Η άσκηση στην πνευμονική υπέρταση

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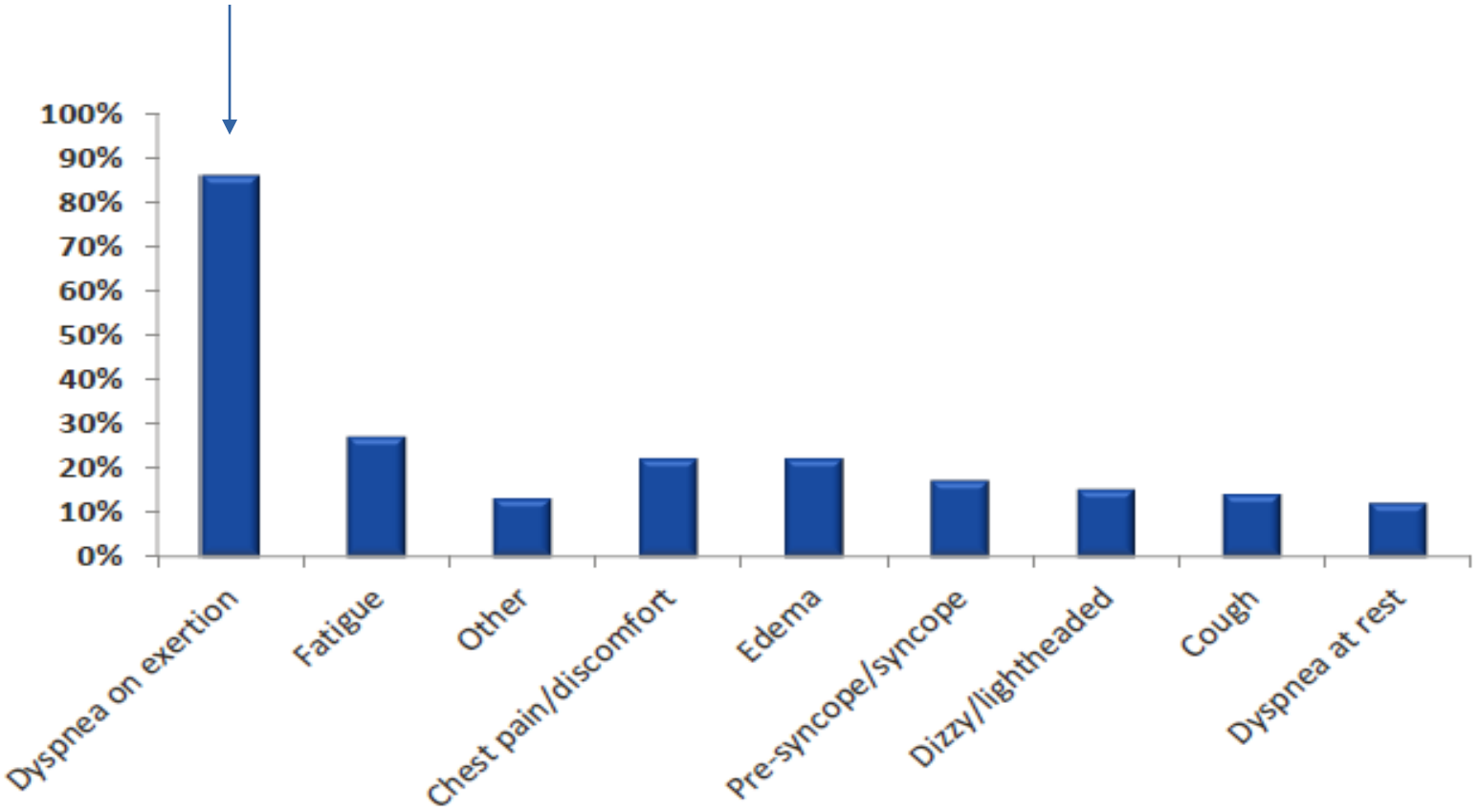
- Η άσκηση στη διάγνωση της ΠΥ
- Η άσκηση στην πρόγνωση της ΠΥ
- Η άσκηση στην παρακολούθηση του θεραπευτικού αποτελέσματος
- Η άσκηση ως θεραπευτικό μέσο

PH and clinical presentation: REVEAL registry



-Low specificity of symptoms
-Delayed diagnosis (average 2.8 years between symptom onset and RHC)
-Exercise testing is recommended early for patient assessment

Brown LM et al, Chest 2011

Εκτίμηση της λειτουργικής ικανότητας στην ΠΥ

- World Health Organization (WHO) functional classification

-απλός, εύκολος, ισχυρά σχετιζόμενος με πρόγνωση δείκτης

-υποκειμενικός

- 6MWT

-απλή, φθηνή, εύκολη και αναπαραγώγιμη δοκιμασία

-τρόπος εκτέλεσης, “ceiling effect”, όχι μεταβολικό και καρδιοαναπνευστικό κόστος άσκησης

- CPET

-περισσότερο ακριβή και χρονοβόρος δοκιμασία, απαιτεί εμπειρία

-παρέχει πολλές περισσότερες πληροφορίες

- Stress ECHO

- RHC during exercise

Paollilo et al. Eur J Prev Cardiol 2011; ESC/ERS guidelines. Eur Heart J 2016

ERS TASK FORCE

Recommendations on the use of exercise testing in clinical practice

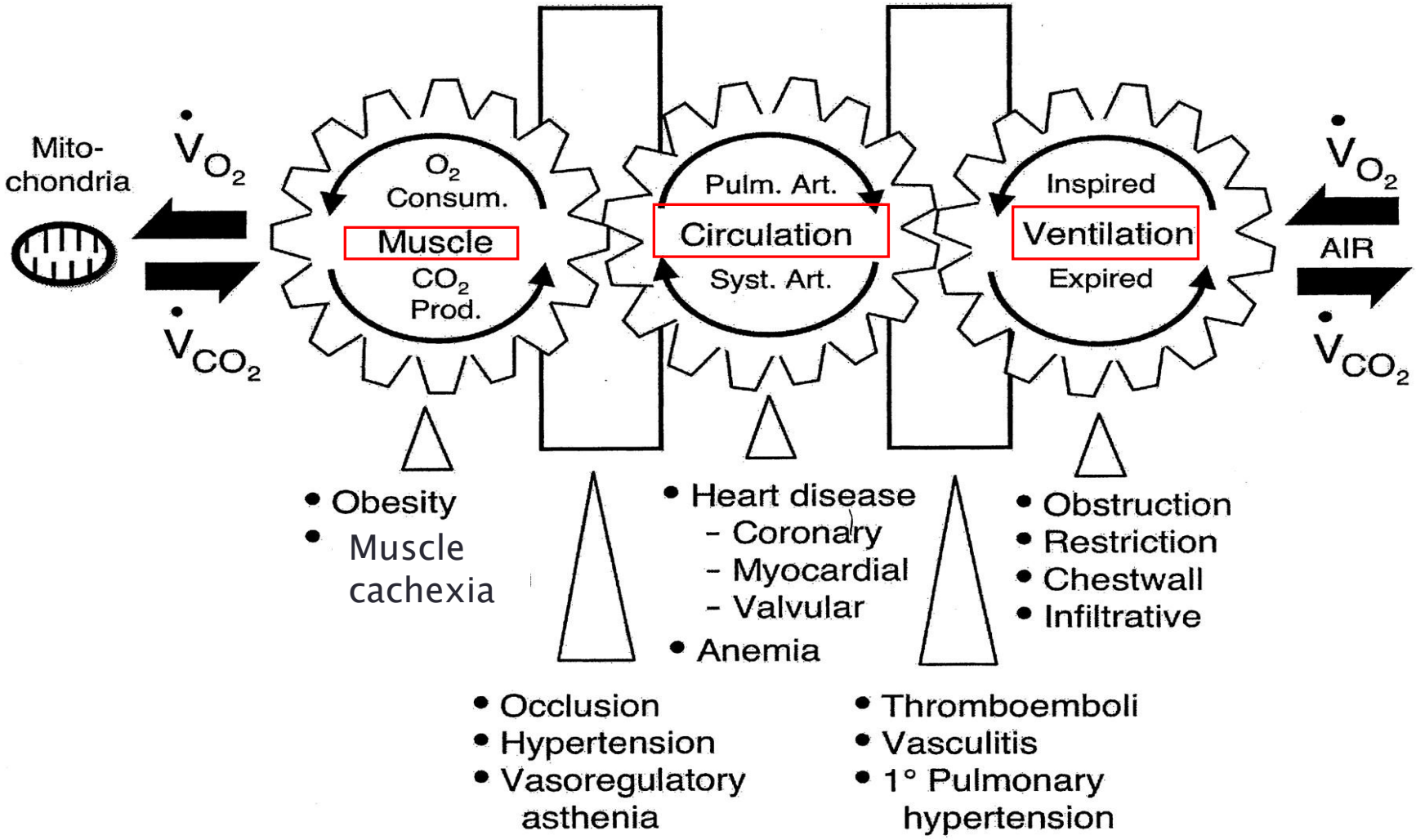
"Cardiopulmonary exercise testing (CPET) should be considered the ***gold standard*** for evaluating the ***causes of exercise intolerance*** in patients with ***pulmonary and cardiac*** **disease**, and is based on the principle that ***system failure*** typically ***occurs*** while the system (e.g. muscle–energetic, cardiovascular or pulmonary) is ***under stress***."

Principles of Exercise Testing and Interpretation, 4th edn.
K Wasserman, J Hansen, D Sue, W Stringer, B Whipp, eds

"Η CPET αποτελεί την δοκιμασία άσκησης που δίνει την δυνατότητα της ταυτόχρονης εκτίμησης της ***κυτταρικής, αναπνευστικής, καρδιαγγειακής, αιμοποιητικής, νευροψυχιατρικής και μυοσκελετικής*** απάντησης σε καθορισμένο βαθμό άσκησης, δηλαδή σε καθορισμένο βαθμό μεταβολικού stress.

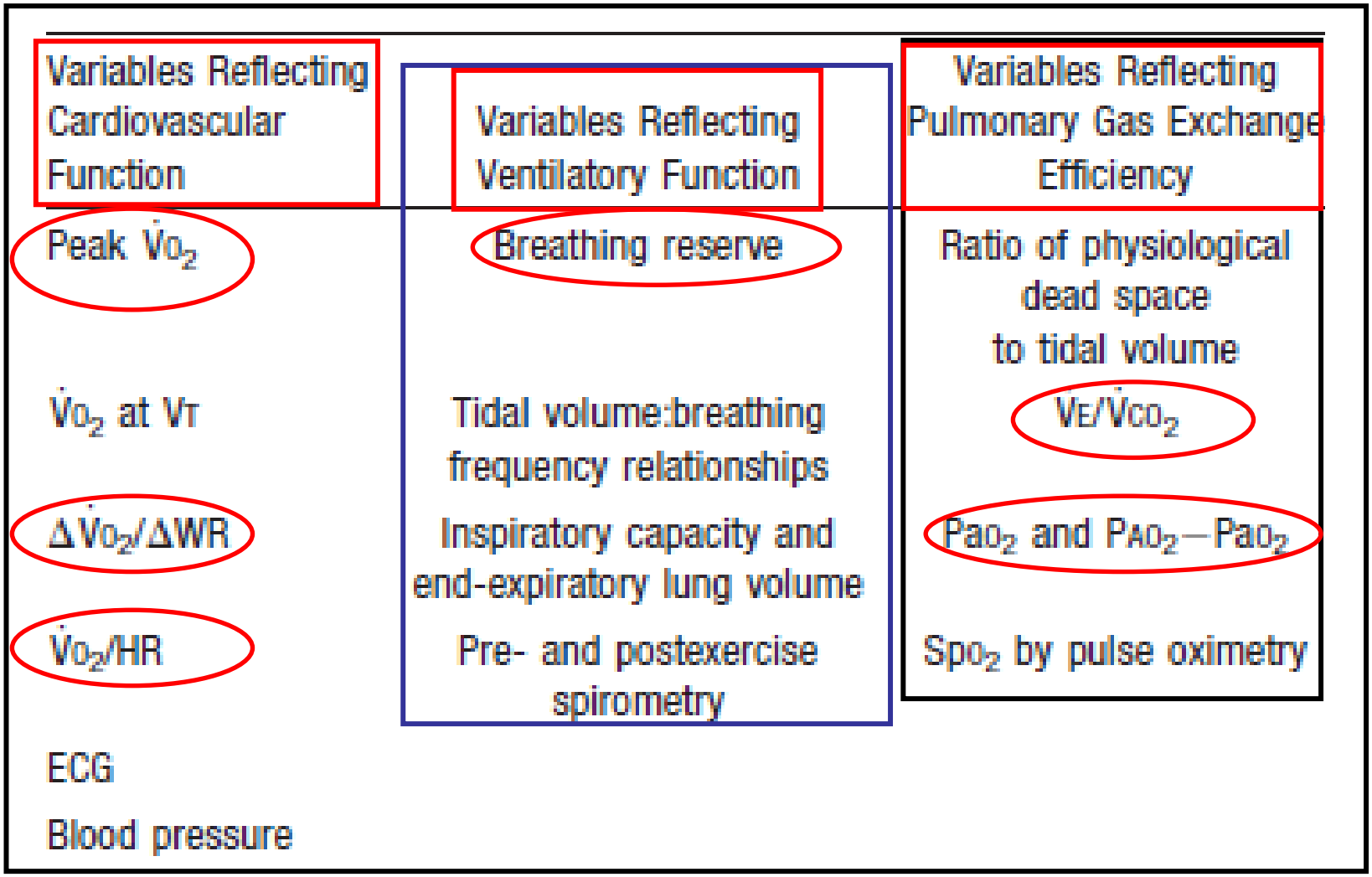
Internal respiration

External respiration



Wasserman K, et al. Principles of exercise testing and interpretation, 2004

Μεταβλητές CPET και φυσιολογικές λειτουργίες II



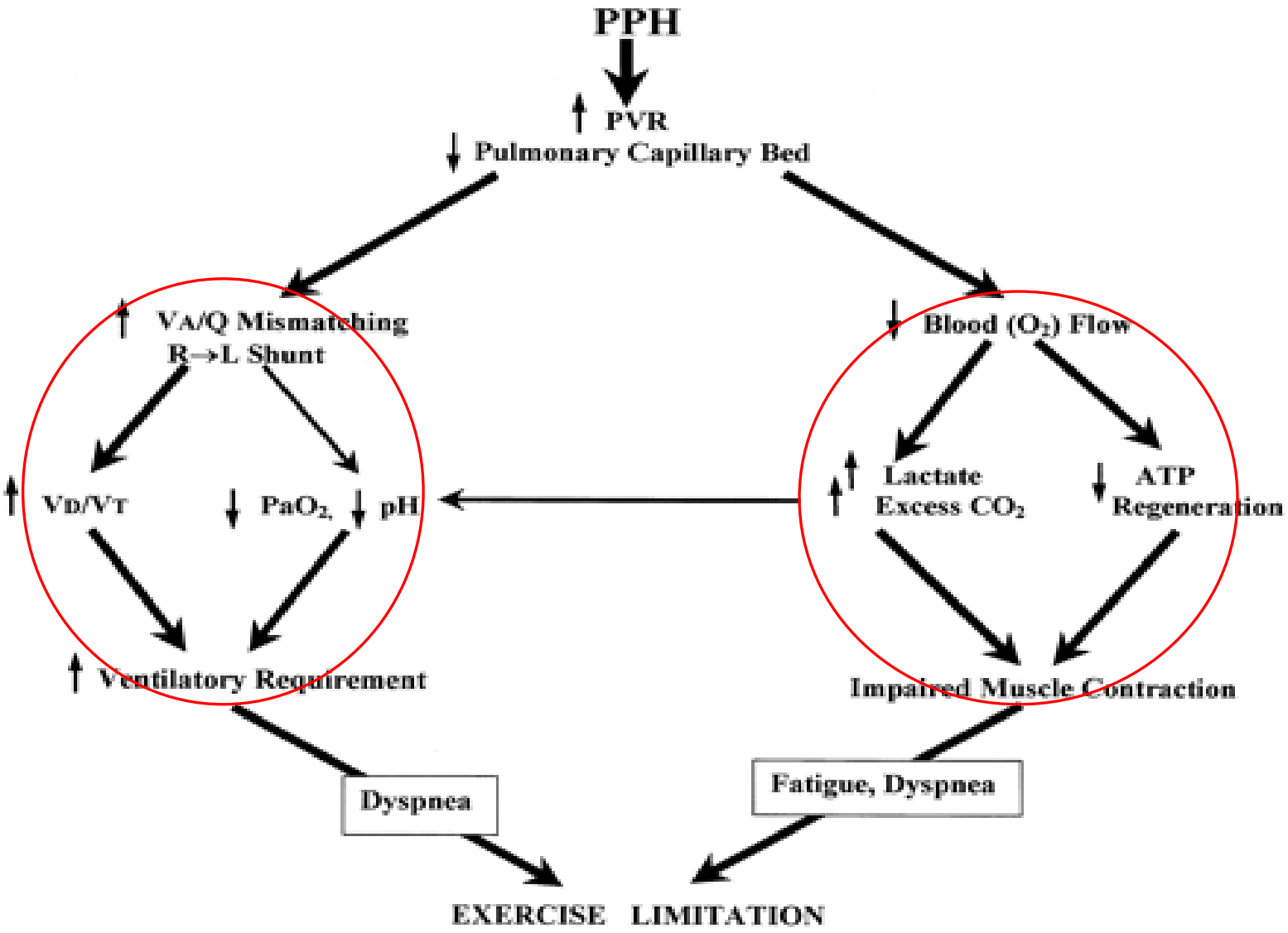
Arena and Sietsema. Circulation, 2011

Μεταβλητές CPET: φυσιολογικές τιμές

Variables	Criteria of Normality
$\dot{V}O_2$max or $\dot{V}O_2$peak	> 84% predicted
Anaerobic threshold	> 40% $\dot{V}O_2$max predicted; wide range of normal (40–80%)
Heart rate (HR)	HRmax > 90% age predicted
Heart rate reserve (HRR)	HRR < 15 beats/min
Blood pressure	< 220/90
O_2 pulse ($\dot{V}O_2$/HR)	> 80%
Ventilatory reserve (VR)	MVV − $\dot{V}E$max: > 11 L or $\dot{V}E$max/MVV × 100: < 85%. Wide normal range: 72 ± 15%
Respiratory frequency (f_R)	< 60 breaths/min
$\dot{V}E/\dot{V}CO_2$ (at AT)	< 34
V_D/V_T	< 0.28; < 0.30 for age > 40 years
Pa_{O_2}	> 80 mm Hg
$P(A-a)O_2$	< 35 mm Hg

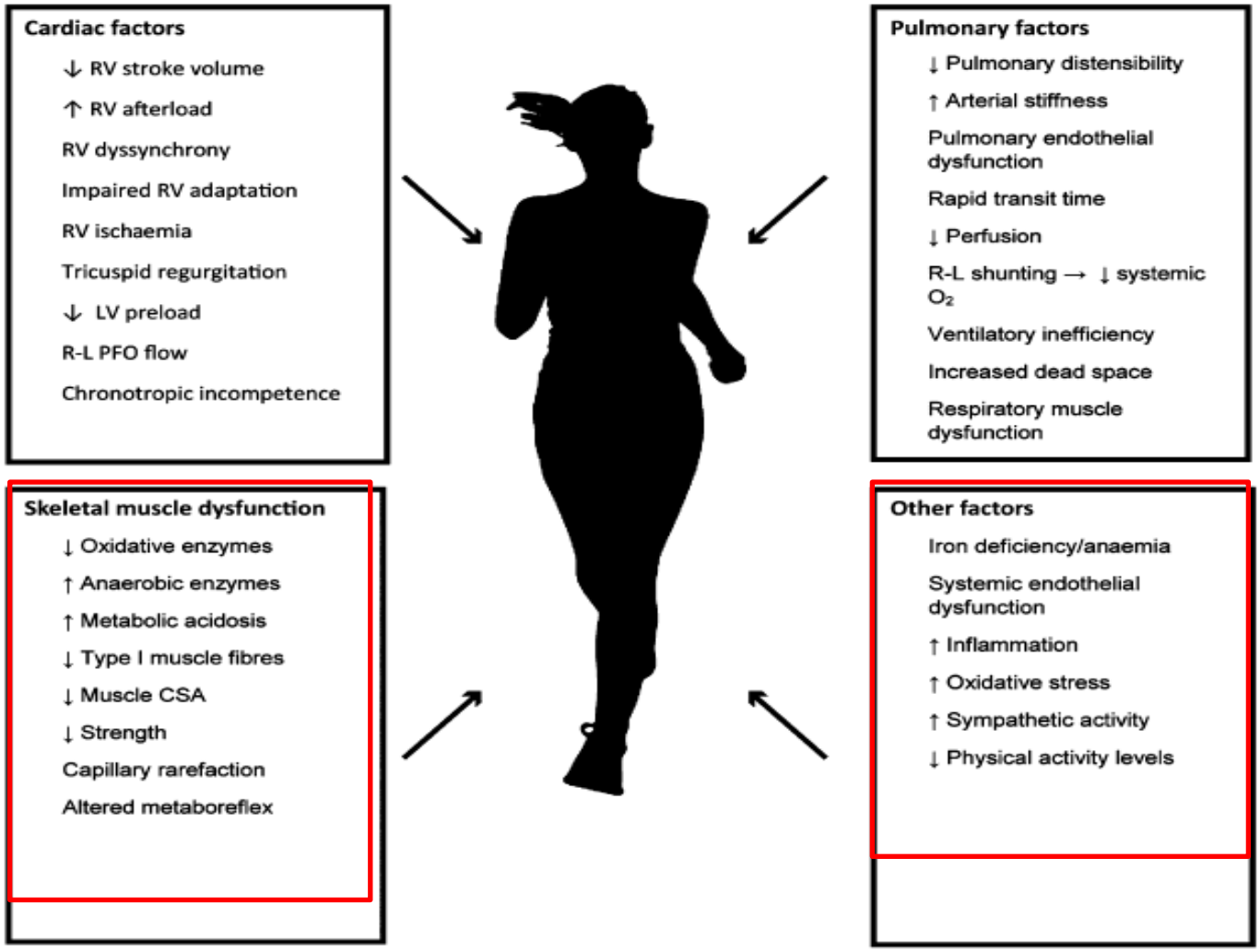
ATS/ACCP statement. Am J Respir Crit Care Med 2003

Παθοφυσιολογία της ελάπτωσης της ικανότητας για άσκηση στην ΠΥ



Sun et al. Circulation 2002

Παθολογία άσκησης σε ασθενείς με ΠΑΥ: νεότερα δεδομένα



Tran et al Respirology 2017

The role of cardiopulmonary exercise tests in pulmonary arterial hypertension

Stefania Farina[1], Michele Correale[2], Noemi Bruno[1,3], Stefania Paolillo[4], Elisabetta Salvioni[1], Roberto Badagliacca[5] and Piergiuseppe Agostoni[1,6], on behalf of the "Right and Left Heart Failure Study Group" of the Italian Society of Cardiology

Eur Respir Rev 2018; 27: 170134

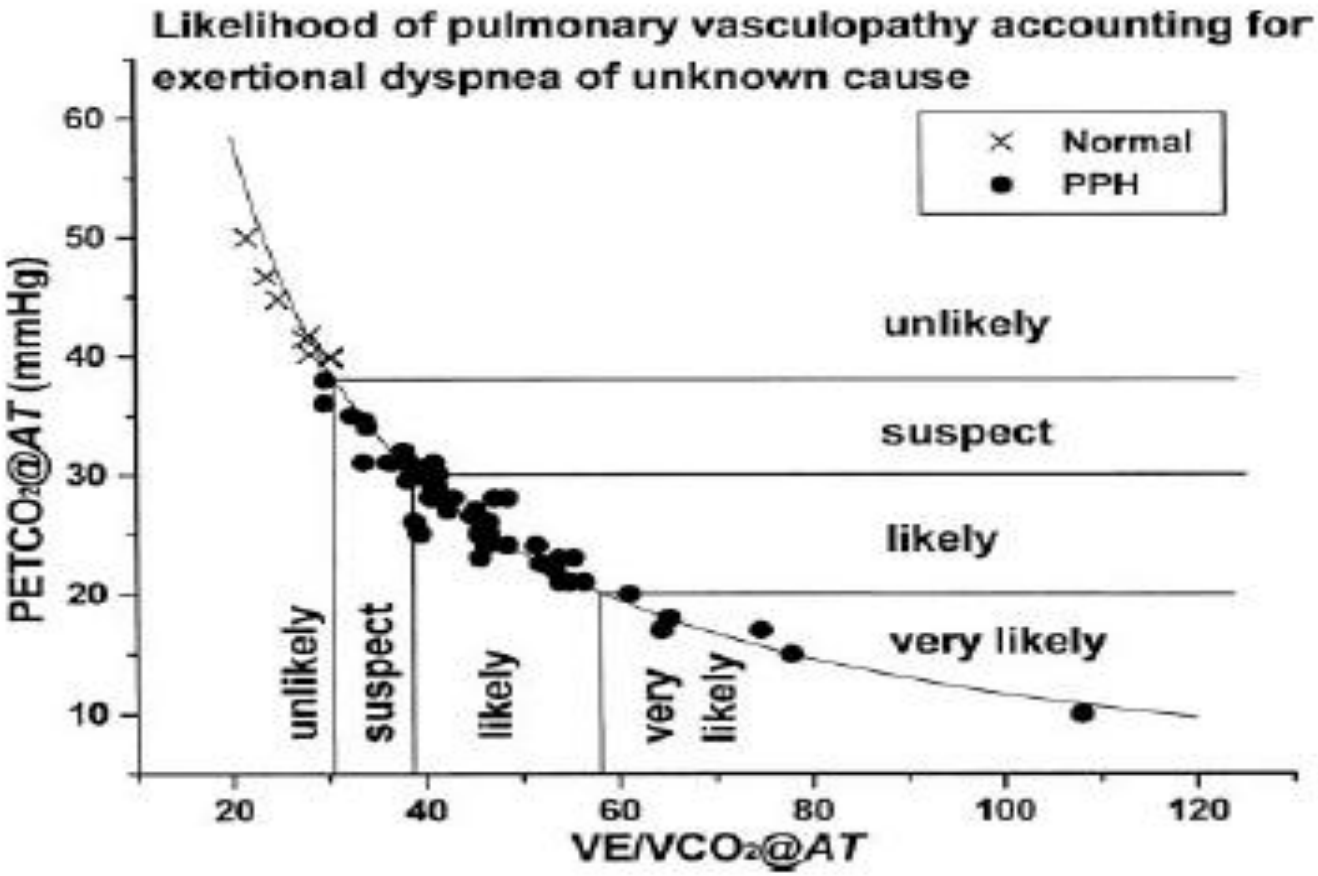
TABLE 2 Common cardiopulmonary exercise test findings in patients with pulmonary arterial hypertension

Reduced parameters	Increased parameters
Peak V'_{O_2}	V_D/V_T during exercise (>30%)
WR	P_{A-aO_2} differences during exercise (up to 45 mmHg or over)
O_2 pulse	Peak VE/VCO2
V'_{O_2}/WR	VE/VCO2@AT
P_{ETCO_2} at rest	
P_{ETCO_2} at AT	
O_2 saturation during exercise (drop >3% without P_{aCO_2} rise)	

Η CPET στη διάγνωση της ΠΥ

End-tidal P_{CO_2} Abnormality and Exercise Limitation in Patients With Primary Pulmonary Hypertension*

Yuji Yasunobu, MD; Ronald J. Oudiz, MD; Xing-Guo Sun, MD; James E. Hansen, MD, FCCP; and Karlman Wasserman, MD, PhD, FCCP



52 PPH patients vs. 9 controls

Yasunobu et al. CHEST 2005

End-tidal P_{CO_2} Abnormality and Exercise Limitation in Patients With Primary Pulmonary Hypertension*

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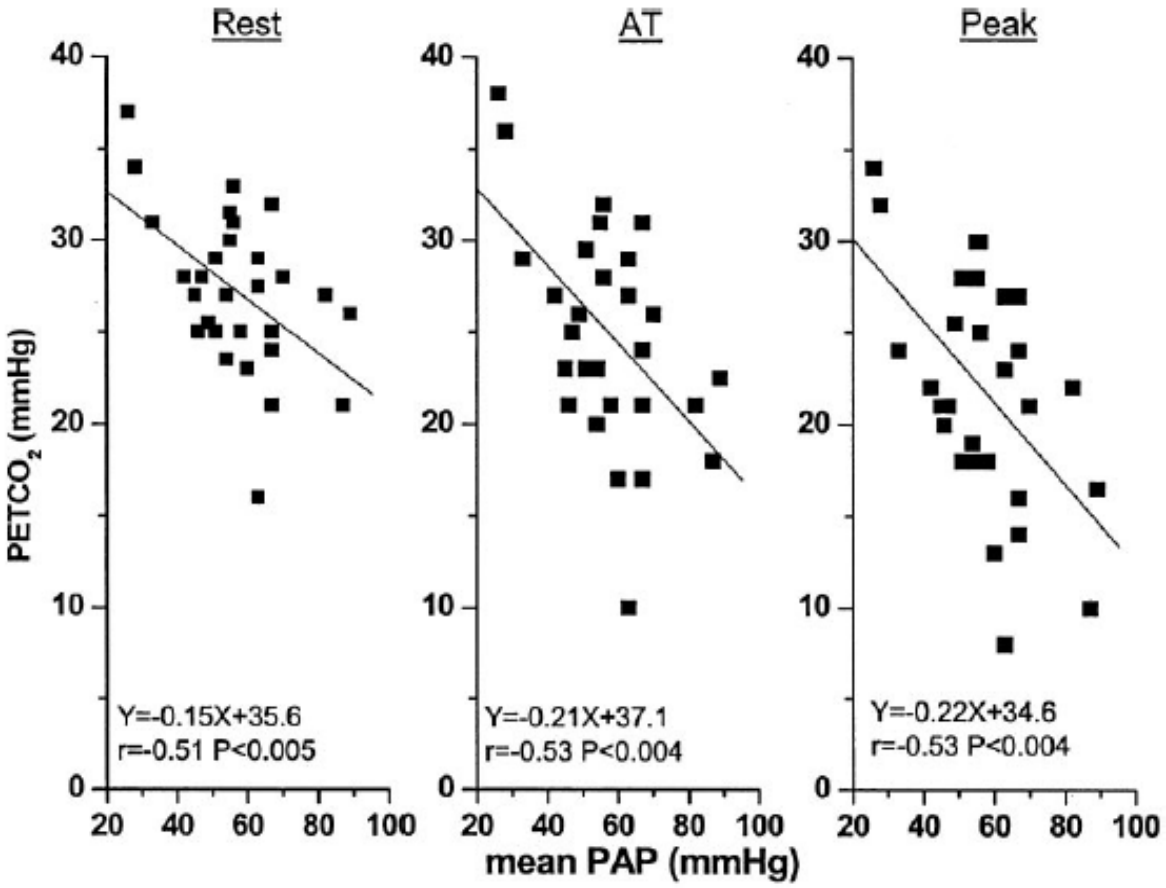
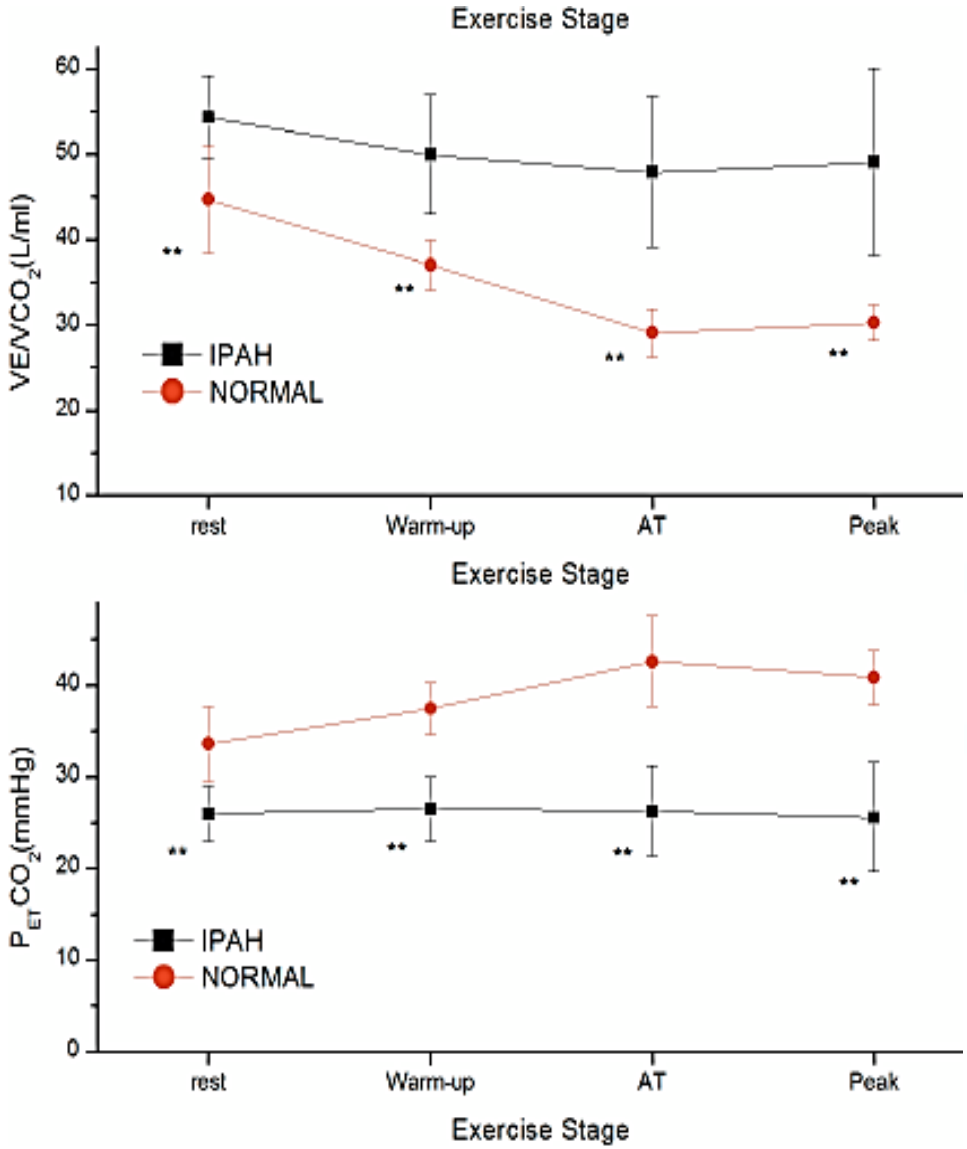


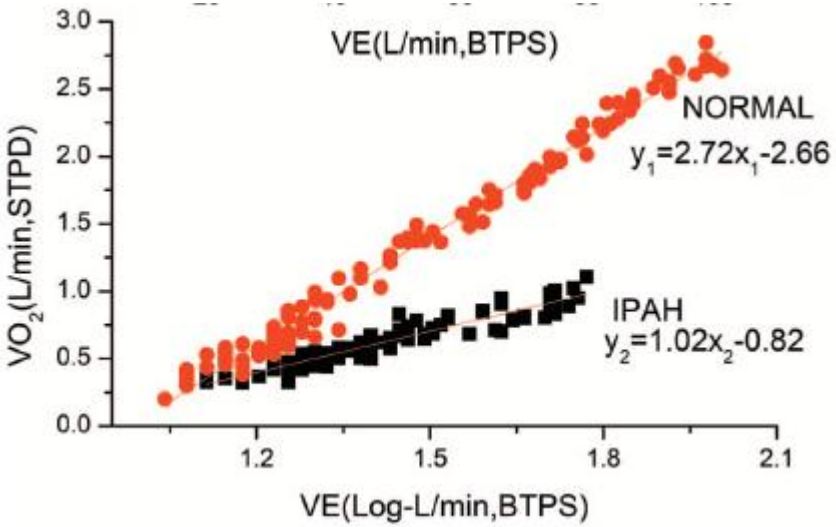
29 PPH patients with RHC and CPET

Yasunobu et al, CHEST 2005

Usefulness of Decrease in Oxygen Uptake Efficiency to Identify Gas Exchange Abnormality in Patients with Idiopathic Pulmonary Arterial Hypertension



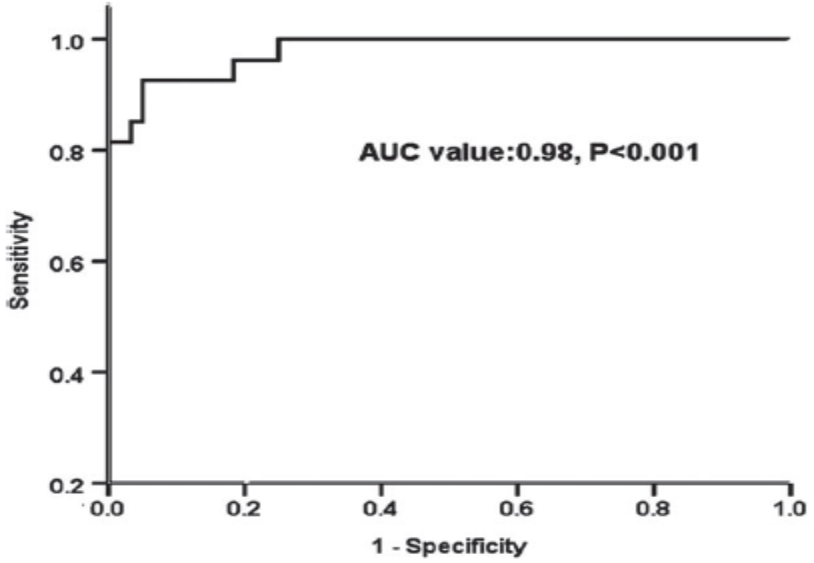
32 IPAH patients vs 16 controls (all underwent maximal CPET)



Tan et al. PLOS One, 2014

Cardiopulmonary exercise testing improves diagnostic specificity in patients with echocardiography-suspected pulmonary hypertension

	OR (95% CI)	*P* Value	β-Coefficient	OR (95% CI)	*P* Value
Age	0.98 (0.95-1.00)	0.08	−0.09	0.92 (0.85-0.98)	0.012
Sex	2.15 (0.71-6.5)	0.17			
BMI	0.78 (0.66-0.93)	0.006	−0.75	0.47 (0.26-0.85)	0.012
CPET parameters					
VO_2 peak, mL/min/kg	0.86 (0.77-0.95)	0.005			
AT, mL/min/kg	0.75 (0.61-0.93)	0.008	−0.35	0.71 (0.52-0.96)	0.03
$P_{ET}CO_2$, mm Hg	0.72 (0.62-0.83)	<0.001			
Lowest VE/VCO_2	1.37 (1.17-1.61)	<0.001			
VE/VCO_2 slope	1.37 (1.17-1.59)	<0.001	0.56	1.76 (1.24-2.48)	0.001



88 pts with potential PH based on Echo:
27 PH (PAH or CTEPH), **61 non-PH**

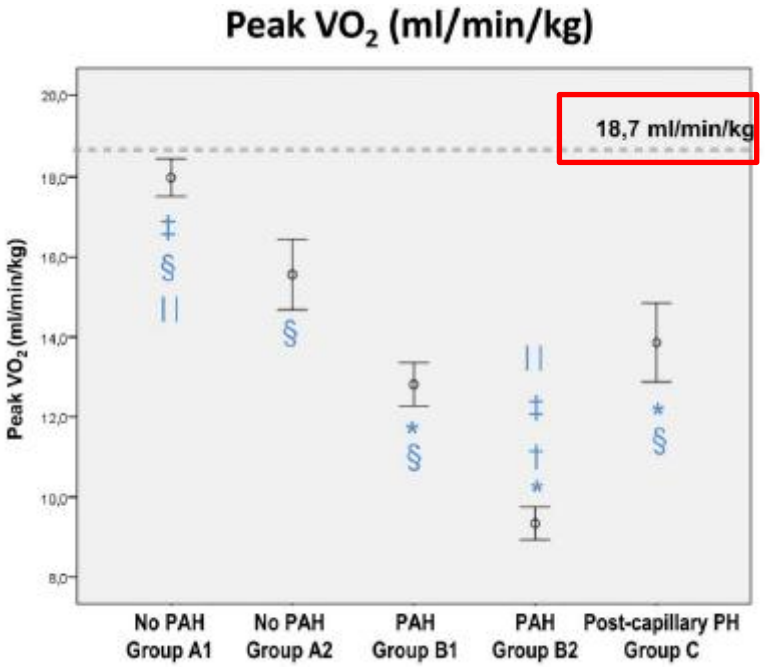
Zhao et al. Clin Cardiol 2016

Cardiopulmonary exercise testing for detecting pulmonary arterial hypertension in systemic sclerosis

Daniel Dumitrescu,[1,2] Christian Nagel,[3,4] Gabor Kovacs,[5] Tom Bollmann,[6] Michael Halank,[7] Jörg Winkler,[8] Martin Hellmich,[9] Ekkehard Grünig,[3] Horst Olschewski,[5] Ralf Ewert,[6] Stephan Rosenkranz[1,2]

Table 2 Differences in key gas exchange parameters between patients without PAH (group A), patients with PAH (group B) and patients with postcapillary PAH (group C)

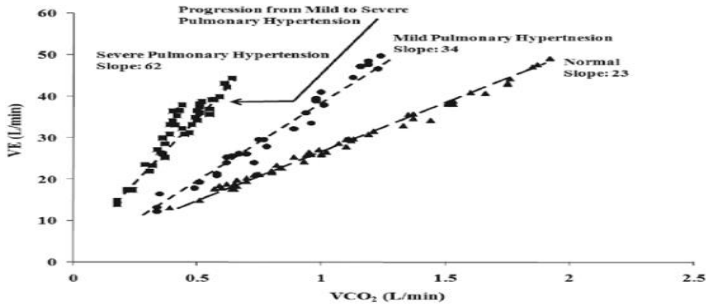
Group	Peak VO_2 (mL/min/kg)	*AT* (mL/min/kg)	Peak O_2 pulse (mL/beat)	VE/VCO_2@*AT* (no unit)	Nadir VE/VCO_2 (no unit)	$P_{ET}CO_2$ @*AT* (mm Hg)	Peak $P_{ET}CO_2$ (mm Hg)	$P_{ET}CO_2$ difference peak–start (mm Hg)
(1) No PAH	17.5±4.7	11.0±2.3	9.0±2.2	32.4±5.4	30.9±5.0	35.0±4.7	36.2±4.7	2.8±3.0
(2) PAH	11.0±2.9*	8.0±2.2*	6.8±1.9*	44.7±12.2*	43.0±10.5*	26.8±7.1*	27.7±6.7*	−0.5±2.7*
(3) Postcapillary PH	13.9±3.1†‡	10.1±1.9†	7.7±1.8	36.5±5.4†‡	35.5±5.6†‡	32.6±6.6†	33.3±5.7†	1.8±3.2‡



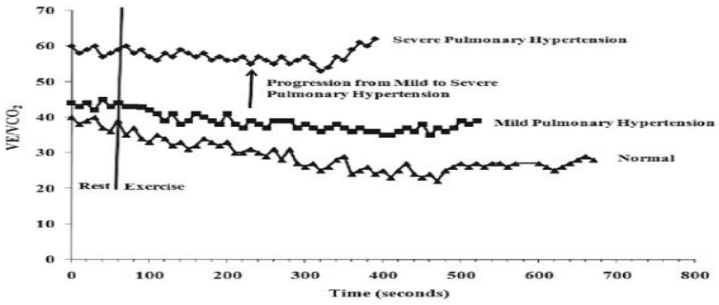
173 consecutive SSc patients, who all underwent RHC and CPET

Heart 2017;**103**:774–782.

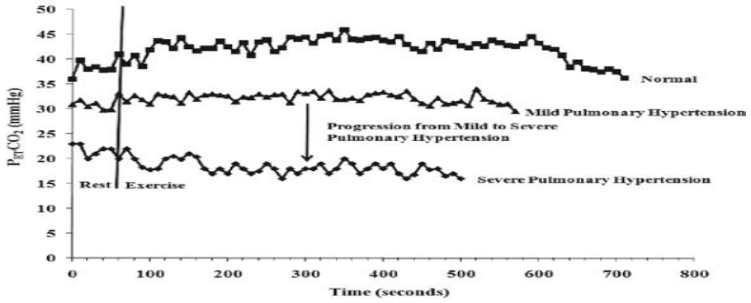
Cardiopulmonary exercise testing in patients with pulmonary arterial hypertension: An evidence-based review



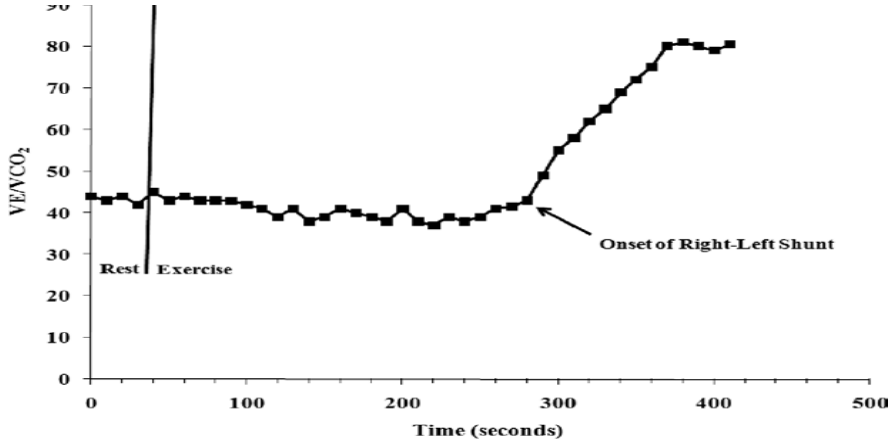
(a) VE/VCO_2 slope



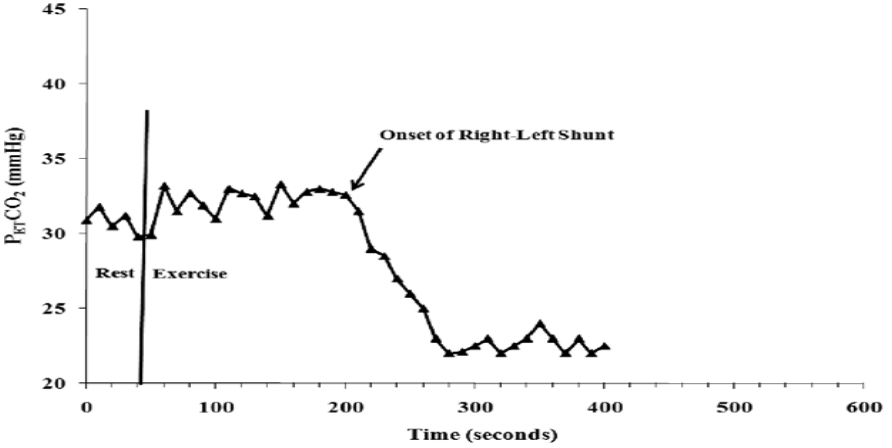
(b) VE/VCO_2 ratio



(c) $P_{ET}CO_2$



(a) VE/VCO_2 ratio response



(b) $P_{ET}CO_2$ response

Arena et al, J Heart Lung Transplant 2010

Η CPET στην προγνωστική εκτίμηση των ασθενών με ΠΑΥ

Σημαντικές παράμετροι για την βαρύτητα και την πρόγνωση της PAH

Better prognosis	Determinants of prognosis	Worse prognosis
No	Clinical evidence of RV failure	Yes
Slow	Rate of progression of symptoms	Rapid
No	Syncope	Yes
I, II	WHO-FC	IV
Longer (>500 m)[a]	6MWT	Shorter (<300 m)
Peak O_2 consumption >15 mL/min/kg	Cardio-pulmonary exercise testing	Peak O_2 consumption <12 mL/min/kg
Normal or near-normal	BNP/NT-proBNP plasma levels	Very elevated and rising
No pericardial effusion TAPSE[b] >2.0 cm	Echocardiographic findings[b]	Pericardial effusion TAPSE[b] <1.5 cm
RAP <8 mmHg and CI ≥2.5 L/min/m^2	Haemodynamics	RAP >15 mmHg or CI ≤2.0 L/min/m^2

McLaughlin et al. J Am Coll Cardiol. 2009

Σημαντικές παράμετροι για την βαρύτητα και την πρόγνωση της ΠΑΥ

Table 13 Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% pred.) VE/VCO_2 slope ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/l	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal, pericardial effusion	RA area >26 cm^2 Pericardial effusion
Haemodynamics	RAP <8 mmHg CI ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 l/min/m^2 SvO_2 <60%

ESC/ERS guidelines for the diagnosis and treatment of PH, Eur Heart J 2015

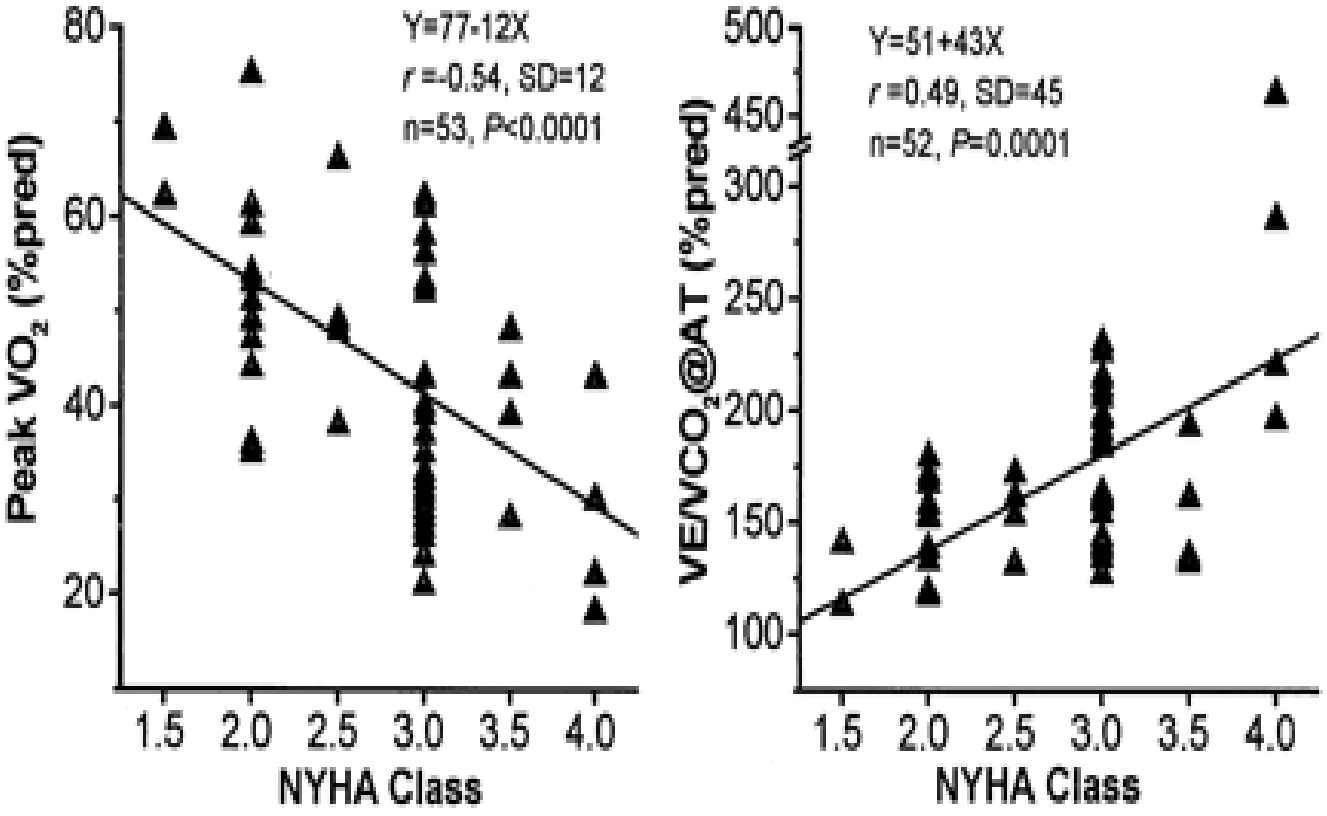
Χρήσιμοι παράμετροι της CPET για τον καθορισμό της βαρύτητας της ΠΑΥ

Peak VO_2 % predicted
Peak VO_2 (ml/kg/min)
AT
Peak O_2 pulse
PET_{CO2} at rest
PET_{CO2} at AT
PET_{CO2} during recovery
VE/VCO_2 slope
$\Delta VO_2/\Delta$work slope
Peak heart rate
Δ O_2 saturation (between peak exercise and rest)

Paollilo et al. Eur J Prev Cardiol 2011

Exercise Pathophysiology in Patients With Primary Pulmonary Hypertension

Xing-Guo Sun, MD; James E. Hansen, MD; Ronald J. Oudiz, MD; Karlman Wasserman, MD, PhD



53 PPH patients with RHC and cycle CPET

Circulation 2002

End-tidal P_{CO_2} Abnormality and Exercise Limitation in Patients With Primary Pulmonary Hypertension*

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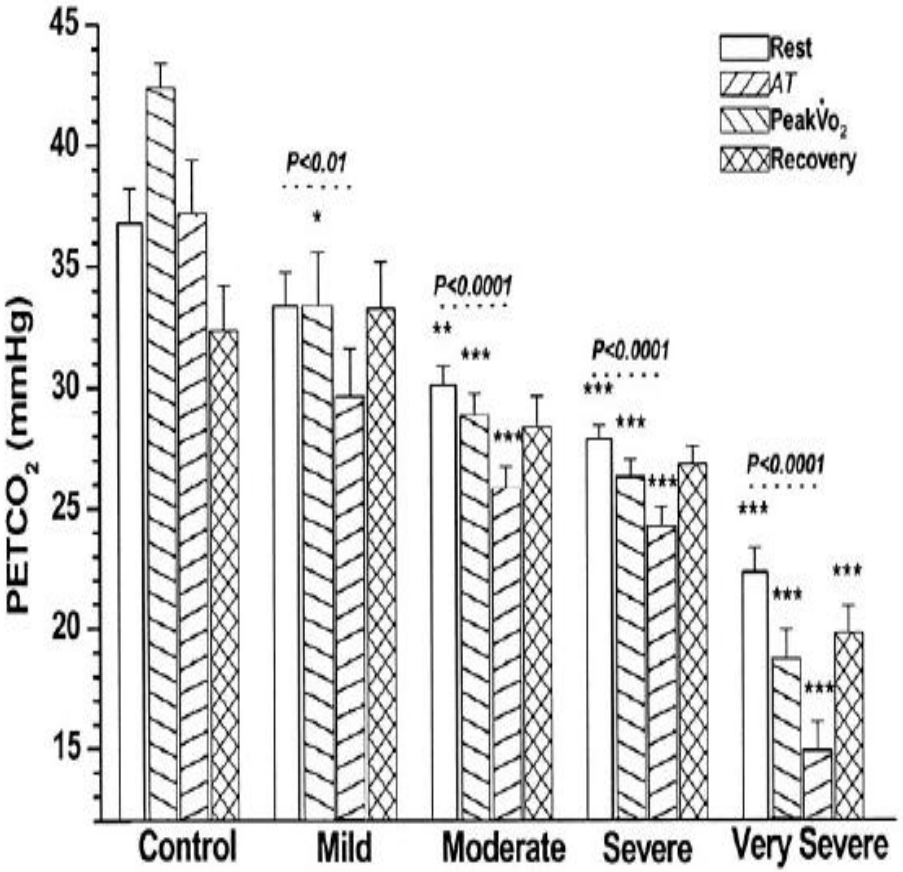
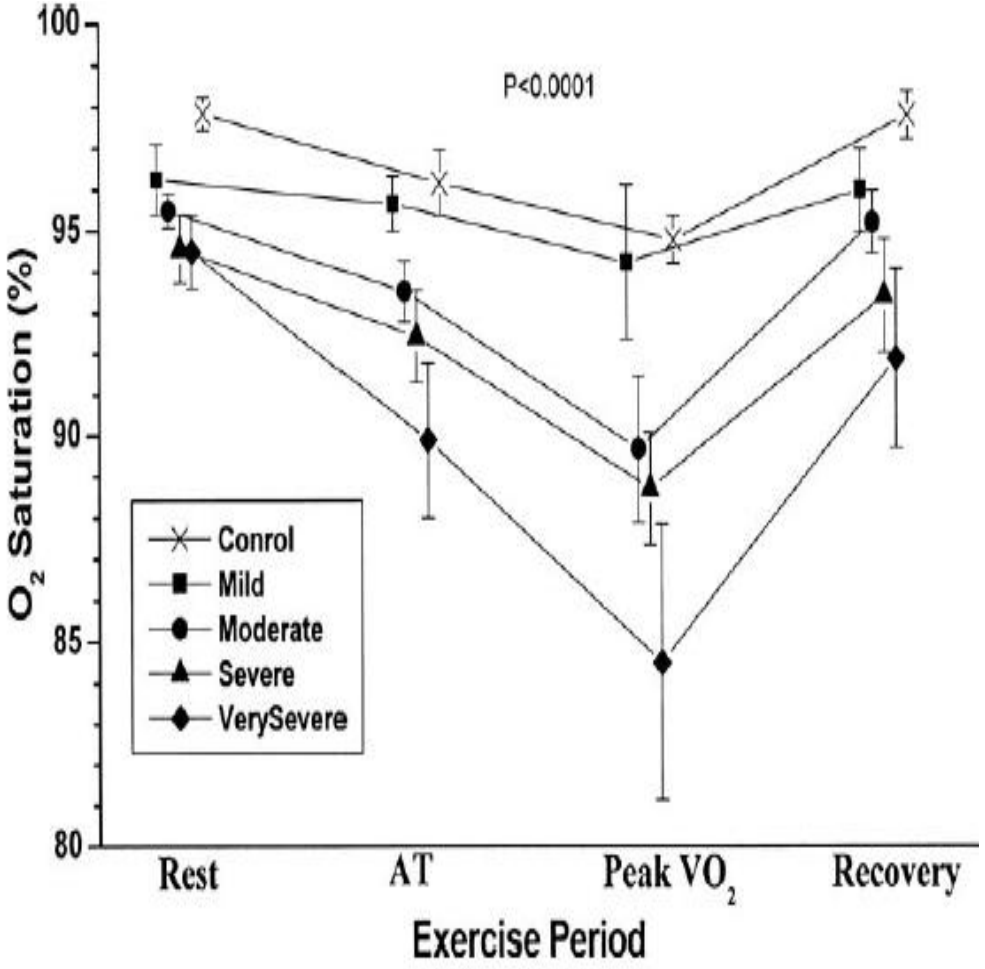


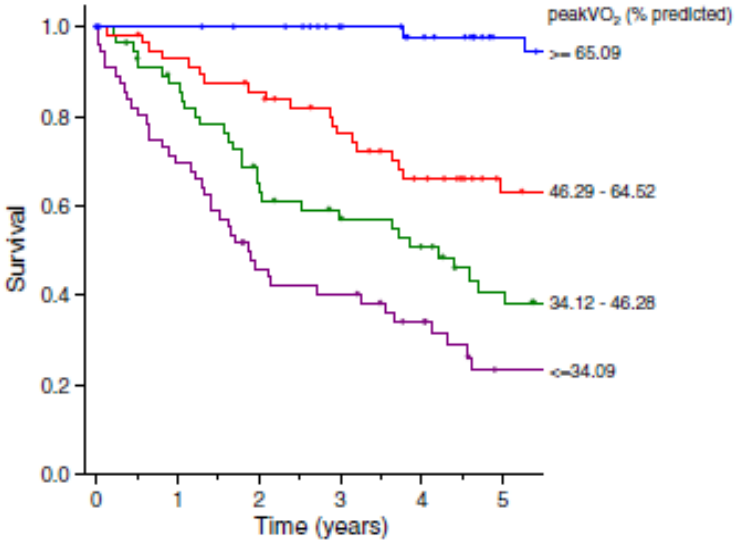


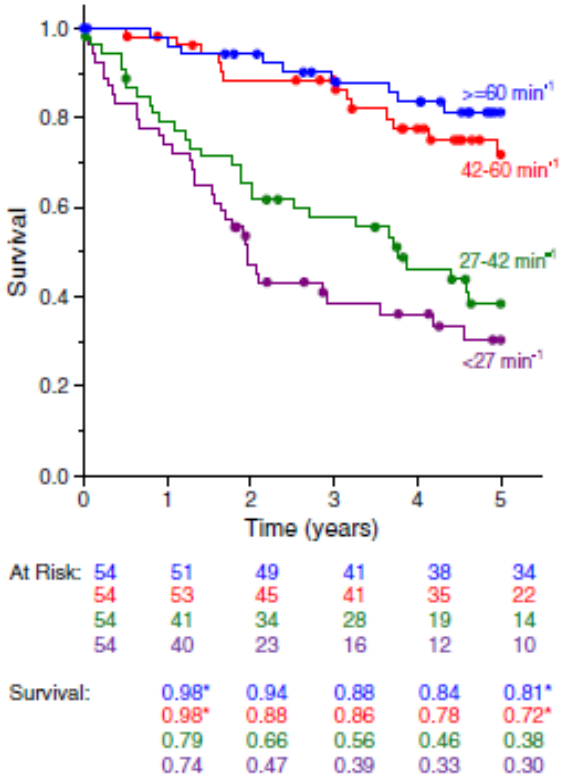
52 PPH patients vs 9 controls

CHEST 2005

Incremental prognostic value of cardiopulmonary exercise testing and resting haemodynamics in pulmonary arterial hypertension

Roland Wensel [a,b,*], Darrel P. Francis [a], F. Joachim Meyer [c], Christian F. Opitz [d], Leonhard Bruch [e], Michael Halank [f], Jörg Winkler [g], Hans-Jürgen Seyfarth [h], Sven Gläser [i], Friedrich Blumberg [j], Anne Obst Michael Dandel [k], Roland Hetzer [k], Ralf Ewert [i]





226 pts with idiopathic or familiar PAH

International journal of cardiology 2013

Ventilatory efficiency testing as prognostic value in patients with pulmonary hypertension

Martin Schwaiblmair*, Christian Faul, Wolfgang von Scheidt and Thomas M Berghaus

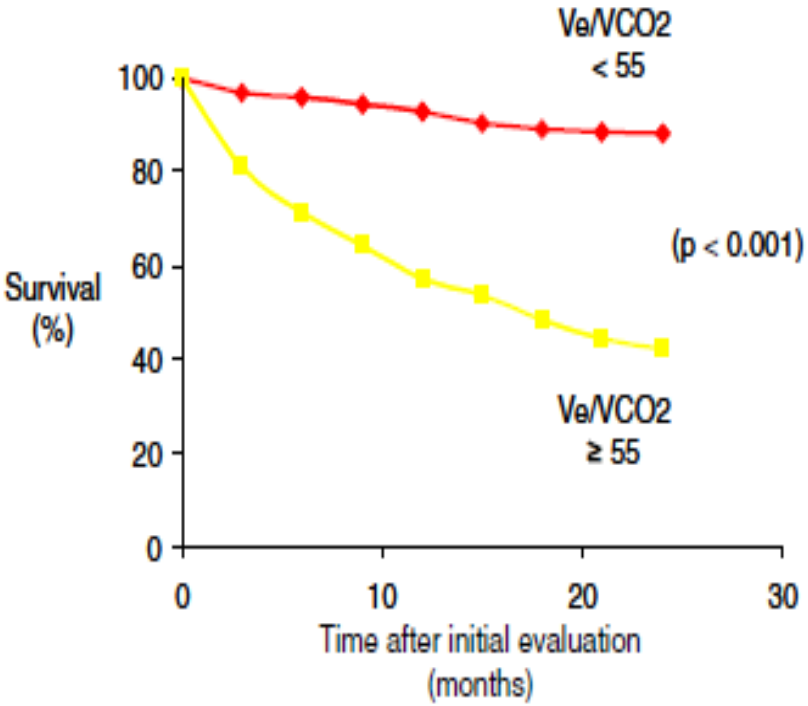


Figure 2 Kaplan-Meier plot relating survival to Ve/VCO2 at anaerobic threshold.

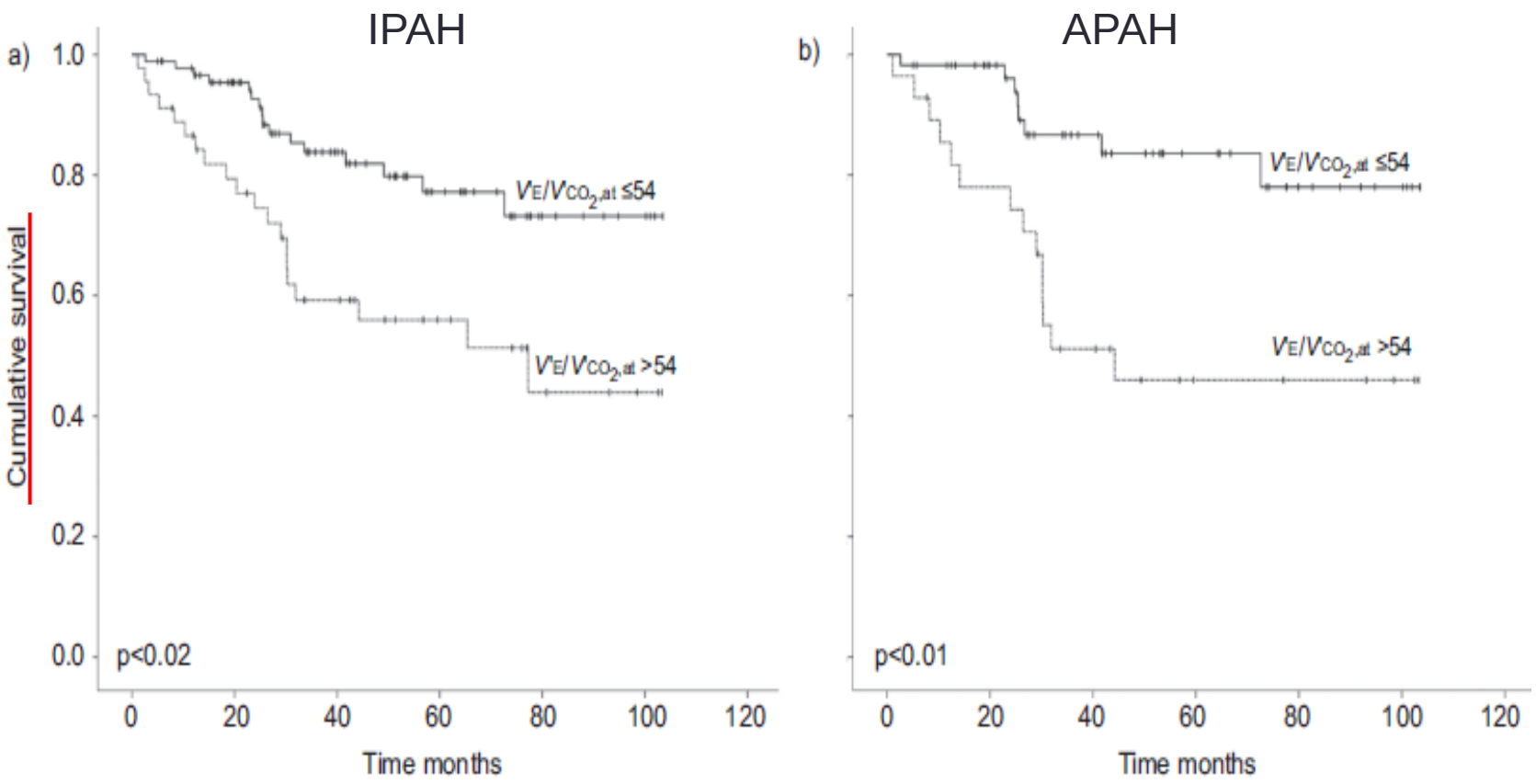
	Survivors (n = 87)	Nonsurvivors (n = 29)	p
PAP, mmHg	42.0 ± 2.5	39.6 ± 2.6	ns
CI, L*min-1*m-2	2.30 ± 0.12	2.31 ± 0.21	ns
PVR, dynes * s * cm-5	633.8 ± 68.2	594.1 ± 76.6	ns
RAP, mmHg	7.22 ± 0.79	8.55 ± 1.88	ns
W, watts	67.7 ± 8.0	35.7 ± 1.5	0.023
VO2, ml/min/kg	14.6 ± 1.4	10.9 ± 1.0	ns
AT, ml/min/kg	9.65 ± 0.87	7.09 ± 1.07	ns
O2 pulse, ml/min/beat	9.80 ± 0.81	7.79 ± 0.64	ns
Ve/VO2 - AT	42.1 ± 2.1	56.9 ± 2.6	0.001
Ve/VCO2 - AT	47.5 ± 2.2	64.4 ± 2.3	< 0.001
AaDO2 – peak exercise, mmHg	52.8 ± 2.8	67.5 ± 4.2	0.009
a-et CO2, mmHg	6.8 ± 0.8	10.5 ± 1.1	0.014
Ve/VCO2 slope	47.0 ± 3.2	65.4 ± 7.5	0.014

Survival of **86 PPH** and **31 CTPH** patients **at 24 months**

BMC Pulmonary Medicine 2012

Exercise testing to predict outcome in idiopathic *versus* associated pulmonary arterial hypertension

Gaël Deboeck*, Cristina Scoditti#, Sandrine Huez*, Jean-Luc Vachiéry*, Michel Lamotte*, Linda Sharples¶, Christian Melot+ and Robert Naeije§

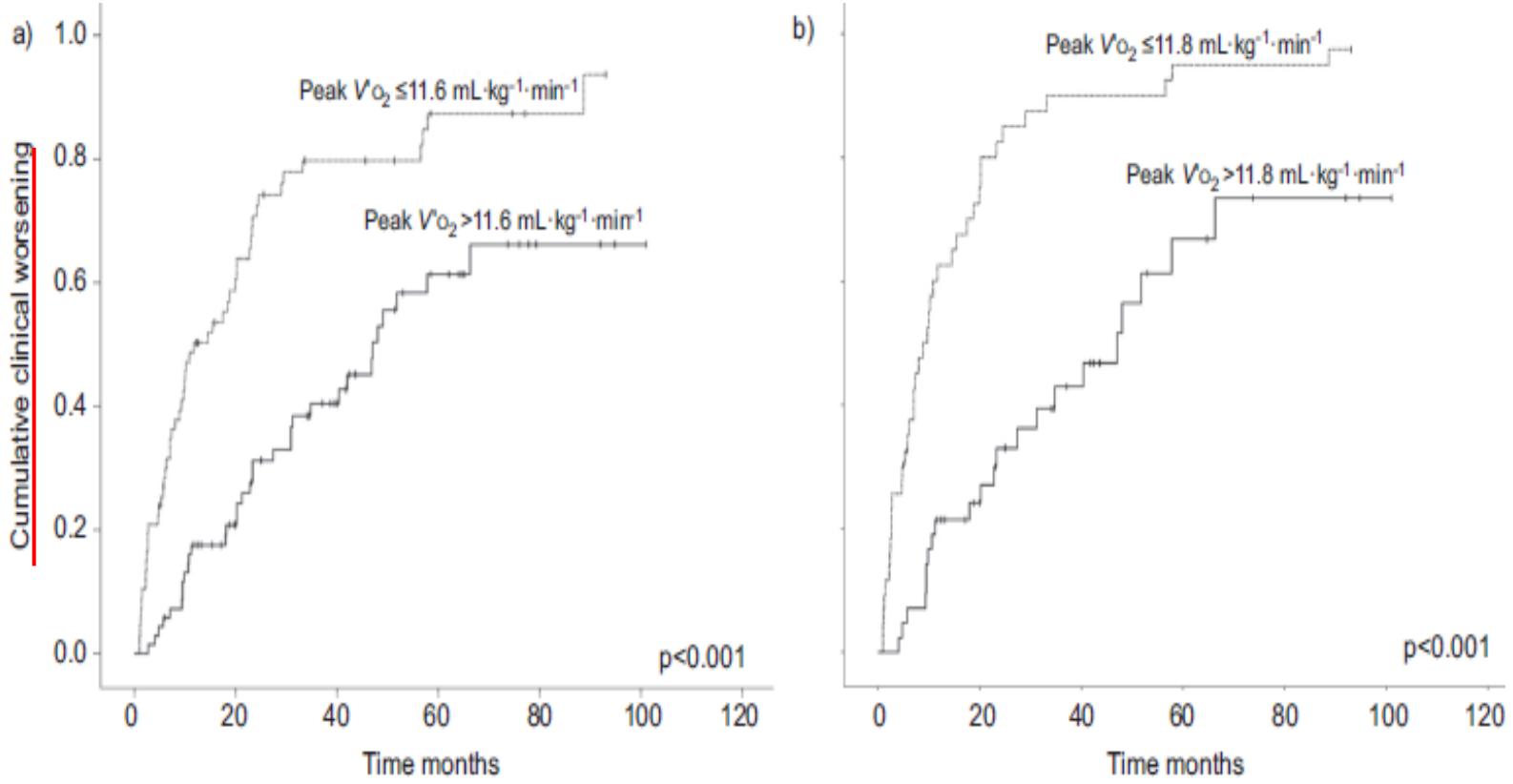


a) **86 IPAH** patients and b) **50 APAH** patients

Eur Respir J 2012

Exercise testing to predict outcome in idiopathic *versus* associated pulmonary arterial hypertension

Gaël Deboeck*, Cristina Scoditti[#], Sandrine Huez*, Jean-Luc Vachiéry*, Michel Lamotte*, Linda Sharples[¶], Christian Melot[+] and Robert Naeije[§]

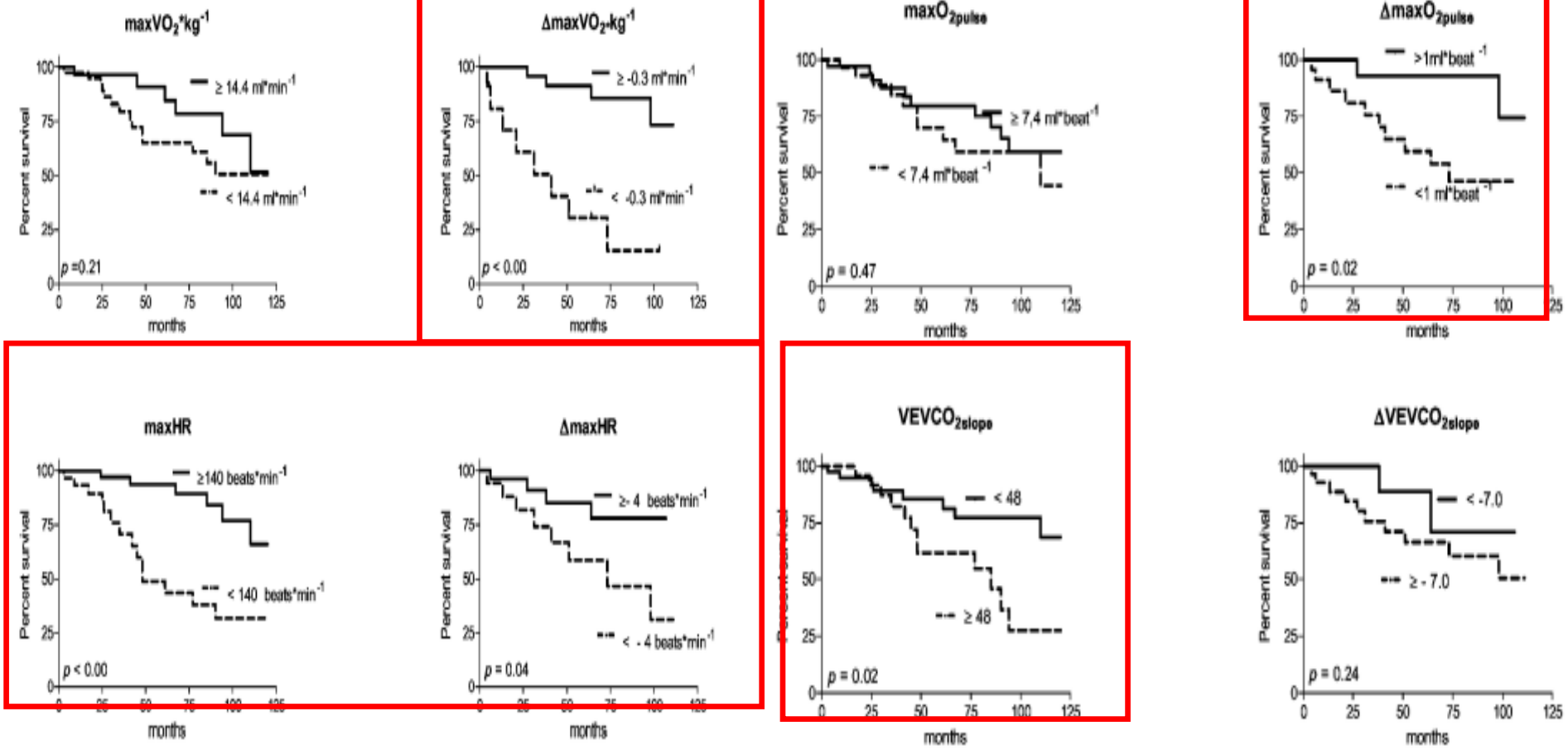


a) **86 IPAH** patients and b) **50 APAH** patients

Eur Respir J 2012

Prognostic Relevance of Changes in Exercise Test Variables in Pulmonary Arterial Hypertension

baseline **change** **baseline** **change**



65 IPAH at baseline **and 43 of them** after **13 months** median follow-up

Groepenhoff et al. PLOS ONE 2013

Παρακολούθηση ασθενών με ΠΑΥ

Table 14 Suggested assessment and timing for the follow-up of patients with pulmonary arterial hypertension

	At baseline	Every 3–6 months[a]	Every 6–12 months[a]	3–6 months after changes in therapy[a]	In case of clinical worsening
Medical assessment and determination of functional class	+	+	+	+	+
ECG	+	+	+	+	+
6MWT/Borg dyspnoea score	+	+	+	+	+
CPET	+		+		+[e]
Echo	+		+	+	+
Basic lab[b]	+	+	+	+	+
Extended lab[c]	+		+		+
Blood gas analysis[d]	+		+	+	+
Right heart catheterization	+		+[f]	+[e]	+[e]

ESC/ERS guidelines for the diagnosis and treatment of PH, Eur Heart J 2015

Ο ρόλος της CPET στην αξιολόγηση της **ανταπόκρισης στη θεραπεία** ασθενών με ΠΑΥ

Treatment Goals of Pulmonary Hypertension

Journal of the American College of Cardiology
Vol. 62, No. 25, Suppl D, 2013

Table 1 Variables Used in Clinical Practice to Determine Response to Therapy and Prognosis in Patients With PAH

Functional class
I or II
Echocardiography/CMR
Normal/near-normal RV size and function
Hemodynamics
Normalization of RV function (RAP $<$8 mm Hg and CI $>$2.5 to 3.0 l/min/m^2)
6-min walk distance
$>$380 to 440 m; may not be aggressive enough in young individuals
Cardiopulmonary exercise testing
Peak VO_2 $>$15 ml/min/kg and $EqCO_2$ $<$45 l/min/l/min
B-type natriuretic peptide level
Normal

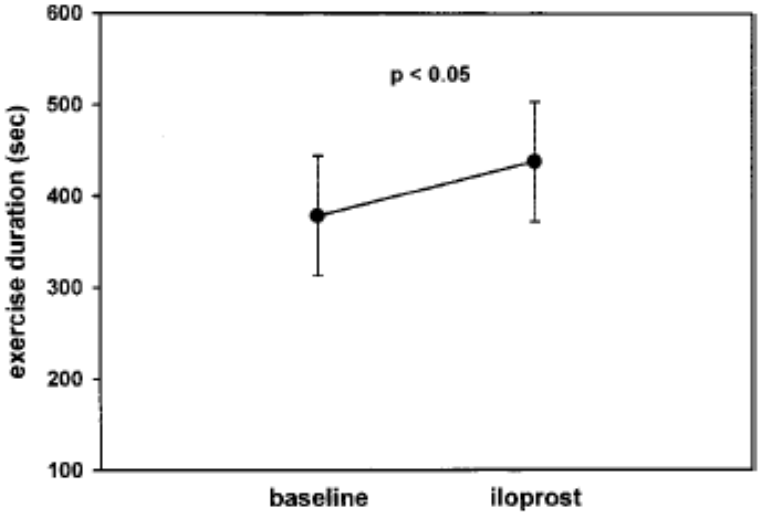
CI = cardiac index; CMR = cardiac magnetic resonance; $EqCO_2$ = ventilatory equivalent for carbon dioxide; PAH = pulmonary arterial hypertension; RAP = right atrial pressure; RV = right ventricular; VO_2 = peak oxygen consumption.

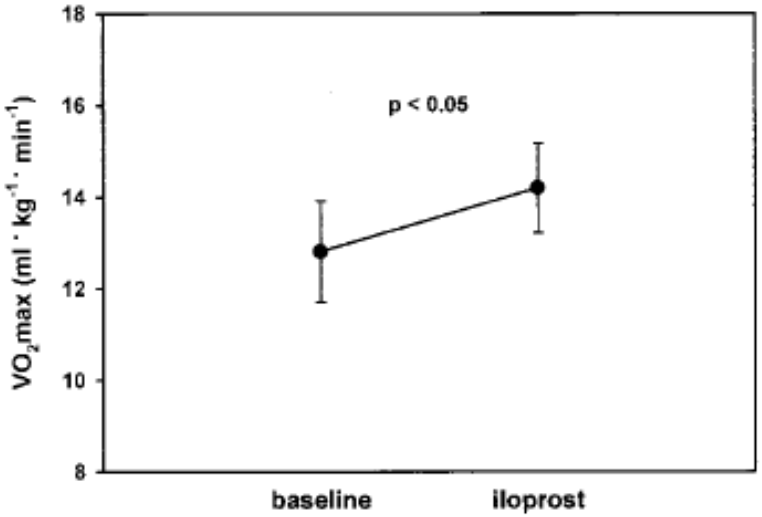
McLaughlin et al, JACC 2013

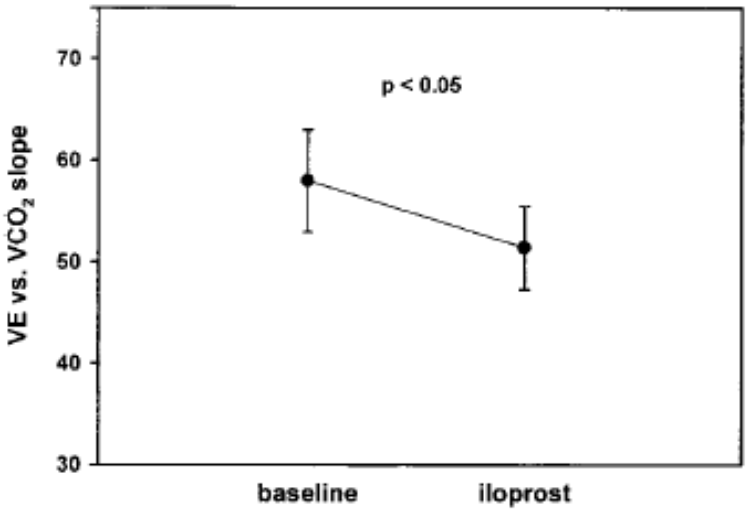
Effects of Iloprost Inhalation on Exercise Capacity and Ventilatory Efficiency in Patients With Primary Pulmonary Hypertension

Roland Wensel, Christian F. Opitz, Ralf Ewert, Leonhard Bruch and Franz X. Kleber

Circulation 2000;101;2388-2392





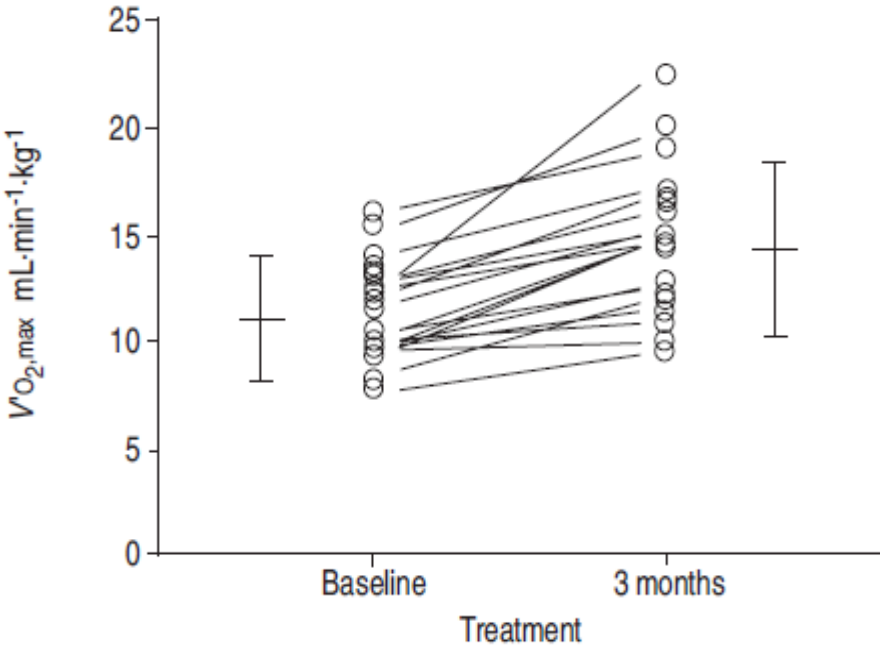


11 patients with PPH, before and after the inhalation **of 17mg of iloprost.**

Bosentan treatment in patients with primary pulmonary hypertension receiving nonparenteral prostanoids

M.M. Hoeper, N. Taha, A. Bekjarova, R. Gatzke, E. Spiekerkoetter

	Baseline	3 months	p-value
Work rate W	43±20	63±17	<0.0001
$f_{c,max}$ beats·min^{-1}	133±16	139±16	0.03
$V'_{O_2,max}$ mL·min^{-1}·kg^{-1}	11.0±2.3	13.8±3.6	<0.0001
AT mL·min^{-1}·kg^{-1}	10.2±2.2	11.7±2.9	0.007
Peak oxygen pulse mL·beat^{-1}	5.7±1.5	6.8±2.0	0.0004
$V'_{E,max}$ L·min^{-1}	45.8±14.5	57.6±15.0	<0.0001
V'_E/V'_{CO_2} at AT#	52.3±14.9	44.9±10.3	0.004
Peak SBP mmHg¶	120±17	139±21	<0.0001

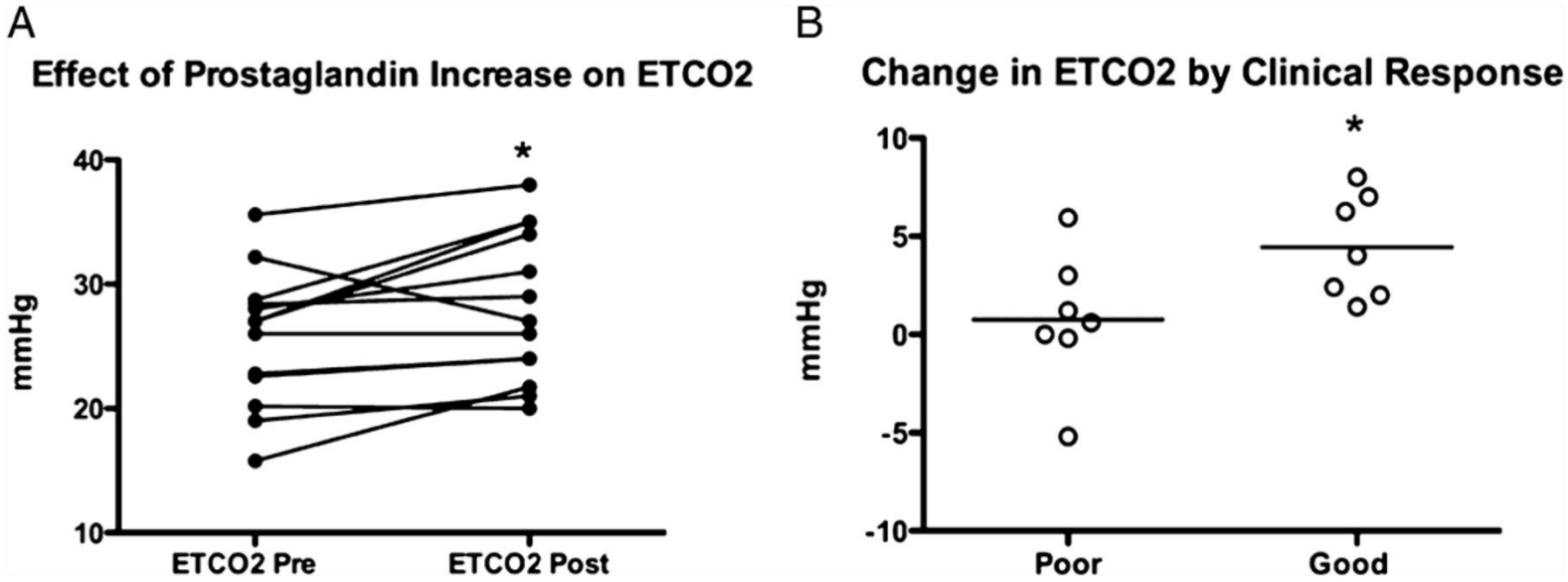


20 patients with PPH under inhaled iloprost or oral beraprost alone (baseline) and **3 months after bosentan add-on**.

Eur Respir J 2003

End Tidal CO_2 Tension

Pulmonary Arterial Hypertension vs Pulmonary Venous Hypertension and Response to Treatment

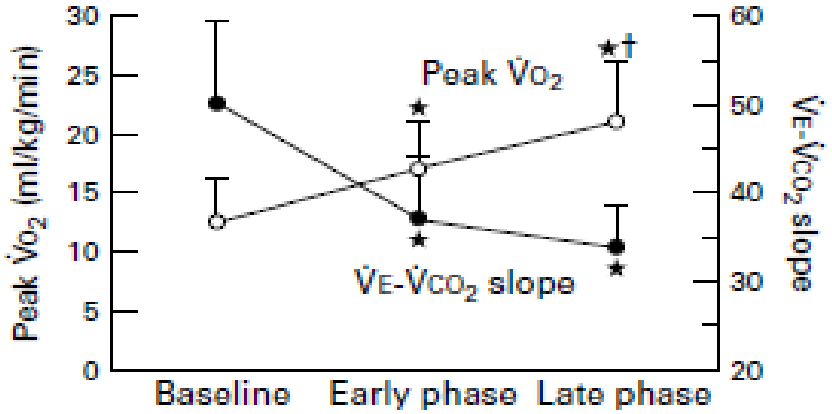


14 PAH patients on prostaglandin,
11 months median follow-up

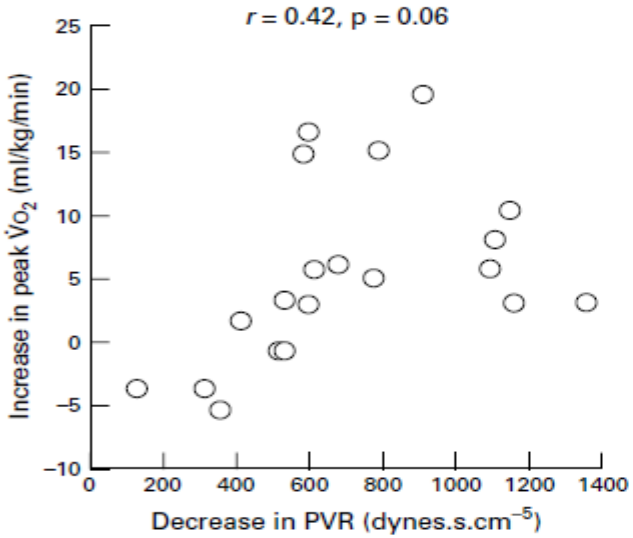
Hemnes et al, CHEST 2011

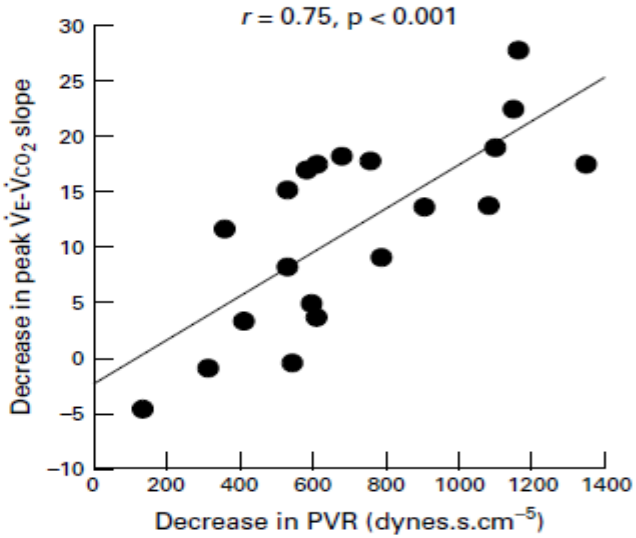
Acute and chronic effects of surgical thromboendarterectomy on exercise capacity and ventilatory efficiency in patients with chronic thromboembolic pulmonary hypertension

T Iwase, N Nagaya, M Ando, T Satoh, F Sakamaki, S Kyotani, H Takaki, Y Goto, Y Ohkita, M Uematsu, N Nakanishi, K Miyatake



20 patients with CTPH **before, 1m** and **4m** after surgery





Heart 2001

Use of exercise testing in the evaluation of interventional efficacy: an official ERS statement

Luis Puente-Maestu[1,2,3], Paolo Palange[4], Richard Casaburi[5], Pierantonio Laveneziana[6,7], François Maltais[8], J. Alberto Neder[9,10], Denis E. O'Donnell[11], Paolo Onorati[4,12], Janos Porszasz[5], Roberto Rabinovich[13], Harry B. Rossiter[5,14], Sally Singh[15], Thierry Troosters[16,17] and Susan Ward[18]

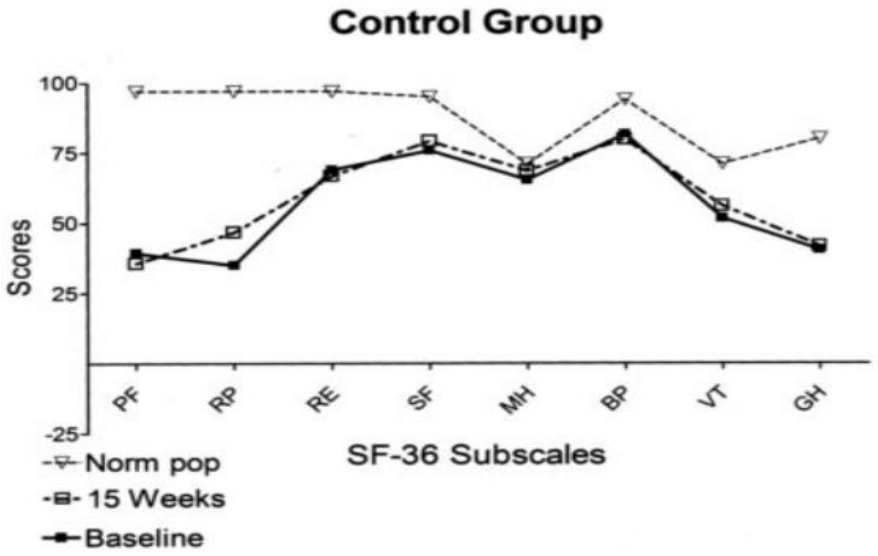
TABLE 4 Responsiveness of the different tests to bronchodilators for chronic obstructive pulmonary disease (COPD) vasodilators for pulmonary arterial hypertension (PAH) or pirfenidone for idiopathic pulmonary fibrosis (IPF)

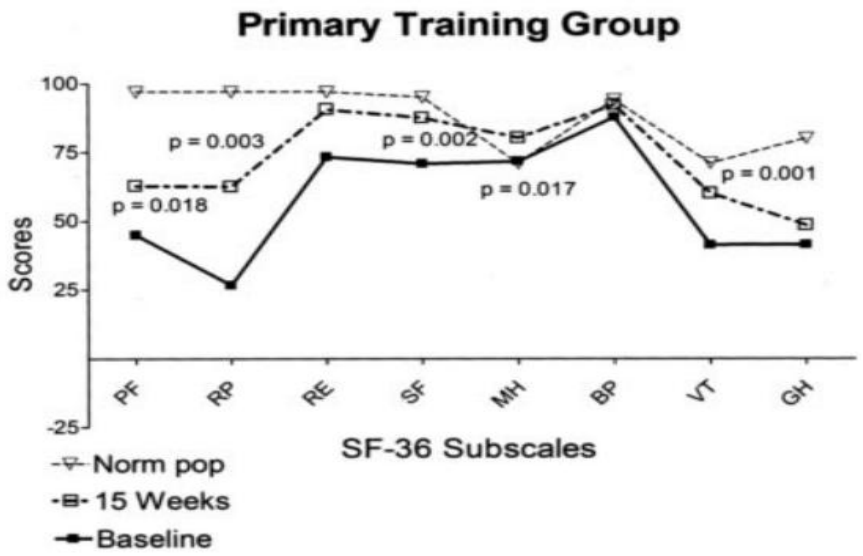
	Variable	COPD	PAH
IET	V'_{O_2peak}	Modest and inconsistent ↑; few studies	1.5–2 mL·min^{-1}·kg^{-1} or ↑ 9–14%
CWRET	V'_E-V'_{CO_2} indices	Anecdotal evidence	↓3–6 units/10–30%
	tLIM	14/26 (54%) and 3/11 (27%) of reviewed studies on long- and short-acting bronchodilators, respectively, showed ↑ >MCID (105 s) Limited comparative evidence suggest that it is more responsive than other tests	
	Isotime IC and dyspnoea	Most studies show ↑ >0.2 L and are associated with improvements in dyspnoea intensity of ⩾1 unit on a Borg scale	
ISWT	Time/distance	Inconsistent ↑; few studies	
ESWT	Time/distance	Inconsistent ↑; few studies	No ↑; few studies

Eur Respir J 2016

Η άσκηση ως θεραπευτικό εργαλείο στην ΠΥ

Exercise and Respiratory Training Improve Exercise Capacity and Quality of Life in Patients With Severe Chronic Pulmonary Hypertension





Δ6MWD=111m, p<0.001
No adverse event

30 pts with PAH or CTPH, NYHA=2-3
3 weeks hospital training
12 weeks home-based training

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Exercise and Respiratory Training Improve Exercise Capacity and Quality of Life in Patients With Severe Chronic Pulmonary Hypertension

TABLE 3. Respiratory and Hemodynamic Variables at Baseline and After Intervention

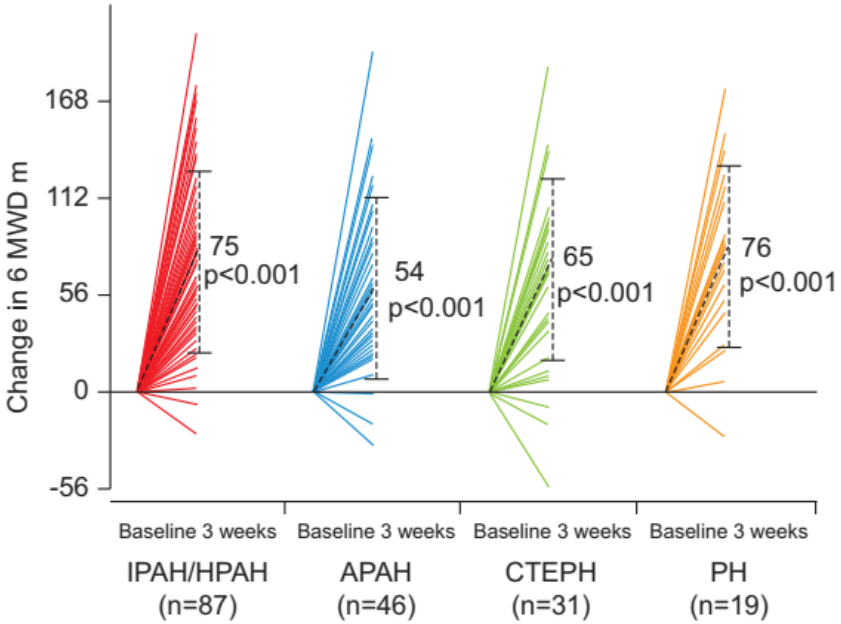
	Control Group (n=15)			Primary Training Group (n=15)		
	Baseline	3 wk	15 wk	Baseline	3 wk	15 wk
$Workload_{max}$, W	64±22	60±24	67±20	70±17	85±26*†	90±25*†
Borg scale	15±2	15±1	16±1*	15±2	15±2	15±2
HR_{rest}, bpm	71±17	74±11	72±11	72±11	73±11	75±11
HR_{max}, bpm	108±19	107±22	110±20	118±16	125±15*†	132±17*†
VE_{max}, L · min	41.6±14.6	40.5±14.1	43.4±15.3	44.2±13.8	47.1±15.1	48.5±15.1
$\dot{V}o_{2\ peak}$, mL · min^{-1} · kg^{-1}	11.9±3.1	11.6±3.4	11.4±3.3	13.2±3.1	14.5±3.5*†	15.4±3.7*†
$\dot{V}o_{2\ \%\ predicted}$, %	46.3±10.7	45.9±14.6	49.8±12.7	51.6±16.3	56.5±18.0*	60.3±19.6*
Workload at AT, W	35±17	31±16	36±17	45±14	56±21*†	65±19*†
$\dot{V}o_2$ at AT, mL/min	640.7±187.4	613.4±206.6	610.4±200.4	736.6±210.3	802.3±229.8†	865.4±264.7*†
$Eqco_2$ at AT	42.4±11.3	50.7±10.8*	43.5±10.5	44.4±11.5	42.6±9.8†	42.9±10.4
Echocardiography						
$PASP_{rest}$, mm Hg	68±21	71±23	70±25	61±18	57±18†	54±18†
$PASP_{max\ exercise}$, mm Hg	98±28	104±29	102±30	89±17	84±23†	89±20
Cardiac $index_{rest}$, L · min^{-1} · m^{-2}	1.4±0.3	1.5±0.4	1.6±0.5	1.5±0.5	1.6±0.3	1.6±0.4
Cardiac $index_{max}$, L · min^{-1} · m^{-2}	1.9±0.7	1.8±0.7	1.9±0.7	2.3±0.6	2.3±0.7	2.5±1.1
RV $area_{rest}$, cm^2/m^2	16.2±5.8	16.0±4.3	13.3±4.7	13.0±3.9	14.2±4.3	12.2±3.8
RV $area_{max}$, cm^2/m^2	17.0±6	17.2±4.8	16.4±4.8	13.7±4.0	14.2±4.3	14.0±2.7
RA $area_{rest}$, cm^2/m^2	13.5±4.4	15.5±5.7	13.8±3.3	12.7±3.9	13.2±4.1	12.8±3.8
RA $area_{max}$, cm^2/m^2	15.3±4.8	15.0±5.9	14.7±3.9	13.9±4.5	14.8±4.3	12.3±3.3

Circulation. 2006;114:1482-1489

Eur Respir J 2012; 40: 84–92

Safety and efficacy of exercise training in various forms of pulmonary hypertension

Ekkehard Grünig*,+++, Mona Lichtblau*,+++, Nicola Ehlken*, Hossein A. Ghofrani#, Frank Reichenberger#, Gerd Staehler¶, Michael Halank+, Christine Fischer§, Hans-Jürgen Seyfarthƒ, Hans Klose, Andreas Meyer##, Stephan Sorichter¶¶, Heinrike Wilkens++, Stephan Rosenkranz§§, Christian Opitzƒƒ, Hanno Leuchte***, Gabriele Karger###, Rudolf Speich¶¶¶ and Christian Nagel***

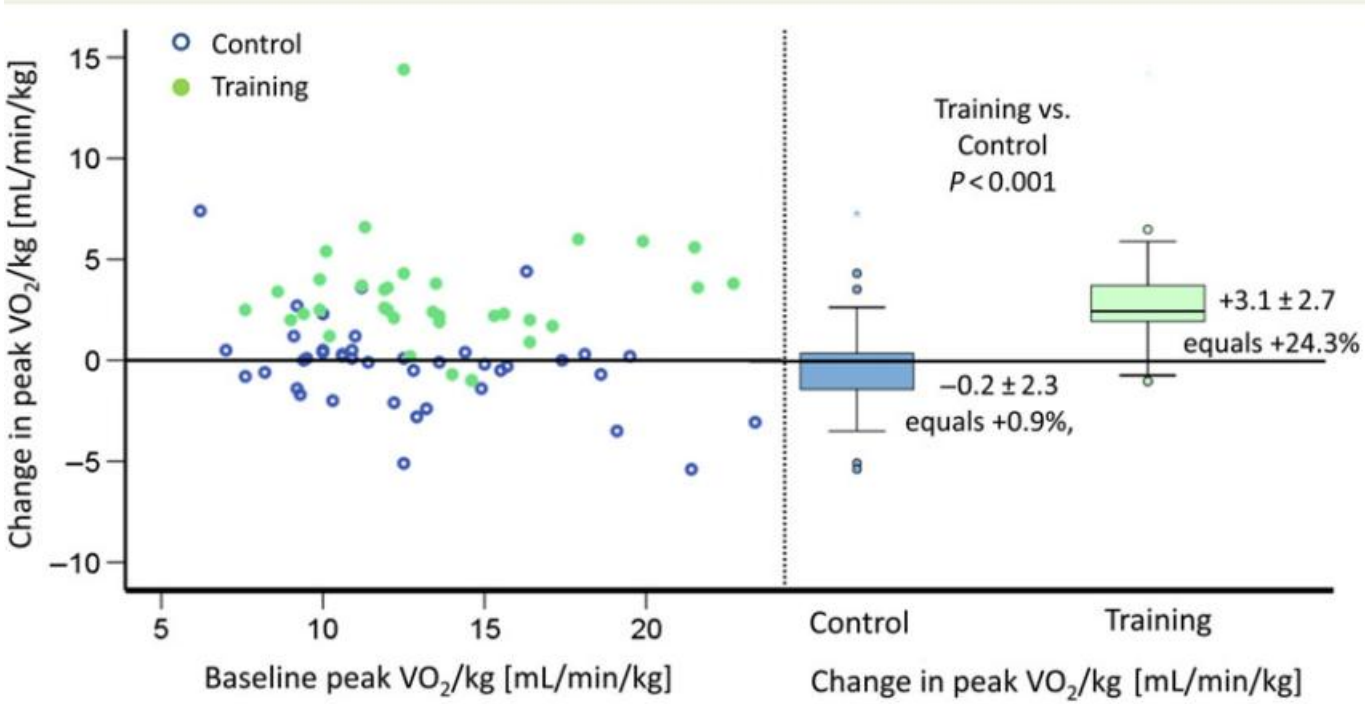


183 patients with PH of various forms and severity

Safety and efficacy of exercise training in various forms of pulmonary hypertension

Characteristics	Baseline		3 weeks				15 weeks			
	Mean ± SD	95% CI	Mean ± SD	Median	95% CI	p-value	Mean ± SD	Median	95% CI	p-value
Subjects n	183		183				103			
6MWD by PH aetiology m										
All	425 ± 106	410–441	493 ± 110		478–510	<0.001	506 ± 104		486–528	<0.001
IPAH/HPAH (n=87/87/53)	448 ± 89	429–467	523 ± 89		503–542	<0.001	543 ± 74		522–563	<0.001
APAH (n=46/46/18)	427 ± 113	393–461	482 ± 123		445–518	<0.001	454 ± 132		392–516	<0.001
CTEPH (n=31/31/18)	417 ± 110	377–457	482 ± 126		436–528	<0.001	512 ± 81		473–551	0.001
PH (n=19/19/11)	327 ± 100	279–375	403 ± 86		362–444	<0.001	407 ± 118		328–486	<0.001
Cardiopulmonary exercise testing										
Peak $V'O_2$ per kg $mL \cdot min^{-1} \cdot kg^{-1}$	12.2 ± 3.5		13.6 ± 4			<0.001	13.9 ± 3.8			<0.001
Peak $V'O_2$ $mL \cdot min^{-1}$	907 ± 276		1006 ± 308			<0.001	1011 ± 292			<0.001
$EqCO_2$ at AT	45.2 ± 9.6		43.6 ± 10.6			0.249	44.3 ± 10.8			0.225
$V'O_2$ at AT $mL \cdot min^{-1}$	692 ± 214		712 ± 236			0.216	790 ± 261			0.007
Oxygen pulse	7.5 ± 2.1		7.9 ± 2.4			<0.001	7.7 ± 2.4			0.001
PASP rest mmHg	59 ± 20		57 ± 20			0.028	56 ± 20			0.016
PASP maximum mmHg	91 ± 26		91 ± 26			0.542	95 ± 26			0.512
Heart rate rest min^{-1}	77 ± 13		74 ± 11			<0.001	80 ± 13			0.009
Heart rate maximum min^{-1}	122 ± 19		127 ± 22			<0.001	133 ± 20			<0.001
RRsys rest mmHg	117 ± 17		114 ± 15			0.016	113 ± 14			0.019
RRdia rest mmHg	78 ± 14		75 ± 9			<0.001	77 ± 9			0.128
RRsys maximum mmHg	150 ± 26		151 ± 24			0.615	150 ± 24			0.719
RRdia maximum mmHg	86 ± 14		86 ± 12			0.617	87 ± 12			0.667
Borg scale	15.6 ± 2		15.6 ± 2			0.896	15.7 ± 2			0.100
Workload maximum W	64 ± 24		77 ± 28			<0.001	80 ± 27			<0.001

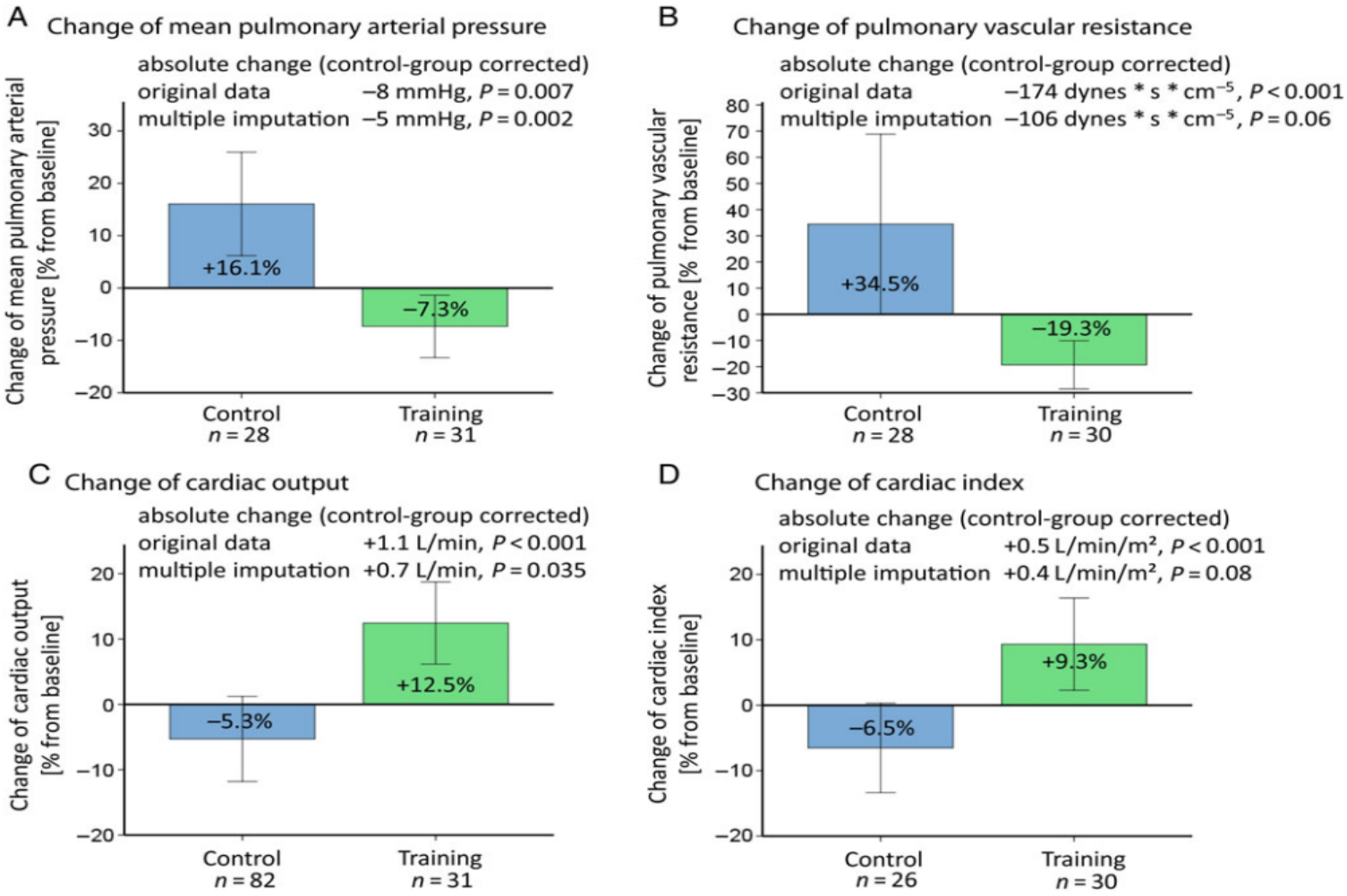
Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial



87 patients with
PAH or CTPH
RCT of 15 weeks of training

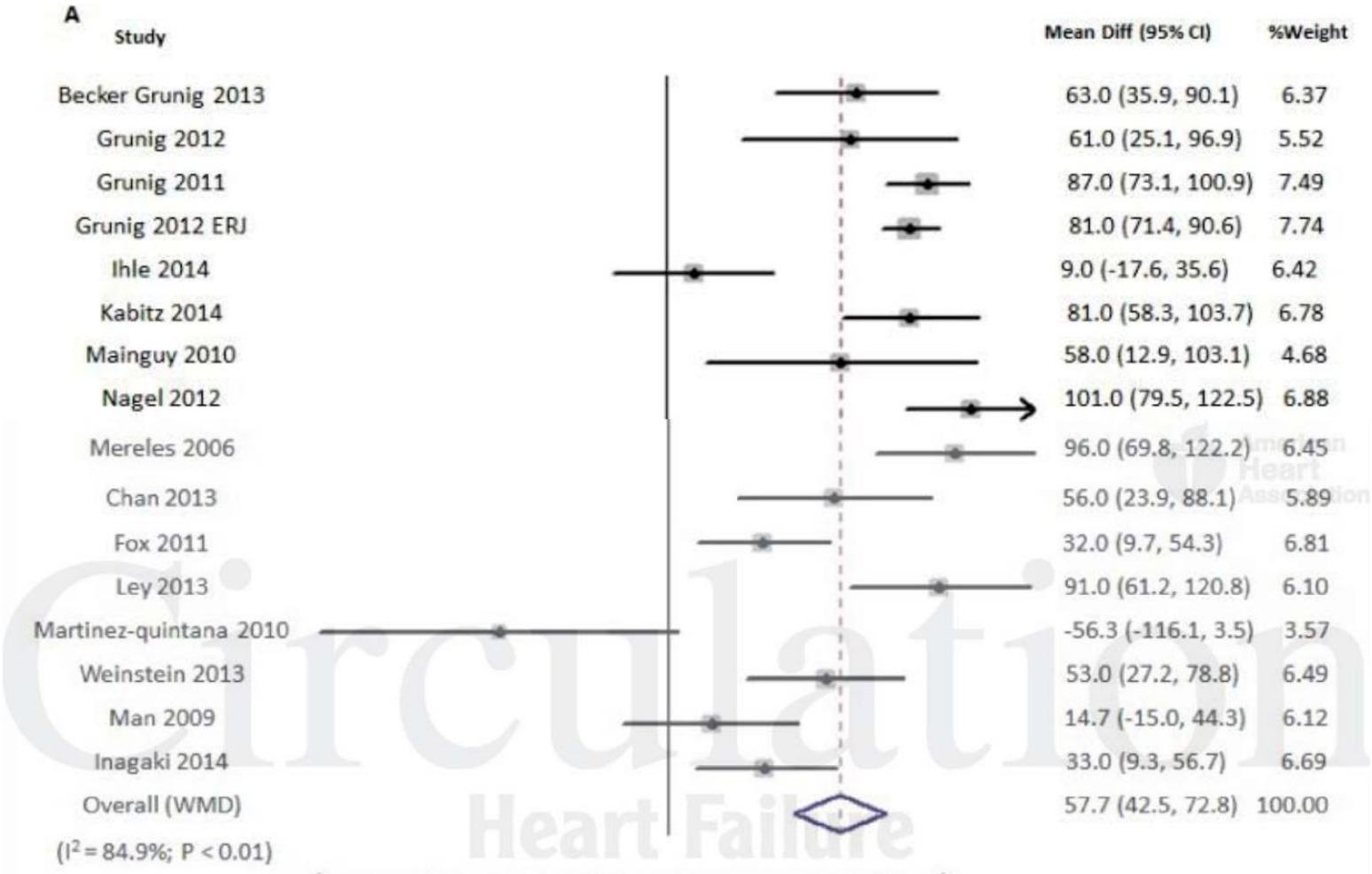
European Heart Journal (2016) **37**, 35–44
doi:10.1093/eurheartj/ehv337

Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial



Efficacy and Safety of Exercise Training in Chronic Pulmonary Hypertension: A Systematic Review and Meta-Analysis

Ambarish Pandey, Sushil Garg, Monica Khunger, Sonia Garg, Dharam J. Kumbhani, Kelly M. Chin and Jarett D. Berry



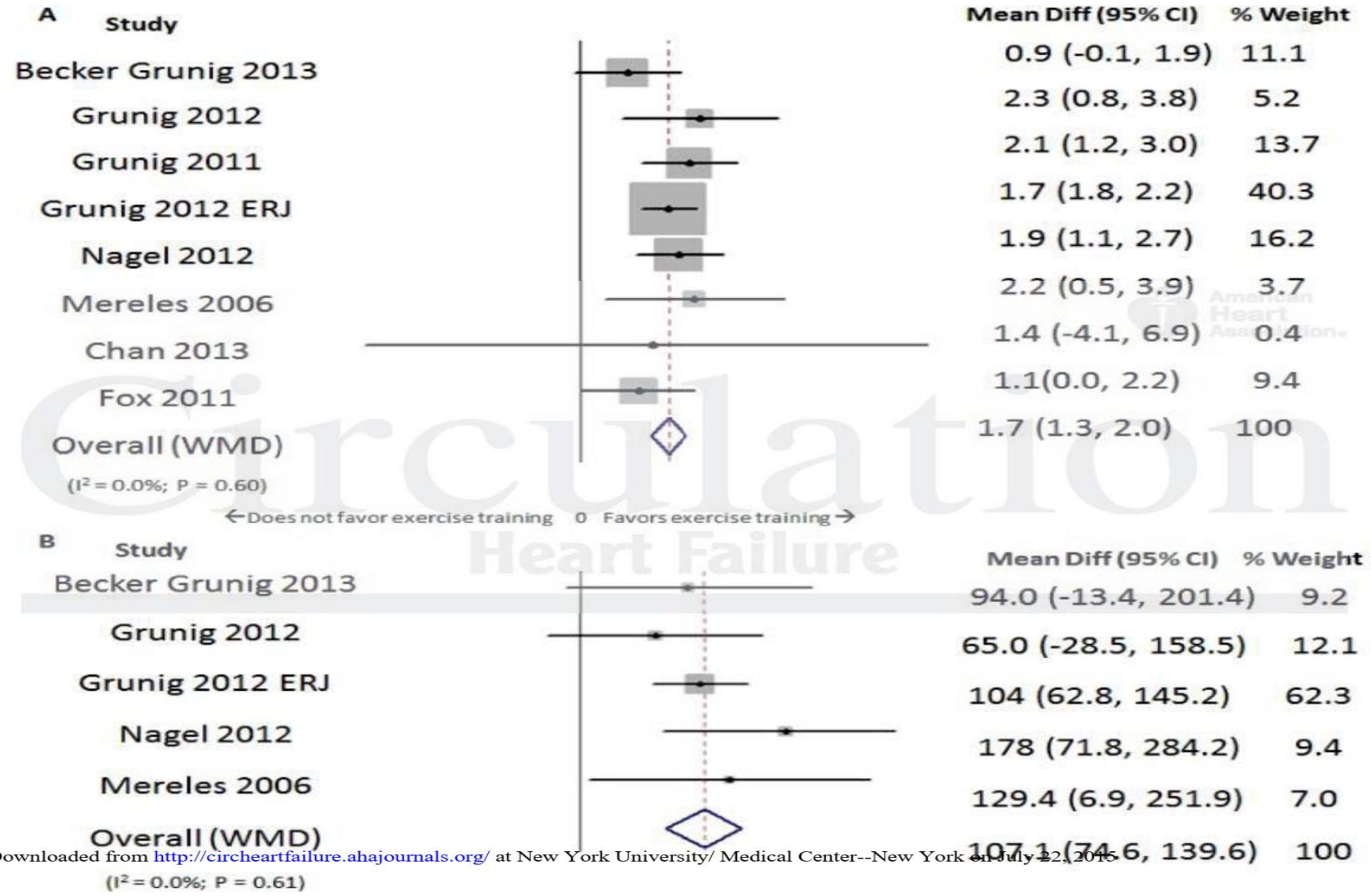
-16 studies
-484 pts

Effect of rehabilitation on 6MWD

Circ Heart Failure 2015

Efficacy and Safety of Exercise Training in Chronic Pulmonary Hypertension: A Systematic Review and Meta-Analysis

Effect on peak VO2 (A) ml/kg/min (B) ml/min



EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

ERS statement on exercise training and rehabilitation in patients with severe chronic pulmonary hypertension

2018 as doi: 10.1183/13993003.00332-2018

In studies among 784 PH patients in total:

As exercise training appears to be effective, cost-efficient and safe, but is scarcely reimbursed, support from health care institutions, commissioners of health care and research funding institutions are of high need. There is a strong need to establish specialised rehabilitation programmes for PH patients to enhance patient access to this treatment intervention.

Συμπεράσματα

- Η ανάπτυξη ΠΥ συνοδεύεται από **πρώιμα και μη ειδικά** συμπτώματα κατά την άσκηση

- Η αύξηση των πνευμονικών αγγειακών αντιστάσεων οδηγεί, αφενός, σε μείωση του **ΚΛΟΑ** και **περιφερική υποάρδευση** και, αφετέρου, σε αύξηση του **νεκρού χώρου** και **υπεραερισμό**

- Κατά την CPET: **χαμηλό peak VO2**, **AT**, **όγκος παλμού**, **WR** σε συνδυασμό με υψηλό **VE/VCO2** και χαμηλό **PETCO2**: ειδικά για ΠΥ

- Η υψηλή peak VO2 (>15 ml/kg/min) και ο χαμηλός VE/VCO2 (<36) είναι, μεταξύ άλλων, ιδιαίτερα σημαντικές παράμετροι για την αναγνώριση ασθενών **καλύτερης πρόγνωσης**

- Η peak VO2, το πηλίκο VE/VCO2 και η PETCO2 αποτελούν χρήσιμες παραμέτρους για την παρακολούθηση της **ανταπόκρισης στη θεραπεία**

- Η ένταξη σε **εξατομικευμένο πρόγραμμα άσκησης** είναι ασφαλής και βελτιώνει σημαντικά την ικανότητα για άσκηση των ασθενών με ΠΥ


ΕΥΧΑΡΙΣΤΩ
ΠΟΛΥ