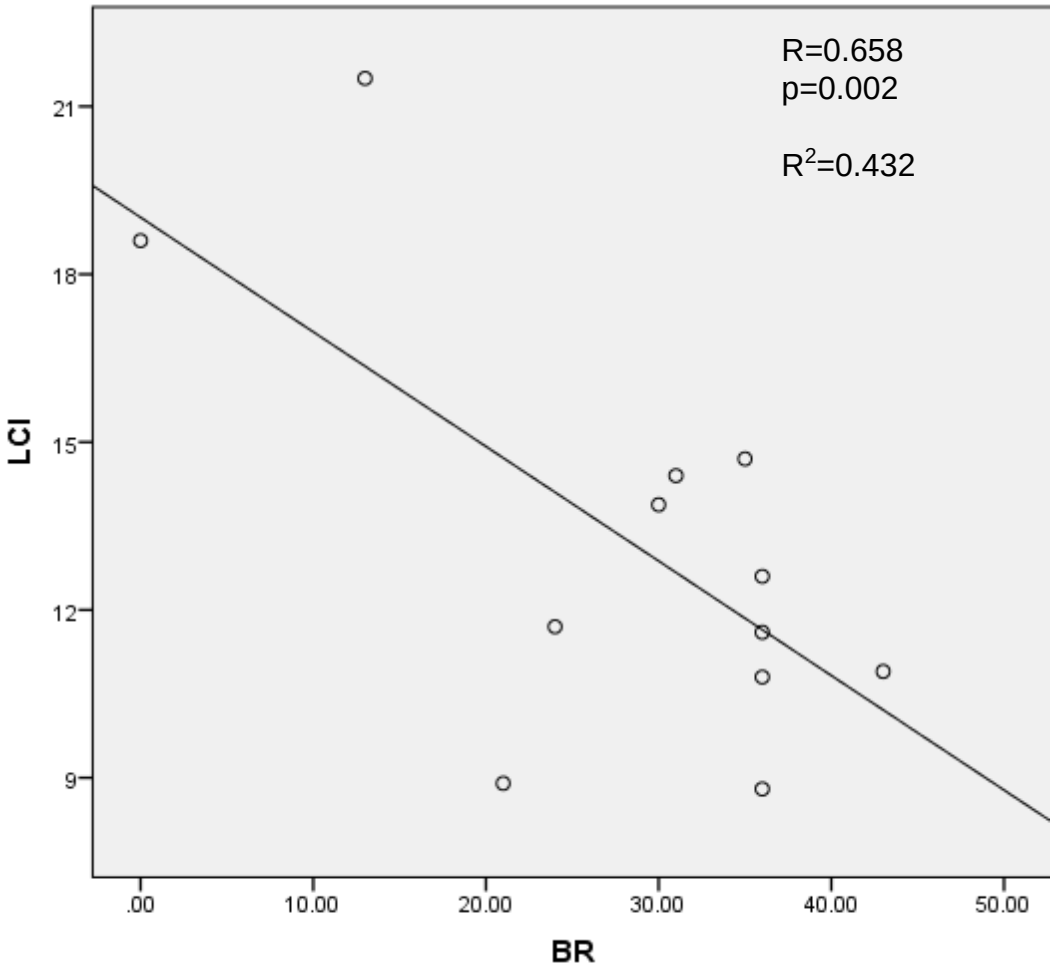
What about other CPET parameters?

- VO2 peak
- Breathing reserve

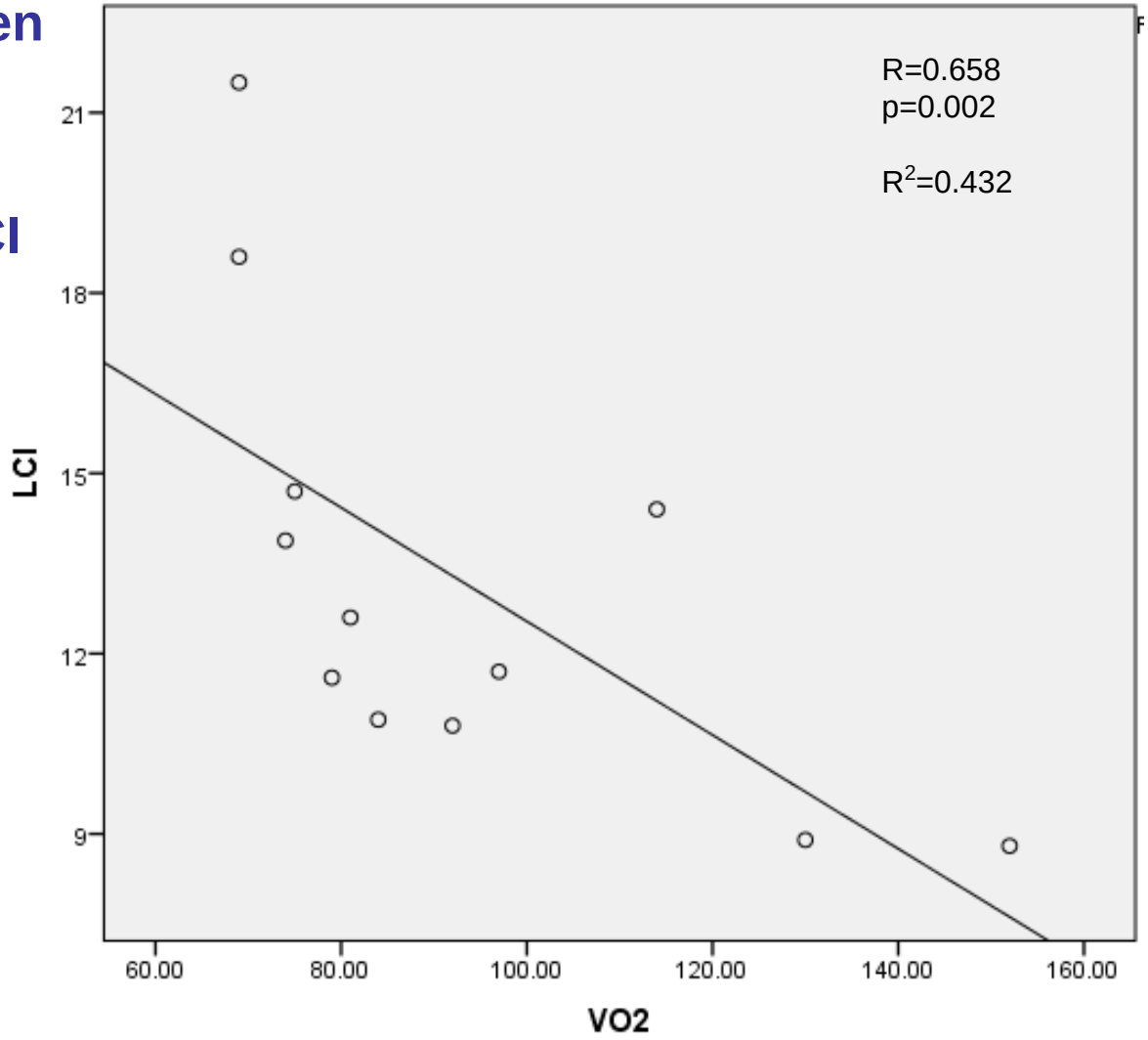
BR and LCI

- Good correlation between BR and LCI
- BR can predict LCI in 43%



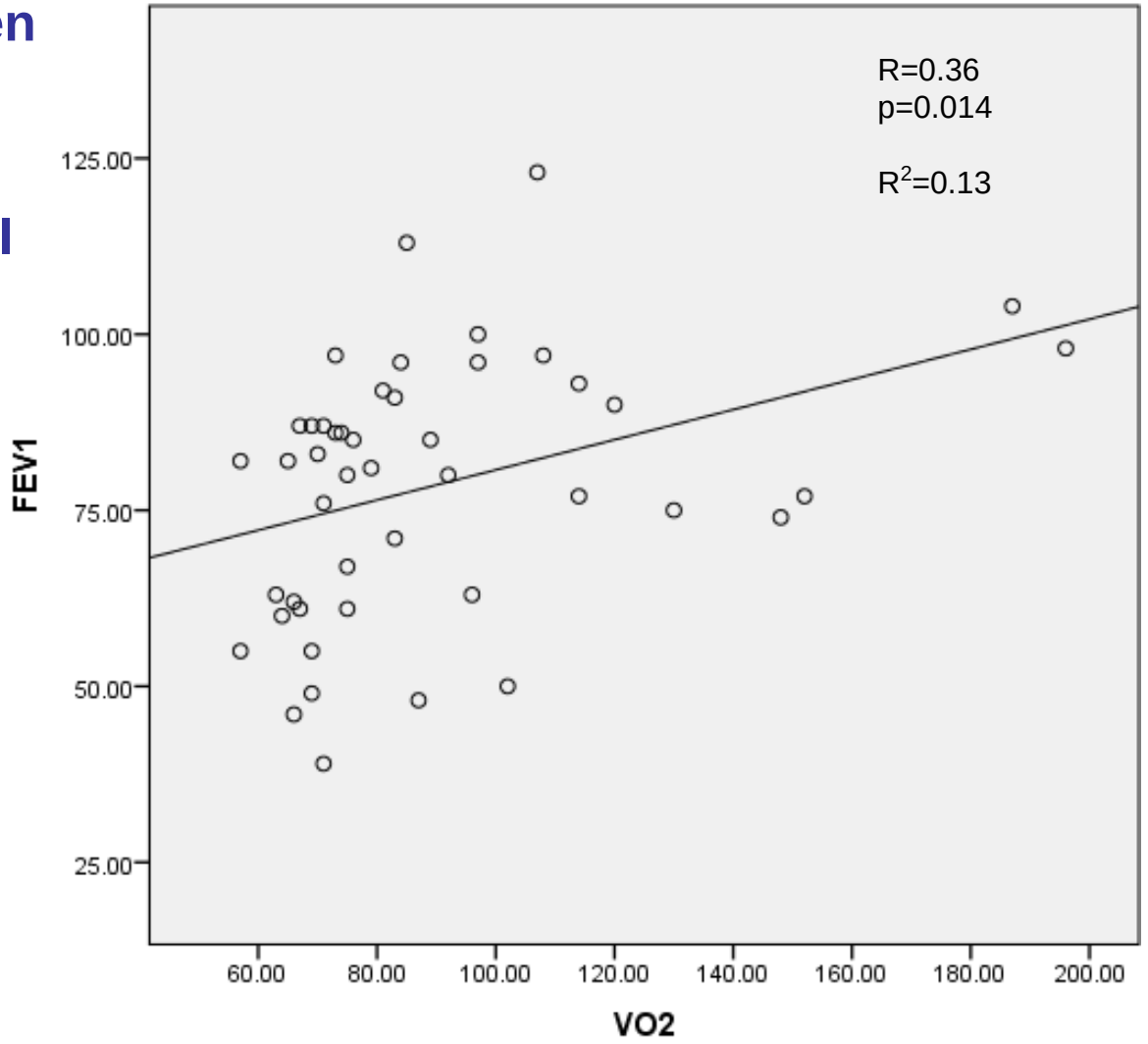
VO2 peak and LCI

- Good correlation between VO2 peak and LCI
- Vo2 peak can predict LCI in 43%



VO2 peak and FEV1

- Weak correlation between VO2 peak and FEV1
- Vo2 peak can predict LCI in 13%



VO2 peak + BR and LCI

- Vo2 peak + BR can predict LCI in 85%

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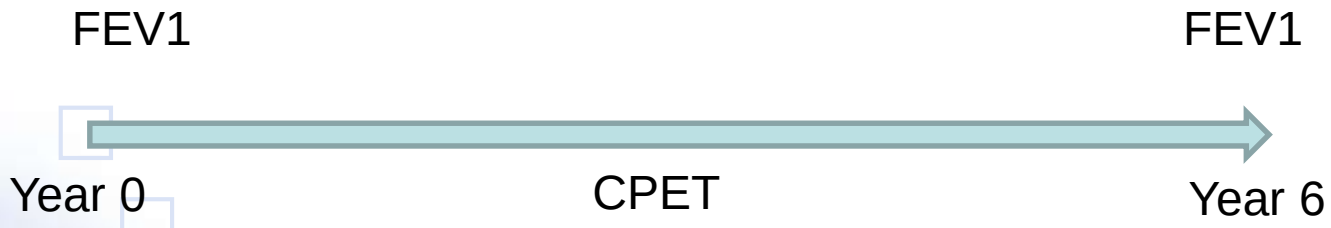
Does DH have a role in predicting lung disease progression?

DH in predicting deterioration

- **FEV1 change in 6 years**



DH in predicting deterioration

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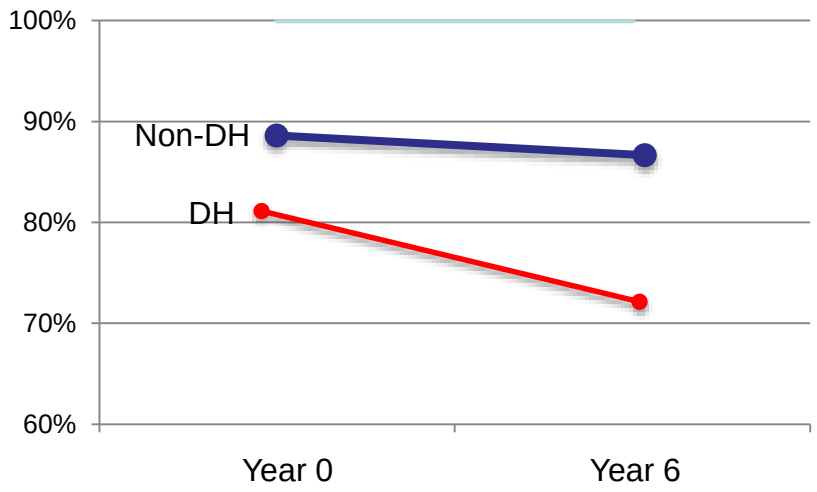
- **FEV1 change in 6 years**

	DH (13)	Non DH (18)	p
FEV1 in year 0	82±26%	88±20%	0.23
%Drop in FEV1	10±11%	2±8%	0.016

DH is associated with lung function deterioration



Conclusions

- Patients with CF have lower exercise capacity and lower aerobic capacity
- There is a correlation between CPET parameters
  - ✓ Work capacity
  - ✓ Vo2 max
  - ✓ Breathing reserve
  - ✓ Dynamic hyperinflation

  } and lung functions (LCI, FEV1)
- Dynamic hyperinflation is associated with lung function deterioration

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Thanks

- PFT technicians
- Yulia Gendler
- Prof Blau
- The CF team at Schneider
- The patients