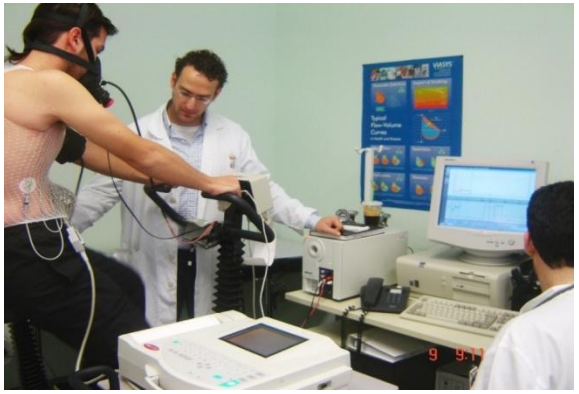
Η εφαρμογή της Καρδιοαναπνευστικής Κόπωσης στην Πνευμονική Αρτηριακή Υπέρταση



Διονυσία Μπίρμπα, Καρδιολόγος, Ακαδημαϊκή Υπότροφος

Ελένη Τριανταφυλλίδη, Διευθύντρια ΕΣΥ Καρδιολογίας

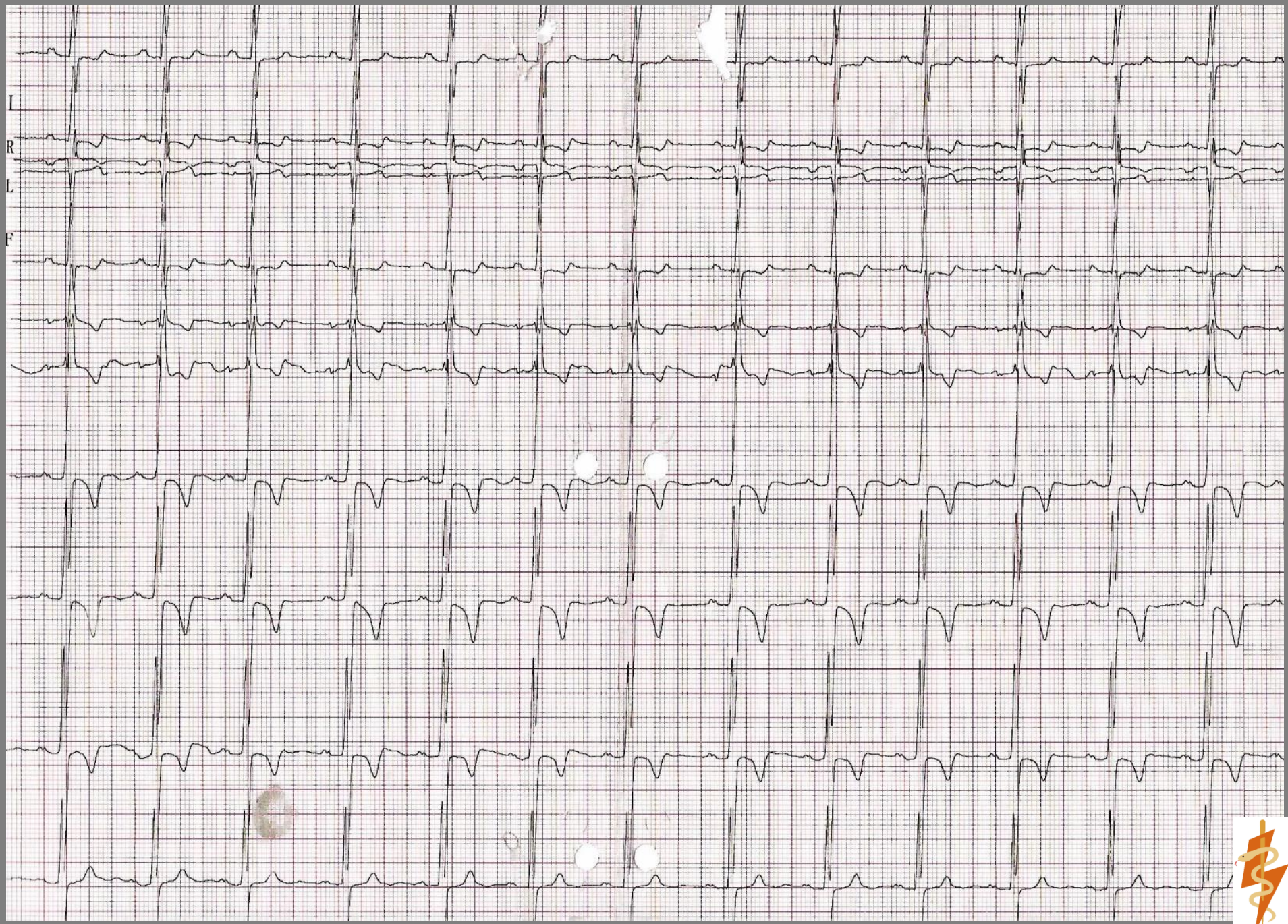
Εργαστήριο Καρδιοαναπνευστικής Κόπωσης

Β΄ Πανεπιστημιακή Καρδιολογική Κλινική

ΑΤΤΙΚΟ Νοσοκομείο

Ιατρικό Ιστορικό

- Άνδρας ασθενής, 20 ετών
- Χειρουργηθείσα μεσοκολπική επικοινωνία σε ηλικία 7 ετών
- Πλέον πρόσφατη προσκομιζόμενη ηχωκαρδιογραφική εκτίμηση (2014):Φυσιολογικές διαστάσεις καρδιακών κοιλοτήτων, ακέραιο μεσοκολπικό διάφραγμα, πνευμονική αρτηρία διατεταμένη= 35 mm, υπολογιζόμενη συστολική πίεση στην πνευμονική αρτηρία 40mmHg.
- Εισαγωγή στο Τζάνειο (11/2018) λόγω συγκοπτικού επεισοδίου
- Παραπομπή στο Αττικό (12/2018) για περαιτέρω διερεύνηση



Βασικός εργαστηριακός έλεγχος και Διερεύνηση αιτίων συγκοπτικού επεισοδίου

- Hct 44%
- Hb 15.7g/dl
- Urea 28 mg/dl
- Cr 0.9 mg/dl
- NT pro- BNP 256 pg/ml
- Troponin 7 pg/ml

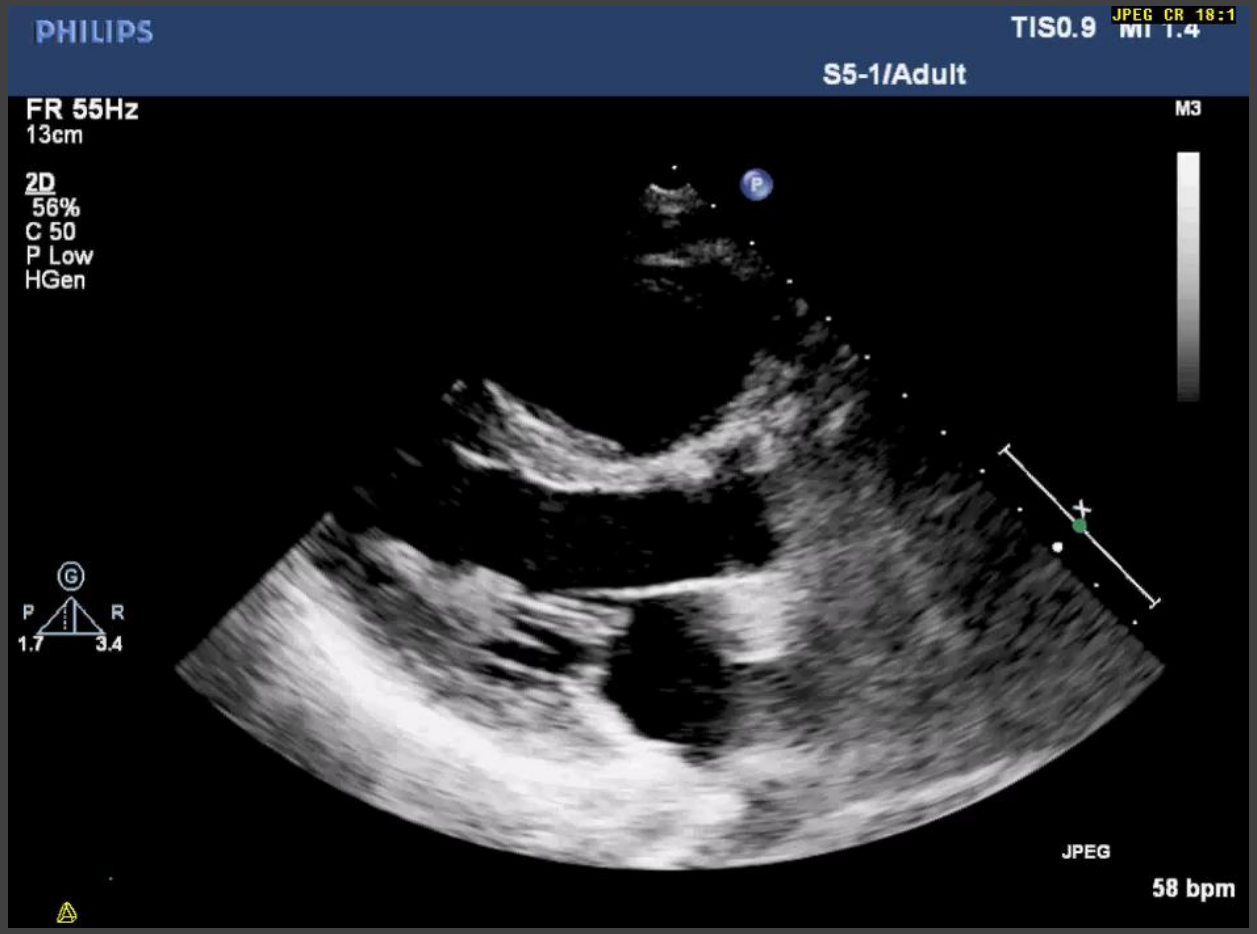
➢**Αξονική εγκεφάλου**: χωρίς παθολογικά ευρήματα

➢**Αξονική θώρακος HRCT**: διατεταμένοι κεντρικοί πνευμονικοί αρτηριακοί κλάδοι με ικανοποιητική σκιαγράφηση χωρίς σαφή ενδοαυλικά ελλείμματα πλήρωσης

➢ **Holter ρυθμού 24ωρου:** χωρίς παθολογικά ευρήματα

Triplex καρδιάς

- Αριστερή κοιλία με φυσιολογικές διαστάσεις-λειτουργία (ΚΕ 55%)
- Συστολο-διαστολική επιπέδωση ΜΚΔ
- Δεξιά κοιλία διατεταμένη (45mm) στην τομή 4 κοιλοτήτων με επηρεασμένη συστολική λειτουργία (TAPSE= 9 mm, S= 5cm/sec)
- Μέτρια ανεπάρκεια τριγλώχινος (RVSP= 100mmHg)
- RA area 20cm^2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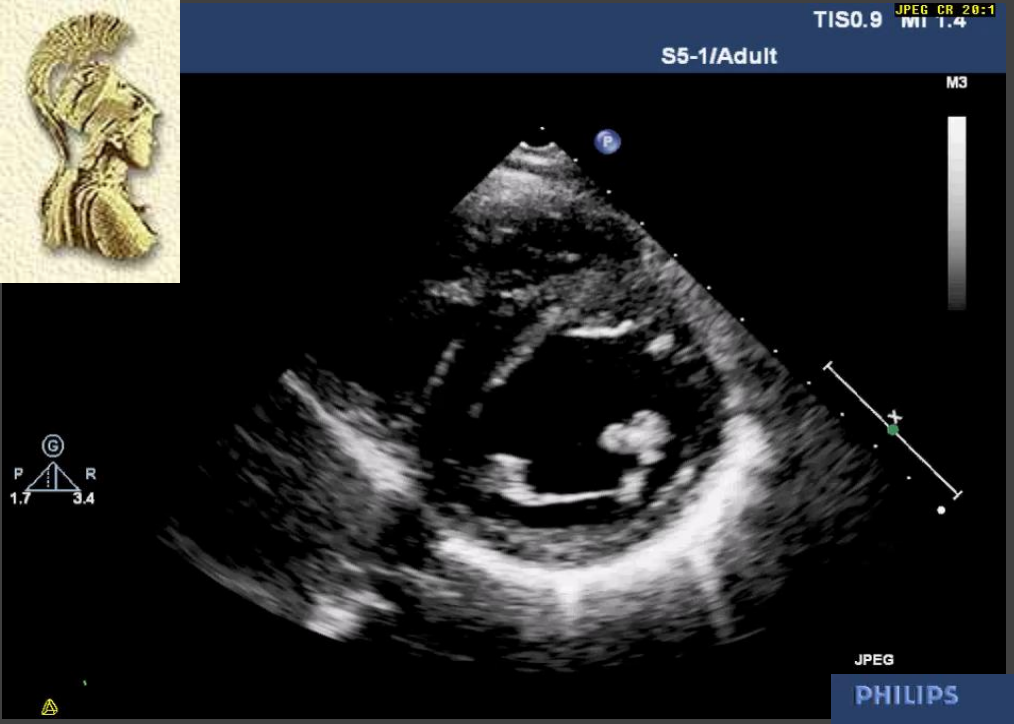
58 bpm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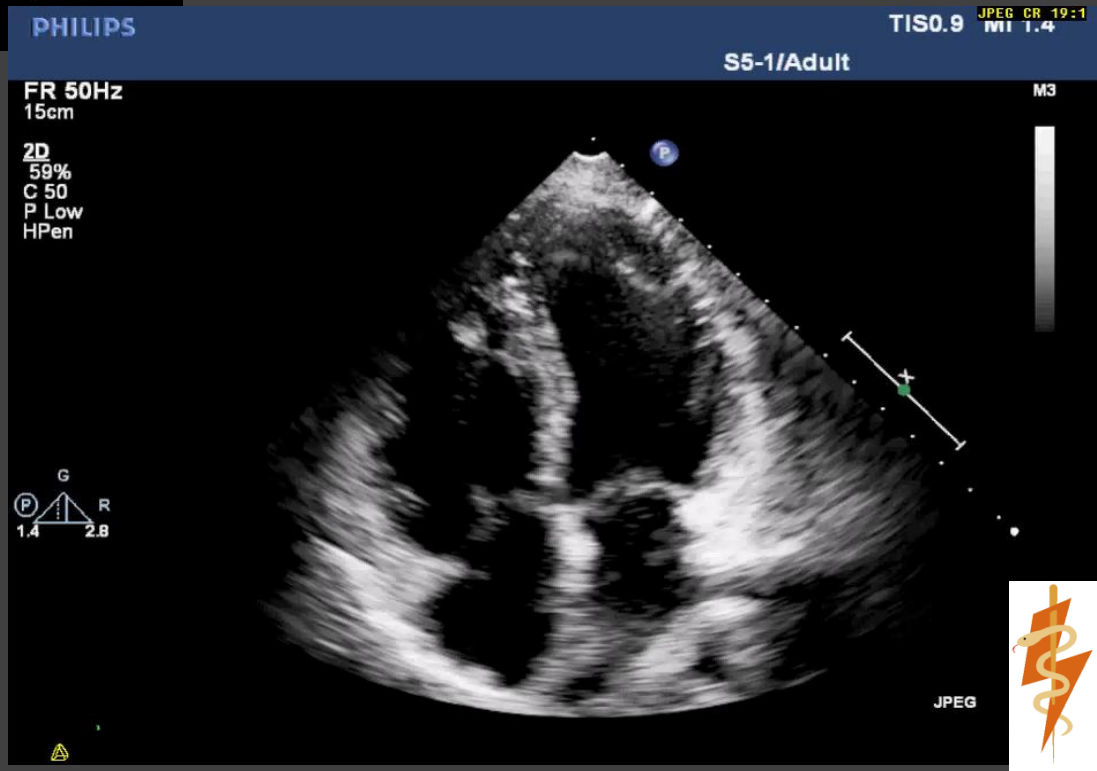
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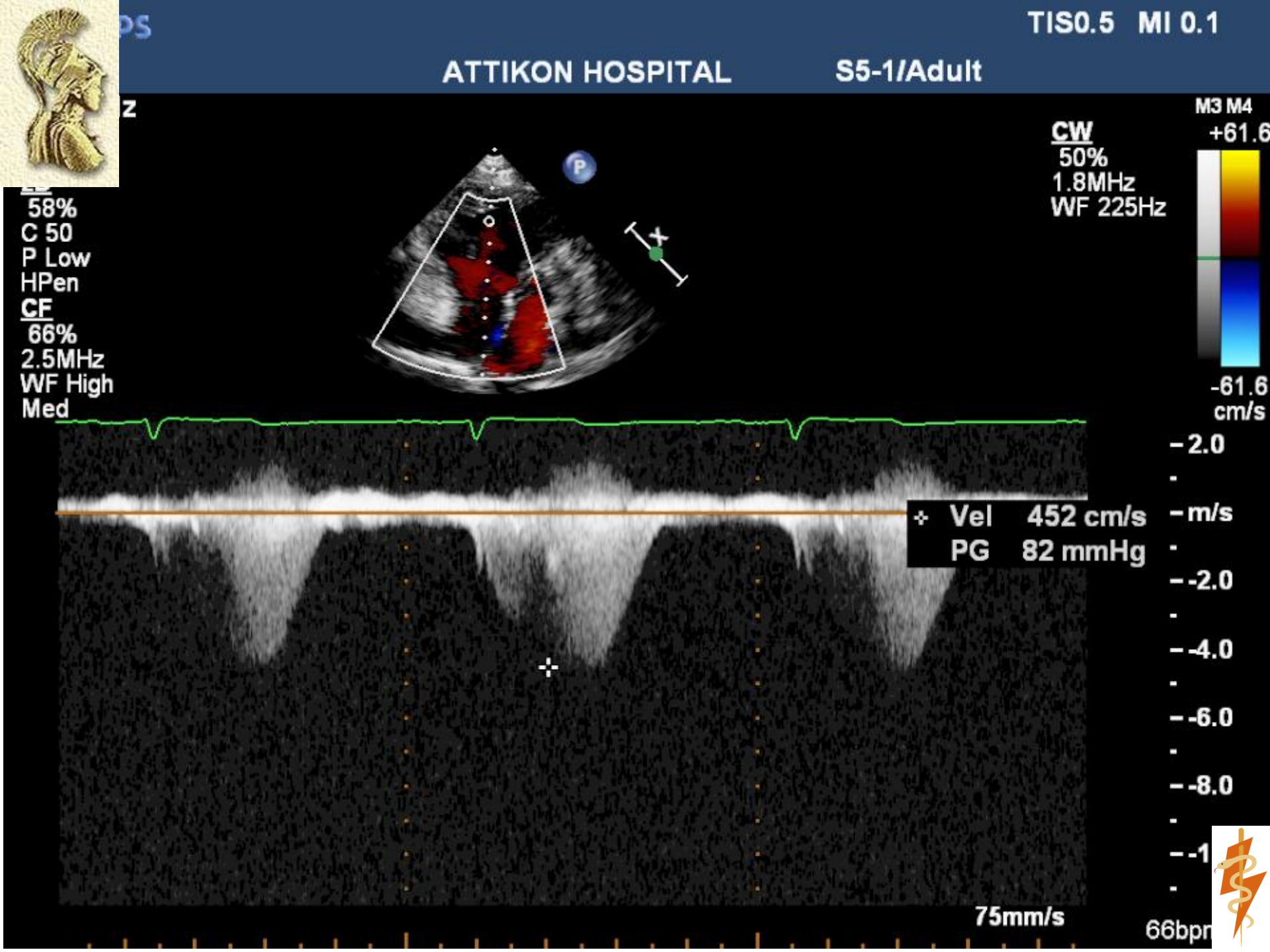
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C 50
P Low
HPen
CF
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WF High
Med
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-4.0
-6.0
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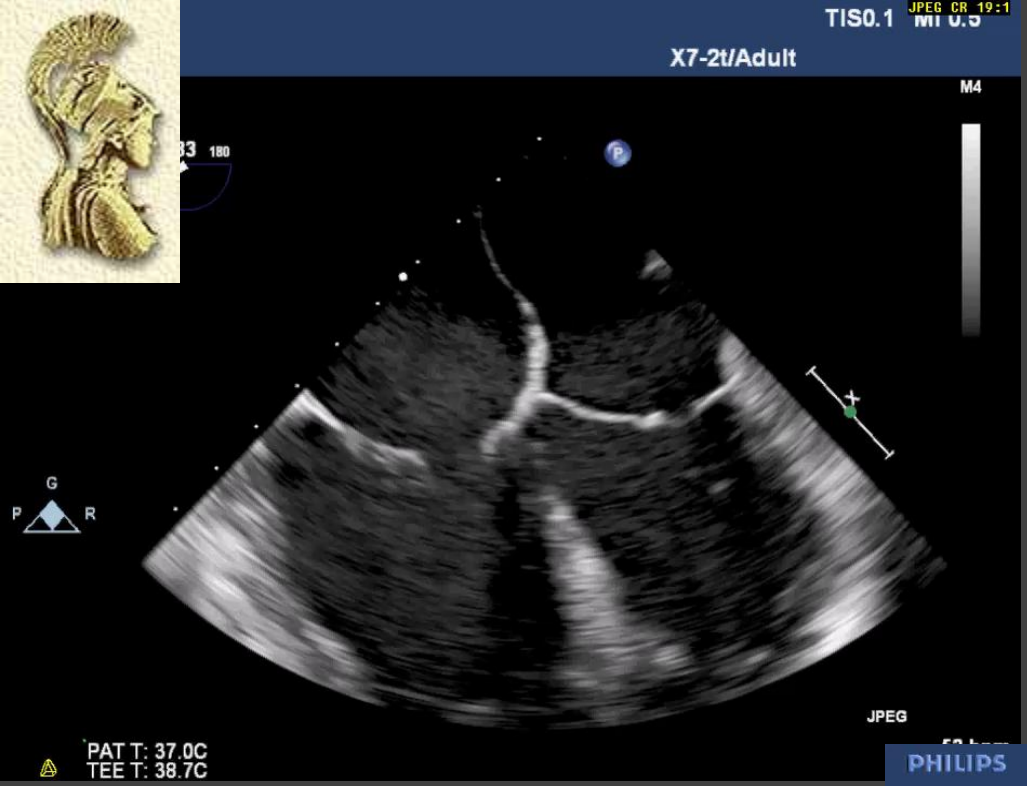
75mm/s
66bpm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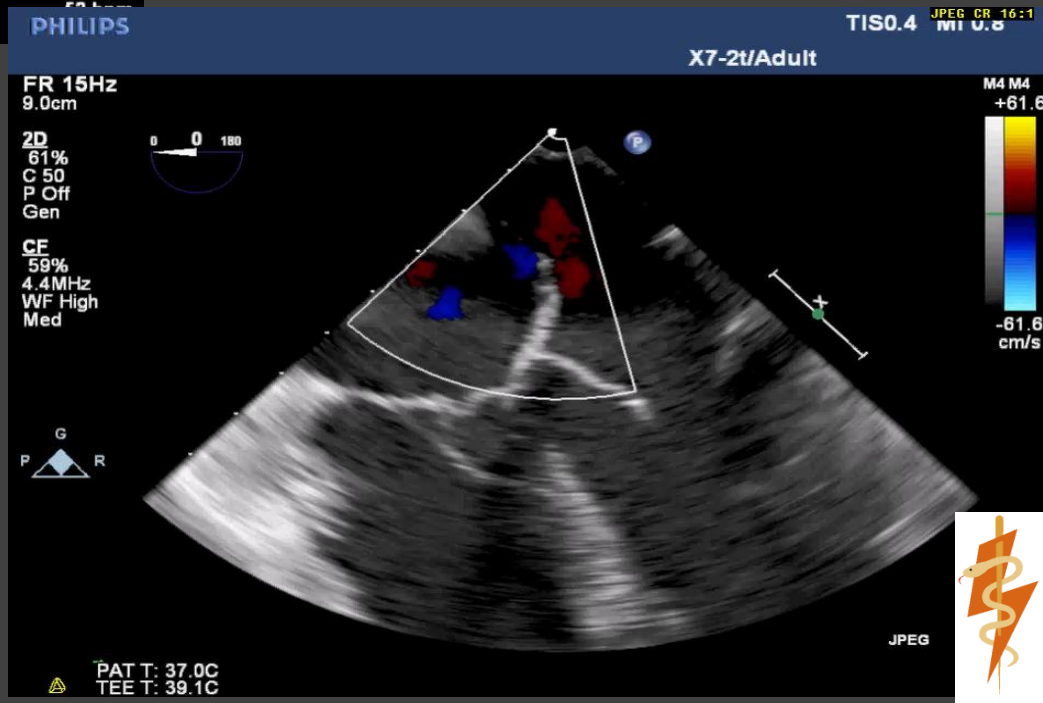
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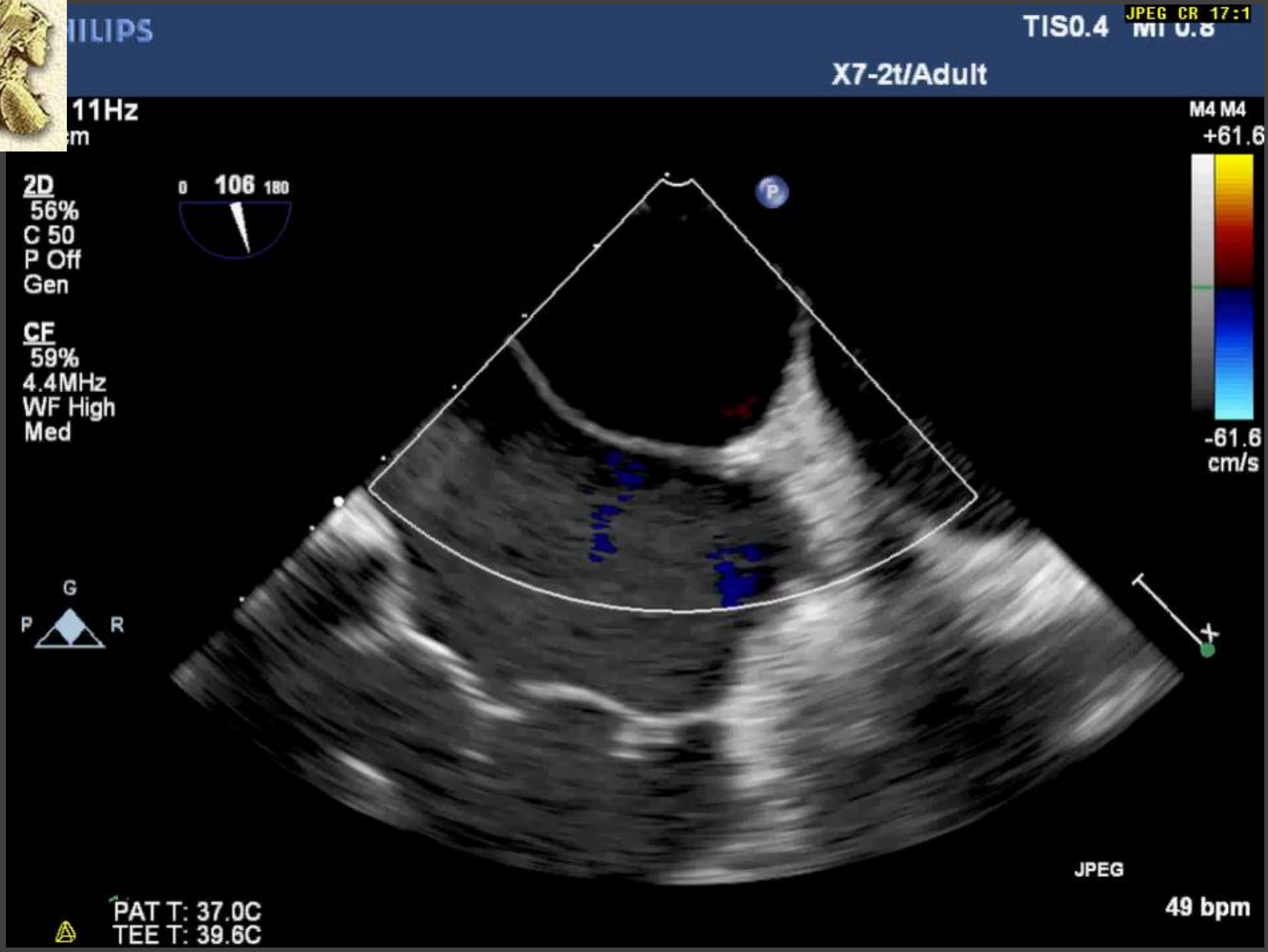


Χωρίς ροή δια του μεσοκολπικού διαφράγματος

Διερεύνηση αιτίων πνευμονικής υπέρτασης

- Εργαστηριακός έλεγχος για **δευτεροπαθείς αιτίες** πνευμονικής αρτηριακής υπέρτασης αρνητικός (HIV, υπερηχογράφημα άνω κοιλίας, κολλαγονικός έλεγχος).
- **Διοισοφάγειο υπερηχοκαρδιογράφημα και MRI καρδιάς**: αναδεικνύουν την σταθερότητα του μεσοκολπικού διαφράγματος και την απουσία άλλων συγγενών καρδιακών βλαβών.
- **Σπιρομέτρηση-Διάχυση πνευμόνων**: FVC=75%, FEV1=85%, TLCO-SB=66% .
- **Δοκιμασία εξάλεπτης βάδισης** 510 m.

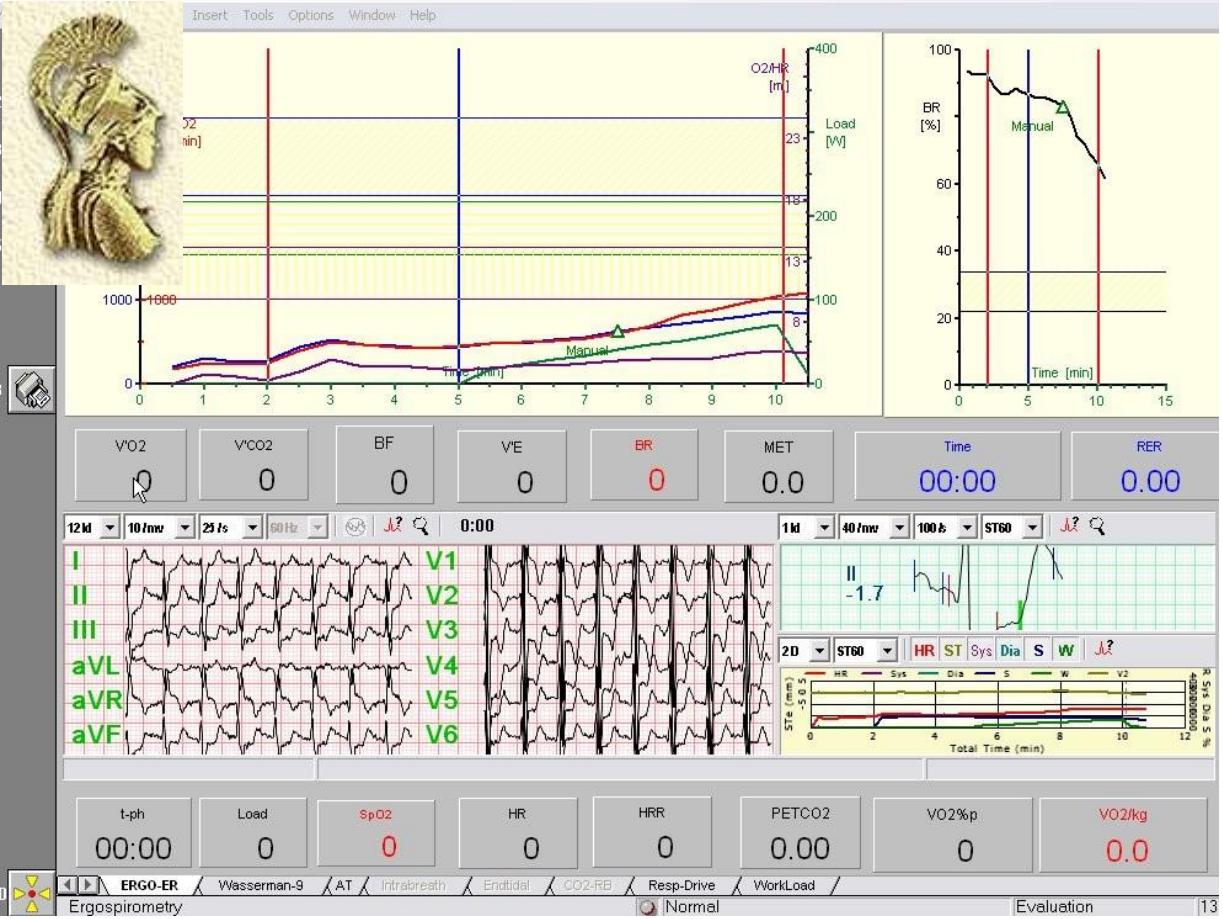
Δεξιός καρδιακός καθετηριασμός (12/2018)

- PA **108/58/73** mmHg
- RV 103/2 mmHg
- RA 7 mmHg
- CO 5.5 l/kg
- CI 3.65 l/min/m2
- PVR **12** Wood units
- PCWP 8mmHg

Table 3 Haemodynamic definitions of pulmonary hypertension[a]

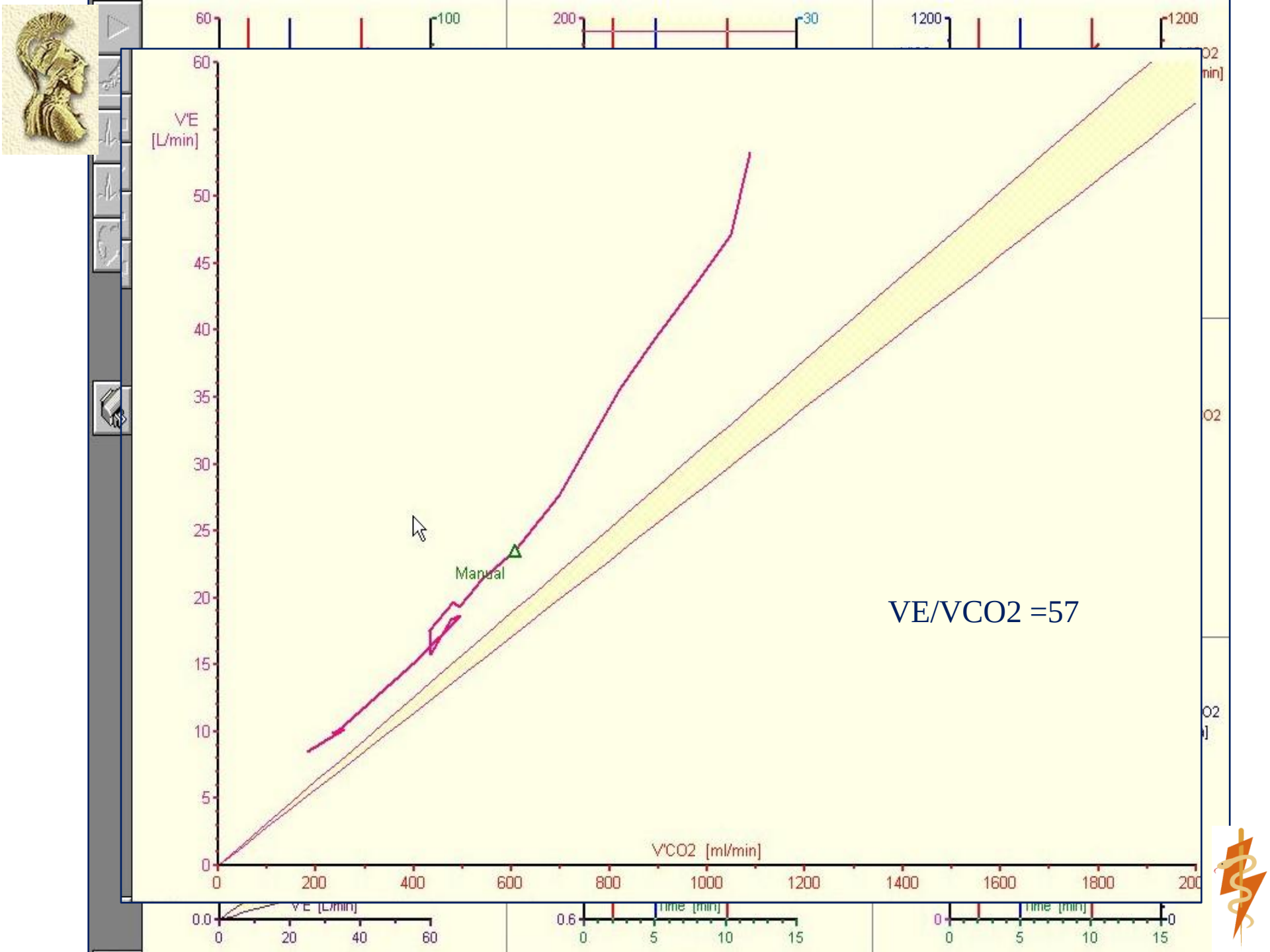
Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]	
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]	

CO = cardiac output; DPG = diastolic pressure gradient (diastolic PAP − mean PAWP); mPAP = mean pulmonary arterial pressure; PAWP = pulmonary arterial wedge press
PH = pulmonary hypertension; PVR = pulmonary vascular resistance; WU = Wood units.
[a]All values measured at rest; see also section 8.0.
[b]According to *Table 4*.
[c]Wood Units are preferred to dynes.s.cm^{-5}.

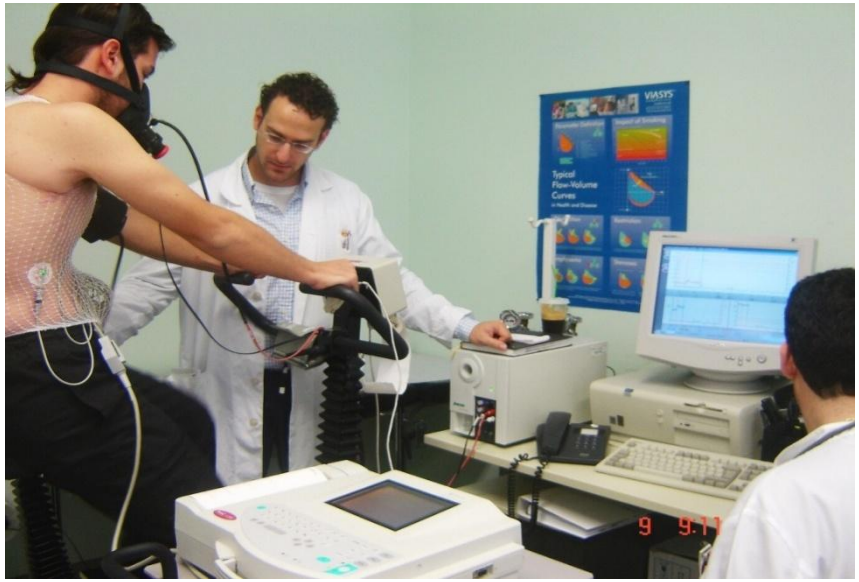


- 12W/12W ramp protocol
- **5.00 min**
- **Load 71W (38%), Mets 4.6**
- **VO2 15.9 ml/kg/min (32%)**
- **AT 11.6 ml/kg/min (23%)**
- **VE/VCO2 57**
- RER 1.22
- **O2 Pulse 5.4ml/beats (46%)**
- VE 47 L/min
- BR 66%
- SO2 98%-98%

1η Καρδιοαναπνευστική κόπωση
12/2018
(προ έναρξης αγωγής)


V'E
[L/min]
V'CO2 [ml/min]
Manual
VE/VCO2 =57

Role of exercise testing in PAH management



- Exercise testing can aid the clinician in:

  a. outlining **the nature** of a patient's exercise limitation,

  b. noninvasively assessing **disease severity**,

  c. establishing **prognosis** and

  d. evaluating the **response to therapy**.

- The **change in exercise capacity parallels** other clinical indicators of **disease severity**, such as: a. survival, b. hemodynamic parameters and c. time to clinical worsening.

- The clinician uses various exercise modalities in evaluating and managing patients with PAH: a. 6MWT, b. CPET, c. Exercise Echocardiography.

Oudiz et al. Respir.Crit.Care Med 2005;26(4): 379-84

Βασικές μετρήσεις

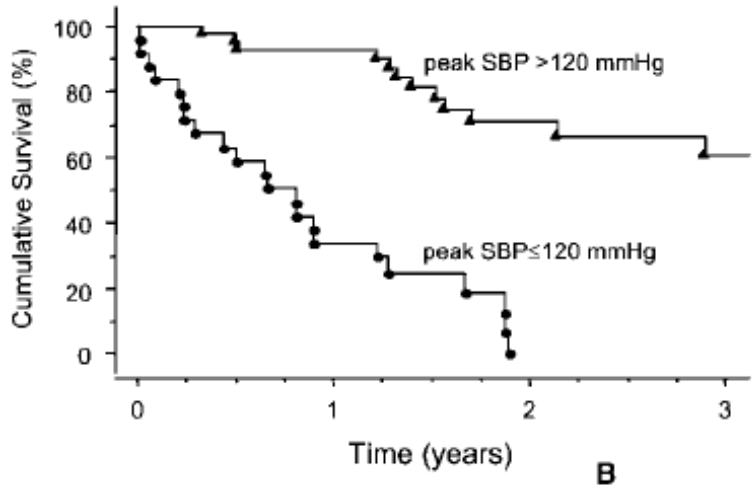
VO_2 peak	>84% προβλεπόμενης τιμής
Αναερόβιος ουδός (AT)	40%-80% προβλεπόμενης VO_2
Αναπνευστικό πηλίκο (VCO2/VO2)	1.05-1.30
Καρδιακή συχνότητα (HR)	>90% προβλεπόμενης τιμής
Εφεδρεία καρδιακής συχνότητας (HRR)	<15 bpm
O_2 παλμού (VO2 peak/HR)	>80%
Αρτηριακή πίεση (BP)	<220/90 mm Hg
Αναπνευστική συχνότητα (BF)	<60 αναπνοές/min
Κατά λεπτό αερισμός (VE)	lt/min
Αναπνευστική εφεδρεία (BR)	MVV-VE /MVV >20-40%
Κορεσμός O_2 (Sat)	πτώση <4%
Κλίση VE/VCO_2	< 34
Κλίση O_2 ανάνηψης (O2 recovery)	> 650

Καρδιοαναπνευστική δοκιμασία κόπωσης σε ασθενείς με πνευμονική αρτηριακή υπέρταση

- Μείωση **peak VO_2** (μειωμένη ικανότητα του ασθενούς για μέγιστη άσκηση).
- Μείωση του **$PETCO_2$**
- Μείωση του **AT** (πρώιμη εμφάνιση αναερόβιου μεταβολισμού, η οποία φαίνεται να αποτελεί έναν ανεξάρτητο προγνωστικό παράγοντα για την εξέλιξη της πνευμονικής υπέρτασης).
- Μείωση του **O_2 pulse** (μείωση του όγκου παλμού και της καρδιακής παροχής).
- Αύξηση **$VE/VCO_2 \geq 35$** (ανεπάρκεια του αναπνευστικού συστήματος ως προς την ανταλλαγή αερίων κατά τη διάρκεια της άσκησης).
- Αποκορεσμός της αιμοσφαιρίνης (**Δsat >4-5%**).

Η προγνωστική σημασία της CPET στην Πνευμονική Υπέρταση

A

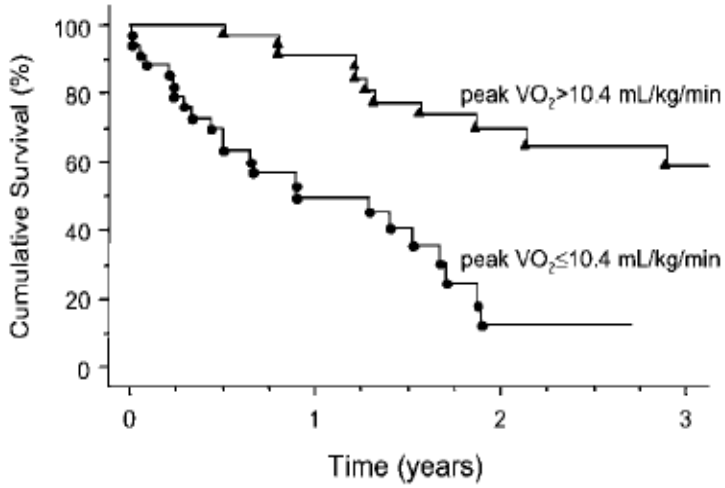


B

Background—Primary pulmonary hypertension (PPH) is a life-threatening disease. Prognostic assessment is an important factor in determining medical treatment and lung transplantation. Whether cardiopulmonary exercise testing data predict survival has not been reported previously.

Methods and Results—We studied 86 patients with PPH (58 female, age 46±2 years, median NYHA class III) between 1996 and 2001 who were followed up in a tertiary referral center. Right heart catheterization was performed and serum uric acid levels were measured in all patients. Seventy patients were able to undergo exercise testing. At the start of the study, the average pulmonary artery pressure was 60±2 mm Hg, average pulmonary vascular resistance was 1664±81 dyne · s · cm^{-5}, average serum uric acid level was 7.5±0.35 mg/dL, and average peak oxygen uptake during exercise (peak Vo_2) was 11.2±0.5 mL · kg^{-1} · min^{-1}. During follow-up (mean: 567±48 days), 28 patients died and 16 underwent lung transplantation (1-year cumulative event-free survival: 68%; 95% CI 58 to 78). The strongest predictors of impaired survival were low peak Vo_2 (P<0.0001) and low systolic blood pressure at peak exercise (peak SBP; P<0.0001). In a multivariable analysis, serum uric acid levels (all P<0.005) and diastolic blood pressure at peak exercise independently predicted survival (P<0.05). Patients with peak Vo_2 ≤10.4 mL · kg^{-1} · min^{-1} and peak SBP ≤120 mm Hg (ie, 2 risk factors) had poor survival rates at 12 months (23%), whereas patients with 1 or none of these risk factors had better survival rates (79% and 97%, respectively).

Conclusions—Peak Vo_2 and peak SBP are independent and strong predictors of survival in PPH patients. Hemodynamic parameters, although also accurate predictors, provide no independent prognostic information. (*Circulation*. 2002;106:319-324.)



Assessment of Survival in Patients With Primary Pulmonary Hypertension: Importance of Cardiopulmonary Exercise Testing
Roland Wensel, Christian F. Opitz, Stefan D. Anker, Jörg Winkler, Gert Höffken, Franz X. Kleber, Rakesh Sharma, Manfred Hummel, Roland Hetzer and Ralf Ewert
Circulation 2002;106;319-324; originally published online Jun 24, 2002;

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Authors/Task Force Members: Nazzareno Galiè[a] (ESC Chairperson) (Italy), Marc Humbert[a,b] (ERS Chairperson) (France), Jean-Luc Vachiery[c] (Belgium), Simon Gibbs (UK), Irene Lang (Austria), Adam Torbicki (Poland), Gérald Simonneau[a]

Table 6 Clinical classification of pulmonary arterial hypertension associated with congenital heart disease (updated from Simonneau *et al.*[5])

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
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, neurofibromatosis 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

increased, systemic-to-pulmonary shunting is still prevalent, whereas cyanosis at rest is not a feature.

3. PAH with small/coincidental defects[b]

Marked elevation in PVR in the presence of small cardiac defects (usually ventricular septal defects <1 cm and atrial septal defects <2 cm of effective diameter assessed by echo), which themselves do not account for the development of elevated PVR; the clinical picture is very similar to idiopathic PAH. Closing the defects is contra-indicated.

4. PAH after defect correction

Congenital heart disease is repaired, but PAH either persists immediately after correction or recurs/develops months or years after correction in the absence of significant postoperative haemodynamic lesions.

4. PAH after defect correction

Congenital heart disease is repaired, but PAH either persists immediately after correction or recurs/develops months or years after correction in the absence of significant postoperative haemodynamic lesions.

Review Article

Atrial septal defects and pulmonary arterial hypertension

Heba Nashat, Claudia Montanaro, Wei Li, Aleksander Kempny, Stephen J. Wort, Konstantinos Dimopoulos, Michael A. Gatzoulis, Sonya V. Babu-Narayan

Department of Adult Congenital Heart Disease, Royal Brompton and Harefield NHS Foundation Trust, National Heart and Lung Institute, Imperial College London, London, UK

Contributions: (I) Conception and design: H Nashat, C Montanaro, SV Babu-Narayan; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Sonya V. Babu-Narayan, MBBS, BSc, PhD, FRCP, FESC. Department of Adult Congenital Heart Disease, National Heart & Lung Institute, Imperial College London, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK. Email: s.babu-narayan@rbht.nhs.uk.

Abstract: Atrial septal defects (ASD) are a common congenital heart defect. The majority of patient with ASDs often follow an uncomplicated course of events. However, a proportion of patients with ASDs, may have their condition complicated by pulmonary hypertension (PH), with a subsequent significant impact on management, morbidity and mortality. The presence of PH, influences the suitability for defect closure. In this review we describe the different types of ASDs, the classification of PH related to congenital heart disease (CHD), when ASD closure is contraindicated and the management of patients who develop pulmonary arterial hypertension (PAH), including the most extreme form, Eisenmenger syndrome (ES).

- 10% of adults with CHD develop PAH
- Vascular remodeling due to a defect with left-to- right shunt
- Increased pulmonary blood flow-endothelial dysfunction-smooth muscle hypertrophy-proliferation-distortion of the pulmonary vasculature
- ASDs are less commonly associated with significant PH
- Genetic disposition additional to their hemodynamic lesion further contributing to the pulmonary vascular remodeling and more aggressive disease

Progressive Pulmonary Hypertension Post Atrial Septal Defect Device Closure—Early Symptomatic Improvement may not Predict Outcome

C. O'Donnell, FRACP[a,*], P.N. Ruygrok, FRACP[b], K. Whyte, FRACP[c] and N.J. Wilson, FRACP[a]

[a] *The Green Lane Paediatric and Congenital Cardiac Service, Starship Children's Hospital, Auckland, New Zealand*
[b] *Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand*
[c] *Respiratory Services, Auckland City Hospital, Auckland, New Zealand*

Background: For patients with an atrial septal defect and pulmonary hypertension it can be difficult to determine whether it is safe to intervene. With newer treatments for pulmonary hypertension and transcatheter techniques avoiding surgical stressors, it has been hoped that we can occlude previously inoperable defects safely.

Methods: We undertook a subgroup analysis of outcomes for patients with mean pulmonary artery pressure (PAp) ≥30 mm Hg from within our database of patients undergoing transcatheter ASD closure from 1997 to 2004.

Results: Data for 11 patients were reviewed. Mean age of the patients at intervention was 38 years (5–69 years). Eight patients have had symptomatic improvement with no evidence of progressive pulmonary hypertension. There was one death due to unrelated causes. Two patients have developed progressive pulmonary vascular disease with one death.

Conclusions: Despite early symptomatic improvement, adverse outcomes may occur in patients with elevated pulmonary vascular resistance undergoing transcatheter ASD closure. Careful haemodynamic evaluation is vital. Modest elevation of pulmonary vascular resistance and the presence of left to right shunt (Qp:Qs > 1.5:1) are reassuring.

(Heart, Lung and Circulation 2010;19:713–716)

- Pulmonary vascular disease is an uncommon finding associated with the diagnosis of an ASD, occurring in only 5-10% of patients
- More frequent in those presenting at > 40 years of age and in women
- ASD may not be the sole aetiology of pulmonary hypertension
- Despite early symptomatic improvement ASD closure in patients with pulmonary hypertension may shorten life expectancy
- Full haemodynamic assessment is important

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

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%

6MWD = 6-minute walking distance; BNP = brain natriuretic peptide; CI = cardiac index; CMR = cardiac magnetic resonance; NT-proBNP = N-terminal pro-brain natriuretic peptide; pred. = predicted; RA = right atrium; RAP = right atrial pressure; SvO_2 = mixed venous oxygen saturation; VE/VCO_2 = ventilatory equivalents for carbon dioxide; VO_2 = oxygen consumption; WHO = World Health Organization.

[a]Most of the proposed variables and cut-off values are based on expert opinion. They may provide prognostic information and may be used to guide therapeutic decisions, but application to individual patients must be done carefully. One must also note that most of these variables have been validated mostly for IPAH and the cut-off levels used above may not necessarily apply to other forms of PAH. Furthermore, the use of approved therapies and their influence on the variables should be considered in the evaluation of the risk.

[b]Occasional syncope during brisk or heavy exercise, or occasional orthostatic syncope in an otherwise stable patient.

[c]Repeated episodes of syncope, even with little or regular physical activity.

Haemodynamic definitions and updated clinical classification of pulmonary hypertension

Gérald Simonneau[1,2], David Montani[1,2], David S. Celermajer[3], Christopher P. Denton[4], Michael A. Gatzoulis[5], Michael Krowka[6], Paul G. Williams[7] and Rogerio Souza[8]

Number 4 in the series
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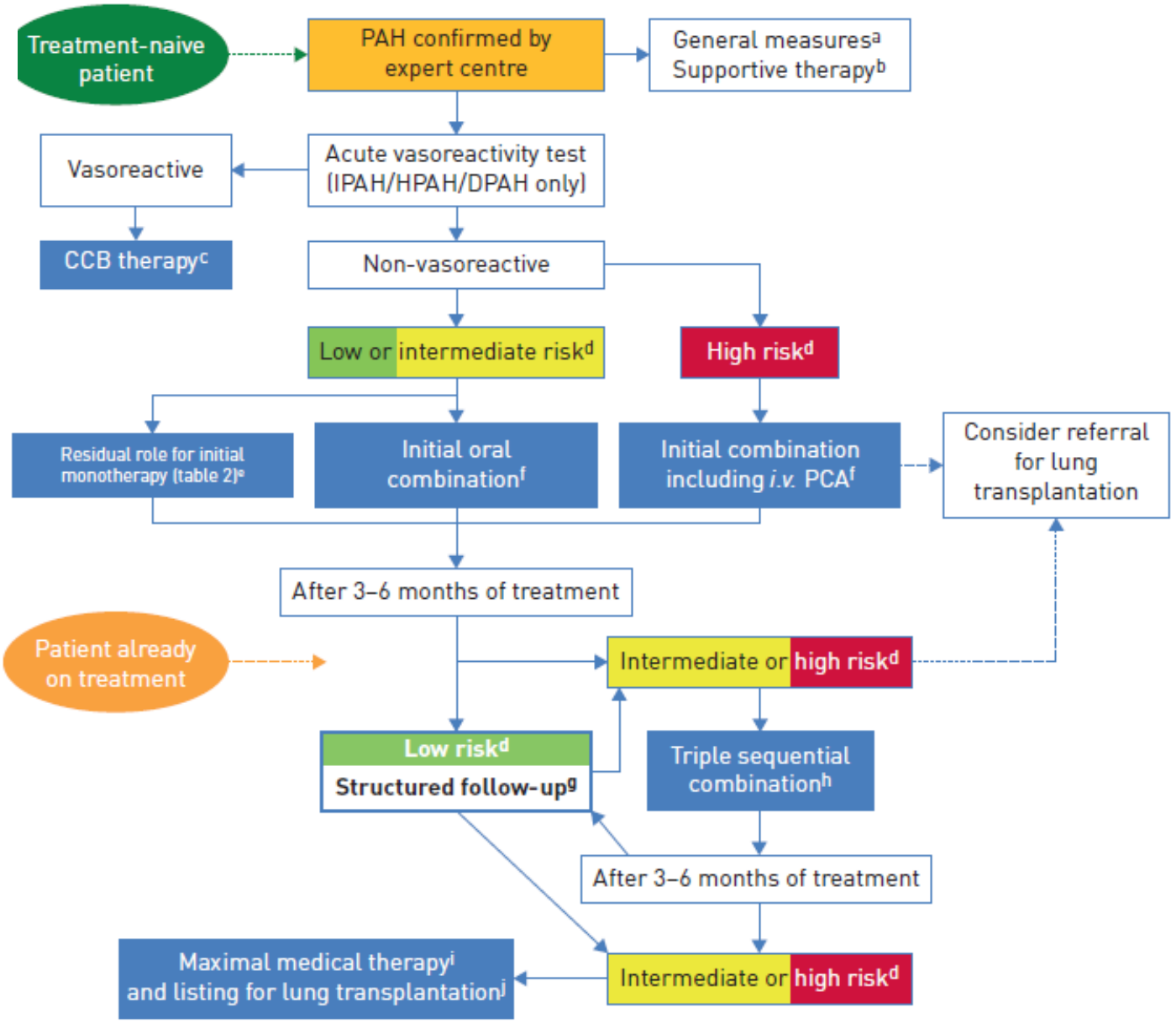

SERIES
WORLD SYMPOSIUM ON PULMONARY HYPERTENSION

Haemodynamic definitions and updated clinical classification of pulmonary hypertension

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TABLE 2 Potential role for initial monotherapy in specific pulmonary arterial hypertension (PAH) subsets

IPAH, HPAH and drug-induced PAH patient responders to acute vasoreactivity tests and with WHO FC I/II and sustained haemodynamic improvement (same or better than achieved in the acute test) after at least 1 year on CCBs only
Long-term-treated historical PAH patients with monotherapy (>5–10 years) stable with low-risk profile
IPAH patients >75 years old with multiple risk factors for heart failure with preserved LVEF (high blood pressure, diabetes mellitus, coronary artery disease, atrial fibrillation, obesity)
PAH patients with suspicion or high probability of pulmonary veno-occlusive disease or pulmonary capillary haemangiomatosis
Patients with PAH associated with HIV infection or portal hypertension or uncorrected congenital heart disease, as they were not included in RCTs of initial combination therapy
PAH patients with very mild disease (*e.g.* WHO FC I, PVR 3–4 WU, mPAP <30 mmHg, normal right ventricle at echocardiography)
Combination therapy unavailable or contraindicated (*e.g.* severe liver disease)

IPAH: idiopathic PAH; HPAH: heritable PAH; CCB: calcium channel blocker; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; LVEF: left ventricular ejection fraction; RCT: randomised controlled trial; WHO: World Health Organization; FC: Functional Class; WU: Wood Units; mPAP: mean PAP.

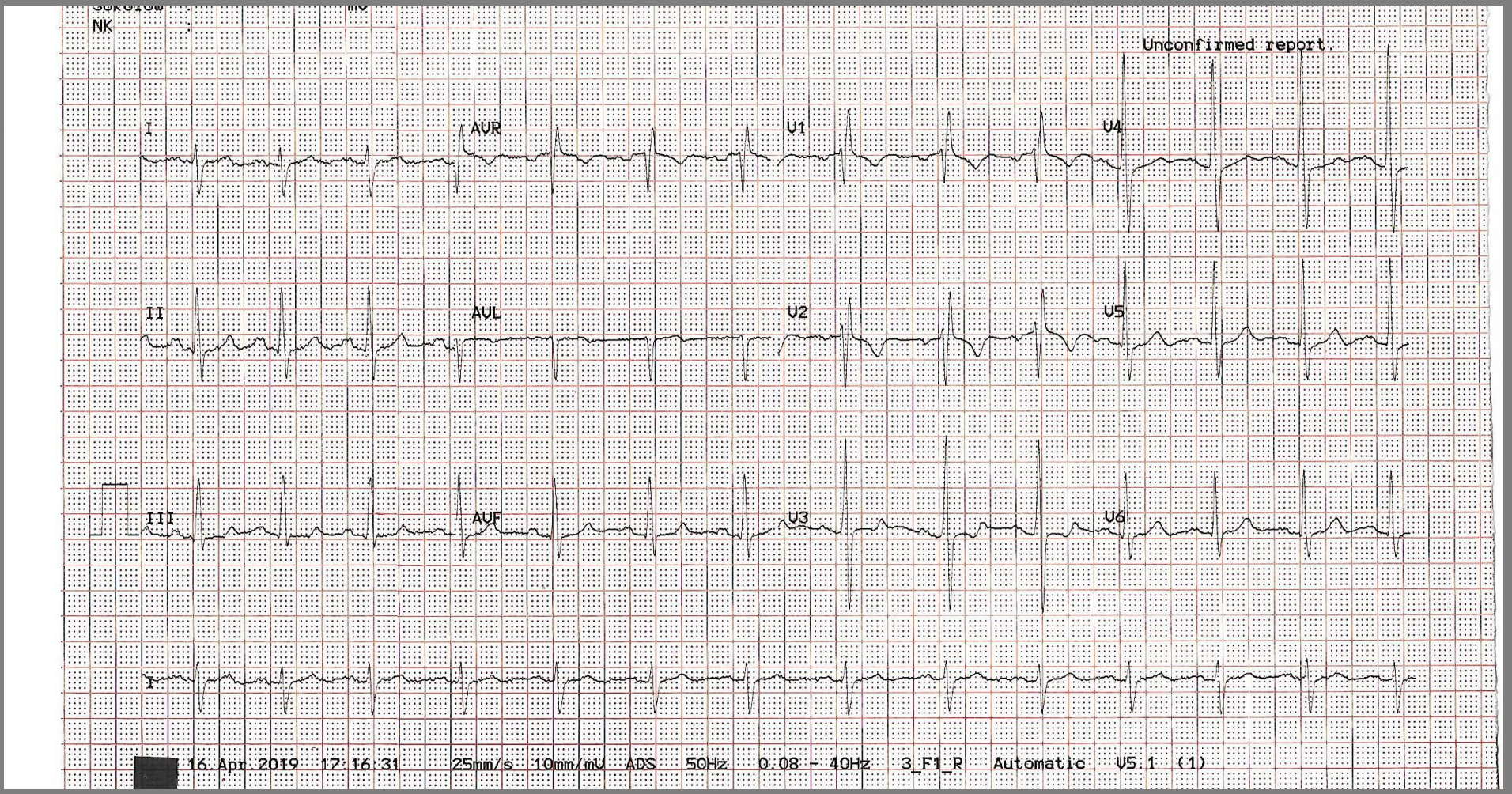
2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Table 19 Recommendations for efficacy of drug monotherapy for pulmonary arterial hypertension (group 1) according to World Health Organization functional class. The sequence is by pharmacological group, by rating and by alphabetical order

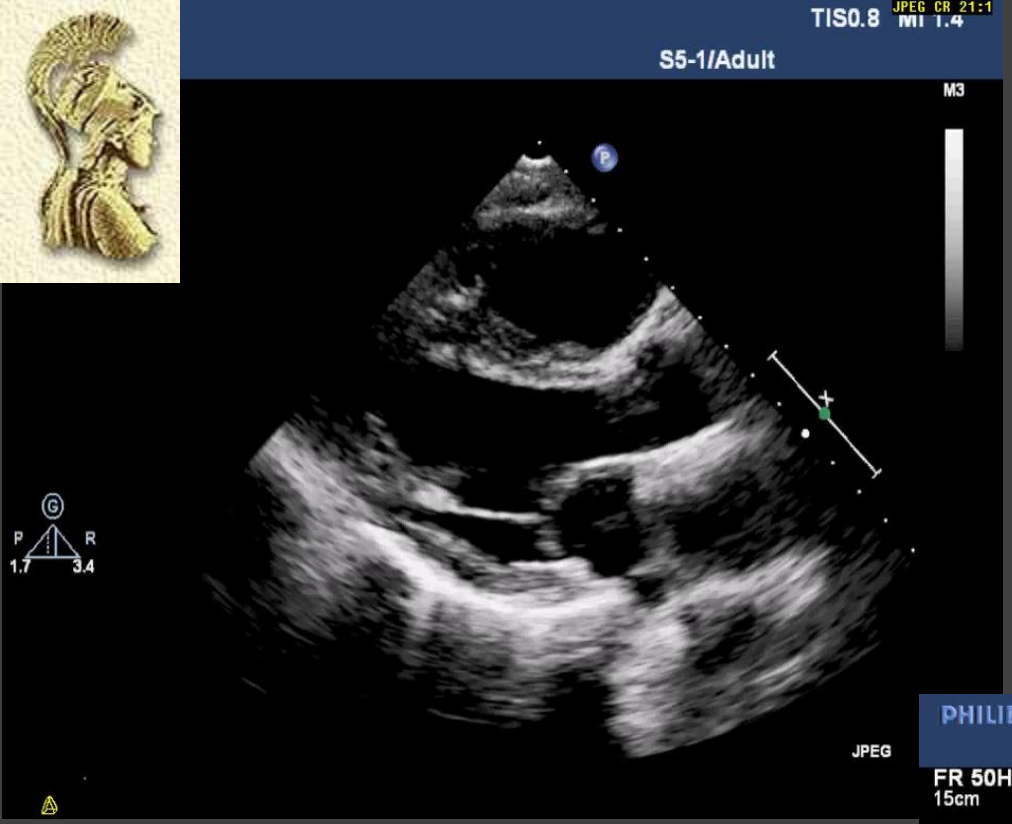
Measure/treatment			Class[a]-Level[b]						Ref.[c]
			WHO-FC II		WHO-FC III		WHO-FC IV		
Calcium channel blockers			I	C[d]	I	C[d]	-	-	84,85
Endothelin receptor antagonists	Ambrisentan		I	A	I	A	IIb	C	194
	Bosentan		I	A	I	A	IIb	C	196–200
	Macitentan[e]		I	B	I	B	IIb	C	201
Phosphodiesterase type 5 inhibitors	Sildenafil		I	A	I	A	IIb	C	205–208
	Tadalafil		I	B	I	B	IIb	C	211
	Vardenafil[g]		IIb	B	IIb	B	IIb	C	212
Guanylate cyclase stimulators	Riociguat		I	B	I	B	IIb	C	214
Prostacyclin analogues	Epoprostenol	Intravenous[e]	-	-	I	A	I	A	220–222
	Iloprost	Inhaled	-	-	I	B	IIb	C	229–231
		Intravenous[g]	-	-	IIa	C	IIb	C	232
	Treprostinil	Subcutaneous	-	-	I	B	IIb	C	233
		Inhaled[g]	-	-	I	B	IIb	C	237
		Intravenous[f]	-	-	IIa	C	IIb	C	234
		Oral[g]	-	-	IIb	B	-	-	238–240
	Beraprost[g]		-	-	IIb	B	-	-	218
IP receptor agonists	Selexipag (oral)[g]		I	B	I	B	-	-	241,248

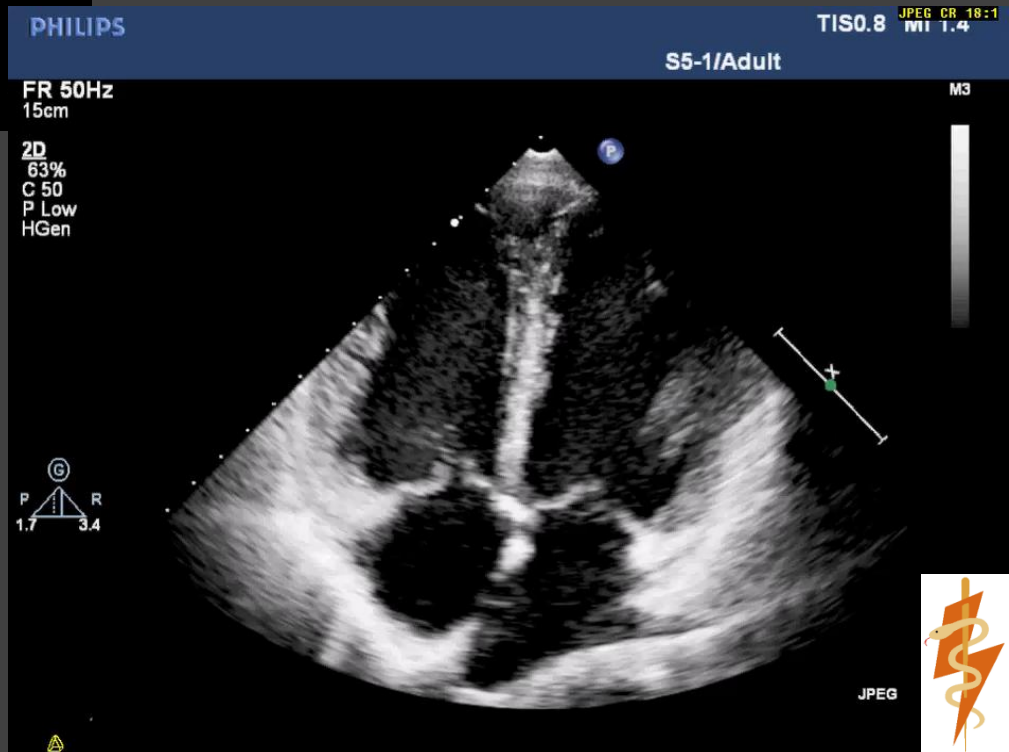
Φαρμακευτική αντιμετώπιση

- Έναρξη αγωγής με Tadalafil (12/2018)
- Προσθήκη Macitentan μετά από ένα μήνα (1/2019).
- Τοποθέτηση υποδόριας αντλίας συνεχούς έγχυσης Treprostenil με σταδιακή τιτλοποίηση της δόσης (4/2019).

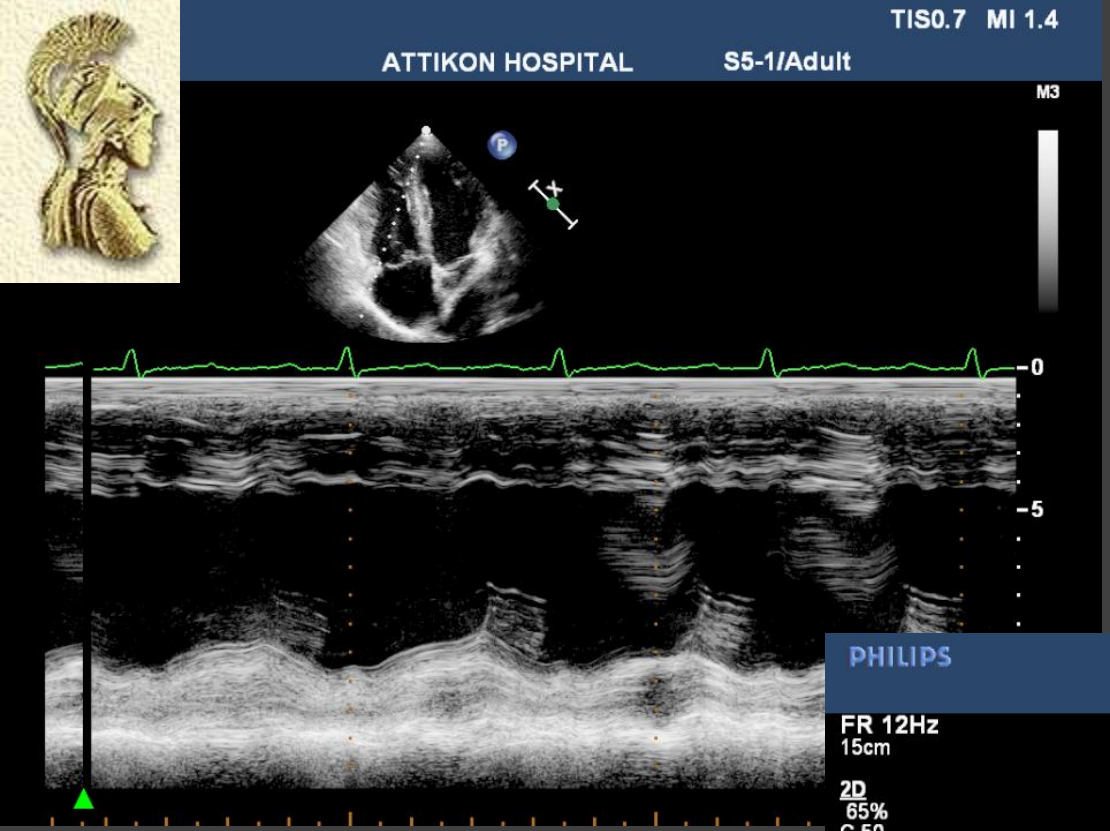

NK
Unconfirmed report.
I
AUR
V1
V4
II
AUL
V2
V5
III
AUF
V3
V6
I
16 Apr 2019 17:16:31 25mm/s 10mm/mV ADS 50Hz 0.08 - 40Hz 3_F1_R Automatic V5.1 (1)

	Baseline (12/18)
Therapy	**None**
Echocardiography	
TR velocity	4.8
RVSP	100
IVC	17
RV diameter (4ch)	45
TAPSE	9
S-TDI	5
Pericardial fluid	NO

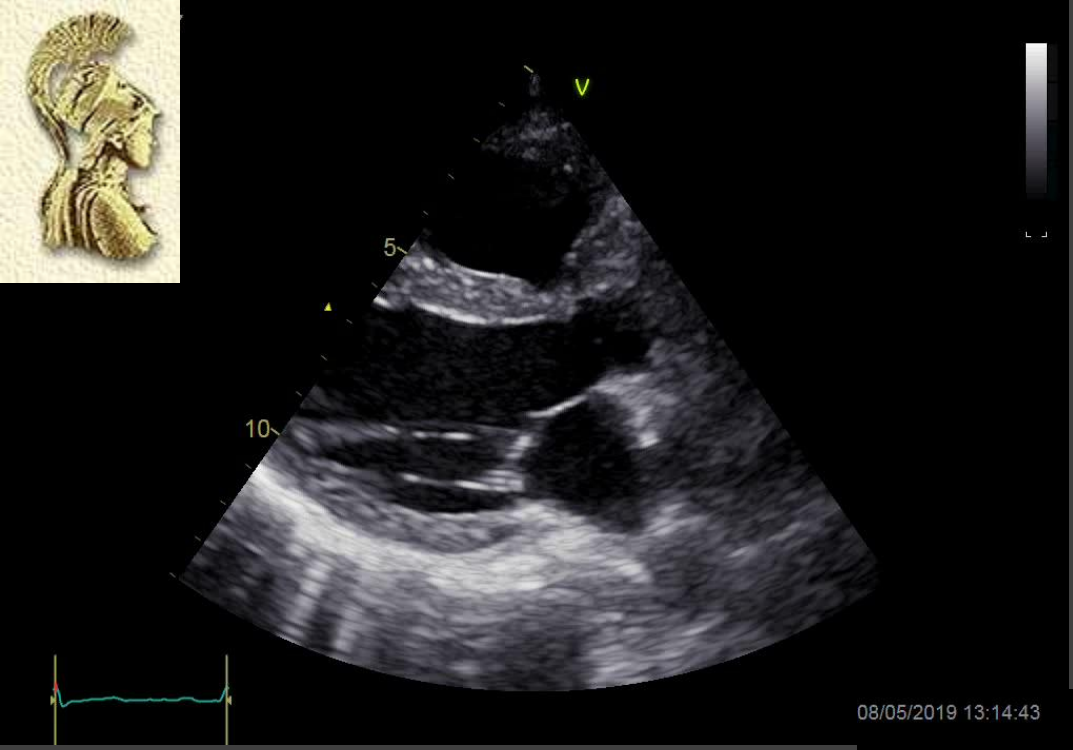




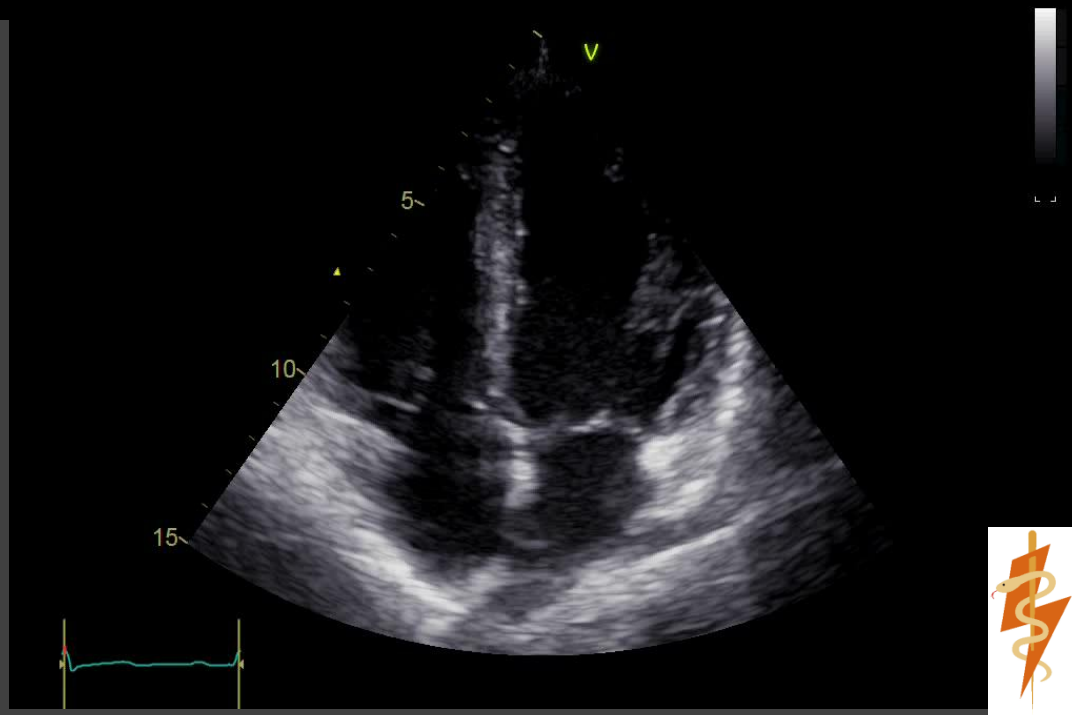
2ο Triplex καρδιάς (4/19)



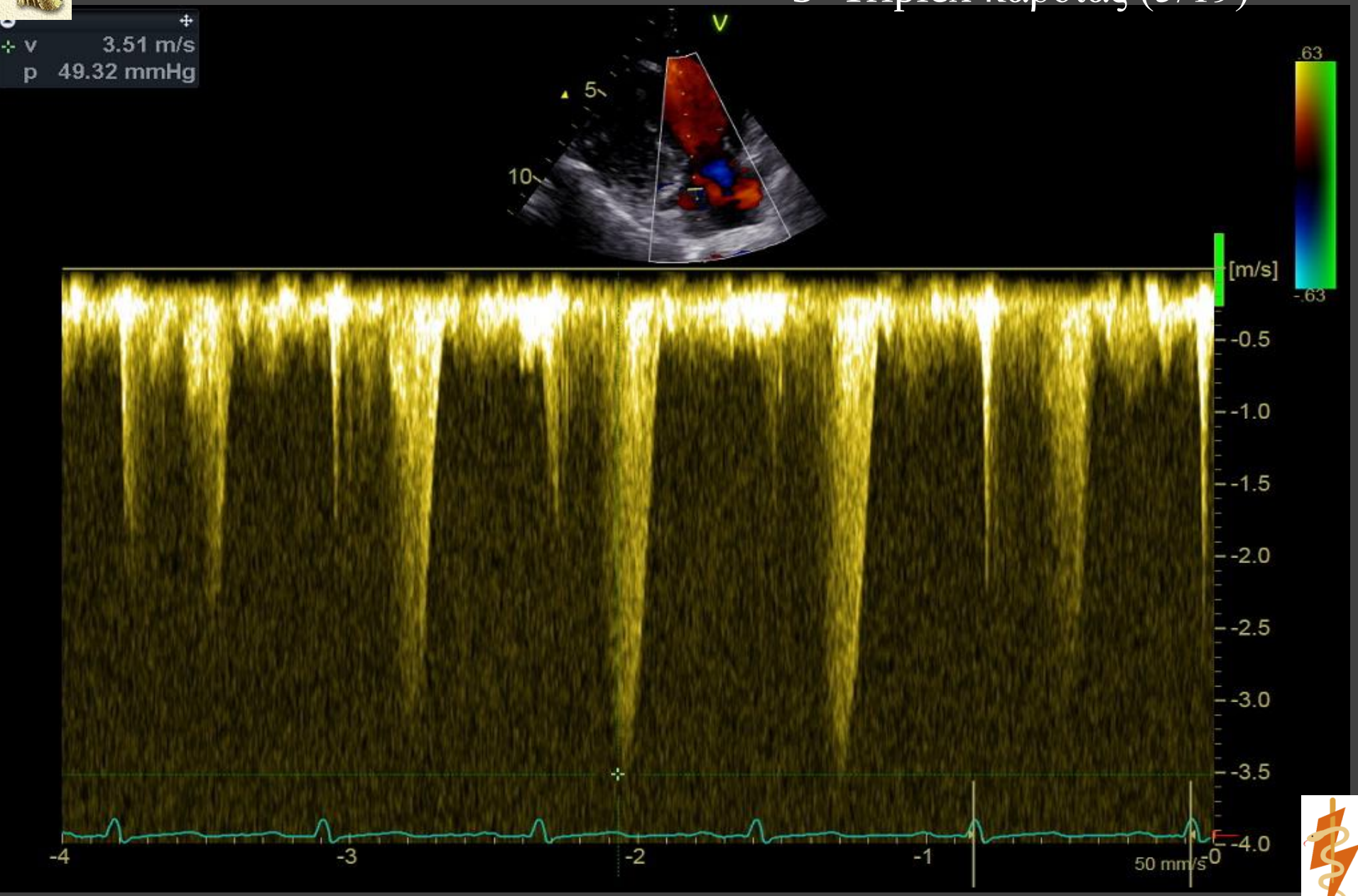
2ο Triplex καρδιάς (4/19)



3ο Triplex καρδιάς (5/19)

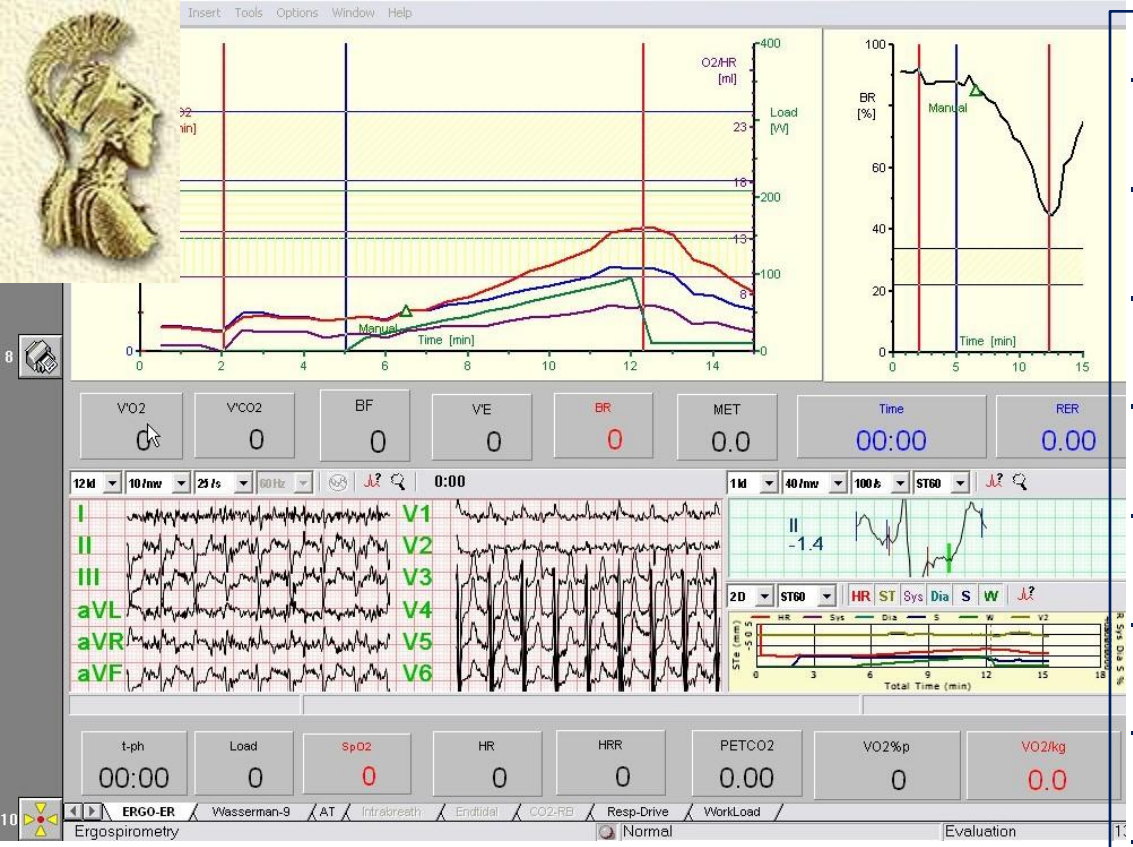


3ο Triplex καρδιάς (5/19)



	Baseline (12/18)	1st re-evaluation (4/19)	
Therapy	**None**	**Tadalafil+ Macitentan**	👍
Right Heart Catheterization			
Ra	7	4	👍
RV	108/2	64/6	👍
PA	108/58/**73**	64/30/**44**	👍
PCWP	8	7	👍
PVR	12	6	👍
CI	3.65	3.60	

	Baseline (12/18)	1st re-evaluation (4/19)	
Therapy	**None**	**Tadalafil+ Macitentan**	👍
Exercise			
6 MWT (meters)	510	585	👍
CPET –Time (min)	5.00	7.00	👍
VO2 (% predicted)	32	46	👍
VO2 (ml/min/kg)	15.9	22.4	👍
Work load (watt)	71 (38%)	94 (49%)	👍
VE/VCO2	57	50	👍
O2 pulse	46	66	👍
Pre- Syncope	YES	YES/NO	👍



-Time 7:16min

-Load 98W (55%), 6 Mets

-peakVO2 20.9 ml/kg/min (41%)

-AT 10.2ml/min/kg (20%)

-O2 pulse 6.6ml/beats (59%)

-SO2 97%-96%

-VE 75L/min (63%)

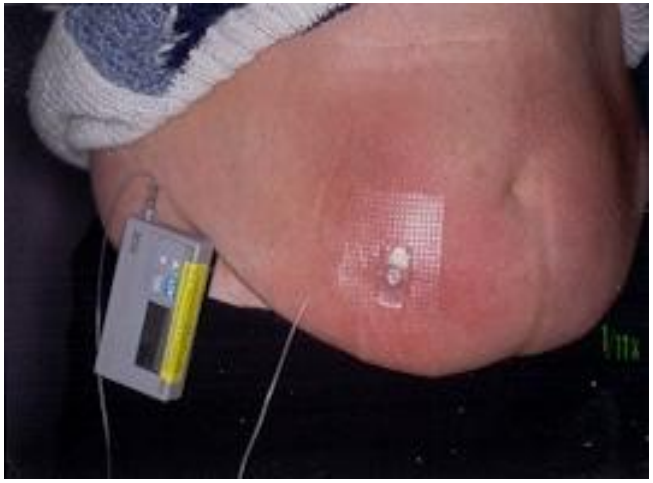
-VE/VCO2 42

-RER 1.46

CPET (6/2019) υπό Macitentan, Tadalafil, Treprostenil sc (34 ng/ml/min)

6MWT (5/2019)= 610 meters

CHRONIC INFUSIONS OF TREPROSTENIL



Active as a subcutaneous injection
Stable at room temperature
Plasma half-life: SC~3h, IV~45'
Smaller pump, **Lower risk of iv infections**

Disadvantages: **severe skin reactions, site pain**

Intravenous approved in USA with
Flolan to Remodulin match (1:3 ng/kg/min)

CHEST Original Research
PULMONARY HYPERTENSION

Efficacy of Long-term Subcutaneous Treprostinil Sodium Therapy in Pulmonary Hypertension*

Irene Lang, MD, PhD; Miguel Gomez-Sanchez, MD; Meinhard Kneussl, MD, PhD; Robert Naeije, MD, PhD; Pilar Escribano, MD; Nika Skoro-Sajer, MD; and Jean-Luc Vachiery, MD

(CHEST 2006; 129:1636–1643)

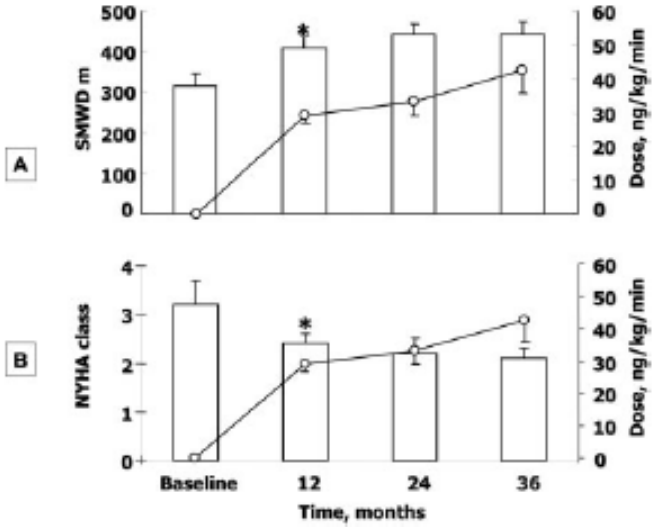


FIGURE 1. Effect of long-term subcutaneously infused treprostinil on exercise capacity and NYHA class. *Top, A*: Improvement in SMWD at 12 months. The effect persisted after 24 months and 36 months. *Bottom, B*: Improvement in NYHA class.

Θέματα προς συζήτηση

- Η εξέλιξη της πνευμονικής αρτηριακής υπέρτασης παρά την σύγκλειση της μεσοκολπικής επικοινωνίας
- Η σημαντική μείωση των πνευμονικών πιέσεων και αντιστάσεων με τη γρήγορη έναρξη τριπλής θεραπείας συνδυασμού
- Η επιλογή μεταξύ υποδορίου και ενδοφλεβίου προστανοειδούς
- Η νεαρή ηλικία ενός τόσου επιβαρυμένου ασθενούς και η ανάγκη αποδοχής ενός γεγονότος χρονίας νόσου με ειδική φαρμακευτική αγωγή 24ωρης χρήσης
- Η καθυστερημένη απάντηση της καρδιοαναπνευστικής κόπωσης (πιθανά απαιτούνται τουλάχιστον 3-4 μήνες για να φανούν οι μεταβολές μετά την εντατικοποίηση της αγωγής)