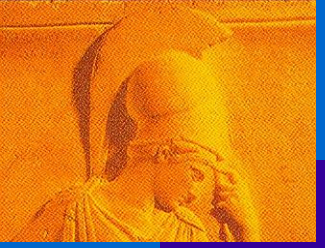


Πνευμονική Υπερταση και Ρευματικά Νοσήματα

- *Στέλλα Μπρίλη*

– *Α! Πανεπιστημιακή Καρδιολογική Κλινική*

– *Ιπποκράτειο Νοσοκομείο Αθηνών*

Pathogenesis of PAH

RISK FACTORS AND ASSOCIATED CONDITIONS

- CTD
- CHD
- Portal hypertension
- HIV
- Drugs and toxins
- Pregnancy

SUSCEPTIBILITY

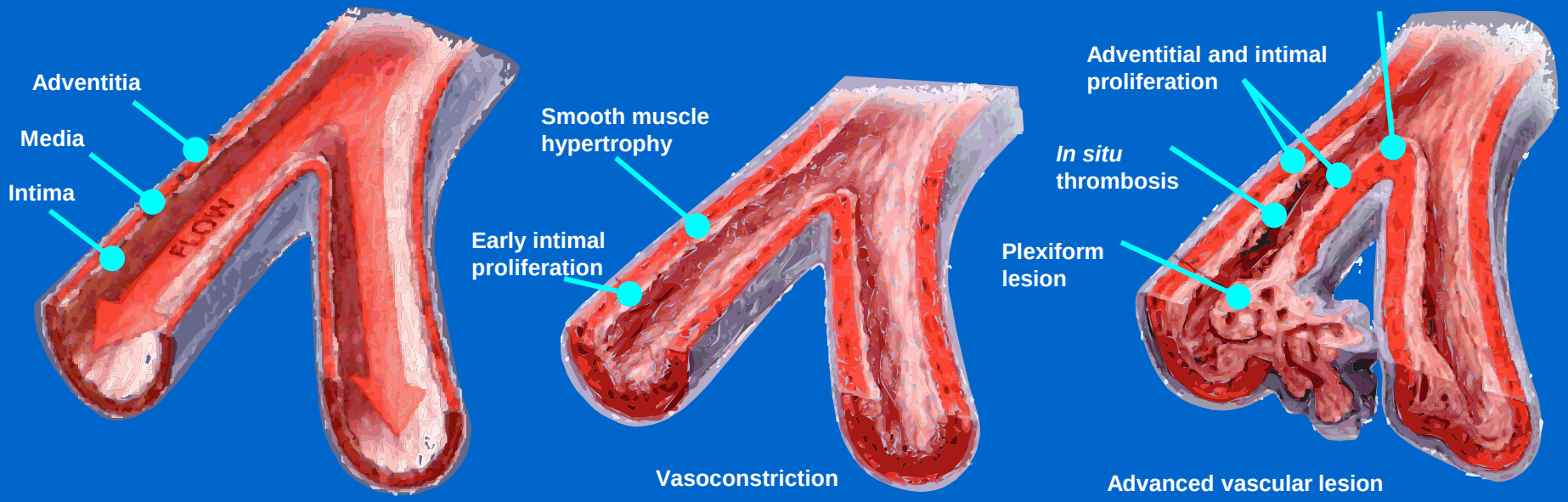
- BMPR2 mutation
- Other genetic factors

VASCULAR INJURY

Endothelial dysfunction

- ↓NO synthase
- ↓PGI_2 production
- ↑Thromboxane production
- ↑ET-1 production

Vascular smooth muscle dysfunction



Normal	Reversible disease	Irreversible disease

BMPR2 = bone morphogenetic protein type 2 receptor; CHD = congenital heart disease; CTD = connective tissue disease; ET = endothelin; HIV = human immunodeficiency virus; NO = nitric oxide; PAH = pulmonary arterial hypertension;PGI_2 = prostacyclin

Adapted from Gaine S. *JAMA* 2000;284:3160–8.

Κλινική ταξινόμηση πνευμονικής υπέρτασης
4ο Παγκόσμιο Συμπόσιο, Dana Point California 2008

1. Πνευμονική αρτηριακή υπέρταση (ΠΑΥ)

- Ιδιοπαθής
- Κληρονομούμενη
- Προκαλούμενη από φάρμακα και τοξίνες
- Σχετιζόμενη με:
  - Συγγενείς καρδιοπάθειες
  - Νοσήματα του συνδετικού ιστού
  - Πυλαία Υπέρταση
  - HIV
  - Σχιστοσωμίαση
  - Χρόνια αιμολυτική αναιμία
- Εμμένουσα ΠΥ του νεογνού

1΄ Πνευμονική φλεβοαποφρακτική νόσος και/ή πνευμονική τριχοειδική αιμαγγειωμάτωση

2. Σχετιζόμενη με αριστερή καρδιακή νόσο

- Συστολική δυσλειτουργία
- Διαστολική δυσλειτουργία
- Βαλβιδοπάθειες

Simonneau G, et al. J Am Coll Cardiol 2009;54:S43-S54

3. Αναπνευστικές νόσοι και/ή υποξαιμία

- ΧΑΠ
- Διάμεσες πνευμονοπάθειες
- Άλλες πνευμονοπάθειες μικτού περιοριστικού και αποφρακτικού τύπου
- Σύνδρομο υπνικής άπνοιας
- Παθήσεις με κυψελιδικό υποαερισμό
- Χρόνια παραμονή σε μεγάλο υψόμετρο
- Διαταραχές της ανάπτυξης

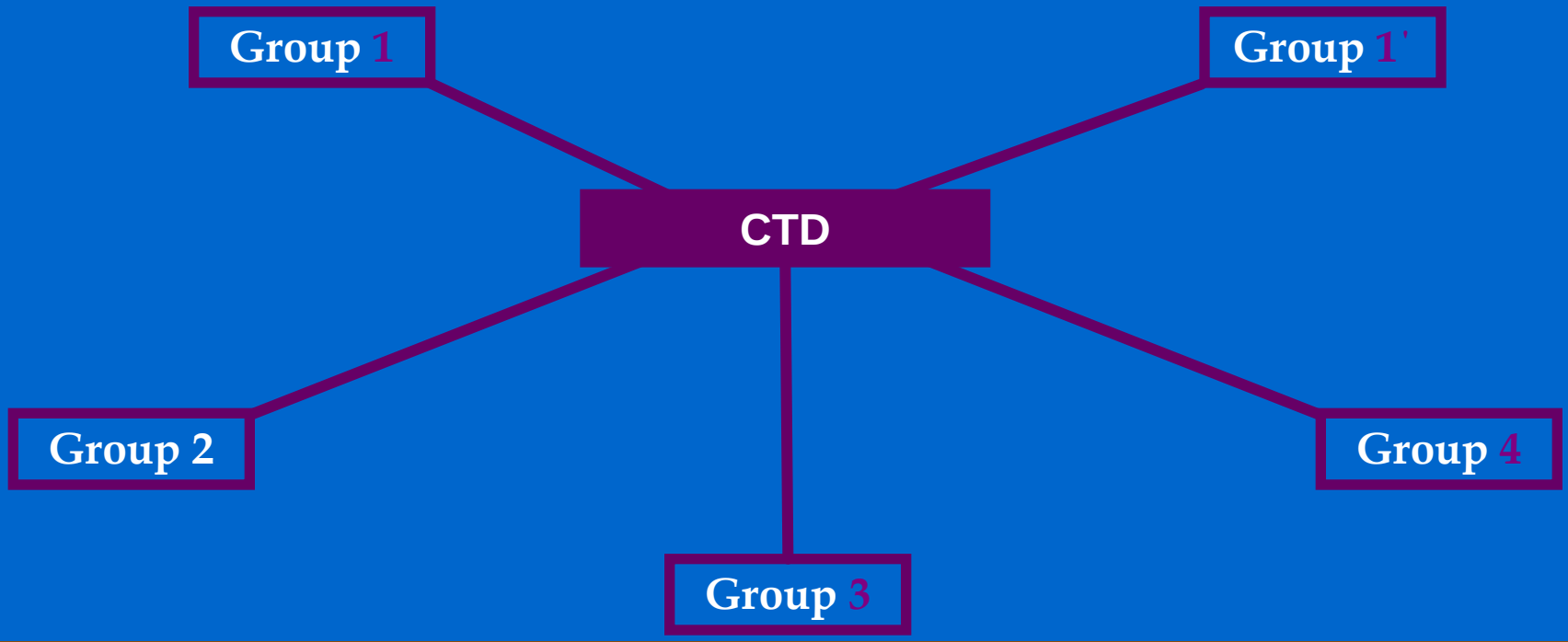
4. Χρόνια θρομβοεμβολική νόσος

5. Πνευμονική υπέρταση ασαφούς ή πολυπαραγοντικής αιτιολογίας

- Αιματολογικές διαταραχές (μυελοϋπερπλαστικά σύνδρομα, σπληνεκτομή)
- Συστηματικές διαταραχές (π.χ. σαρκοείδωση)
- Μεταβολικές διαταραχές
- Άλλα (αποφρακτικοί όγκοι, ίνωση μεσοθωρακίου, ΧΝΑ υπό αιμοκάθαρση)

Μοναδικά χαρακτηριστικά της ΠΑΥ σχετιζόμενης με CTD

- Μοναδικός φαινότυπος της ΠΑΥ σχετιζόμενης με ΝΣΙ
  - αλληλοεπικάλυψη με αριστερή καρδιακή νόσο, αναπνευστικές νόσους, πνευμονική φλεβοαποφρακτική νόσο που δικαιολογεί την υψηλή θνησιμότητα και τη μη ανταπόκριση των ασθενών με ΝΣΙ στις ειδικές θεραπείες για την ΠΑΥ



- Πτωχότερη ανταπόκριση της δεξιάς κοιλίας στις αυξημένες πιέσεις σε ασθενείς με ΝΣΙ σε σχέση με τους ασθενείς με ιδιοπαθή ΠΑΥ

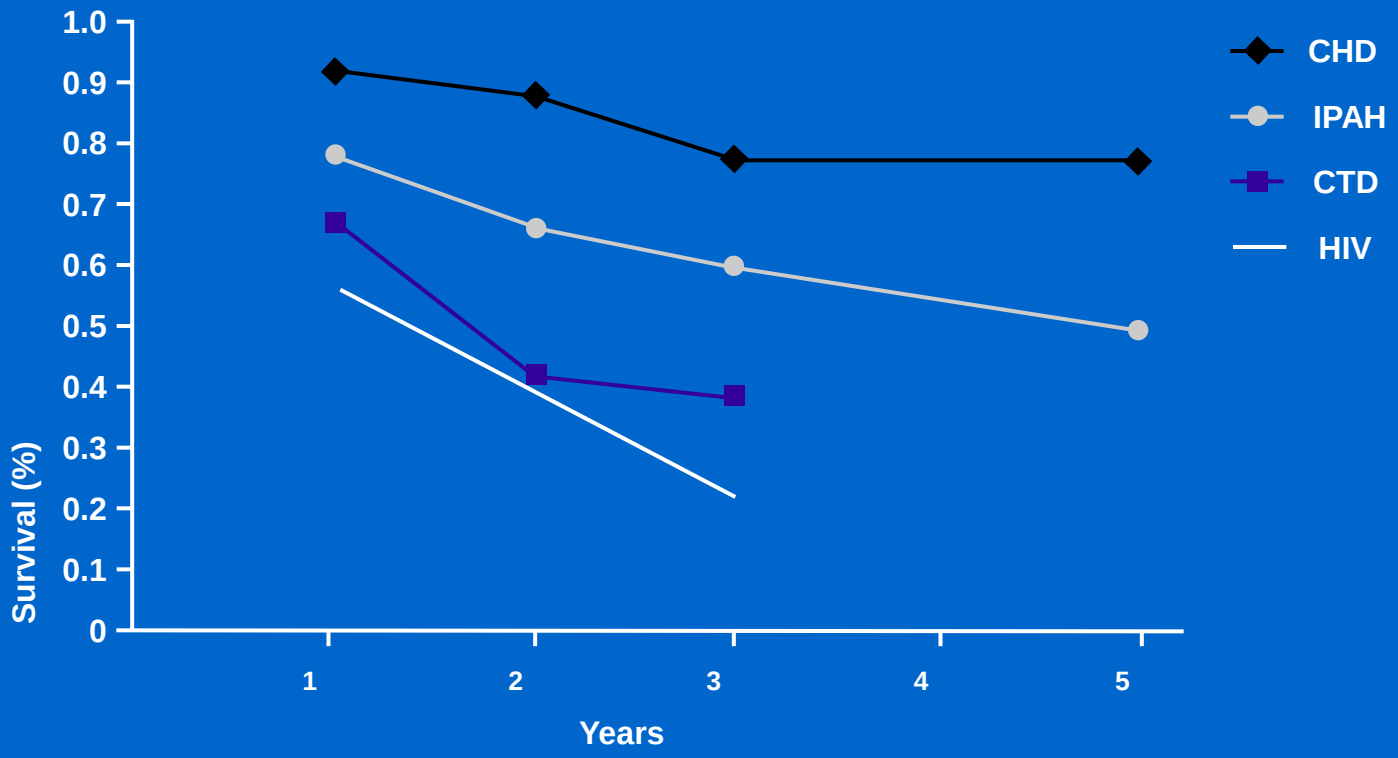
Dimitroulas et al. Current Pharmaceutical Design 2012; 18; 1457-1464

CTD: Connective Tissue Disease

Νοσήματα κολλαγόνου και πνευμονική υπέρταση

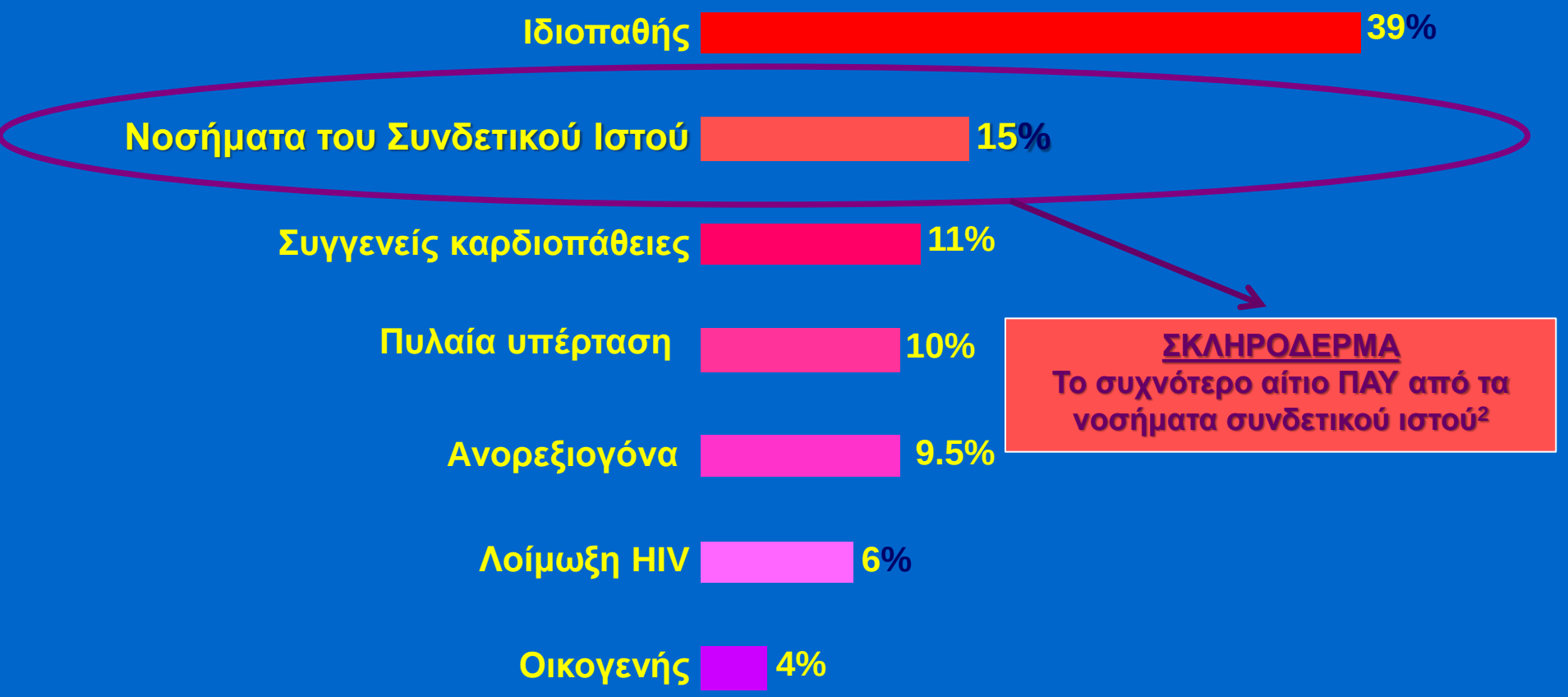
- ***Η ΡΑΗ έχει συσχετισθεί με κάθε γνωστή μορφή κολλαγονώσεως***
- Κοινά ιστολογικά χαρακτηριστικά με την ιδιοπαθή
- Η πνευμονική συμμετοχή στις κολλαγονώσεις ποικίλλει
- Τα επίπεδα της ΕΤ-1 είναι αυξημένα
  - ακόμα και χωρίς πνευμονική υπέρταση

PAH: survival based on aetiology



McLaughlin VV, *et al. Chest* 2004;126 (Suppl 1):78–92.

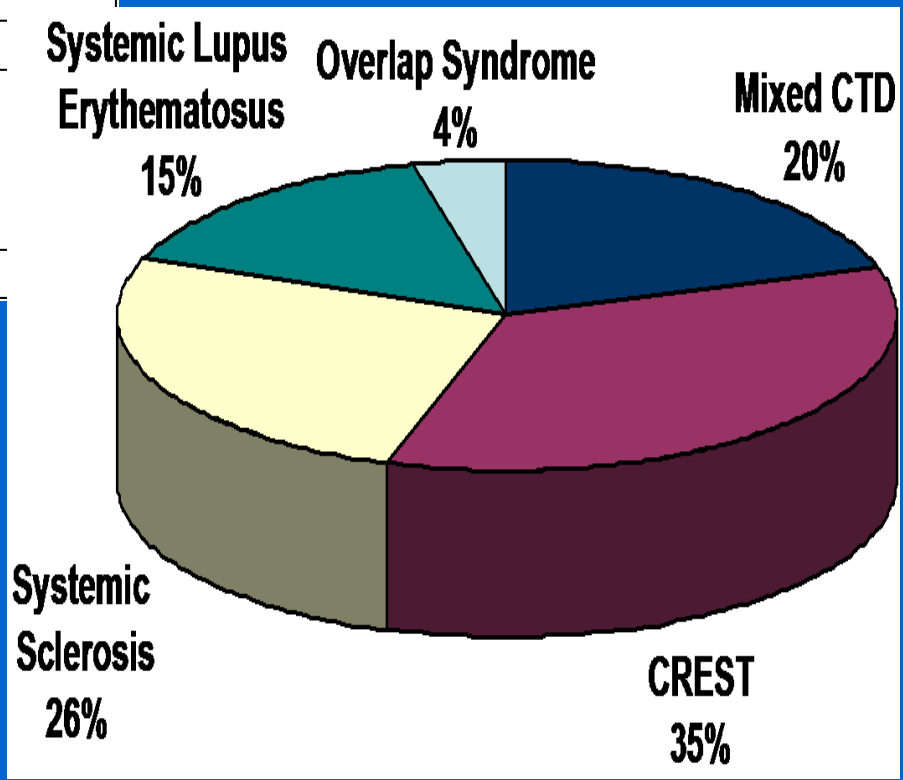
Νοσήματα συνδετικού ιστού: Η 2η συχνότερη αιτία εμφάνισης ΠΑΥ[1,2]



1.Humbert et al. Am J Respir Crit Care Med 2006; 173; 1023-1030
2.Dimitroulas et al. Current Pharmaceutical Design 2012; 18;1457-1464

Δημογραφικά χαρακτηριστικά ασθενών κατά την έναρξη

	ARIES-E N=383
Female	302 (78.9%)
Male	81(21.1%)
Age	51.1 (SD 15.1)
Idiopathic PAH	241 (62.9%)
PAH-CTD	124 (32.4%)
PAH-Anorexigen	6 (1.6%)
PAH-HIV	11 (2.9%)
WHO FC	
I	12 (3.1%)
II	163 (42.6%)
III	178 (46.5%)
IV	30 (7.8%)
6-Minute Walk Distance (metres)	347 (SD 85.39)



Oudiz RZ et al.J Am Coll Cardiol 2009;54(21);1971-1981

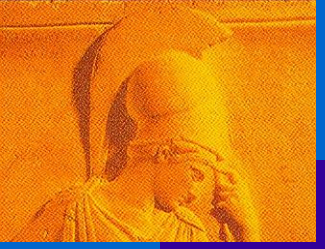
Οι ασθενείς με ΠΑΥ σχετιζόμενη με CTD είναι μεγαλύτερης ηλικίας σε σχέση με τους ασθενείς άλλων τύπων ΠΑΥ

Table 1—*Demographic and Baseline Characteristics of Patients Meeting Traditional Hemodynamic Criteria in the REVEAL Registry by World Health Organization Group I Diagnosis at Enrollment*

Characteristic	All Patients[a]	IPAH	All Patients With APAH[b]	APAH Subgroup[c]			
				CHD	CVD/ CTD	Portal HT	Drugs/Toxins
Patients, No. (%)	2,525 (100)	1,166 (46.2)	1,280 (50.7)	250 (19.5)	639 (49.9)	136 (10.6)	134 (10.5)
[illegible] SD, y	53.0 ± 14.0	53.1 ± 14.5	53.4 ± 13.4	45.5 ± 13.1	[illegible]	53.3 ± 9.6	49.5 ± 10.6
Age at diagnosis, mean ± SD, y	50.1 ± 14.4	49.9 ± 14.8	50.7 ± 13.8	41.6 ± 13.3	55.5 ± 13.4	51.0 ± 9.5	46.0 ± 10.0
[illegible] No. (%)	2,098 (83.1)	971 (83.3)	1,054 (82.3)	236 (94.4)	[illegible]	124 (91.2)	129 (96.3)
65-74, No. (%)	324 (12.8)	138 (11.8)	181 (14.1)	11 (4.4)	135 (21.1)	11 (8.1)	5 (3.7)
75 +, No. (%)	103 (4.1)	57 (4.9)	45 (3.5)	3 (1.2)	37 (5.8)	1 (0.7)	0 (0.0)
Female, No. (%)	2,007 (79.5)	936 (80.3)	1,014 (79.2)	184 (73.6)	576 (90.1)	68 (50.0)	113 (84.3)
Time from diagnosis to enrollment, mo							
Mean ± SD	35.6 ± 37.9	38.0 ± 40.4	32.7 ± 34.9	46.6 ± 50.3	26.9 ± 27.3	27.5 ± 31.1	42.6 ± 32.7
Median	24.9	26.7	23.1	33.8	18.1	17.1	39.5
(IQR)	(8.0, 50.9)	(8.3, 53.8)	(7.8, 46.7)	(16.2, 59.8)	(6.4, 40.2)	(5.7, 36.7)	(12.9, 65.7)
Newly diagnosed, No. (%)	357 (14.1)	177 (15.2)	170 (13.3)	20 (8.0)	94 (14.7)	22 (16.2)	15 (11.2)
Previously diagnosed, No. (%)	2,168 (85.9)	989 (84.8)	1,110 (86.7)	230 (92.0)	545 (85.3)	114 (83.8)	119 (88.8)
Functional class at enrollment,[d] No. (%)							
I	175 (7.6)	89 (8.3)	80 (6.9)	13 (5.7)	32 (5.7)	14 (11.4)	10 (7.8)
II	846 (36.7)	391 (36.4)	423 (36.6)	87 (38.3)	182 (32.2)	50 (40.7)	60 (46.5)
III	1,153 (50.0)	534 (49.7)	584 (50.5)	117 (51.5)	311 (54.9)	54 (43.9)	55 (42.6)
IV	130 (5.6)	60 (5.6)	69 (6.0)	10 (4.4)	41 (7.2)	5 (4.1)	4 (3.1)
6MWD at enrollment,[e] mean ± SD, m	366 ± 126	374 ± 129	356 ± 123	382 ± 121	322 ± 120	397 ± 115	410 ± 95
No.	2,034	921	1,050	210	518	105	122
		P value[f] < .001					

Badesch DB et al. Chest 2010;137:376-387

CTD: Connective Tissue Disease

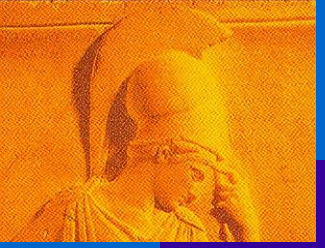


Pulmonary hypertension in systemic sclerosis and systemic lupus erythematosus

TABLE 1 Prevalence of systemic sclerosis-associated pulmonary arterial hypertension

Prevalence	Diagnostic threshold
Echocardiogram based	
43%	$P_{pa,sys} \geq 35$ mmHg
35%	$P_{pa,sys} > 30$ mmHg
59%	$P_{pa,sys} \geq 40$ mmHg
16%	$P_{pa,sys} > 40$ mmHg
26.7%	$P_{pa,sys} \geq 40$ mmHg
21% limited, 26% diffuse	$P_{pa,sys} > 30$ mmHg or > 35 mmHg
Right heart catheterisation based	
2.93 per million[#]	$\bar{P}_{pa} \geq 25$ mmHg at rest with $P_{pcw} < 15$ mmHg
5%	$\bar{P}_{pa} > 25$ mmHg at rest with $P_{pcw} \leq 15$ mmHg
7%	$\bar{P}_{pa} > 32$ mmHg
16%	$\bar{P}_{pa} \geq$ mmHg at rest with $P_{pcw} \leq 12$ mmHg
29%	$\bar{P}_{pa} \geq 20$ mmHg or $P_{pa,sys} \geq 35$ mmHg
12%	$\bar{P}_{pa} > 25$ mmHg
7.85%[¶]	$\bar{P}_{pa} \geq 25$ mmHg at rest or ≥ 30 mmHg during exercise, with $P_{pcw} < 15$ mmHg

Eur Respir Rev 2011; 20: 122, 277–286



What is Systemic Sclerosis?

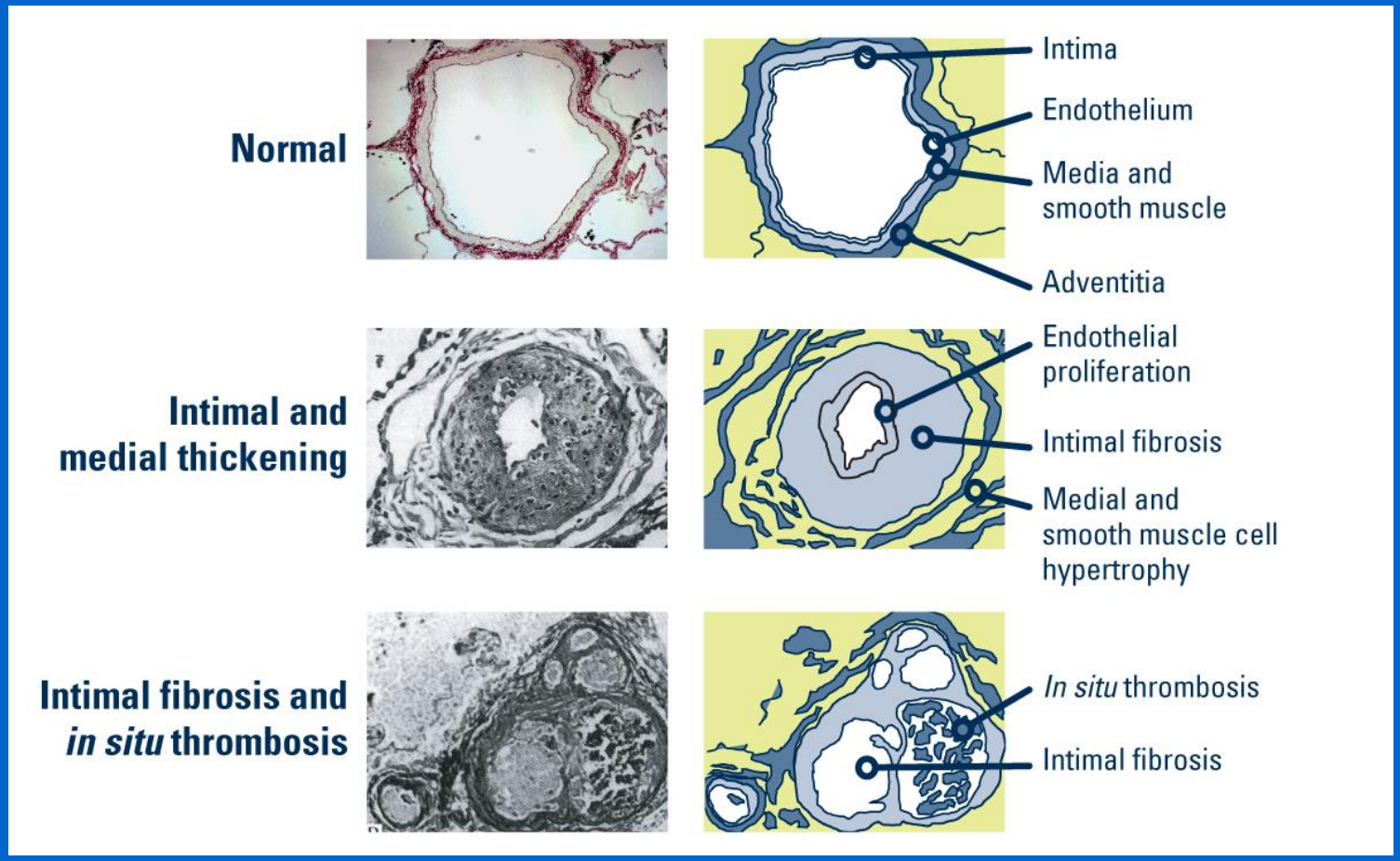
- Chronic autoimmune connective tissue disease characterised by excessive collagen deposition in the skin and internal organs such as the gastrointestinal tract, kidney, heart and lung

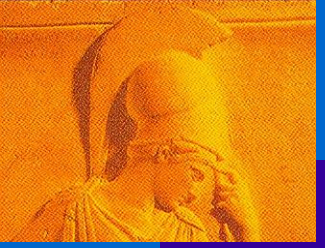
- Symptoms may be caused by vascular dysfunction, inflammation and progressive fibrosis which lead to occlusion of the microvasculature

1. Mouthon L *et al. Eur Respir J* 2005
2. Denton CP *et al. Trends Immunol* 2005

What is Systemic Sclerosis?

The nature of the vascular dysfunction in SSc:





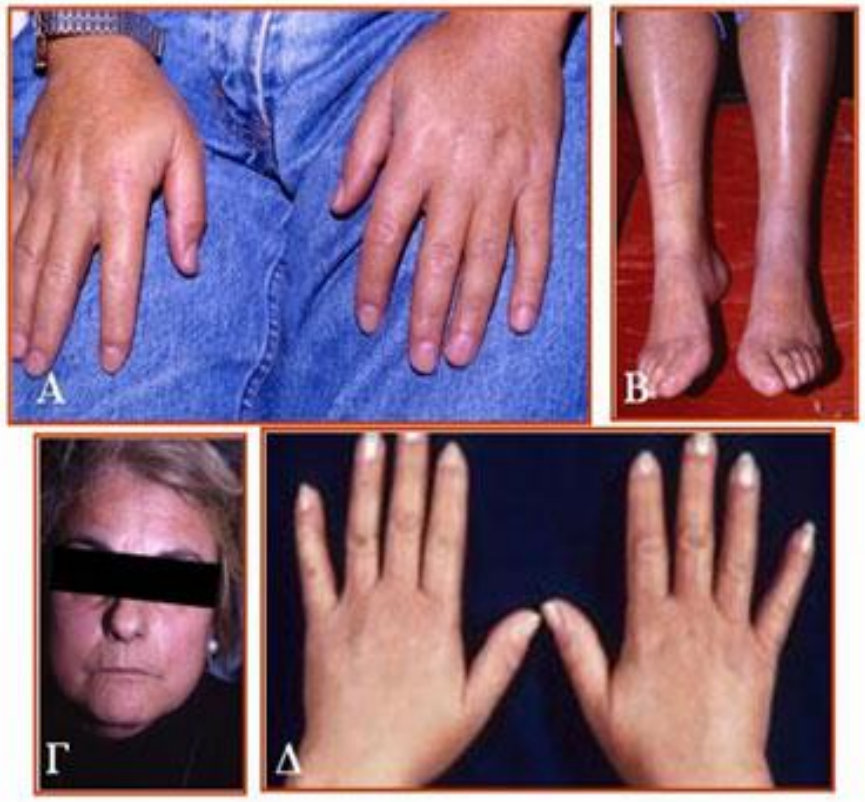
PAH in Systemic Sclerosis

- Systemic sclerosis (SSc); also known as scleroderma
- Pulmonary Arterial Hypertension (PAH) occurs in approximately one in seven scleroderma patients
- Pulmonary complications, namely PAH and pulmonary fibrosis, are a common cause of death in SSc patients
- Symptoms such as breathlessness, fatigue on exercise and syncope are common to other respiratory or cardiac complaints
- PAH should be considered in the daily management of SSc patients and screening is the key to establishing early diagnosis
- International guidelines recommend screening by Doppler echocardiography annually and/or in the presence of unexplained breathlessness[5]

1. Hachulla E *et al. Ann Rheum Dis* 2004
2. Steen V *et al. Ann Rheum Dis* 2007
3. Runo JR *et al. Lancet* 2003
4. McGoon M *et al. Chest* 2004
5. Galiè *et al. Eur Heart J* 2004

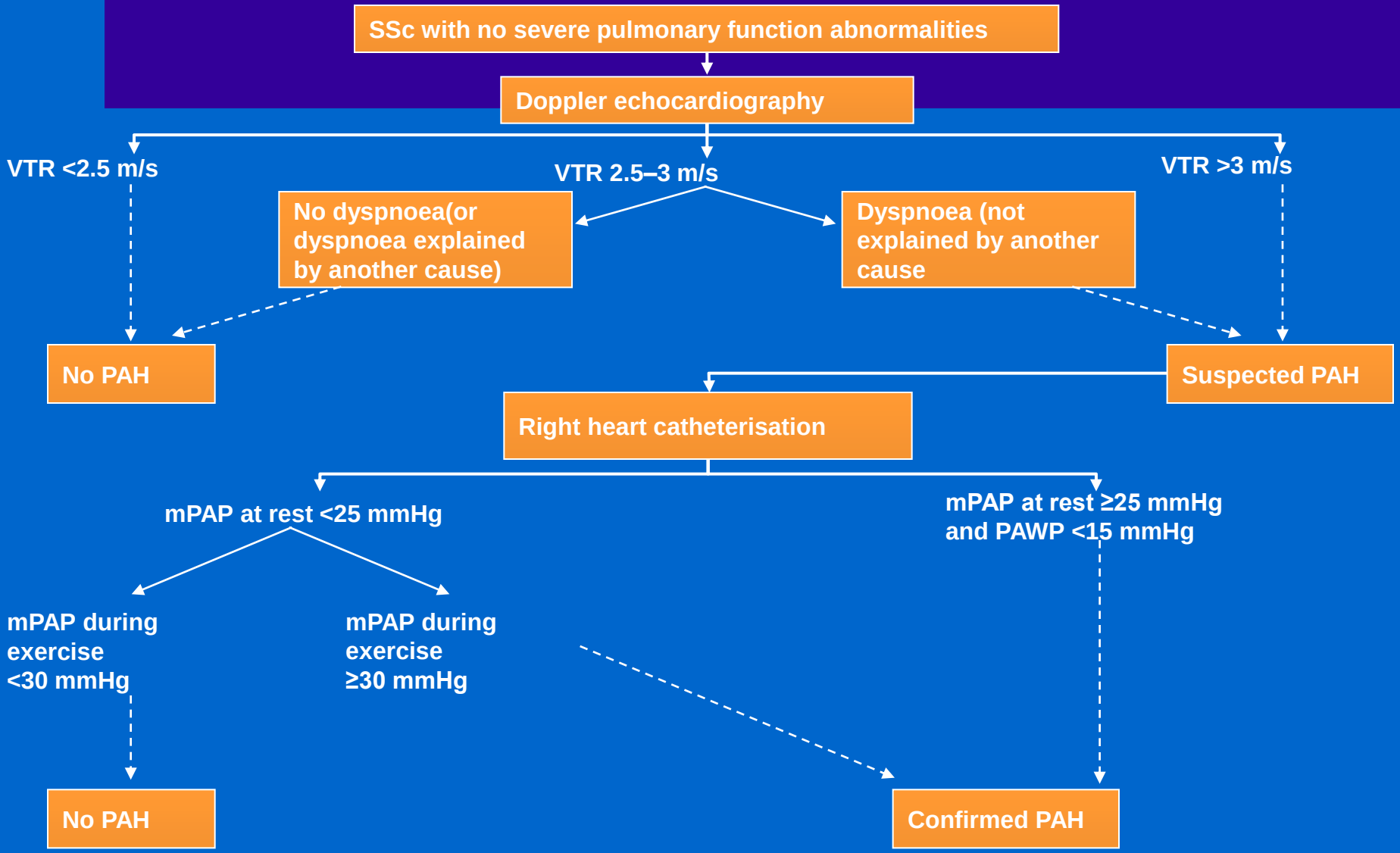
Νοσήματα κολλαγόνου και πνευμονική υπέρταση

- Στην Ελλάδα
  - επιπολασμός σκληροδέρματος: 1.
  - επίπτωση: 120 νέα περιστατικά/έτος
- PAH σε σκληρόδερμα: ~30%



Συστηματική σκλήρυνση. **Α, Β:** Διάχυτο δερματικό σκληρόδερμα
Γ: Περιορισμένο δερματικό σκληρόδερμα. **Δ:** "Αλλαντοειδής" διόγκωση δακτύλων.

Screening algorithm for PAH in SSc



Hachulla E, *et al. Arthritis Rheum* 2005;52:3792–800.

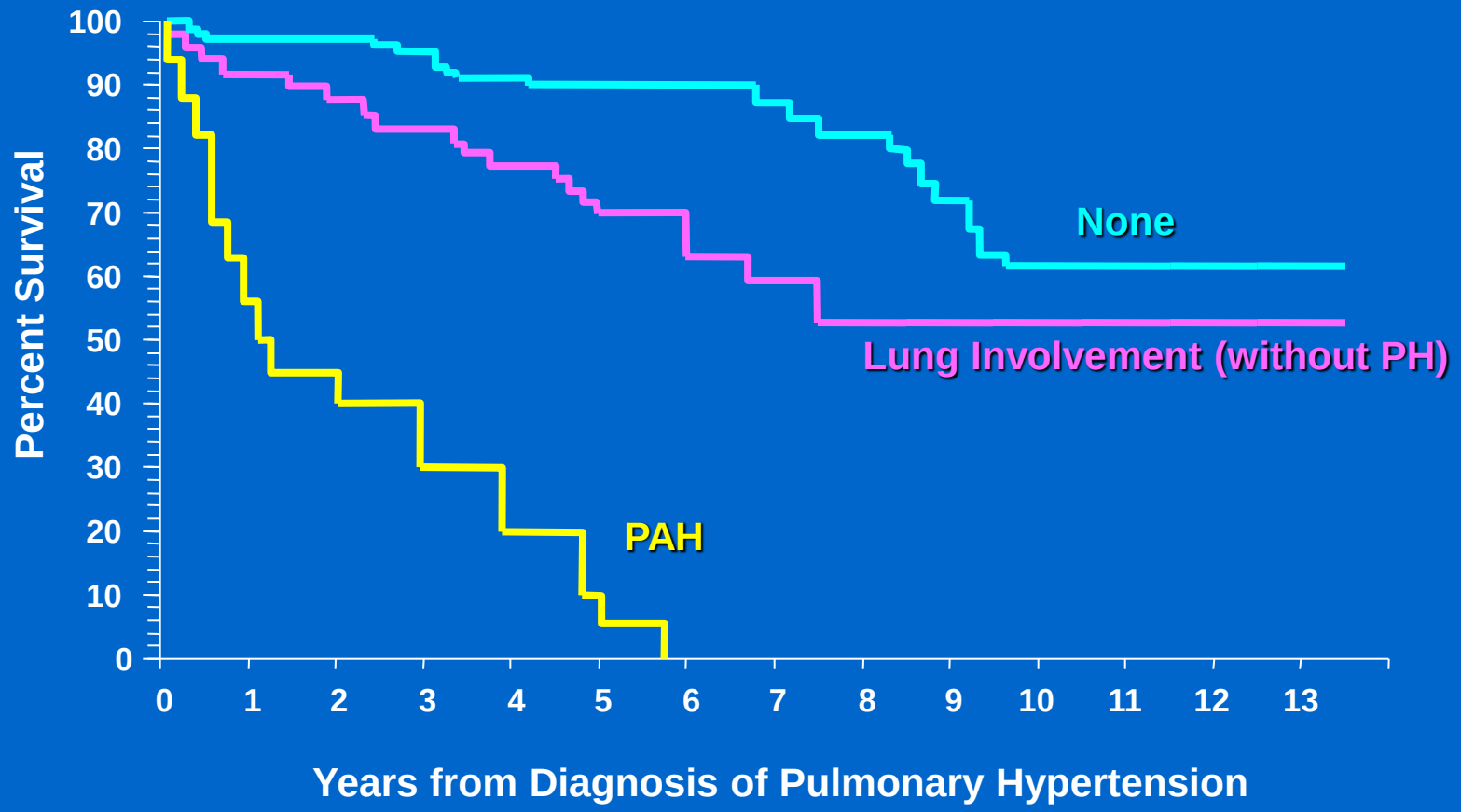
ΠΑΥ: Μία από τις κύριες αιτίες θνησιμότητας στους ασθενείς με σκληρόδερμα

TABLE 2. Causes of death observed in the total population

Causes of death, *n* (%)	All patients (*n* = 546)
Total number of deaths	47 (8.6)
Scleroderma-related causes of death	24 (4.4)
PAH	17
Pulmonary fibrosis	2
Gastrointestinal	2
Renal crisis	3
Non-scleroderma-related causes of death	23 (4.2)
Cancer	8
Infection	4
Cardiovascular or cerebrovascular atherosclerosis	2
Other cause	2
Unknown cause	7

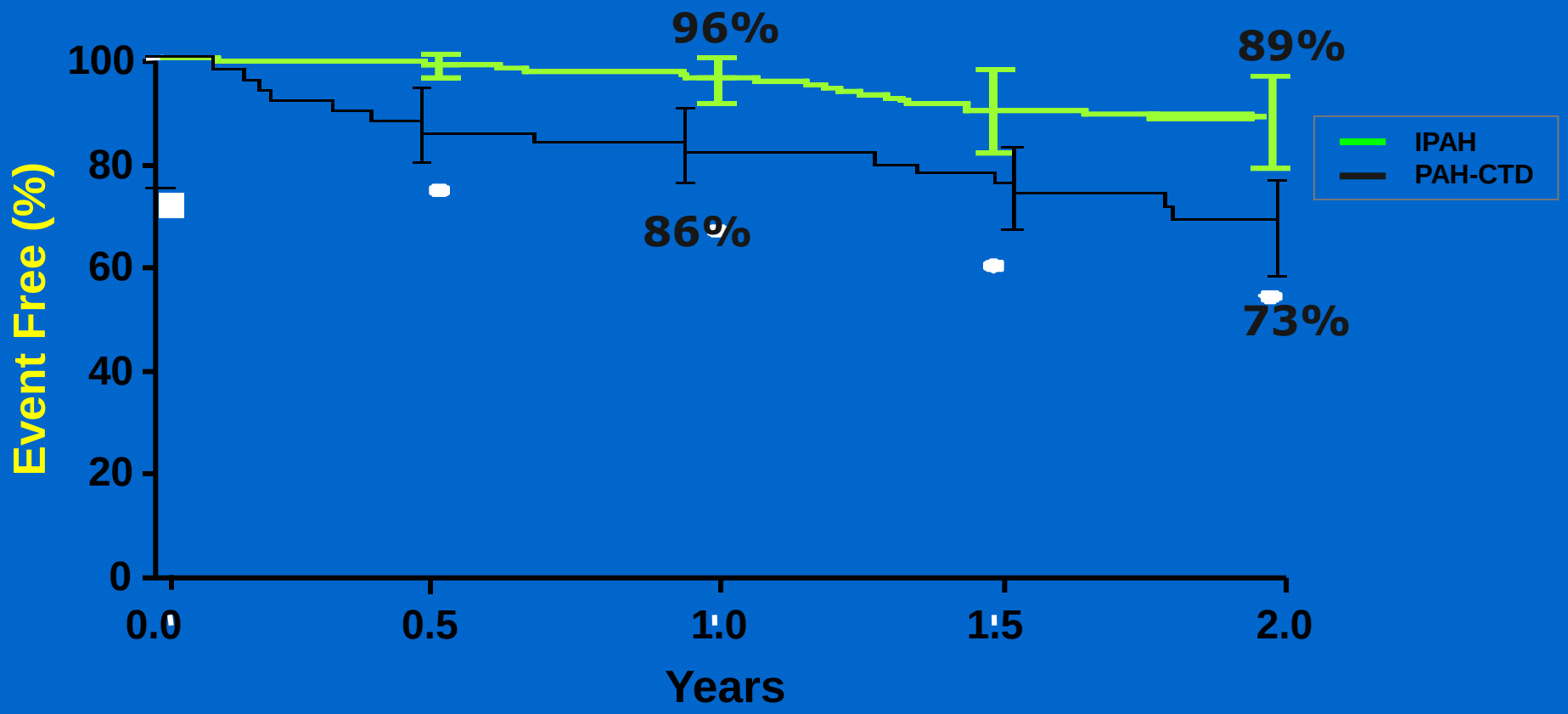
Hachulla et al. Rheumatology 2009;48;304-308

Survival Estimates in Scleroderma By Organ Involvement



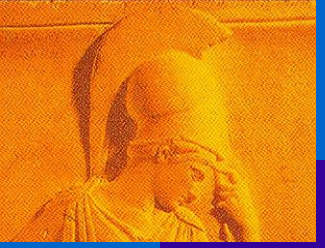
Koh et al. *Brit J Rheumatol* 1996

Η PAH-CTD έχει χειρότερη πρόγνωση από την ιδιοπαθή ακόμα και υπό θεραπεία



In the long-term follow-up of the pivotal trials for bosentan, patients with PAH-CTD had worse long-term survival compared with patients with idiopathic PAH (73% vs. 89%, respectively)

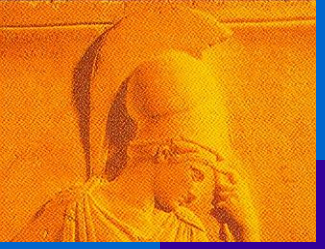
McLaughlin *et al. Eur Respir J* 2005;25:244-9
Denton *et al. Ann Rheum Dis* 2006;65:1336-1340



- ***Pulmonary Arterial Hypertension in Systemic Lupus***
- ***Erythematosus: Current Status and Future Direction***

	IPAH	CTD	SLE-aPAH	SSc-aPAH
Total # of patients	1251	641	110	399
Patients newly diagnosed at enrollment (%)	14	15	14	16
Age (years)	50.1 ± 17.5	57.1 ± 13.7	45.5 ± 11.9	61.8 ± 11.1
Sex, (#)				
Female	987	578	104	353
Male	264	63	6	46
Race (%)				
White	74.8	71.8	37.4	83.9
African-American	11.7	16.5	31.8	10.9
Hispanic	8.3	7.5	17.8	3.6
Other	5.2	4.2	13.1	1.6
Raynaud phenomenon (%)	1.4	26.5	13.6	32.6
Renal insufficiency (%)	3.9	6.9	4.6	8.7
Time between diagnostic RHC and enrollment (months)	41.1 ± 44.1	27.2 ± 29.9	34.4 ± 39.1	24.2 ± 24.1
BNP (pg/mL)	245.6 ± 427.2	432.8 ± 789.1	263.8 ± 338.8	552.2 ± 977.8
DLCO (%)	63.6 ± 22.1	44.9 ± 18	53.3 ± 19.5	41.2 ± 16.3
Immunosuppressive therapy (%)	1.3	11.9	22	6.8
Alive at 1 year (%)	93	86	94	82

Clinical and Developmental Immunology
Volume 2012, Article ID 854941,



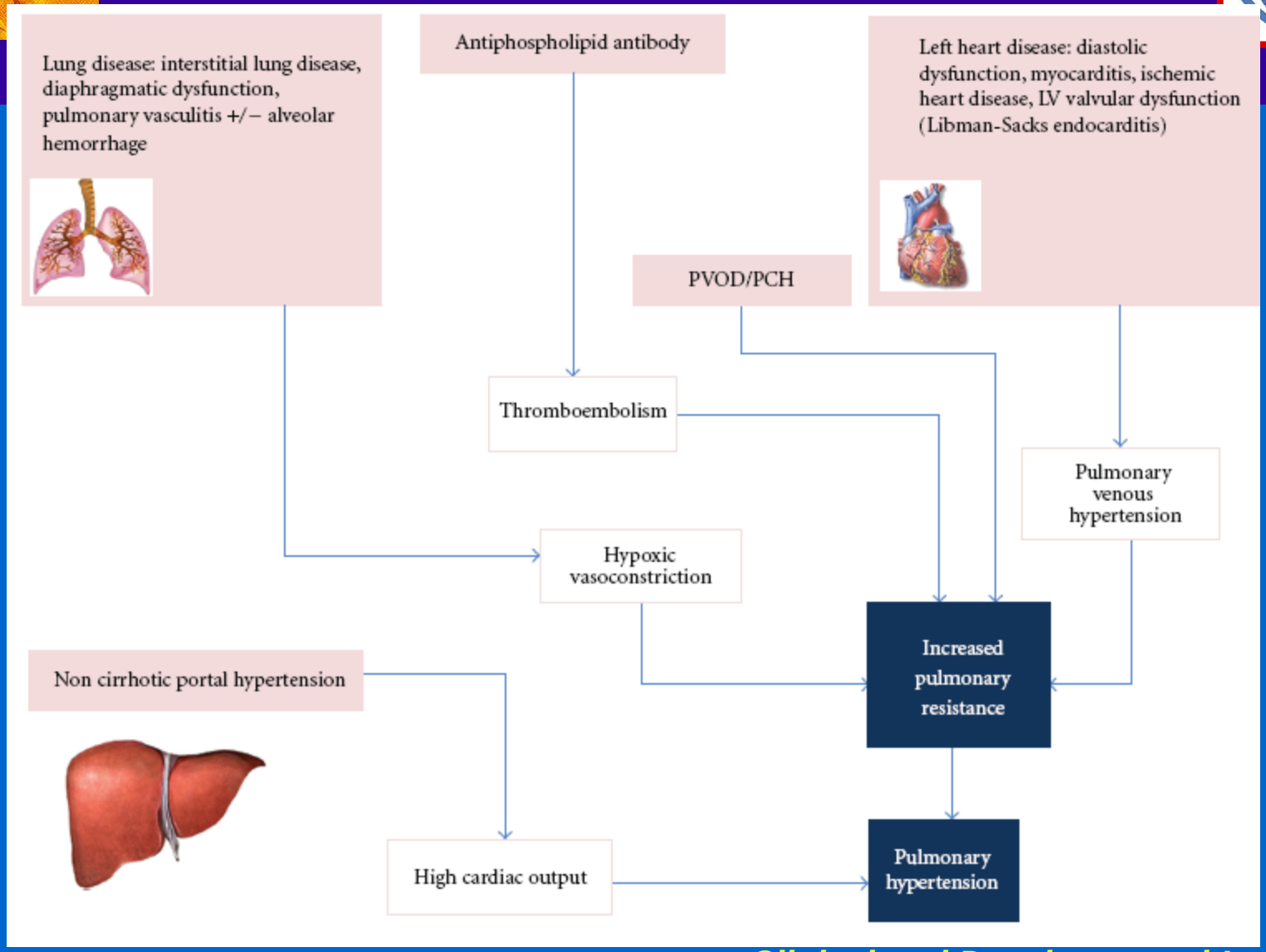
Pulmonary hypertension in systemic sclerosis and systemic lupus erythematosus

TABLE 5 Prevalence of systemic lupus erythematosus associated-pulmonary arterial hypertension

Prevalence	Diagnostic threshold	Ref.
Echocardiogram based		
2.8%	RVSP >45 mmHg	[77]
4.9%	$P_{pa,sys}$ >30 mmHg	[78]
9%	Clinical findings#	[80]
10%	P_{pa} >55 mmHg	[81]
11%	$P_{pa,sys}$ >30 mmHg and $\bar{P}_{pa}$ >20 mmHg	[82]
13%	$P_{pa,sys}$ ⩾35 mmHg	[85]
14%	RVSP >30 mmHg	[83]
14%	$P_{pa,sys}$ >30 mmHg	[86]
14%	RVSP ⩾40 mmHg	[84]
Right heart catheterisation based		
0.005%	$\bar{P}_{pa}$ >40 mmHg	[76]
5%	$\bar{P}_{pa}$ >30 mmHg	[77]
9.3%	$\bar{P}_{pa}$ >40 mmHg	[79]

Eur Respir Rev 2011; 20: 122, 277–286

Pulmonary Arterial Hypertension in Systemic Lupus Erythematosus: Current Status and Future Direction



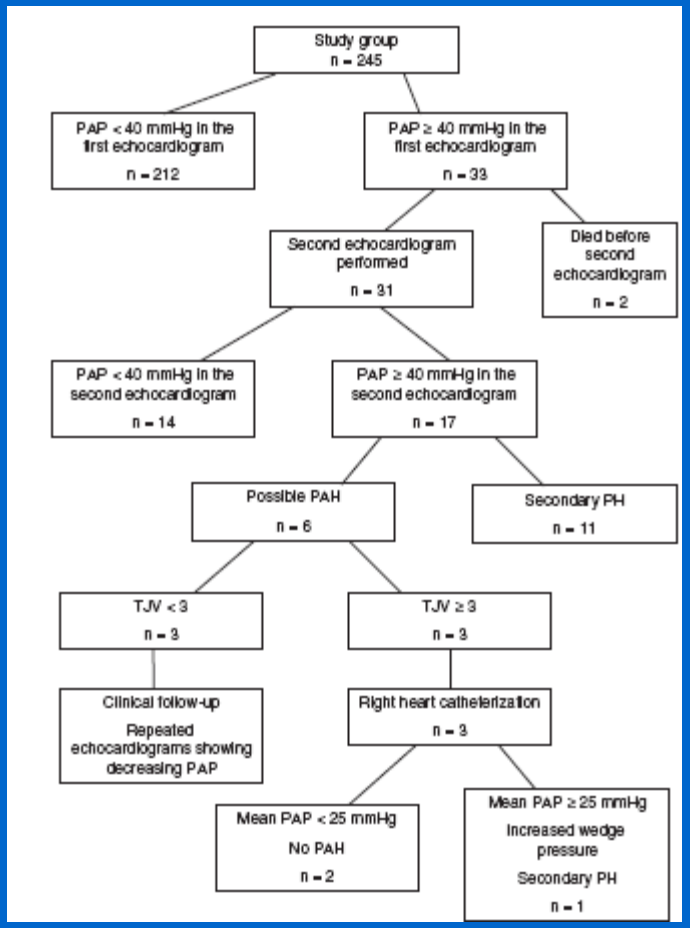
Clinical and Developmental Immunology
Volume 2012, Article ID 854941,

- ***Pulmonary Arterial Hypertension in Systemic Lupus***
- ***Erythematosus: Current Status and Future Direction***

(i) Female gender
(ii) Isolated reduction in diffusion
(iii) Raynaud phenomenon §
(iv) Serositis §
(v) Renal disease
(vi) Digital gangrene
(vii) Cutaneous vasculitis/livedo reticularis
(viii) Rheumatoid factor
(ix) Anti-U1 RNP §
(x) Anticardiolipin antibodies §
(xi) Antiendothelial cell antibodies

Clinical and Developmental Immunology
Volume 2012, Article ID 854941,

Pulmonary hypertension in systemic lupus erythematosus: prevalence, predictors and diagnostic strategy



Autoimmunity Reviews 12 (2013) 410–415

Studies	Drug/design	Patients and baseline characteristics			Outcome
Intensive Immunosuppressive therapy (IIT) trials					
Miyamichi-Yamamoto et al. [19]	IIT: IV cyclophosphamide + oral glucocorticoids + vasodilator therapy (VT) Observational cohort study from a single center with historical control	(i) 8 patients with SLE-aPAH (ii) MPAP = 39.5 ± 9.2 (iii) PVR = 8.75 ± 5.43 (iv) NYHA FC = I, II, III (v) 6MWD = 442 ± 54 (vi) Age = 42 ± 8			IIT: (i) Significantly decreased MPAP (ii) Tended to decrease PVR (iii) Normalized hemodynamics in a few patients. IIT + VT improved the pulmonary hemodynamics and long-term prognosis of patients with CTD-aPAH.
Jais et al. [20]	IIT: IV cyclophosphamide + glucocorticoids ± VT Retrospective, uncontrolled study		Rx with IIT	Rx with IIT + VT	(i) SLE-aPAH patients with less severe disease may respond to treatment with IIT. (ii) For patients with more severe disease, VT should be started, possibly in combination with IIT. (iii) These retrospective and uncontrolled data need to be confirmed by randomized controlled trials.
		$N = 13$	9	4	
		MPAP	48 ± 12	58 ± 10	
		PVR	8.6 ± 3.5	14.3 ± 1.3	
		NYHA FC	II, III	III, IV	
		6MWD	347 ± 80	381 ± 71	
		Age	31 ± 10	38 ± 9	
Sanchez et al. [21]	IV cyclophosphamide ± glucocorticoids Retrospective study	(i) 13 patients with SLE-aPAH (ii) MPAP (avg.) = 54 (iii) PVR (avg.) = 19 (iv) NYHA FC = II, III			(i) Of the responders [R] 62% had SLE. (ii) R's had a significantly improved 6MWD and hemodynamic parameters. (iii) R's had a better survival than non responders [NR].

Rubin et al. [24]	Bosentan Double-blind placebo-controlled trial	(i) 16 patients with SLE (ii) MPAP = 55 ± 16 (iii) PVR = 12.68 ± 8.48 (iv) NYHA FC = III, IV (v) 6MWD = 330 ± 74 (vi) Age = 49 ± 16	Statistically significant improvement in exercise capacity, NYHA FC and increase in time to clinical worsening.
Subcutaneous, inhaled, and intravenous prostanoids			
Oudiz et al. [25]	Subcutaneous treprostinil Double-blind placebo-controlled trial	(i) 25 patients with SLE (ii) MPAP = 52 ± 2 (iii) NYHA FC = II, III, IV (iv) 6MWD = 280 ± 13 (v) Age = 54 ± 2	Improved exercise capacity, dyspnea fatigue symptoms, hemodynamics and trend toward improved quality of life.
Olschewski et al. [26]	Inhaled Iloprost Randomized placebo-controlled trial	(i) 35 patients with CTD (ii) MPAP = 52.8 ± 11.5 (iii) PVR = 12.86 ± 4.88 (iv) NYHA FC = III, IV (v) 6MWD = 332 ± 93 (vi) Age = 51 ± 13	(i) Statistically significant benefit in combined endpoint of 10% improvement in 6MWD and FC improvement and absence of clinical deterioration. (ii) No subgroup analysis done for SLE.
Robbins et al. [27]	Intravenous epoprostenol Case series	(i) 6 patients with SLE (ii) MPAP = 57 ± 9 (iii) PVR = 14 ± 7 (iv) NYHA FC = III, IV (v) Age = 26–35	Dramatic improvement in FC and marked improvement in hemodynamics.

Pulmonary hypertension in systemic lupus erythematosus: prevalence, predictors and diagnostic strategy

Take-home messages

- PH, and particularly PAH, is not a major clinical problem in patients with SLE.
- Screening echocardiograms of asymptomatic lupus patients without a clinical suspicion of PH is not recommended.
- Two consecutive PAP values ≥ 40 mm Hg estimated by echocardiogram are the best initial procedure to decide further testing for the diagnosis of PH.

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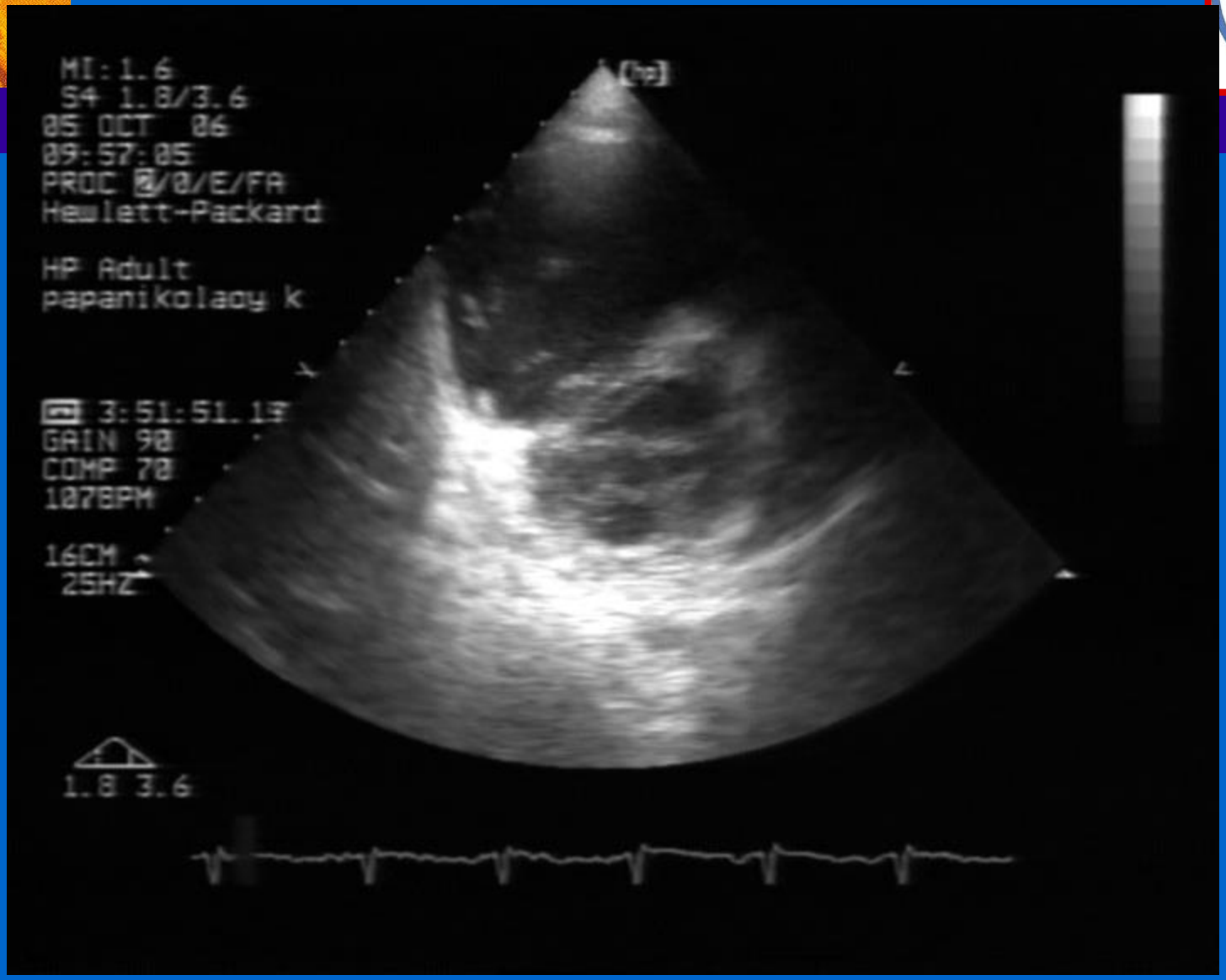
A 25 year old female presented with shortness of breath on exertion and chest pain since the last five months. She referred that during the last month she has been deteriorating with shortness of breath and arrhythmias even at the mildest exertion. On physical examination it was revealed that she had a photosensitive rash of the face and trunk. A normal S1, a loud S2 and a systolic murmur at the lower left sternal border were heard at auscultation.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PROC 0/0/E/FA
Hewlett-Packard
HP Adult
papanikolaou k
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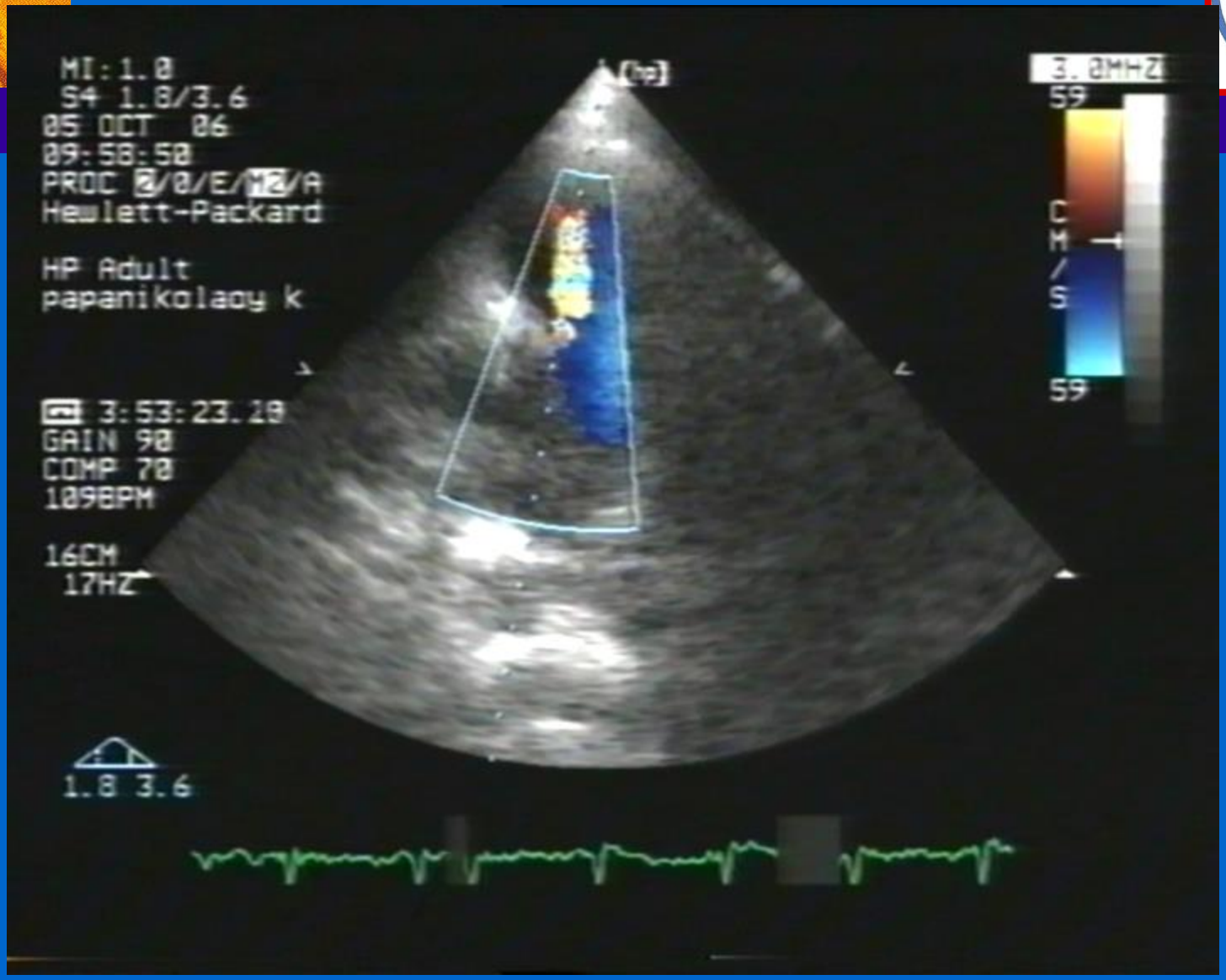
GAIN 90
COMP 70
107BPM
16CM
25HZ
1.8 3.6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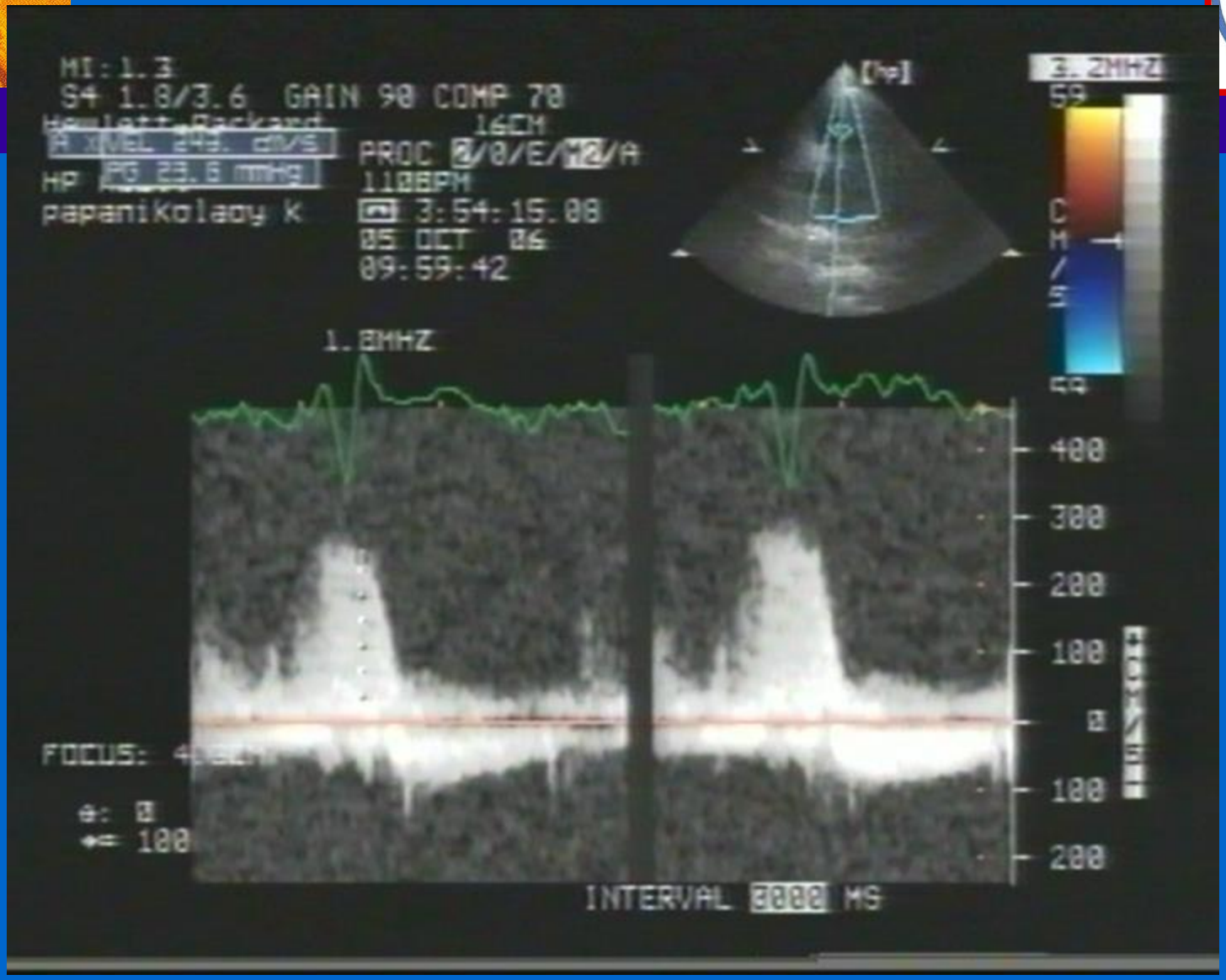
1.8 3.6
3.0MHZ
59
CM/S
59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papanikolaou K
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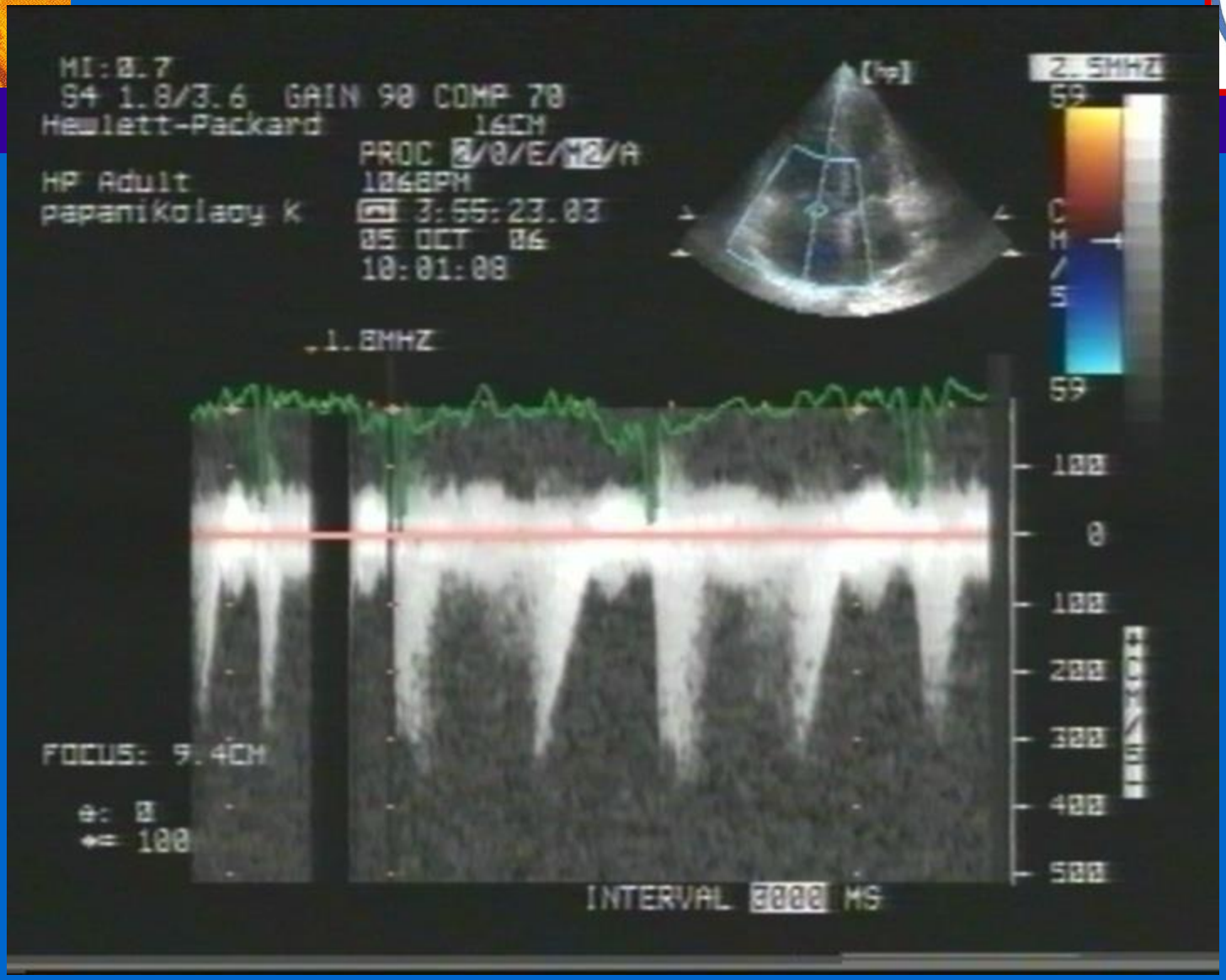
09:59:42
3.2MHZ
1.8MHZ
400
300
200
100
0
100
200
INTERVAL 0000 MS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Hewlett-Packard 16CM
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05 OCT 06
10:01:08
2.5MHZ
59
CM/S
59
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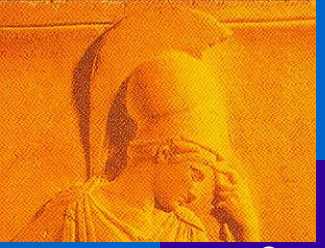
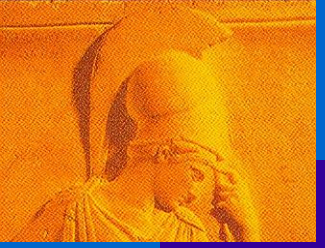
0
100
200
300
400
500
FOCUS: 9.4CM
0
100
INTERVAL 0000 MS



- Right heart catheterization before treatment
- RA: 5 mmHg
- RV: 80/5 mmHg
- PA: 80/40 mmHg
- O_2 consumption: 200 ml O_2/min/m2
- CO: 3L/min
- PVR: 1394 $dyn_x sec_x cm^{-5}$
- PAR: 1315 $dyn_x sec_x cm^{-5}$
- SVR: 1880 $dyn_x sec_x cm^{-5}$



-*normal V/Q scan*

-*normal pulmonary function tests but a mild decrease of DLCO 73% of predicted*

-*normal renal function*

-*normal thyroid tests*

-*negative tests for anti-phospholipid syndrome*

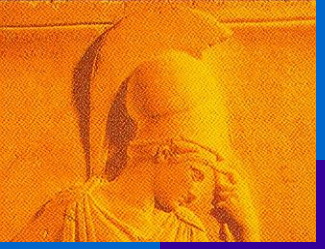
- *negative screening test for HIV infection*

- *mild hypochromic microcytic anaemia*

- *ANA (+) (1:1280)*

- *Anti –dsDNA (+)*

- *Low complement (C3/C4)*



Treatment

The patient was put on Bosentan, coumadin as well as on methylprednisolone 32 mgr with gradual tapering and on cyclophosphamide 1 gr IV/q month x 6.

Right heart catheterrization after treatment

RA: 4 mmHg

RV: 74/4 mmHg

PA: 74/31 mmHg

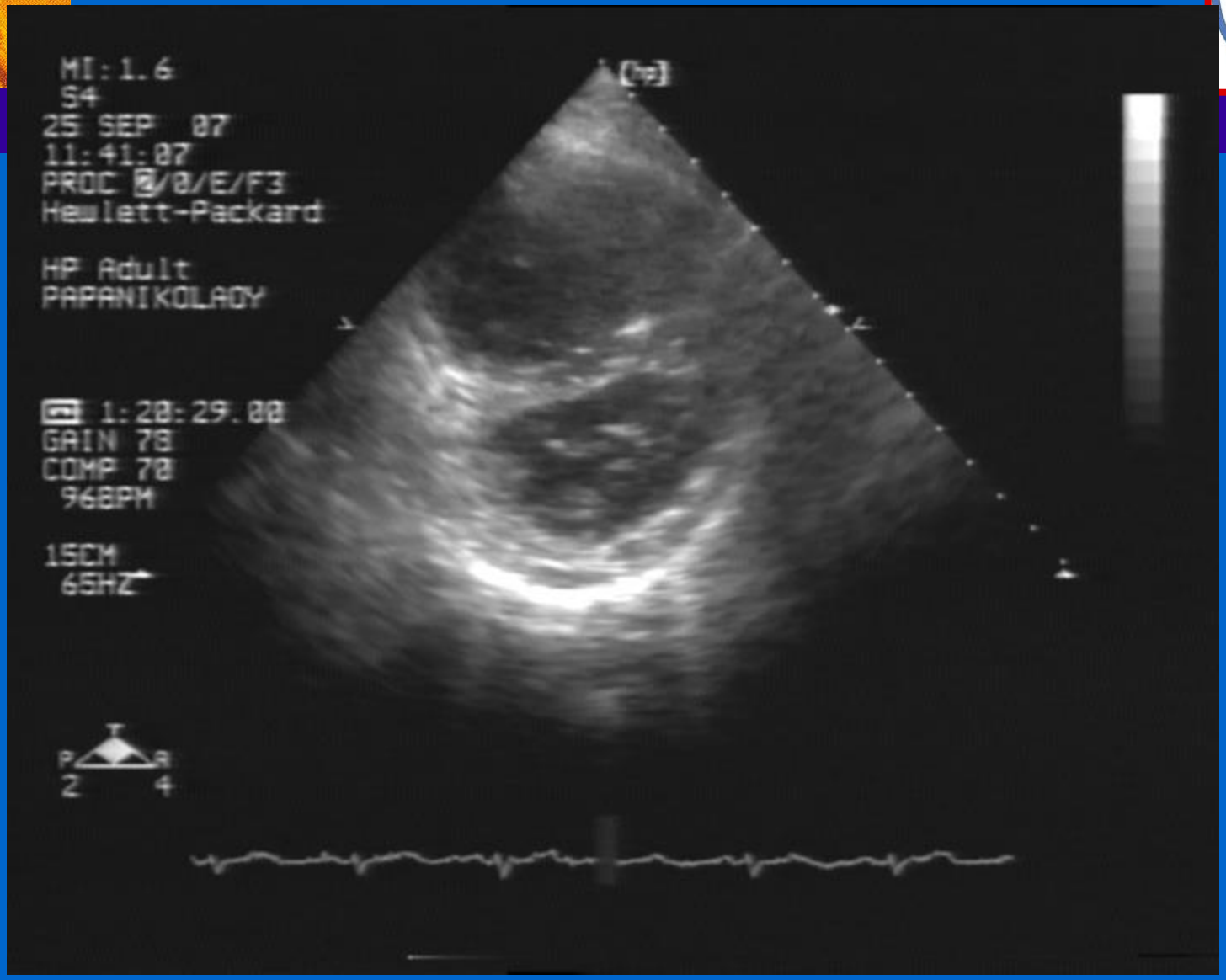
O_2 Consumption: 223 ml O_2/min/m^2

Καρδιακή Παροχή: 4,9 L/min

PVR: 791 dyn x sec x cm^{-5}

PAR: 694 dyn x sec x cm^{-5}

SVR: 1336 dyn x sec x cm^{-5}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Hewlett-Packard
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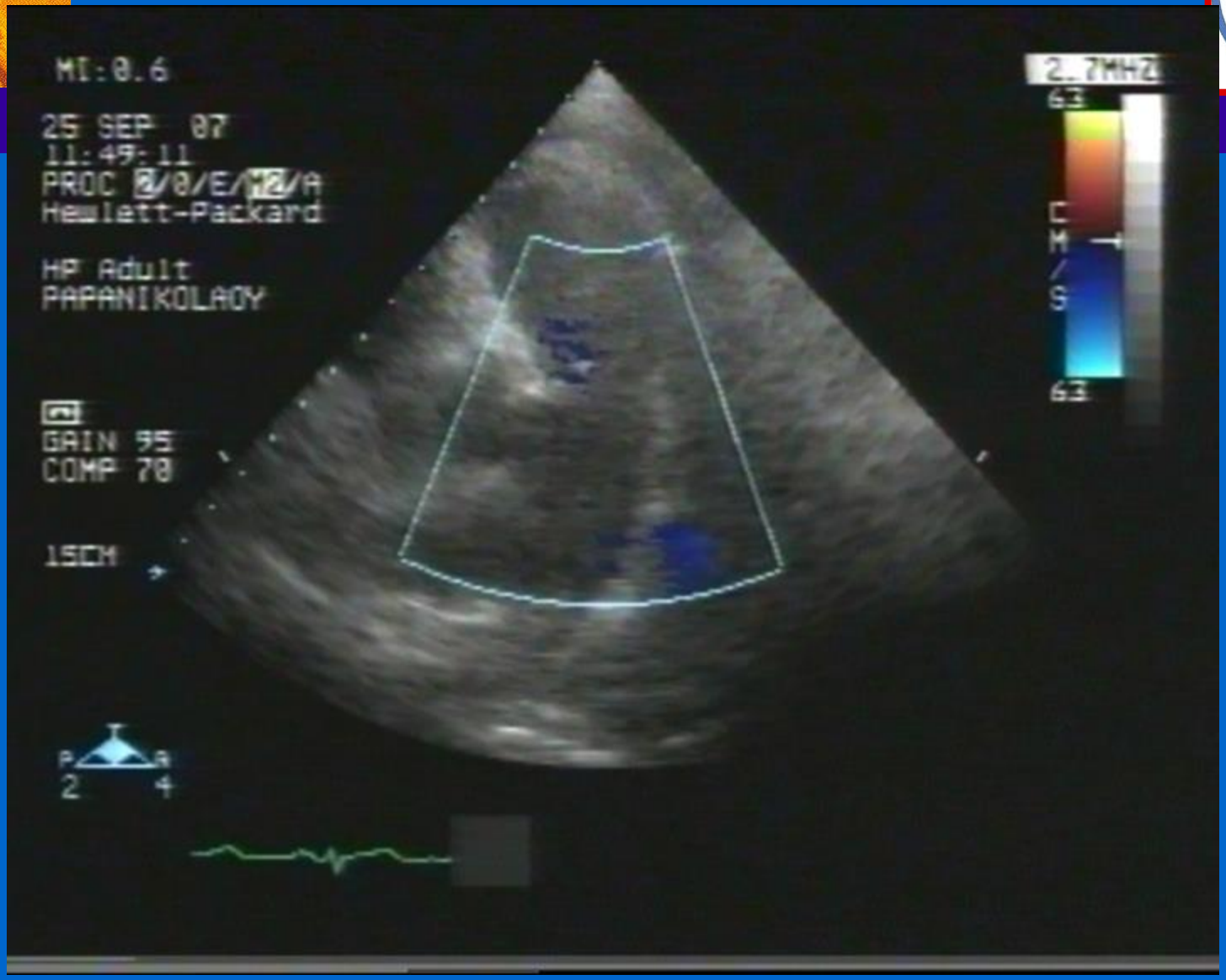
968PM
15CM
65HZ
P
A
2
4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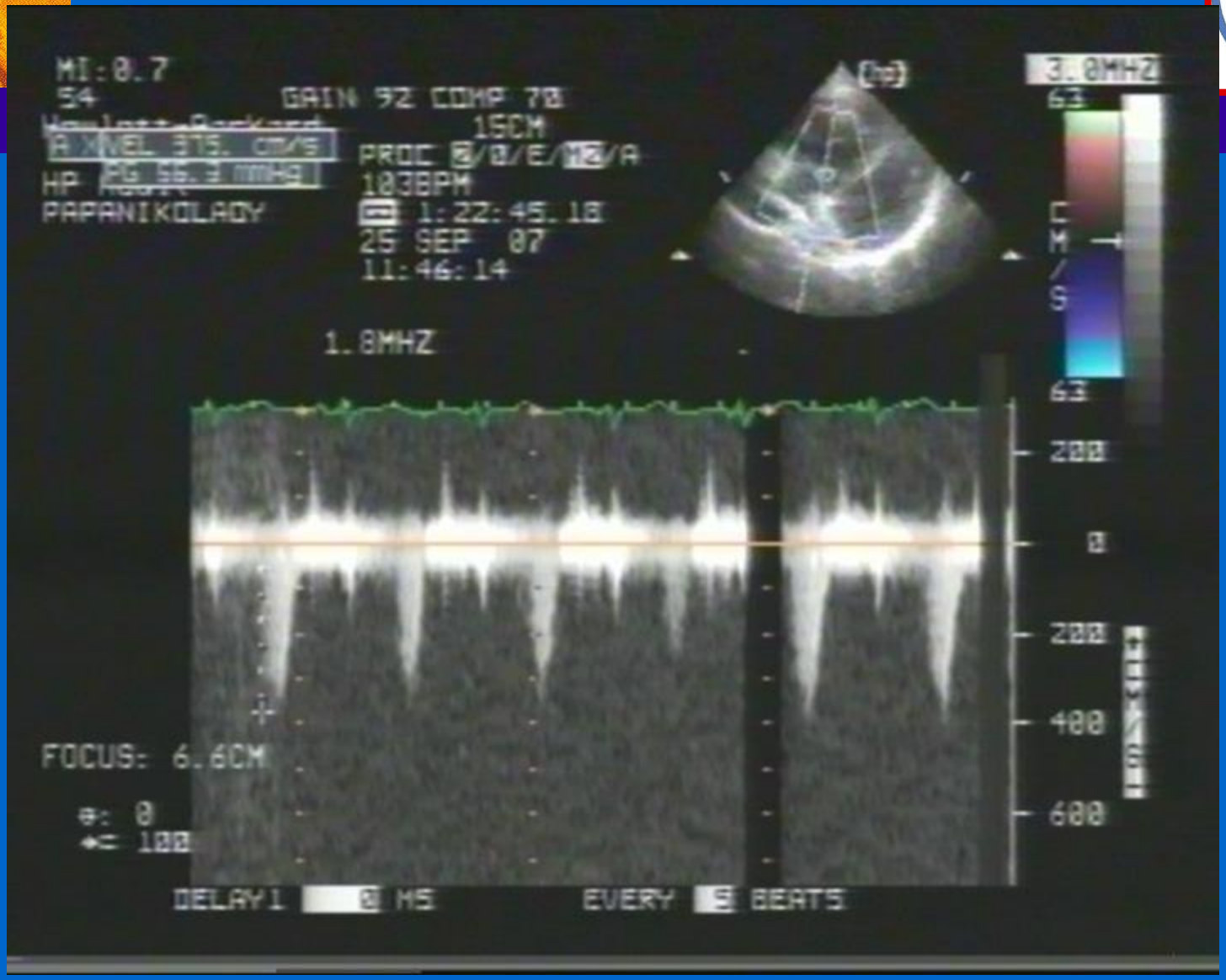
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PROC
1038PM
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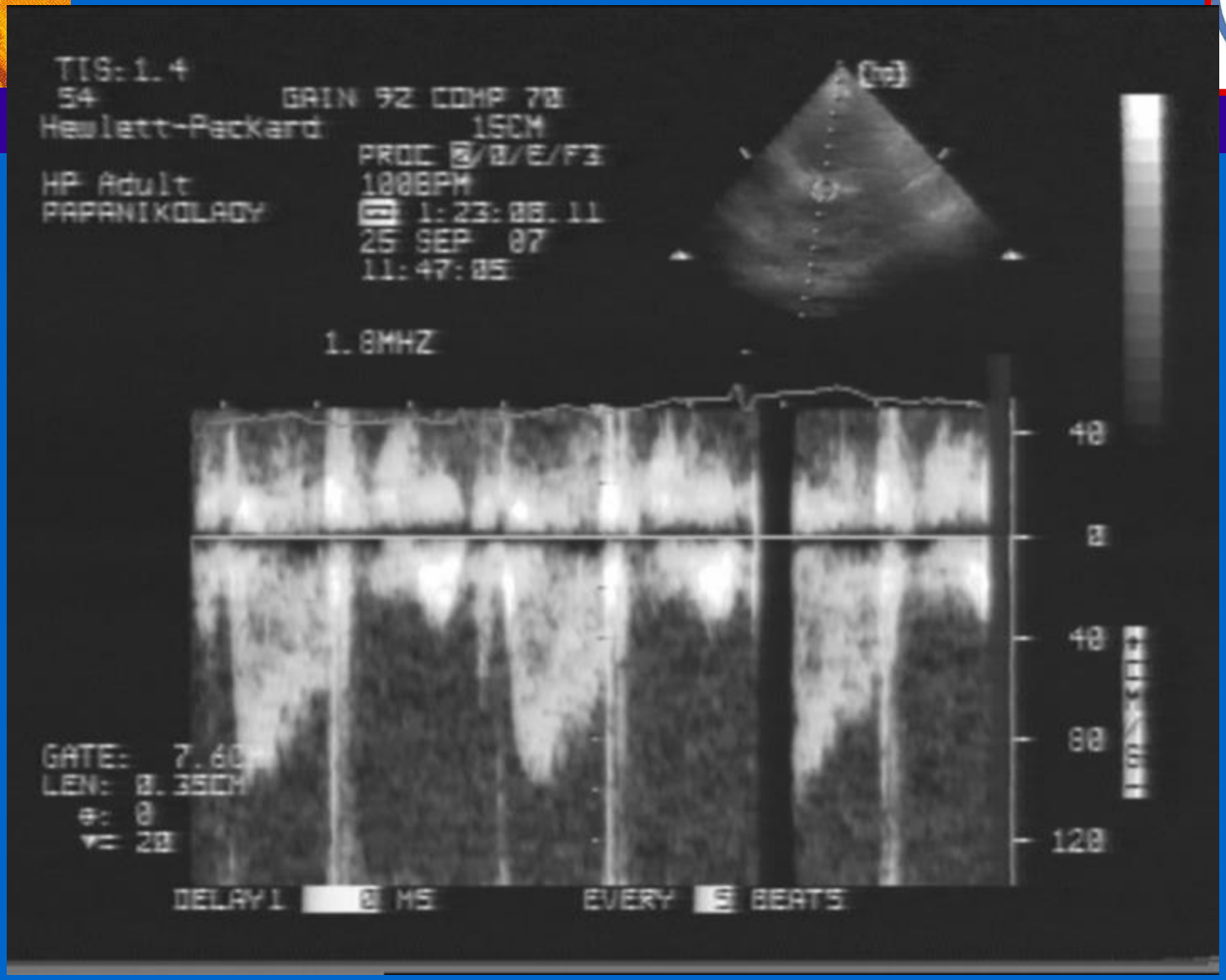
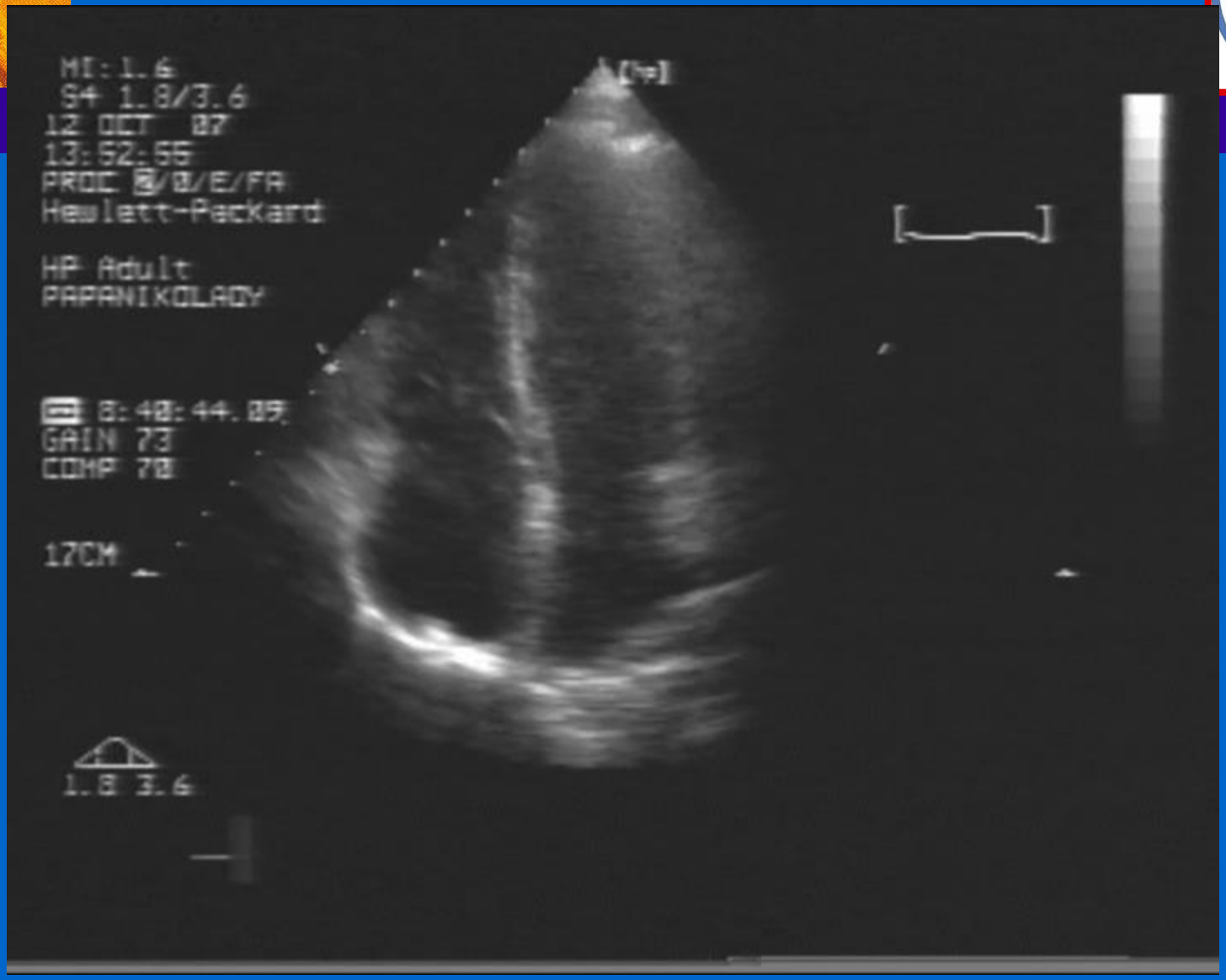
11:46:14
PAPANIKOLAOU
1.8MHZ
3.0MHZ
63
CM/S
63
200
0
200
400
600
FOCUS: 6.6CM
DELAY 1
MS
EVERY
BEATS


TIS:1.4
54
GAIN 92 COMP 70
Hewlett-Packard
15CM
PROC B/D/E/F3
HP Adult
1008PM
PAPANIKOLAOU
1:23:08.11
25 SEP 07
11:47:05
1.8MHZ
40
0
40
80
120
GATE: 7.6
LEN: 0.35CM
0
20
DELAY 1 0 MS
EVERY 5 BEATS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12 OCT 07
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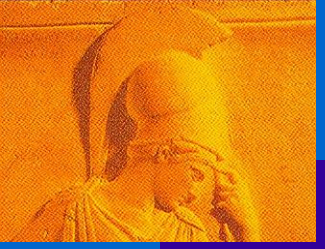
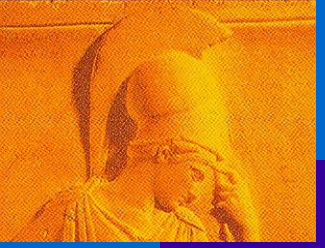
8:40:44.05
GAIN 73
COMP 70
17CM
1.8 3.6



The 6-minute work increased to over 600 m and the O_2 Sat reached 96%.

The patient has no complains or restrictions.



–*Thank you*