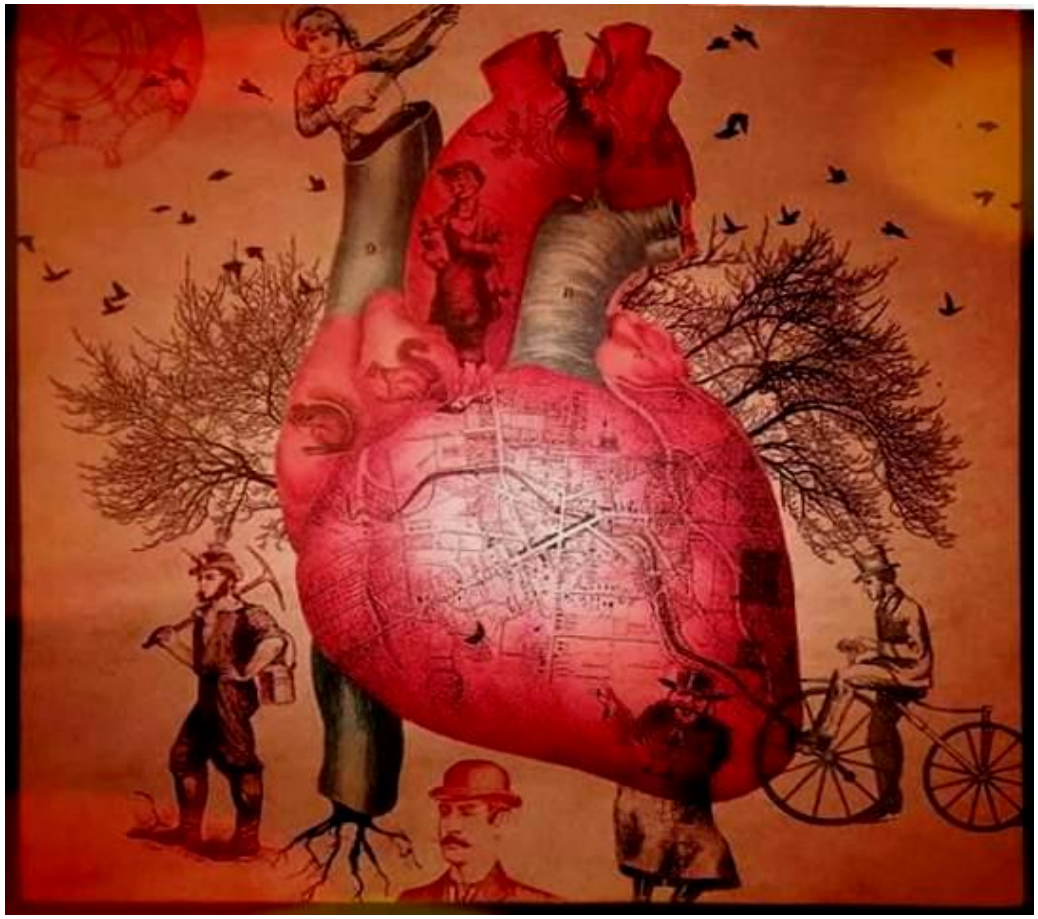
1ο Πανελλήνιο Συνέδριο Πνευμονικής Υπέρτασης



Σταγάκη Ελένη

Πνευμονολόγος, Εντατικολόγος

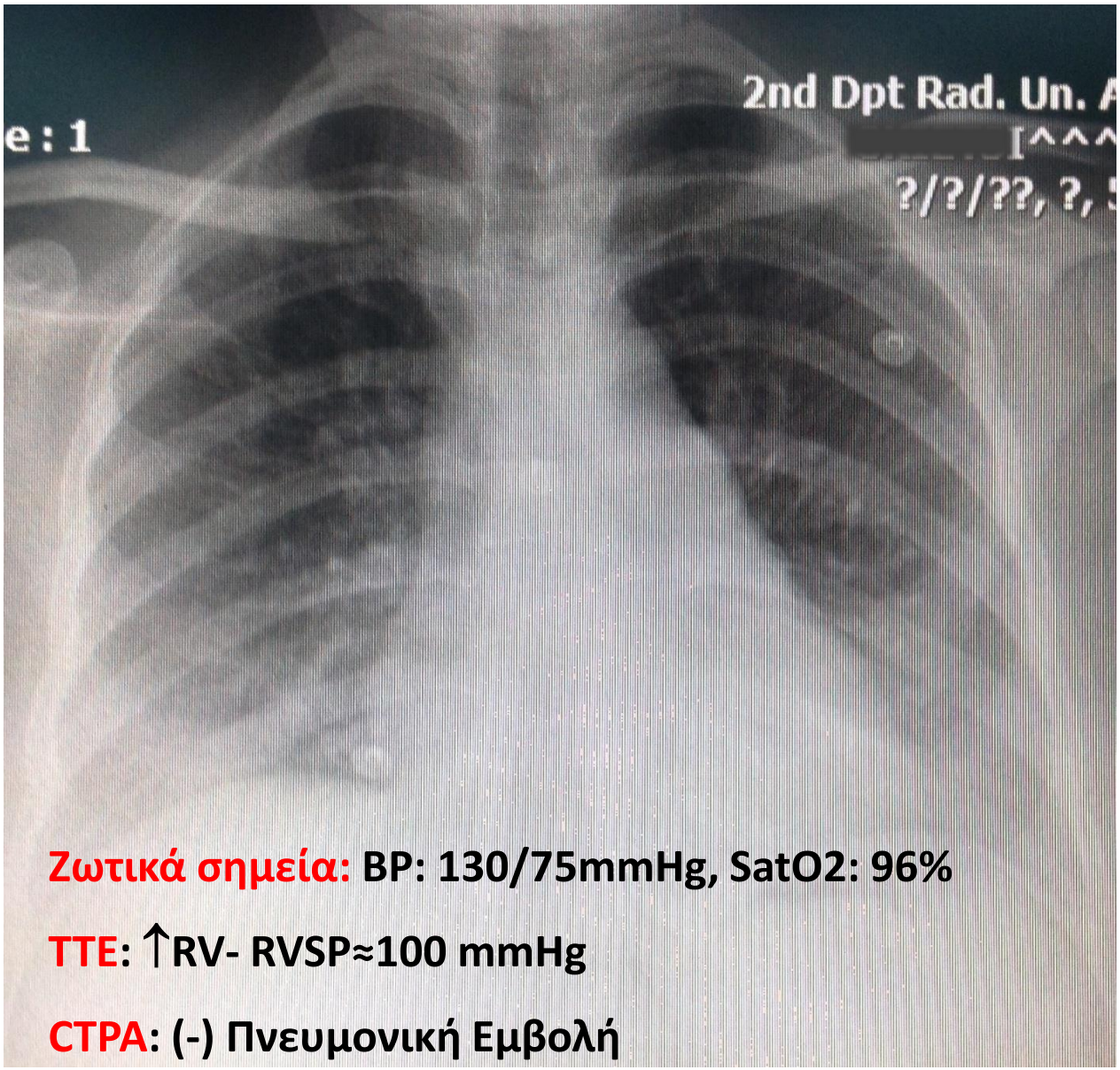
Επιστημονική Συνεργάτις Διακλινικού Ιατρείου ΠΥ ΠΓΝ «Αττικόν»

Παρουσίαση περιστατικού

♀ 31y, μη καπνίστρια,
μητέρα ενός αγοριού 7ετών

Με ατομικό αναμνηστικό
Σκλήρυνση κατά πλάκας (2009)/ INF-b (2010)

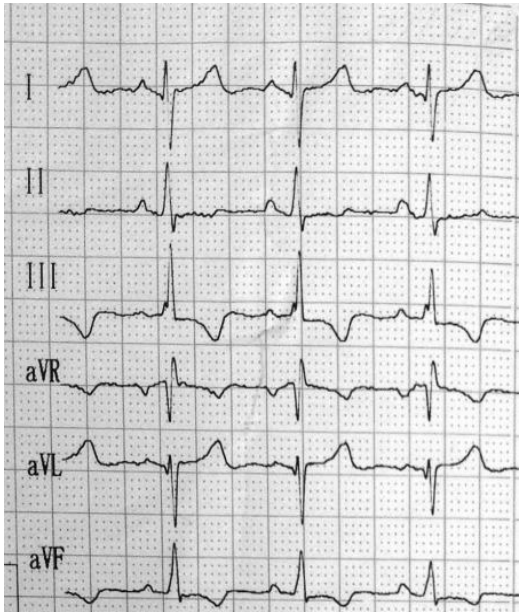
8 Νοε 2015
ΤΕΠ ΠΓΝ «ΑΤΤΙΚΟΝ» για προσυγκοπτικό επεισόδιο
Προσυγκοπτικά επεισόδια 2y
Δύσπνοια επιδεινούμενη, θωρακαλγία στην κόπωση 3m

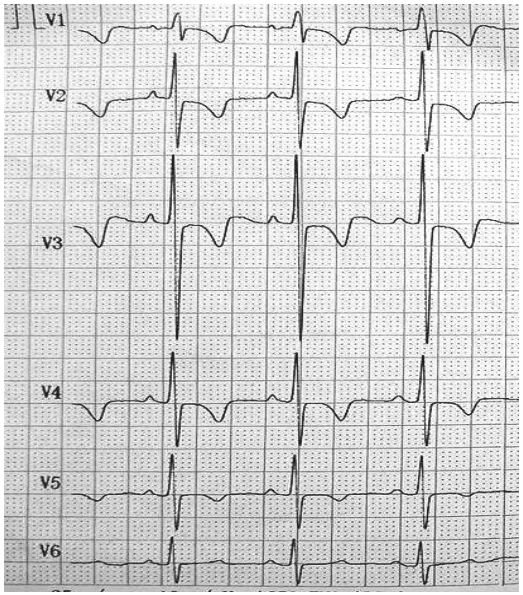


Ζωτικά σημεία: BP: 130/75mmHg, SatO2: 96%

TTE: ↑RV- RVSP≈100 mmHg

CTPA: (-) Πνευμονική Εμβολή





Παραπέμπεται στο ιατρείο Πνευμονικής Υπέρτασης

Διερεύνηση

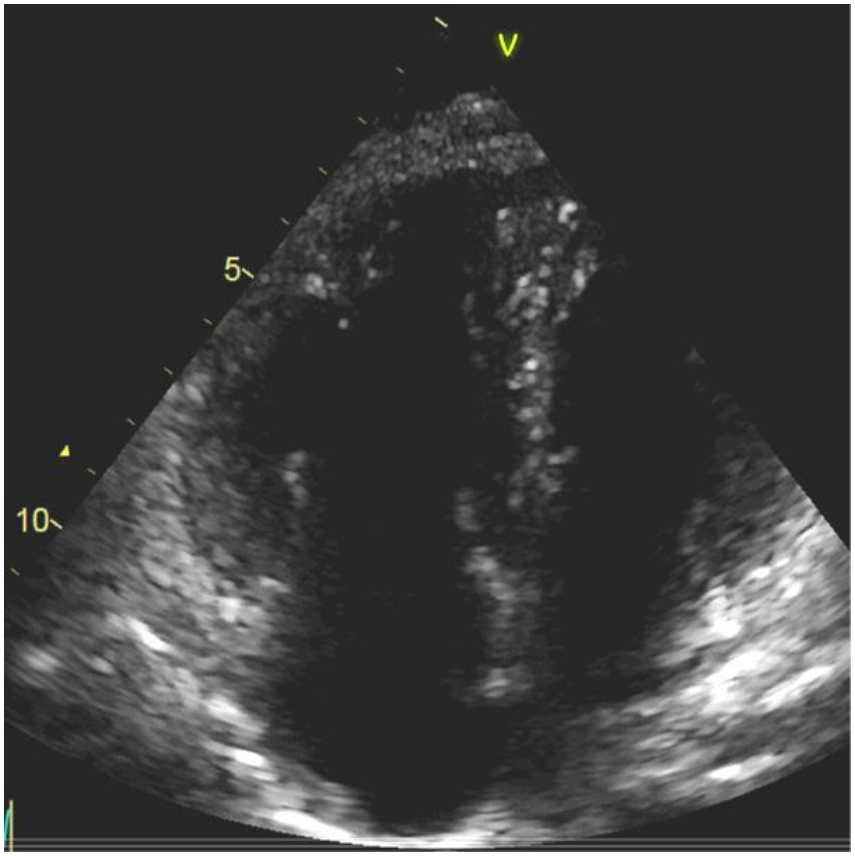
Παρούσα κατάσταση

WHO class	III
6MWT	312m

Echocardiography

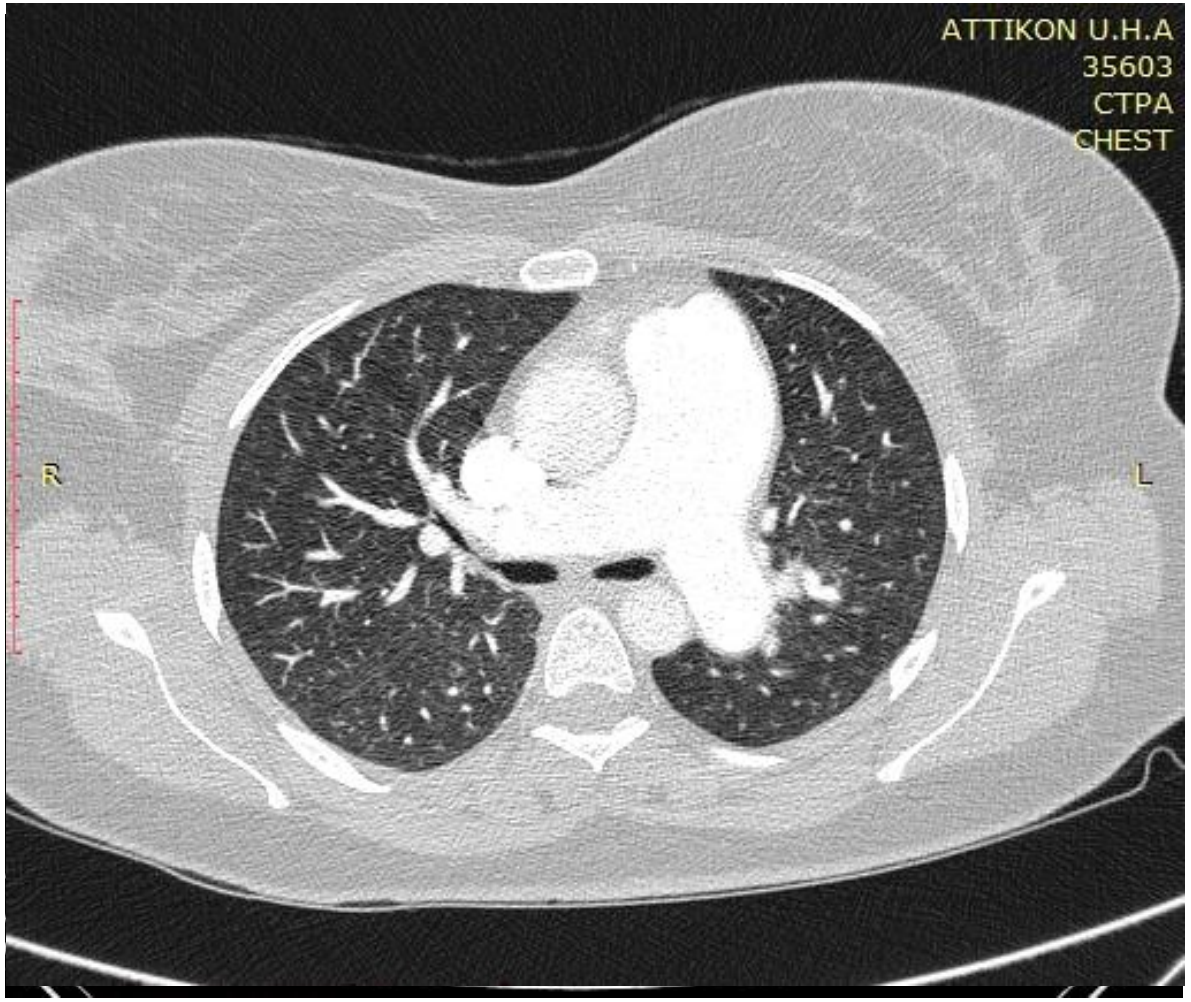
TRVmax	4,8	m/s
RVSP	95	mmHg
TAPSE	16	mm

Διάταση RV
Με διάχυτη υποκινησία
D-shape LV



Διερεύνηση

PFT's εφο
DLCO 72 %
pro BNP 182 pg/ml



Χωρίς ιδιαίτερα ευρήματα από:
Q scanning πνευμόνων
Απλό εργαστηριακό ανοσολογικό, θυρεοειδικό
HIV (-)

Διερεύνηση

RHC 1

RHC -1		Results
RAP	(mmHg)	5
PAP	(mmHg)	74/42/53
PAWP	(mmHg)	10
CO	(l/min)	3.3
CI	(l/min/m²)	1.9
PVR	(Wood Units)	13
SvO2	(%)	78

Test αγγειοδραστικότητας (-)
(iv epoprostenol- 12ng/kg/min)

Clinical classification of Pulmonary Hypertension (ESC/ERS guidelines 2015)

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

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

Table 7 Updated risk level of drugs and toxins known to induce pulmonary arterial hypertension

Definite	Likely	Possible
• Aminorex • Fenfluramine • Dexfenfluramine • Toxic rapeseed oil • Benfluorex • Selective serotonin reuptake inhibitors[a]	• Amphetamines • Dasatinib • L-tryptophan • Methamphetamines	• Cocaine • Phenylpropanolamine • St John's Wort • Amphetamine-like drugs • Interferon α and β • Some chemotherapeutic agents such as alkylating agents (mytomycine C, cyclophosphamide)[b]

[a]Increased risk of persistent pulmonary hypertension in the newborns of mothers with intake of selective serotonin reuptake inhibitors.
[b]Alkylating agents are possible causes of pulmonary veno-occlusive disease.

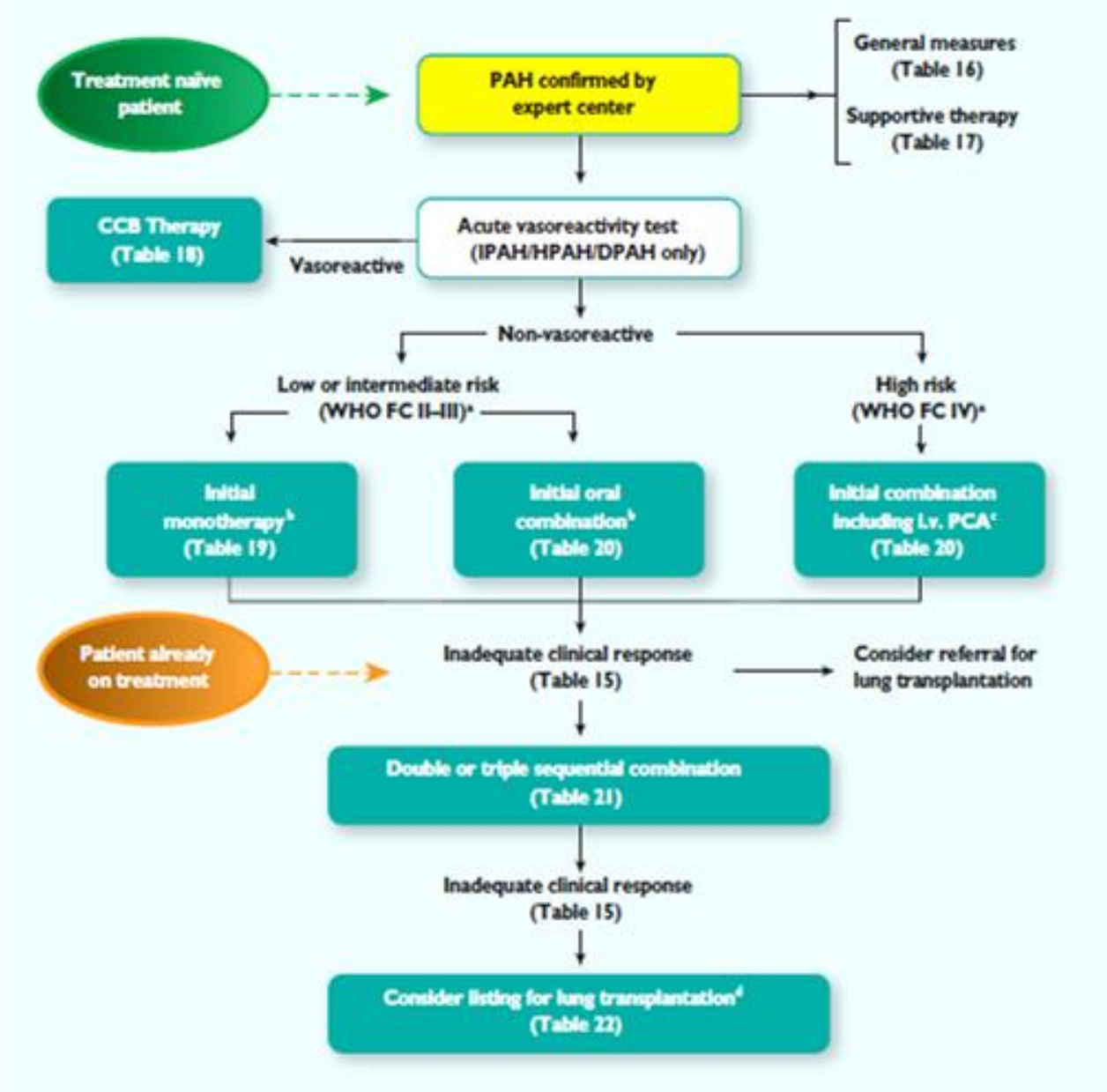
PH guidelines 2015

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 ≥45
NT-proBNP plasma levels	BNP <50 ng/l * NT-proBNP <300 ng/ml	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%

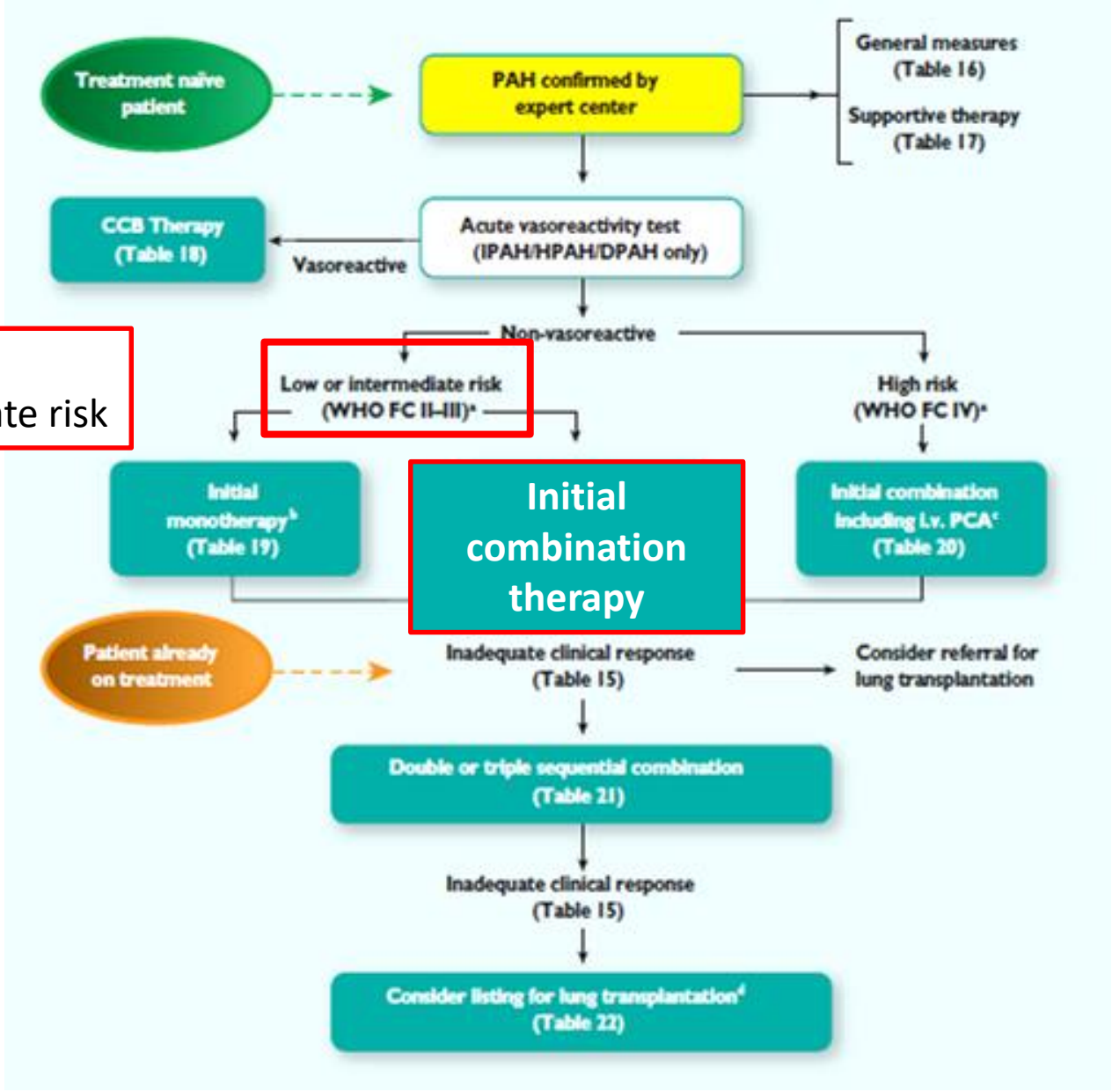
ESC/ERS PH guidelines 2015

Evidence based treatment algorithm for PAH patients



Evidence based treatment algorithm for PAH patients

WHO-FC III
Intermediate risk



Θεραπεία

Measure/ treatment	Class[a]-Level[b]						Ref.[c]
	WHO-FC II		WHO-FC III		WHO-FC IV		
Ambrisentan + tadalafil[d]	I	B	I	B	IIb	C	247
Other ERA + PDE-5i	IIa	C	IIa	C	IIb	C	-
Bosentan + sildenafil + i.v. epoprostenol	-	-	IIa	C	IIa	C	246
Bosentan + i.v. epoprostenol	-	-	IIa	C	IIa	C	198, 245
Other ERA or PDE-5i + s.c. treprostinil			IIb	C	IIb	C	-
Other ERA or PDE-5i + other i.v. prostacyclin analogues			IIb	C	IIb	C	-

1. Διακοπή
Interferone-b

Αντικατάσταση με γκλατιραμέρη(copaxone)

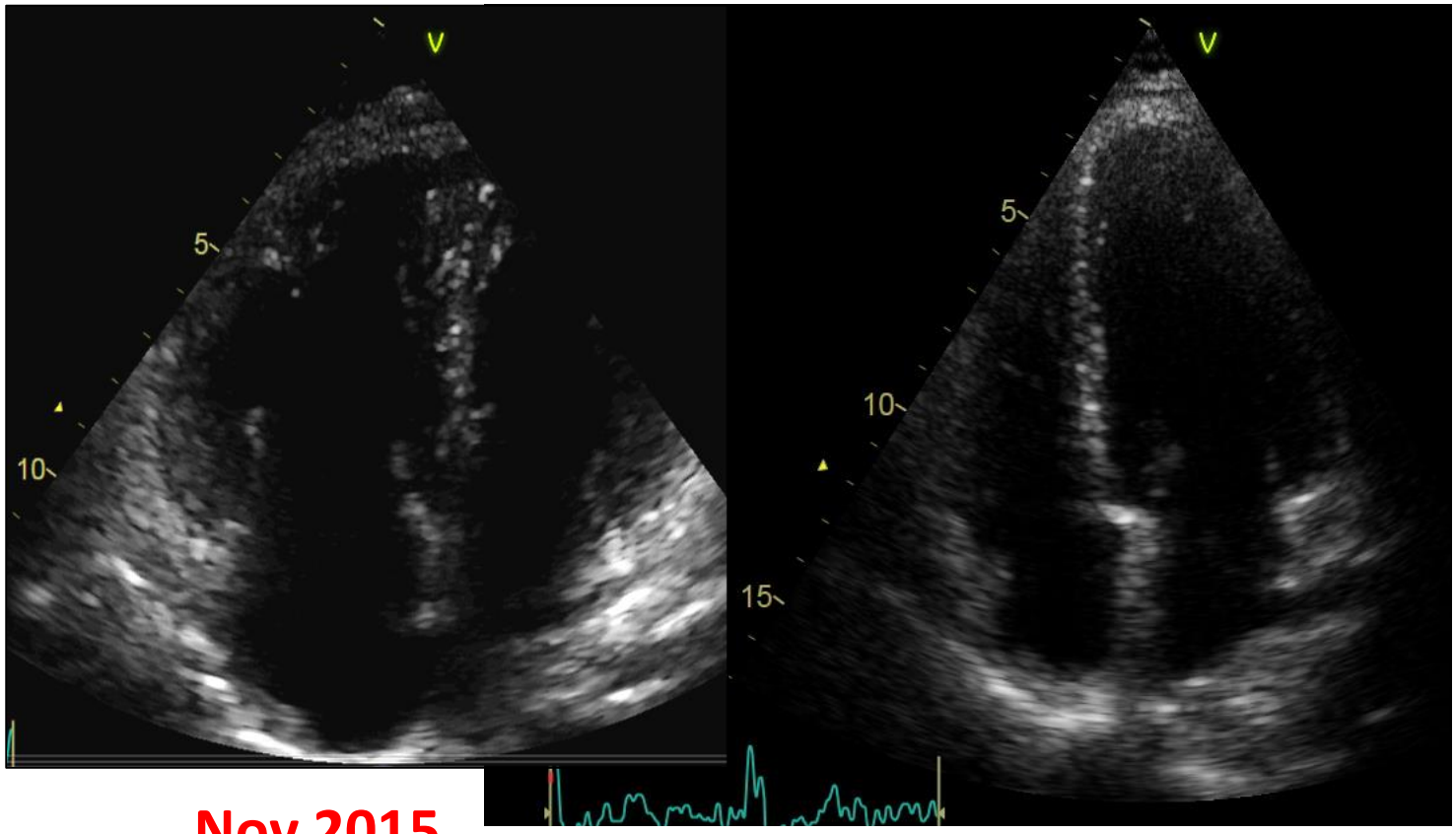
2. 3m
Ambrisentan 10mg
+
Tadalafil 40mg

Recommendations for *efficacy* of initial drug combination therapy for PAH (group 1) according to WHO FC

Παρακολούθηση- Follow up

PARAMETERS		Nov 2015	Sep 2016	Feb 2017
NYHA		III	II	II early
6MWT		312	510	536
nT-pro BNP	(pg/ml)	184		32
TTECHO				
TRVmax	(m/s)	4.9	3.6	2.8
RVSP	(mmHg)	95	60	35-40
TAPSE	(mm)	16	21	20
RHC				
RAP	(mmHg)	5	6	
PAP (S/D/m)	(mmHg)	74/42/53	49/21/30	
PAWP	(mmHg)	10	7	
CO	(l/min)	3.3	6.5	
CI	(l/min/m²)	1.9	3.8	
PVR	WU	13 →	3.5	
SVO2	(%)	78	82	

Παρακολούθηση- Follow up

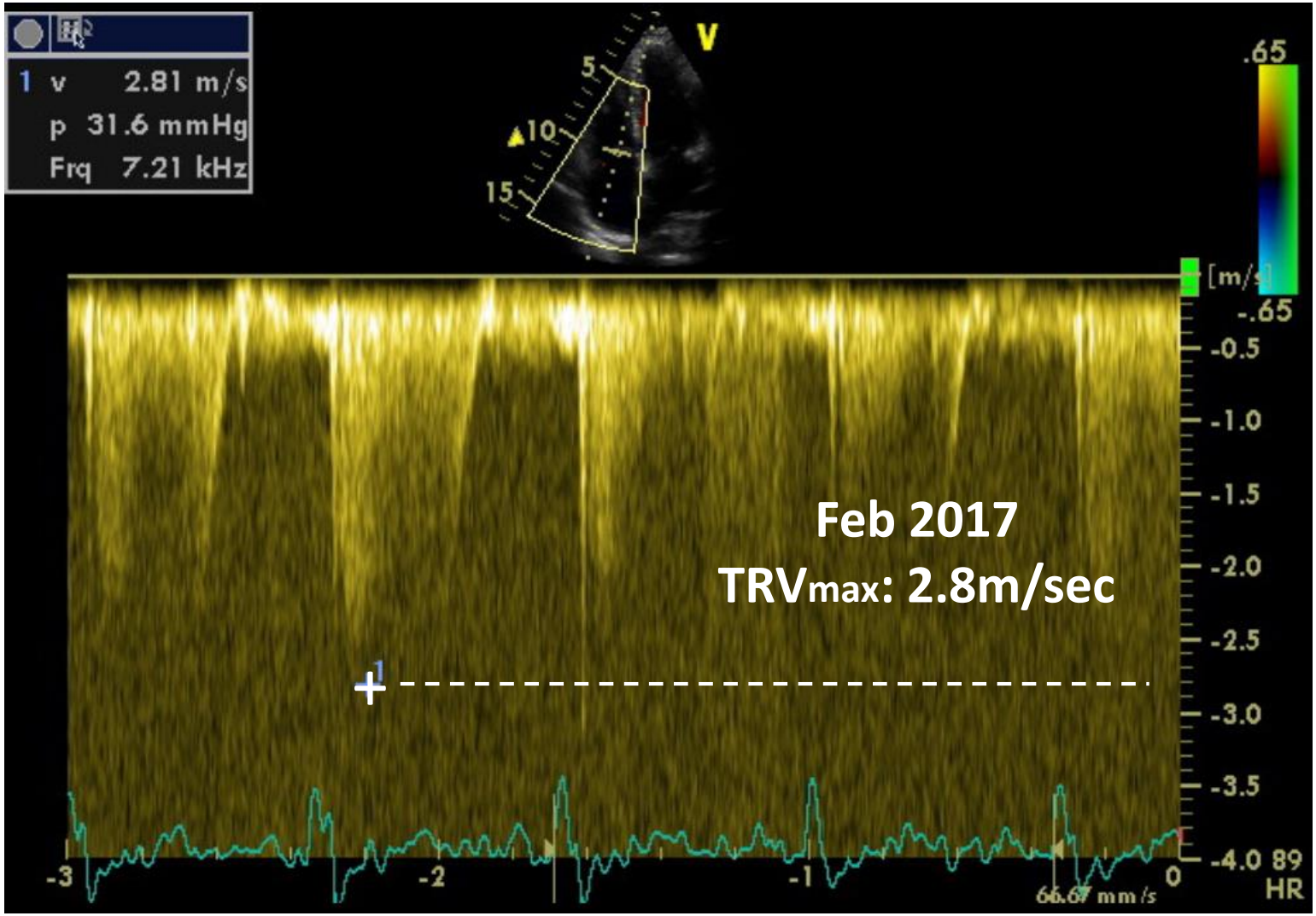


Nov 2015

Feb 2017

BYLYRE13FEB24.wmv

Παρακολούθηση- Follow up



Risk assessment 2

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 ≥45
NT-proBNP plasma levels	BNP <50 ng/l * NT-proBNP <300 ng/ml	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%

Συζήτηση-Υπάρχουσα Βιβλιογραφία

Γυναίκα με ΠΑΥ από interferone-b, με σχεδόν πλήρη αναστροφή μετά τη διακοπή του triggering factor και θεραπεία με συνδυασμό ειδικών για ΠΑΥ φαρμάκων

MULTIPLE SCLEROSIS JOURNAL | MSJ

Cardic

Case report

Short Report

Interferon beta-1a long-term therapy related to pulmonary arterial hypertension in multiple sclerosis patients

Anthony Fok, Trevor Williams, Catriona A McLean and Ernest Butler

Pulmonary arterial hypertension in patients treated with interferon

Laurent Savale, Marie-Camille Chaumais, Olivier Sitbon, Marc Humbert

European Respiratory Journal 2015 46: 1851-1853; **DOI:** 10.1183/13993003.01376-2015

Govern EM[1], Judge EP[2], Kavanagh E[3], Gaine S[2], Lynch T[4].

Gibbons E, Promislow S, Davies RA, Chandy G, Stewart DJ, Vladamir CD, Pugliese C, Dunne R, Mielniczuk LM.

Interferon-induced pulmonary hypertension: an update

Current Opinion in Pulmonary Medicine. 22(5):415–420, SEP 2016

Laurent Savale; Marie-Camille Chaumais; and 3 more

References	N°	Delay between IFN-β initiation and PAH diagnosis (years)	Hemodynamics at diagnosis			Outcomes
			mPAP (mmHg)	CO (l/min)	PVR (WU)	
Ledinek *et al.* [7]	1	3	47	3.4	12.3	Improvement on PDE-5i and ERA. No hemodynamic assessment during follow-up
Caravita *et al.* [9]	2	1	69	NA	NA	Improvement on PDE-5i. No hemodynamic assessment during follow-up
Savale *et al.* [8]	3[a]	6	52	9.3	3.1	Near normalization of hemodynamics after ASD closure
	4	5	62	3.59	15.9	Dead
	5	7	52	3.85	11.7	Reversible case[b]
	6	8	69	4.42	11.3	Dramatic Improvement on PDE-5i and ERA.
	7	10	70	1.5	43.3	Dead
Prella *et al.* [12]	8	15	48	2.4	14.5	Near normalization of hemodynamic on ERA and PDE-5i at 6 months
Govern *et al.* [10•]	9	5	52	NA	NA	Reversible case[b]
Gibbons *et al.* [11]	10	3	47	3.25	13.5	Reversible case[b]
Fok *et al.* [14]	11	9	50	4.7	8.27	PAH worsening due to continued use of interferon leading to lung transplantation
	12	7	44	2.8	15.8	Clinical improvement. No hemodynamic assessment during follow-up
Piroddi *et al.* [17]	13	6	NA	NA	NA	Clinical improvement. No hemodynamic assessment during follow-up

Interferon-induced pulmonary hypertension: an update

Current Opinion in Pulmonary Medicine. 22(5):415–420, SEP 2016

Laurent Savale; Marie-Camille Chaumais; and 3 more

References	N°	Delay between IFN-β initiation and PAH diagnosis (years)	Hemodynamics at diagnosis			
			mPAP (mmHg)	CO (l/min)	PVR (W	
Ledinek *et al.* [7]	1	3	47	3.4	12.3	
Caravita *et al.* [8]	2	1	69	NA	NA	
Gibbons *et al.* [11]	10	3	47	3.25	13.5	Reversible case[b]
Fok *et al.* [14]	11	9	50	4.7	8.27	PAH worsening due to continued use of interferon leading to lung transplantation
	12	7	44	2.8	15.8	Clinical improvement. No hemodynamic assessment during follow-up
Piroddi *et al.* [17]	13	6	NA	NA	NA	Clinical improvement. No hemodynamic assessment during follow-up

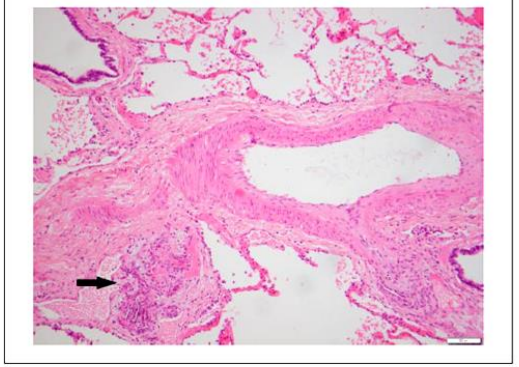


Figure 1. Haematoxylin and eosin–stained section of the explant lung showing intimal and medial hypertrophy with an adjacent plexiform lesion forming (arrow). Magnification 100×.

- **Γυναίκες 100%**
- **«Καθαρά περιστατικά»**
- **Μεγάλος χρόνος για τη διάγνωση → 10 χρόνια**
- **Πολύ σοβαρή ΠΑΥ, Αναστρέψιμη**
- **Πολύ σπάνιο (?)** *Papani et al. Multidisciplinary Respiratory Medicine (2017) 12:1*

Συζήτηση- Take Home Messages

- **Υψηλό δείκτη εγρήγορσης**
  - **Σπάνιο**
  - **Δύσκολη συσχέτιση χρόνου εμφάνισης**
  - **Υποκείμενο νόσημα**
- **Συνεργασία ειδικοτήτων**
- **Κατηγορία που «γέννησε την ΠΥ» και πιθανά στο μέλλον να αποτελέσει ξανά σημαντική κατηγορία ασθενών με ΠΥ**

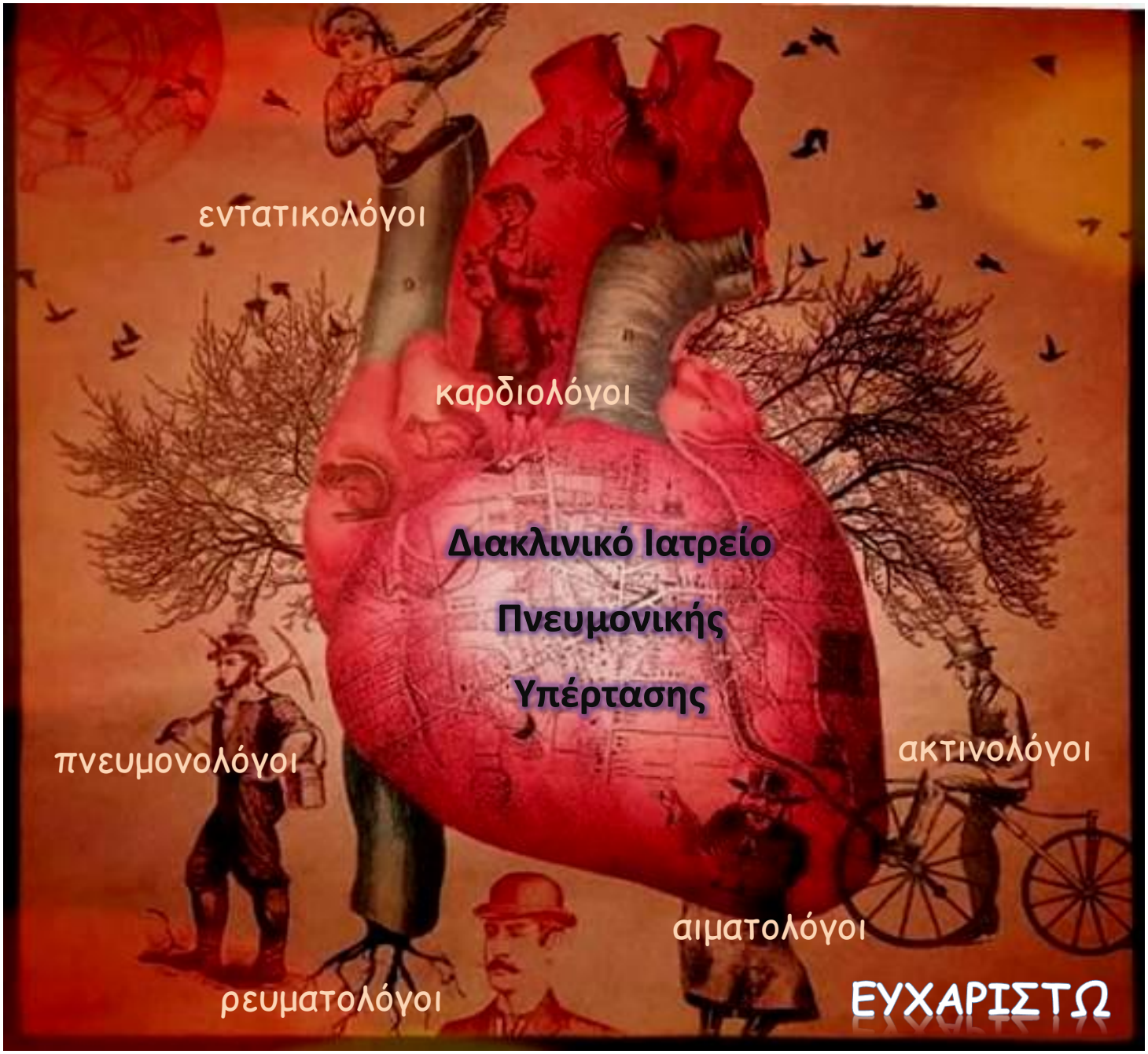
Συζήτηση- Take Home Messages

- **Υψηλό δείκτη εγρήγορσης**
  - **Σπάνιο**
  - **Δύσκολη συσχέτιση χρόνου εμφάνισης**
  - **Υποκείμενο νόσημα**
- **Συνεργασία ειδικοτήτων**
- **Κατηγορία που «γέννησε την ΠΥ» και πιθανά στο μέλλον να αποτελέσει ξανά σημαντική κατηγορία ασθενών με ΠΥ**

Drug-induced pulmonary arterial hypertension: a recent outbreak

David Montani, Andrei Seferian, Laurent Savale, Gérald Simonneau, Marc Humbert

European Respiratory Review 2013 22: 244-250; **DOI:** 10.1183/09059180.00003313


εντατικολόγοι
καρδιολόγοι
Διακλινικό Ιατρείο
Πνευμονικής
Υπέρτασης
πνευμονολόγοι
ακτινολόγοι
αιματολόγοι
ρευματολόγοι
ΕΥΧΑΡΙΣΤΩ