Pericardial diseases

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2015 ESC Guidelines for the diagnosis and management of pericardial diseases

1. Introduction (1)

- **The pericardium** (from the Greek p1ri´, 'around' and ka´rdion, 'heart') is a **double-walled sac** containing the heart and the roots of the great vessels.
- **The pericardial sac has two layers,** a **serous visceral** layer (also known as epicardium when it comes into contact with the myocardium) and a **fibrous parietal** layer. It encloses the pericardial cavity, which contains pericardial fluid.
- The pericardium fixes the heart to the mediastinum, gives protection against infection and provides lubrication for the heart.

1. Introduction (2)

- Pericardial diseases may be either isolated disease or part of a systemic disease.
- The main pericardial syndromes that are encountered in clinical practice include pericarditis (acute, subacute, chronic and recurrent), pericardial effusion, cardiac tamponade, constrictive pericarditis and pericardial masses.
- All medical therapies for pericardial diseases are off-label, since no drug has been registered until now for a specific pericardial indication.

2. Epidemiology, aetiology and classification of pericardial diseases (1)

2.1 Epidemiology

- The incidence of acute pericarditis has been reported as 27.7 cases per 100,000 population per year in an Italian urban area.
- Pericarditis is responsible for 0.1% of all hospital admissions and 5% of emergency room admissions for chest pain.
- Data collected from a Finnish national registry (2000–9) showed a standardized incidence rate of hospitalizations for acute pericarditis of 3.32 per 100,000 person-years.

2. Epidemiology, aetiology and classification of pericardial diseases (2)

2.1 Epidemiology

- Men ages 16–65 years were at higher risk for pericarditis (relative risk 2.02) than women in the general admitted population, with the highest risk difference among young adults compared with the overall population.
- Acute pericarditis caused 0.20% of all cardiovascular admissions.
- The proportion of caused admissions declined by an estimated 51% per 10-year increase in age.

2. Epidemiology, aetiology and classification of pericardial diseases (3)

2.1 Epidemiology

- The in-hospital mortality rate for acute pericarditis was 1.1% and was increased with age and severe co-infections (pneumonia or septicaemia).
- Recurrences affect about 30% of patients within 18 months after a first episode of acute pericarditis.

2. Epidemiology, aetiology and classification of pericardial diseases (4)

2.2 Aetiology

- A simple aetiological classification for pericardial diseases is to consider infectious and non-infectious causes.
- The aetiology is varied and depends on the epidemiological background, patient population and clinical setting.
- In developed countries, viruses are usually the most common aetiological agents of pericarditis, whereas tuberculosis (TB) is the most frequent cause of pericardial diseases in the world and developing countries, where TB is endemic. In this setting, TB is often associated with human immunodeficiency virus (HIV) infection, especially in sub-Saharan Africa.

Aetiology of pericardial diseases

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

Aetiology of pericardial diseases

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.

3. Pericardial syndromes (1)

- 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’.

3. Pericardial syndromes (2)

3.1 Acute pericarditis

- **Acute pericarditis is an inflammatory pericardial syndrome with or without pericardial effusion.**
- **Additional signs and symptoms may be present according to the underlying aetiology or systemic disease (i.e. signs and symptoms of systemic infection such as fever and leucocytosis, or systemic inflammatory disease or cancer).**

3. Pericardial syndromes (3)

3.1 Acute pericarditis

- **Widespread ST-segment elevation** has been reported as a typical hallmark sign of acute pericarditis **as well as PR depression**.
- **However, changes in the ECG imply inflammation of the epicardium, since the parietal pericardium itself is electrically inert.**
- **Typical ECG changes have been reported in up to 60% of cases.**
- **The temporal evolution of ECG changes with acute pericarditis is highly variable from one patient to another and is affected by therapy.**
- **Major differential diagnoses include acute coronary syndromes with ST-segment elevation and early repolarization.**

3. Pericardial syndromes (4)

3.1 Acute pericarditis

- Elevation of markers of inflammation [i.e. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] is a common and supportive finding in patients with acute pericarditis and may be helpful for monitoring the activity of the disease and efficacy of therapy.
- Patients with concomitant myocarditis may present with an elevation of markers of myocardial injury [i.e. creatine kinase (CK), troponin].

3. Pericardial syndromes (5)

3.1 Acute pericarditis

- A chest X-ray is generally normal in patients with acute pericarditis since an increased cardiothoracic ratio only occurs with pericardial effusions exceeding 300 ml.
- In the case of pleuropulmonary diseases, signs of pleuropericardial involvement may be found in patients with pericarditis.

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.

Definitions and diagnostic criteria for pericarditis

3.1.1 Clinical management and therapy (4)

- A minimal restriction of 3 months (after the initial onset of the attack) has been arbitrarily defined according to expert consensus.
- We suggest applying this restriction only to athletes, while a shorter period (until remission) may be suitable for non-athletes.
- Aspirin or NSAIDs are mainstays of therapy for acute pericarditis. Different anti-inflammatory drugs have been proposed.

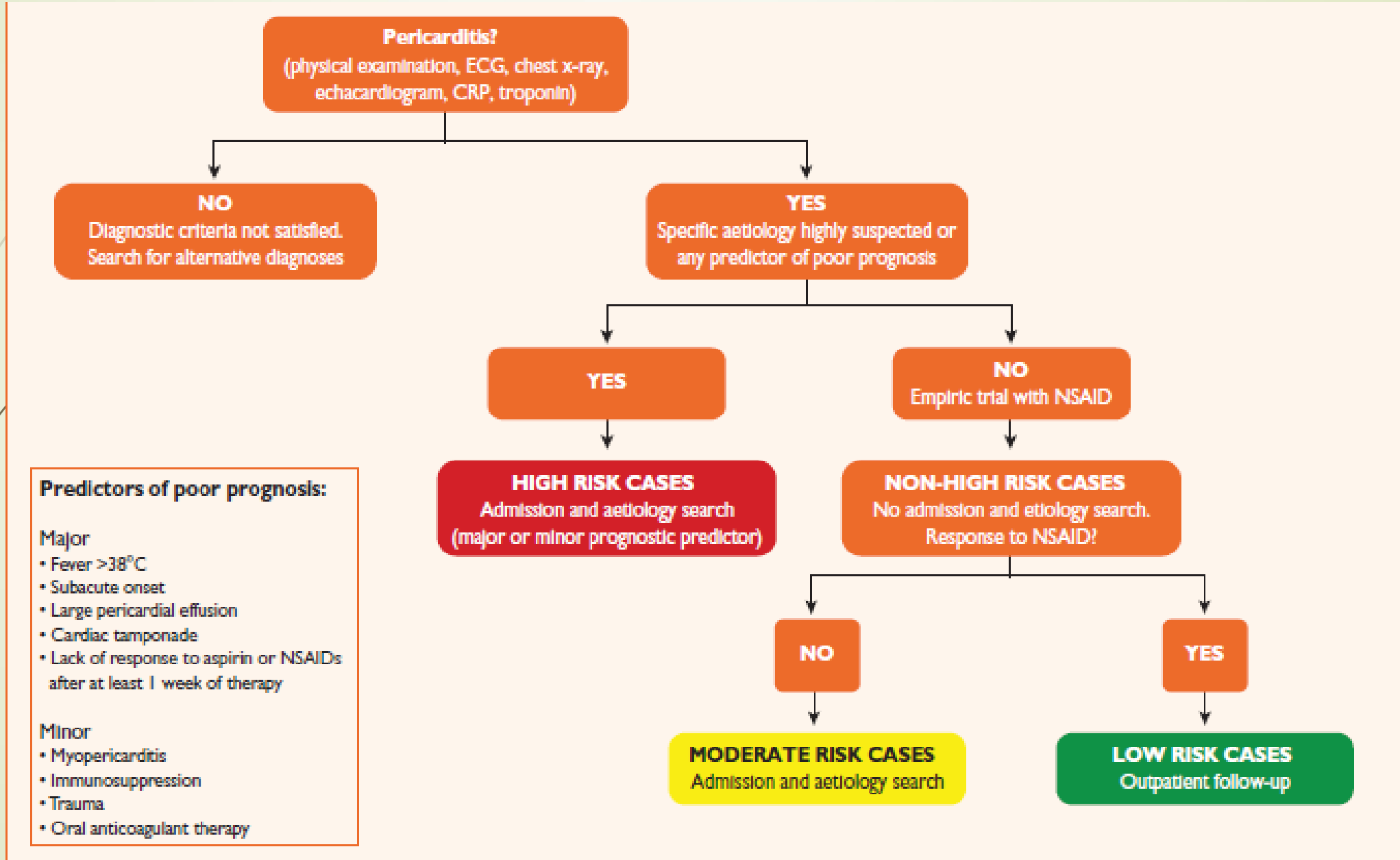
3.1.1 Clinical management and therapy (6)

- Colchicine is recommended at low, weight-adjusted doses to improve the response to medical therapy and prevent recurrences.
- Tapering of colchicine is not mandatory but may be considered to prevent persistence of symptoms and recurrence.
- Corticosteroids should be considered as a second option in patients with contraindications and failure of aspirin or NSAIDs because of the risk of favouring the chronic evolution of the disease and promoting drug dependence

3.1.1 Clinical management and therapy (7)

- In this case they are used with colchicine. If used, low to moderate doses (i.e. prednisone 0.2–0.5 mg/kg/day or equivalent) should be recommended instead of high doses (i.e. prednisone 1.0 mg/kg/day or equivalent).
- The initial dose should be maintained until resolution of symptoms and normalization of CRP, then tapering should be considered.

Proposed triage of pericarditis



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

3.1.2 Prognosis (1)

- Most patients with acute pericarditis (generally those with presumed viral or idiopathic pericarditis) have a good long-term prognosis.
- Cardiac tamponade rarely occurs in patients with acute idiopathic pericarditis, and is more common in patients with a specific underlying aetiology such as malignancy, TB or purulent pericarditis.
- Constrictive pericarditis may occur in <1% of patients with acute idiopathic pericarditis, and is also more common in patients with a specific aetiology.

3.1.2 Prognosis (2)

- The risk of developing constriction can be classified as low (<1%) for idiopathic and presumed viral pericarditis; intermediate (2–5%) for autoimmune, immunemediated and neoplastic aetiologies; and high (20–30%) for bacterial aetiologies, especially with TB and purulent pericarditis.
- Approximately 15–30% of patients with idiopathic acute pericarditis who are not treated with colchicine will develop either recurrent or incessant disease, while colchicine may halve the recurrence rate.

3.2 Incessant and chronic pericarditis

- The term ‘incessant’ has been adopted for cases with persistent symptoms without a clear-cut remission after the acute episode.
- The term ‘chronic’ generally refers—especially for pericardial effusions—to disease processes lasting >3 months.
- The Task Force suggests that the term ‘acute’ should be adopted for new-onset pericarditis, ‘incessant’ for pericarditis with symptoms persisting for >4–6 weeks (that is generally the approximate length of conventional anti-inflammatory therapy and its tapering), and ‘chronic’ for pericarditis lasting >3 months.

3.3 Recurrent pericarditis (1)

- Recurrent pericarditis is diagnosed with a documented first episode of acute pericarditis, a symptom-free interval of 4–6 weeks or longer and evidence of subsequent recurrence of pericarditis.
- Diagnosis of recurrence is established according to the same criteria as those used for acute pericarditis.
- CRP, computed tomography (CT) and/or CMR may provide confirmatory findings to support the diagnosis in atypical or doubtful cases showing pericardial inflammation through evidence of edema and contrast enhancement of the pericardium.

3.3 Recurrent pericarditis (2)

- The recurrence rate after an initial episode of pericarditis ranges from 15 to 30%, and may increase to 50% after a first recurrence in patients not treated with colchicine, particularly if treated with corticosteroids.
- In developed countries, the aetiology is often not identified in most immunocompetent patients, and it is generally presumed to be immune-mediated.
- A common cause of recurrence is inadequate treatment of the first episode of pericarditis.
- In up to 20% of cases, when additional virological studies have been conducted on pericardial fluid and tissue, a viral aetiology is detected.

3.3.1 Therapy (1)

- Recurrent pericarditis therapy should be targeted at the underlying aetiology in patients with an identified cause.
- Aspirin or NSAIDs remain the mainstay of therapy.
- Colchicine is recommended on top of standard anti-inflammatory therapy, without a loading dose and using weight-adjusted doses (i.e. 0.5 mg once daily if body weight is <70 kg or 0.5 mg twice daily if it is ≥70 kg, for ≥6 months) in order to improve the response to medical therapy, improve remission rates and prevent recurrences.

3.3.1 Therapy (2)

- In cases of incomplete response to aspirin/NSAIDs and colchicine, corticosteroids may be used, but they should be added at low to moderate doses to aspirin/NSAIDs and colchicine as triple therapy, not replace these drugs, in order to achieve better control of symptoms.

3.3.1 Therapy (3)

- Corticosteroids at low to moderate doses (i.e. prednisone 0.2–0.5 mg/kg/day) should be avoided if infections, particularly bacterial and TB, cannot be excluded and should be restricted to patients with specific indications (i.e. systemic inflammatory diseases, post-pericardiotomy syndromes, pregnancy) or NSAID contraindications (true allergy, recent peptic ulcer or gastrointestinal bleeding, oral anticoagulant therapy when the bleeding risk is considered high or unacceptable) or intolerance or persistent disease despite appropriate doses.

3.3.1 Therapy (4)

- Although corticosteroids provide rapid control of symptoms, they favour chronicity, more recurrences and side effects.
- If corticosteroids are used, their tapering should be particularly slow.
- A critical threshold for recurrences is a 10–15 mg/day dose of prednisone or equivalent.
- At this threshold, very slow decrements as small as 1.0–2.5 mg at intervals of 2–6 weeks are useful.
- In cases of recurrence, every effort should be made not to increase the dose or to reinstate corticosteroids.

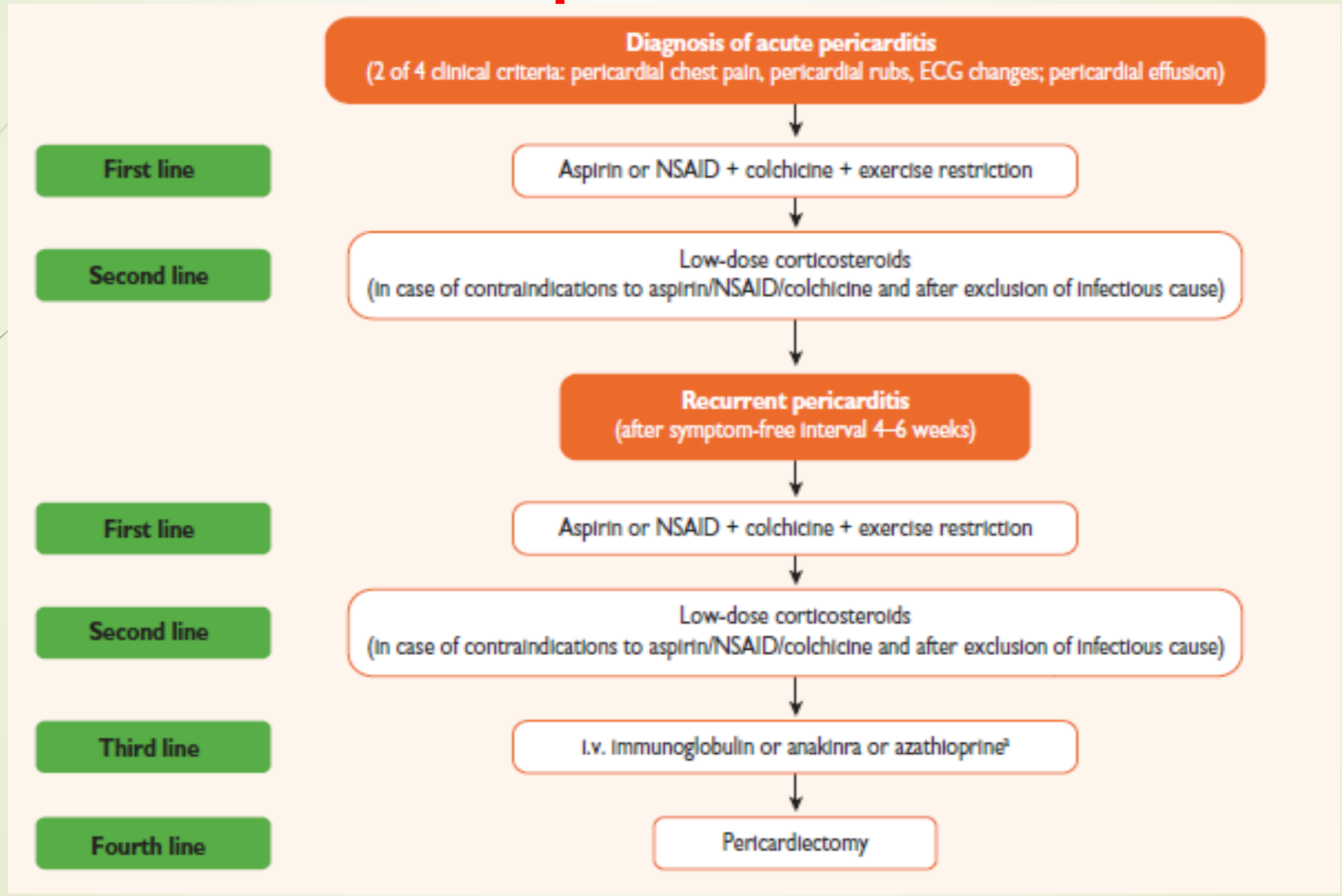
3.3.1 Therapy (7)

- An alternative effective approach to minimize systemic side effects related to corticosteroids may be intrapericardial administration of non-absorbable corticosteroids, but this technique requires further investigation.
- For those patients who require unacceptably high long-term doses of corticosteroids (e.g. prednisone 15–25 mg/day) or who do not respond to anti-inflammatory therapies, several drugs have been used, including azathioprine, IVIG (immunomodulatory but also anti-viral) and anakinra, a recombinant IL-1b receptor antagonist, but strong evidence-based data are lacking.

Commonly prescribed anti-inflammatory therapies for 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

Therapeutic algorithm for acute and recurrent pericarditis



3.4 Pericarditis associated with myocardial involvement (myopericarditis)

- The classical presentation is chest pain associated with other signs of pericarditis (pericardial rubs, ST-segment elevation and pericardial effusion) plus the elevation of markers of myocardial damage (i.e. troponins).
- Limited clinical data on the causes of myopericarditis suggest that viral infections are among the most common causes in developed countries, while other infectious causes are more common in developing countries (especially TB).

3.4 Pericarditis associated with myocardial involvement (myopericarditis)

- Many cases of myopericarditis are subclinical. In other patients, cardiac symptoms and signs are masked by pronounced systemic manifestations of infection or inflammation.
- In many cases, myopericarditis manifestations are preceded by or are sometimes concomitant with an acute respiratory illness (especially acute tonsillitis, pneumonia) or gastroenteritis.
- The increased sensitivity of troponin assays and contemporary widespread use of troponins has greatly increased the reported number of cases.

3.4.1 Definition and diagnosis (1)

- The diagnosis of predominant pericarditis with myocardial involvement, or 'myopericarditis', can be clinically established if patients with definite criteria for acute pericarditis show elevated biomarkers of myocardial injury (troponin I or T, CK-MB fraction) without newly developed focal or diffuse impairment of left ventricular function in echocardiography or CMR.
- The term myopericarditis indicates a primarily pericarditic syndrome with minor myocardial involvement, which describes the majority of combined pericarditis and myocarditis cases encountered in clinical practice.

3.4.1 Definition and diagnosis (4)

- In cases of pericarditis with suspected associated myocarditis, coronary angiography (according to clinical presentation and risk factor assessment) is recommended in order to rule out acute coronary syndromes.
- CMR is recommended for the confirmation of myocardial involvement and to rule out ischaemic myocardial necrosis in the absence of significant coronary disease; this has clinical and therapeutic implications.

3.4.2 Management (1)

- Empirical anti-inflammatory therapies (i.e. aspirin 1500–3000 mg/day) or NSAIDs (ibuprofen 1200–2400 mg/day or indomethacin 75–150 mg/day) are usually prescribed to control chest pain, while corticosteroids are prescribed as a second choice in cases of contraindication, intolerance or failure of aspirin/NSAIDs.

3.5 Pericardial effusion (1)

- The normal pericardial sac contains 10–50 ml of pericardial fluid as a plasma ultrafiltrate that acts as a lubricant between the pericardial layers.
- Any pathological process usually causes an inflammation with the possibility of increased production of pericardial fluid (exudate).
- An alternative mechanism of accumulation of pericardial fluid may be decreased reabsorption due to a general increase in systemic venous pressure as a result of congestive heart failure or pulmonary hypertension (transudate).

3.5 Pericardial effusion (2)

- Pericardial effusion may be classified according to its onset (acute or subacute vs. chronic when lasting >3 months), distribution (circumferential or loculated), haemodynamic impact (none, cardiac tamponade, effusive-constrictive), composition (exudate, transudate, blood, rarely air, or gas from bacterial infections) and, in particular, by its size based on a simple semiquantitative echocardiographic assessment as mild (>10 mm), moderate (10–20 mm) or large (>20 mm).

3.5 Pericardial effusion (3)

- A significant proportion of patients with pericardial effusion are asymptomatic and pericardial effusion constitutes an incidental and unexpected finding on X-ray or echocardiogram performed for other reasons.
- According to these series, many cases remain idiopathic in developed countries (up to 50%), while other common causes include cancer (10–25%), infections (15–30%), iatrogenic causes (15–20%) and connective tissue diseases (5–15%), whereas TB is the dominant cause in developing countries (>60%), where TB is endemic.

3.5 Pericardial effusion (3)

- In the setting of pericarditis with pericardial effusion, the prevalence of malignant or infectious aetiologies ranges from 15 to 50% depending on the published series.

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

3.5.1 Clinical presentation and diagnosis (2)

- Classic symptoms include dyspnoea on exertion progressing to orthopnoea, chest pain and/or fullness.

- Additional occasional symptoms due to local compression may include nausea (diaphragm), dysphagia (oesophagus), hoarseness (recurrent laryngeal nerve) and hiccups (phrenic nerve).

3.5.1 Clinical presentation and diagnosis (2)

- Non-specific symptoms include cough, weakness, fatigue, anorexia and palpitations, and reflect the compressive effect of the pericardial fluid on contiguous anatomic structures or reduced blood pressure and secondary sinus tachycardia.
- Fever is a non-specific sign that may be associated with pericarditis, either infectious or immune mediated (i.e. systemic inflammatory diseases).

3.5.1 Clinical presentation and diagnosis (3)

- Physical examination may be absolutely normal in patients without haemodynamic compromise.
- When tamponade develops, classic signs include neck vein distension with elevated jugular venous pressure at bedside examination, pulsus paradoxus and diminished heart sounds on cardiac auscultation in cases of moderate to large effusions.
- Pericardial friction rubs are rarely heard; they can usually be detected in patients with concomitant pericarditis.

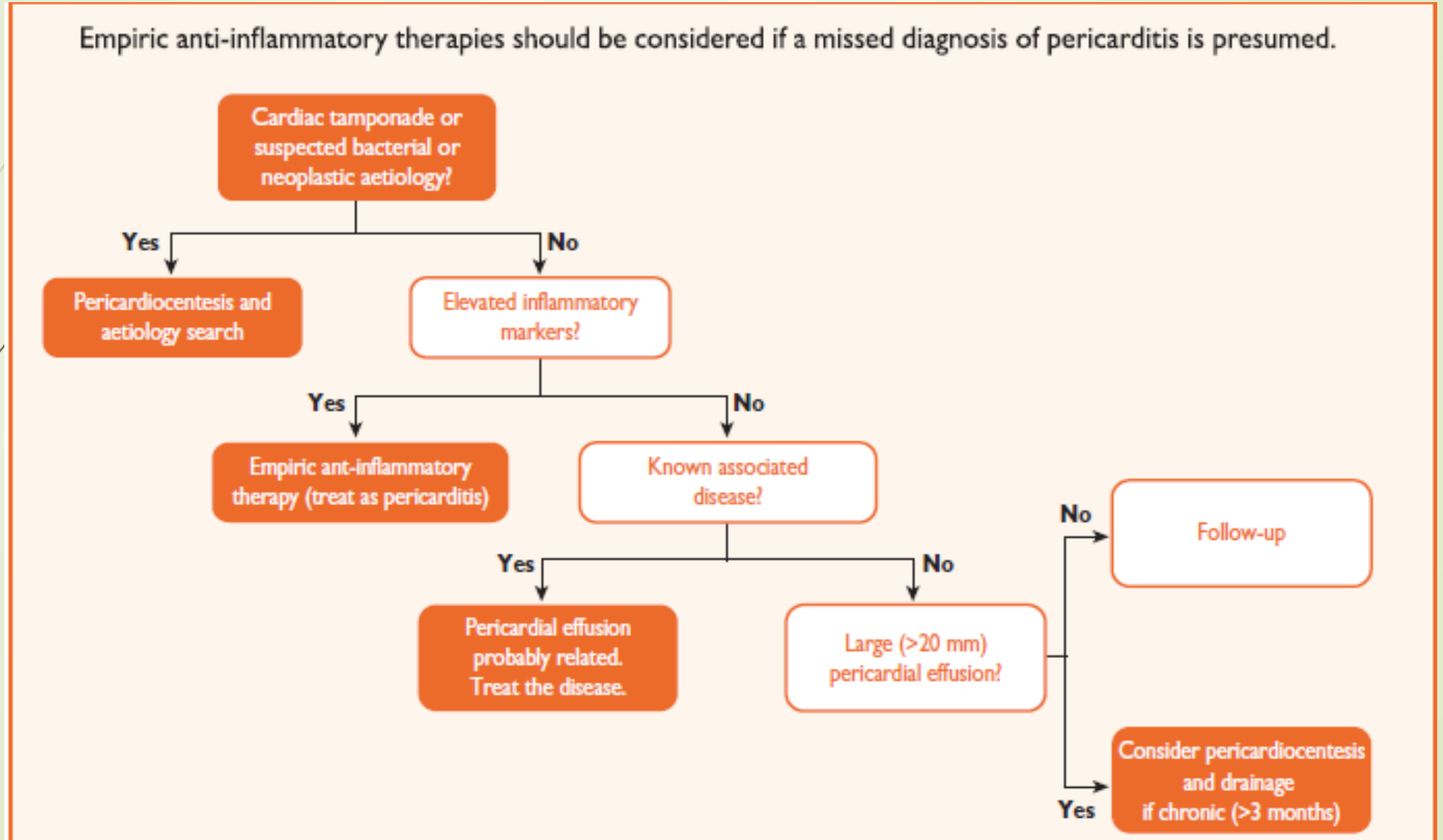
3.5.1 Clinical presentation and diagnosis (4)

- The diagnosis of pericardial effusion is generally performed by echocardiography, which also enables semiquantitative assessment of the pericardial effusion size and its haemodynamic effects.
- Although echocardiography remains the primary diagnostic tool for the study of pericardial diseases because of its widespread availability, portability and limited costs, CT and CMR provide a larger field of view, allowing the detection of loculated pericardial effusion and pericardial thickening and masses, as well as associated chest abnormalities.

3.5.2 Triage and management (2)

- Cardiac tamponade without inflammatory signs is associated with a higher risk of a neoplastic aetiology (likelihood ratio 2.9), whereas a severe effusion without cardiac tamponade and inflammatory signs is usually associated with a chronic idiopathic aetiology (likelihood ratio 20).
- In chronic effusion with no definite aetiology, there are no data on non-steroidal anti-inflammatory drugs (NSAIDs), colchicine and corticosteroids.
- If markers of inflammation are elevated, a trial of NSAIDs and/or colchicine and/or low-dose corticosteroids may be tried.

A simplified algorithm for pericardial effusion triage and management



3.5.3 Therapy (1)

- Therapy of pericardial effusion should be targeted at the aetiology as much as possible.
- In about 60% of cases, the effusion is associated with a known disease and the essential treatment is that of the underlying disease.
- When pericardial effusion is associated with pericarditis, management should follow that of pericarditis.
- When a pericardial effusion becomes symptomatic without evidence of inflammation or when empiric anti-inflammatory drugs are not successful, drainage of the effusion should be considered.

3.5.4 Prognosis and follow-up (1)

- The prognosis of pericardial effusion is essentially related to the aetiology.
- The size of the effusion is correlated with the prognosis, as moderate to large effusions are more common for specific aetiologies such as bacterial and neoplastic conditions.

3.5.4 Prognosis and follow-up (2)

- Large idiopathic chronic effusions (>3 months) have a 30–35% risk of progression to cardiac tamponade.
- Also, subacute (4–6 weeks) large effusions not responsive to conventional therapy and with echocardiographic signs of collapse of the right chambers may have an increased risk of progression according to some authors, who recommend preventive drainage in such cases.

3.5.4 Prognosis and follow-up (3)

- A mild idiopathic effusion (<10 mm) is usually asymptomatic, generally has a good prognosis and does not require specific monitoring.
- Moderate to large effusions (<10 mm) may worsen, and especially severe effusions may evolve towards cardiac tamponade in up to one-third of cases.
- For idiopathic moderate effusions, an appropriate timing for echocardiographic follow-up may be an echocardiogram every 6 months.

3.6 Cardiac tamponade (1)

- Cardiac tamponade is a life-threatening, slow or rapid compression of the heart due to the pericardial accumulation of fluid, pus, blood, clots or gas as a result of inflammation, trauma, rupture of the heart or aortic dissection.
- Clinical signs in a patient with cardiac tamponade include tachycardia, hypotension, pulsus paradoxus, raised jugular venous pressure, muffled heart sounds, decreased electrocardiographic voltage with electrical alternans and an enlarged cardiac silhouette on chest X-ray with slow-accumulating effusions.

3.6 Cardiac tamponade (2)

- A key diagnostic finding is pulsus paradoxus (conventionally defined as an inspiratory decrease in systolic arterial pressure of >10 mmHg during normal breathing).
- Pulsus paradoxus is due to exaggerated ventricular interdependence occurring in cardiac tamponade, when the overall volume of cardiac chambers becomes fixed and any change in the volume of one side of the heart causes the opposite changes in the other side (i.e. inspiratory increase of venous return and right chambers with decreased volume of left chambers and reduced systemic blood pressure).

3.6 Cardiac tamponade (5)

- In a patient with clinical suspicion of cardiac tamponade, several diagnostic tools are required.
- An ECG may show signs of pericarditis, with especially low QRS voltages and electrical alternans.
- Both ECG signs are generally considered to be an expression of the damping effect of pericardial fluid and swinging heart.
- Echocardiography is the single most useful diagnostic tool to identify pericardial effusion and estimate its size, location and degree of haemodynamic impact.

3.6 Cardiac tamponade (6)

- The treatment of cardiac tamponade involves drainage of the pericardial fluid, preferably by needle pericardiocentesis, with the use of echocardiographic or fluoroscopic guidance, and should be performed without delay in unstable patients.
- Alternatively, drainage is performed by a surgical approach, especially in some situations such as purulent pericarditis or in urgent situations with bleeding into the pericardium.

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

3.7 Constrictive pericarditis (1)

- Constrictive pericarditis can occur after virtually any pericardial disease process, but only rarely follows recurrent pericarditis.
- The risk of progression is especially related to the aetiology: low (<1%) in viral and idiopathic pericarditis, intermediate (2–5%) in immune-mediated pericarditis and neoplastic pericardial diseases and high (20–30%) in bacterial pericarditis, especially purulent pericarditis.
- A few large historical series of patients with constrictive pericarditis have been described from tertiary referral centres (Stanford, Mayo Clinic, Cleveland Clinic and Groote Schuur Hospital) reporting cases after pericardiectomy.

3.7 Constrictive pericarditis (2)

- The most common reported causes in developed countries were idiopathic or viral (42–49%), post-cardiac surgery (11–37%), postradiation therapy (9–31%) (mostly for Hodgkin's disease or breast cancer), connective tissue disorder (3–7%), post-infectious causes (TB or purulent pericarditis in 3–6%) and miscellaneous causes (malignancy, trauma, drug-induced, asbestosis, sarcoidosis, uremic pericarditis in ,10%). TB is now only a rare cause of constrictive pericarditis in developed countries, while it is a major cause in developing countries.
- However, this disorder may be increasing among immigrants from underdeveloped nations and patients with HIV infection.

3.7.1 Clinical presentation (2)

- The delay between the initial pericardial inflammation and the onset of constriction is variable and is possibly a direct evolution from subacute/chronic pericarditis to constrictive pericarditis.
- Venous congestion, hepatomegaly, pleural effusions and ascites may occur.
- Haemodynamic impairment of the patient can be additionally aggravated by a systolic dysfunction due to myocardial fibrosis or atrophy in more advanced cases

Constrictive pericarditis vs. restrictive cardiomyopathy: a brief overview of features for the differential diagnosis

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.

3.7.3 Therapy (1)

- Although the mainstay of treatment of chronic permanent cases is surgery, medical therapy may have a role in at least three conditions.
- First, medical therapy of specific etiologies (i.e. tuberculous pericarditis) may be useful to prevent the progression to constriction.
- Antituberculosis antibiotics may significantly reduce the risk of constriction from >80% to <10%.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.1 Chest X-ray

- Although chest X-ray can detect pericardial calcifications, presenting as a curvilinear density at the extreme margin of the silhouette, particularly on the lateral view, other techniques (i.e. echocardiography, CT) yield much greater accuracy in assessing the heart and lungs, providing information with regard to cardiac size and the presence of pulmonary pathology (e.g., pulmonary congestion, pneumonia, TB, lung cancer), pleural effusion and hilar and mediastinal enlargement.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.2 Echocardiography

- **Transthoracic echocardiography is the first-line imaging test in patients with suspected pericardial disease**, because it accurately detects pericardial effusion and cardiac tamponade, as well as ventricular dysfunction due to myocardial involvement.
- **Patients with purely fibrinous acute pericarditis may have a normal echocardiogram**, the presence of a pericardial effusion is consistent with acute pericarditis and is one of the criteria for its diagnosis.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.2 Echocardiography

- **Echocardiography may help to differentiate acute pericarditis from myocardial ischemia by excluding wall motion abnormalities consistent with coronary flow distribution in the setting of patients with acute chest pain.**
- **However, 5% of patients with acute pericarditis and myocardial involvement may demonstrate wall motion abnormalities.**

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.3 Computed tomography

- CT should be regarded as a valuable complementary imaging modality to echocardiography.
- **CT is the most accurate technique to image calcified tissue.**
- Current multidetector CT scanners combine acquisition speed, high contrast and spatial resolution with volumetric scanning to provide excellent anatomical detail of the heart and pericardium.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.3 Computed tomography

- The anatomical region of interest covered by CT can be limited to the heart and pericardium ('card CT'), although in patients with neoplastic, inflammatory or aortic disease it may encompass the chest entirely and possibly also include the abdomen and pelvis.
- Low-radiation cardiac CT is feasible using prospective electrocardiographic triggering.
- In patients with neoplastic disease, pericardial involvement may occur by direct tumour invasion or metastatic spread. CT is important in treatment planning and patient follow-up.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.4 Cardiac magnetic resonance

- Over the years, CMR has shifted from a morphologic imaging modality towards a comprehensive one, allowing visualization and tissue characterization of the pericardium (and heart) in patients with pericardial disease and appraisal of the consequences of pericardial abnormalities on cardiac function and filling patterns.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.4 Cardiac magnetic resonance

- In patients with congenital pericardial pathology and pericardial malignancy, CMR shares the advantages of CT, but allows better tissue characterization and the possibility of evaluating the functional consequences.
- Moreover, novel techniques, such as diffusion-weighted and dynamic contrast-enhanced magnetic resonance imaging, open perspectives for improved tissue characterization in patients with pericardial tumors.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.5 Nuclear medicine

- In selected cases, positron emission tomography (PET) alone, or preferably in combination with CT (PET/CT), can be indicated to depict the metabolic activity of pericardial disease.
- Pericardial uptake of 18F-fluorodeoxyglucose (FDG) tracer in patients with solid cancers and lymphoma is indicative of (malignant) pericardial involvement, thus providing essential information on the diagnosis, staging and assessment of the therapeutic response.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.5 Nuclear medicine

- The uptake is usually intense and often associated with a focal soft tissue mass.
- PET/CT is also of value in identifying the nature of inflammatory pericarditis. In particular, tuberculous pericarditis yields higher FDG uptakes than idiopathic forms.
- However, differentiation between benign and malignant pericardial disease, as well as differentiation between physiological and pathological cardiac FDG uptake by PET/CT, remains challenging.

4. Multimodality cardiovascular imaging and diagnostic work-up

4.1.6 Cardiac catheterization

- Cardiac catheterization is not routinely used for the diagnosis of pericardial disease, as current non-invasive techniques are usually able to solve the differential diagnosis of a patient with the suspicion of heart disease involving the pericardium.

- However, right heart catheterization may be useful in certain circumstances.

4.2 Proposal for a general diagnostic work-up (4)

- Major risk factors include fever >38 C, subacute course, large pericardial effusion (diastolic echo-free space >20 mm in width) or cardiac tamponade and failure of aspirin or NSAIDs.
- Minor risk factors are pericarditis associated with myocarditis, immunodepression, trauma and oral anticoagulant therapy.

5. Specific aetiologies of pericardial syndromes

5.1 Viral pericarditis

- Most cases of acute pericarditis in developed countries are based on viral infections or are autoreactive.
- Acute viral pericarditis often presents as a self-limited disease, with most patients recovering without complications.
- However, as a consequence of acute viral pericarditis, cardiac tamponade, recurrent pericarditis and, more rarely, constrictive pericarditis may also develop.

5. Specific aetiologies of pericardial syndromes

5.1 Viral pericarditis

- Cardiotropic viruses can cause pericardial and myocardial inflammation via direct cytolytic or cytotoxic effects and/or via T and/or B cell–driven immune-mediated mechanisms.
- Persistence of viral nucleic acid without virus replication in the peri(myo)cardium is known to sustain ongoing inflammation and effusions via (auto)immune processes directed against specific cardiac proteins by molecular mimicry.

5. Specific aetiologies of pericardial syndromes

5.1 Viral pericarditis

- In contrast, serological tests were found to be futile in the diagnosis of viral pericarditis.
- Whereas no up-regulation of pro-inflammatory cytokine expression is noted in the serum, TNF-a, vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), IL-6, IL-8 and interferon-gamma (IFN-g) are increased in the pericardial effusions of patients with pericarditis, indicating the presence of local inflammatory reactions.

5. Specific aetiologies of pericardial syndromes

5.1 Viral pericarditis

- DNA of varicella zoster virus, herpes simplex virus and adenoviruses is only rarely detected in pericarditis patients.
- Cytomegalovirus (CMV)-associated pericarditis is mainly found in immunocompromised and HIV patients.
- In developing countries with a delayed rollout of antiretroviral therapy, HIV-associated inflammatory reactions (often related to TB) of the pericardium and myocardium are common complications.