

Pericardial Diseases

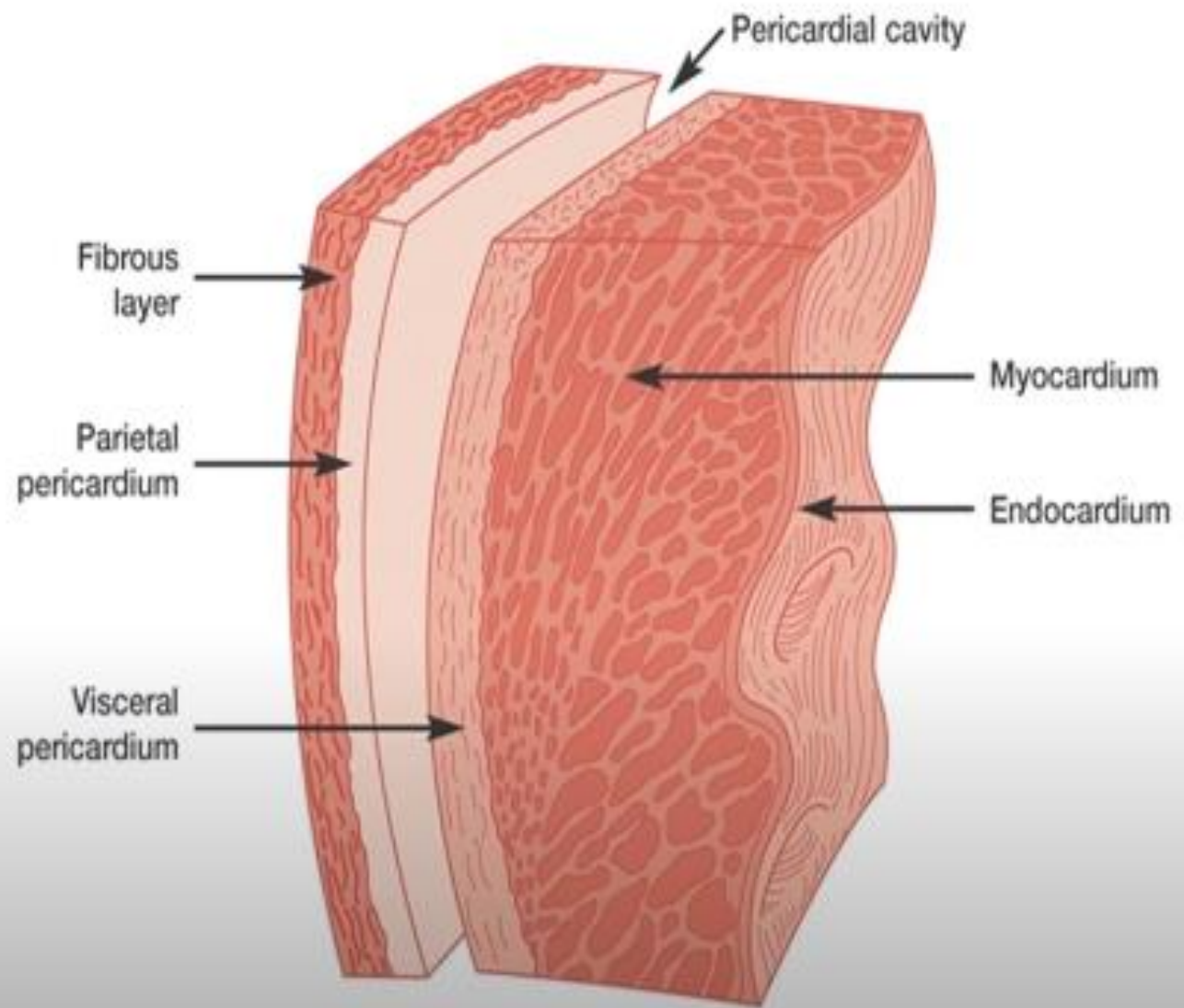
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Outline

- Acute and chronic pericarditis
- Pericardial effusion/ Tamponade
- Pericardial constriction



Acute pericarditis

Table 3 Aetiology of pericardial diseases. The pericardium may be affected by all categories of diseases, including infectious, autoimmune, neoplastic, iatrogenic, traumatic, and metabolic

A. Infectious causes:
Viral (common): Enteroviruses (coxsackieviruses, echoviruses), herpesviruses (EBV, CMV, HHV-6), adenoviruses, parvovirus B19 (possible overlap with aetiological viral agents of myocarditis).
Bacterial: <i>Mycobacterium tuberculosis</i> (common, other bacterial rare), <i>Coxiella burnetii</i> , <i>Borrelia burgdorferi</i> , rarely: <i>Pneumococcus</i> spp, <i>Meningococcus</i> spp, <i>Gonococcus</i> spp, <i>Streptococcus</i> spp, <i>Staphylococcus</i> spp, <i>Haemophilus</i> spp, <i>Chlamydia</i> spp, <i>Mycoplasma</i> spp, <i>Legionella</i> spp, <i>Leptospira</i> spp, <i>Listeria</i> spp, <i>Providencia stuartii</i> .
Fungal (very rare): <i>Histoplasma</i> spp (more likely in immunocompetent patients), <i>Aspergillus</i> spp, <i>Blastomyces</i> spp, <i>Candida</i> spp (more likely in immunocompromised host).
Parasitic (very rare): <i>Echinococcus</i> spp, <i>Toxoplasma</i> spp
B. Non-infectious causes:
Autoimmune (common): Systemic autoimmune and auto-inflammatory diseases (systemic lupus erythematosus, Sjögren syndrome, rheumatoid arthritis, scleroderma), systemic vasculitides (i.e. eosinophilic granulomatosis with polyangiitis or allergic granulomatosis, previously named Churg-Strauss syndrome, Horton disease, Takayasu disease, Behçet syndrome), sarcoidosis, familial Mediterranean fever, inflammatory bowel diseases, Still disease.

Neoplastic:

Primary tumours (rare, above all pericardial mesothelioma).
Secondary metastatic tumours (common, above all lung and breast cancer, lymphoma).

Metabolic: Uraemia, myxoedema, anorexia nervosa, other rare.

Traumatic and Iatrogenic:

Early onset (rare):

- Direct injury (penetrating thoracic injury, aoesophageal perforation).
- Indirect injury (non-penetrating thoracic injury, radiation injury).

Delayed onset: Pericardial injury syndromes (common) such as postmyocardial infarction syndrome, postpericardiotomy syndrome, posttraumatic, including forms after iatrogenic trauma (e.g. coronary percutaneous intervention, pacemaker lead insertion and radiofrequency ablation).

Drug-related (rare): Lupus-like syndrome (procainamide, hydralazine, methyl dopa, isoniazid, phenytoin); antineoplastic drugs (often associated with a cardiomyopathy, may cause a pericardiopathy): doxorubicin, daunorubicin, cytosine arabinoside, 5-fluorouracil, cyclophosphamide; penicillins as hypersensitivity pericarditis with eosinophilia; amiodarone, methysergide, mesalazine, clozapine, minoxidil, dantrolene, practolol, phenylbutazone, thiazides, streptomycin, thiouracils, streptokinase, p-aminosalicylic acid, sulfa-drugs, cyclosporine, bromocriptine, several vaccines, GM-CSF, anti-TNF agents.

Other (common): Amyloidosis, aortic dissection, pulmonary arterial hypertension and chronic heart failure.

Other (uncommon): congenital partial and complete absence of the pericardium.

CMV = cytomegalovirus; EBV = Epstein-Barr virus; GM-CSF = granulocyte-macrophage colony-stimulating factor; HHV = human herpesvirus; spp = species; TNF = tumor necrosis factor.

Table 3 Aetiologic diagnosis of moderate to large pericardial effusions according to major published series

Feature	Corey et al. ¹⁷	Sagrista-Sauleda et al. ¹⁸	Levy et al. ¹⁹	Reuter et al. ²⁰	Ma et al. ²¹
Patients	57	322	204	233	140
Study years	1993	1990–96	1998–2002	1995–2001	2007–09
Country	USA	Spain	France	South Africa	China
Effusion size	>5 mm	>10 mm	NR	NR	Moderate to large ^a
Cardiac tamponade	NR	37	NR	NR	NR
Evaluation	Subxiphoid pericardiotomy	TB, ANA, TSH, pericardiocentesis, and biopsy	BCx, TSH, ANA, Q fever, viral rectal, and throat swabs	HIV, sputum, TB, BCx, blood chemistry, and serology	Pericardiocentesis
Idiopathic (%)	7	29	48	14	9
Cancer (%)	23	13	15	9	39
Infections (%)	27	2	16	72	29
Connective tissue diseases (%)	12	5	10	5	6
Metabolic (%)	24	6	11	0	0
Iatrogenic (%)	0	16	0	0	9

A selection of the most frequent aetiological diagnoses is reported (thus overall sum in columns may be <100%).

NR, not reported; TB, aetiology search for tuberculosis; BCx, blood cultures.

^aAll effusions requiring pericardiocentesis.

Presentation

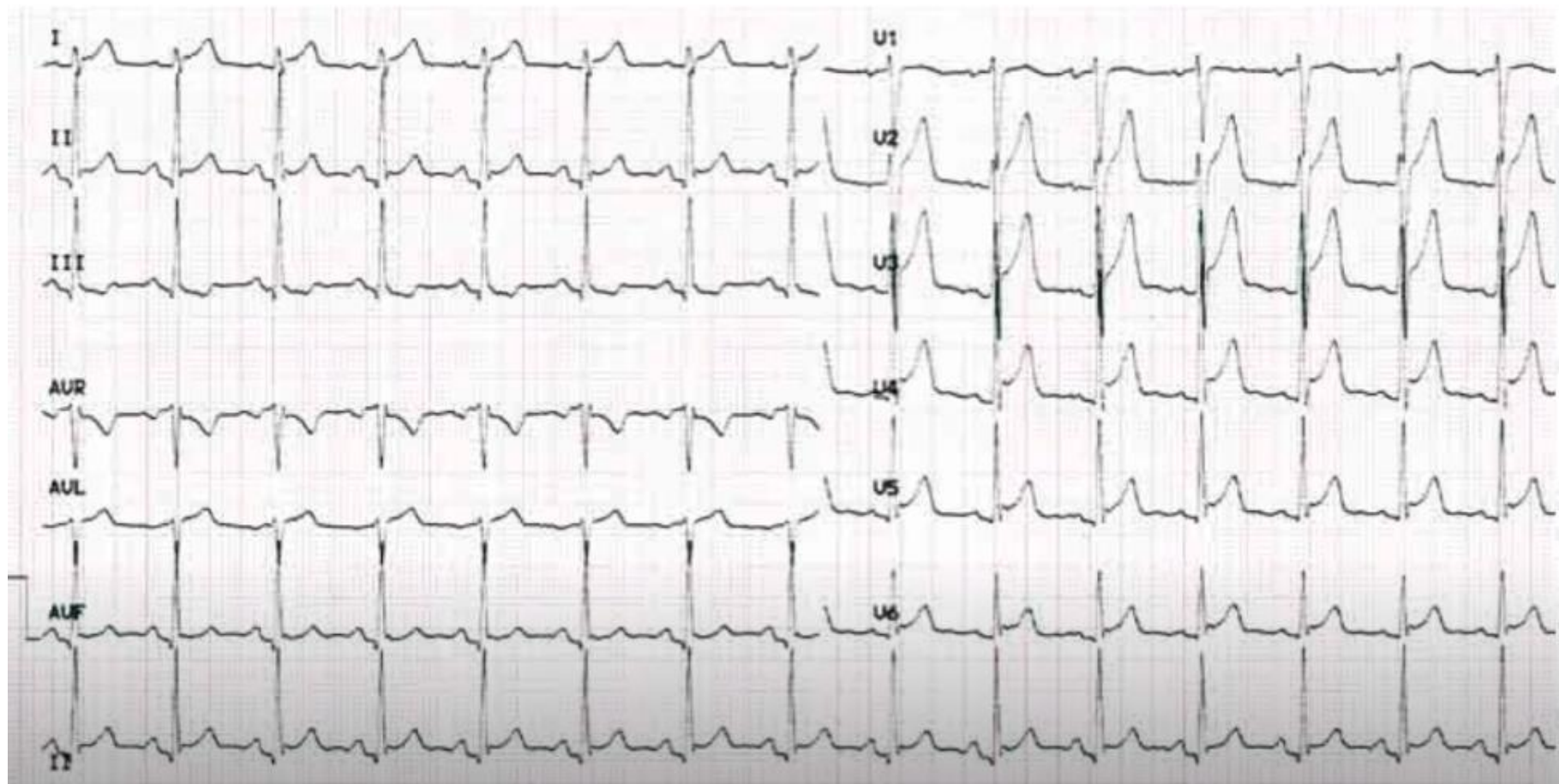
- Sharp
- Retrosternal
- Pleuritic
- Positional (Supine vs lean forward)
- Radiate to trapezius ridge
- Fever
- Antecedent viral symptoms

Physical exam

- Low grade fever (worse prognosis)
- Pericardial rub (~ 1/3)
- High pitched, scratchy
- 1-3 components
- Auscultation:
- Left sternal border
- Leaning forward or resting on elbow/knees

ECG

- Diffuse STE
- PR depression



Labs

- **Inflammatory biomarkers (80%)**

- ☐ ESR

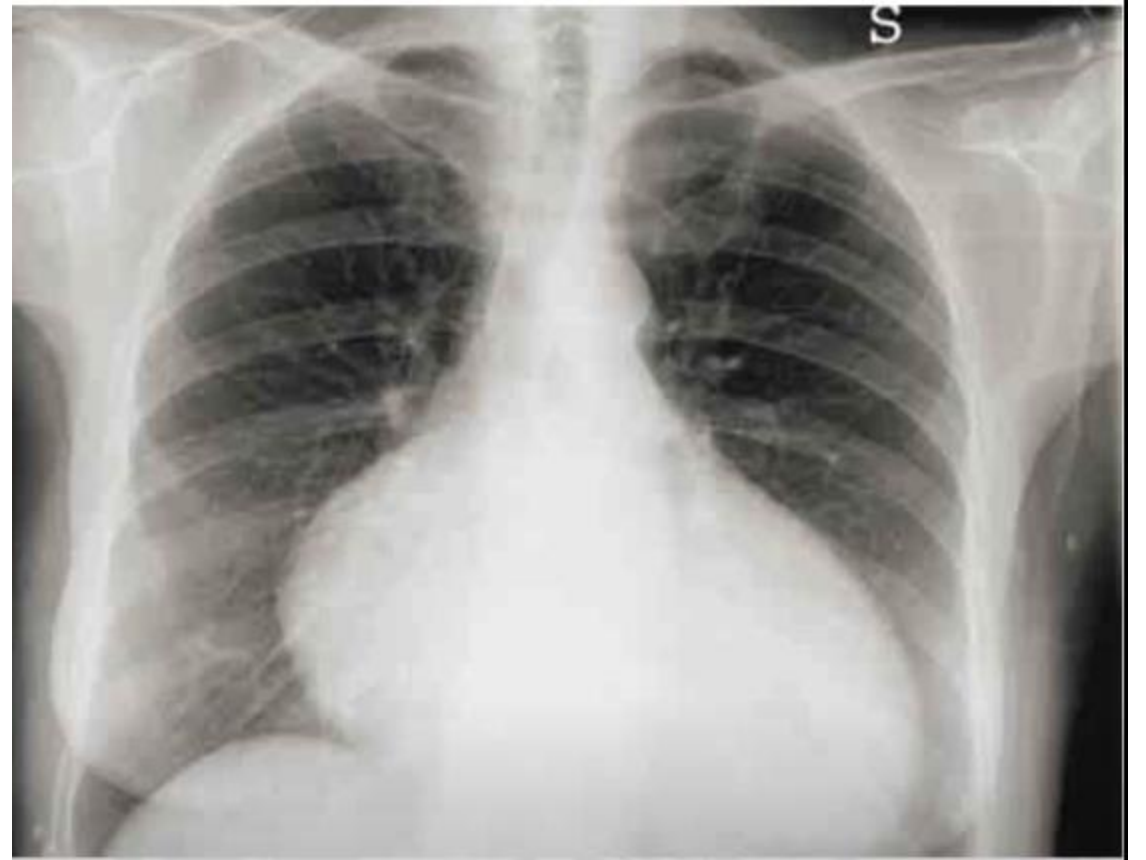
- ☐ CRP

- **Troponin (30%)**

- ☐ High values: Consider myopericarditis

Imaging

- Usually normal
- Exceptions:
 - -Pleuropulmonary disease
 - -Large pericardial effusion



Echocardiography

- Effusion: 50-60%
- Usually small
- If large: Increased risk of
 - ❑ septic etiology
 - ❑ Complications

CT scan

- Pericardial thickness (normal: 0.7 – 2.0 mm)
- Effusion
- Malignancy
- Pericardial cysts
- Perioperative assessment

MRI

- Pericardial thickness (nl: 1.2-1.7 mm)
- Effusion & Hemodynamic impact
- Myocarditis
- Pericardial inflammation

Diagnosis Criteria

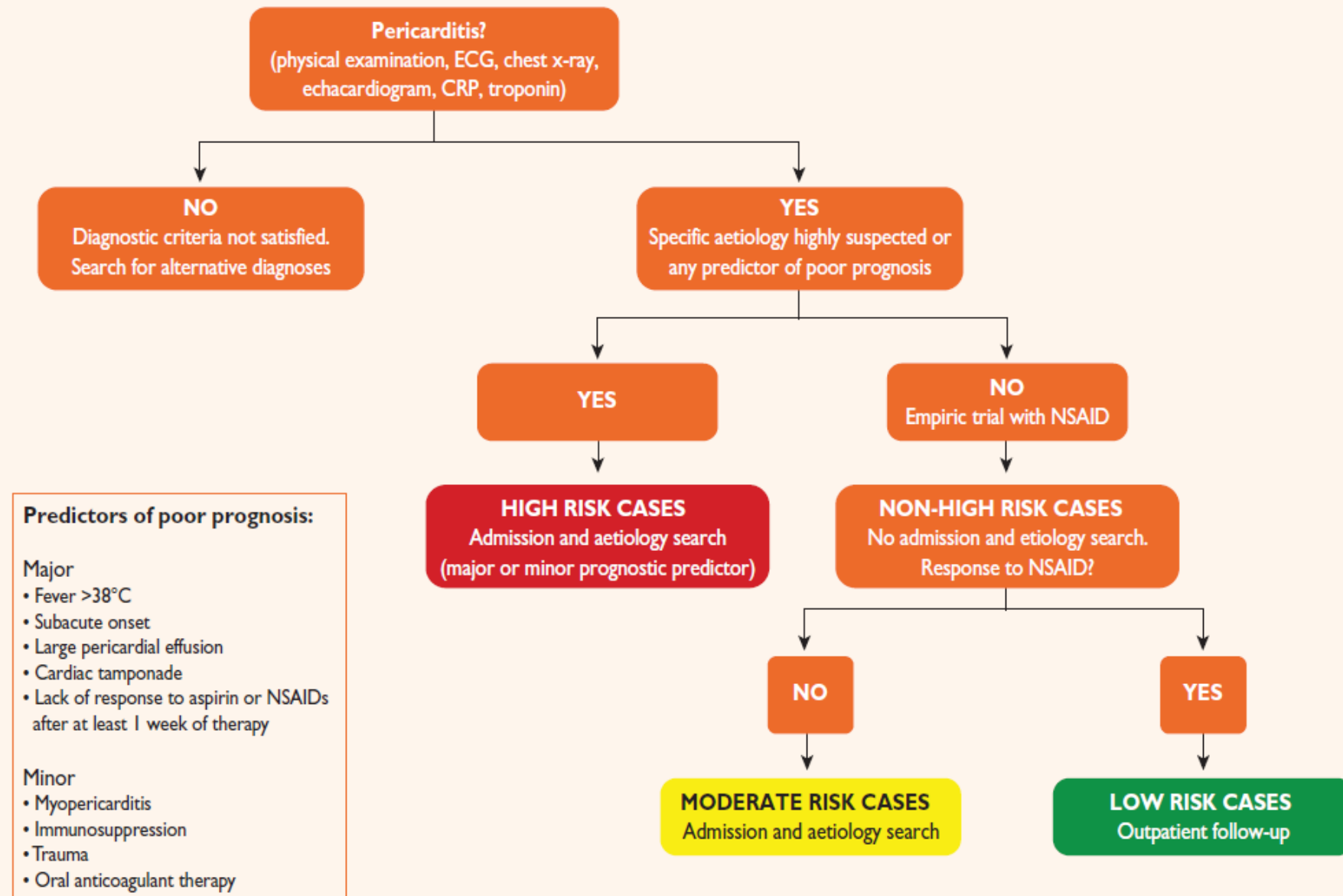
- Clinical: (≥ 2 of the following)
 - Typical chest pain
 - Exam (rub)
 - ECG
- Imaging: New/worsening effusion

Table 1 Classification of pericardial effusion

Onset	Acute (<1 week)
	Subacute (>1 week but <3 months)
	Chronic (>3 months)
Size	Mild (<10 mm)
	Moderate (10–20 mm)
	Large (>20 mm)
Distribution	Circumferential
	Loculated
Haemodynamic effect	Without cardiac tamponade
	With cardiac tamponade
	Effusive-constrictive
Composition/type	Transudate
	Exudate
	Hydropericardium (transudate, plasma ultrafiltrate)
	Haemopericardium (blood in pericardial space)
	Chylopericardium (chylous pericardial fluid)
	Pyopericardium (purulent pericardial effusion)
	Pneumopericardium (air in the pericardium)

No precise definition is available for acute and subacute pericardial effusion, while the definition of chronic as >3 months is more clearly defined.

Ris



CRP = C-reactive protein; ECG = electrocardiogram.

Proposed triage of acute pericarditis according to epidemiological background and predictors of poor prognosis at presentation (modified from refs 5, 6, 8, and 12). At least one predictor of poor prognosis is sufficient to identify a high risk case. Major criteria have been validated by multivariate analysis,(9) minor criteria are based on expert opinion and literature review. Cases with moderate risk are defined as cases without negative prognostic predictors but incomplete or lacking response to non-steroidal anti-inflammatory drug (NSAID) therapy. Low risk cases include those without negative prognostic predictors and good response to anti-inflammatory therapy. Specific aetiology is intended as non-idiopathic aetiology

Treatment

Drug	Usual dosing ^a	Tx duration ^b	Tapering ^a
Aspirin	750–1000 mg every 8h	1–2 weeks	Decrease doses by 250–500 mg every 1–2 weeks
Ibuprofen	600 mg every 8h	1–2 weeks	Decrease doses by 200–400 mg every 1–2 weeks
Colchicine	0.5 mg once (<70 kg) or 0.5 mg b.i.d. (≥70 kg)	3 months	Not mandatory, alternatively 0.5 mg every other day (< 70 kg) or 0.5 mg once (≥70 kg) in the last weeks

Steroids

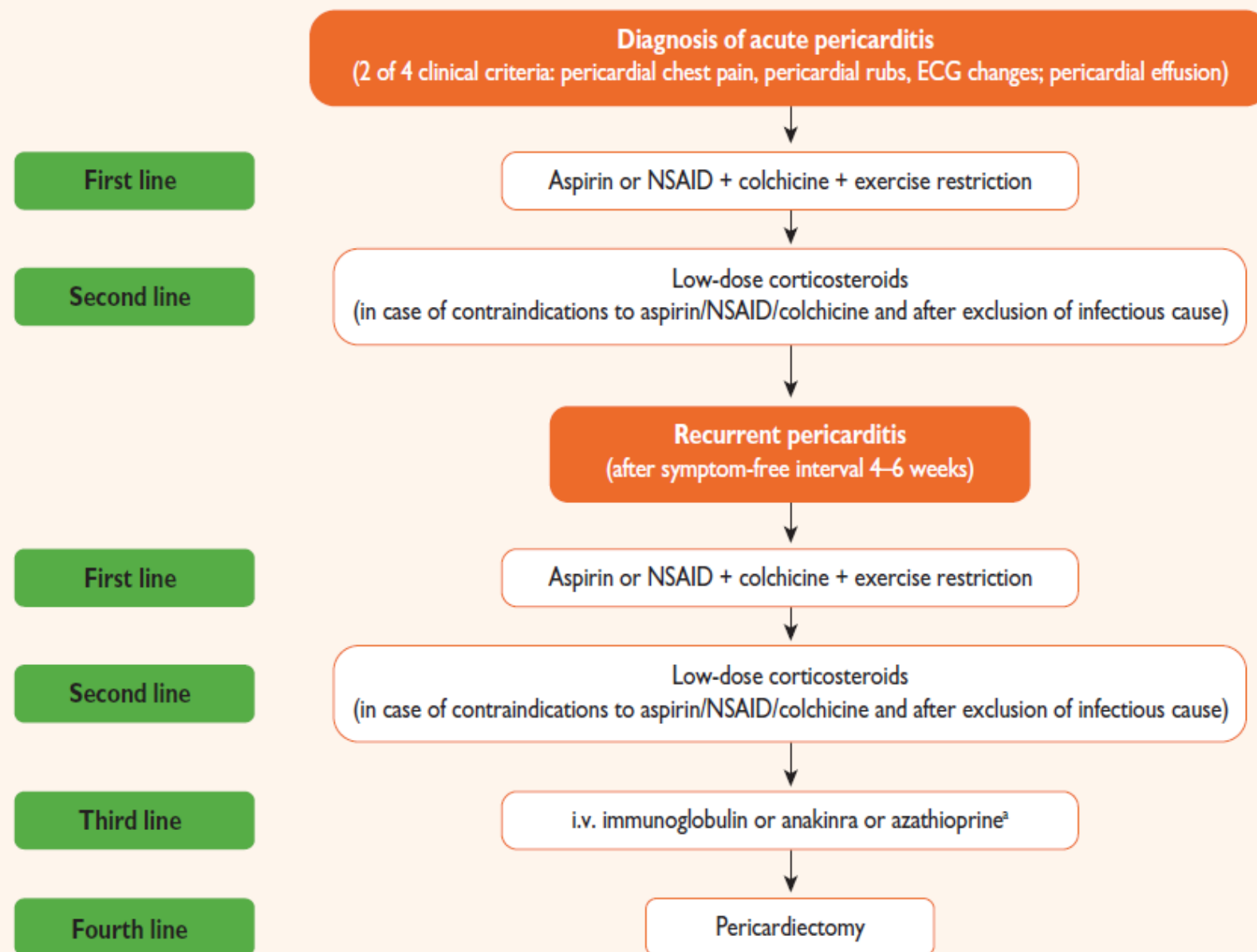
- Systemic inflammatory diseases
 - Pregnancy
 - NSAIDs contraindications
 - Failure of treatment with SAIDs
 - Renal failure
 - Anticoagulant use
-
- Higher risk of recurrence

Recurrent pericarditis

- Recurrent: episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer.
- Chronic Pericarditis: lasting for >3 months.

Recurrent pericarditis

Drug	Usual initial dose ^a	Tx duration ^b	Tapering ^a
Aspirin	500–1000 mg every 6–8 hours (range 1,5–4 g/day)	weeks-months	Decrease doses by 250–500 mg every 1–2 weeks ^b
Ibuprofen	600 mg every 8 hours (range 1200–2400 mg)	weeks-months	Decrease doses by 200–400 mg every 1–2 weeks ^b
Indomethacin	25–50 mg every 8 hours: start at lower end of dosing range and titrate upward to avoid headache and dizziness.	weeks-months	Decrease doses by 25 mg every 1–2 weeks ^b
Colchicine	0.5 mg twice or 0.5 mg daily for patients <70 kg or intolerant to higher doses.	At least 6 months	Not necessary, alternatively 0.5 mg every other day (<70 kg) or 0.5 mg once (≥70 kg) in the last weeks



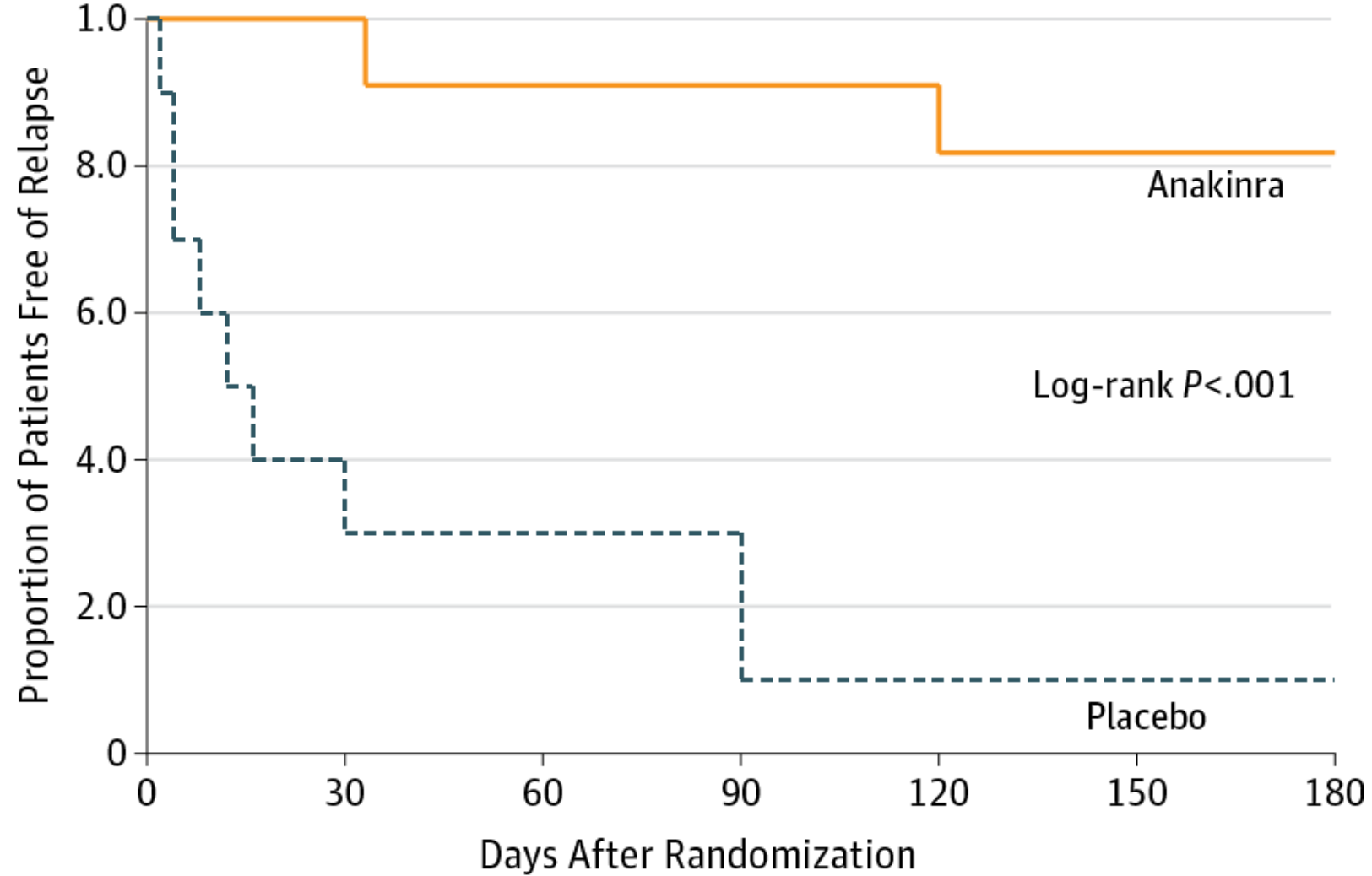
Low-dose corticosteroids are considered when there are contraindications to other drugs or when there is an incomplete response to aspirin/NSAIDs plus colchicine; in this case physicians should consider adding these drugs instead of replacing other anti-inflammatory therapies.

³Azathioprine is steroid-sparing and has a slow onset of action compared with IVIG and anakinra. Cost considerations may apply considering the cheaper solution first (e.g. azathioprine) and resorting to more expensive options (e.g. IVIG and anakinra) for refractory cases.

AIRTRIP Randomized Clinical Trial

Effect of Anakinra on Recurrent Pericarditis Among Patients With Colchicine Resistance and Corticosteroid Dependence The AIRTRIP Randomized Clinical Trial

- *Antonio Brucato, MD1; Massimo Imazio, MD, FESC2; Marco Gattorno, MD3; et alGeorge Lazaros, MD2,4; Silvia Maestroni, MD1; Mara Carraro, RN2; Martina Finetti, MD3; Davide Cusmetti, MD1; Alessandra Carobbio, MSc1; Nicolino Ruperto, MD, MPH3; Renzo Marcolongo, MD5; Monia Lorini, MD1; Alessandro Rimini, MD3; Anna Valenti, MD1; Gian Luca Erre, MD6; Maria Pia Sormani, PhD3; Riccardo Belli, MD2; Fiorenzo Gaita, MD7; Alberto Martini, MD3,8*
- **JAMA. 2016;316(18):1906-1912. doi:10.1001/jama.2016.15826**



No. at risk

Placebo	10	4	3	3	1	1
Anakinra	11	11	10	10	10	9

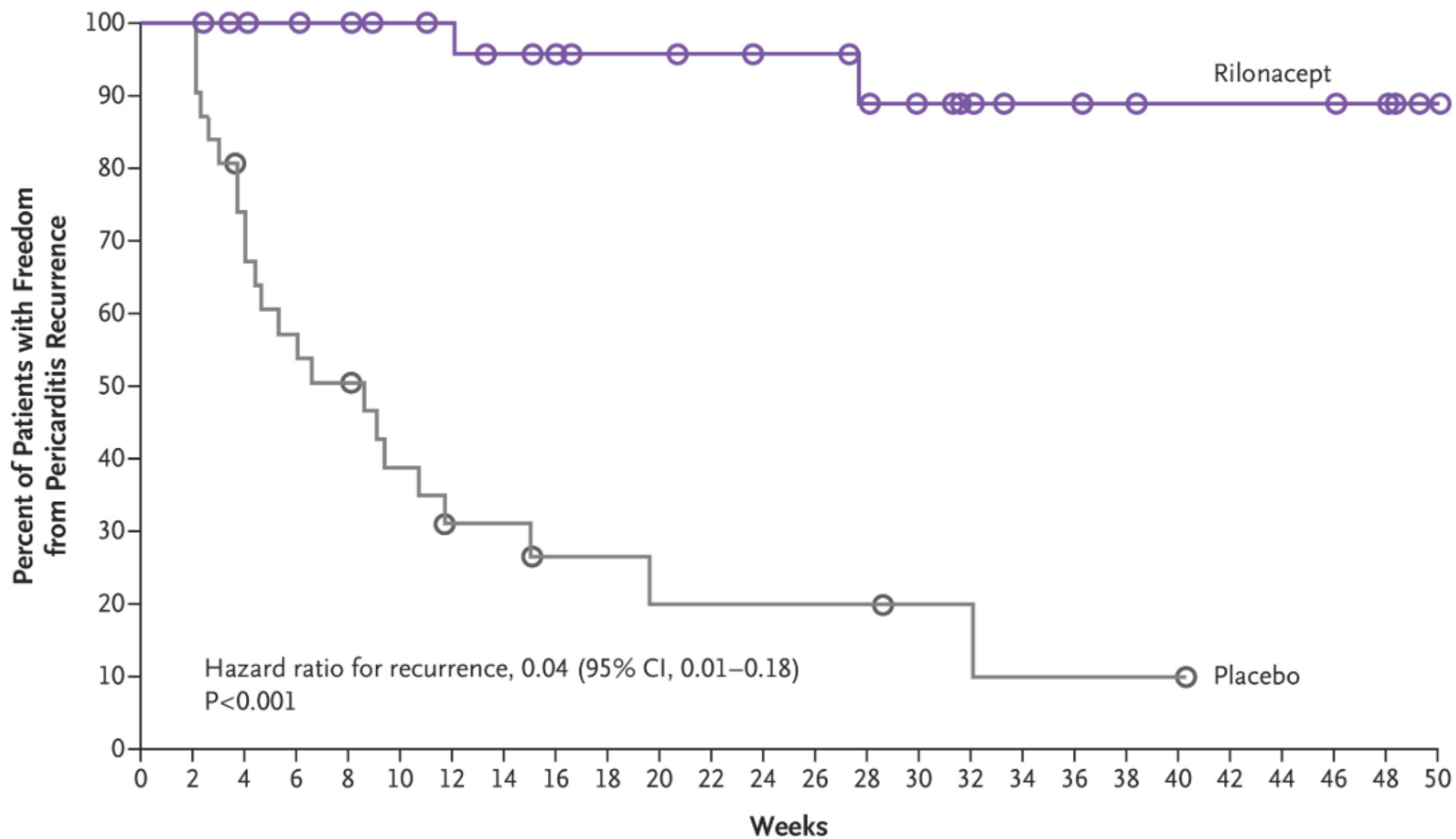
No. of treatment failures

Placebo	6	1	0	2	0
Anakinra	0	1	0	0	1

ORIGINAL ARTICLE

Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis

Allan L. Klein, M.D., Massimo Imazio, M.D., Paul Cremer, M.D.,
Antonio Brucato, M.D., Antonio Abbate, M.D., Ph.D., Fang Fang, Ph.D.,
Antonella Insalaco, M.D., Martin LeWinter, M.D., Basil S. Lewis, M.D.,
David Lin, M.D., Sushil A. Luis, M.B., B.S., Stephen J. Nicholls, M.B., B.S., Ph.D.,
Arian Pano, M.D., Alistair Wheeler, M.D., and John F. Paolini, M.D., Ph.D.,
for the RHAPSODY Investigators*

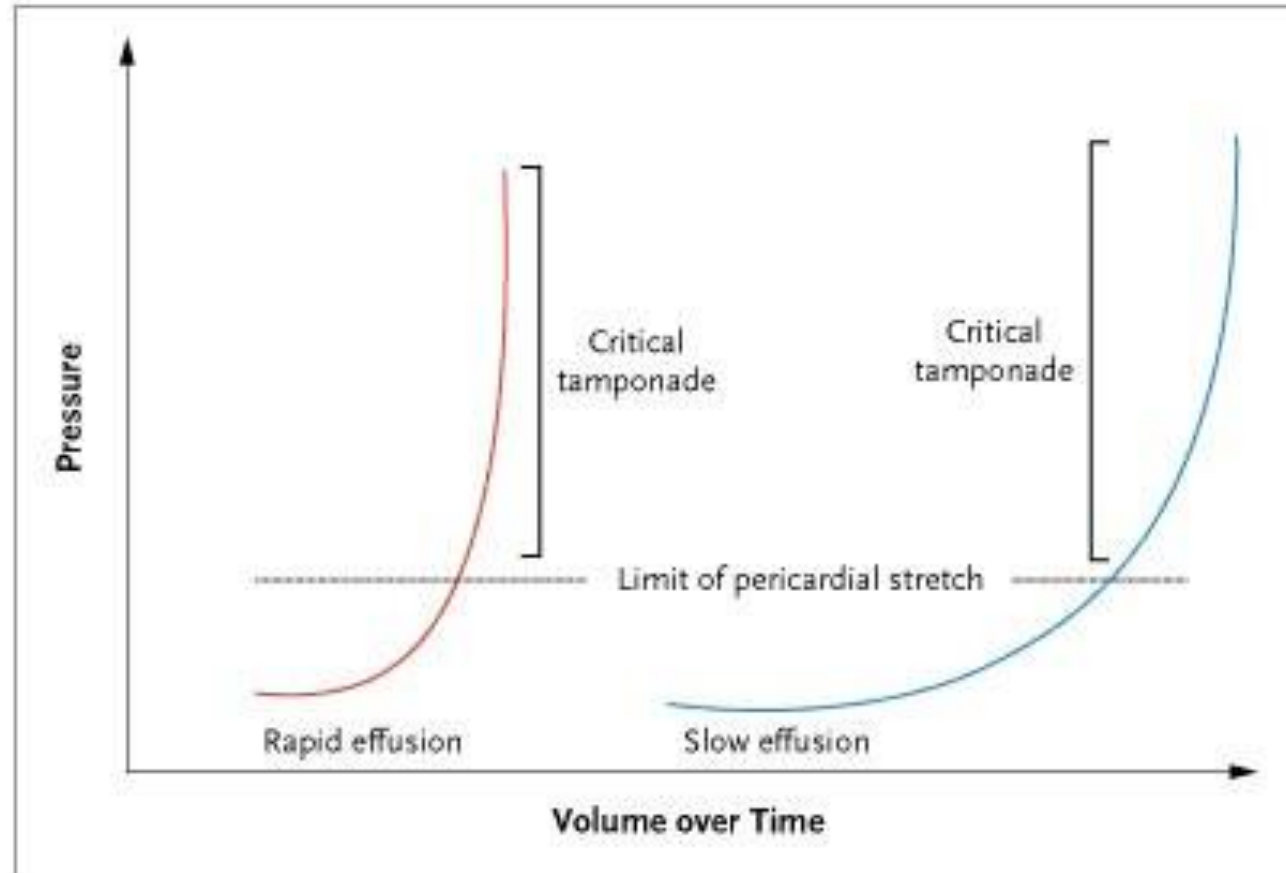


No. at Risk

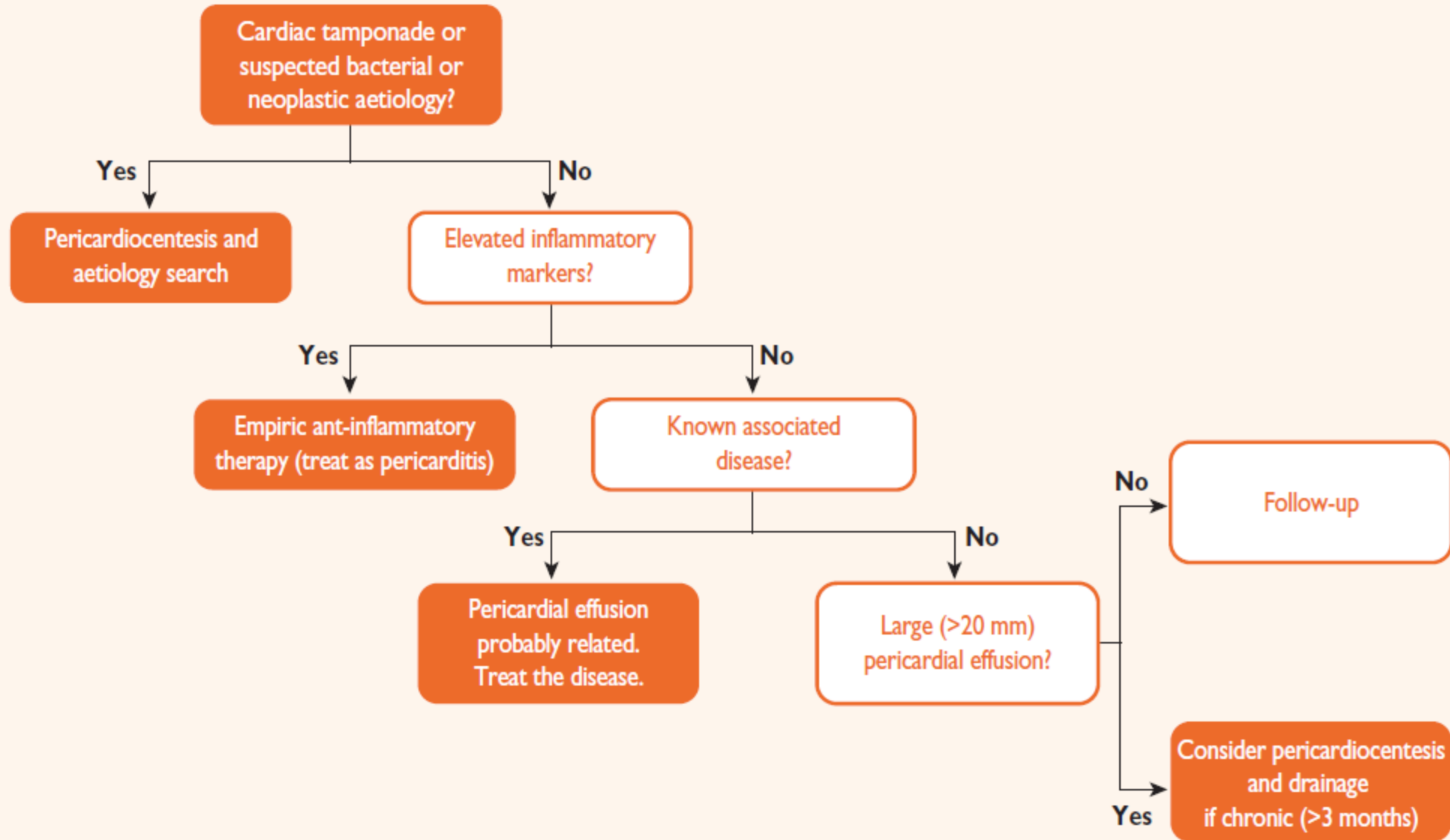
Rilonacept	30	30	28	27	26	24	23	21	20	17	17	16	15	15	13	11	9	7	7	6	5	5	5	5	4	1
Placebo	31	31	22	17	15	10	7	7	4	4	3	3	3	3	3	2	2	1	1	1	1					

Tamponade

- Volume and rate



Empiric anti-inflammatory therapies should be considered if a missed diagnosis of pericarditis is presumed.

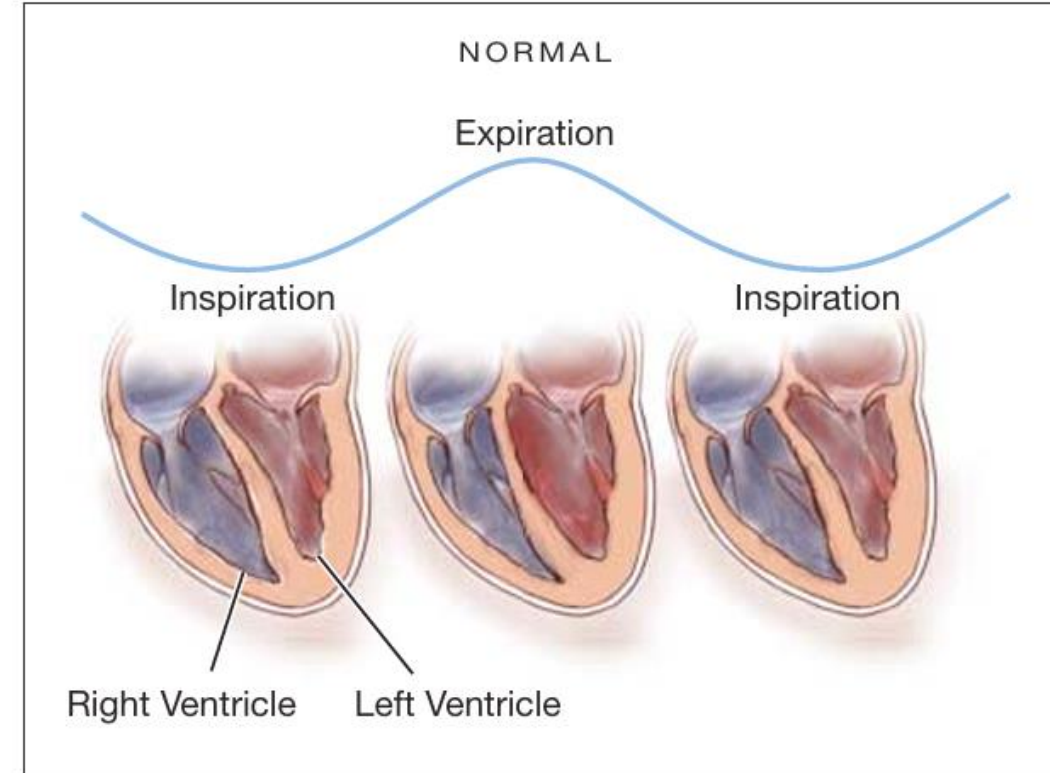
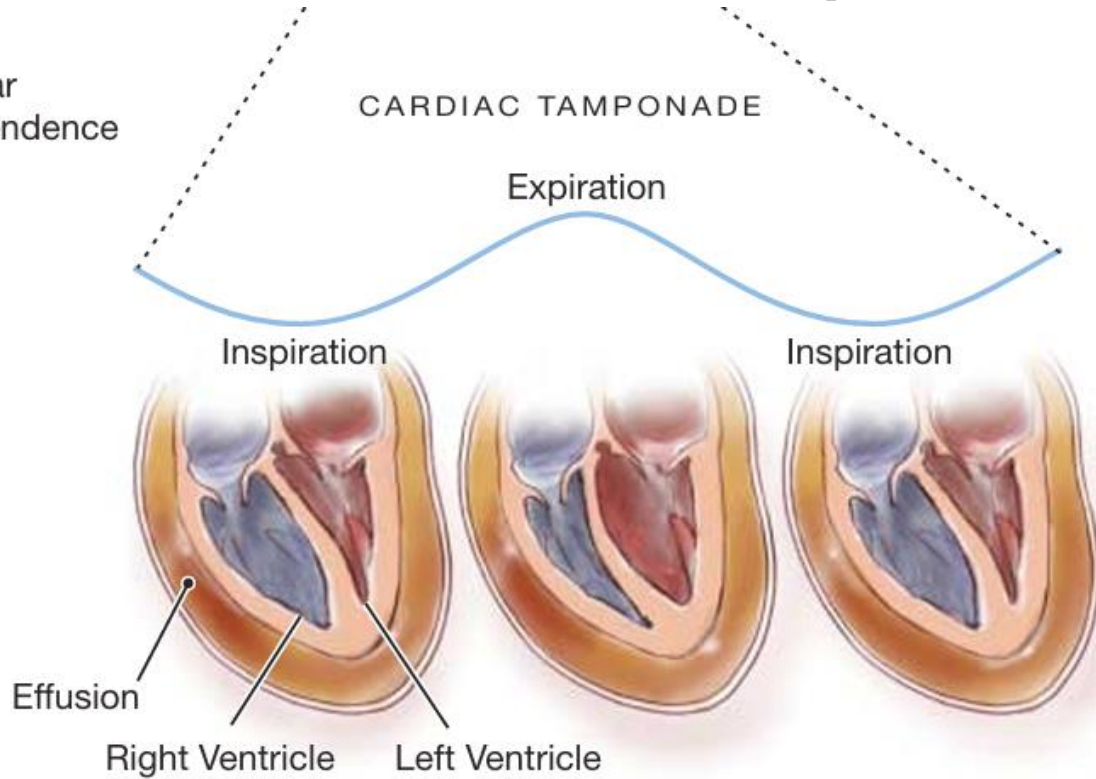


Physical exam

- Elevated venous pressure
- Muffled heart sounds
- Tachycardia
- Hypotension (Absolute or relative)
- Narrow pulse pressure
- Beck's triad: Hypotension, JVD, muffled heart sounds (more common in acute tamponade)

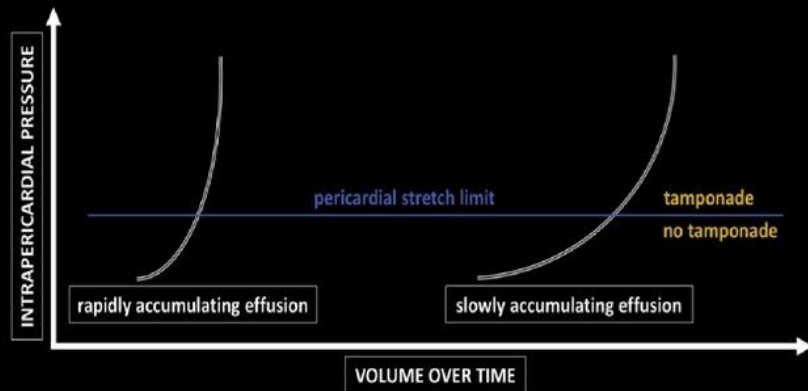
Ventricular interdependence

B Ventricular Interdependence



Pericardial Effusion

Tamponade physiology depends on: 1) rate of rise of effusion 2) pericardial compliance
—and not necessarily effusion size



Right-Sided Chamber Collapse

Occurs when intrapericardial pressure > intracardiac pressure
Intrapericardial pressure (P) = Intrapericardial fluid volume (V) x Pericardial stiffness ($\Delta P/\Delta V$)

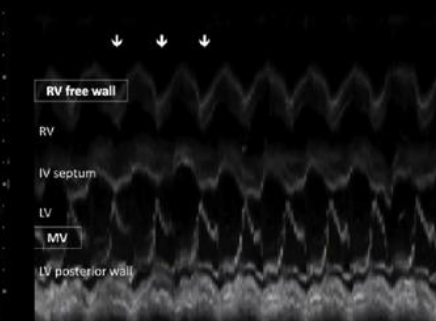
Diastolic RV collapse

Specificity 75-90%

Severity correlated with duration of chamber collapse

Systolic RA collapse

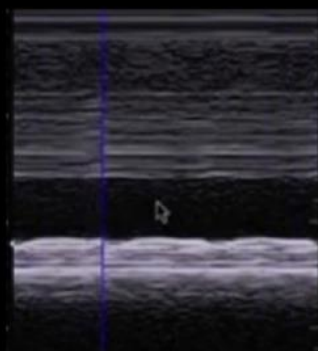
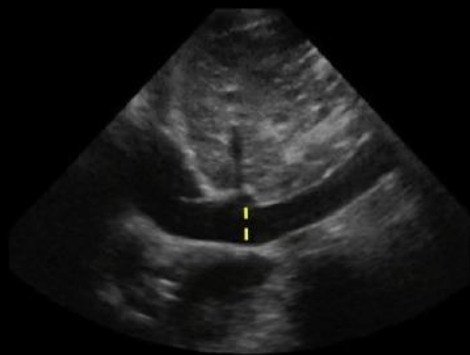
Sensitivity: 50% (early) to 100% (late)
Earliest sign of tamponade



Plethoric Inferior Vena Cava

Increased intrapericardial pressure → compression of RA → hindrance of venous return

Sensitivity 95-97%



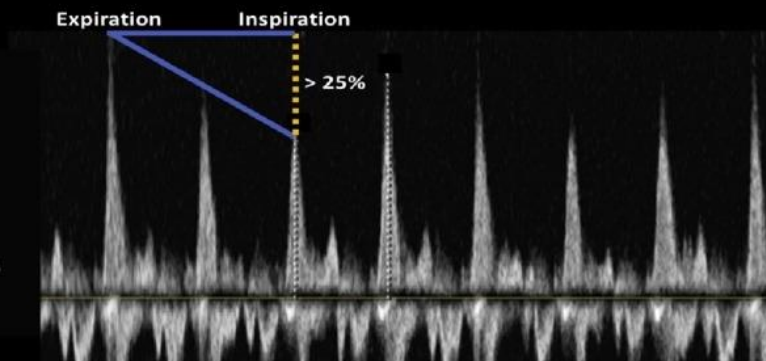
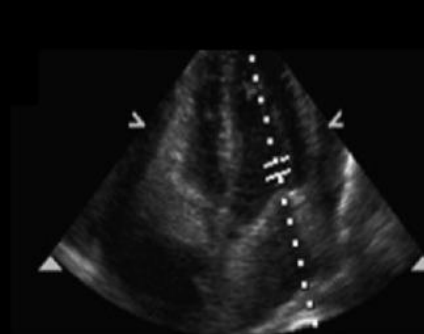
Alerhand, et al. Am J Emerg Med. 2019

Doppler Surrogate of Pulsus Paradoxus

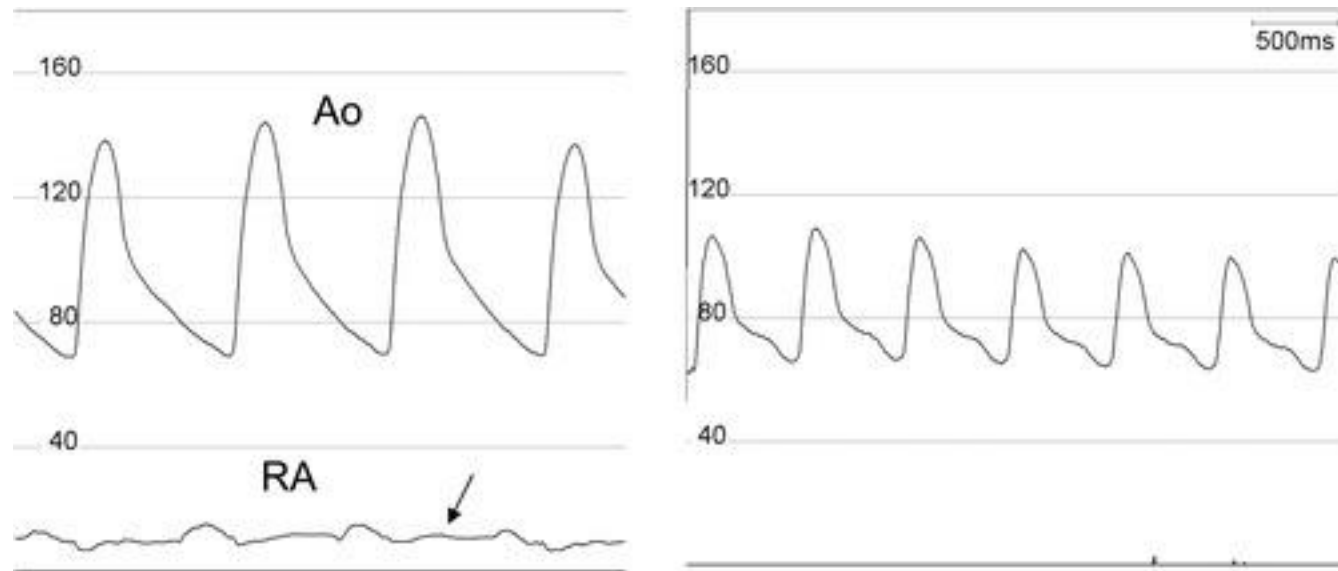
Exaggerated respiratory cycle changes in mitral (MV) and tricuspid valve (TV) in-flow velocities as surrogate for changes in blood flow through the left and right heart, respectively.

- A reflection of exaggerated ventricular interdependence -

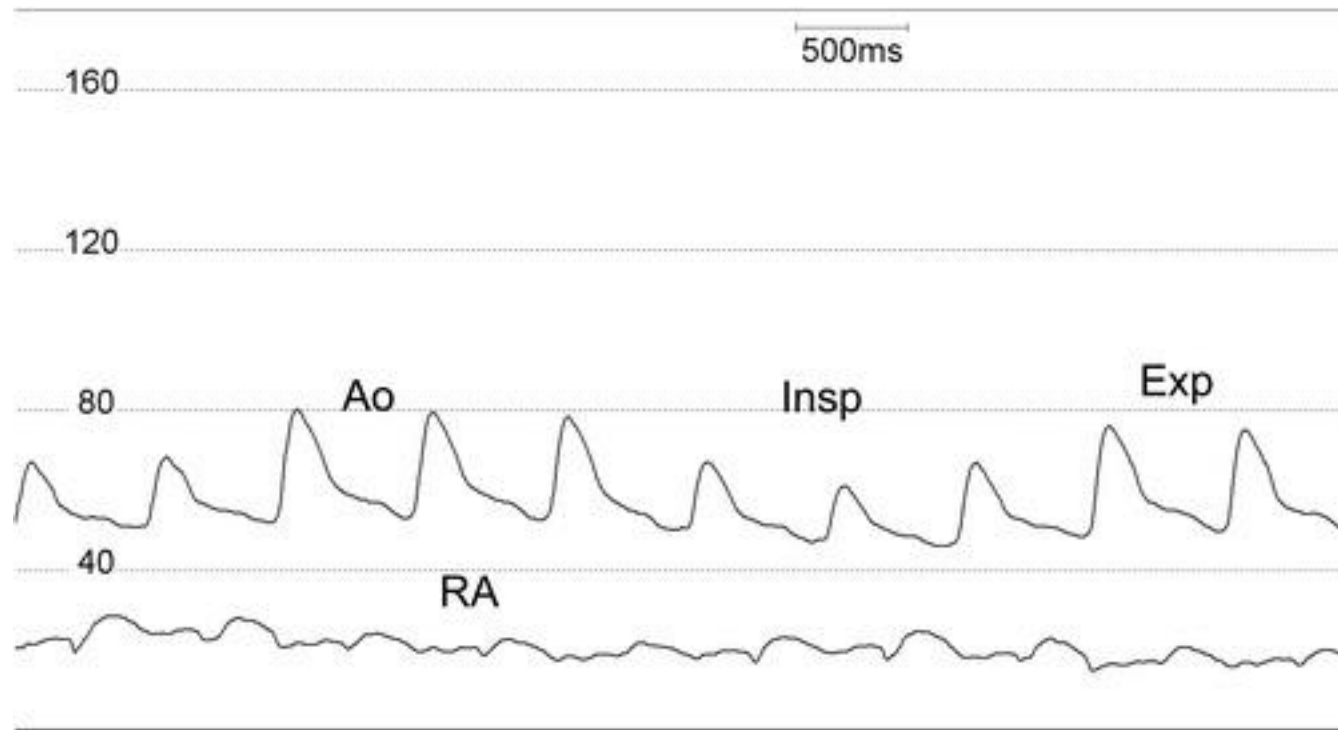
During inspiration: > 25% decrease for MV and > 40% increase for TV



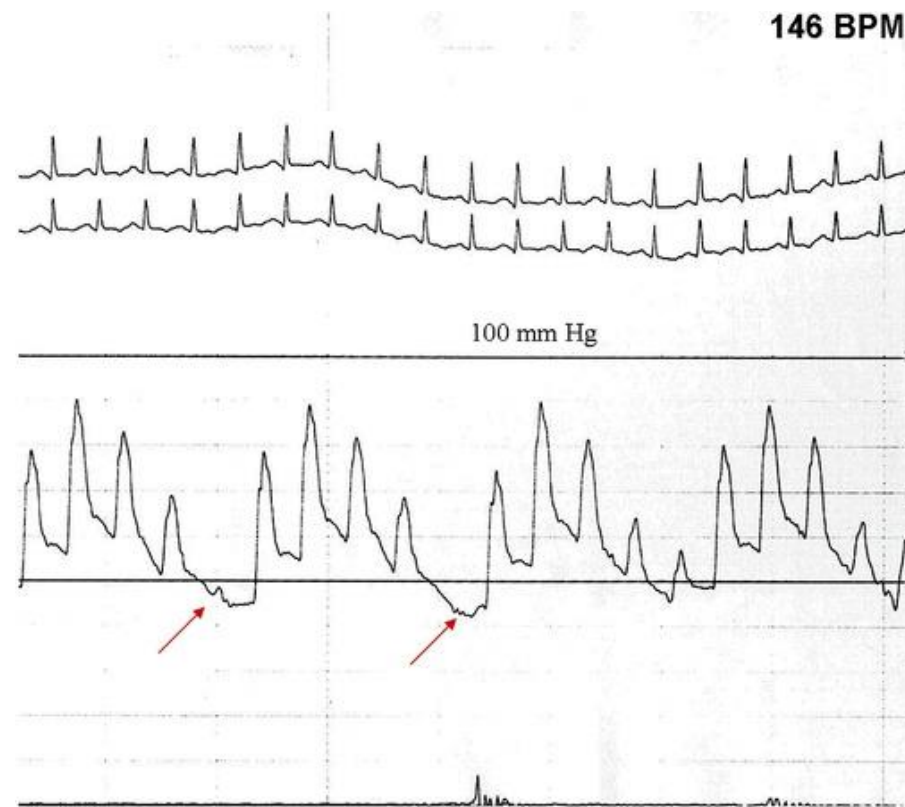
Hemodynamics



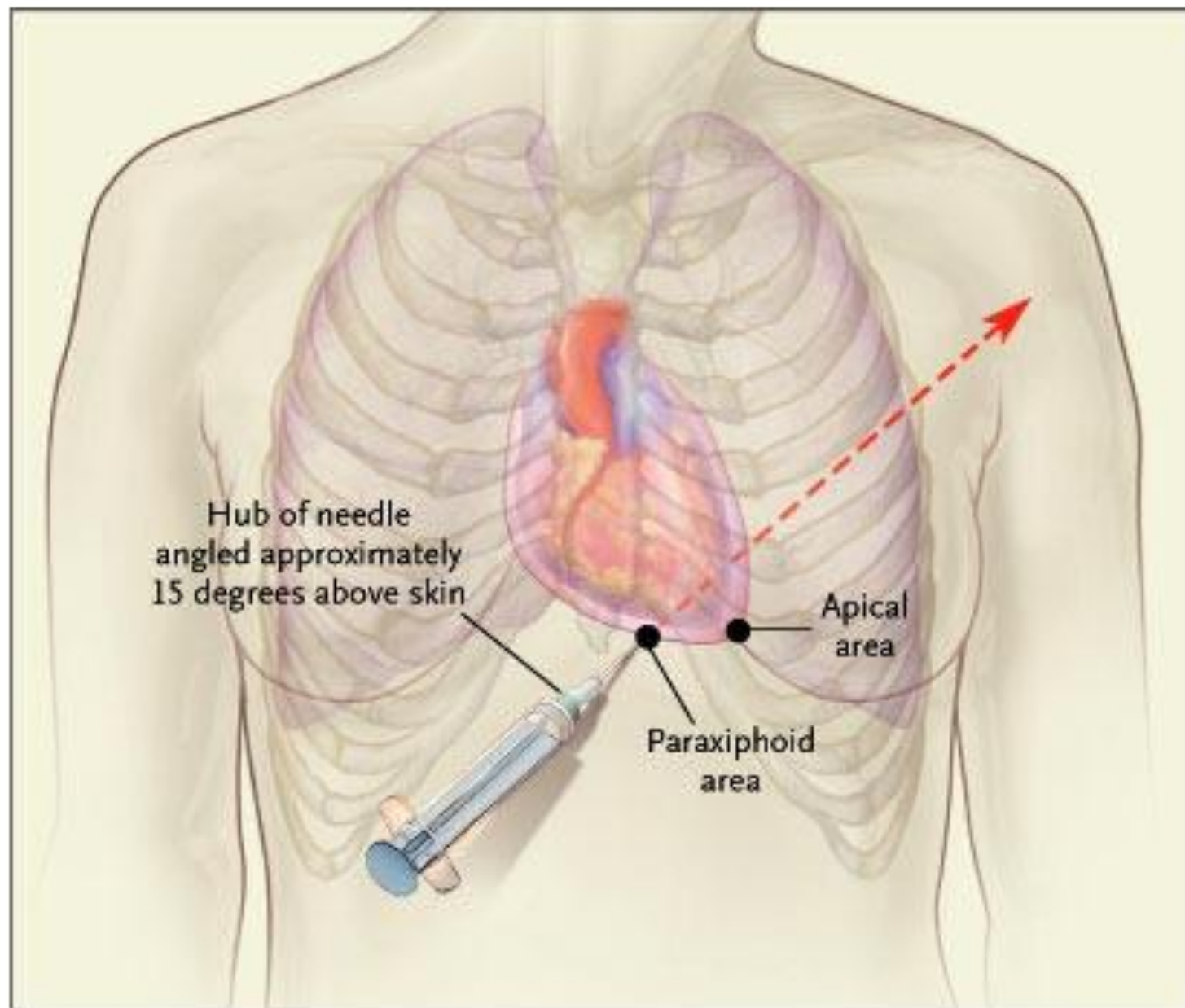
David R. Holmes et al. *J Am Coll Cardiol Interv* 2009; 2:705-717.



David R. Holmes et al. *J Am Coll Cardiol Interv* 2009; 2:705-717.



David R. Holmes et al. *J Am Coll Cardiol Interv* 2009; 2:705-717.



Constrictive Pericarditis

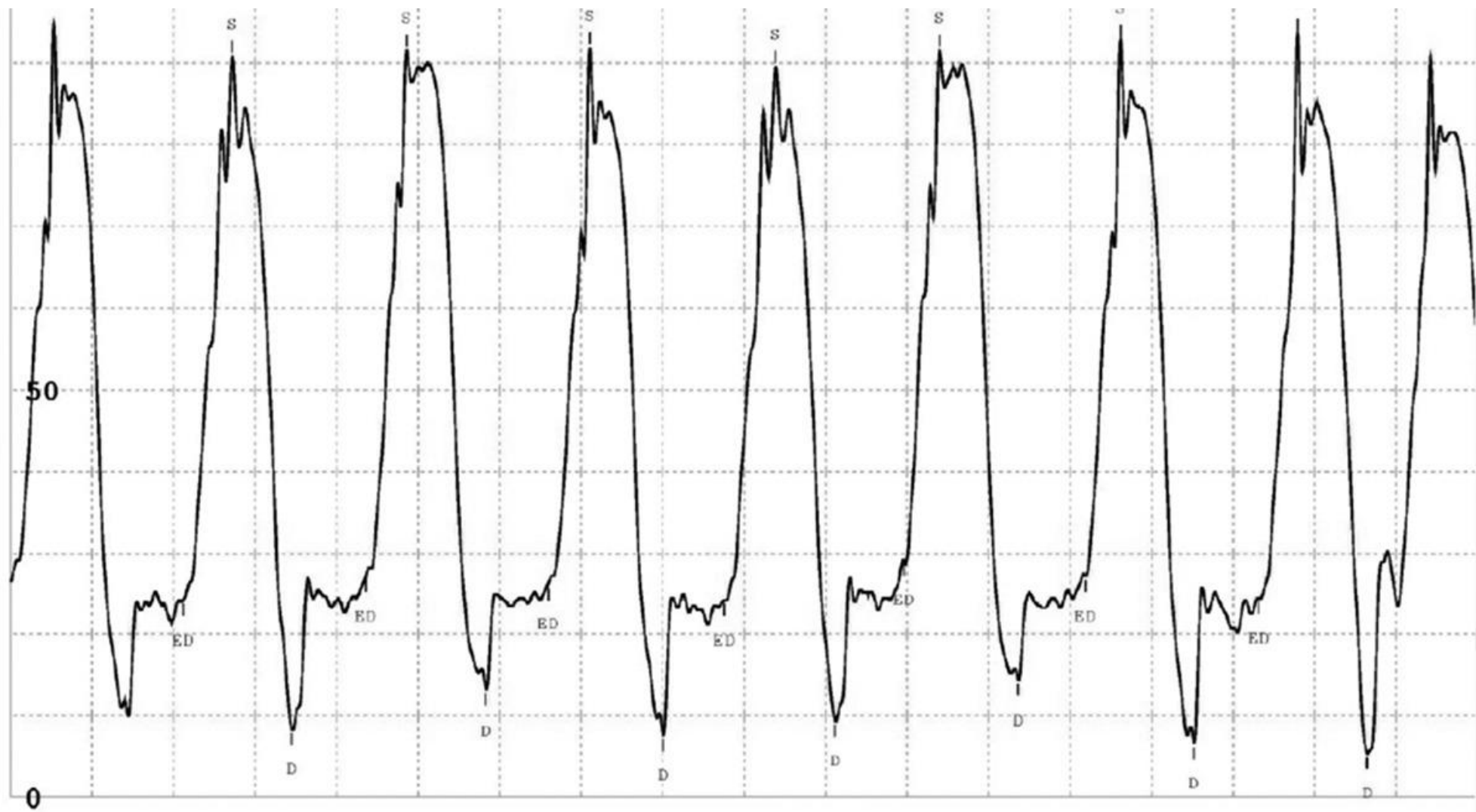
- Etiologies
- Worldwide: TB is the most common
- US: Post cardiac surgery, radiation therapy, idiopathic

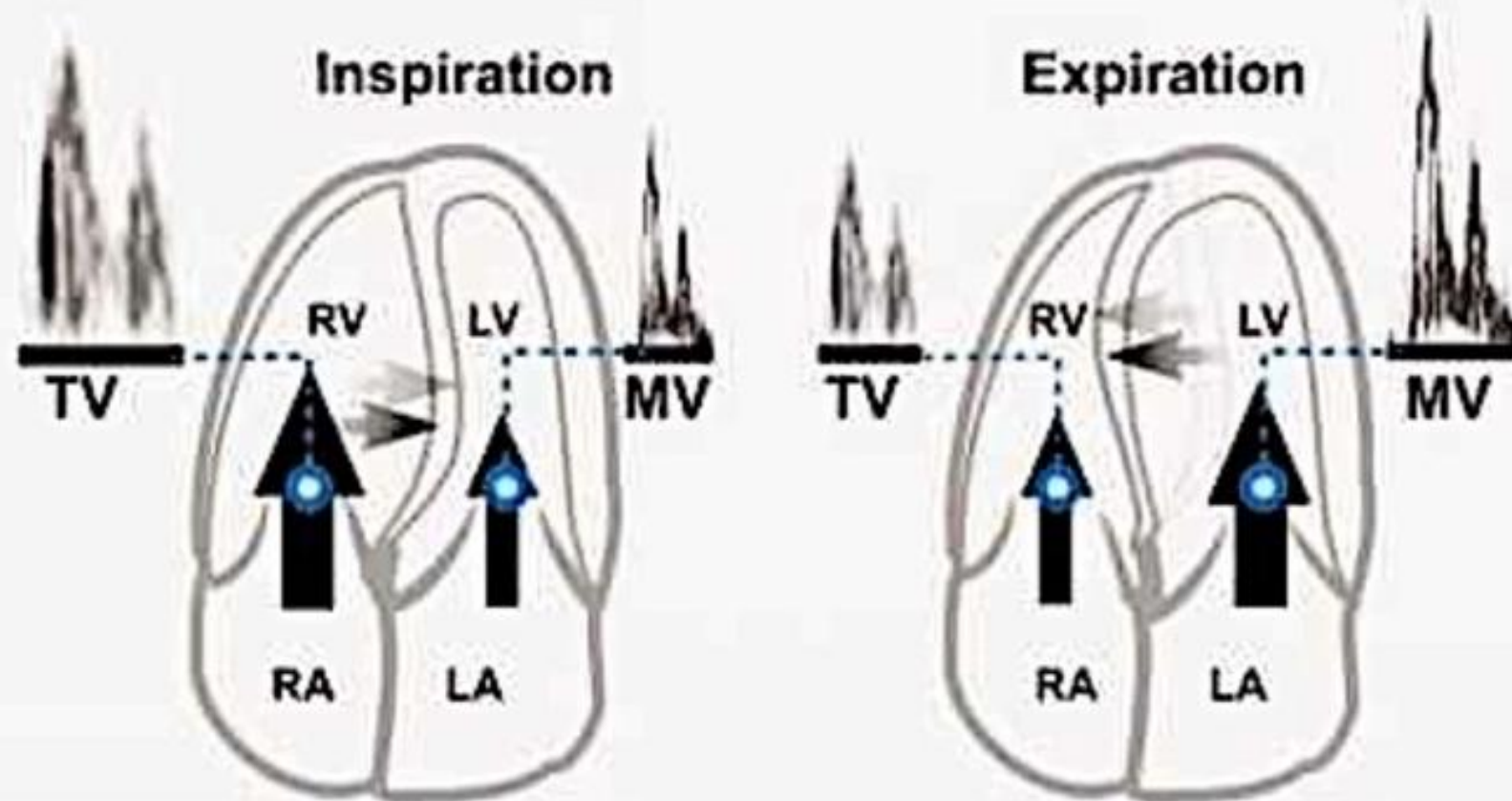
Pathophysiology

- Impaired cardiac filling
- Inelastic pericardium
- Restricted cardiac chamber expansion to a fixed volume.
- Early/mid diastolic ventricular filling abruptly ceases
- Venous congestion:
Peripheral edema
- Ascites
- Hepatic congestion.

Physical exam

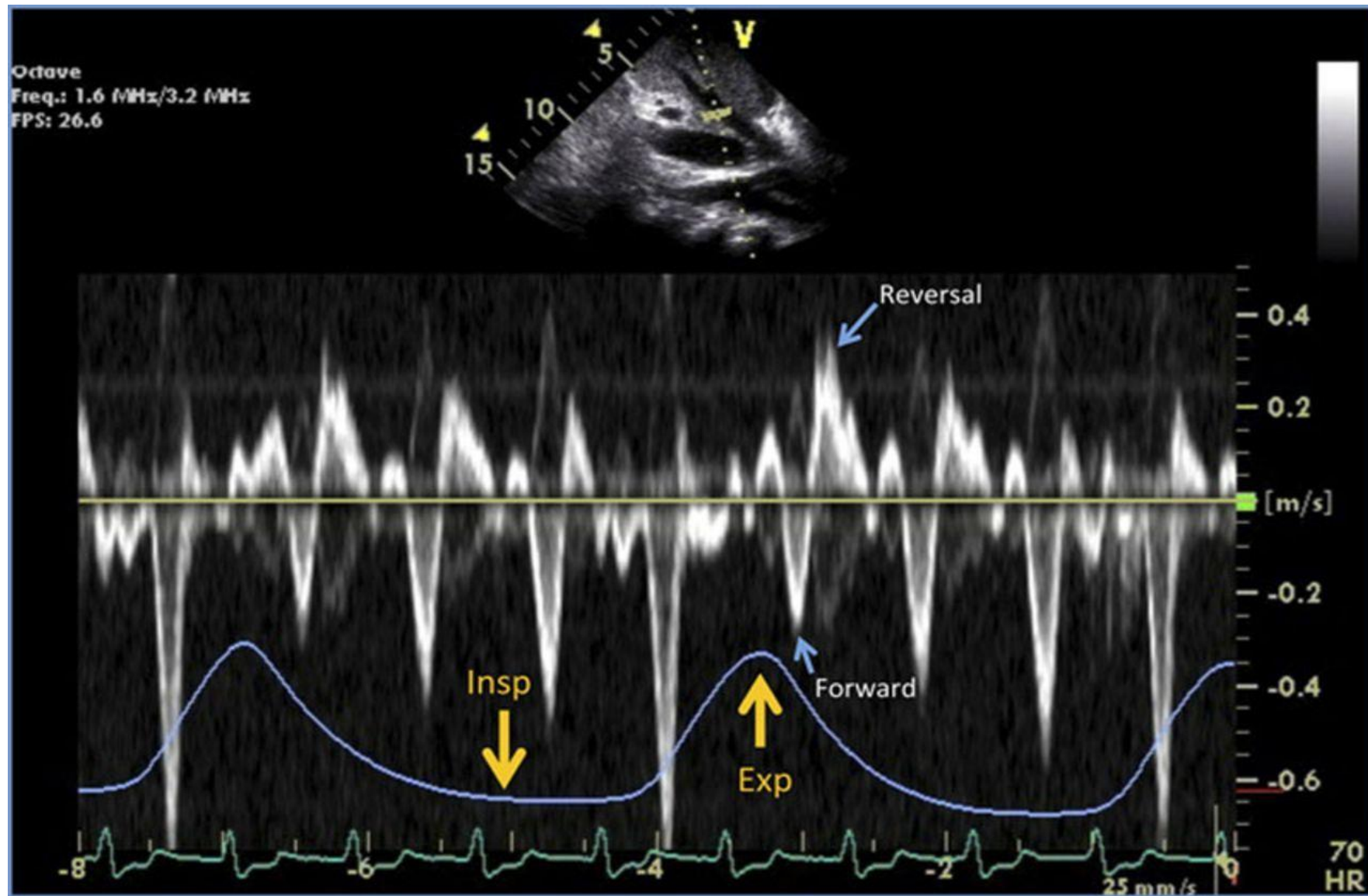
- Jv: prominent y-descent
- Kussmaul sign: Inspiratory increase in Jugular venous pressure
- Pericardial knock
- Hepatomegaly, spider angiomas, palmar erythema, peripheral edema



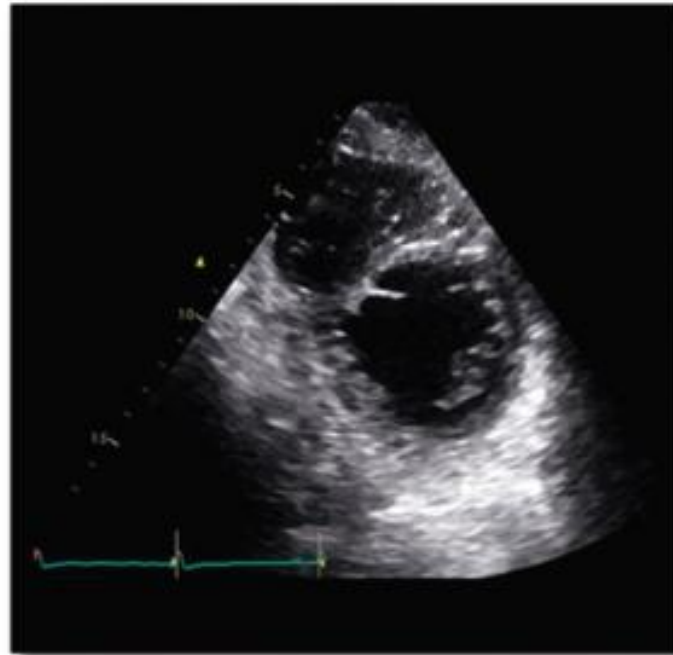


Constrictive Pericarditis

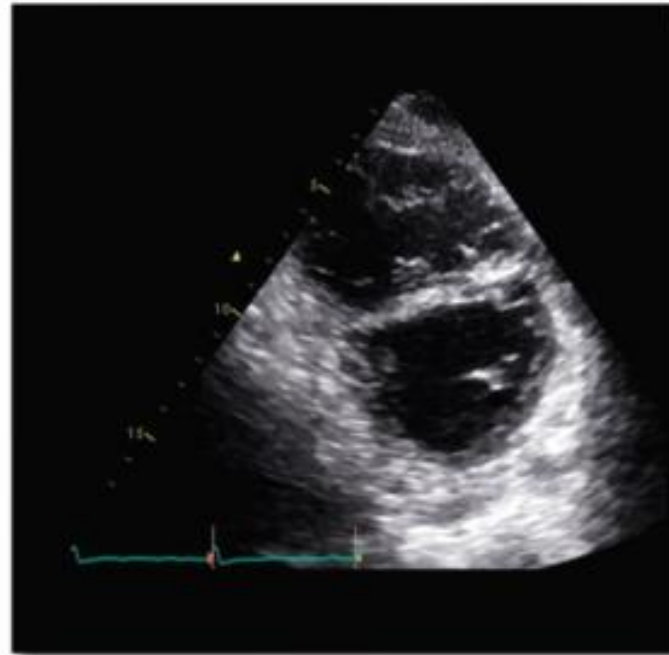
Reciprocal patterns of ventricular filling as assessed on pulsed Doppler examination of mitral (MV) and tricuspid (TV) inflow



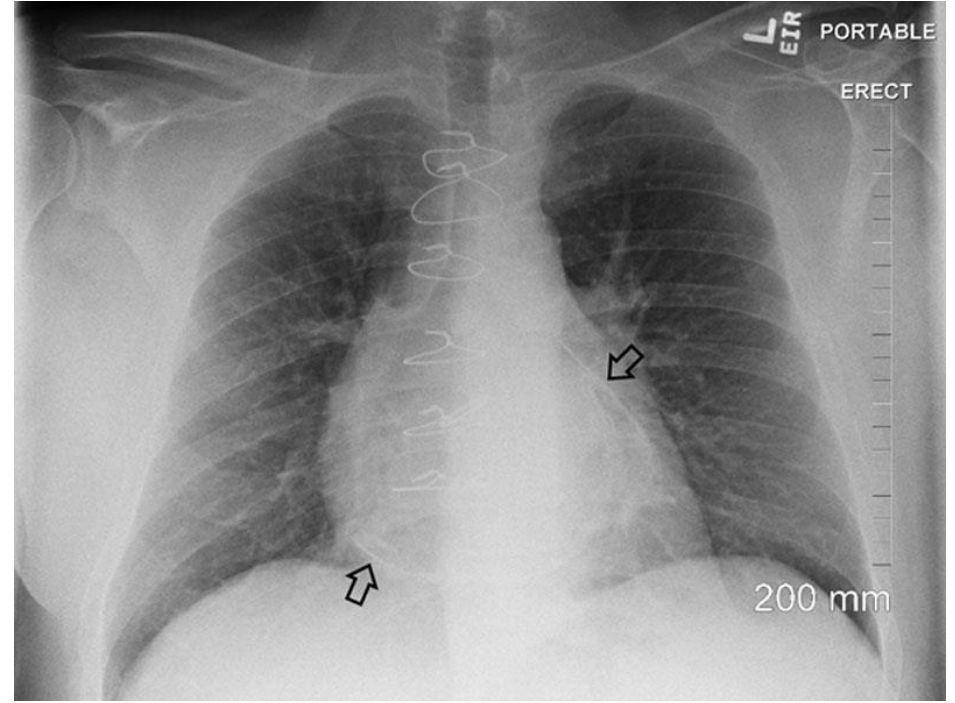
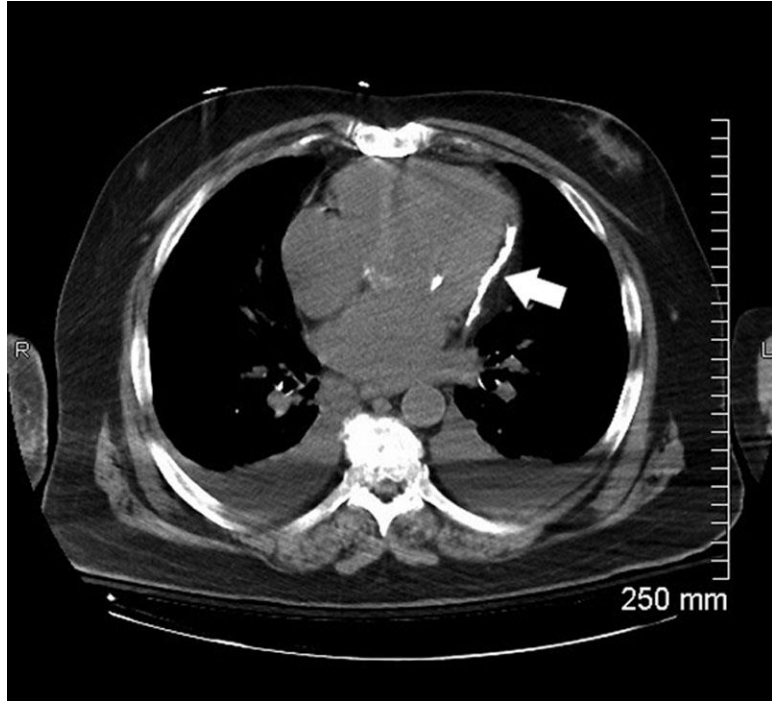
Respirophasic Ventricular Septal Shift With Echocardiography



A



B



Treatment

- Diuresis
- Surgery (5-15% perioperative mortality) , early intervention is preferred.
- Surgical risk factors: Age, NYHA class, organ failure, prior radiation Rx , other cardiac disease.