

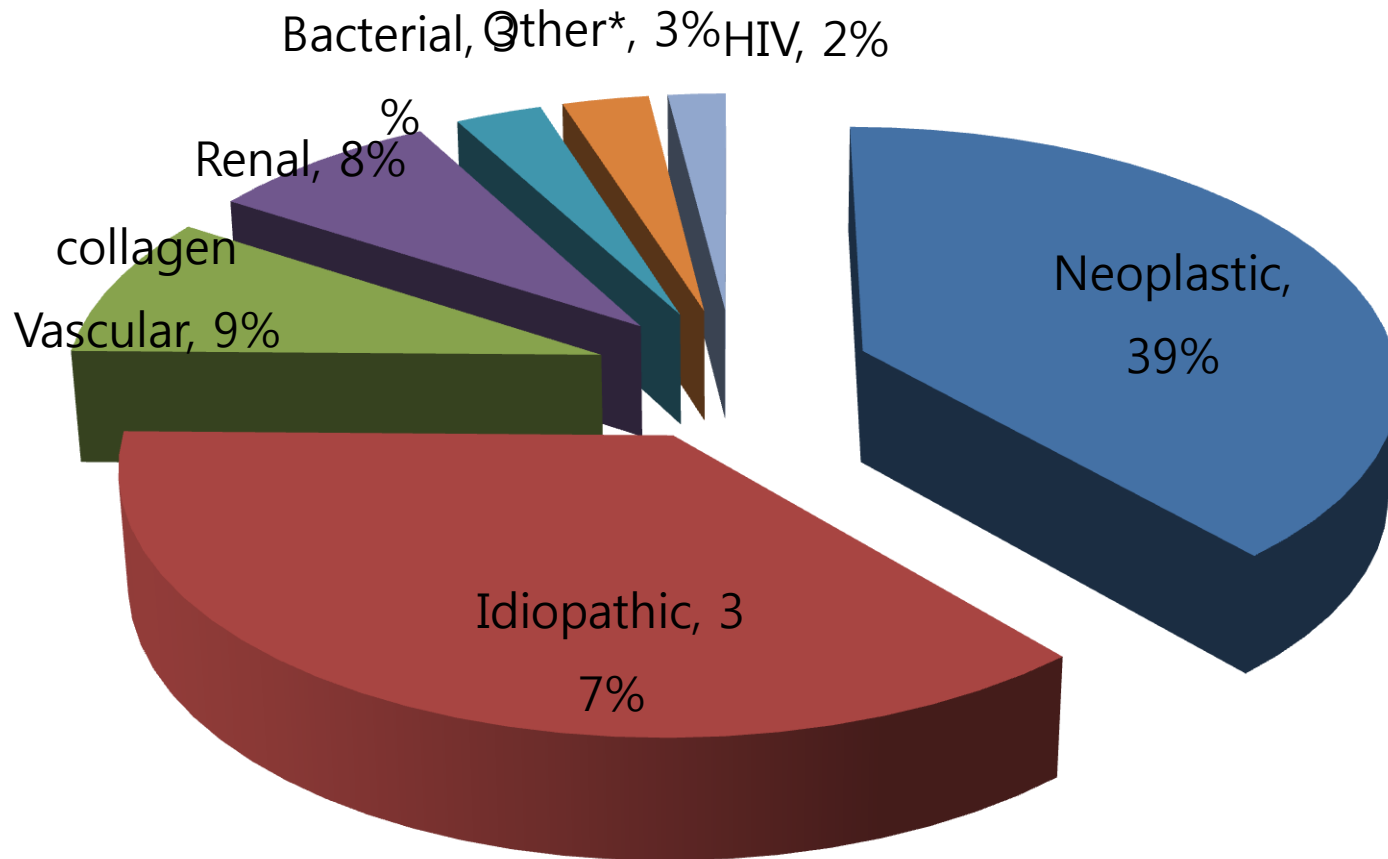
Noninfectious nonsurgical pericardial disease

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Etiology of pericardial disease

Comprehensive category	Primary Etiology Category
A. Infectious causes (2/3)	Viral (common), bacterial, fungal (very rare), parasitic (very rare)
B. Non-Infectious cause (1/3)	
Autoimmune (common) (< 10%)	SLE, systemic vasculitis, Kawasaki disease
Neoplastic (5-7%)	Primary tumors (rare), secondary metastatic tumors (common)
Metabolic	Uremia, myxedema, anorexia nervosa
Traumatic & Iatrogenic	
Drug-related (rare)	
Other (common)	Amyloidosis, pulmonary arterial hypertension , aortic dissection
Other (uncommon)	Congenital absence of pericardium

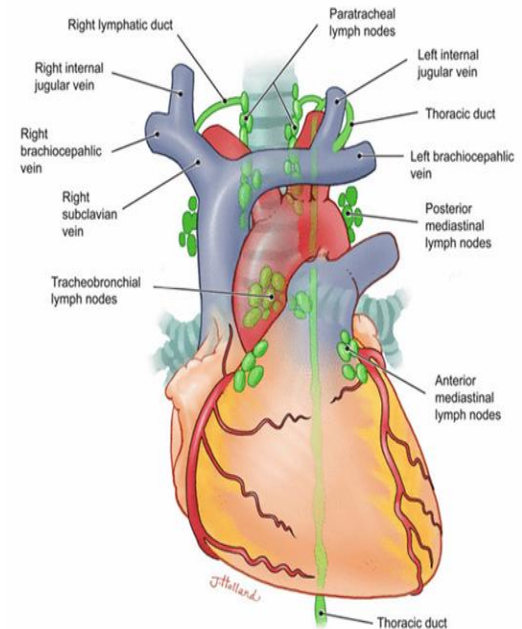
Associated etiologies of pts with PE



- Boston children's hospital
- 116 pts with moderate to large PE
- *Other : hypothyroidism, sepsis, anorexia nervosa

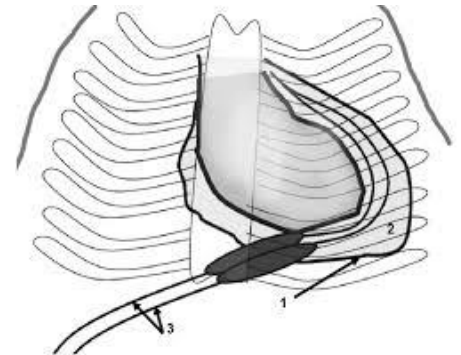
Neoplastic

- up to 21% of patients with cancer
- late in the course of the disease, unfavorable event
- cancers of the lung and breast, lymphoma, and leukemia
- one of four pathways
 - retrograde lymphatic extension : predominant
 - hematogenous spread
 - direct contiguous extension
 - transvenous extension
- subclinical effusion
- CT to be superior in assessing tumor involvement of the pericardium and paracardiac extent



Neoplastic PE

- Cytology Ix : hemorrhagic, no trauma Hx, (+) → poor Px
- Tx
 - 목표: symptomatic, 재발 방지
 - Pericardiocentesis
 - Percutaneous balloon pericardiotomy : 재발 시
 - Pericardial window creation
 - Pericardial sclerotherapy



Neoplastic

- Chemotherapeutic agents (anthracyclines or cyclophosphamide)
 - acute pericarditis or myocarditis.
 - dose-dependent
- Mediastinal irradiation
 - effusive constrictive pericarditis
 - PE & constriction of the heart by the fibrosed visceral pericardium

Hematopoietic stem cell transplant recipients

- 0.2-17%
- Risk factor : GVHD, age 증가, allo-HCT, myeloablative conditioning, delayed neutrophil engraftment, CMV exposed donor

SLE

- 3-24% (1-2.5% tamponade), no constriction
- Co-existing pleuritis

Table 1 Comparison of demographic data, clinical features and laboratory findings of tamponade versus non-tamponade systematic lupus erythematosus (SLE) patients

<i>Demographics</i>	<i>No tamponade (n = 32)</i>	<i>Tamponade (n = 9)</i>	<i>P value</i>
Age (years)	31.8 ± 14.0	32.9 ± 12.1	0.81
Gender	23M/9F	0M/9F	0.0001
Race	25AA/7C	5AA/3C/1A	0.21
SLE duration from Dx (years)	5.3 ± 6.9	6.9 ± 6.2	0.62
Arthritis	21	4	0.28
Rash	4	0	0.56
CNS	4	0	0.56
Renal	17	4	0.28
Thrombocytopenia	5	1	1
Taking corticosteroids on presentation	18	3	0.28
Anticardiolipin antibody	4	2	1
Lupus anticoagulant	2	0	1
ESR	80.6 ± 34.2	101.7 ± 20.1	0.25
WBC	10.8 ± 14.4	8.6 ± 5.1	0.65
C3	75.4 ± 50.8	45.8 ± 23.0	0.28
C4	14.7 ± 9.9	7.8 ± 4.0	0.05

Abbreviations: M: male; F: female; AA: African American; C: Caucasian; A: Asian; Dx: diagnosis; CNS: central nervous system; ESR: erythrocyte sedimentation rate; WBC: white blood cell count; C3, C4: complement 3, 4.

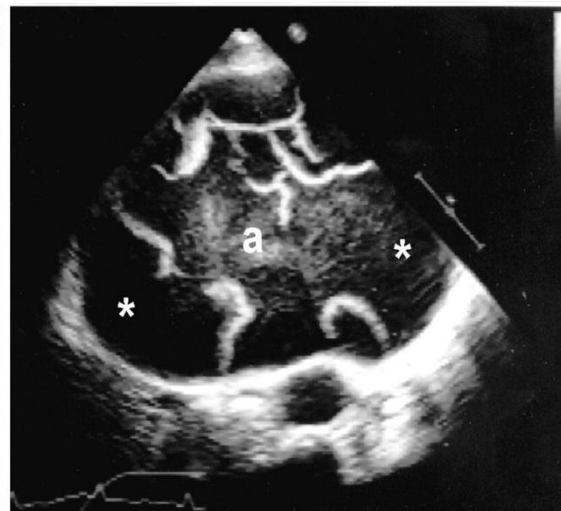
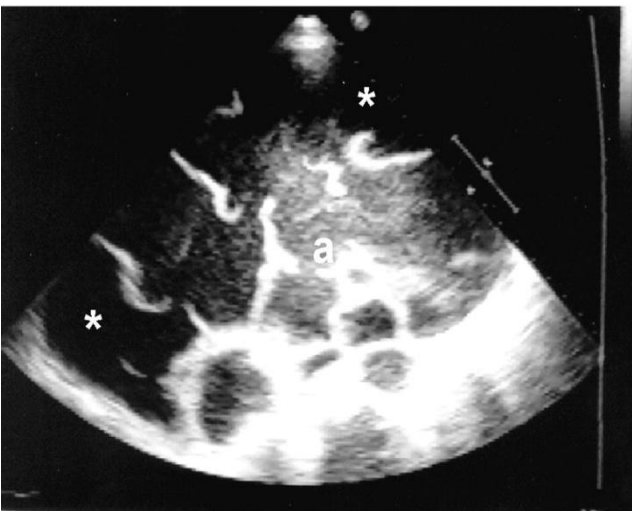
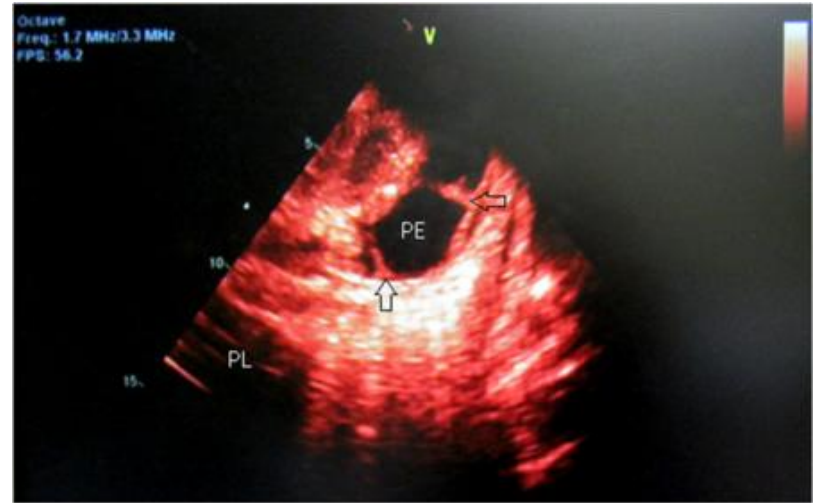
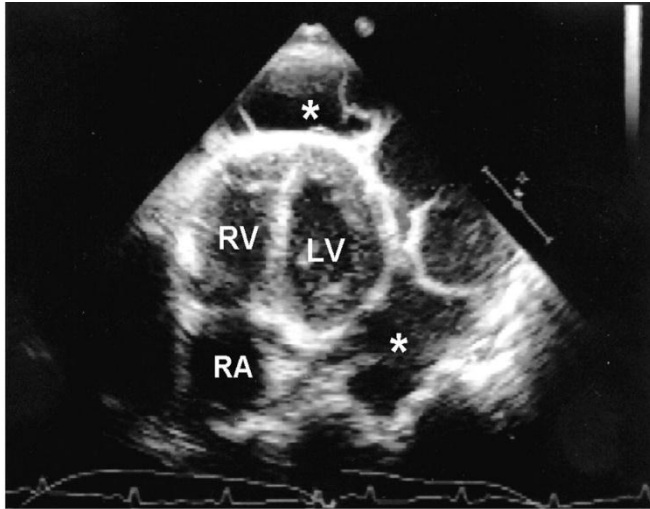
SLE

Table 1 Frequency of selected presenting clinical features of childhood-onset SLE

	Balkaran <i>et al</i> [5]	Spinosa <i>et al.</i> [6]	Abdwani <i>et al.</i> [7]	Hiraki <i>et al.</i> [8]	Agarwal <i>et al.</i> [9]	Gulay <i>et al.</i> [10]
Country	Trinidad	Brazil	Oman	Canada	India	Phillipines
Sample size	33	47	50	256	70	78
<i>Clinical features (%)</i>						
Malar rash	36	32	-	61	57	65
Musculoskeletal	70	32	76	61	66	41
Renal disease	64	38	64	45	77	63
Fever	76	34	62	39	94	-
Weight loss	-*	26	52	29	30	-
Ulcers	-	9	-	33	-	54
Alopecia	-	17	36	22	46	40
Pleuritis/ Pleural effusion	9	17	26	12	3	14
Pericarditis/ Pericardial effusion	24	4	22	12	3	15
Neuropsychiatric	-	36	18	16	21	31

* denotes no data was presented for that clinical feature.

SLE



Two-dimensional transthoracic echocardiography was also remarkable for mobile fibrinous strands (arrows) between the visceral and parietal pericardium,

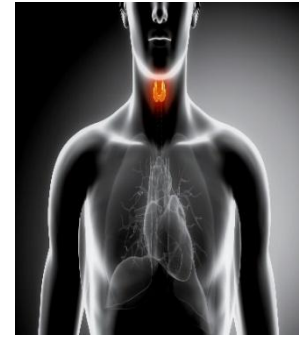
Kawasaki disease

Table 2 Univariate and multivariable analysis of factors associated with coronary artery lesions (CAL) in the acute phase

	Univariate analysis			Multivariable analysis*		
	OR	CI	p Value	aOR	CI	p Value
Sex: male	1.76	0.94 to 3.28	0.08	2.99	1.12 to 7.97	0.03
Extreme age (<6 months or >5 years)	2.24	1.18 to 4.23	0.01	3.73	1.41 to 9.89	0.01
LV shortening fraction <30%	0.68	0.24 to 1.99	0.49	–	–	–
Pericardial effusion	3.00	1.34 to 6.72	0.01	5.26	1.53 to 18.03	0.01
Mitral regurgitation	2.51	1.22 to 5.16	0.01	–	–	–
CRP (10 mg/l increase)†	1.03	1.01 to 1.07	0.03	–	–	–
Haemoglobin (1 g/dl increase) †	0.50	0.38 to 0.67	<0.00001	0.59	0.42 to 0.83	0.003
WBC ($1 \times 10^9/l$ increase)†	1.05	1.00 to 1.11	0.06	–	–	–
Platelet count $>450000/mm^3$ in the late phase†	4.00	1.57 to 10.22	0.004	–	–	–
>2 Day-course of IVIg‡	2.60	1.18 to 5.61	0.02	–	–	–
Late diagnosis (>10 days)	3.81	1.76 to 8.24	0.001	–	–	–
IVIg resistance	7.82	2.07 to 29.58	0.002	23.58	2.45 to 226.58	0.006

*Regression performed with 151 patients; †data available in 165 patients; ‡data available in 157 patients.
CRP, C-reactive protein; IVIg, intravenous immunoglobulins; LV, left ventricular; WBC, white blood cell count.

Hypothyroidism



- In adults, : 10 to 30 % of patients with hypothyroidism
- In the pediatric population : rare, a/w Down syndrome
- related to the severity and duration of the disease
 - 3% in early, mild stage disease, 80% in myxedema
- increased capillary permeability with leakage of plasma proteins into the interstitium.(VEGF, abnormal lymphatic drainage, increased water and salt retention)
- Straw color : high protein & cholesterol, lymphocyte dominant
- Thyroid replacement, The time to resolution varied between 2 to 12 months

Hypothyroidism

Case	Age (years)/ Gender	Ht (%)	Wt (%)	Etiology of thyroid disease	Trisomy 21	Presenting complaint	Pleural effusion also present	Tamponade/ hemodynamic involvement	Levothyroxine (mcg/kg/day)	Bone age (years)	TSH mU/L	FT4 pmol/L (ng/dL)	T3 pmol/L (pgl/dL)	Anti-microsomal antibodies	Time to resolution of effusion (months)
1	7 / F	3	25	Congenital	No	Chest pain	Yes	No	4.41	---	160.49	2.4 (0.19)	---	---	1
2	4.8 / F	3	25	Autoimmune	No	Heart failure	No	Yes	4.42	3	>750	---	---	6400	1
3	14.7 / F	>3	>3	Autoimmune	No	Short stature	No	No	1.08	15	258	<3.4 (<0.26)	1.1 (71.4)	negative	4
4	15.9 / F	>50	25	Medication induced	No	Chest pain	No	No	0.56	14.8	94.2	1.9 (0.15)	0.7 (45.5)	1/102,400	2
5	3.2 / F	<3	<3	Autoimmune	Yes	Cardiology follow up	No	No	2.13	---	43	1.5 (0.12)	---	negative	12
6	7.7 / F	3	50	Autoimmune	No	Precocious puberty	No	No	2.81	5.7	1660	<3.23 (<0.25)	0.4 (26)	6400	5

Anorexia nervosa

- The pathophysiology : unclear
 - Malnutrition >> protein malnutrition
- Docx et al.
 - Echo in 128 AN pts
 - 22% - clinically silent effusions
 - significantly resolved with three months of re-feeding.
 - risk factors : BMI \leq 13.5 kg/m, weight loss \geq 25% and IGF-1 level \leq 100 ng/mL.
 - due to the reduction in pericardial fat and myocardial muscle wasting



Anorexia nervosa

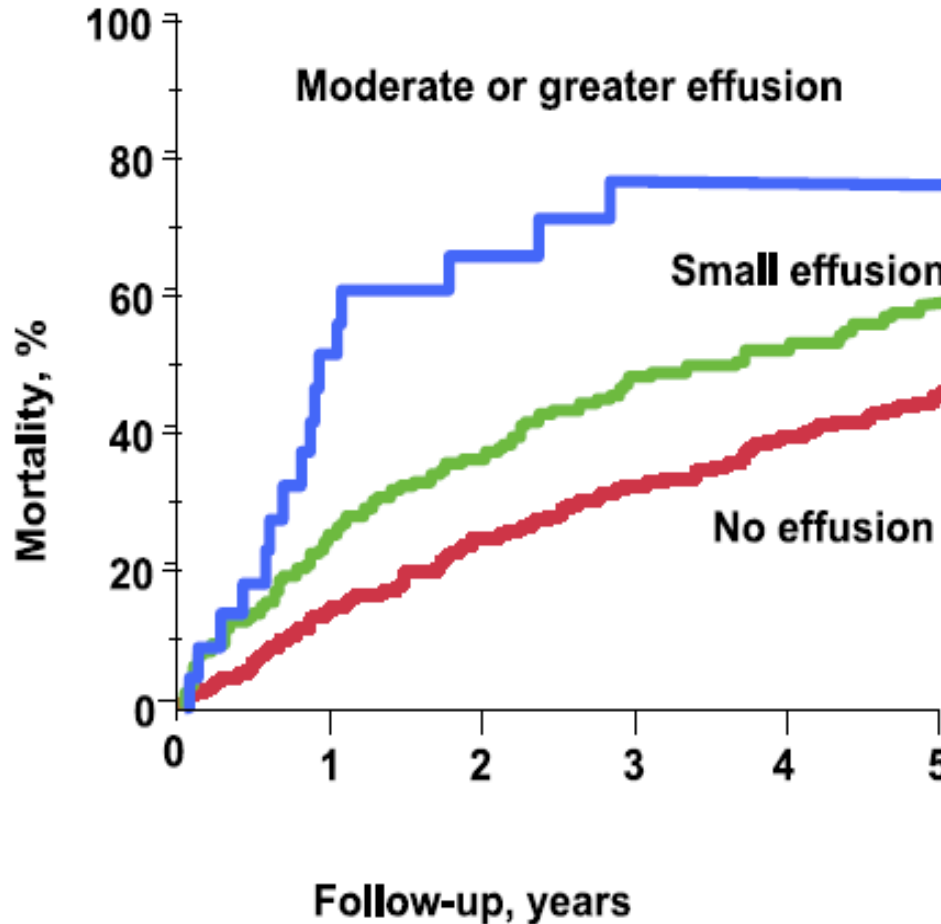
	Silvennan [4]	Von Walter**	Silveti [5]	Frolich [9]	Inagaki [10]	Ramacciotti [6]	Polli [2]	Cho [3]	Docx [7]
Year	1983	1996	1998	2001	2003	2003	2006	2008	2010
Journal	Ped Cardiol	Monatszeitschrift Kinderheilkunde	G Ital Cardiol	Eur Child Adolesc Psychiatry	Int J Eat Disord	Eat Weight disord	Int J Eat Disord	Korean J Pediatr	Eating Disorders
N	4	81	23	65	1	15	1	3	128
Mean age	19.5 ± 3.3	*	14.7 ± 2	15.2 ± 2.1	*	*	*	14.2 ± 0.9	14.4 ± 1.5
% with effusions	*	19.8	61	15.4	*	71.4	*	*	22.2
Mean BMI with effusion	10.8 ± 1.0	*	***	13.5 ± 1.2	14.2	*	11.8	11.7 ± 1.8	13.6 ± 1.1
Mean BMI without effusion	*	*	*	14.1	*	*	*	*	15.8 ± 1.6
Mean % weight loss with effusion	46.5 ± 6.2	*	*	*	43.7	*	23.0	31.0 ± 3.7	25.0 ± 9.0
Concern for tamponade?	No	No	No	No	No	No	Yes	No	No

Renal disease and ESRD

- 2-21%
- 3 pathologies
 - uremic pericarditis : before renal replacement therapy or within 8 weeks of its initiation, d/t retention of toxic metabolites
 - dialysis pericarditis : after being stabilized on dialysis (usually ≥ 8 weeks after its initiation), chronic pericardial effusion, continuous volume overload
 - constrictive pericarditis : very rare
- Since pericardial effusion is often bloody in uremic patients, anticoagulation should be carefully considered or avoided in patients starting dialysis.

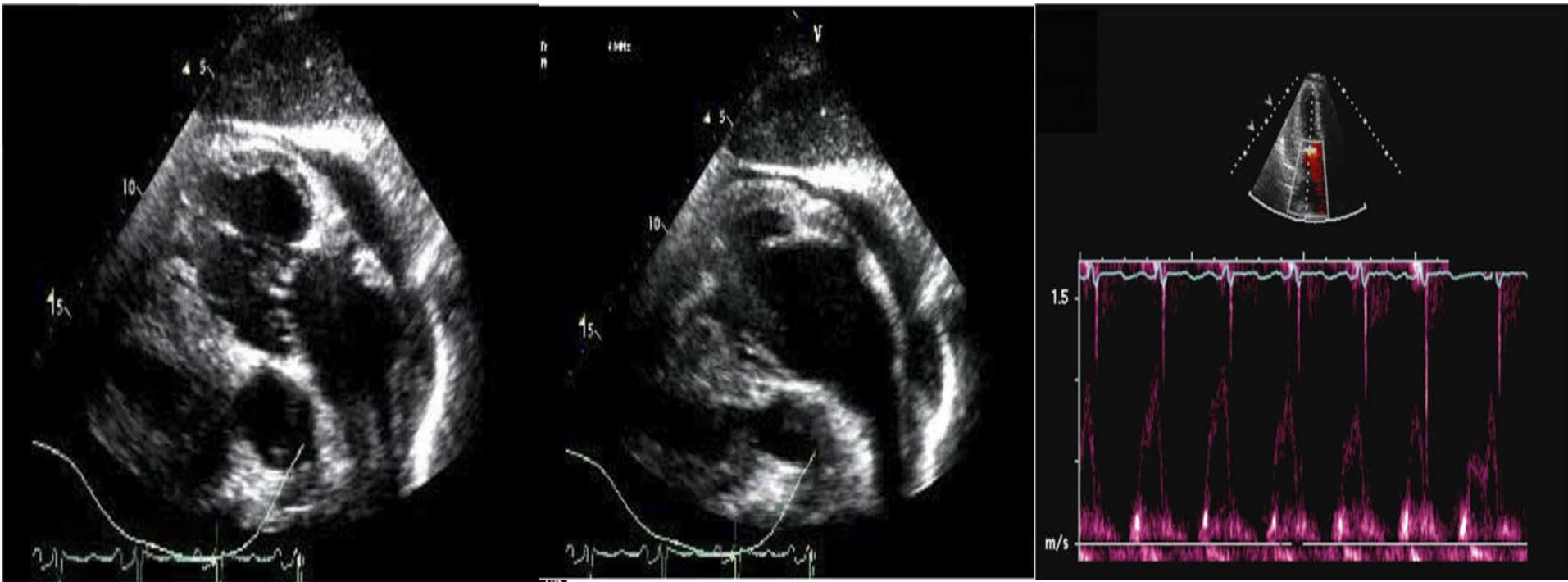
Pericardial involvement in pulmonary arterial hypertension

- 25–30% hemody
- relate to in right- and lymph effusion
- a/w CT and an
- poor pr
- Pericard



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Pericardial involvement in pulmonary arterial hypertension



Diagnosis of cardiac tamponade in a patient with severe PAH is challenging.
left atrial early diastolic collapse !!

ESC 2015 Proposal for a general diagnostic work-up

- In all cases of suspected pericardial disease a first diagnostic evaluation is recommended with
 - auscultation
 - ECG
 - transthoracic echocardiography
 - chest X-ray
 - routine blood tests, markers of inflammation (i.e., CRP and/or ESR), WBC, differential count, renal function and liver tests and myocardial lesion tests (CK, troponins)

ESC 2015 Proposal for a general diagnostic work-up

- It is recommended to search for independent predictors of an identifiable and specifically treatable cause of pericarditis (i.e. bacterial, neoplastic, systemic inflammatory diseases).
- Major factors include
 - fever $> 38^{\circ}\text{C}$
 - subacute course (symptoms developing over several days or weeks)
 - large pericardial effusion (diastolic echo-free space > 20 mm in width)
 - cardiac tamponade
 - failure of aspirin or NSAIDs

Pericardial fluid biochemical and cell-count characteristics

Cause	White Blood Cells/ μ l	% Lymphocytes	LDH P/S	LDH Pericardial/Upper Normal Serum Level	Protein P/S	Protein Pericardial/Upper Normal Serum Level	Glucose P/S
Neoplastic	3.3 (0.1–6.5)	45 (22–68)	4.3 (0.6–8)	4.4 (0.8–8)	0.8 (0.6–1)	0.6 (0.5–0.7)	0.8 (0.4–1.2)
Bacterial	2.8 (0.4–5.2)	8 (5–11)	2.3 (0.6–4)	2.1 (0.3–3.9)	0.8 (0.6–1)	0.6 (0.4–0.8)	0.3 (0–0.6)
Tuberculous	1.7 (0.1–3.3)	50 (42–58)	8.2 (4.2–12.2)	5.2 (5–5.4)	0.8 (0.7–0.9)	0.6 (0.3–0.9)	0.7 (0.6–0.9)
Acute pericarditis	7.8 (0–19.8)	44 (13–75)	2.9 (0.8–5)	3.5 (0–7.5)	0.9 (0.7–1.1)	0.7 (0.6–0.8)	0.9 (0.5–1.3)
Idiopathic	2.2 (0–5.8)	67 (43–91)	2.6 (0.4–4.8)	1.8 (0.2–3.4)	0.8 (0.6–1)	0.6 (0.5–0.7)	0.9 (0.6–1.2)
Trauma	2.7 (1.2–4.2)	46 (39–53)	1.4 (0.9–1.9)	1.5 (0.7–2.3)	1 (0.9–1.1)	0.7 (0.6–0.8)	0.9 (0.5–1.3)
Uremic	2.9 (0.1–5.7)	49 (23–65)	1.6 (0.2–3)	1.6 (0.6–2.6)	0.8 (0.6–1)	0.6 (0.4–0.8)	0.9 (0.5–1.3)
Collagen disease	7.5 (0–21)	51 (13–89)	0.9 (0.5–1.3)	1.2 (0.2–2.2)	0.9 (0.5–1.3)	0.7 (0.5–0.9)	0.8 (0.3–1.3)
Postpericardiectomy	5 (0–10.1)	29 (0–60)	3.9 (3.6–4.2)	2.5 (2.3–2.7)	0.6 (0.3–0.9)	0.5 (0.3–0.7)	0.8 (0.5–1.1)
Radiation	2.4	90	2.8	3.1	0.9	0.7	0.8
Heart failure	0.2	31	0.7	0.7	0.5	0.5	1.2
Indeterminate	2.3 (0.4–4.2)	44 (7–75)	2.5 (0–5.5)	2.3 (0.1–4.5)	0.8 (0.7–0.9)	0.6 (0.5–0.7)	1.1 (0.7–1.5)

Demographics and clinical characteristics

Cause	No. of Patients	Women/Men	Mean Age \pm SD	Tamponade Present: Yes/No/Not Available	Amount Aspirated (cm ³)	Fluid Serous/Serosanguineous/Bloody
Neoplastic	42	23/19	57 \pm 16.4 [†]	32/6/4*	727 \pm 377	8/9/21*
Bacterial	4	2/2	45 \pm 18.1	3/1/0	582 \pm 365	1/2/1
Tuberculous	2	0/2	61 \pm 22.3	1/1/0	625 \pm 247	1/1/0
Acute pericarditis	17	6/11	54 \pm 17 [†]	11/6/0	607 \pm 241	5/7/5
Idiopathic	22	11/11	65 \pm 13.2*	11/11/0 [†]	731 \pm 404	11/6/5 [†]
Trauma	5	2/3	64 \pm 10.7	4/1/0	576 \pm 496	0/1/4
Uremic	7	2/5	56 \pm 9.3	3/4/0	933 \pm 452	4/0/3
Collagen disease	5	2/3	62 \pm 6.6	3/2/0	414 \pm 191	3/1/1
Postpericardiotomy	4	1/3	48 \pm 32.3	3/1/0	1,002 \pm 931	1/1/2
Radiation	1	1/0	68	0/1/0	400	0/1/0
Heart failure	1	0/1	68	0/1/0	800	1/0/0
Indeterminate	10	5/5	59 \pm 24.4	8/1/1	628 \pm 333	3/5/2
Overall	120	55/65	61 \pm 17.8	79/36/5	696 \pm 396	38/34/44

[†] A result that is significantly different compared with results denoted by * in the same column (p < 0.05).

ESC 2015 Proposal for a general diagnostic work-up

Table 15 Main analyses to be performed on pericardial fluid

Analysis	Test
General chemistry	Protein level >3 g/dL, protein fluid/serum ratio >0.5, LDH >200 IU/L, fluid/serum ratio >0.6 ^a , blood cell count.
Cytology	Cytology (higher volumes of fluid, centrifugation, and rapid analysis improve diagnostic yield).
Polymerase chain reaction (PCR)	PCR for TB.
Microbiology	Mycobacterium cultures, aerobic and anaerobic cultures.

ESC 2015 Proposal for a general diagnostic work-up

- Percutaneous or surgical pericardial biopsy : suspected neoplastic or tuberculous pericarditis
- Further testing : according to the clinical conditions