1ο ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ ΠΝΕΥΜΟΝΙΚΗΣ ΥΠΕΡΤΑΣΗΣ ΑΘΗΝΑ 9-11/6/2017

Γιώργος Π. Αναστασιάδης
Καρδιολόγος
Επιμελητής Καρδιολογικής κλινικής ΓΝΑ ΛΑΙΚΟ

Σύγχρονες προκλήσεις στην αντιμετώπιση περιστατικών με αιμολυτική αναιμία και πνευμονική υπέρταση

Δεν έχω σύγκρουση συμφερόντων

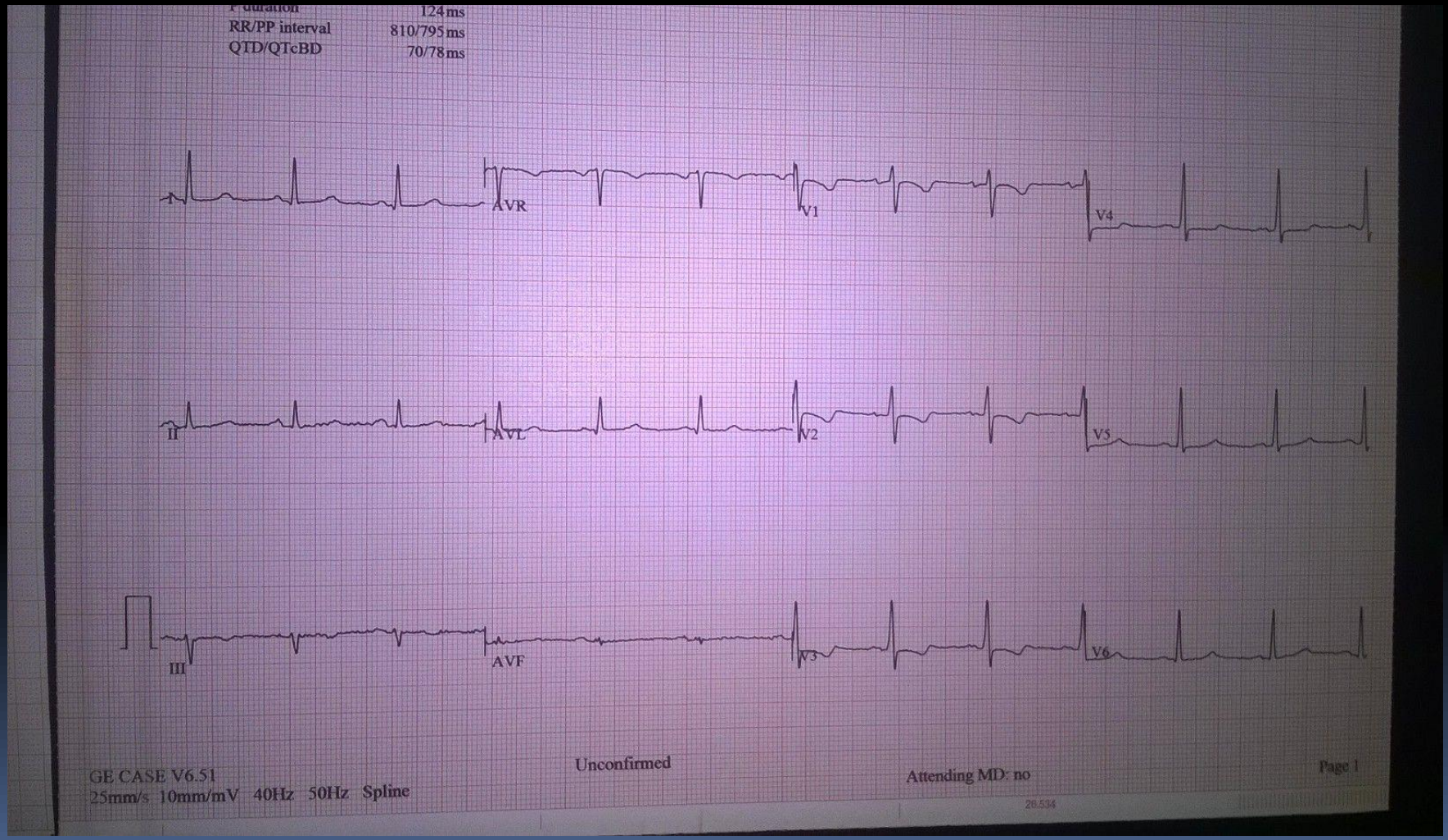
Ιστορικό

- Πρόκειται για γυναίκα ασθενή ηλικίας 50 ετών με σύνθετη ετερόζυγη δρεπανοκυτταρική νόσο που παρακολουθείται από πολλών ετών στο κέντρο αιμοσφαιρινοπαθειών του νοσοκομείου
- Σε πρόγραμμα μεταγγίσεων από την παιδική ηλικία ως το 1990 με ταυτόχρονη θεραπεία αποσιδήρωσης με Desferral
- *Σε αγωγή με υδροξυουρία από το 1994 λόγω επώδυνων κρίσεων*

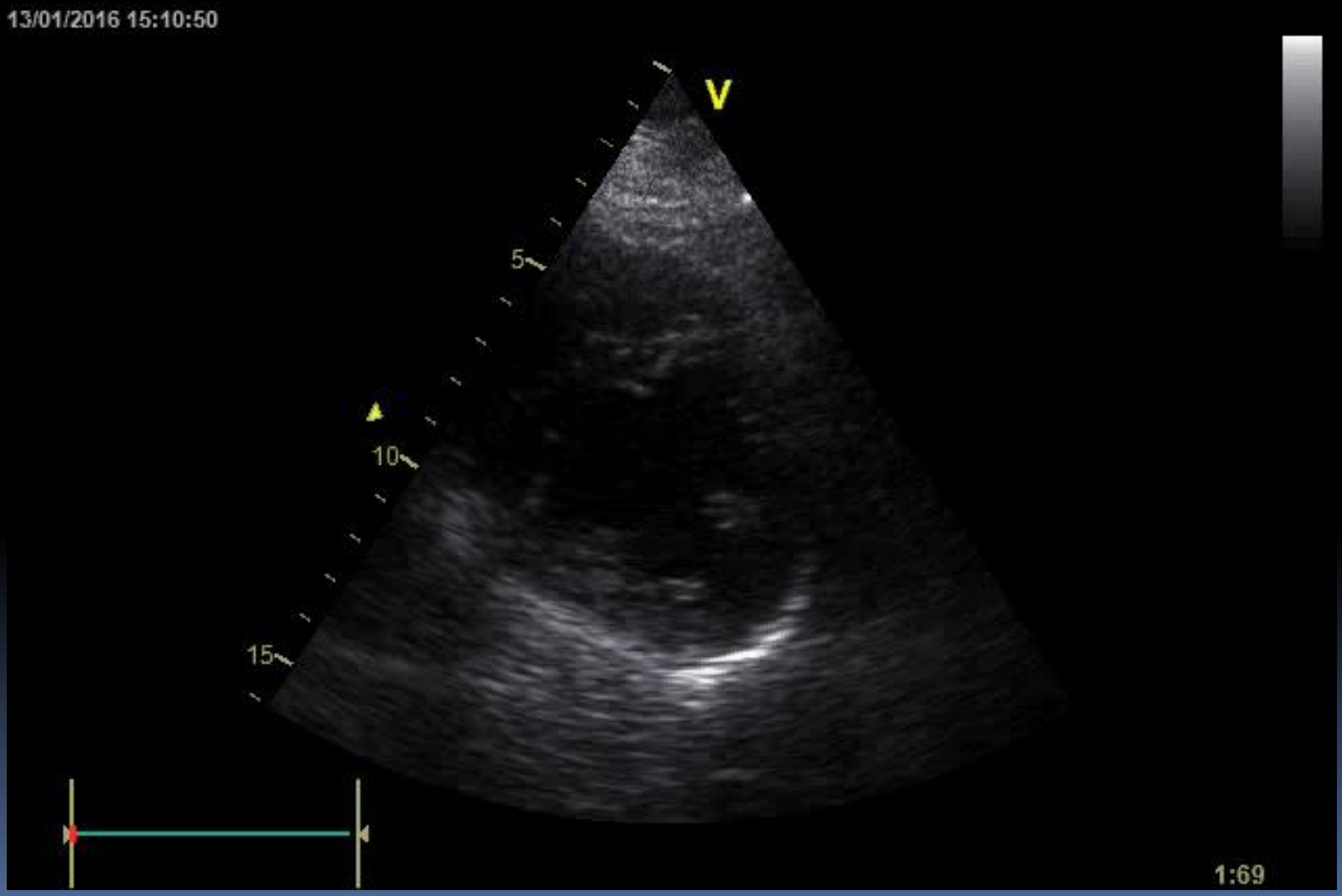
Ιστορικό

- Αρθροπλαστική ισχίων, δεξιού το 2008 και αριστερού το 2014 μετά από την οποία διαγνώστηκε DVT και έλαβε αντιπηκτική αγωγή με Rivaroxaban για 6 μήνες. Μετά από τη διάγνωση 2 επεισοδίων επιπολής θρομβοφλεβίτιδας την τελευταία διετία ετέθη σε ασπιρίνη 100mg.
- Έλεγχος θρομβοφιλίας αρνητικός εκτός από αυξημένα επίπεδα VIII.

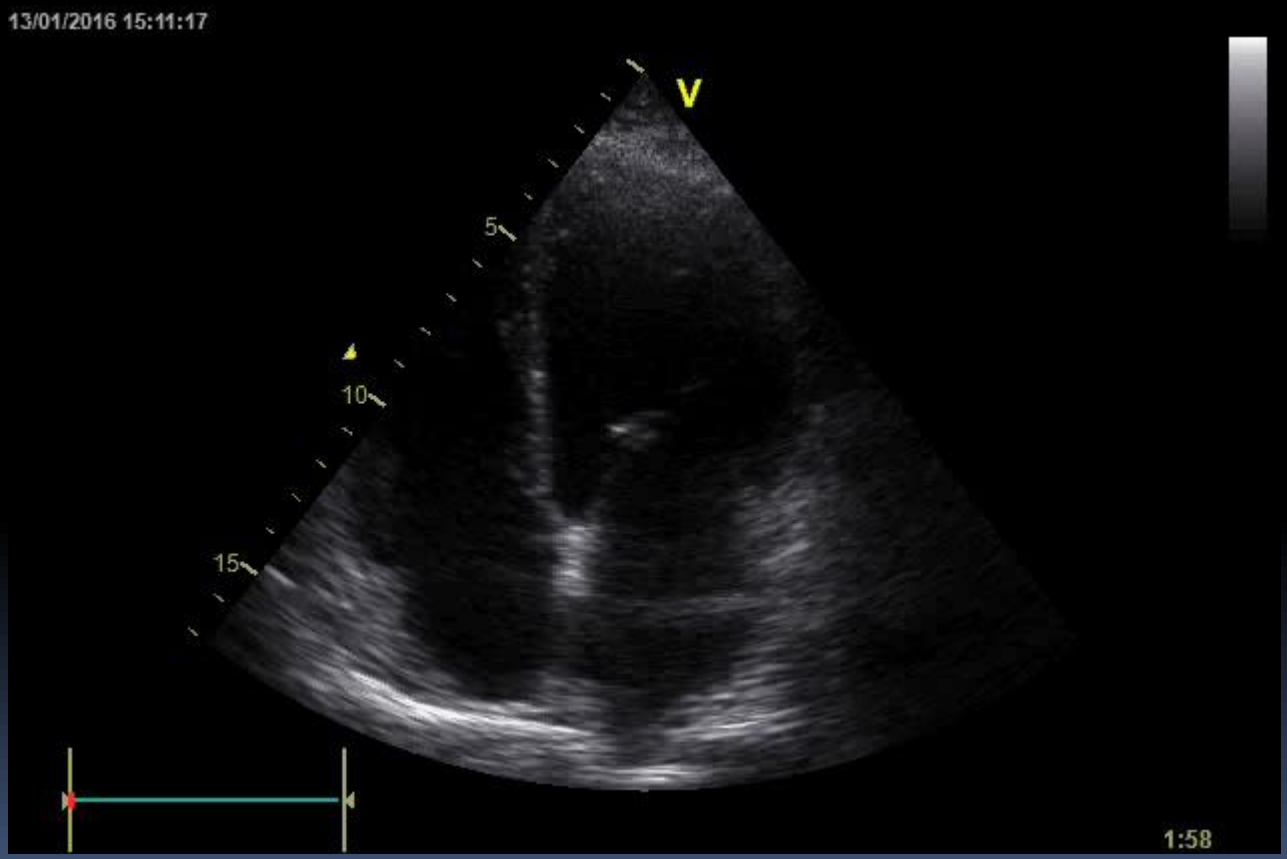
НКГ 1


124 ms
RR/PP interval 810/795 ms
QTD/QTcBD 70/78 ms
I
AVR
V1
V4
II
AVL
V2
V5
III
AVF
V3
V6
GE CASE V6.51
25mm/s 10mm/mV 40Hz 50Hz Spline
Unconfirmed
Attending MD: no
Page 1

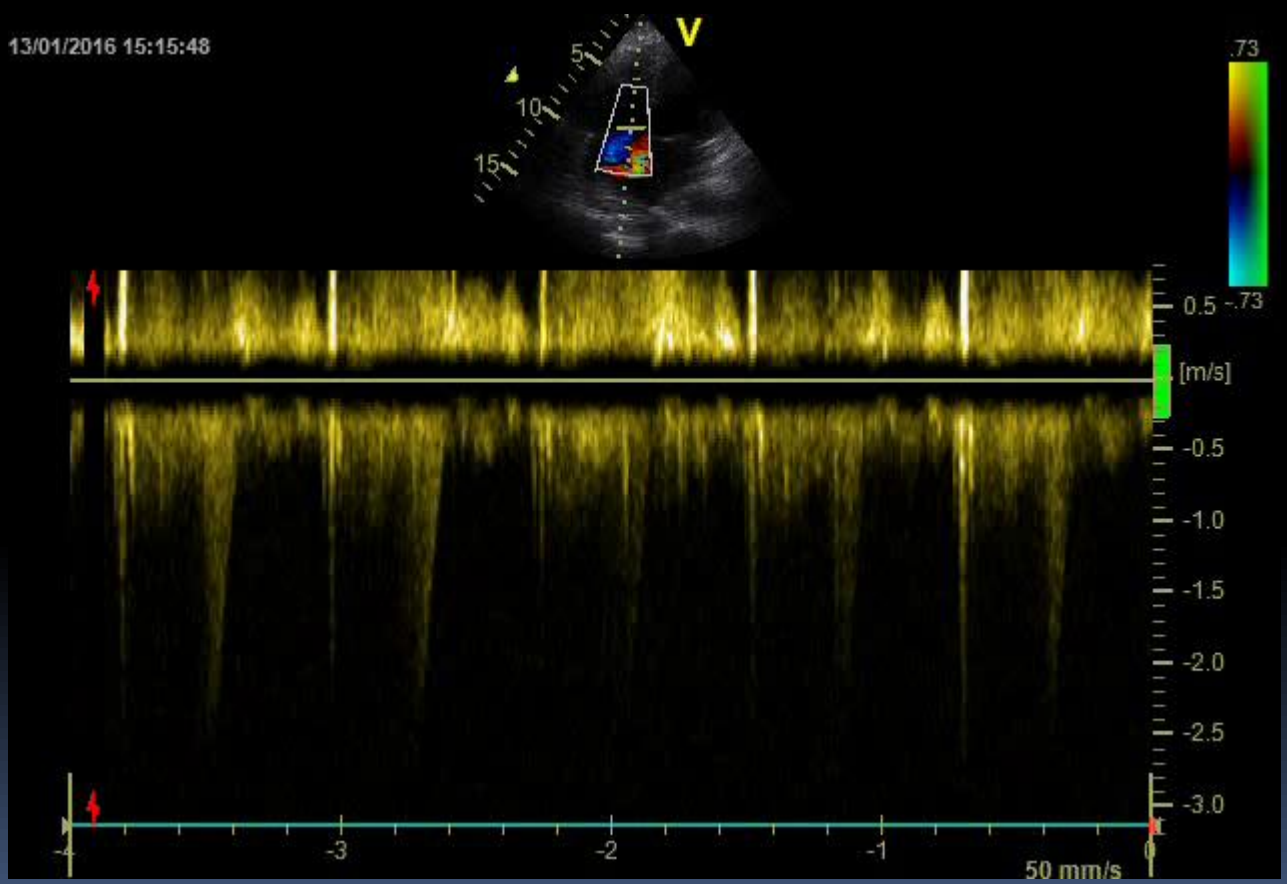
Echo-SAX



Echo-4ch



Echo-TRV


13/01/2016 15:15:48
V
5
10
15
.73
0.5
-.73
[m/s]
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
-4
-3
-2
-1
0
50 mm/s

Ιστορικό

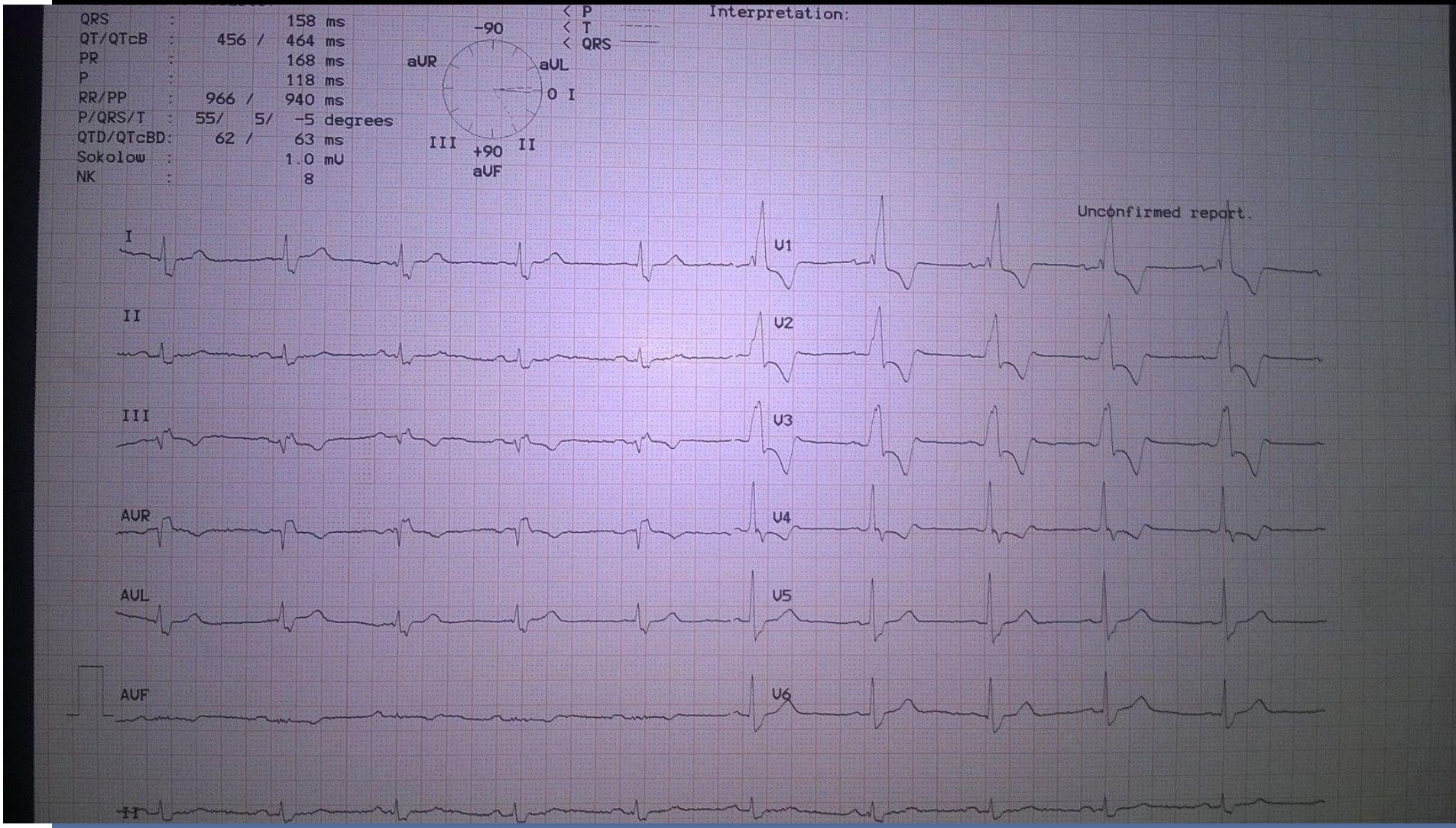
- Προ 3 μηνών νοσηλεία λόγω ΑΕΕ (ισχαιμικό έμφρακτο στο δεξιό θάλαμο και στο δεξιό παρεγκεφαλιδικό ημισφαίριο.
- Στη διάρκεια της νοσηλείας της υπεβλήθη σε ανοσολογικό, θυρεοειδικό και έλεγχο θρομβοφιλίας που ήταν αρνητικός.
- Ο έλεγχος των φλεβών κάτω άκρων δεν ανέδειξε εικόνα θρόμβωσης.
- Τίθεται έκτοτε σε πρόγραμμα αφαιμαξομεταγγίσεων.

Ιστορικό

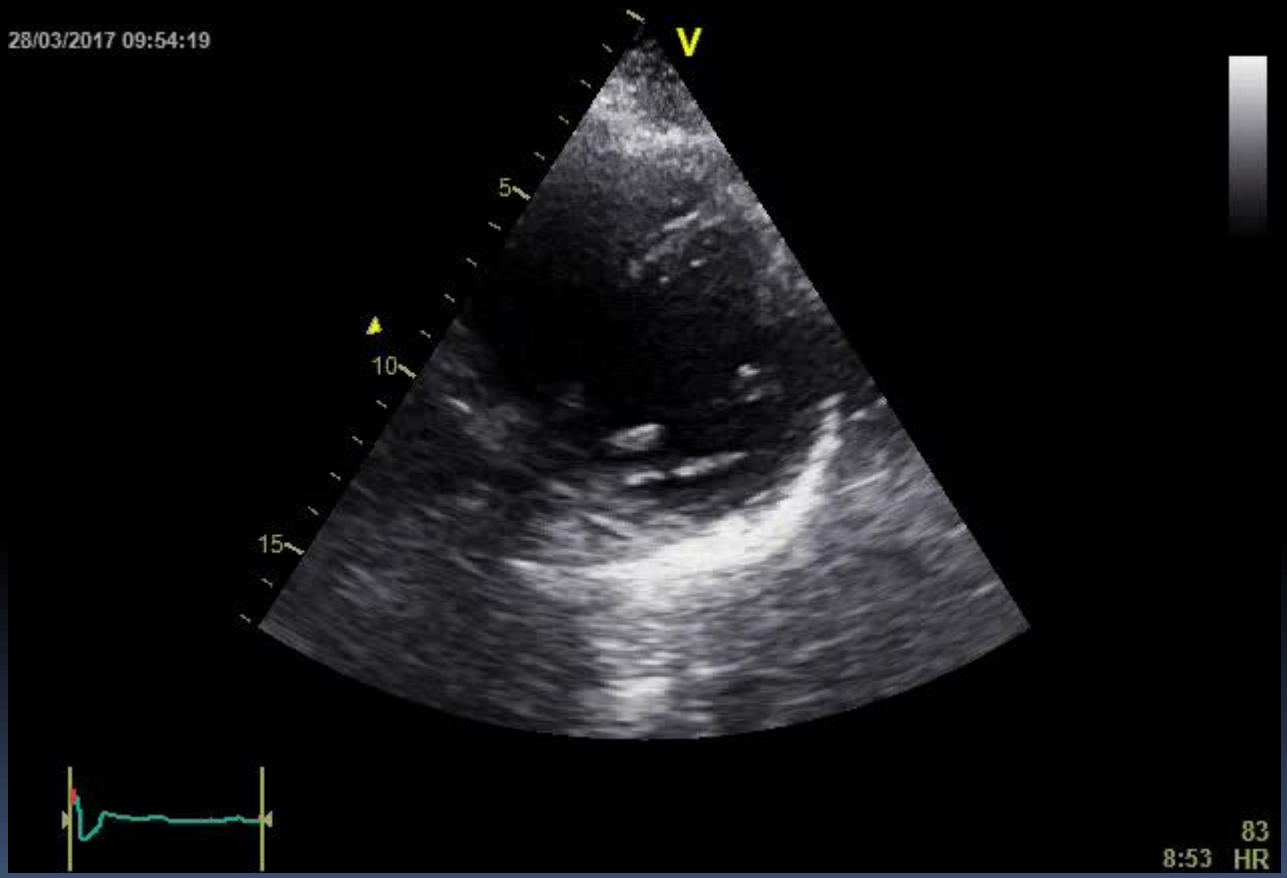
- Εξέρχεται με αγωγή Salospir 100, Xarelto 20, Siklos, Lumaren, Filicine και σύσταση για 24ωρη καταγραφή καρδιακού ρυθμού και διενέργεια TEE προς αναζήτηση εμβολογόνου εστίας.
- Στο TTE διάταση δεξιών κοιλοτήτων και αυξημένη TRV
- Εργαστηριακός έλεγχος εξόδου:

  Hb 10g/dl, PLT 393000, Cr. 0,56 mg/dl
  Χολερυθρίνη ολ. 2,6 αμ. 0,6, φερριτίνη 548

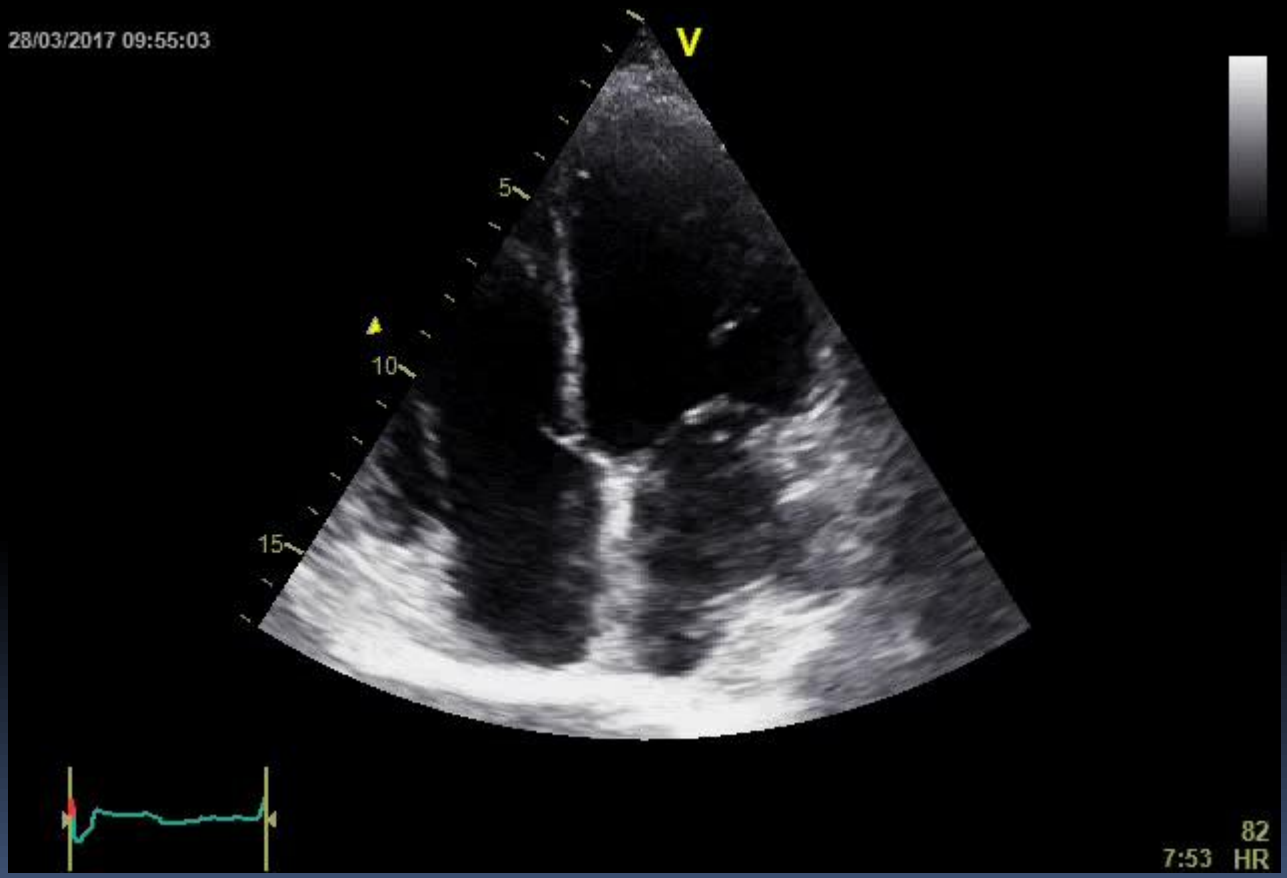
НКГ 2


QRS : 158 ms
QT/QTcB : 456 / 464 ms
PR : 168 ms
P : 118 ms
RR/PP : 966 / 940 ms
P/QRS/T : 55/ 5/ -5 degrees
QTD/QTcBD: 62 / 63 ms
Sokolow : 1.0 mV
NK : 8
-90
aVR
aVL
0 I
III
+90
II
aVF
P
T
QRS
Interpretation:
Unconfirmed report.
I
II
III
AVR
AVL
AVF
II
V1
V2
V3
V4
V5
V6

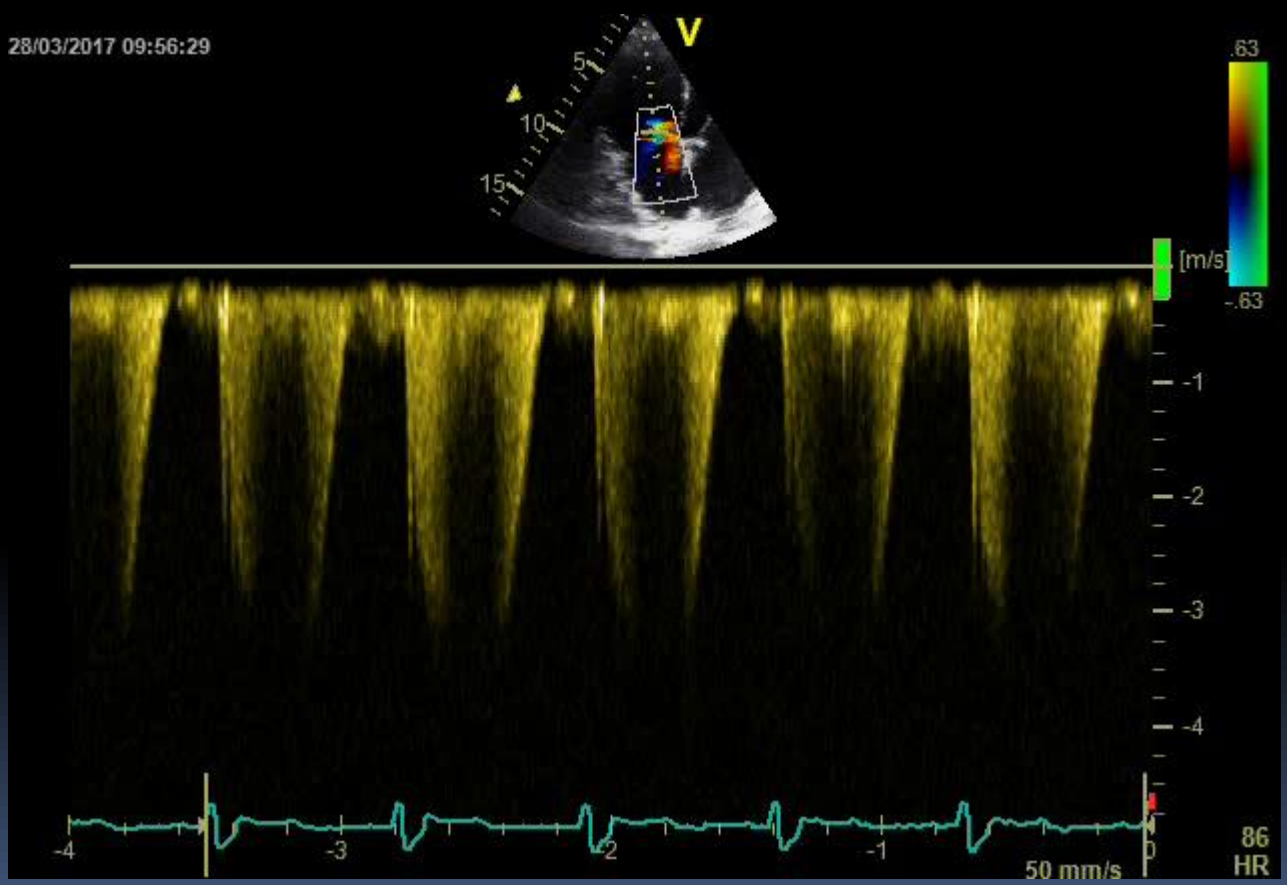
Echo-SAX



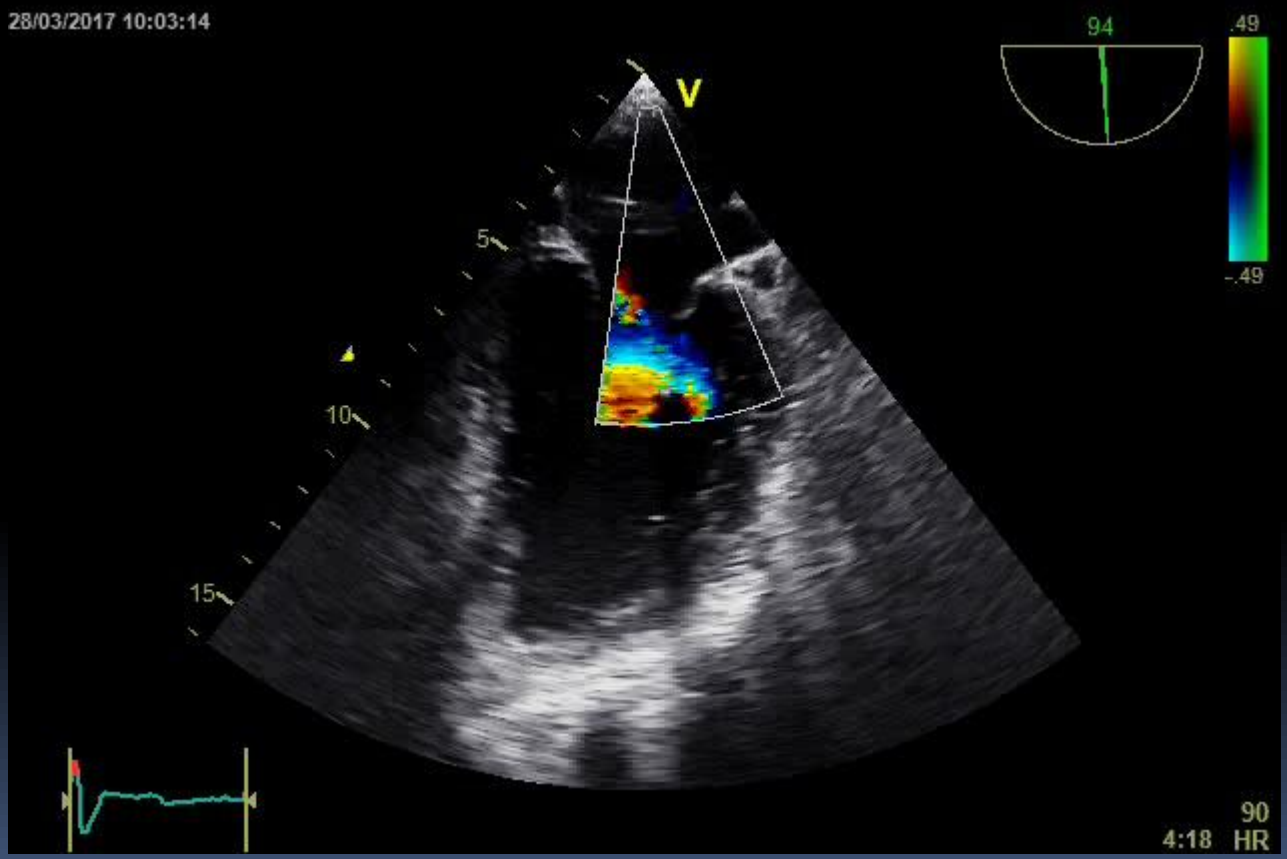
Echo-4Ch



Echo-TRV



TEE



Echo-SAX subxif

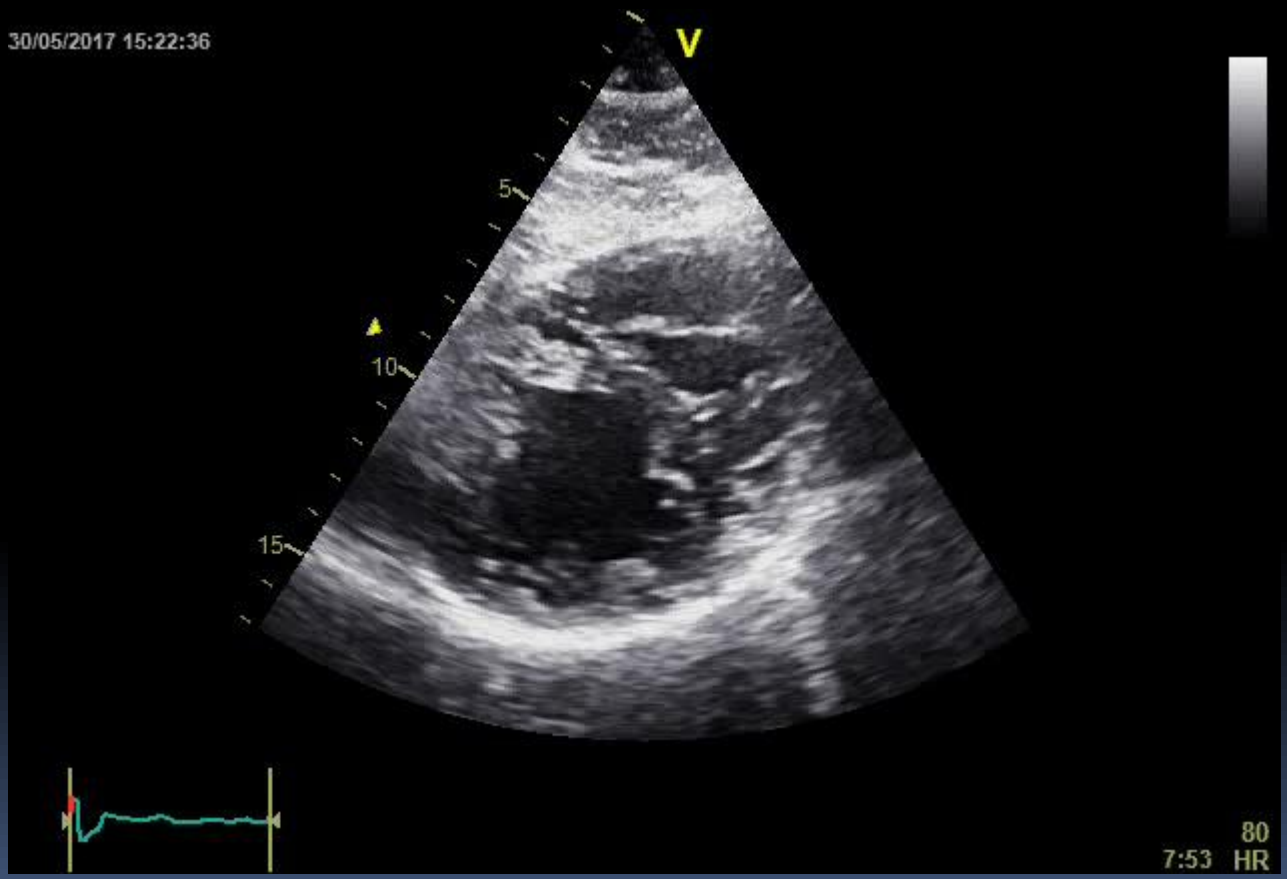
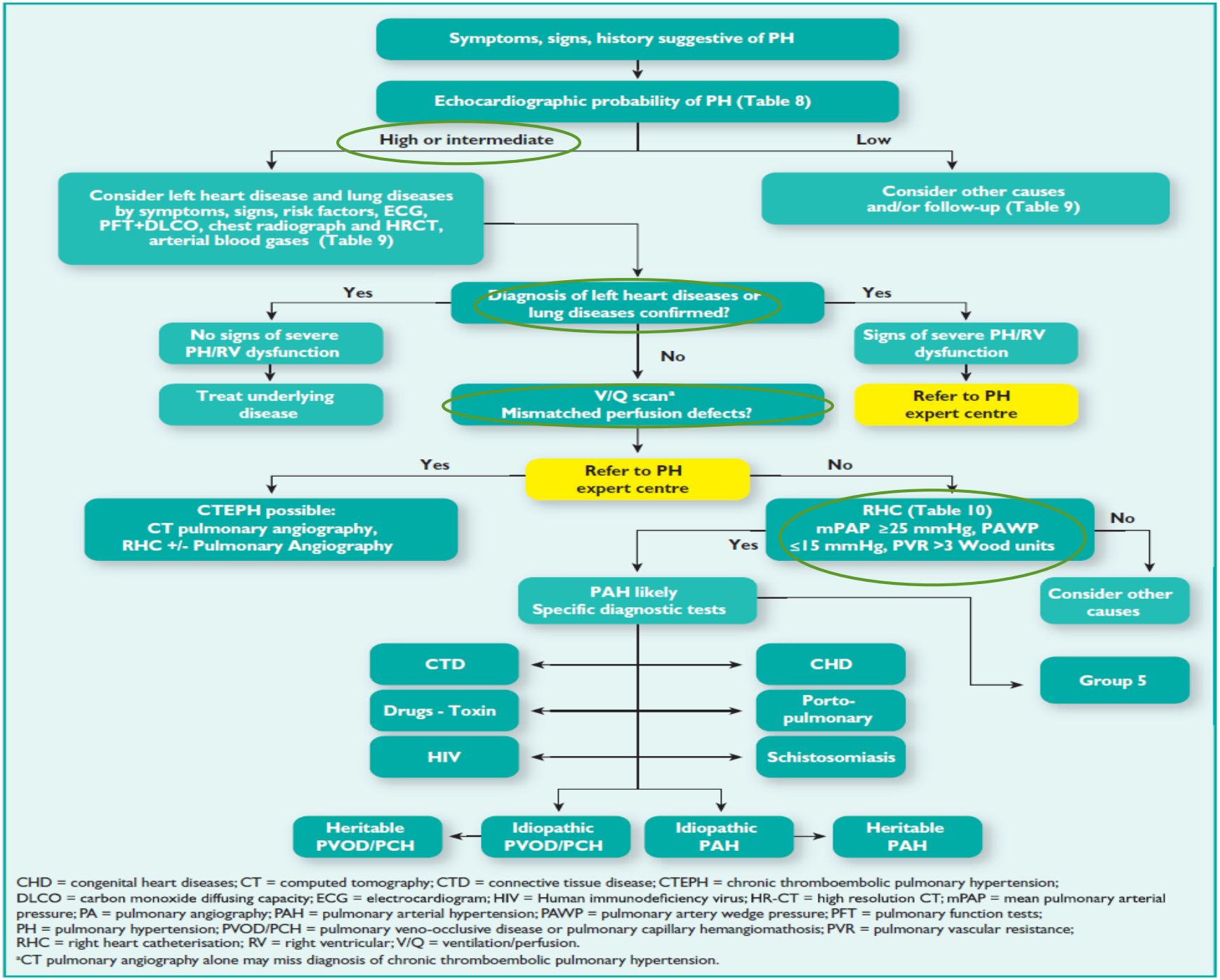


Table 8A Echocardiographic probability of pulmonary hypertension in symptomatic patients with a suspicion of pulmonary hypertension

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo 'PH signs'[a]	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

Table 9 Diagnostic management suggested according to echocardiographic probability of pulmonary hypertension in patients with symptoms compatible with pulmonary hypertension, with or without risk factors for pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension

Echocardiographic probability of PH	Without risk factors or associated condition for PAH or CTEPH[d]	Class[a]	Level[b]	With risk factors or associated conditions for PAH or CTEPH[c]	Class[a]	Level[b]	Ref[c]
Low	Alternative diagnosis should be considered	IIa	C	Echo follow-up should be considered	IIa	C	
Intermediate	Alternative diagnosis, echo follow-up, should be considered	IIa	C	Further assessment of PH including RHC should be considered[e]	IIa	B	45, 46
	Further investigation of PH may be considered[e]	IIb					
High	Further investigation of PH (including RHC[e]) is recommended	I	C	Further investigation of PH[e] including RHC is recommended	I	C	



CHD = congenital heart diseases; CT = computed tomography; CTD = connective tissue disease; CTEPH = chronic thromboembolic pulmonary hypertension; DLCO = carbon monoxide diffusing capacity; ECG = electrocardiogram; HIV = Human immunodeficiency virus; HR-CT = high resolution CT; mPAP = mean pulmonary arterial pressure; PA = pulmonary angiography; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PFT = pulmonary function tests; PH = pulmonary hypertension; PVOD/PCH = pulmonary veno-occlusive disease or pulmonary capillary hemangiomathosis; PVR = pulmonary vascular resistance; RHC = right heart catheterisation; RV = right ventricular; V/Q = ventilation/perfusion.

[a]CT pulmonary angiography alone may miss diagnosis of chronic thromboembolic pulmonary hypertension.

Σπινθηρογράφημα αιμάτωσης πνευμόνων

ΗΜΕΡΟΜΗΝΙΑ	ΗΛΙΚΙΑ	ΦΥΛΟ	ΠΑΡΑΠΕΜΠΩΝ
30-3-2017	50	Θ	

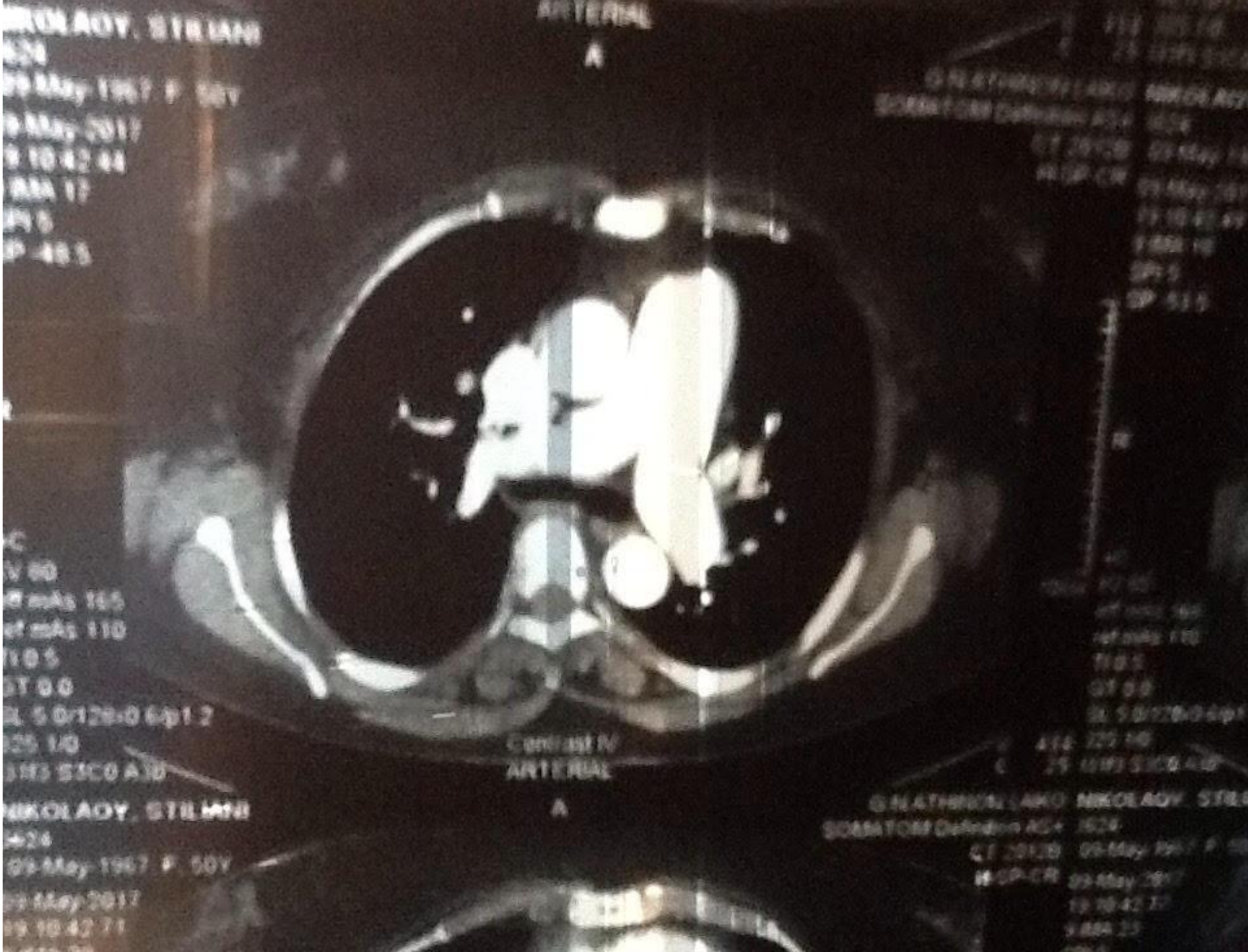
ΕΚΘΕΣΗ ΡΑΔΙΟΪΣΟΤΟΠΙΚΗΣ ΜΕΛΕΤΗΣ

Στο σπινθηρογράφημα αιματώσεως πνευμόνων με ^{99m}Tc-MAA παρατηρούνται μικρά τριγωνικά ελλείμματα διάχυσης του ραδιοφαρμάκου και στους δύο πνεύμονες ιδία δεξιά συμβατά με παρουσία μικροεμβολών.

Συμπέρασμα: Μελέτη ενδεικτική παρουσίας μικροεμβολικής νόσου.

Γνωμάτευση CT θώρακα

- Καλή ροή του σκιαγραφικού στα αγγεία του μεσοθωρακίου χωρίς εικόνα πνευμονικής εμβολής.


ARTERIAL
A
Contrast IV
ARTERIAL
A

Δεξιός καθετηριασμός

- RA 6mmHg
- RV 55/6mmHg
- PA 53/22/33mmHg
- PW 9mmHg
- CO 4,26lt/min
- CI 2,34lt/min/m²
- PVR 5,63WU
- SVR 18,07WU

RHC

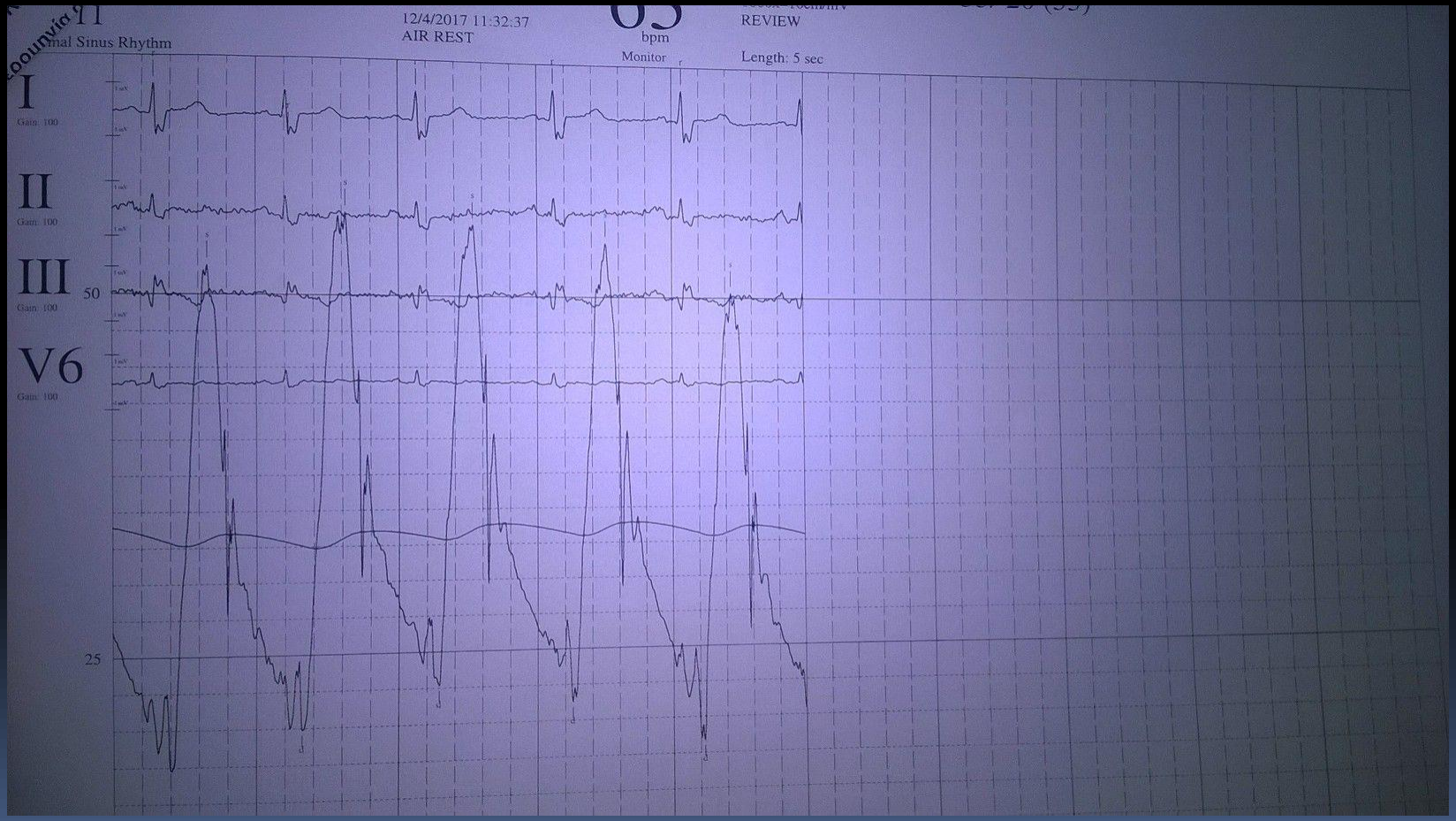

12/4/2017 11:32:37
AIR REST
bpm
Monitor
REVIEW
Length: 5 sec
I
II
III
V6
Gain: 100
50
25

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]	

Διαστρωμάτωση κινδύνου

- NTpBNP 433ng/l
- SvO2 57%
- RA area 17,5cm²
- Hb 10gr/dl
- RAP 6mmHg
- CI 2,34lt/min/m²

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%

Table 4 Comprehensive clinical classification of pulmonary hypertension (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 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, 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

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 thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

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expert reviews
in molecular medicine

Pathophysiology and therapy for haemoglobinopathies
Part I: sickle cell disease

Catherine Madigan and Punam Malik

ποια αλλαγή συμβαίνει στην αιμοσφαιρίνη σε ομοζυγώτη της Δρεπανοκυτταρικής αναιμίας;

- δεν προκαλεί μείωση ή διακοπή της σύνθεσης μιας πρωτεϊνικής αλυσίδας
- προκαλεί παραγωγή μιας διαφορετικής αλυσίδας

δημιουργία μιας παθολογικής αιμοσφαιρίνης S

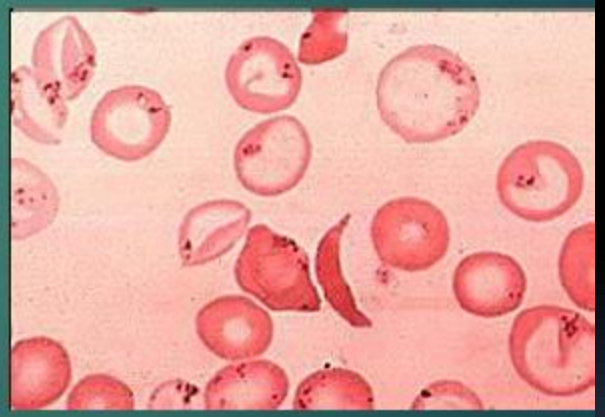
Αιμοσφαιρίνη S

ποιες συνέπειες έχει η κυκλοφορία της παθολογικής αιμοσφαιρίνης S;

- σε συνθήκες υποοξυγοναιμίας καθιζάνει
  - δίνει στα ερυθρά ένα χαρακτηριστικό δρεπανοειδές σχήμα

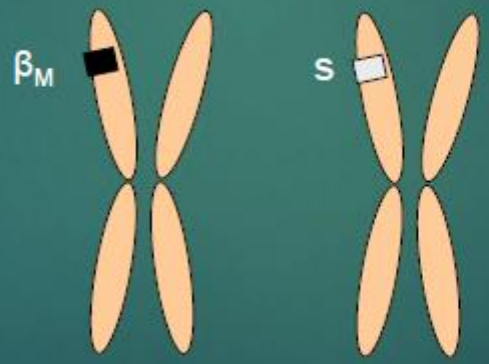
τα δρεπανοκύτταρα

- αιμολύονται εύκολα
- η καθίζησή τους στα τριχοειδή
  - δημιουργεί θρόμβους αίματος
- μπορεί να συμβεί μετά από
  - μια λοίμωξη
  - ένα έντονο στρες
  - μια εγχείρηση



Τι ονομάζουμε Μικροδρεπανοκυτταρική αναιμία;

- είναι μια μεικτή κατάσταση
- ο άρρωστος είναι διπλά ετεροζυγώτης
  - έχει το στίγμα της Δρεπανοκυτταρικής και
  - το στίγμα της Μεσογειακής αναιμίας



ΜΟΡΦΕΣ ΔΡΕΠΑΝΟΚΥΤΤΑΡΙΚΗΣ ΝΟΣΟΥ

- ΟΜΟΖΥΓΗ ΔΡΕΠΑΝΟΚΥΤΤΑΡΙΚΗ ΝΟΣΟΣ:HbS/HbS
- ΕΤΕΡΟΖΥΓΗ ΔΡΕΠΑΝΟΚΥΤΤΑΡΙΚΗ ΝΟΣΟΣ:HbS/HbA
- ΣΥΝΘΕΤΗ ΕΤΕΡΟΖΥΓΗ ΔΡΕΠΑΝΟΚΥΤΤΑΡΙΚΗ ΚΑΙ ΑΙΜΟΣΦΑΙΡΙΝΟΠΑΘΕΙΑ C: HbS/HbC
- ΣΥΝΘΕΤΗ ΕΤΕΡΟΖΥΓΗ ΚΑΤΑΣΤΑΣΗ ΔΡΕΠΑΝΟΚΥΤΤΑΡΙΚΗΣ ΚΑΙ ΜΟΡΦΩΝ β-ΜΕΣΟΓΕΙΑΚΗΣ ΑΝΑΙΜΙΑΣ:HbS/HbB
- ΣΠΑΝΙΟΤΕΡΟΙ ΣΥΝΔΥΑΣΜΟΙ ΜΕ ΑΛΛΕΣ ΠΑΘΟΛΟΓΙΚΕΣ ΑΙΜΟΣΦΑΙΡΙΝΕΣ.

Pulmonary Hypertension Associated With Hemoglobinopathies

Prevalent But Overlooked

Dimitrios Farmakis, MD, PhD; Athanasios Aessopos, MD, PhD

Hemoglobinopathies constitute a heterogeneous group of hereditary hemoglobin disorders characterized by either reduced (thalassemias) or defective (sickle cell disease) globin chain synthesis that results in chronic hemolytic anemia. They represent the most common monogenetic disorders in humans, and although traditionally confined to specific geographic areas and populations (the Mediterranean Basin and the Middle and Far East in the case of β-thalassemia; Sub-Saharan Africa and African-Americans in the case of sickle cell disease), they have currently expanded to a global distribution because of the immigration of those populations to the Western world.[1] Although their clinical severity is variable, the hemoglobinopathies are generally demanding conditions, particularly in the homozygous state, characterized by reduced survival, multiorgan complications, frequent hospitalizations, and need for lifelong management, thus posing a significant medical and socioeconomic burden.

Cardiovascular complications are among the leading causes of mortality and morbidity in hemoglobinopathies.[1] In the wide spectrum of cardiovascular manifestations of these patients, pulmonary hypertension (PH) holds a prominent place. It has been postulated that hemoglobinopathies, along with HIV infection and schistosomiasis, may be the most common causes of PH worldwide given the high prevalence of PH in those populations.[2]

Epidemiology

β-Thalassemia

PH is a frequent finding in patients with hemoglobinopathies, but the reported prevalence varies in the different conditions and according to the method used for screening (Table 1). In thalassemia intermedia, a form of β-thalassemia that accounts for 20% to 25% of cases, PH has been recognized as the most striking cardiovascular finding and the main cause of heart failure. In a preliminary report, all 7 patients with thalassemia intermedia with heart failure had preserved systolic left ventricular (LV) function and severe PH as shown by right-sided heart catheterization.[3] This initial report was followed by a systematic study of 110 patients with thalassemia intermedia with a mean age of 33 years[4]; PH was observed echocardiographically in approximately 60% of cases, and all 6 patients with heart failure had preserved systolic LV function and underwent right-sided heart catheterization that confirmed the presence of PH.[5] A later study comparing cardiovascular involvement between thalassemia intermedia and the most prevalent form of the disease, namely, thalassemia major, in a cohort of 205 patients confirmed the above findings.[7] In thalassemia major, in contrast, the main cardiac manifestation is LV dysfunction.[6,7] Striking rates of PH of 75% and 79% were reported in 2 previous studies in small populations of patients with thalassemia major,[3,4] but those patients were generally poorly treated and had an increased prevalence of systolic LV dysfunction. Recent trials in optimally treated populations with thalassemia major showed that PH was rather rare and mild, with pulmonary artery pressure elevation, mostly borderline, encountered in approximately 10% of cases in different cohorts.[5–7]

Sickle Cell Disease

In homozygous sickle cell anemia, PH is a frequent finding and has been considered a major determinant of prognosis.[18] In a cohort of 195 patients with a mean age of 36 years, 32% of patients had PH by echocardiography, and PH was the strongest predictor of mortality within 18 months.[10] Similarly, in a subsequent trial in 235 patients with a mean age of 35 years, PH was present in 40% of cases, and together with diastolic LV dysfunction, it was the strongest predictor of mortality.[12] In sickle-thalassemia, a compound heterozygous state with 1 thalassemia and 1 sickle allele, PH has been observed with a rather lower frequency and a definitely lesser severity.[15–17] It should be stressed that with the exception of thalassemia intermedia, in which PH was confirmed by right-sided heart catheterization in 2 of the previously cited trials,[8,9] the vast majority of studies in thalassemia and sickle cell disease used echocardiography as a screening tool, and therefore, the reported prevalence may be overestimated by at least some of those trials.

Pathophysiology

The hemoglobinopathies are not the only hemolytic states associated with PH. In fact, this association is much broader, and it has been observed that other chronic hemolytic

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Παθοφυσιολογία ΠΥ στις αιμοσφαιρινοπάθειες

- Χρόνια ιστική υποξία
- Υψηλή καρδιακή παροχή
- Αιμόλυση
- Υπερπηκτικότητα
- Σπληνεκτομή
- Αιμοσιδήρωση
- Χρόνια πνευμονική βλάβη

Table 1. Prevalence of Pulmonary Hypertension in Different Hemoglobinopathies

Study	Publication Year	Hemoglobinopathy	N	Method for PH Diagnosis	Echocardiographic Criterion for PH	Prevalence of PH, %
Grisaru et al[3]	1990	Thalassemia major	35	Echo	PAT/RVET	75
Du et al[4]	1997	Thalassemia major	33	Echo	TPG+RAP >30 mm Hg	79
Derchi et al[5]	1999	Thalassemia major	130	Echo	TPG	10
Aessopos et al[6]	2004	Thalassemia major	202	Echo	TPG >30 mm Hg	10
Aessopos et al[7]	2005	Thalassemia major and thalassemia intermedia	131 74	Echo	TPG >30 mm Hg	10 60
Aessopos et al[8]	1995	Thalassemia intermedia with heart failure	7	RHC		100
Aessopos et al[9]	2001	Thalassemia intermedia	110	Echo and RHC	TPG >30 mm Hg	59
Gladwin et al[10]	2004	Sickle cell anemia	195	Echo	TRV ≥2.5 m/s	32
Machado et al[11]	2006	Sickle cell anemia	226	Echo	TRV ≥2.5 m/s	35
Sachdev et al[12]	2007	Sickle cell anemia	235	Echo	TRV ≥2.5 m/s	40
De Castro et al[13]	2008	Sickle cell anemia, sickle thalassemia, sickle-HbC, sickle-HbO_{Arab}	125	Echo	TRV ≥2.5 m/s	32
Klings et al[14]	2008	Sickle cell anemia	97	Echo	TRV ≥2.5 m/s	43
		sickle-HbC	27			28
Moyssakis et al[15]	2005	Sickle thalassemia	43	Echo	TPG >30 mm Hg	21
Voskaridou et al[16]	2007	Sickle thalassemia	84	Echo	TPG+RAP ≥35 mm Hg or TRV ≥2.5 m/s	33
Aessopos et al[17]	2009	Sickle thalassemia	115	Echo	TPG >30 mm Hg	27

PH indicates pulmonary hypertension; Echo, echocardiography; PAT/RVET, pulmonary valve acceleration time to right ventricular ejection time ratio; TPG, tricuspid systolic pressure gradient; RAP, right atrial pressure; RHC, right heart catheterization; sickle-HbC, sickle cell–hemoglobin C; sickle-HbOArab, sickle cell–hemoglobin O-Arab; and TRV, tricuspid regurgitation velocity.

Hemodynamic and Functional Assessment of Patients with Sickle Cell Disease and Pulmonary Hypertension

Anastasia Anthi[1,2*], Roberto F. Machado[1,2*], Maria L. Jison[2], Angelo M. Taveira-DaSilva[3], Lewis J. Rubin[4], Lori Hunter[1,2,5], Christian J. Hunter[1,2], Wynona Coles[1,2], James Nichols[1,2], Nilo A. Avila[6], Vandana Sachdev[1], Clara C. Chen[7], and Mark T. Gladwin[1,2]

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Παθοφυσιολογία ΠΥ στις αιμοσφαιρινοπάθειες

- Μελέτες με σπινθηρογράφημα αερισμού-αιμάτωσης πνευμόνων ανέδειξαν ευρήματα συμβατά με CTEPH στο 12% ασθενών με SCD και PH.
- Συνήθη νεκροτομικά ευρήματα σε ασθενείς με SCD αποτελούν οι μικροθρομβώσεις ή/και οι θρομβοεμβολικές αλλοιώσεις.
- Νεκροτομικές μελέτες σε ασθενείς με SCD και PH υποδηλώνουν την πιθανότητα συμμετοχής των θρομβοεμβολών.

Review Series

SICKLE CELL DISEASE: CHALLENGES AND PROGRESS

Pathophysiology and treatment of pulmonary hypertension in sickle cell disease

Victor R. Gordeuk,[1] Oswaldo L. Castro,[2] and Roberto F. Machado[1]

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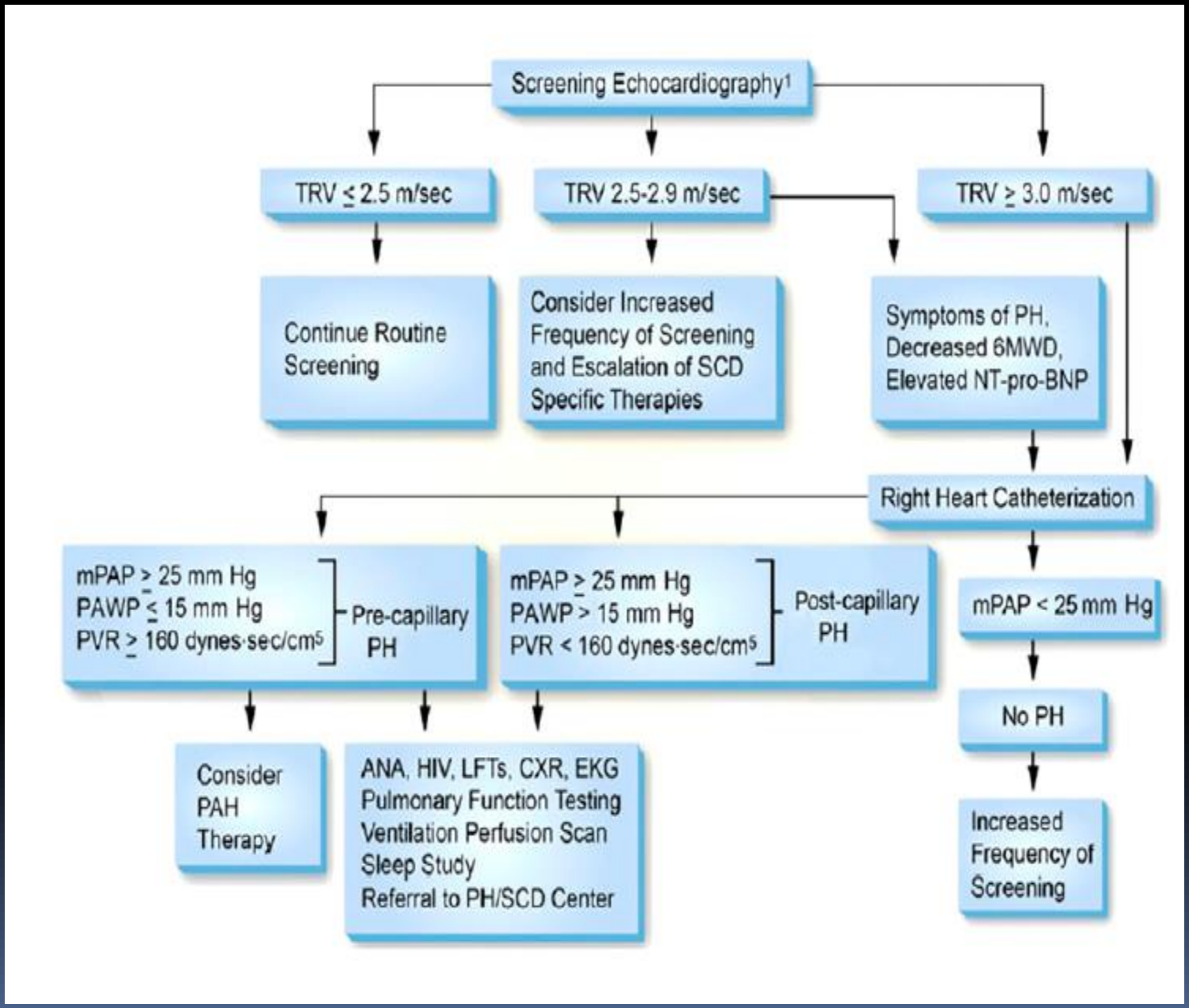
Screening Echocardiography[1]
TRV ≤ 2.5 m/sec
TRV 2.5-2.9 m/sec
TRV ≥ 3.0 m/sec
Continue Routine Screening
Consider Increased Frequency of Screening and Escalation of SCD Specific Therapies
Symptoms of PH, Decreased 6MWD, Elevated NT-pro-BNP
Right Heart Catheterization
mPAP ≥ 25 mm Hg
PAWP ≤ 15 mm Hg
PVR ≥ 160 dynes·sec/cm5
Pre-capillary PH
mPAP ≥ 25 mm Hg
PAWP > 15 mm Hg
PVR < 160 dynes·sec/cm5
Post-capillary PH
mPAP < 25 mm Hg
No PH
Increased Frequency of Screening
Consider PAH Therapy
ANA, HIV, LFTs, CXR, EKG
Pulmonary Function Testing
Ventilation Perfusion Scan
Sleep Study
Referral to PH/SCD Center

- Συνοψίζοντας πρόκειται για μια ασθενή με σύνθετη ετερόζυγη δρεπανοκυτταρική νόσο με ιστορικό φλεβικών και αρτηριακών **θρομβώσεων** υπό αγωγή με υδροξυουρία και **ήδη** σε πρόγραμμα αφαιμαξομεταγγίσεων και αντιπηκτική αγωγή στην οποία διαπιστώνεται προτριχοειδική πνευμονική υπέρταση πιθανώς σε έδαφος **κυρίως** περιφερικής θρομβοεμβολικής πνευμονικής νόσου

ΕΡΩΤΗΜΑΤΑ

- Σε ποια κατηγορία ΠΥ ταξινομείται η συγκεκριμένη ασθενής;
- Θα λάβει αντιπηκτική αγωγή, τι είδους και για πόσο διάστημα;
- Οι παραπάνω αποφάσεις θα ήταν διαφορετικές αν δεν υπήρχε το ιστορικό DVT;
- Θα χορηγήσουμε ειδική θεραπεία ΠΑΥ και αν ναι ποια θα είναι η πρώτη μας επιλογή;
- Σε περίπτωση που επιλέξουμε από την αρχή θεραπεία συνδυασμού ποιες θα είναι οι επιλογές μας;

AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society Clinical Practice Guideline: Diagnosis, Risk Stratification, and Management of Pulmonary Hypertension of Sickle Cell Disease

Elizabeth S. Klings*, Roberto F. Machado*, Robyn J. Barst†, Claudia R. Morris, Kamal K. Mubarak, Victor R. Gordeuk, Gregory J. Kato, Kenneth I. Ataga, J. Simon Gibbs, Oswaldo Castro, Erika B. Rosenzweig, Namita Sood, Lewis Hsu, Kevin C. Wilson, Marilyn J. Telen, Laura M. DeCastro, Lakshmanan Krishnamurti, Martin H. Steinberg, David B. Badesch, and Mark T. Gladwin; on behalf of the ATS *Ad Hoc* Committee on Pulmonary Hypertension of Sickle Cell Disease

This Official Clinical Practice Guideline of the American Thoracic Society was approved by the ATS Board of Directors, November 2013. These Guidelines were also endorsed by the American College of Chest Physicians, October 2013, and by the Pulmonary Hypertension Association, November 2013

Recommendation: For patients with SCD who have RHC-confirmed PH, venous thromboembolism, and no additional risk factors for bleeding, we suggest indefinite anticoagulant therapy rather than a limited duration of therapy (weak recommendation, low-quality evidence).

Values and preferences: This recommendation attaches a relatively high value to the prevention of recurrent venous thromboembolic events and a lower value to the risks and burdens of anticoagulant therapy.

Recommendation: For all patients with SCD who have elevated TRV alone, or elevated NT-pro-BNP alone, and for most patients with SCD who have RHC-confirmed PH, we recommend *against* targeted PAH therapy (strong recommendation, moderate-quality evidence).

Remarks: Targeted PAH therapy refers to prostacyclin agonist, endothelin receptor antagonist, soluble guanylate cyclase stimulator, and phosphodiesterase-5 inhibitor therapy.

Values and preferences: This recommendation places a greater value on avoiding expensive and potentially harmful agents in patients who may not benefit and a lower value on avoiding the complications of invasive hemodynamic testing by using noninvasive results for decision making.

Recommendation: For select patients with SCD who have an RHC-confirmed marked elevation of their pulmonary vascular resistance, normal pulmonary artery wedge pressure, and related symptoms, we suggest a trial with either a prostacyclin agonist or an endothelin receptor antagonist (weak recommendation, low-quality evidence).

Remarks: This group of patients with SCD is characterized by a mean pulmonary arterial pressure (mPAP) of $\geqslant$25 mm Hg with a pulmonary artery wedge pressure $<$ 15 mm Hg, plus increased pulmonary vascular resistance (PVR) of $\geqslant$160 dyn $\cdot$ seconds $\cdot$ cm^{-5} (2 Wood units). Patients with SCD who have confirmed PH are now categorized as being within WHO group 5, instead of WHO group 1. As a result, use of targeted PAH therapy in such patients is considered off-label.

Values and preferences: This recommendation places a greater value on improving symptoms and hemodynamic measures and a lower value on the costs, burdens, and risks of therapy.

Recommendation: For patients with SCD who have an RHC-confirmed marked elevation of their pulmonary vascular resistance, a normal pulmonary artery wedge pressure, and related symptoms, we recommend *against* phosphodiesterase-5 inhibitor therapy as a first-line treatment (strong recommendation, moderate-quality evidence).

Remarks: The recommendation is based on the observation that phosphodiesterase-5 inhibitor therapy may increase the risk of hospitalization for vaso-occlusive crisis.

Values and preferences: This recommendation places a higher value on avoiding serious complications and a lower value on symptomatic and hemodynamic improvement.

Ευχαριστώ
για
την προσοχή σας