



ACTION

Pneumologi in azione nell'ipertensione
arteriosa polmonare (PAH)

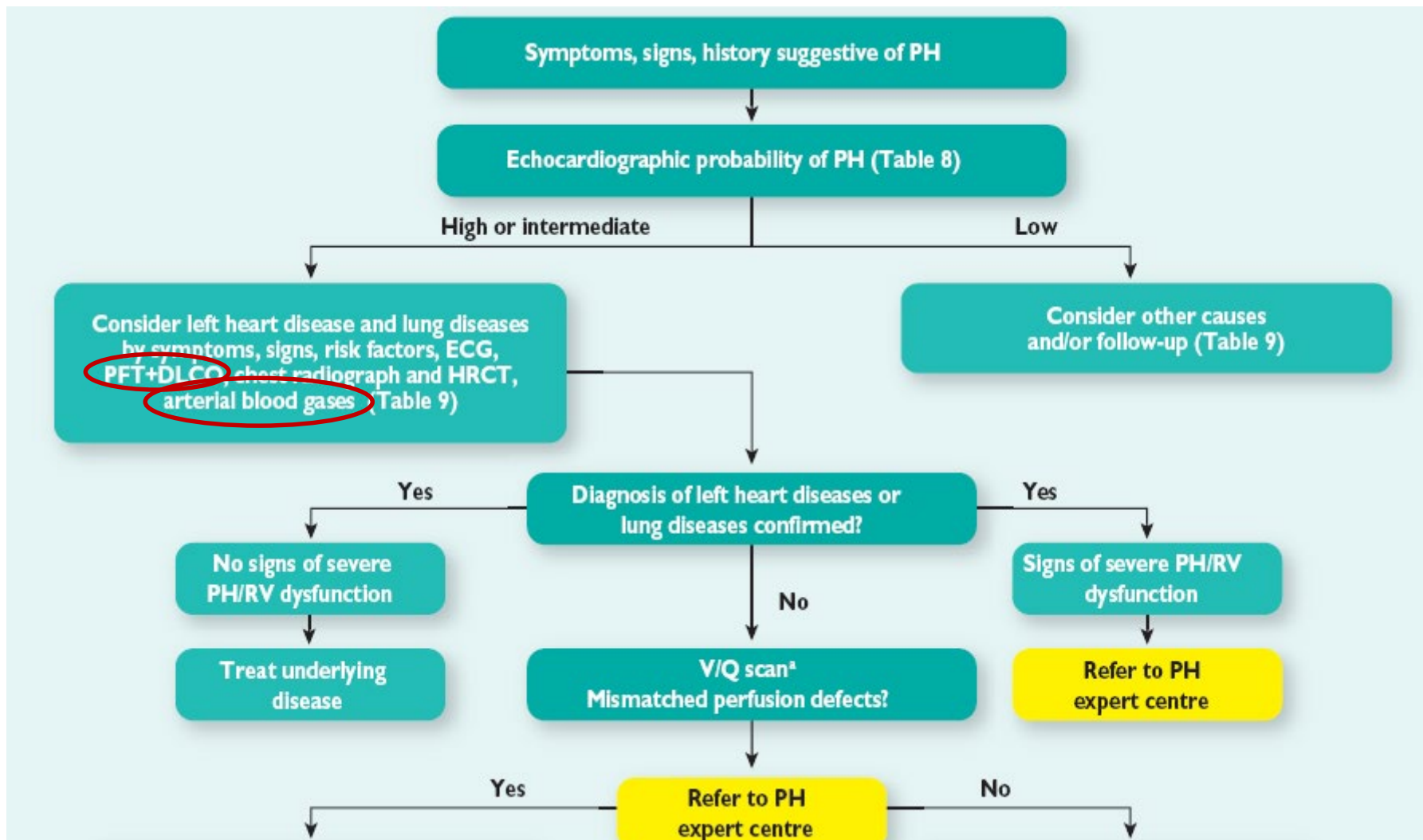
MILANO

13 // 14 dicembre 2018

PALAZZO DELLE STELLINE

**Prove di funzionalità
respiratoria:
un aiuto alla diagnosi**

Dr.ssa Maria Rosa Mirenda





- ✓ Spirometria semplice
- ✓ Spirometria globale
(pletismografia)
- ✓ DLCO
(singolo respiro)

Lung function in pulmonary hypertension

A.T. Low ^{a,*}, A.R.L. Medford ^b, A.B. Millar ^c, R.M.R. Tulloh ^a

^a University Hospitals Bristol NHS Foundation Trust, Upper Maudlin Street, Bristol, United Kingdom

^b North Bristol Lung Centre, Southmead Hospital, Southmead Road, Bristol, United Kingdom

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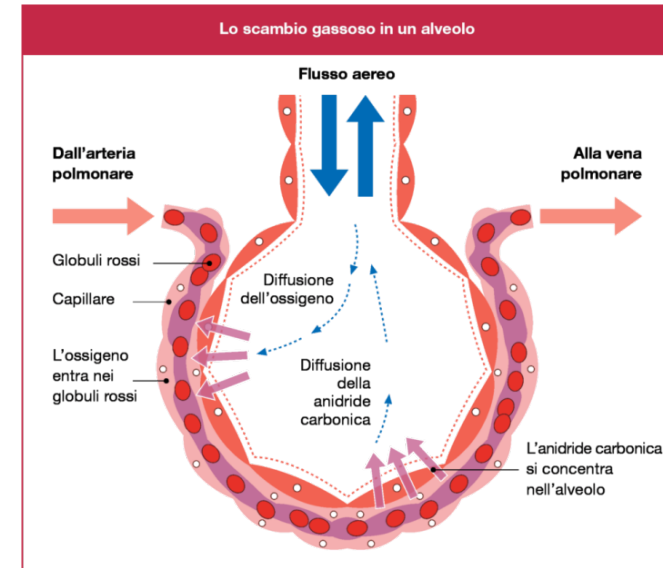
Age: 50 Height(cm): 164 Weight(kg): 55.0 Gender: Femm. RaceCaucasica

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
VC	Litri	3.06	2.67	87			
FVC	Litri	3.08	2.67	87			
FEV1	Litri	2.63	2.16	82			
FEV1/FVC	%	80	81				
FEV1/SVC	%		81				
PEF	L/sec	6.41	5.57	87			
FEF25-75%	L/sec	3.27	2.16	66			
FEF25%	L/sec	5.63	5.52	98			
FEF50%	L/sec	3.93	3.66	93			
FEF75%	L/sec	1.58	0.83	53			
Lung Volumes							
TLC	Litri	5.03	4.34	86			
RV	Litri	1.77	1.68	95			
RV/TLC	%	36	39				
FRC PL	Litri	2.72	3.07	113			
FRC N2	Litri	2.72					
Raw	cmH2O/L/sec	<2.24	2.14				
sRaw	cmH2O/L/s/L		7.19				
Diffusion							
DLCO	mL/mmHg/min	24.6	11.3	46			
DL Adj	mL/mmHg/min	24.6	11.3	46			
DLCO/VA	mL/mHg/min/L	4.88	2.88	59			
DL/VA Adj	mL/mHg/min/L	4.88	2.88	59			
VA	Litri	5.03	3.91	78			

Flusso

Il ruolo della DLCO

- ✓ Consente di valutare **la capacità di diffusione dei gas O₂ e CO₂** attraverso la membrana alveolo-capillare. Il test di diffusione valuta l'integrità di tale membrana.
- ✓ Si sfrutta **monossido di carbonio**, gas che ha un'elevata affinità per l'emoglobina e il cui trasferimento è limitato quindi unicamente dalla diffusione
- ✓ Il test di diffusione del monossido di carbonio viene effettuato facendo inalare al soggetto una miscela con **CO a bassissime concentrazioni (0.3%)** ed elio (He) ad una concentrazione del 10% mediante respiro singolo.



SERIES “ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING”

Interpretative strategies for lung function tests

R. Pellegrino, G. Viegi, V. Brusasco, R.O. Crapo, F. Burgos, R. Casaburi, A. Coates, C.P.M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen and J. Wanger

Alterazione	DLCO (% del teorico)
lieve	< 80% e $\geq$ 60%
media	< 60% e $\geq$ 40%
elevata	< 40%

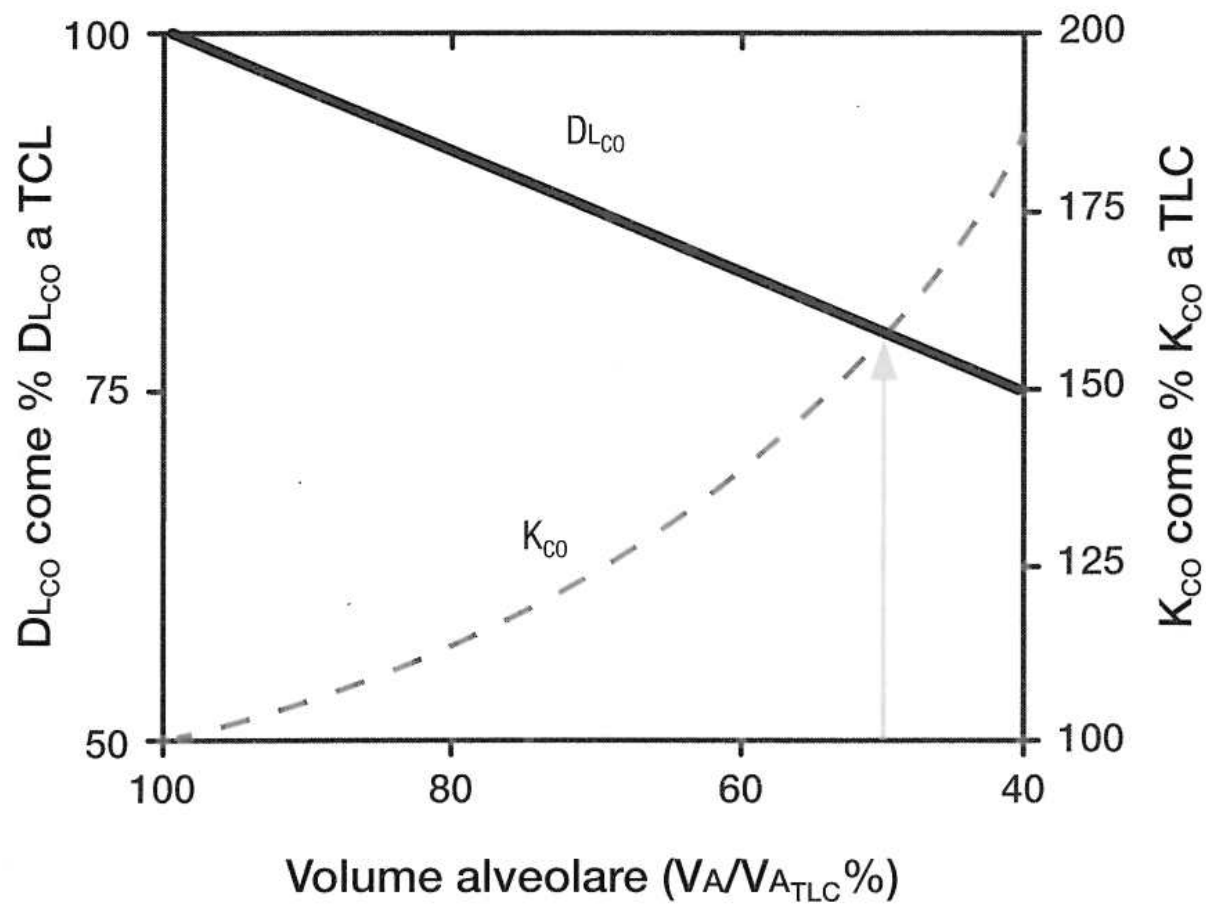
75% dei pazienti con PAH ha una DLCO < 80%

DLCO 59-71%

ATS/ERS, 2005

Respiratory Medicine, 2015

$$DLCO = K_{CO} \times VA \text{ ml/min/mmHg}$$



~~$DLCO/VA$~~

Loss of alveolar membrane diffusing capacity and pulmonary capillary blood volume in pulmonary arterial hypertension

Samar Farha^{1*}, Daniel Laskowski^{1,2}, Deepa George², Margaret M Park^{2,3}, WH Wilson Tang³, Raed A Dweik^{1,2} and Serpil C Erzurum^{1,2}

Equazione di Roughton e Forster:

$$1/DL = 1/Dm + 1/\theta \times Vc$$

DL = DLCO

Dm= capacità di diffusione di membrana

Vc = volume capillare

Θ = reazione del CO con il sangue (corretta per la concentrazione emoglobinica)

Variable	Healthy N = 41	PAH N = 28	p-value
Age (years)	34 ±2	45 ±2	<0.01
Gender (M/F)	17/24	6/22	0.09
Smoking history (never/current/ ex smoker)	40/0/1	24/1/3	0.1
Height (cm)	169 ±1	167 ±3	0.3
Weight (kg)	79 ±3	89 ±7	0.2
O ₂ Saturation (% of Hgb)	98 ±0.2	96 ±0.4	<0.01
FE _{NO} (ppb)	19 ±2	18 ±2	0.7
FVC (%)	98 ±2	91 ±3	0.2
FEV ₁ (%)	93 ±2	80 ±4	<0.01
FEV ₁ /FVC	81 ±1	75 ±1	<0.01
TLC (%)	85 ±2	82 ±2	0.4
V _A (L)	4.9 ±0.2	4.3 ±0.2	0.1
DL _{CO} (ml/min/mmHg)	24 ±1	17 ±1	<0.01
DL _{NO} (ml/min/mmHg)	94 ±4	66 ±5	<0.01
D _m (ml/min/mmHg)	48 ±2	33 ±2	<0.01
V _c (ml)	78 ±4	63 ±5	<0.01
D _m /V _c (1/min/mmHg)	0.6 ±0.02	0.6 ±0.04	0.8
Hgb (g/dl)	13.3 ±0.3	13.5 ±0.4	0.9

↓ **D_m**

- ✓ ispessimento della membrana alveolocapillare per processi fibrotici e proliferativi
- ✓ edema interstiziale

↓ **V_c**

- ✓ ↑ resistenze vascolari
- ✓ ↓ output cardiaco
- ✓ trombosi locale

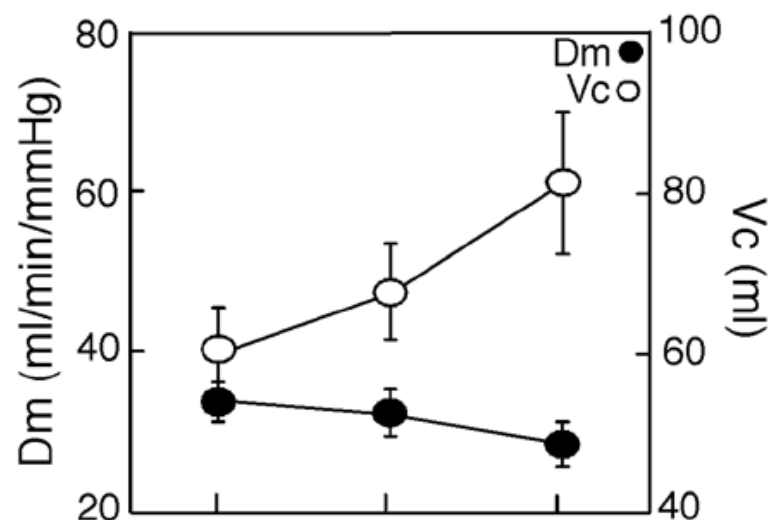
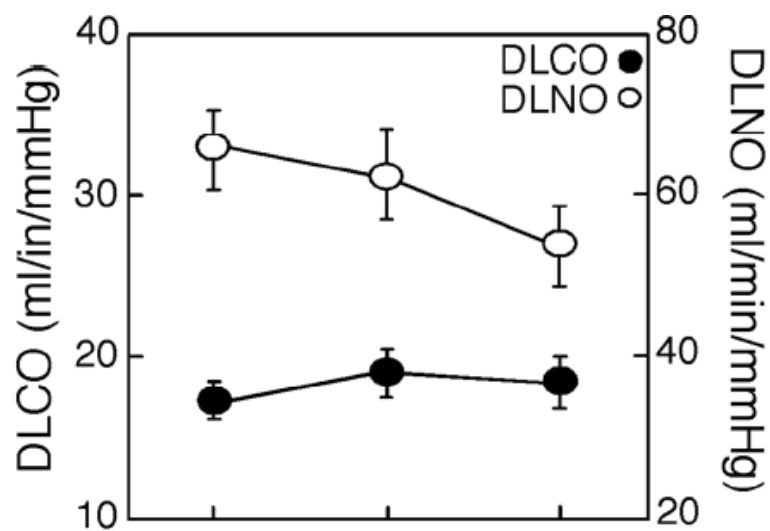


Table 3 Changes over time in the PAH group

Variable	Estimated unit/year change	Wilcoxon SR p-value
FEV ₁ (ml)	-144	0.1
FEV ₁ (%)	-3	0.12
FVC (ml)	-190	0.2
FVC (%)	-5	0.2
FEV ₁ /FVC	0.8	0.4
V _A (ml)	20	0.4
FE _{NO} (ppb)	0.5	0.4
TLC (%)	0.7	0.5
DL _{CO} (ml/min/mmHg)	-1.2	0.7
DL _{NO} (ml/min/mmHg)	-24	0.01
D _m (ml/min/mmHg)	-12	0.01
V _c (ml)	11	0.07
D _m /V _c (1/min/mmHg)	-0.4	0.04
Hgb (g/dl)	0.05	0.6

Severely reduced diffusion capacity in idiopathic pulmonary arterial hypertension: patient characteristics and treatment responses

Pia Trip¹, Esther J. Nossent¹, Frances S. de Man^{1,2}, Inge A.H. van den Berk³, Anco Boonstra¹, Herman Groepenhoff¹, Edward M. Leter⁴, Nico Westerhof^{1,2}, Katrien Grünberg⁵, Harm-Jan Bogaard¹ and Anton Vonk-Noordegraaf¹

	DLco <45% pred	DLco ≥45% pred	p-value
Survival years			0.002 [†]
1	87	95	
3	54	86	
5	38	80	

Demographics	DLco <45% pred	DLco ≥45% pred	p-value
Patients n	48	118	
Age at diagnosis years	67 [53–75]	46 [35–60]	<0.001
Sex male	24 (50)	22 (19)	0.013
Body mass index kg·m ⁻²	26 ± 4	27 ± 6	0.035
Smoking	33 (77)	54 (48)	0.033
Current smoker	8 (19)	20 (18)	0.765
Former smoker	25 (58)	34 (30)	0.065
Pack years	25 [0–40]	0 [0–13]	0.009
Medical history			
Coronary disease	13 (27)	1 (1)	0.008
Hypertension	14 (29)	26 (22)	0.207
Diabetes mellitus	12 (25)	11 (9)	0.513
Thyroid disease	4 (8)	12 (10)	0.701
Pulmonary disease COPD (GOLD I–II)	5 (10)	6 (5)	0.845

TABLE 2 Computed tomography findings in patients according to the diffusing capacity of the lung for carbon monoxide (DLco)

	Presence of fibrosis			Presence of emphysema		
	DLco <45% pred [#]			DLco ≥45% pred [†]		
	None	Mild	Moderate	None	Mild	Moderate
None	14 (32)	9 (21)	8 (18)	64 (67)	24 (25)	4 (4)
Mild	3 (7)	4 (9)	4 (9)	1 (1)	1 (1)	1 (1)
Moderate	0 (0)	2 (5)	0 (0)	1 (1)	0 (0)	0 (0)
WHO functional class				0.050 [#]		
I		0 (0)			6 (6)	
II		9 (21)			32 (29)	
III		27 (61)			61 (56)	
IV		8 (18)			10 (9)	
Pulmonary function						
FEV ₁ % pred		85 ± 16			91 ± 16	0.010 ^{††}
FVC % pred		99 ± 16			102 ± 17	0.206 ^{††}
FEV ₁ /FVC %		68 ± 9			74 ± 9	<0.001 ^{††}
TLC % pred		92 ± 16			99 ± 12	0.004 ^{††}
VA % pred		78 ± 14			85 ± 11	0.001 ^{††}

Predicting Survival in Pulmonary Arterial Hypertension

Insights From the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL)

Raymond L. Benza, MD; Dave P. Miller, MS; Mardi Gomberg-Maitland, MD, MSc;
Robert P. Frantz, MD; Aimee J. Foreman, MA; Christopher S. Coffey, PhD; Adaani Frost, MD;
Robyn J. Barst, MD; David B. Badesch, MD; C. Gregory Elliott, MD;
Theodore G. Liou, MD; Michael D. McGoon, MD

Table 2. Variable Coefficients for the Linear Component of the Cox Model

Additions and Subtractions to Linear Component of Equation			
WHO group I subgroup	FPAH, +0.7737	APAH-PoPH, +1.2801	APAH-CTD, +0.4624
Demographics and comorbidities	Male >60 y of age, +0.7779	Renal insufficiency, +0.6422	
NYHA/WHO FC	FC I, -0.8740	FC III, +0.3454	FC IV, +1.1402
Vital signs	SBP <110 mm Hg, +0.5128	Heart rate >92 bpm, +0.3322	
6MWD test	6MWD $\geq$ 440 m, -0.5455	6MWD <165 m, +0.5210	
BNP	BNP <50 pg/mL or N-terminal-proBNP <300 pg/mL, -0.6922	BNP >180 pg/mL or N-terminal-proBNP >1500 pg/mL, +0.6791	
Echocardiogram	Any pericardial effusion, +0.3014		
Pulmonary function test	% Predicted DLCO $\geq$ 80%, -0.5317	% Predicted DLCO $\leq$ 32%, +0.3756	
Right heart catheterization (mm Hg, Wood units)	mRAP >20 mm Hg within 1 year, +0.5816	PVR >32 Wood units, +1.4062	

APAH indicates associated PAH; FC, functional class; FPAH, familial PAH; mRAP, mean right atrial pressure; PoPH, portopulmonary PAH hypertension; PVR, pulmonary vascular resistance; and SBP, systolic BP.

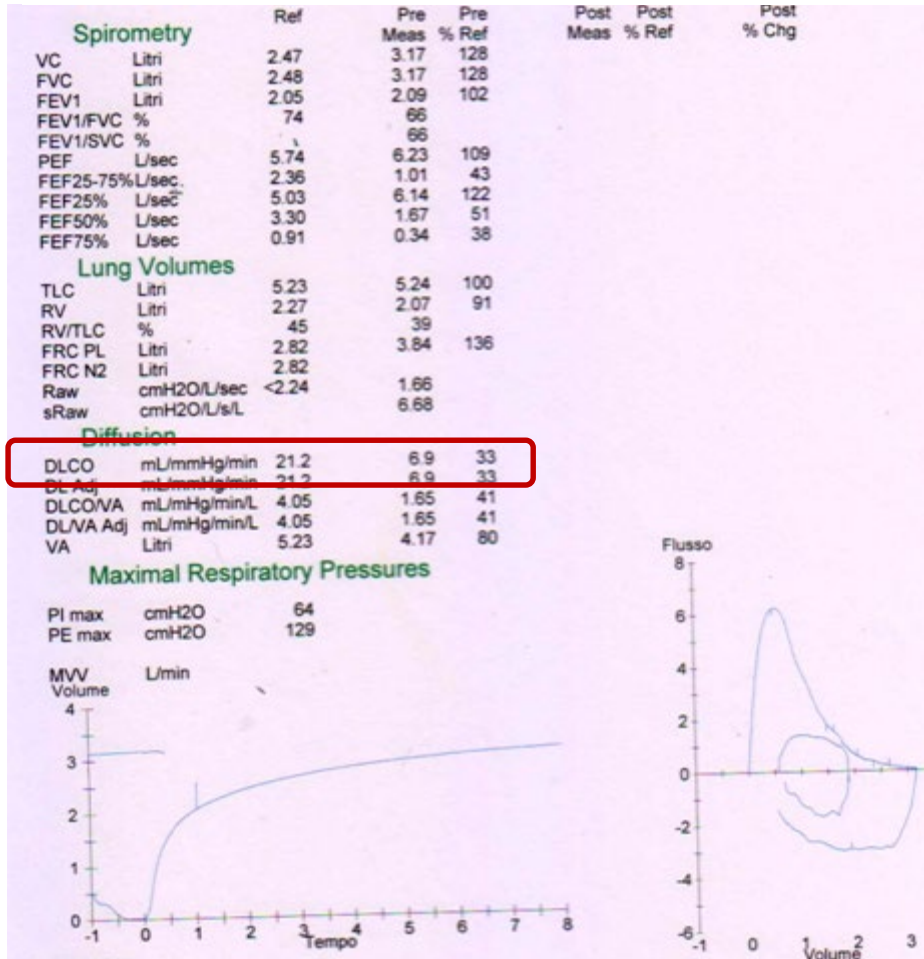
Lung function in pulmonary hypertension

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20-50% dei pazienti
Deficit restrittivo
↓TLC fino al 64%

20-40% deficit ostruttivo
FEV1/FVC < 70%
76% vs 84% p < 0.001

Scambi gassosi nella IPAH

Ipossiemia lieve moderata

paO₂ 72 ± 13 mmHg nelle donne

paO₂ 70 ± 13 mmHg negli uomini

Ipocapnia lieve moderata

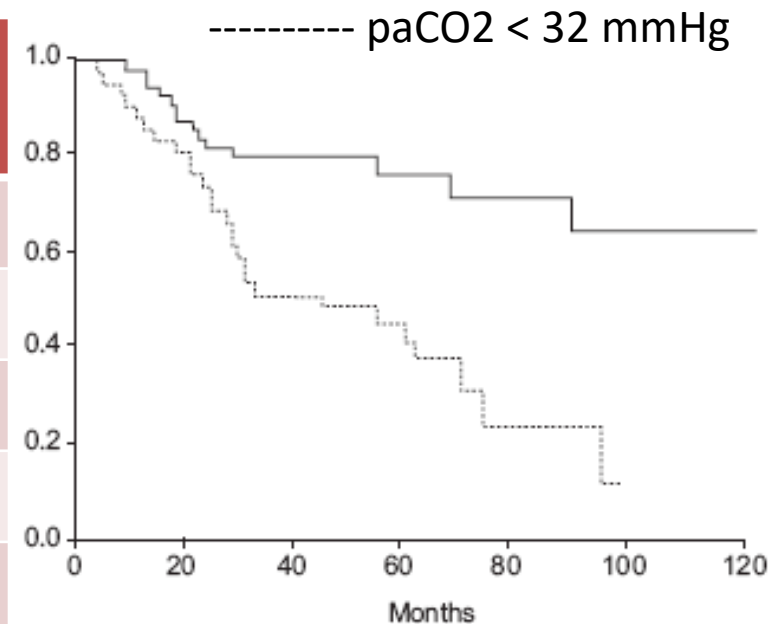
paCO₂ 31 ± 5 mmHg nelle donne

paCO₂ 30 ± 6 mmHg negli uomini

Prognostic value of blood gas analyses in patients with idiopathic pulmonary arterial hypertension

M.M. Hoeper, M.W. Pletz, H. Golpon and T. Welte

	paCO ₂ ≥ 32	paCO ₂ < 32 (p<0,001)
1 anno	98	86
2 anni	82	69
3 anni	80	51
5 anni	77	41
8 anni	65	12



	paCO ₂ ≥ 32	paCO ₂ < 32 (p<0,001)
1 anno	95	88
2 anni	86	70
3 anni	83	57
5 anni	83	46
8 anni	78	15

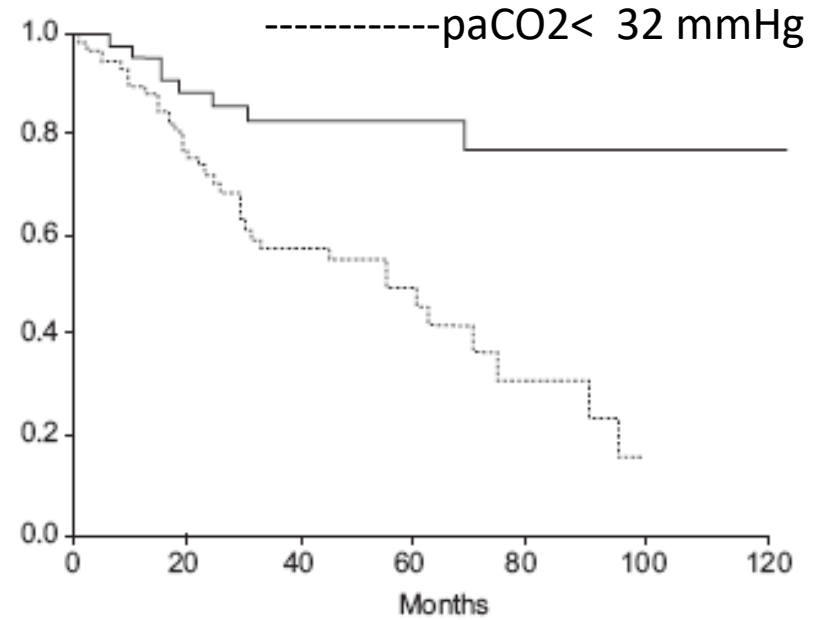


TABLE 2

Correlations between blood gases at rest, haemodynamics and 6-min walking distance (6MWD)

	6MWD	RAP	mPAP	Cardiac index	PVR	Sv,O ₂
<i>Pa</i> ,O ₂						
r	0.298	-0.269	0.108	0.008	0.161	0.227
p-value	0.001	0.007	NS	NS	NS	0.026
<i>Pa</i> ,CO ₂						
r	0.104	-0.054	-0.049	0.235	-0.185	0.226
p-value	NS	NS	NS	0.019	NS	0.026

R=0,362
P < 0,001

I. Pulmonary arterial hypertension
- I.1 Idiopathic - I.2 Heritable - I.2.1 BMPR2 mutation - I.2.2 Other mutations - I.3 Drugs and toxins induced - I.4 Associated with: - I.4.1 Connective tissue disease - I.4.2 Human immunodeficiency virus (HIV) infection - I.4.3 Portal hypertension - I.4.4 Congenital heart disease (Table 6) - I.4.5 Schistosomiasis
I'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
- I'.1 Idiopathic - I'.2 Heritable - I'.2.1 EIF2AK4 mutation - I'.2.2 Other mutations - I'.3 Drugs, toxins and radiation induced - I'.4 Associated with: - I'.4.1 Connective tissue disease - I'.4.2 HIV infection



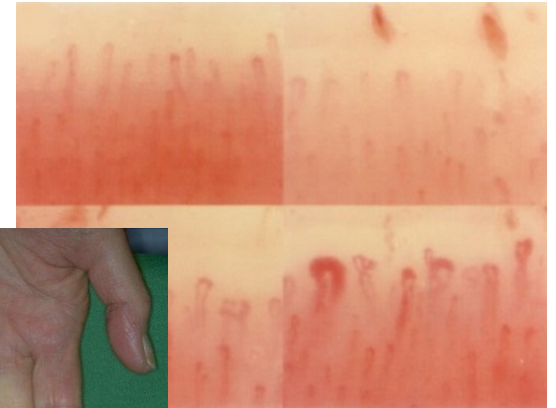
Scleroderma

↓ DLCO

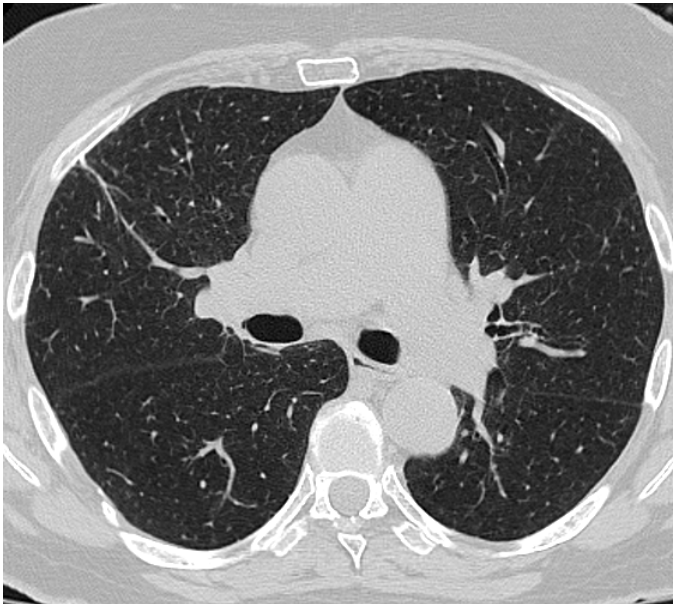
✓ Secondaria all'
interessamento isolato della
componente vascolare



Volumi nella norma



Test
immunosierologici



Scleroderma

↓ DLCO

✓ Secondaria all'
interessamento isolato della
componente vascolare

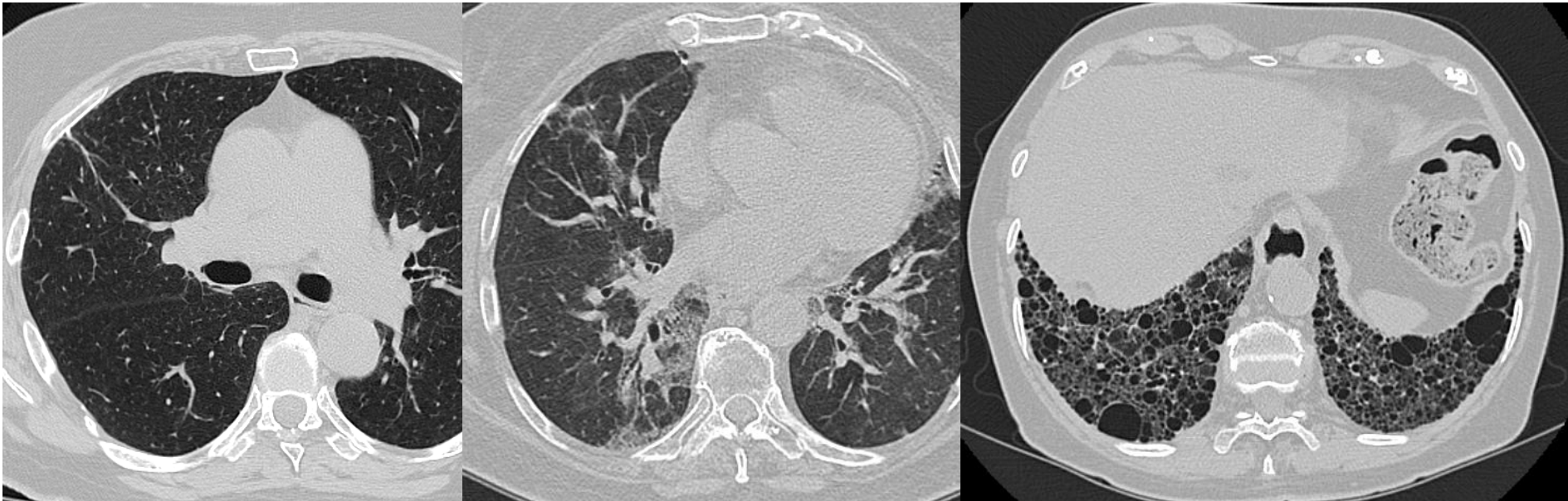


Volumi nella norma

✓ secondaria all'interessamento
parenchimale



Volumi nella norma
Sindrome restrittiva



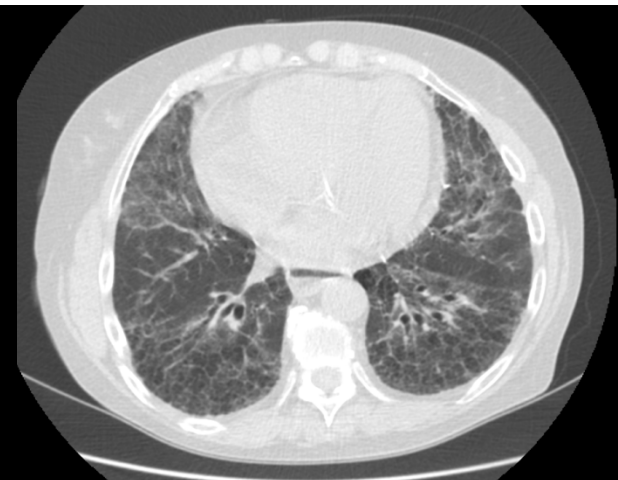
Age: 58 Height(cm): 157 Weight(kg): 58.5 Gender: Femm. RaceCaucasica Birth Date 13/03/1956

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
VC	Litri	2.53	2.29	91			
FVC	Litri	2.56	2.13	83			
FEV1	Litri	2.15	1.71	80			
FEV1/FVC	%	78	81				
FEV1/SVC	%		75				
PEF	L/sec	5.78	4.93	85			
FEF25-75%	L/sec	2.91	1.94	67			
FEF25%	L/sec	5.21	4.91	94			
FEF50%	L/sec	3.56	4.20	118			
FEF75%	L/sec	1.31	0.54	42			

Lung Volumes				
TLC	Litri	4.57	3.31	73
RV	Litri	1.77	1.02	58
RV/TLC	%	39	31	
FRC PL	Litri	2.57	1.60	62
FRC N2	Litri	2.57		
Raw	cmH2O/L/sec	<2.24	1.31	
sRaw	cmH2O/L/s/L		2.96	

Diffusion				
DLCO	mL/mmHg/min	21.7	5.6	26
DL Adj	mL/mmHg/min	21.7	5.6	26
DLCOVA	mL/mHg/min/L	4.75	2.05	43
DLVA Adj	mL/mHg/min/L	4.75	2.05	43
VA	Litri	4.57	2.72	60

Flusso



3. Pulmonary hypertension due to lung diseases and/or hypoxia

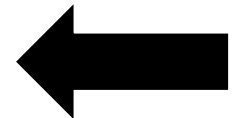
- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
 - 4.2.1 Angiosarcoma
 - 4.2.2 Other intravascular tumors
 - 4.2.3 Arteritis
 - 4.2.4 Congenital pulmonary arteries stenoses
 - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

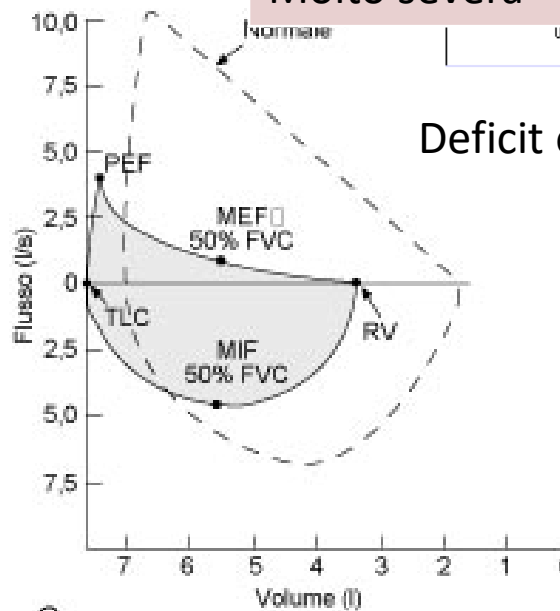


Kco ridotto /VA normale		Kco ridotto/ VA ridotta	
Meccanismi fisiopatogenetici	Condizioni cliniche	Meccanismi fisiopatologici	Condizioni cliniche
Distruzione del microcircolo	Ipertensione polmonare idiopatica	Distruzione alveolare	Enfisema (ridotto volume alveolare accessibile)
	vasculiti	Distruzione alveolare	Malattia interstiziale diffusa del polmone con fibrosi
Rimodellamento e dilatazione del microcircolo	Sindrome epatopolmonare	Distruzione del microcircolo	Bronchiolite obliterante
	MAV		Grave SCC

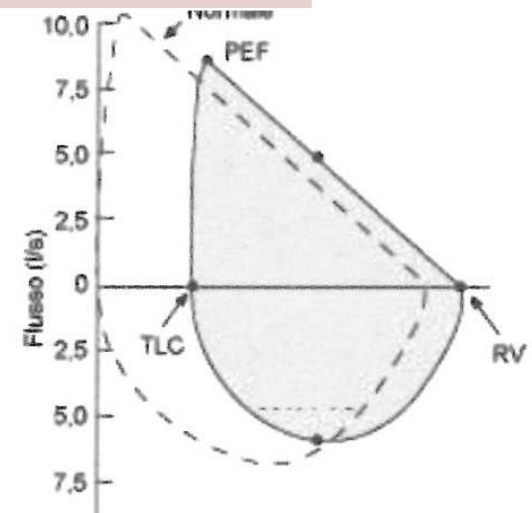
$$DLCO = Kco \times VA$$

	Rif	Migl.	% Rif	1
DLCO	20.6	15.7	76	15.7
DL Adj	20.6	15.7	76	15.7
DLCO/VA	5.99	3.28	55	3.28
VA		4.78		4.78
DL/VA Adj		3.28		3.28

Severità	FEV1 % del predetto
Lieve	>70
Moderata	60-69
Moderata-severa	50-59
Severa	35-49
Molto severa	<35



Deficit restrittivo



C

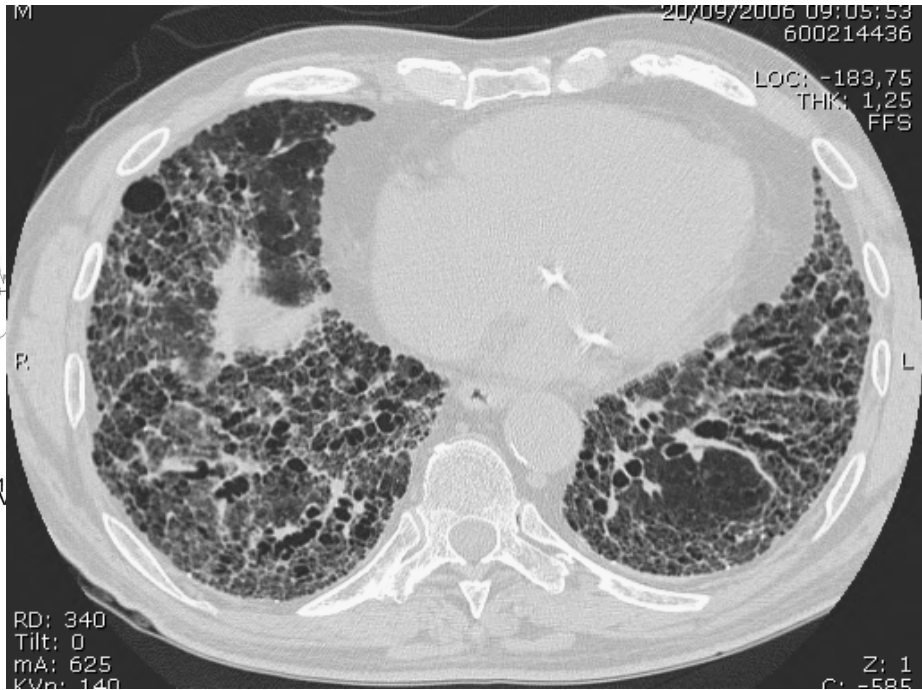
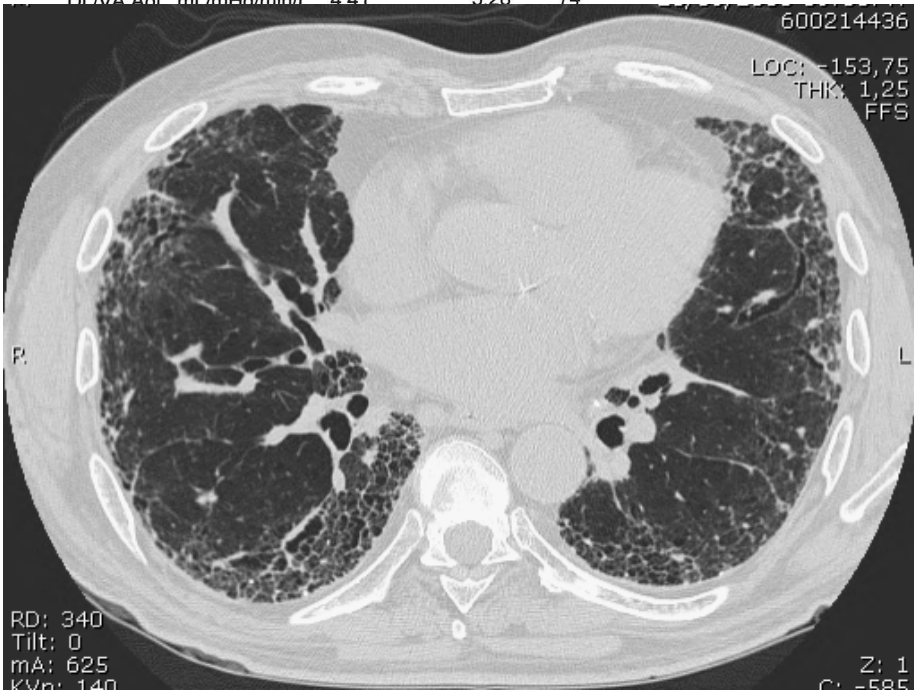
Age: 66 Height(cm): 165 Weight(kg): 85.0 Gender: Femm. RaceCaucasica Birth Date 27/06/1949

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
VC	Litri	2.69	1.58	59			
FVC	Litri	2.70	1.56	58			
FEV1	Litri	2.27	1.22	54			
FEV1/FVC	%	77	78				
FEV1/SVC	%		77				
PEF	L/sec	5.98	5.84	98			
FEF25-75%	L/sec	2.74	1.43	52			
FEF25%	L/sec	5.26	4.07	77			
FEF50%	L/sec	3.55	5.23	147			
FEF75%	L/sec	1.19	0.46	38			

Lung Volumes				
TLC	Litri	5.10	2.88	57
RV	Litri	2.04	1.30	64
RV/TLC	%	41	45	
FRC PL	Litri	2.76	1.55	56
FRC N2	Litri	2.76		
Raw	cmH2O/L/sec	<2.24	3.35	
sRaw	cmH2O/L/s/L		6.72	

Diffusion				
DLCO	mL/mmHg/min	22.5	5.8	26
DL Adj	mL/mmHg/min	22.5	5.8	26
DLCO/VA	mL/mHg/min/L	4.41	3.28	74
DLA/VA Adj	mL/mHg/min/L	4.41	3.28	74

IPF



Age: 73 Height(cm): 163 Weight(kg): 43.0 Gender: Masch. Race: Caucasica Hb:

Spirometry		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
VC	Liters	3.25	1.47	45			
FVC	Liters	3.15	1.36	43			
FEV1	Liters	2.40	0.42	18			
FEV1/FVC	%	74	31				
FEV1/SVC	%	82	29				
PEF	L/sec	7.02	1.67	24			
FEF25-75%	L/sec	2.72	0.15	6			
FEF25%	L/sec	6.31	0.27	4			
FEF50%	L/sec	3.56	0.17	5			
FEF75%	L/sec	1.02	0.09	9			

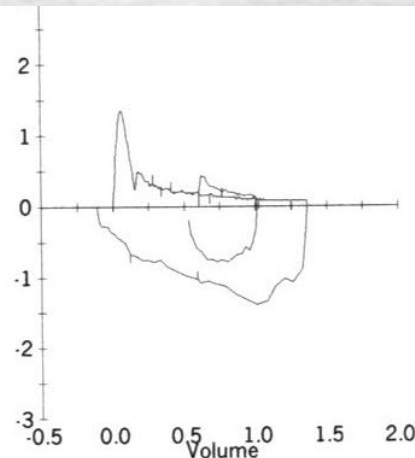
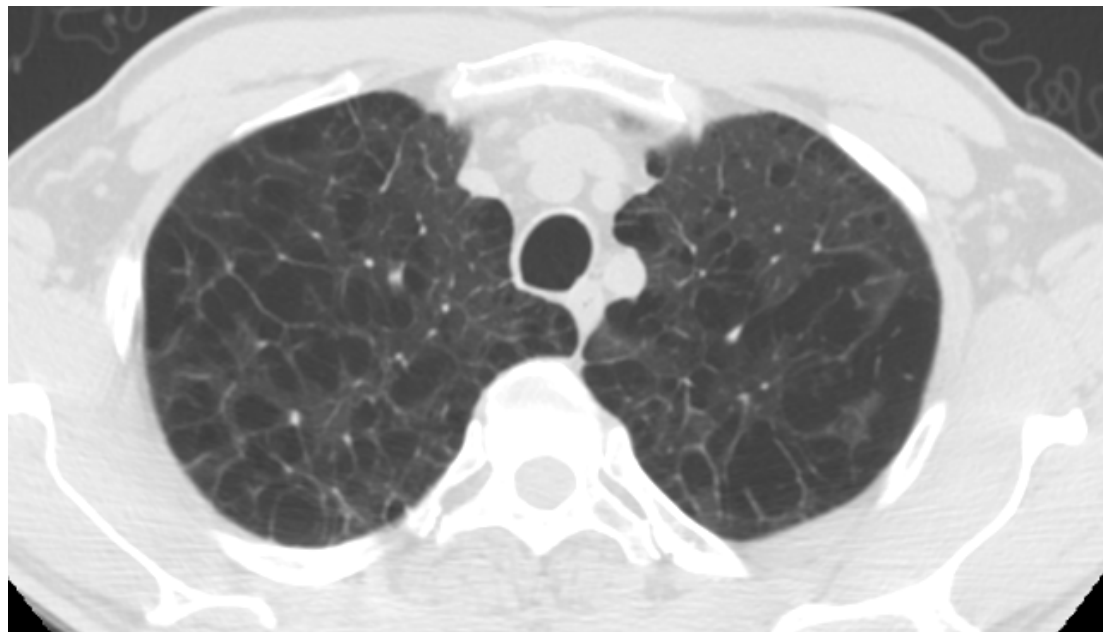
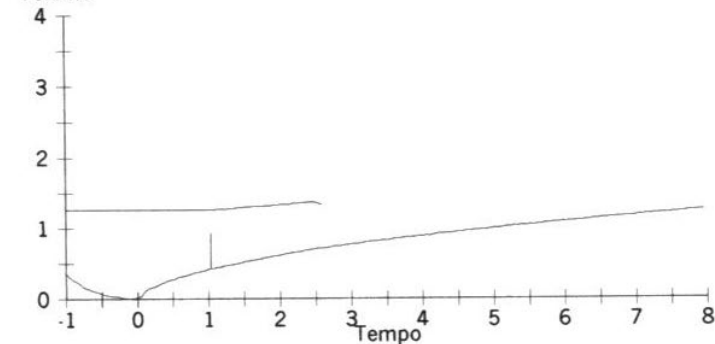
Lung Volumes				
TLC	Liters	5.94	7.61	128
RV	Liters	2.51	6.14	244
RV/TLC	%	42	81	
FRC PL	Liters	3.38	6.87	203
Raw	cmH2O/L/sec	<2.24	13.49	
sRaw	cmH2O/L/s/L		87.29	

Diffusion				
DLCO	mL/mmHg/min	21.7	3.2	15
DL Adj	mL/mmHg/min	21.7	3.2	15
DLCO/VA	mL/mHg/min/L	3.65	1.65	45
DLVA Adj	mL/mHg/min/L	3.65	1.65	45
VA	Liters	5.94	1.95	33

Maximal Respiratory Pressures

PI max	cmH2O	103
PE max	cmH2O	193

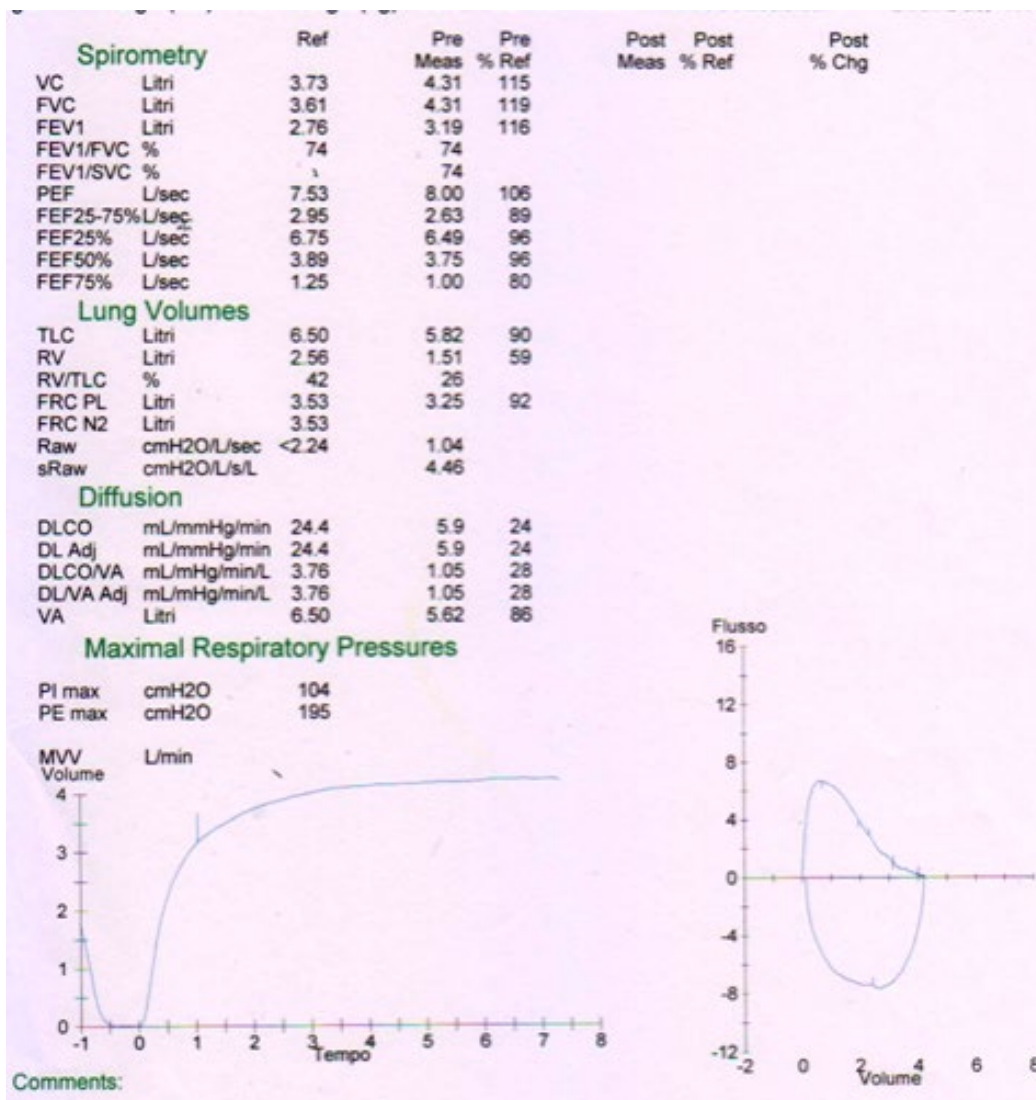
MVV	L/min	77
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Enfisema

Comments:

Pseudonormalizzazione spirometrica



Volumi statici e dinamici nella norma
Severa riduzione della DLCO

CEPF



Necessità di interpretare le prove funzionali alla luce delle immagini TC



Test da sforzo: severità e prognosi in PAH

Table 15 Recommendations for evaluation of the severity of pulmonary arterial hypertension and clinical response to therapy

Recommendations	Class ^a	Level ^b	Ref. ^c
It is recommended to evaluate the severity of PAH patients with a panel of data derived from clinical assessment, exercise tests, biochemical markers and echocardiographic and haemodynamic evaluations (Tables 13 and 14)	I	C	96,97,99
It is recommended to perform regular follow-up assessments every 3–6 months in stable patients (Table 14)	I	C	98
Achievement/maintenance of a low-risk profile (Table 13) is recommended as an adequate treatment response for patients with PAH	I	C	96–99
Achievement/maintenance of an intermediate-risk profile (Table 13) should be considered an inadequate treatment response for most patients with PAH	IIa	C	96–99

Determinants of prognosis* (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%

Test da sforzo: severità e follow up in PAH

Table 15 Recommendations for evaluation of the severity of pulmonary arterial hypertension and clinical response to therapy

Recommendations	Class ^a	Level ^b	Ref. ^c
It is recommended to evaluate the severity of PAH patients with a panel of data derived from clinical assessment, exercise tests, biochemical markers and echocardiographic and haemodynamic evaluations (Tables 13 and 14)	I	C	96,97, 99
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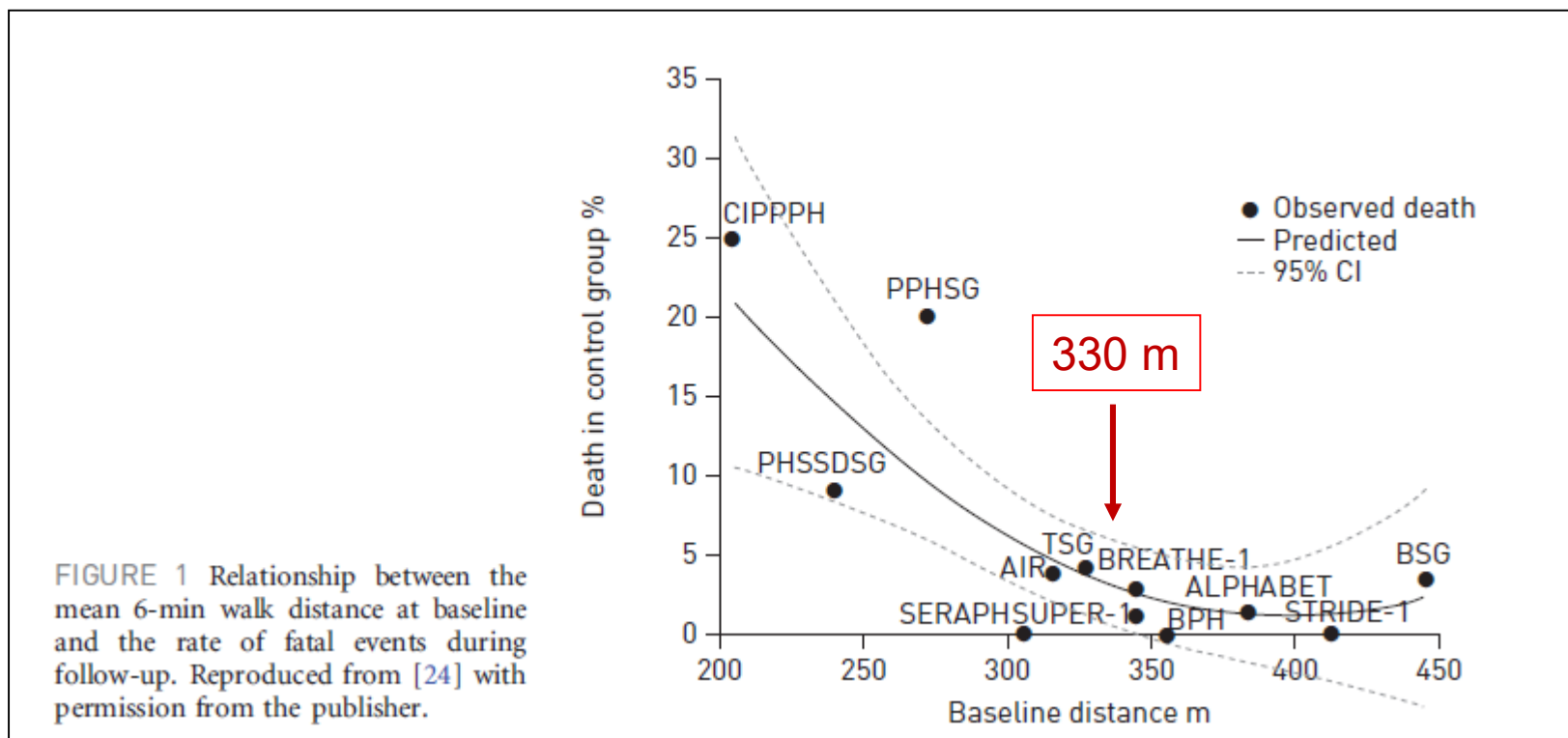
Table 14 Suggested assessment and timing for the follow-up of patients with pulmonary arterial hypertension

	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	+		+		+*
Echo	+		+	+	+
Basic lab ^b	+	+	+	+	+
Extended lab ^c	+		+		+
Blood gas analysis ^d	+		+	+	+
Right heart catheterization	+		+ ^f	+*	+*

6MWT

- **Semplice, poco costoso, accettato da autorità regolatorie (sintomi e capacità funzionale)**
- **Primo end-point utilizzato in primo trial su terapia PAH-specifica (epoprostenolo)**
- **End-point primario più usato (bosentan, ambrisentan, sildenafil, tadalafil, treprostinil....)**
- **Dati basali associati a prognosi**

6MWT e prognosi in PAH



Determinants of prognosis ^a (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
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Predicting Survival in Pulmonary Arterial Hypertension

Insights From the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL)

Raymond L. Benza, MD; Dave P. Miller, MS; Mardi Gomberg-Maitland, MD, MSc;
 Robert P. Frantz, MD; Aimee J. Foreman, MA; Christopher S. Coffey, PhD; Adaani Frost, MD;
 Robyn J. Barst, MD; David B. Badesch, MD; C. Gregory Elliott, MD;
 Theodore G. Liou, MD; Michael D. McGoon, MD



The need to move from 6-minute walk distance to outcome trials in pulmonary arterial hypertension

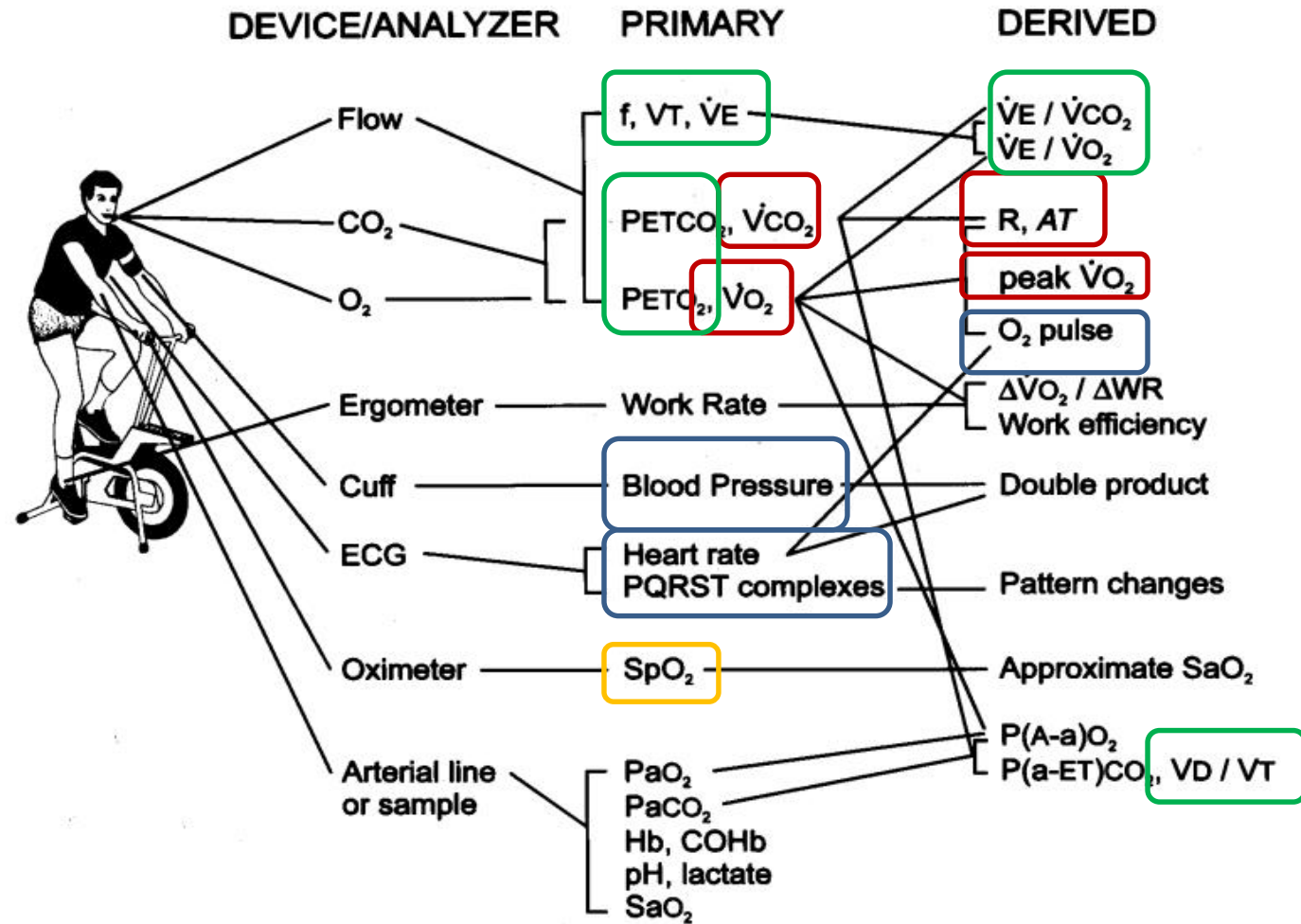
Sean Gaine¹ and G  rald Simonneau²

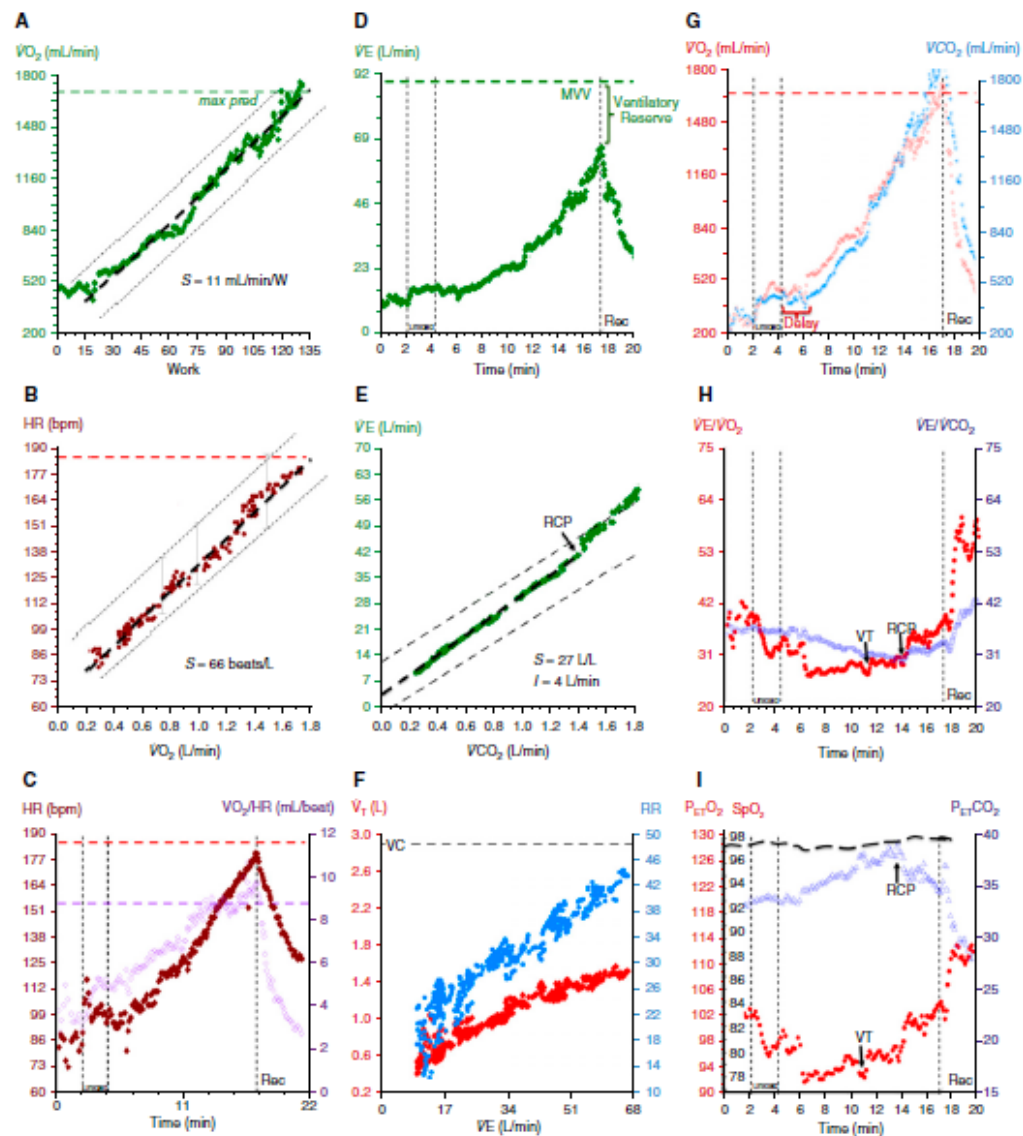
- «ceiling effect»
- Poco specifico (frailty, decondizionamento,...)
- Poco utile in «add-on» terapia
- *Nessuna informazione sulla fisiopatologia*

CPET

PARAMETRI:

- metabolici
- cardiaci
- respiratori





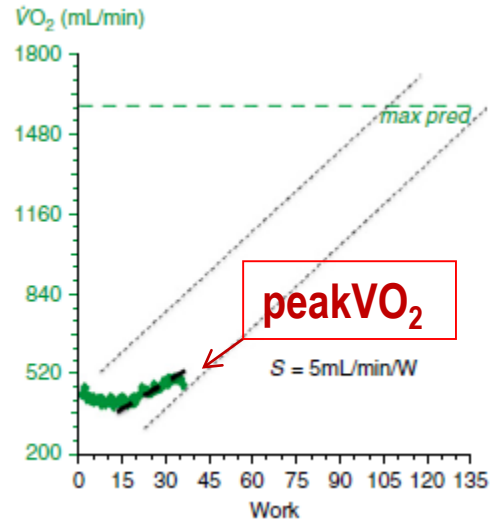
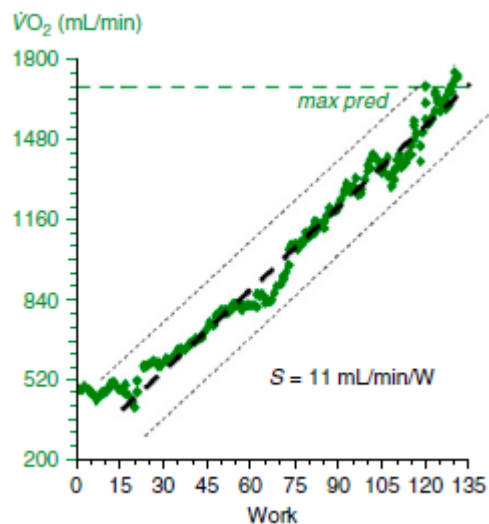
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Exercise Intolerance in Pulmonary Arterial Hypertension

The Role of Cardiopulmonary Exercise Testing

J. Alberto Neder^{1,3}, Roberta P. Ramos^{1,2}, Jaqueline S. Ota-Arakaki², Daniel M. Hirai^{1,3}, Christine L. D'Arsigny⁴, and Denis O'Donnell⁴



Test da sforzo cardiopolmonare: peakVO₂

PAH

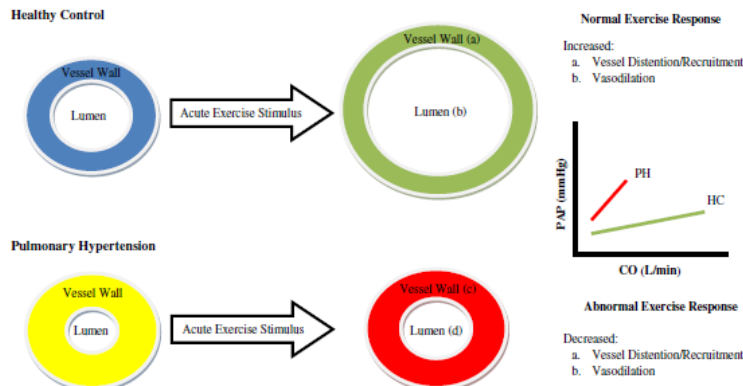
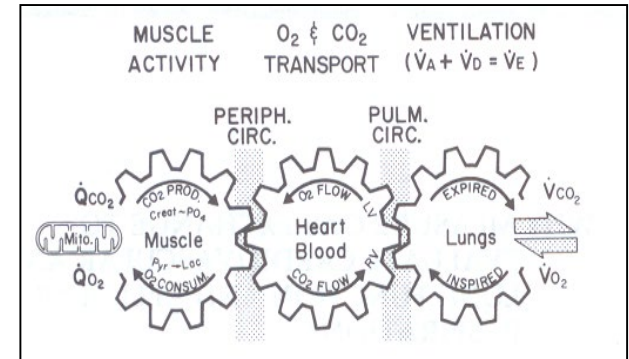
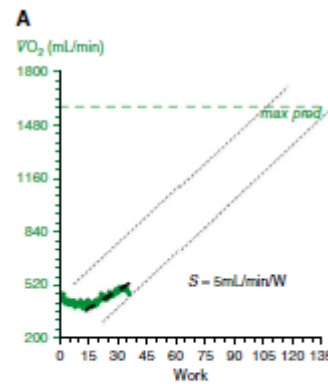
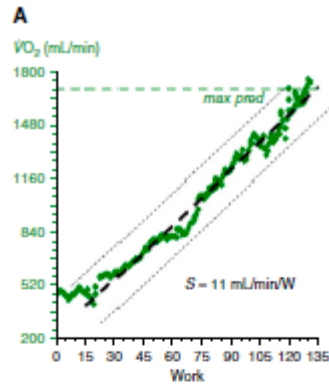
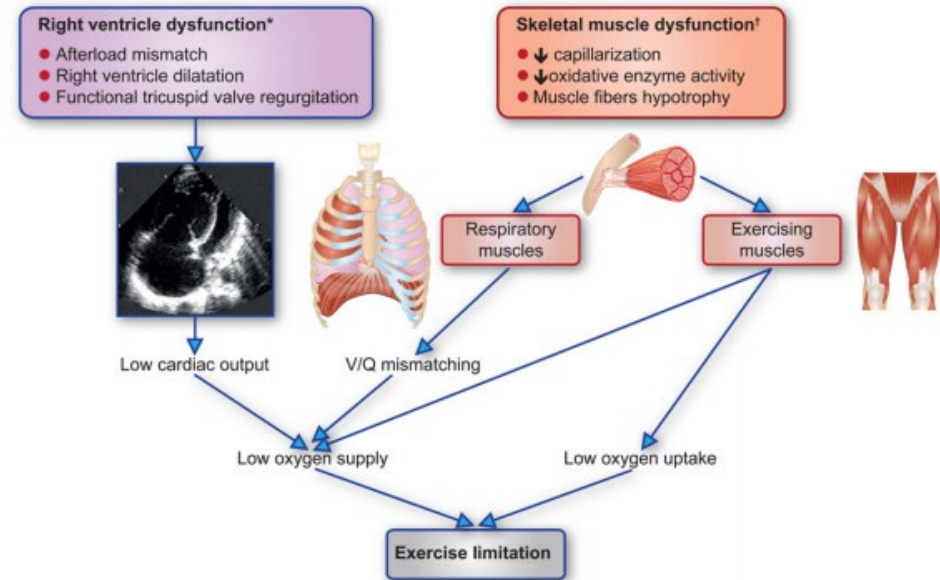


Fig 1 - Comparison between normal and abnormal pulmonary arterial vessel response to acute exercise. Abbreviations: CO, cardiac output; HC, healthy control; PAP, pulmonary artery pressure; PH, pulmonary hypertension.



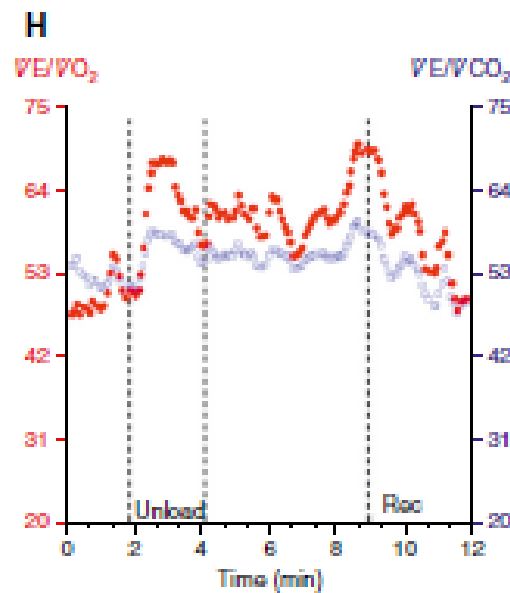
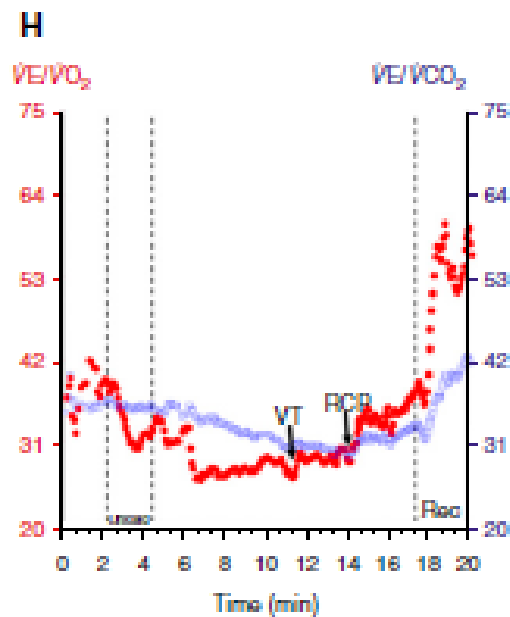
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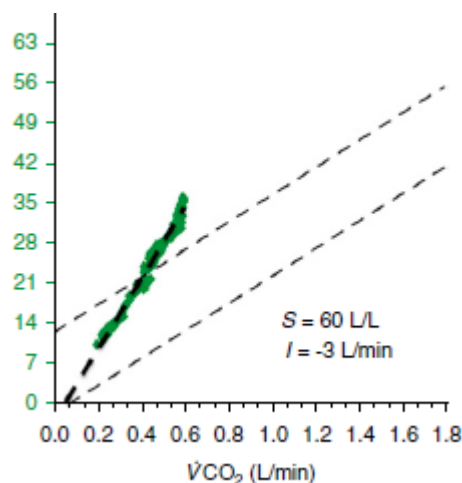
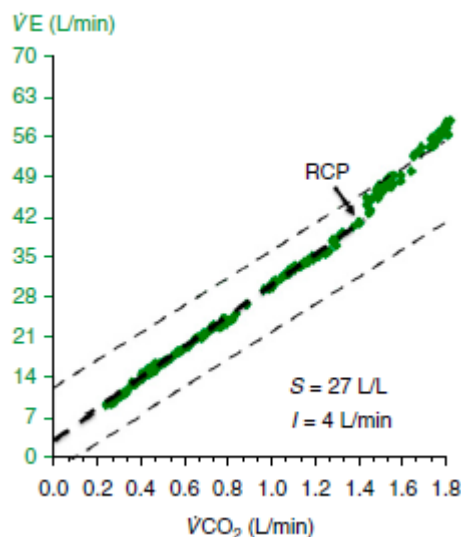
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$$VE = \frac{VCO_2 \times 863}{[PaCO_2 \times (1 - VD/VT)]}$$



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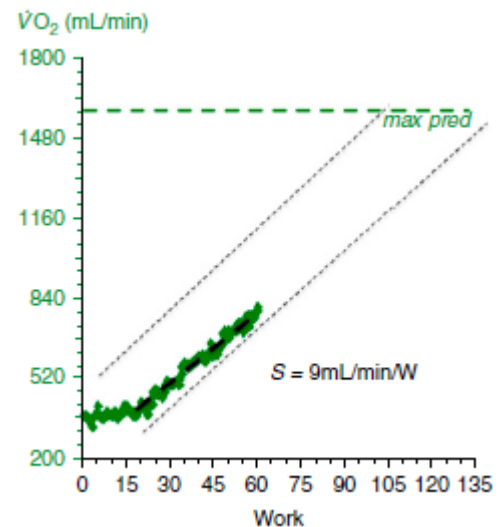
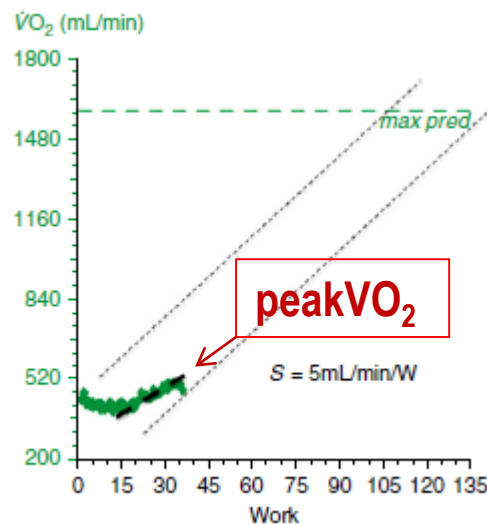
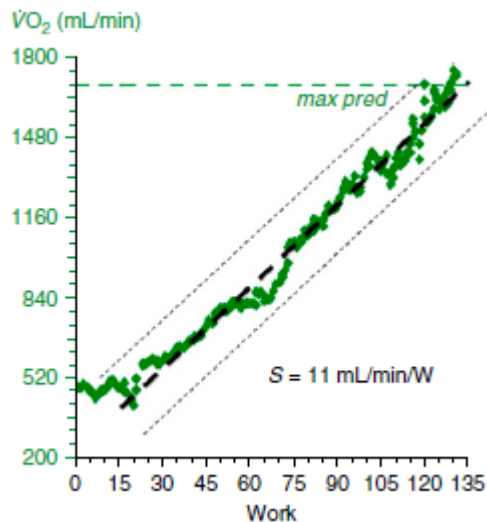
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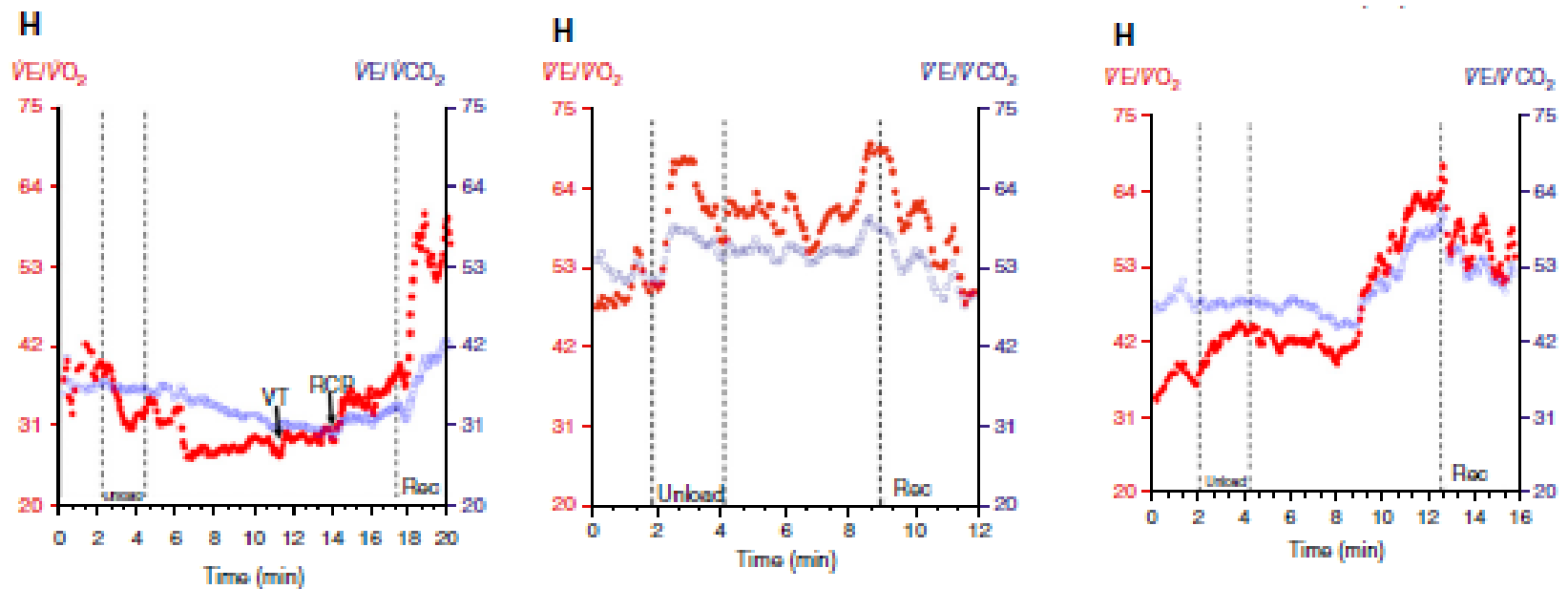
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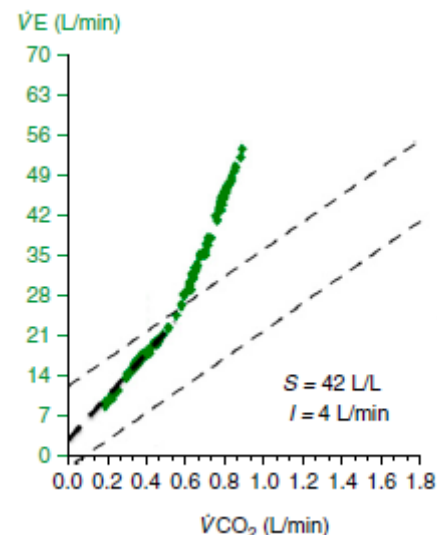
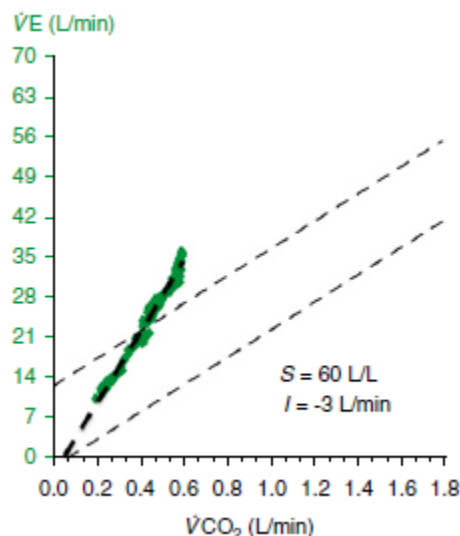
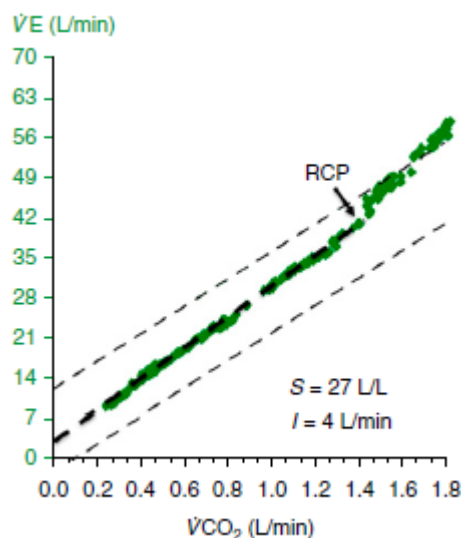
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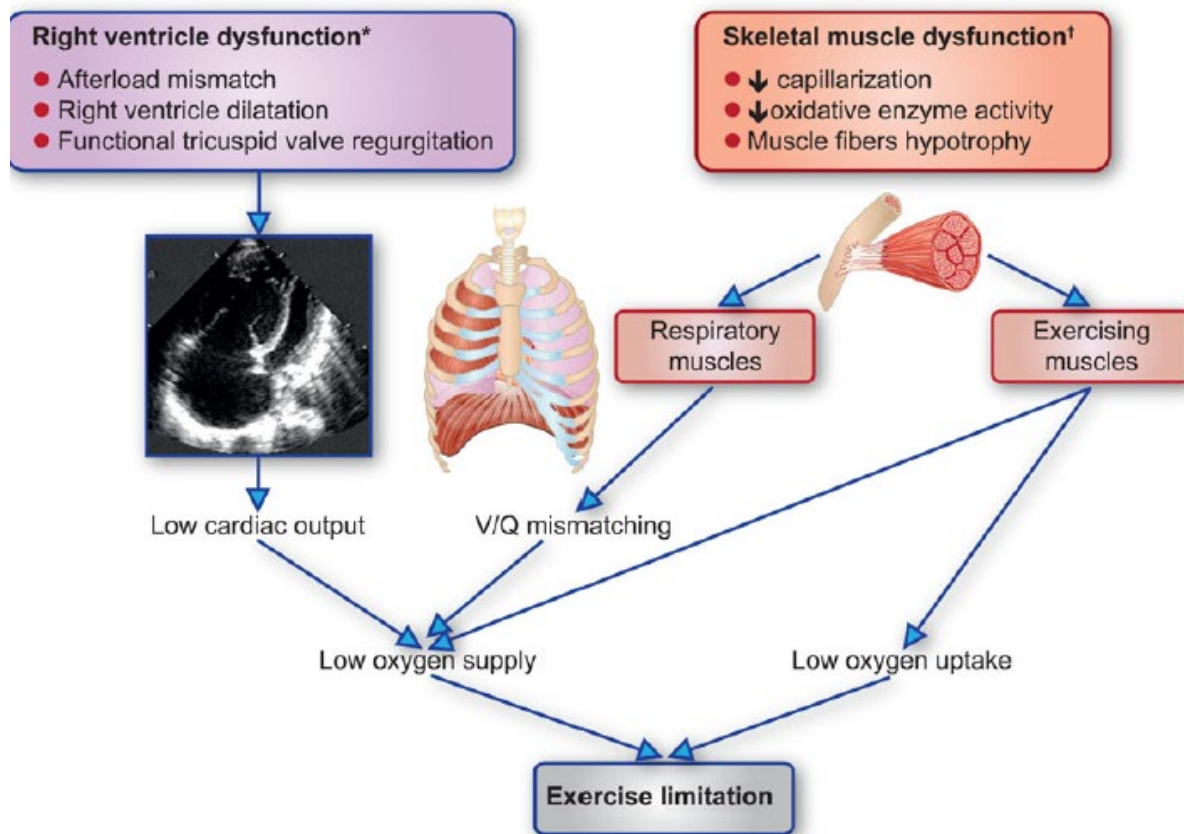
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Exercise training in pulmonary hypertension: improving performance but waiting for outcome

Nazzareno Galie^{1*}, Alessandra Manes², and Massimiliano Palazzini¹



*Improved by approved drug therapy by reducing right ventricular afterload

†Improved by exercise training by increasing capillary density and oxidative enzyme activity

Grazie!

