Pericardial diseases

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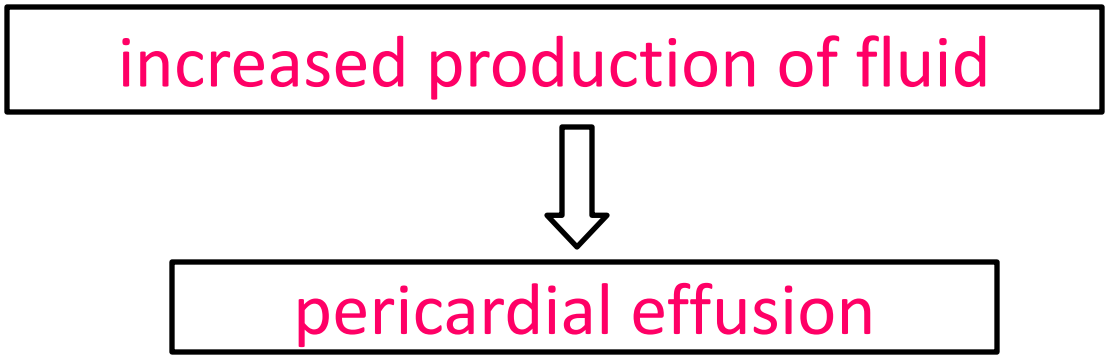
Pericard : anatomical and physyological considerations

- Outer layer - fibrous pericardium
  Inner layer - serous or visceral pericardium (epicardium)
- Proximal portion of aorta and pulmonary artery are enclosed in pericardial sac
- Functions of pericardium:
  - prevents friction between the heart and surrounding structures
  - acts as mechanical and immunological barrier
  - limits distention of the heart

Pericardial fluid

- In normal hearts there is a small amount of pericardial fluid (25-50 ml)
- Produced by visceral pericardium



Most common forms of pericardial syndromes

- Acute and recurrent pericarditis
- Pericardial effusion
- Cardiac tamponade
- Constrictive pericarditis

3. Pericardial syndromes

Pericardial syndromes include different clinical presentations of pericardial diseases with distinctive signs and symptoms that can be grouped in specific 'syndromes'. The classical pericardial syndromes include pericarditis, pericardial effusion, cardiac tamponade and constrictive pericarditis. Pericardial effusion and cardiac tamponade may occur without pericarditis and will be considered in separate chapters. Specific considerations apply to cases with pericarditis and concomitant myocardial inflammatory involvement, usually referred to in the literature as 'myopericarditis'.

Etiology

A. Infectious causes:
Viral (common): Enteroviruses (coxsackieviruses, echoviruses), herpesviruses (EBV, CMV, HHV-6), adenoviruses, parvovirus B19 (possible overlap with aetiologic viral agents of myocarditis).
Bacterial: *Mycobacterium tuberculosis* (common, other bacterial rare), *Coxiella burnetii*, *Borrelia burgdorferi*, rarely: *Pneumococcus* spp, *Meningococcus* spp, *Gonococcus* spp, *Streptococcus* spp, *Staphylococcus spp*, *Haemophilus* spp, *Chlamydia* spp, *Mycoplasma* spp, *Legionella spp*, *Leptospira* spp, *Listeria* spp, *Providencia stuartii*.
Fungal (very rare): *Histoplasma* spp (more likely in immunocompetent patients), *Aspergillus* spp, *Blastomyces* spp, *Candida* spp (more likely in immunocompromised host).
Parasitic (very rare): *Echinococcus* spp, *Toxoplasma* spp

Etiology

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, aesophageal 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, methyldopa, 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.

ESC guidelines 2004

ESC Guidelines

Guidelines on the Diagnosis and Management of Pericardial Diseases Full Text

The Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology

Task Force members, Bernhard Maisch, Chairperson* (Germany), Petar M. Seferović (Serbia and Montenegro), Arsen D. Ristić (Serbia and Montenegro), Raimund Erbel (Germany), Reiner Rienmüller (Austria), Yehuda Adler (Israel), Witold Z. Tomkowski (Poland), Gaetano Thiene (Italy), Magdi H. Yacoub (UK)

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ESC GUIDELINES

2015 ESC Guidelines for the diagnosis and management of pericardial diseases

The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC)

Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS)

Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Table 2 Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Acute pericarditis

Table 4 Definitions and diagnostic criteria for pericarditis (see text for explanation)

Pericarditis	Definition and diagnostic criteria
Acute	Inflammatory pericardial syndrome to be diagnosed with at least 2 of the 4 following criteria: (1) pericarditic chest pain (2) pericardial rubs (3) new widespread ST-elevation or PR depression on ECG (4) pericardial effusion (new or worsening) Additional supporting findings: - Elevation of markers of inflammation (i.e. C-reactive protein, erythrocyte sedimentation rate, and white blood cell count); - Evidence of pericardial inflammation by an imaging technique (CT, CMR).
Incessant	Pericarditis lasting for >4–6 weeks but <3 months without remission.
Recurrent	Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer[a].
Chronic	Pericarditis lasting for >3 months.

Acute pericarditis

- Most common form of pericardial disease

- ~5% of presentations to ED for non-ischemic chest pain
- Incidence of acute pericarditis in a prospective study 28/ 100 000 of the population per year in an urban area in Italy

Acute pericarditis: etiology

- 80-95% of cases - idiopathic (in Western Europe and in North America)

- Such cases are generally presumed to be viral

- Major non-idiopathic etiologies:
  - tuberculosis
  - neoplasia
  - systemic (generally autoimmune disease)

Acute pericarditis: etiology (cont'd)

- Developed countries:

  emerging cases of pericarditis – iatrogenic posttraumatic, following cardiac surgery, PCI, pacemaker insertion, catheter ablation.

In these cases pathogenesis is determined by combination of:

- direct pericardial trauma
- pericardial bleeding
- individual predisposition

Acute pericarditis: etiology (cont'd)

- Developing countries:

  high prevalence of tuberculosis-related pericarditis (70-80%) in Sub-Saharian Africa,

  in ~90% the disease associated with HIV infection

Acute pericarditis: diagnosis

- Typical chest pain (pleuritic CP)
- Pericarial friction rub
- Widespread ST-segment elevation and PR depression
- Pericardial effusion

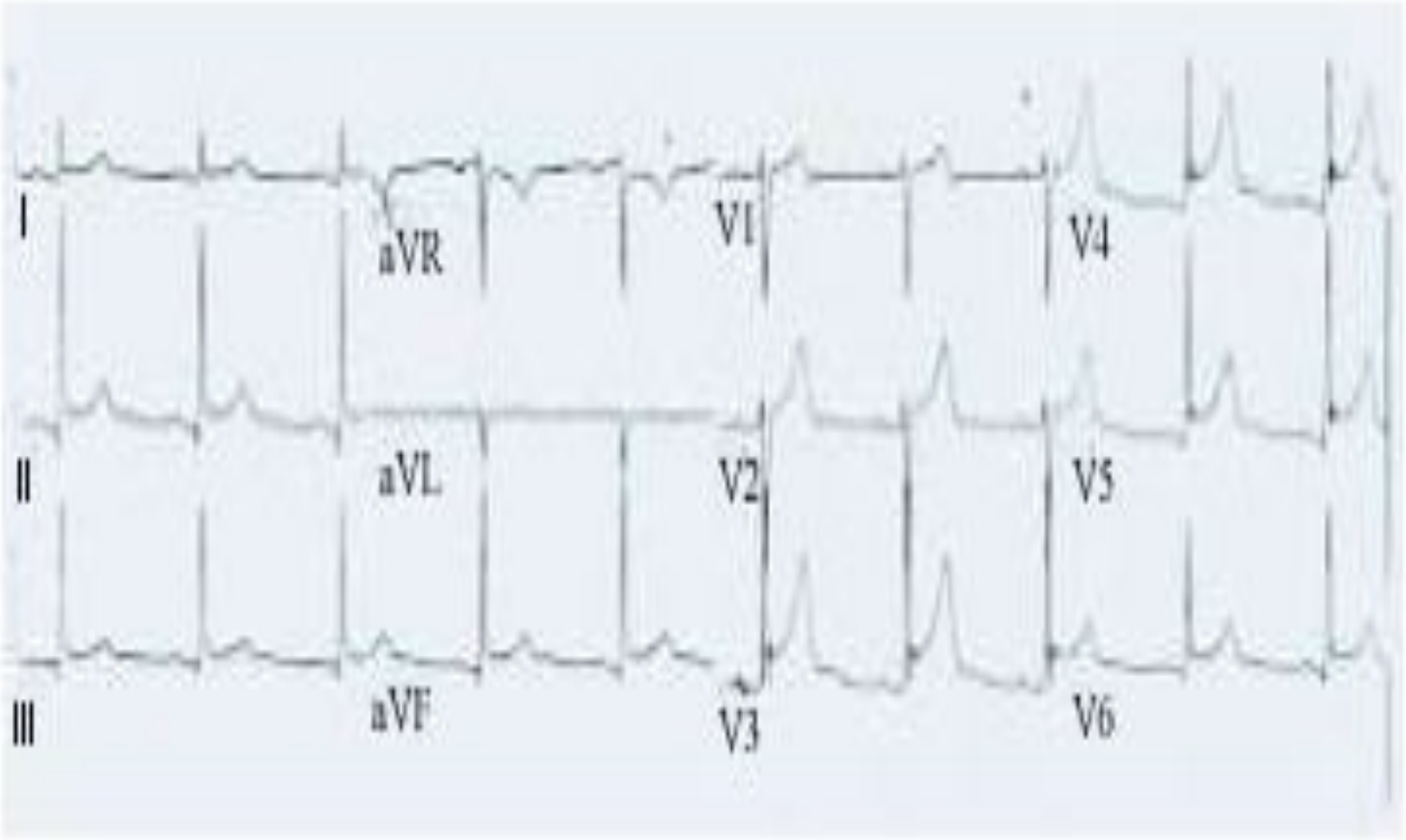
At least 2 of 4 criteria should be present for Dx of acute pericarditis

Acute pericarditis: diagnosis
Basic diagnostic evaluation

- Physical examination – auscultation
- ECG
- Trans-thoracic echocardiography (TTE)
- Chest x-ray
- Blood tests

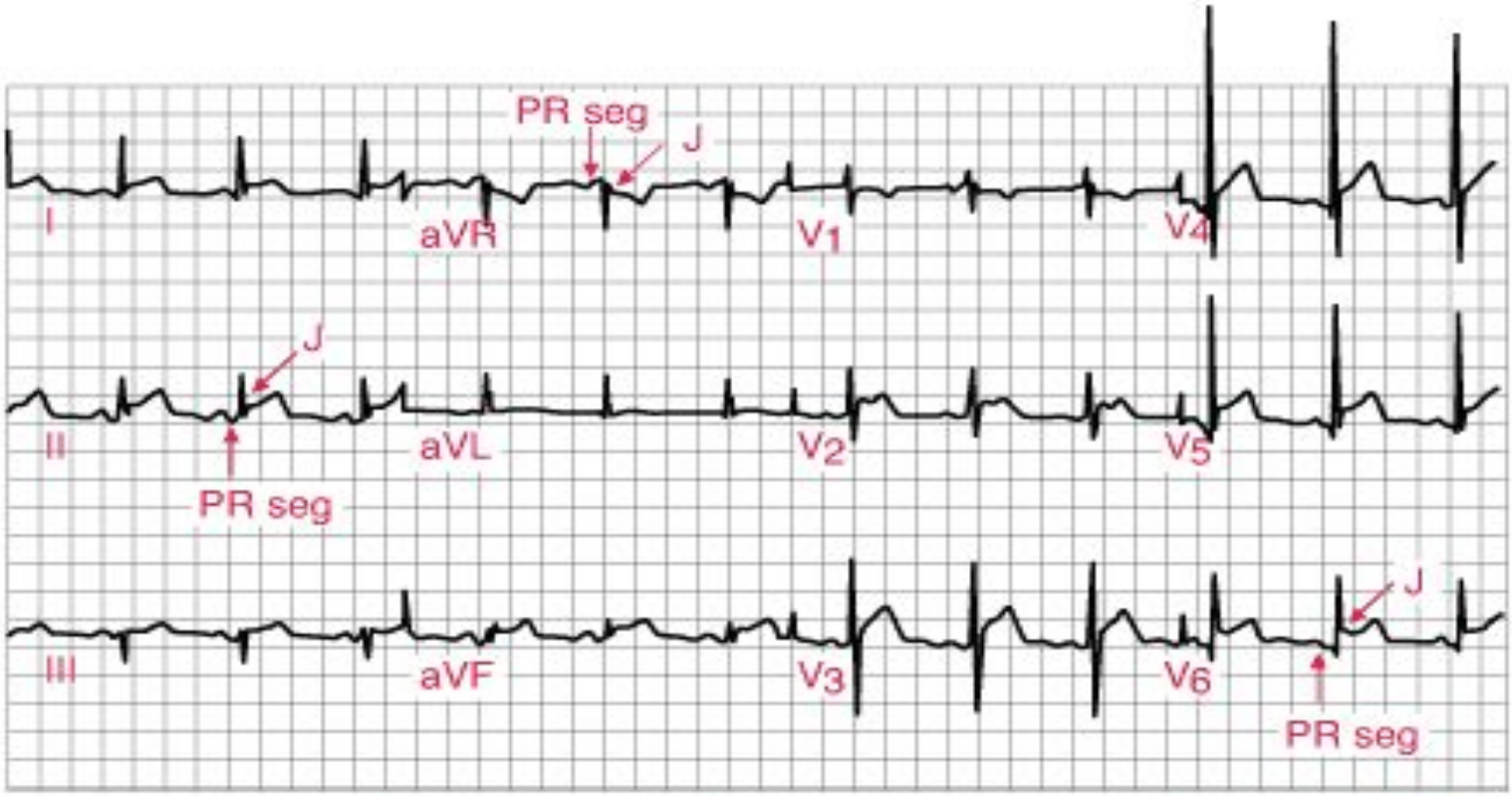
  - routine blood tests
  - markers of inflammation (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR])
  - markers of myocardial damage (CK, Tn)

ECG in acute pericarditis



ECG in acute pericarditis

Acute pericarditis: Stage 1 ECG.



J points, except aVR and V_1, are elevated. T waves are essentially normal. PR segments, except aVR and V_1, are depressed. PR deviations are commonly absent in one limb lead (here, aVL).

ECG in acute pericarditis

TABLE 2
Stages of Acute Pericarditis on ECG

Stage	Changes on ECG
Stage I	Diffuse concave-upward ST-segment elevation with concordance of T waves; ST-segment depression in aVR or V1; PR-segment depression; low voltage; absence of reciprocal ST-segment changes
Stage II	ST segments return to baseline; T-wave flattening
Stage III	T-wave inversion
Stage IV	Gradual resolution of T-wave inversion

Acute pericarditis: diagnosis
Basic diagnostic evaluation

The need for routine etiology search in all cases of pericarditis is controversial and in low risk patients is not considered necessary

Indications for pericardiocentesis

- Cardiac tamponade
- Large or symptomatic pericardial effusion despite medical therapy
- Highly suspected tuberculous, purulent, or neoplastic etiology

ESC guidelines, 2004

Acute pericarditis: diagnostic studies of pericardial fluid

- Protein
- LDH
- Glucose
- Cell count

Less useful for diagnosis of specific etiology but are warranted to distinguish exudate from transudate

Acute pericarditis: diagnostic studies of pericardial fluid

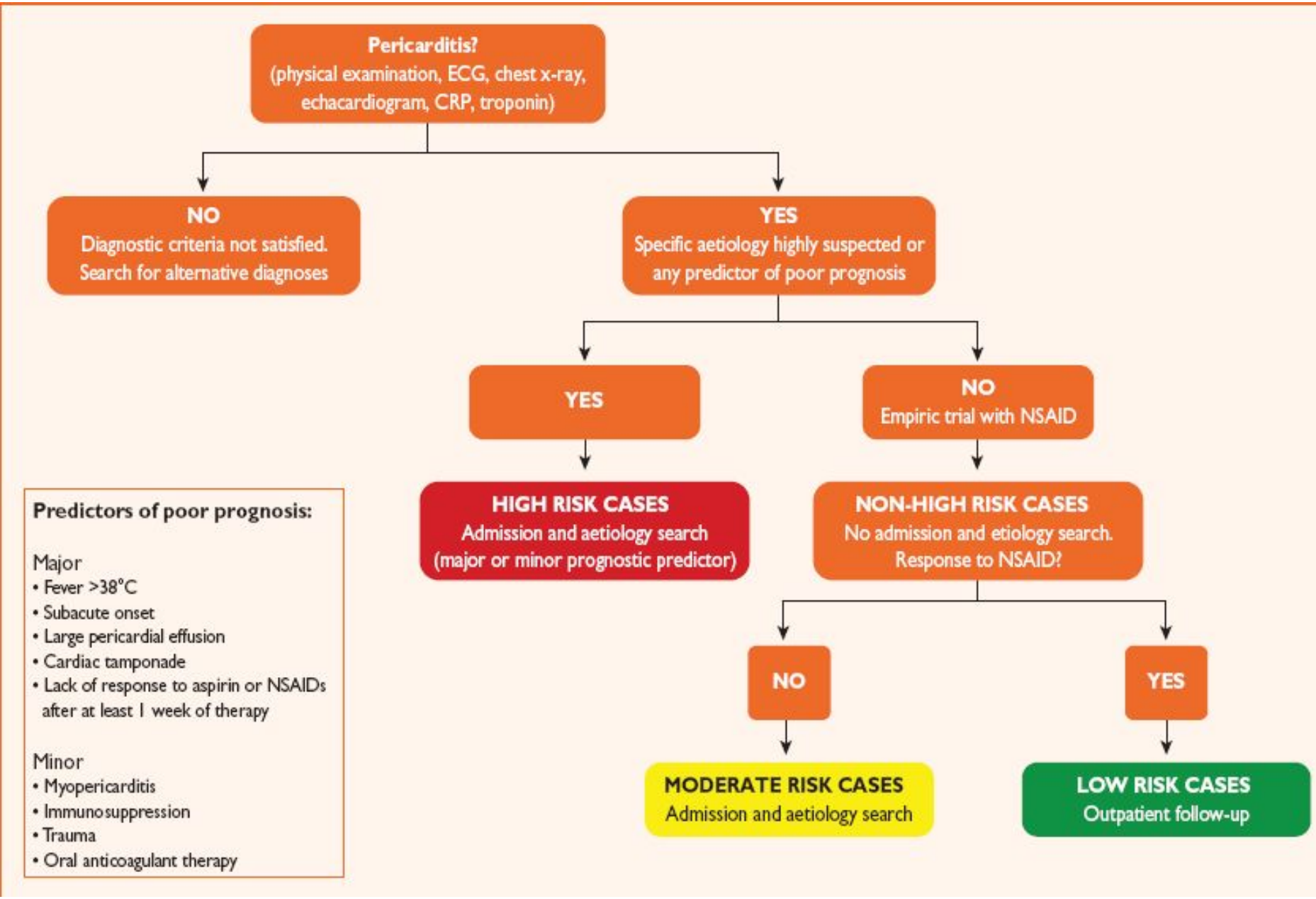
- Adenosin deaminase measurement for TB
- Tumor marker measurement (carcino-embryonic antigen [CEA], cytokeratin 19 fragment)
- Cytology
- Culture and polymerase chain reactions for infections

Acute pericarditis: other diagnostic modalities

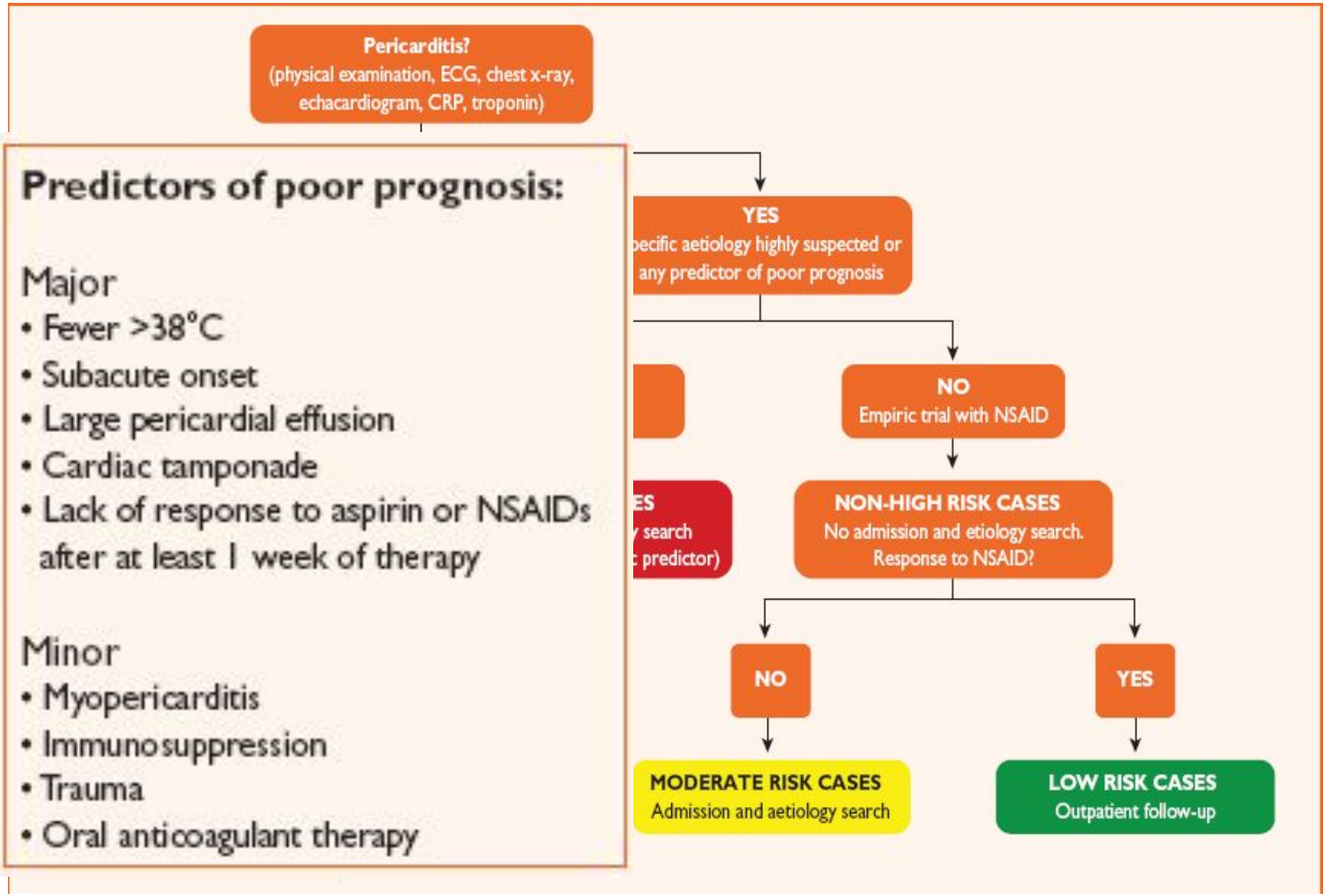
- Pericardial biopsy (during surgical drainage)
  - if cardiac tamponade relapsed after pericardiocentesis
  - in patients without definite diagnosis whose illness lasted for > 3 weeks
- Pericardioscopy with target biopsy

- Thoracic and abdominal CT

Management of pericarditis



Acute pericarditis: risk stratification



Acute pericarditis: risk stratification

- At least one predictor of poor prognosis is sufficient to identify a high risk cases
- Cases of moderate risk – cases without negative prognostic predictors but incomplete or lacking response to NSAID therapy
- Low risk cases – those without negative prognostic predictors and good response to anti-inflammatory therapy

Acute pericarditis: therapy

- Targets toward specific etiology if known
- Empirical therapy for most cases (idiopathic or presumed to be viral)
- Rx until inflammatory marker (CRP, ESR) normalize (~7-14 days), than gradual tapering of the drug can be considered

Acute pericarditis: therapy

Table 5 Commonly prescribed anti-inflammatory therapy for acute pericarditis

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

b.i.d. = twice daily; CRP = C-reactive protein; NSAIDs = non-steroidal anti-inflammatory drugs; Tx = treatment.

[a]Tapering should be considered for aspirin and NSAIDs.

[b]Tx duration is symptoms and CRP guided but generally 1–2 weeks for uncomplicated cases. Gastroprotection should be provided. Colchicine is added on top of aspirin or ibuprofen.

Recommendations	Class[a]	Level[b]	Ref.[c]
Aspirin or NSAIDs are recommended as first-line therapy for acute pericarditis with gastroprotection	I	A	55
Colchicine is recommended as first-line therapy for acute pericarditis as an adjunct to aspirin/NSAID therapy	I	A	10,11, 58,59

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Colchicine for Acute Pericarditis

Massimo Imazio, M.D., Antonio Brucato, M.D., Roberto Cemin, M.D., Stefania Ferrua, M.D., Stefano Maggiolini, M.D., Federico Beqaraj, M.D., Daniela Demarie, M.D., Davide Forno, M.D., Silvia Ferro, M.D., Silvia Maestroni, M.D., Riccardo Belli, M.D., Rita Trinchero, M.D., David H. Spodick, M.D., and Yehuda Adler, M.D., for the ICAP Investigators*

NEJM 2013, Sep 1

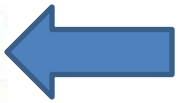
ICAP trial

- Colchicine 0.5 mg x 2/d for 3 months
  (for patients ≤ 70 kg 0.5 mg x 1/d) vs placebo
- In addition to conventional antiinflammatory therapy with Aspirin or Ibuprofen

ICAP trial

EXCLUSION CRITERIA

Patients with any of the following criteria were not eligible to participate in the trial: tuberculous, neoplastic, or purulent pericarditis; severe liver disease or current aminotransferase levels of more than 1.5 times the upper limit of the normal range; a serum creatinine level of more than 2.5 mg per deciliter (221 μmol per liter); skeletal myopathy or a serum creatine kinase level above the upper limit of the normal range; blood dyscrasia; inflammatory bowel disease; hypersensitivity to colchicine or other contraindication to its use; current treatment with colchicine; and life expectancy of 18 months or less. Pregnant or lactating women or women of childbearing potential who were not protected by a contraception method were also ineligible, as were patients with evidence of myopericarditis, as indicated by an elevation in the serum troponin level.[13] All patients provided written informed consent.



ICAP trial

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Placebo (N=120)	Colchicine (N=120)
Age — yr	50.7±17.5	53.5±16.2
Male sex — no. (%)	74 (61.7)	71 (59.2)
Cause of pericarditis — no. (%)		
Idiopathic	93 (77.5)	92 (76.7)
Post–cardiac injury syndrome	23 (19.2)	25 (20.8)
Connective-tissue disease†	4 (3.3)	3 (2.5)
Clinical findings — no. (%)		
Pericarditic chest pain	119 (99.2)	120 (100.0)
Pericardial rub	38 (31.7)	44 (36.7)
ST-segment elevation	26 (21.7)	35 (29.2)
Pericardial effusion‡	82 (68.3)	76 (63.3)
Mild (<10 mm)	76 (63.3)	64 (53.3)
Moderate (10–20 mm)	2 (1.7)	9 (7.5)
Large (>20 mm)	4 (3.3)	3 (2.5)
Cardiac tamponade	2 (1.7)	2 (1.7)
Elevated C-reactive protein level	89 (74.2)	85 (70.8)
Medications — no. (%)		
Aspirin	96 (80.0)	86 (71.7)
Ibuprofen	18 (15.0)	24 (20.0)
Prednisone	6 (5.0)	10 (8.3)

ICAP trial

Table 2. Trial Outcomes.*

Outcome	Placebo (N=120)	Colchicine (N=120)	P Value
Incessant or recurrent pericarditis: primary end point — no. (%)‡	45 (37.5)	20 (16.7)	<0.001†
Symptom persistence at 72 hr — no. (%)	48 (40.0)	23 (19.2)	0.001
Remission at 1 wk — no. (%)	70 (58.3)	102 (85.0)	<0.001
Incessant course — no. (%)	20 (16.7)	9 (7.5)	0.046
Recurrent course — no. (%)	25 (20.8)	11 (9.2)	0.02
No. of recurrences per patient	0.52±0.81	0.21±0.52	0.001
Time to first recurrence — wk	17.7±9.0	24.7±11.0	<0.001
Cardiac tamponade — no. (%)	3 (2.5)	0	0.25
Constrictive pericarditis — no. (%)	1 (0.8)	0	1.00
Pericarditis-related hospitalization — no. (%)	17 (14.2)	6 (5.0)	0.02
Mean follow-up — mo	22.3±8.7	22.9±8.7	0.61

* Plus–minus values are means ±SD.
† The P value was calculated by means of the log-rank test.
‡ The type of background antiinflammatory therapy had no significant effect on the proportions of patients with incessant or recurrent pericarditis.

ICAP trial

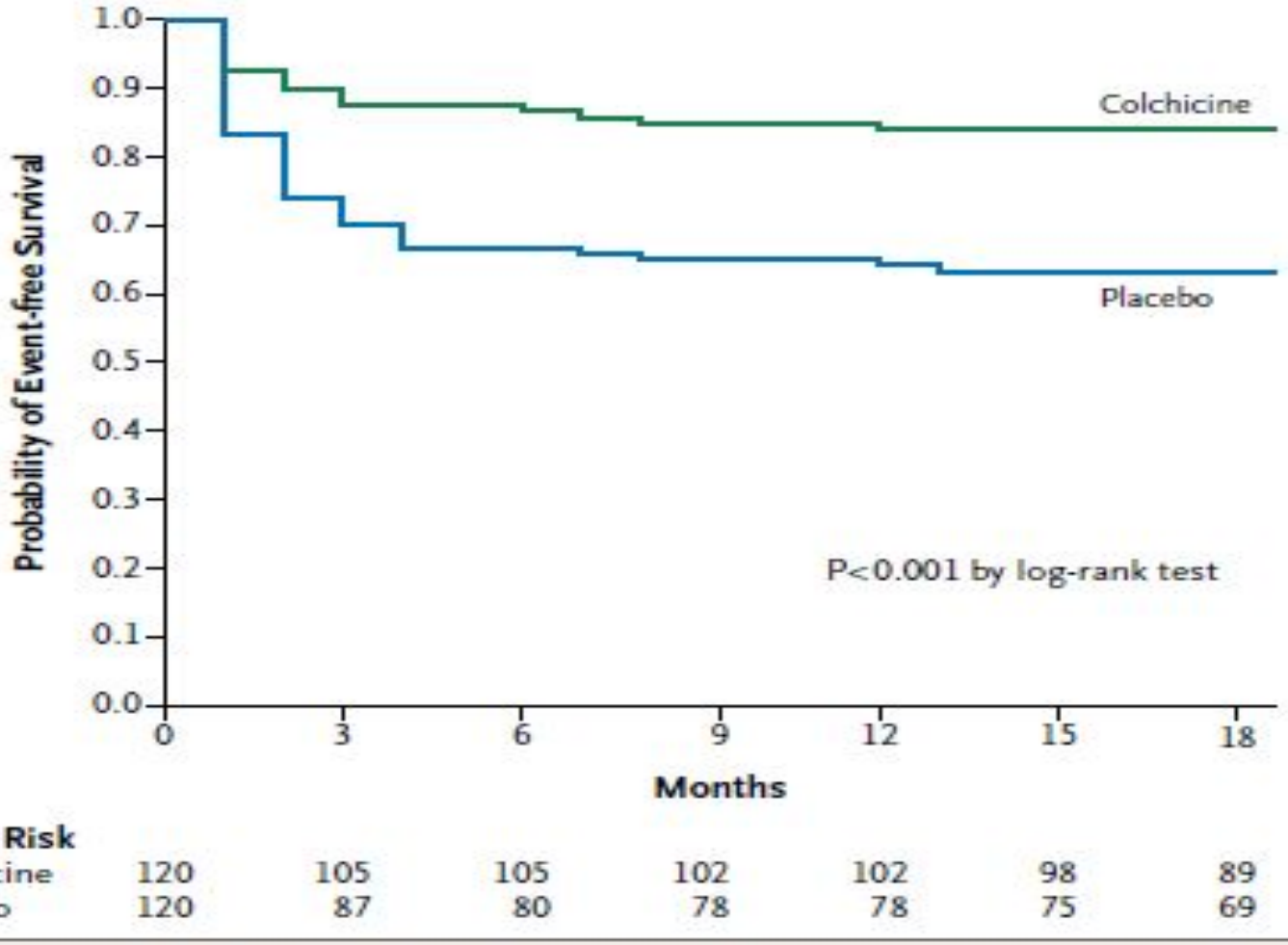


Figure 2. Kaplan–Meier Survival Curves for Freedom from Incessant or Recurrent Pericarditis (Primary Outcome).

ICAP trial

Table 3. Adverse Events.

Adverse Event	Placebo (N=120)	Colchicine (N=120)	P Value
	no. (%)		
Overall	12 (10.0)	14 (11.7)	0.84
Gastrointestinal disorder*	10 (8.3)	11 (9.2)	0.67
Hepatotoxicity†	1 (0.8)	2 (1.7)	
Myotoxicity	0	0	
Alopecia	1 (0.8)	1 (0.8)	
Other	0	0	
Serious adverse event‡	0	0	
Drug discontinuation	10 (8.3)	14 (11.7)	0.52
Physician decision	9 (7.5)	12 (10.0)	
Patient decision	1 (0.8)	2 (1.7)	

* Gastrointestinal disorders included diarrhea, nausea, cramping, abdominal pain, and vomiting.

† Hepatotoxicity was defined as an elevation in aminotransferase levels above the normal reference range.

‡ Adverse events were considered to be serious if they were fatal or life-threatening, required hospitalization, or resulted in substantial or permanent disability or a medically significant event (i.e., one that could have jeopardized the patient or required medical or surgical intervention to prevent an adverse outcome).

Recommendations	Class[a]	Level[b]	Ref.[c]
Serum CRP should be considered to guide the treatment length and assess the response to therapy	IIa	C	

Acute pericarditis: therapy

- Corticosteroids increase risk of pericaditis recurrence

- Indications:
  - contraindication for aspirin and NSAID
  - failure of treatment with aspirin and at least another NSAID
  - need for treatment of concomitant systemic condition

Acute pericarditis: therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
Corticosteroids are not recommended as first-line therapy for acute pericarditis	III	C	
Low-dose corticosteroids[d] should be considered for acute pericarditis in cases of contraindication/failure of aspirin/ NSAIDs and colchicine, and when an infectious cause has been excluded, or when there is a specific indication such as autoimmune disease	IIa	C	

Acute pericarditis: therapy

Table 7 Tapering of corticosteroids[35] (dosage information is provided for prednisone)

Starting dose 0.25–0.50 mg/kg/day[a]	Tapering[b]
>50 mg	10 mg/day every 1–2 weeks
50–25 mg	5–10 mg/day every 1–2 weeks
25–15 mg	2.5 mg/day every 2–4 weeks
<15 mg	1.25–2.5 mg/day every 2–6 weeks

Acute pericarditis: therapy (cont'd)

- Rest and avoidance of physical activity are useful adjunctive measures until active disease is no longer evident (absence of pericardial effusion, normalization of inflammatory markers)

- For athlets return to competitive sports not earlier than 6 months after episode of pericarditis particularly with myopericarditis

Acute pericarditis: therapy (cont'd)

Athlets. Return to competitive sports only if:

- asymptomatic
- achieve normalization of ECG abnormalities
- achieve normalization of markers of inflammation
- achieve normalization of LV function, wall motion abnormalities and cardiac dimentions
- no evidence of clinically relevant arrhythmias on Holter monitoring and exercise tolerance test

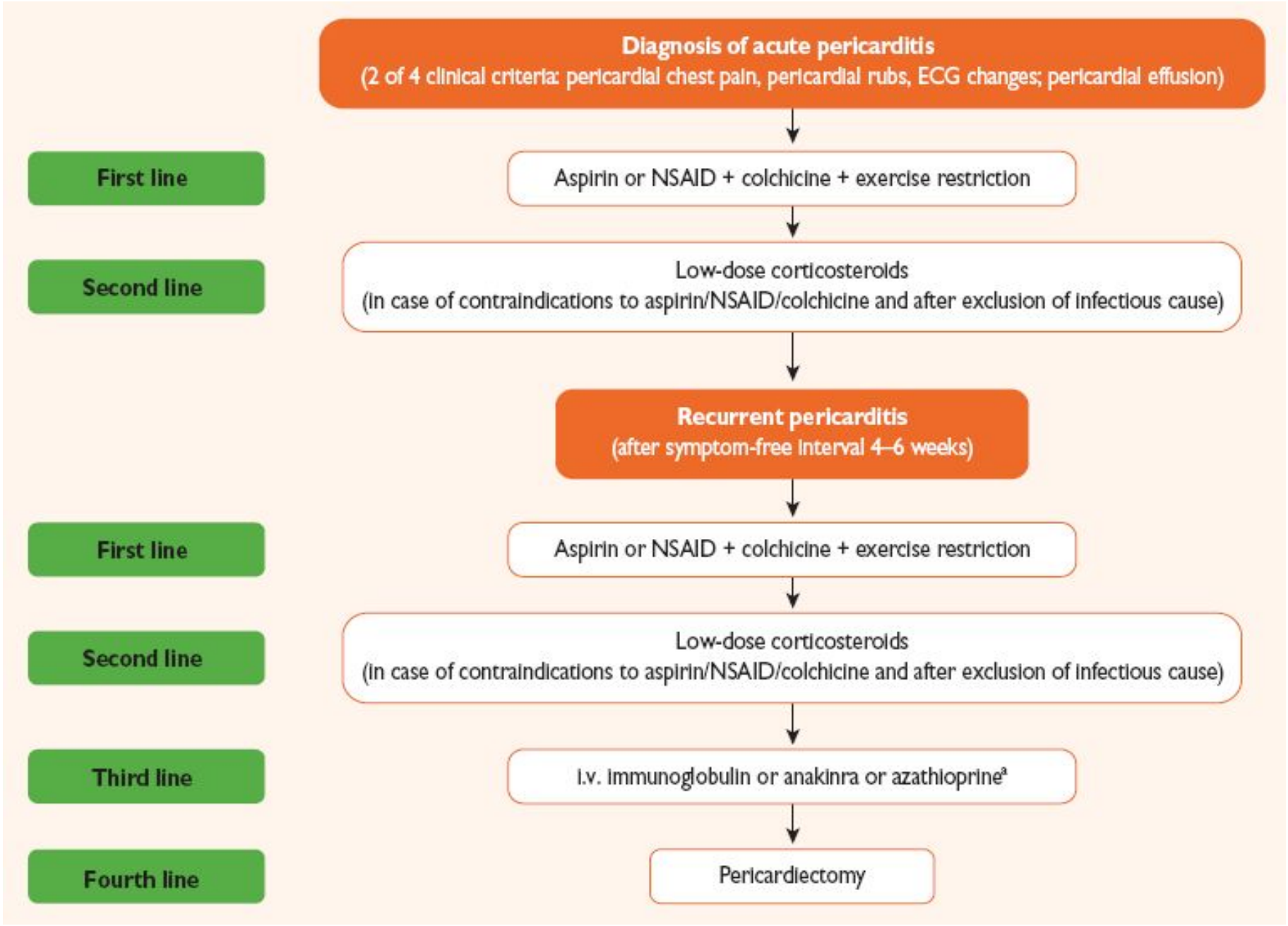
Acute pericarditis: prognosis

- Recurrence is most common complication
- Incidence ~30%
- Autoimmune pathogenetic mechanism is most probable

Recurrent pericarditis

Recurrent	Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer[a].

Recurrent pericarditis



Recommendations for the management of recurrent pericarditis

Recommendations	Class[a]	Level[b]	Ref.[c]
Aspirin and NSAIDs are mainstays of treatment and are recommended at full doses, if tolerated, until complete symptom resolution	I	A	55,56
Colchicine (0.5 mg twice daily or 0.5 mg daily for patients <70 kg or intolerant to higher doses); use for 6 months is recommended as an adjunct to aspirin/ NSAIDs	I	A	13–15, 58,59
Colchicine therapy of longer duration (>6 months) should be considered in some cases, according to clinical response	IIa	C	
CRP dosage should be considered to guide the treatment duration and assess the response to therapy	IIa	C	

Pericardial effusion

Echo (4-chamber view) in pt with large pericardial effusion and cardiac tamponade

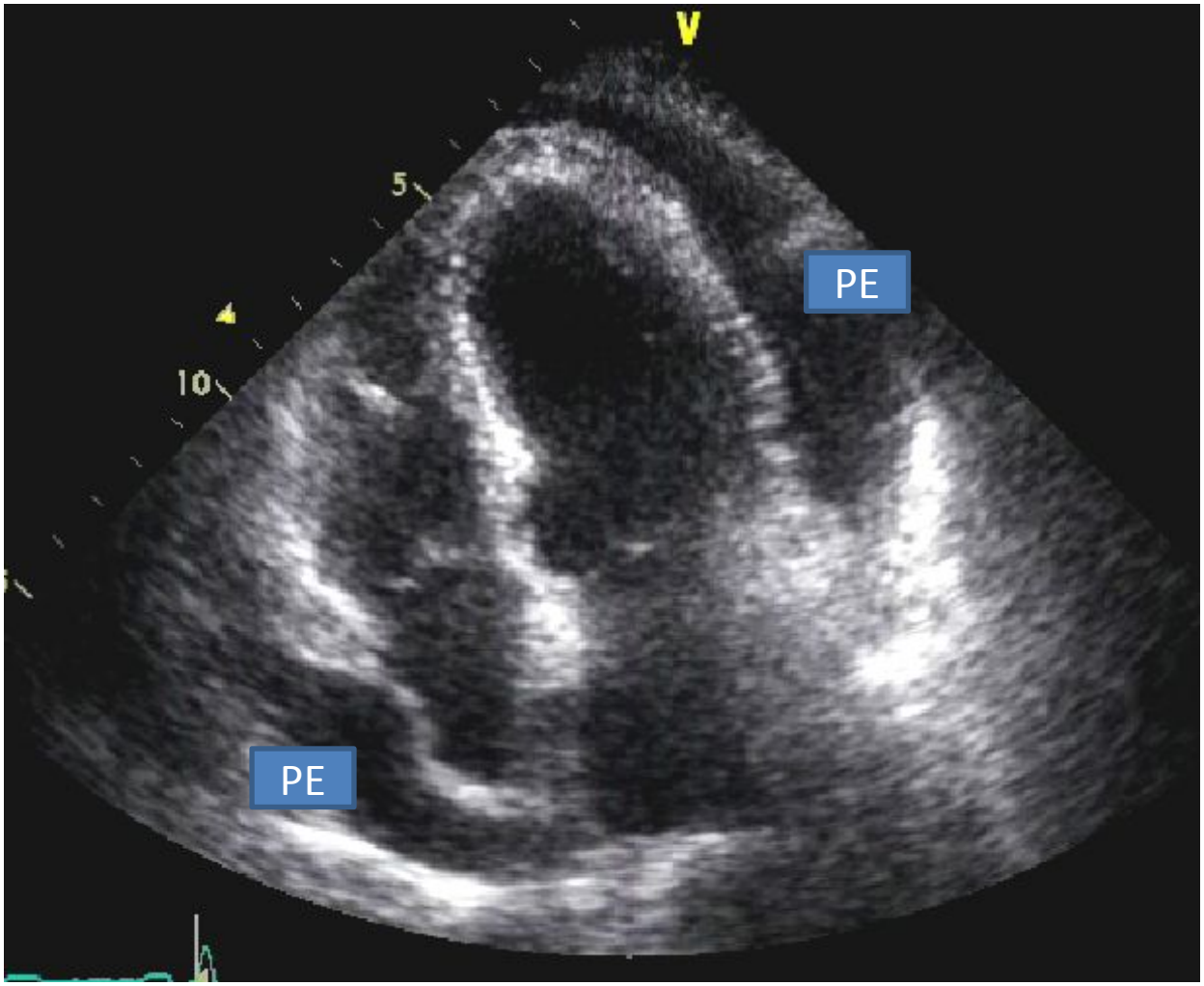


Table 8 Classification of pericardial effusion

Onset	Acute Subacute Chronic (>3 months)
Size	Mild <10 mm Moderate 10–20mm Large >20 mm
Distribution	Circumferential Loculated
Composition	Transudate Exudate

Pericardial effusion

- Large **idiopatic chronic** pericardial effusion defined as collection of pericardial fluid that persists for >3 months and has no apparent cause

- Risk of progression to cardiac tamponade ~30%

- Drainage of large pericardial effusion is recommended after 6-8 weeks of Rx

Pericardial effusion

- Pericardiectomy is recommended in a case of large effusion after pericardiocentesis

- No medical therapy have been proven effective for reduction of an isolated pericardial effusion in the absence of inflammation

Pericardial effusion: etiology

- Pericardial effusion without evidence of inflammation and pericarditis is often a clinical dilema

- The presence of inflammatory signs (elevated CPR and/or ESR) favor diagnose of pericarditis

- Large effusion and cardiac tamponade without inflammatory signs are often associated with neoplastic etiology

Pericardial effusion: etiology

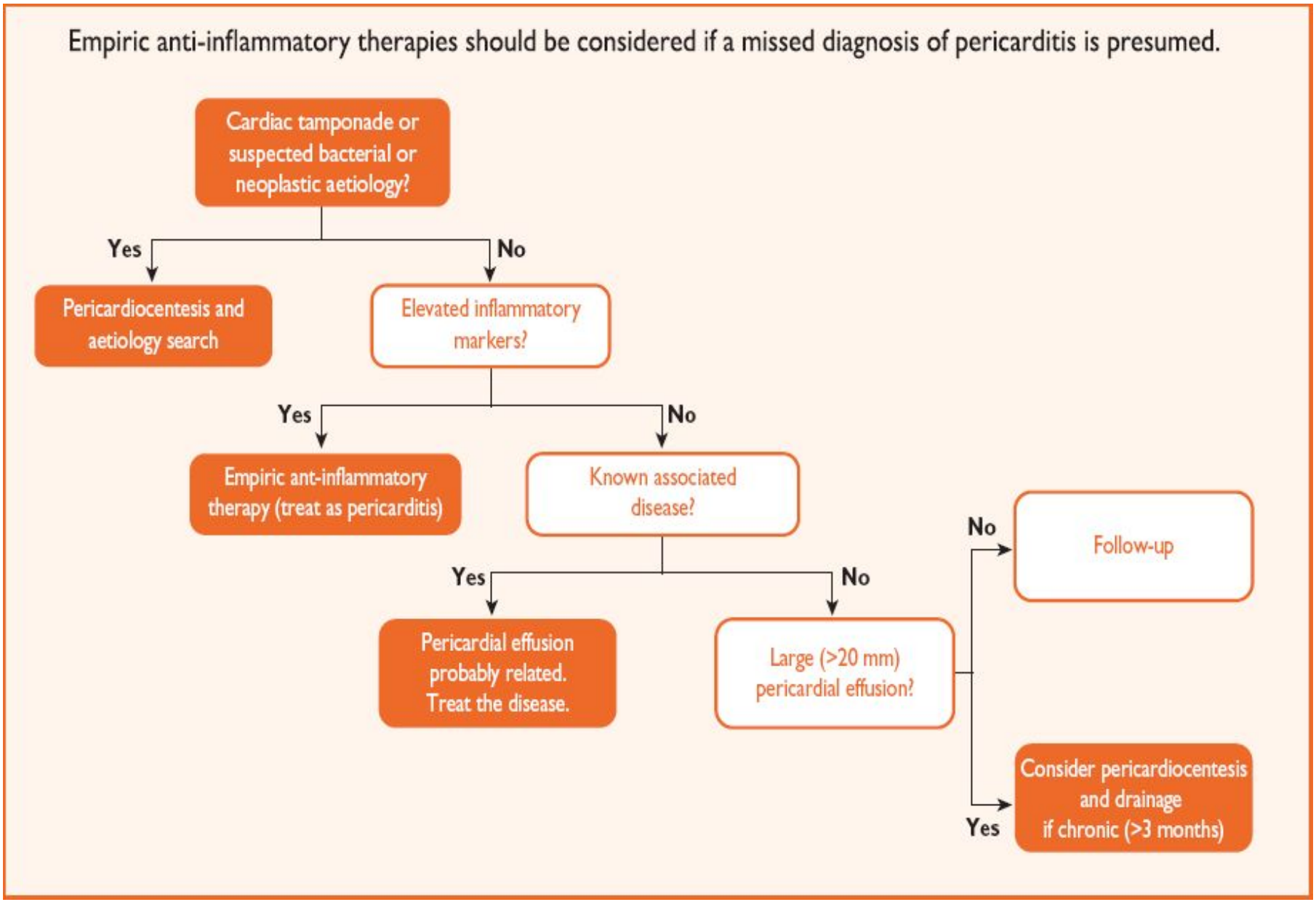
Table 5. Etiology of Isolated Moderate to Large Pericardial Effusions in Major Published Series

Study	Total number of patients	Idiopathic etiology *n* (%)	Neoplasia *n* (%)	Infection *n* (%)	Connective tissue diseases *n* (%)	Metabolic disorders *n* (%)	Other *n* (%)
Corey *et al.* (1993)[35]	57	4 (7)	13 (23)	15 (27)	7 (12)	7 (12)	11 (19)
Sagristà-Sauleda *et al.* (2000)[36]	322	93 (29)	42 (13)	7 (2)	16 (5)	19 (6)	145 (45)
Levy *et al.* (2003)[37]	204	98 (48)	31 (15)	33 (16)	18 (9)	22 (11)	2 (1)

Medscape

Source: Nat Rev Cardiovasc Med © 2009 Nature Publishing Group

Pericardial effusion: management



Pericardial effusion: management

Recommendations for the therapy of pericardial effusion

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended to target the therapy of pericardial effusion at the aetiology	I	C	
Aspirin/NSAIDs/colchicine and treatment of pericarditis is recommended when pericardial effusion is associated with systemic inflammation	I	C	
Pericardiocentesis or cardiac surgery is indicated for cardiac tamponade or for symptomatic moderate to large pericardial effusions not responsive to medical therapy, and for suspicion of unknown bacterial or neoplastic aetiology	I	C	

Pericardial effusion: management

Recommendations for the management of traumatic pericardial effusion and haemopericardium in aortic dissection

Recommendations	Class[a]	Level[b]	Ref.[c]
Urgent imaging technique (transthoracic echocardiogram or CT) is indicated in patients with a history of chest trauma and systemic arterial hypotension	I	B	184
Immediate thoracotomy is indicated in cardiac tamponade due to penetrating trauma to the heart and chest	I	B	185
In the setting of aortic dissection with haemopericardium, controlled pericardial drainage of very small amounts of the haemopericardium should be considered to temporarily stabilize the patient in order to maintain blood pressure at about 90 mmHg	IIa	C	
Pericardiocentesis as a bridge to thoracotomy may be considered in cardiac tamponade due to penetrating trauma to the heart and chest	IIb	B	185

Cardiac tamponade

Table 9 Causes of cardiac tamponade

Common causes:

- Pericarditis
- Tuberculosis
- Iatrogenic (invasive procedure-related, post-cardiac surgery)
- Trauma
- Neoplasm/malignancy

Uncommon causes:

- Collagen vascular diseases (systemic lupus erythematosus, rheumatoid arthritis, scleroderma)
- Radiation induced
- Postmyocardial infarction
- Uraemia
- Aortic dissection
- Bacterial infection
- Pneumopericardium

Cardiac tamponade

Clinical signs

- Beck's triad: hypotension, muffled heart sounds, elevated jugular venous pressure

- pulsus paradoxus >10 mm Hg: difference between the pressure at which Korotkoff sounds **first appear** and that at which they are present with **each heart beat**

Cardiac tamponade

- Electrocardiographic signs
  - reduced voltage
  - electrical alternance

- Echocardiographic signs
  - large peicardial effusion (most often)
  - “swinging” motion
  - repriratory changes in trans-mitral and trans-aortic flow

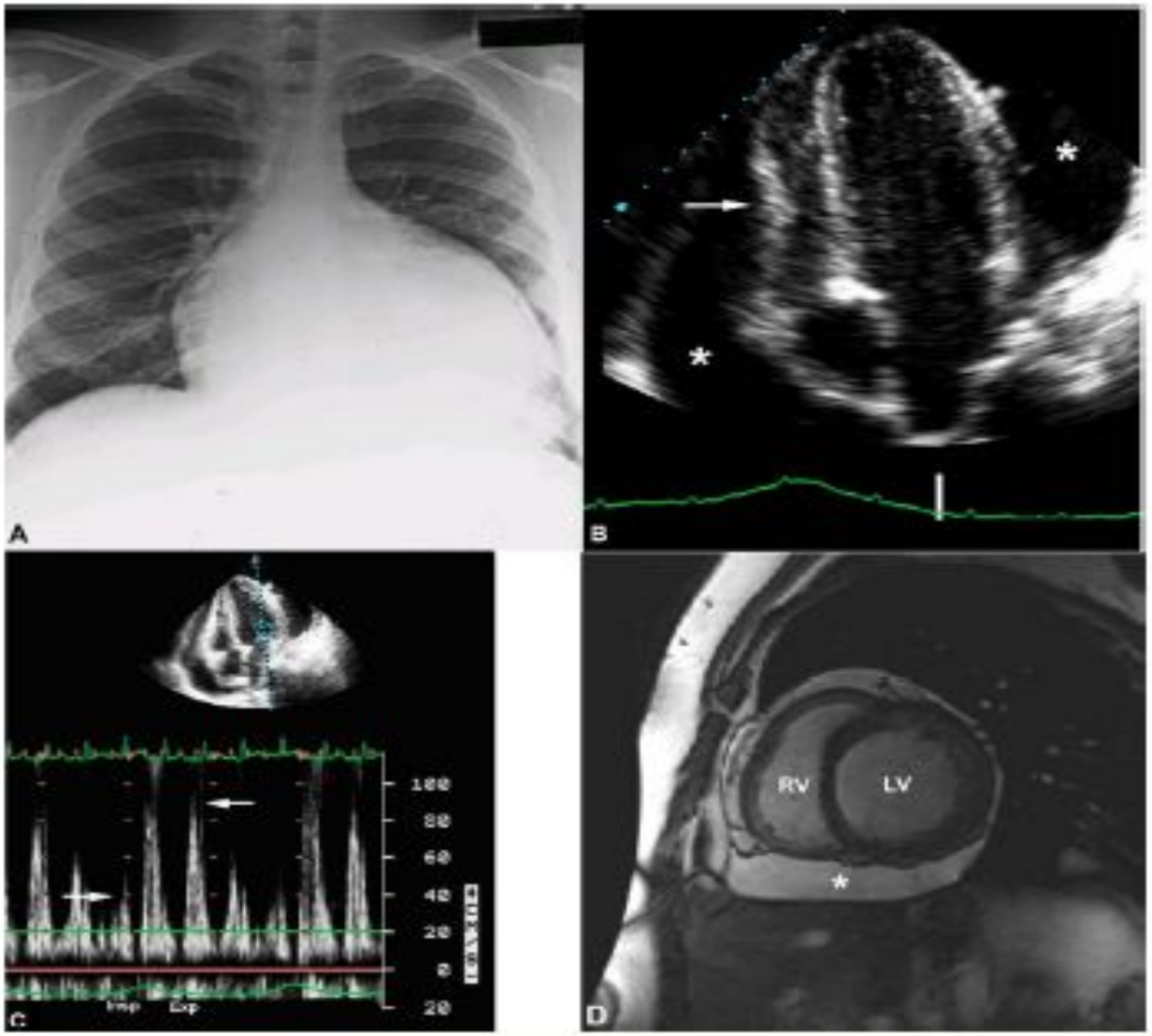


Figure 3. Imaging Findings in Pericardial Tamponade

(A) Chest radiography demonstrating the characteristic water-bottle appearance of the cardiac silhouette. (B) Large circumferential pericardial effusion with diastolic RV inversion and (C) reduced mitral inflow on inspiration (arrows). (D) CMR using bSSFP in a short-axis view demonstrating a circumferential pericardial effusion (*). See Online Video 1. Abbreviations as in Figure 1.

Cardiac tamponade

Recommendations	Class[a]	Level[b]	Ref.[c]
Vasodilators and diuretics are not recommended in the presence of cardiac tamponade	III	C	

Approaches for pericardiocentesis

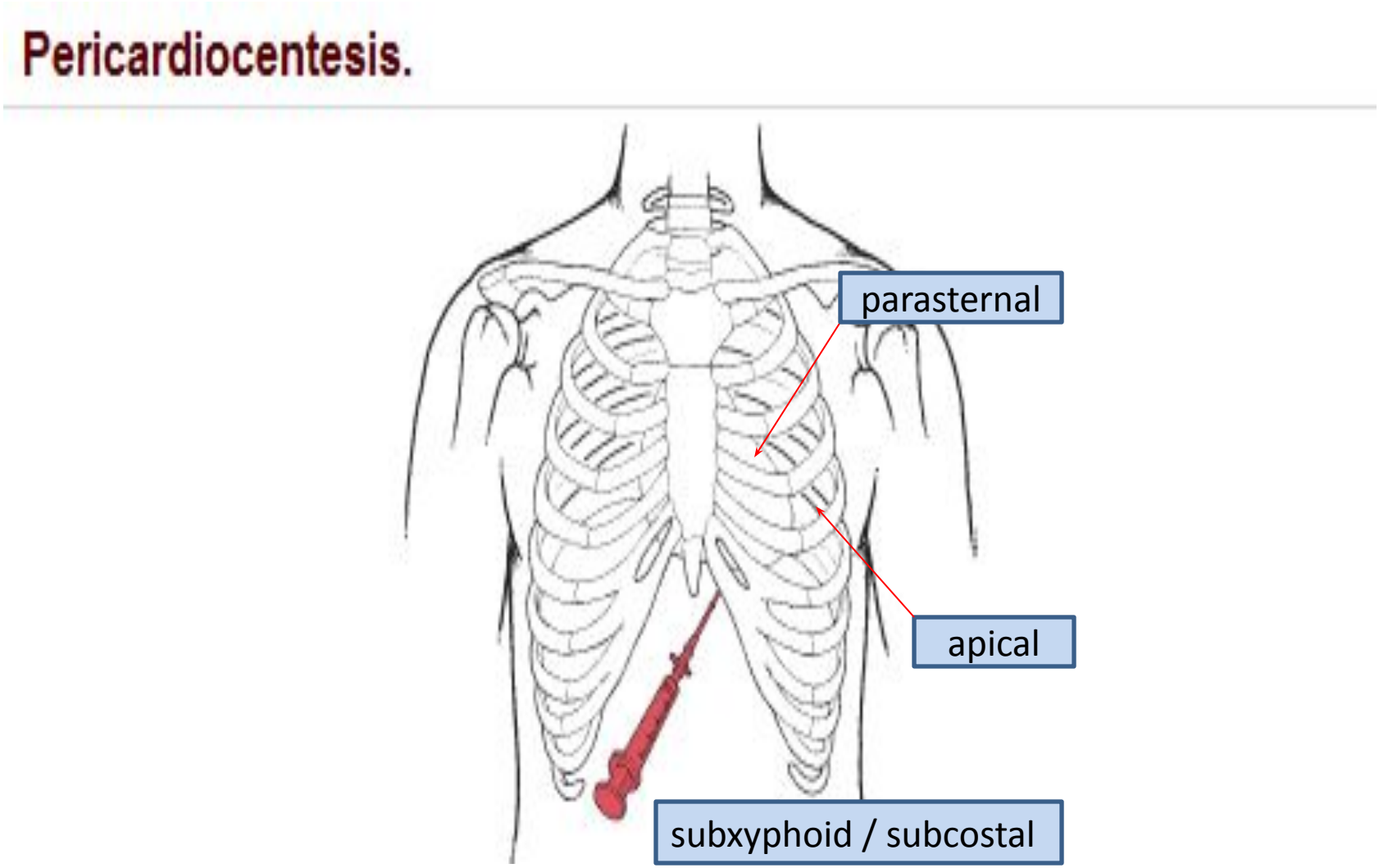


Table 15 Main analyses to be performed on pericardial fluid

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.

LDH = lactate dehydrogenase; TB = tuberculosis.

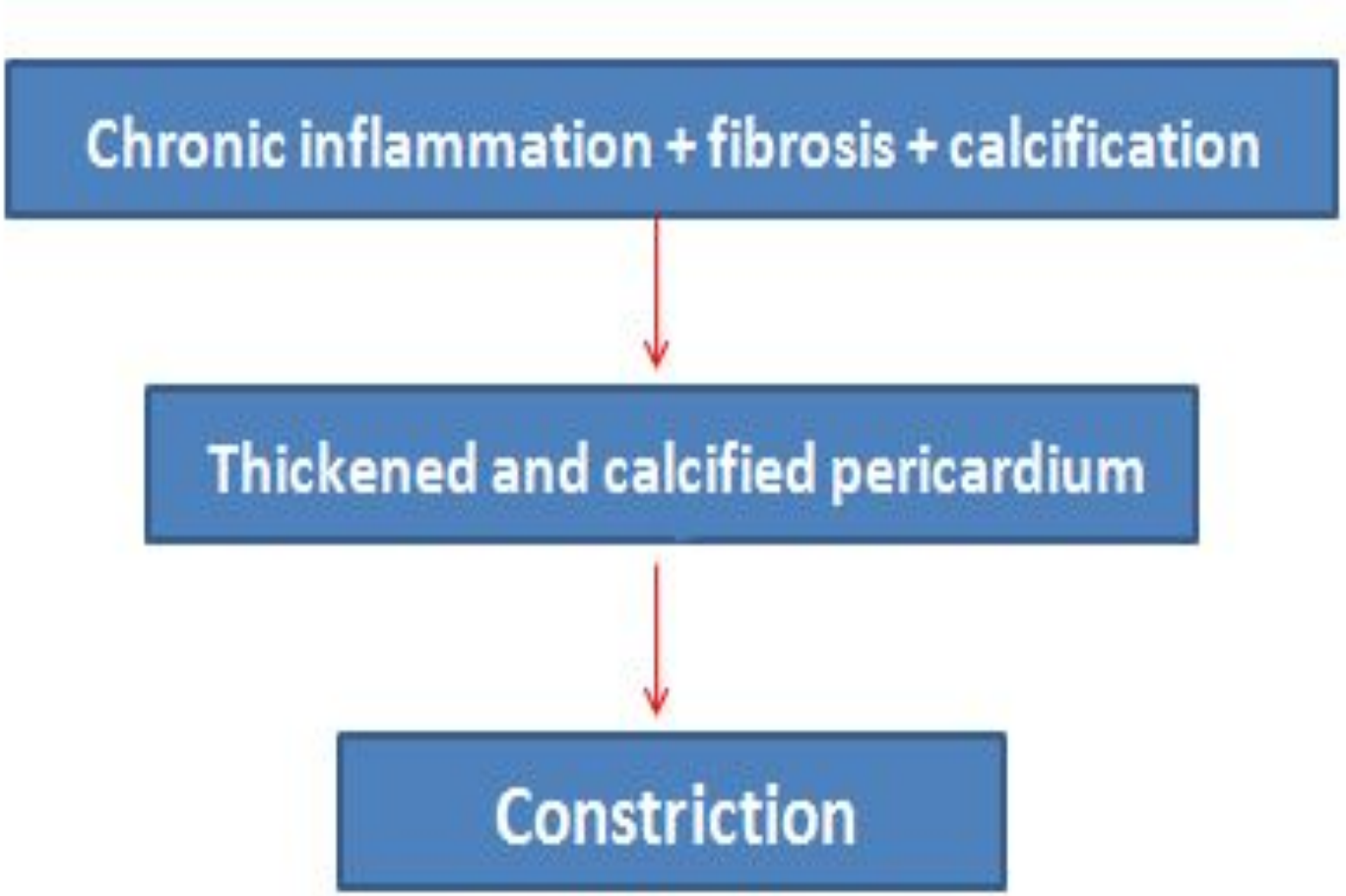
[a]High values of protein and LDH are commonly interpreted as an exudate, as in pleural fluid, but have not been validated for pericardial fluid.

Recommendations for management of neoplastic involvement of the pericardium

Extended pericardial drainage is recommended in patients with suspected or definite neoplastic pericardial effusion in order to prevent effusion recurrence and provide intrapericardial therapy	I	B	
Intrapericardial instillation of cytostatic/ sclerosing agents should be considered since it may prevent recurrences in patients with malignant pericardial effusion	IIa	B	197–204
Intrapericardial cisplatin should be considered in pericardial involvement in the course of lung cancer and intrapericardial instillation of thiotepa should be considered in breast cancer pericardial metastases	IIa	B	197, 198, 200, 204
Radiation therapy should be considered to control malignant pericardial effusion in patients with radiosensitive tumours such as lymphomas and leukaemias	IIa	B	
Pericardiotomy should be considered when pericardiocentesis cannot be performed	IIa	B	205
Percutaneous balloon pericardiotomy may be considered for the prevention of recurrences of neoplastic pericardial effusions	IIb	B	

Constrictive pericarditis

Constrictive pericarditis



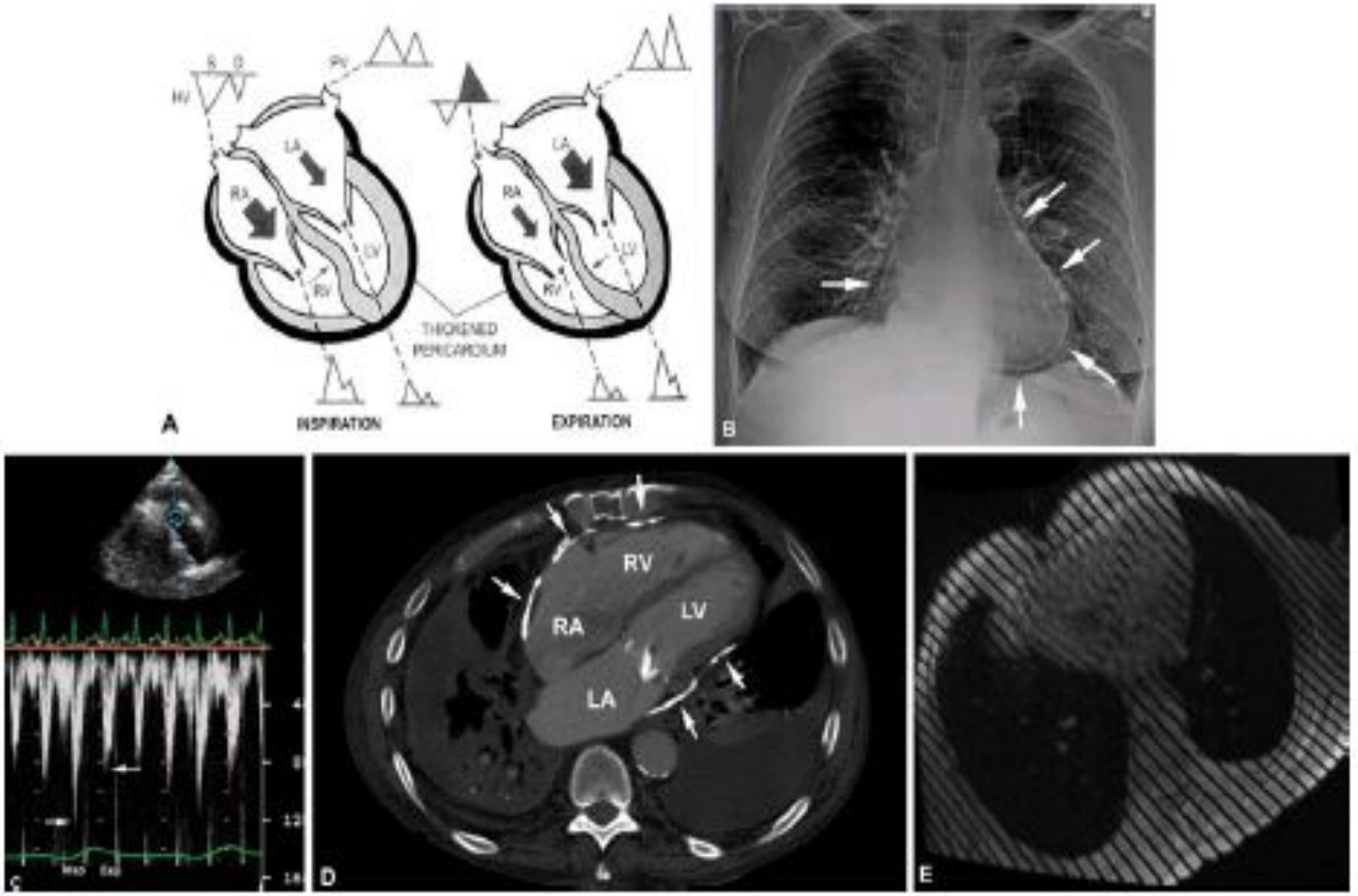


Figure 4. Multimodality Imaging in Constrictive Pericarditis

(A) Physiology of ventricular interdependence highlighting the change in transvalvular flow throughout the respiratory cycle. Reprinted with permission from Oh et al. (28). (B) Chest radiograph with evidence of circumferential pericardial calcification. (C) Pulsed-wave Doppler interrogation across the right ventricular outflow tract demonstrating significant respirophasic variation. (D) Cardiac computed tomography findings of pericardial calcification clustered around the atrioventricular grooves (**arrows**). (E) Persistent continuity of tag lines on CMR tagging sequence throughout the cardiac cycle is diagnostic of pericardial adhesions. See Online Video 2. D = diastole; HV = hepatic veins; LA = left atrium; PV = pulmonary veins; S = systole; other abbreviations as in Figure 1.

Constrictive pericarditis

- Fibrotic pericardium impedes normal diastolic filling because of loss of elasticity

- Usually pericardium is considerably thickened but in ~20% of cases can be of normal thickness

- Types of constrictive pericarditis:
  - chronic (usually)
  - subacute transient
  - occult constriction

Constrictive pericarditis: etiology

- Idiopathic or viral - 42-49%
- Cardiac surgery - 11-37%
- Radiation Rx - 9-31% (mostly for Hodgkin disease or breast cancer)
- Connective tissue disorders (3-7%)
- Infection 3-6% (TB or purulent pericarditis)

Risk of Constrictive Pericarditis After Acute Pericarditis

Massimo Imazio, MD; Antonio Brucato, MD; Silvia Maestroni, MD; Davide Cumetti, MD; Riccardo Belli, MD; Rita Trinchero, MD; Yehuda Adler, MD

Background—Constrictive pericarditis (CP) is considered a rare, dreaded possible complication of acute pericarditis. Nevertheless, there is a lack of prospective studies that have evaluated the specific risk according to different etiologies. The aim of this study is to evaluate the risk of CP after acute pericarditis in a prospective cohort study with long-term follow-up.

Methods and Results—From January 2000 to December 2008, 500 consecutive cases with a first episode of acute pericarditis (age, 51±16 years; 270 men) were prospectively studied to evaluate the evolution toward CP. Etiologies were viral/idiopathic in 416 cases (83.2%), connective tissue disease/pericardial injury syndromes in 36 cases (7.2%), neoplastic pericarditis in 25 cases (5.0%), tuberculosis in 20 cases (4.0%), and purulent in 3 cases (0.6%). During a median follow-up of 72 months (range, 24 to 120 months), CP developed in 9 of 500 patients (1.8%): 2 of 416 patients with idiopathic/viral pericarditis (0.48%) versus 7 of 84 patients with a nonviral/nonidiopathic etiology (8.3%). The incidence rate of CP was 0.76 cases per 1000 person-years for idiopathic/viral pericarditis, 4.40 cases per 1000 person-years for connective tissue disease/pericardial injury syndrome, 6.33 cases per 1000 person-years for neoplastic pericarditis, 31.65 cases for 1000 person-years for tuberculous pericarditis, and 52.74 cases per 1000 person-years for purulent pericarditis.

Conclusions—CP is a relatively rare complication of viral or idiopathic acute pericarditis (<0.5%) but, in contrast, is relatively frequent for specific etiologies, especially bacterial. (*Circulation*. **2011;124:1270-1275.**)

Risk of Constrictive Pericarditis After Acute Pericarditis

- 500 patients
- Mean FU – 72 months
- Constrictive pericarditis – 1.8%
- Idiopathic/Viral (2 of 416 pts) – 0.48%
- Nonviral/Nonidiopathic (7 of 84 pts) – 8.3%

Circulation 2011; 124: 1270

Risk of Constrictive Pericarditis After Acute Pericarditis

Incidence rate per 1000 patients-years	Number of patients (%)	Etiology
0.76	416 (83.2%)	Viral/idiopathic
4.40	36 (7.2%)	Connective tissue disease/ pericardial injury syndrome
6.33	25 (5%)	Neoplastic pericarditis
31.65	(4%) 20	Tuberculous pericarditis
52.74	3 (0.6%)	Purulent pericarditis

Circulation 2011; 124: 1270

Constrictive pericarditis: symptoms

- Right heart failure: range from periferal edema to anasarca
- No pulmonary congestion
- Usually normal heart size
- Fatigability and dyspnea related to diminished cardiac output (CO) response to exertion

Constrictive pericarditis

Pericardial constriction should be considered in any patient with unexplained elevation of jugular venous pressure, particularly with history of cardiac surgery, radiation therapy, or bacterial pericarditis

Table 10 Constrictive pericarditis vs. restrictive cardiomyopathy: a brief overview of features for the differential diagnosis (Modified from Imazio et *al.*[51])

Diagnostic evaluation	Constrictive pericarditis	Restrictive cardiomyopathy
Physical findings	Kussmaul sign, pericardial knock	Regurgitant murmur, Kussmaul sign may be present, S3 (advanced).
ECG	Low voltages, non-specific ST/T changes, atrial fibrillation.	Low voltages, pseudoinfarction, possible widening of QRS, left-axis deviation, atrial fibrillation.
Chest X-ray	Pericardial calcifications (1/3 of cases).	No pericardial calcifications.
Echocardiography	• Septal bounce. • Pericardial thickening and calcifications. • Respiratory variation of the mitral peak E velocity of >25% and variation in the pulmonary venous peak D flow velocity of >20% • Colour M-mode flow propagation velocity (Vp) >45 cm/sec. • Tissue Doppler: peak e' >8.0 cm/s.	• Small left ventricle with large atria, possible increased wall thickness. • E/A ratio >2, short DT. • Significant respiratory variations of mitral inflow are absent. • Colour M-mode flow propagation velocity (Vp) <45 cm/sec. • Tissue Doppler: peak e' <8.0 cm/s.
Cardiac Catheterization	'Dip and plateau' or 'square root' sign, right ventricular diastolic, and left ventricular diastolic pressures usually equal, ventricular interdependence (i.e. assessed by the systolic area index >1.1).[a]	Marked right ventricular systolic hypertension (>50 mmHg) and left ventricular diastolic pressure exceeds right ventricular diastolic pressure (LVEDP >RVEDP) at rest or during exercise by 5 mmHg or more (RVEDP <1/3 RVSP).
CT/CMR	Pericardial thickness >3–4 mm, pericardial calcifications (CT), ventricular interdependence (real-time cine CMR).	Normal pericardial thickness (<3.0 mm), myocardial involvement by morphology and functional study (CMR).

Transient constrictive pericarditis

- 10-20% of cases during resolution of pericardial inflammation

- Patients with newly diagnosed constrictive pericarditis who are hemodynamically stable, can be managed conservatively for 2-3 months period with empiric anti-inflammation therapy, before pericardiectomy is recommended

Effusive constrictive pericarditis

- In 8% of patients with cardiac tamponade who underwent pericardiocentesis and cardiac catheterization
- Diagnostic characteristics of effusive-constrictive pericarditis: failure of right atrial (RA) pressure to fall by 50% or to level below 10 mm Hg after pericardiocentesis
- Usually present with clinical signs of pericardial effusion, constrictive pericarditis, or both

Constrictive pericarditis: treatment

Table 11 Definitions and therapy of main constrictive pericardial syndromes (adapted from Imazio et *al.*[51])

Syndrome	Definition	Therapy
Transient constriction (d.d. permanent constrictive pericarditis, restrictive CMP).	Reversible pattern of constriction following spontaneous recovery or medical therapy.	A 2–3-month course of empiric anti-inflammatory medical therapy.
Effusive-constrictive pericarditis (d.d. cardiac tamponade, constrictive pericarditis).	Failure of the right atrial pressure to fall by 50% or to a level below 10 mmHg after pericardiocentesis. May be diagnosed also by non-invasive imaging.	Pericardiocentesis followed by medical therapy. Surgery for persistent cases.
Chronic constriction (d.d. transient constriction, restrictive CMP).	Persistent constriction after 3–6 months.	Pericardiectomy, medical therapy for advanced cases or high risk of surgery or mixed forms with myocardial involvement.

CMP = cardiomyopathy; d.d. = differential diagnosis.

Thank you for attention

Backup slides

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Multimodality Imaging of Pericardial Diseases

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Boston, Massachusetts; and Toronto, Ontario, Canada

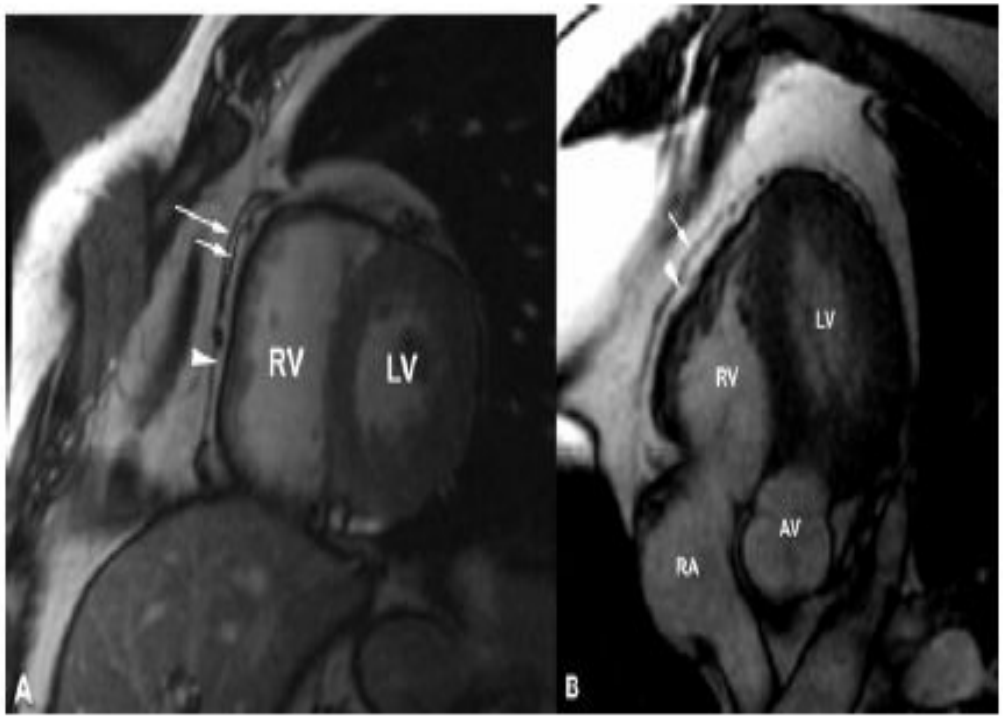


Figure 1. CMR of Normal Pericardium

The CMR bSSFP sequence in short-axis (**left**) and 4-chamber view (**right**) showing the normal pericardial outline and the epicardial fat layer (**arrowhead**). The **left panel** shows a trivial pericardial effusion separating the visceral (**short arrow**) and parietal (**long arrow**) pericardium. In the **right panel**, the separation is not as evident (**long arrow**) and visualization of the pericardial contour is difficult on the lateral border of the LV. AV = aortic valve; bSSFP = balanced steady-state free precession; CMR = cardiac magnetic resonance; LV = left ventricle; RA = right atrium; RV = right ventricle.

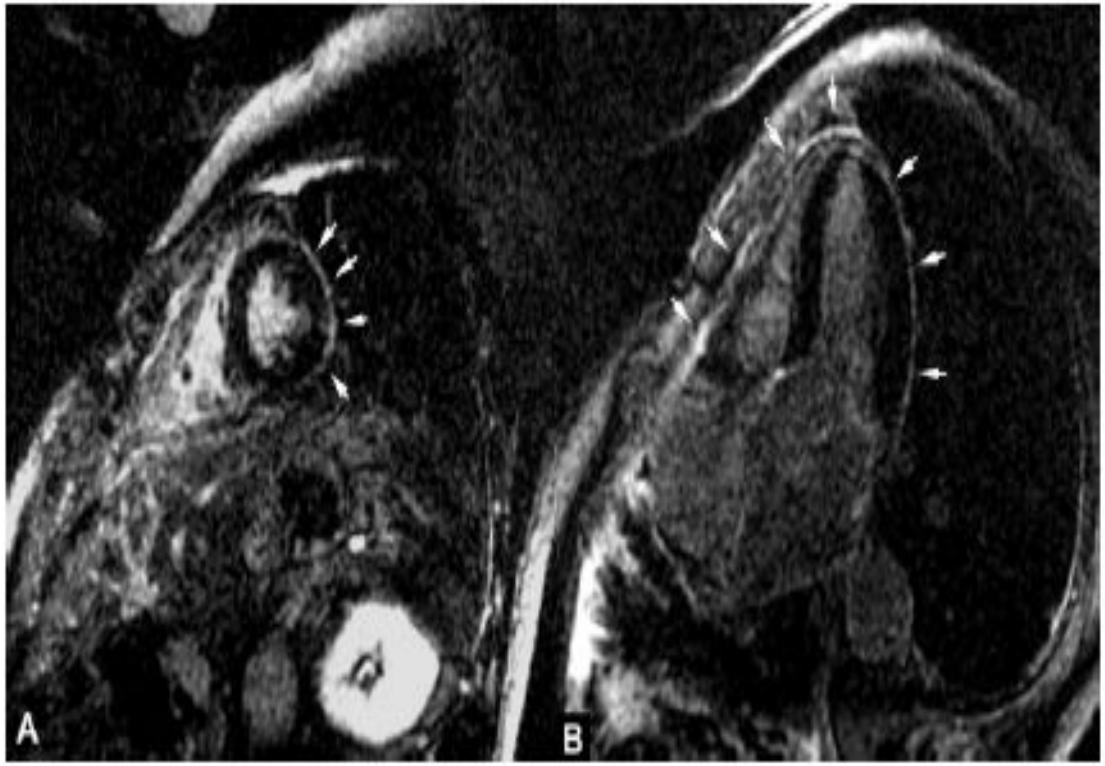


Figure 2. Delayed Enhancement of the Pericardium

Double-inversion recovery delayed-enhancement CMR images after injection of gadolinium demonstrating circumferential enhancement of the pericardium (**arrows**) consistent with pericardial inflammation. Abbreviations as in Figure 1.

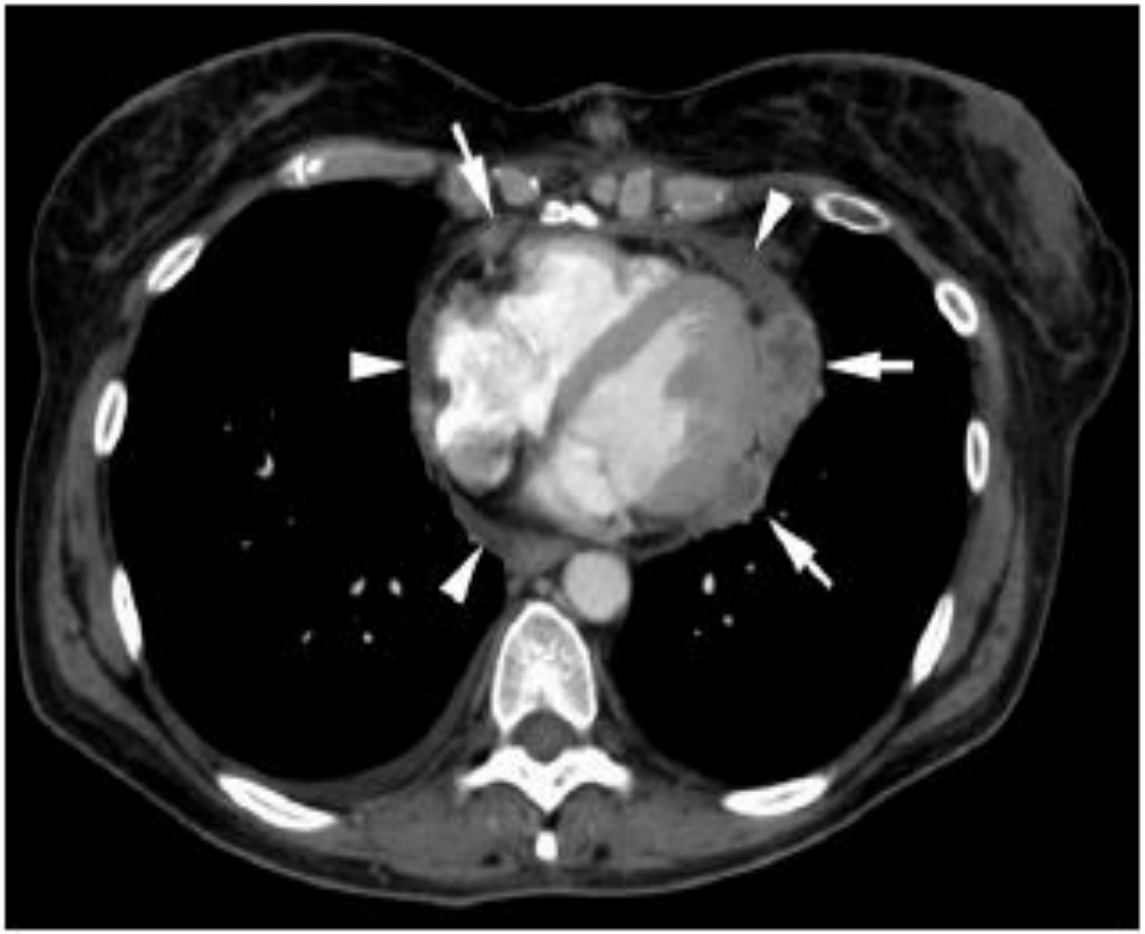


Figure 5. Computed Tomography of the Chest in a Patient With Metastatic Disease

Axial view demonstrating circumferential pericardial thickening (**arrowheads**) and deposition of pericardial metastases (**arrows**).

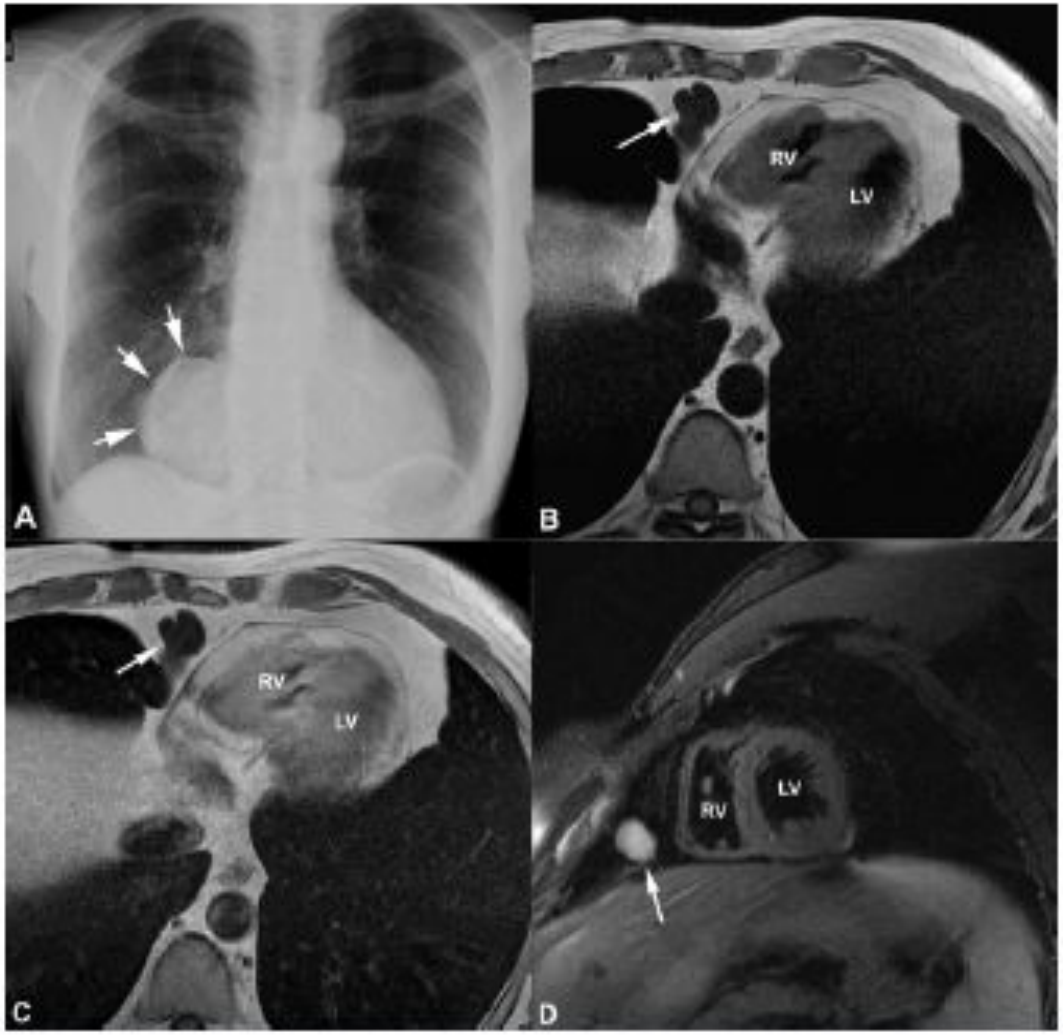


Figure 6. Multimodality Imaging of a Pericardial Cyst

(A) Chest radiograph showing a large pericardial cyst at the right costophrenic angle. In a different patient, CMR T_1-weighted spin echo imaging before (B) and after (C) gadolinium injection showing a circular, septated, hypointense, nonenhancing structure within the paracardiac fat pad at the right costophrenic angle. The hyperintense appearance on subsequent T_2-weighted spin echo imaging (D) is consistent with the diagnosis of a pericardial cyst. Abbreviations as in Figure 1.

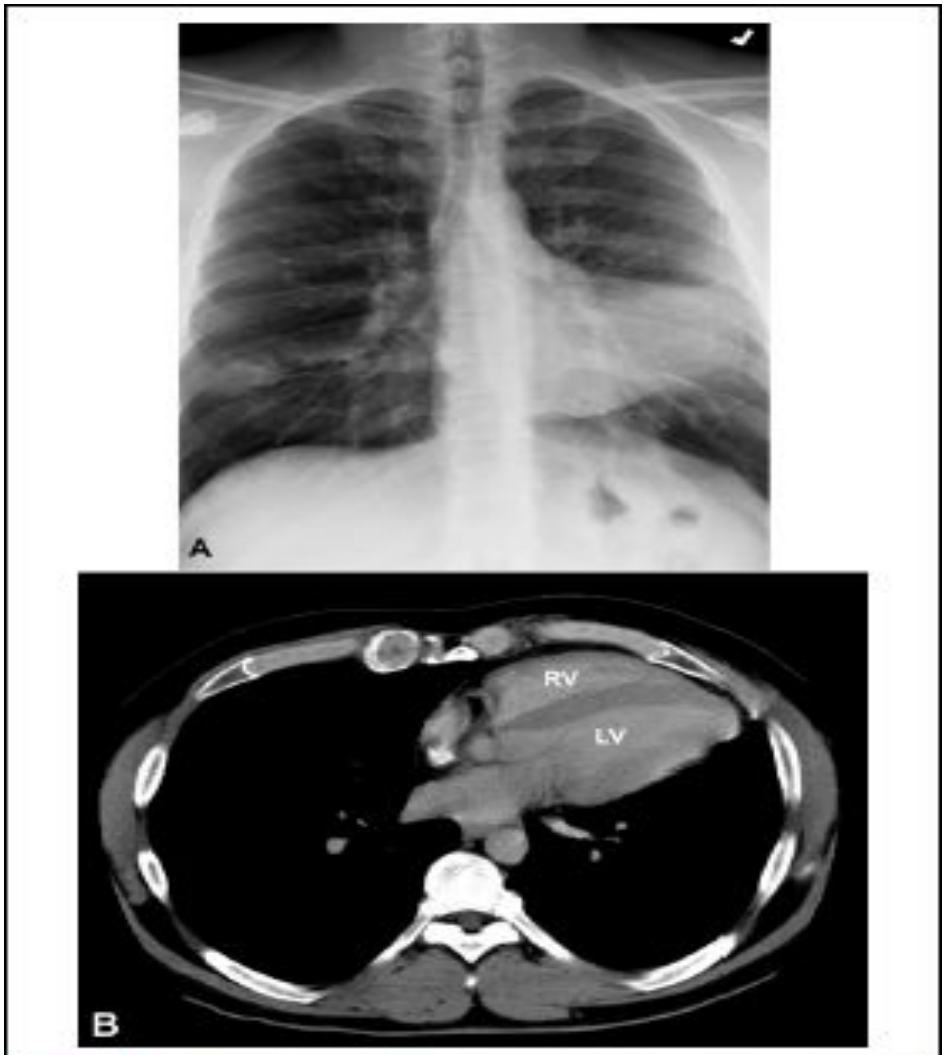
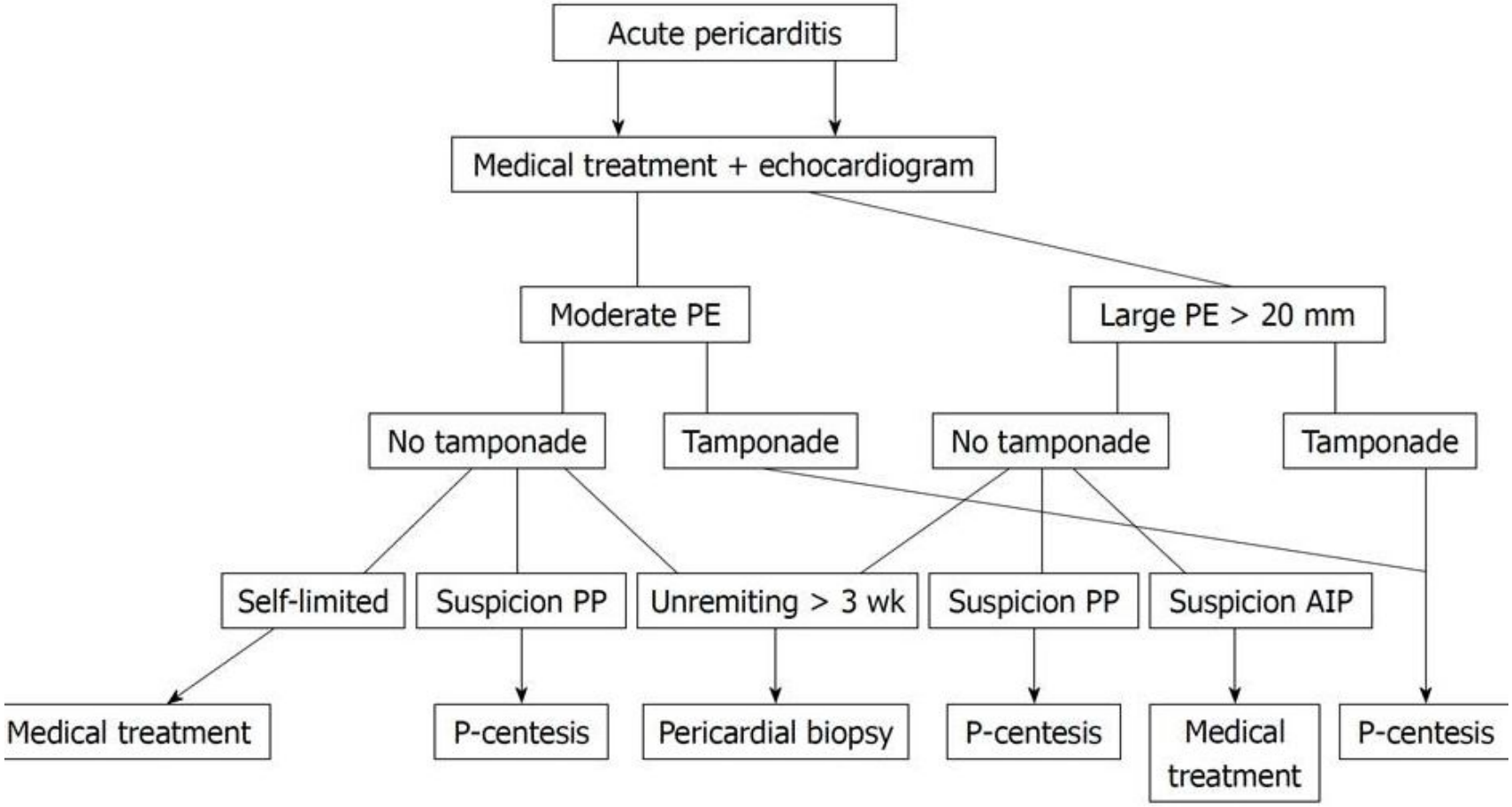
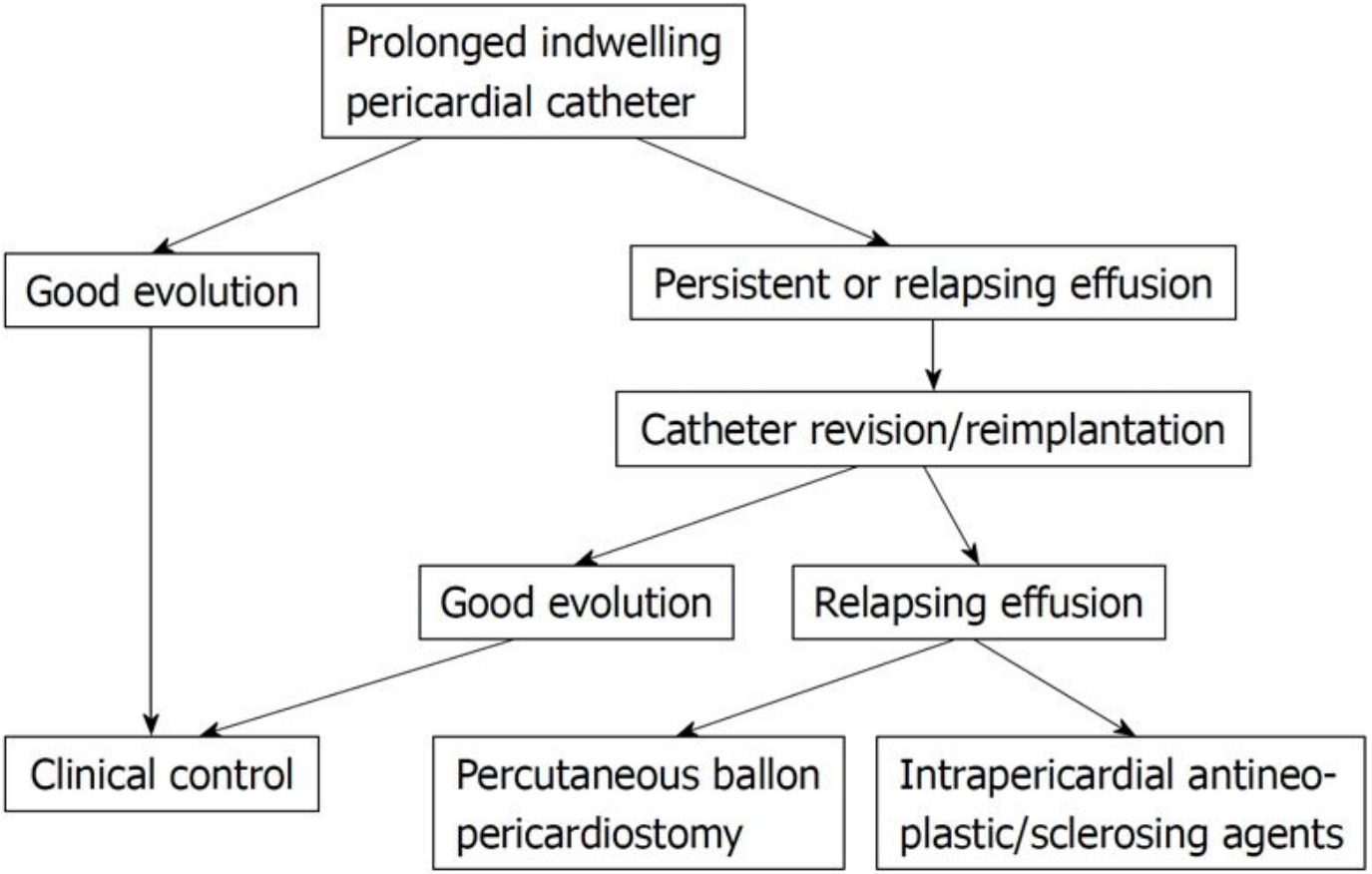


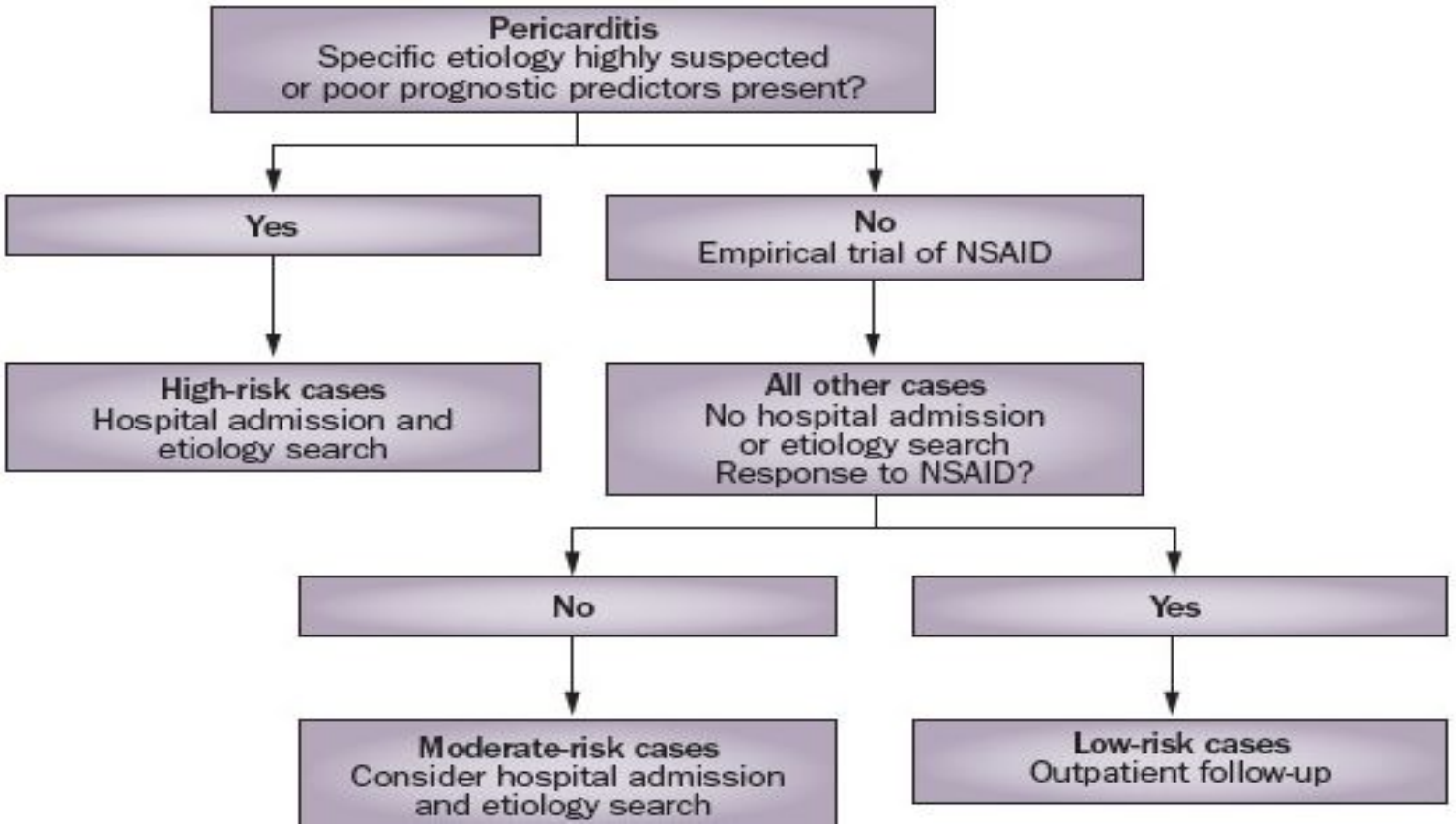
Figure 7. Multimodality Imaging of Congenital Absence of the Pericardium

Chest radiograph (**A**) and chest cardiac computed tomography scan (**B**) demonstrating superior and lateral displacement of the apex without identifiable pericardium over the apex of the heart consistent with congenital absence of the pericardium. Abbreviations as in Figure 1.


Acute pericarditis
Medical treatment + echocardiogram
Moderate PE
Large PE > 20 mm
No tamponade
Tamponade
No tamponade
Tamponade
Self-limited
Suspicion PP
Unremiting > 3 wk
Suspicion PP
Suspicion AIP
Medical treatment
P-centesis
Pericardial biopsy
P-centesis
Medical treatment
P-centesis


Prolonged indwelling pericardial catheter
Good evolution
Persistent or relapsing effusion
Catheter revision/reimplantation
Good evolution
Relapsing effusion
Clinical control
Percutaneous ballon pericardiostomy
Intrapericardial antineo-plastic/sclerosing agents

Triage of patients with acute pericarditis

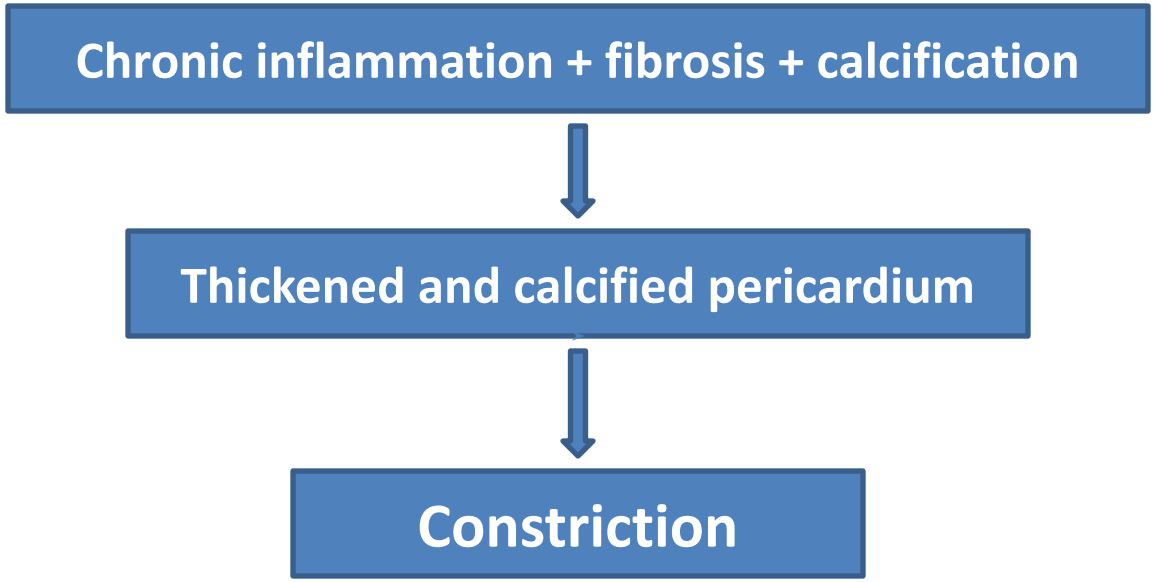


Imazio et al. JACC 2004; 43:1042-6

Causes of pericardial effusion

Inflammation

- Infection
- Noninfectious etiology



Etiology of pericarditis

- Infectious pericarditis
- Pericarditis in systemic autoimmune diseases
- Type 2 (auto)immune process
- Pericarditis and pericardial effusion in diseases of surrounding organs
- Pericarditis in metabolic disorders
- Neoplastic
- Idiopathic

Acute pericarditis: therapy (cont'd)

Table 2. Medical Therapy for Acute and Recurrent Pericarditis

Drug	Initial dose	Maintenance*	Treatment length	Monitoring	Tapering
Aspirin	2–4 g per day in 3 divided doses	As initial dose, consider weekly tapering following normalization of CRP levels	2–4 weeks (longer for complicated cases)	Blood cell count, CRP levels	Every 1–2 weeks after normalization of CRP levels
Ibuprofen	400–600 mg three times per day	As initial dose, consider weekly tapering following normalization of CRP levels	2–4 weeks (longer for complicated cases)	Blood cell count, CRP levels	Every 1–2 weeks after normalization of CRP levels
Indomethacin	25–50 mg three times per day (usually 50 mg)	As initial dose, consider weekly tapering following normalization of CRP levels	2–4 weeks (longer for complicated cases)	Blood cell count, CRP levels	Every 1–2 weeks after normalization of CRP levels
Nimesulide	200 mg per day in 2 divided doses	As initial dose, consider weekly tapering following normalization of CRP levels	2–4 weeks (longer for complicated cases)	Blood cell count, CRP levels	Every 1–2 weeks after normalization of CRP levels
Prednisone	0.2–0.5 mg/kg per day	As initial dose, consider weekly tapering following normalization of CRP levels	2–4 weeks (longer for complicated cases)	Blood cell count, CRP levels‡	See Table 3
Colchicine	Not necessary; see maintenance for initial dose	0.5 mg twice per day (0.5 mg per day for patients who weigh <70 kg)	Following a first attack: 3 months Following a recurrence: 6–12 months	Blood cell count, levels of CRP, transaminases, creatine kinase, and creatinine	May be required in recurrent forms of pericarditis

*Weekly tapering is usual for acute pericarditis, but longer durations may be necessary for recurrences. ‡Additional blood chemistry may be needed to monitor for metabolic effects and complications of corticosteroid therapy in selected patients. Abbreviation: CRP, C-reactive protein.

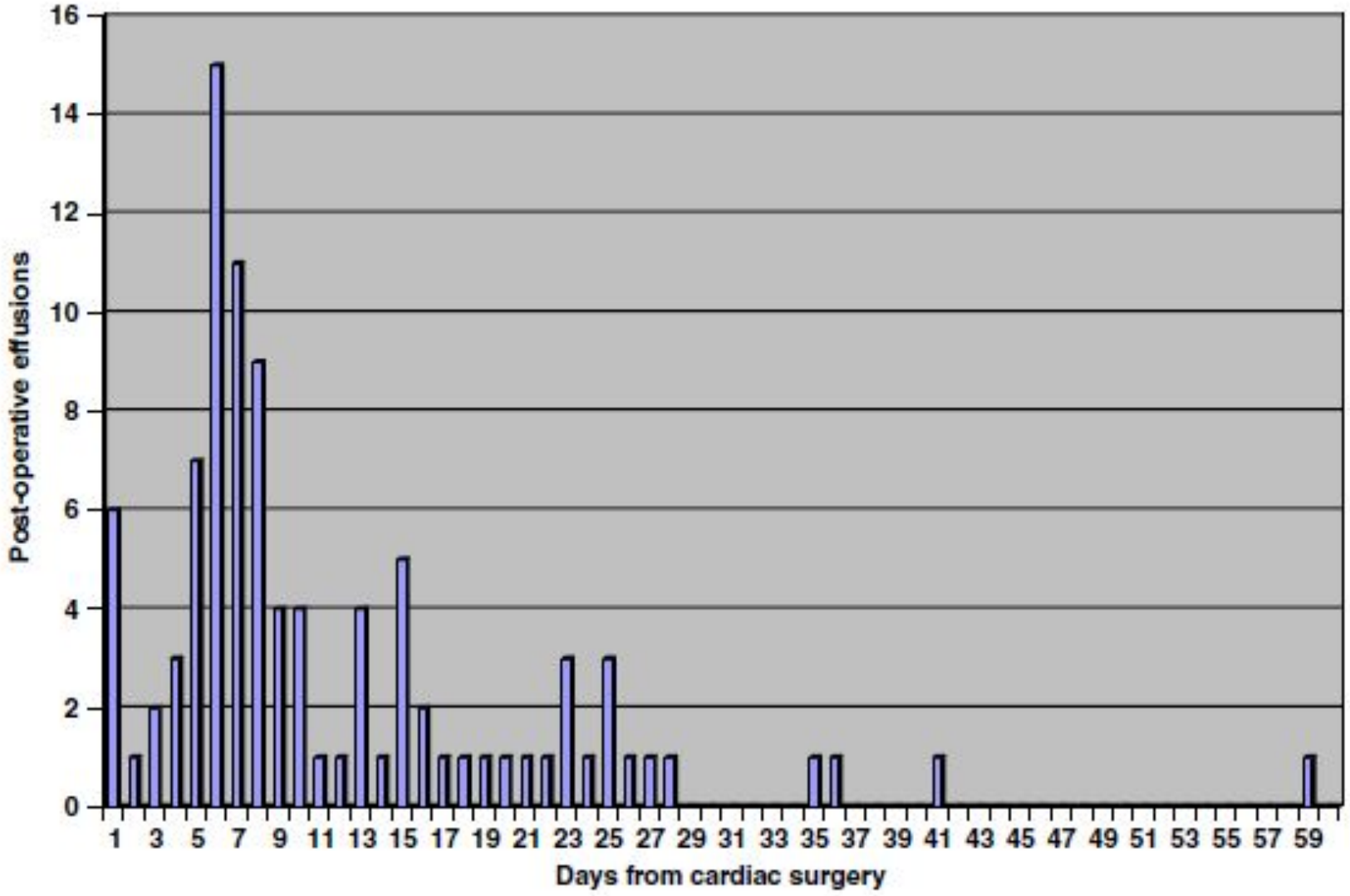
COPPS trial

Colchicine prevents early postoperative pericardial and pleural effusions

Massimo Imazio, MD,[a] Antonio Brucato, MD,[b,j] Maria Elena Rovere, MD,[c,j] Anna Gandino, MD,[d,j] Roberto Cemin, MD,[e,j] Stefania Ferrua, MD,[f,j] Silvia Maestroni, MD,[b,j] Edoardo Zingarelli, MD,[c,j] Alberto Barosi, MD,[d,j] Caterina Simon, MD,[b,j] Fabrizio Sansone, MD,[c,j] Davide Patrini, MD,[g,j] Ettore Vitali, MD,[g,j] Riccardo Belli, MD,[a] Paolo Ferrazzi, MD,[b,j] Rita Trinchero, MD,[a,j] David H. Spodick, MD,[h,j] and Yehuda Adler, MD[i,j] *Torino, Bergamo, Milano, Bolzano, and Rivoli, Italy; Worcester, MA; and Kupat Holim Meubedet, Israel*

Am Heart J 2011; 62:527-32

COPPS trial



Time course of postoperative effusions after cardiac surgery.

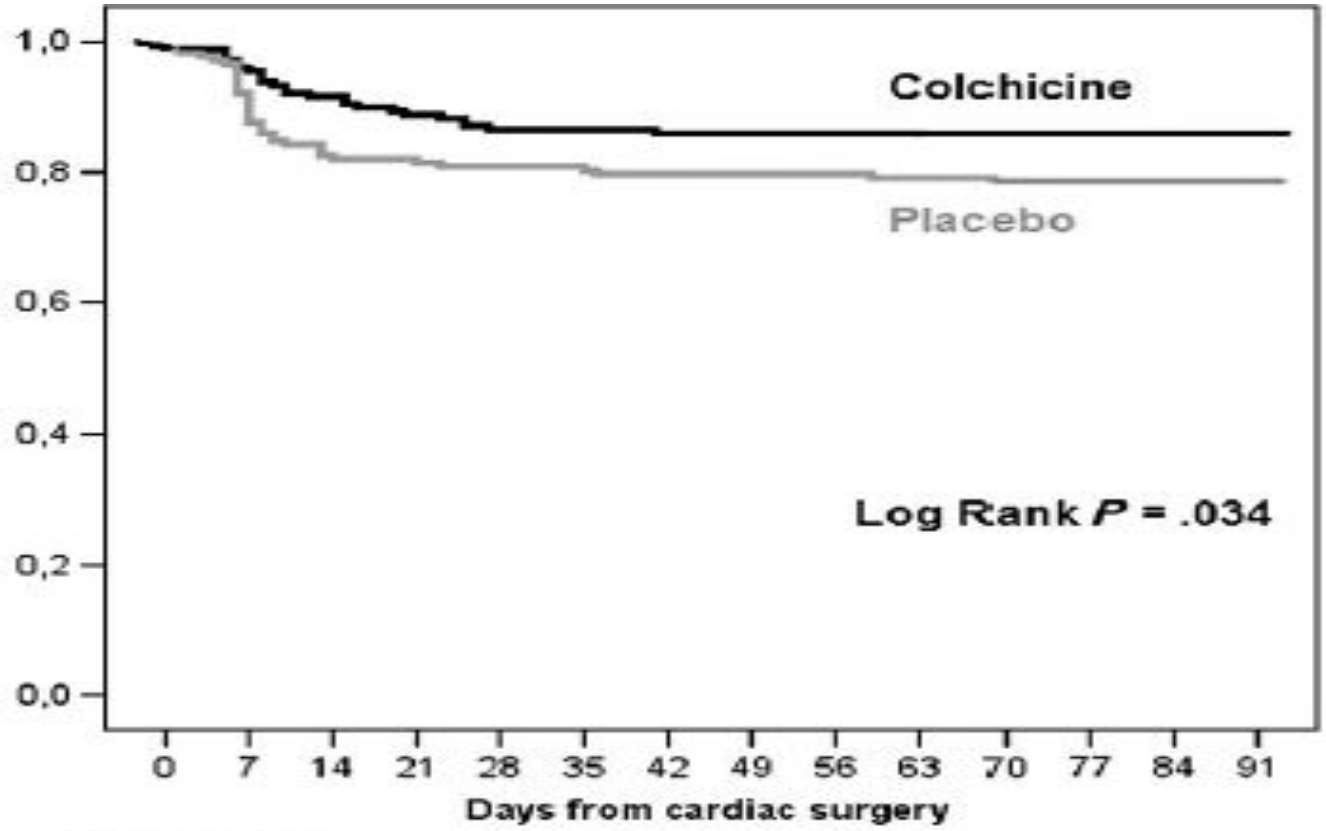
COPPS trial

Table II. Efficacy and safety of colchicine for the primary prevention of postoperative effusions

Patients	Placebo (n = 180)	Colchicine (n = 180)	P	NNT (95% CI)
Postoperative pericardial effusion (n = 64)	41 (22.8%)	23 (12.8%)	.019	10 (5.6-46.1)
Mild <10 mm	33/41 (80.5%)	22/23 (95.7%)	<.001	8 (4.7-18.6)
Moderate 10-20 mm	6/41 (14.6%)	1/23 (4.3%)	.002	8 (4.7-30.3)
Large >20 mm	2/41 (4.9%)	0/23 (0.0%)	.012	
Cardiac tamponade	1/41 (2.5%)	0/23 (0.0%)	.097	
Postoperative pleural effusion (n = 68)	46 (25.6%)	22 (12.2%)	.002	
All postoperative effusions (n = 92)*	57 (31.7%)	35 (19.4%)	.011	
Cardiac surgery stay (d)	10.3 ± 4.3	9.4 ± 3.7	.034	
Rehabilitation stay (d)	13.9 ± 6.8	11.9 ± 6.4	.004	
Overall hospital stay (d)	24.2 ± 8.8	21.3 ± 8.6	.002	
Side effects (n = 25)	9 (5.0%)	16 (8.9%)	NS	
Gastrointestinal (n = 24)	8 (4.4%)	16 (8.9%)	NS	
Other (n = 1)	1 (0.6%)	0 (0.0%)	NS	
Severe adverse events (n = 0)	0 (0.0%)	0 (0.0%)	NS	
Drug withdrawal (n = 33)	12 (6.7%)	21 (11.7%)	NS	
Mean follow-up (m)	18.5	20.2	NS	

NS, Not statistically significant ($P > .05$).
*Including patients with pericardial and/or pleural effusion.

COPPS trial



Kaplan-Meier postoperative pericardial effusion–free survival curve according to study groups (placebo/colchicine) in the first 90 days after cardiac surgery.

Rx of acute pericarditis in children

Table 4. Age-adjusted Doses of Common Anti-inflammatory Drugs for Pericarditis

Drug*	Child dose	Adult dose
Aspirin	60–90 mg/kg per day in 3–4 divided doses	Initial: 2–4 g per day in 3–4 divided doses Maintenance: as initial dose, consider tapering following normalization of CRP levels
Ibuprofen	30–50 mg/kg per day divided every 8 h; start at lower end of dosing range and titrate upward (maximum dose 2.4 g per day)	Initial: 400–600 mg three times per day Maintenance: as initial dose, consider tapering following normalization of CRP levels
Indomethacin	Age ≥2 years: 1–2 mg/kg per day in 2–4 divided doses (maximum dose 4 mg/kg per day, do not exceed 150–200 mg per day)	Initial: 25–50 mg three times per day (usually 50 mg, maximum dose 150 mg per day); extended-release capsule should be given once or twice per day Maintenance: as initial dose, consider tapering following normalization of CRP levels

Rx of acute pericarditis in children

Colchicine	Age ≤5 years: 0.5 mg per day Age >5 years: 1.0–1.5 mg per day in 2–3 divided doses	0.5 mg twice per day (0.5 mg per day for patients who weigh <70 kg or are >70 years old) An initial dose is not necessary and can increase the risk of gastrointestinal intolerance Duration of treatment: following a first attack, 3 months; following a recurrence, 6–12 months For patients with renal impairment: CL_{cr} 35–49 ml/min, 0.5–0.6 mg per day CL_{cr} 10–34 ml/min, 0.5–0.6 mg every 2–3 days CL_{cr} <10 ml/min, avoid chronic use of colchicine, contraindicated by the manufacturer

*All doses to be administered orally. Abbreviations: CL_{cr}, creatinine clearance, CRP, C-reactive protein.