

# Pericardial Diseases (Diagnosis and Management of)

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

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# Guidelines on the Diagnosis and Management of Pericardial Diseases

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# Main Topics

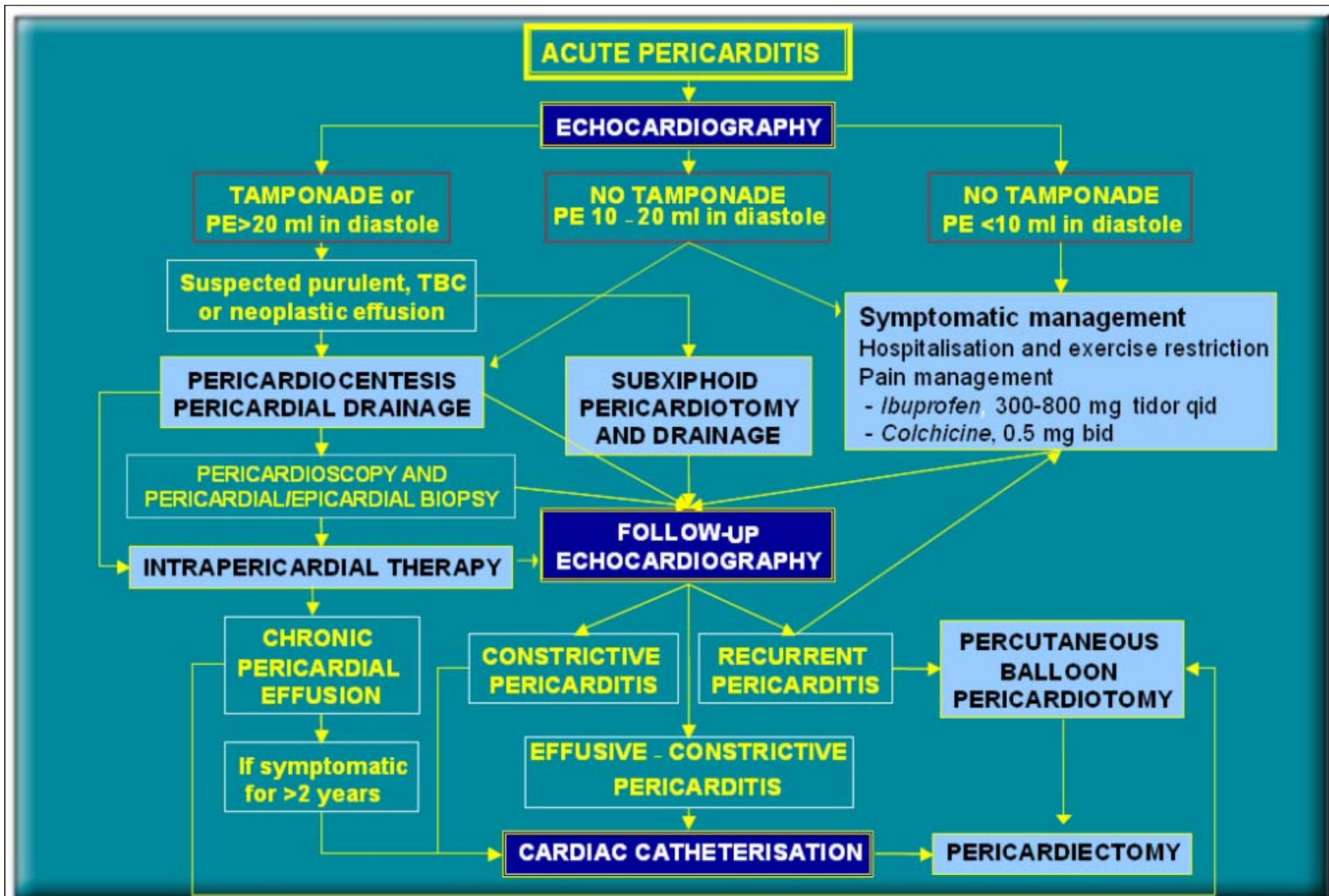
- Acute pericarditis
- Pericardial effusion and cardiac tamponade
- Constrictive pericarditis
- Viral pericarditis
- Bacterial pericarditis
- Pericarditis in renal failure
- Autoreactive pericarditis and pericardial involvement in systemic autoimmune diseases
- The post-cardiac injury syndrome
- Postinfarction pericarditis
- Traumatic pericardial effusion
- Haemopericardium in aortic dissection
- Neoplastic pericarditis
- Pericardial effusion in pregnancy
- Drug- and toxin-related pericardial disease

# Level of Evidence

- **Level of evidence A:**  
Multiple randomized clinical trials or meta-analyses.
- **Level of evidence B:**  
A single randomized trial or large non-randomized studies.
- **Level of evidence C:**  
Consensus opinion of the experts.

# Classes of Recommendations

- **Class I:** evidence and/or general agreement that a given procedure or treatment is useful and effective.
- **Class II:** conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
  - **Class IIa:** Weight of evidence/opinion is in favour of usefulness/efficacy.
  - **Class IIb:** Usefulness/efficacy is less well established by evidence/opinion.
- **Class III:** evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.



# Acute Pericarditis

Diagnostic pathway and sequence of performance  
(level of evidence B for all procedures)

## Technique

### Obligatory (class I)

- Auscultation
- ECG
- Echocardiography
- Blood analyses
- Chest X-ray



# Acute Pericarditis

Diagnostic pathway and sequence of performance  
(level of evidence B for all procedures)

**Mandatory in Tamponade (class I)**

**Optional in large/recurrent effusions or if previous tests inconclusive (class IIa) in small effusions (class IIb) :**  
Pericardocentesis and drainage

**Optional or if previous tests inconclusive (class IIa)**

CT

MRI

Pericardioscopy, Pericardial biopsy

# Diagnosis of Cardiac Tamponade

## Diagnostic Procedure

- Clinical presentation
- Precipitating factors
- ECG
- Chest X-ray
- M-mode/2D echocardiogram
- Doppler
- M-mode colour Doppler
- Cardiac catheterisation
- RV/LV angiography
- Coronary angiography
- Computer tomography

# Acute Pericarditis

## Symptomatic management

- Exercise restriction
- **Hospitalisation** to determine the aetiology and observe for tamponade and the effect of treatment.
- **Pain management**
  - NSAIDs are the mainstay (level of evidence B, class I)
  - Ibuprofen is preferred for its rare side-effects, favourable impact on the coronary flow, and the large dose range (300-800 mg every 6-8 h)
  - Aspirin 300-600 mg every 4-6 h
  - Indomethacin should be avoided in elderly patients (flow reduction in the coronaries).
  - Gastrointestinal protection must be provided.

# Recurrent Pericarditis

## Treatment and prevention of recurrences

- **Colchicine** (0.5 mg bid) added to an NSAID or as monotherapy is well tolerated with fewer side effects than NSAIDs (level of evidence B, class IIa).
- **Percutaneous balloon pericardiotomy** - in recurrences resistant to medical treatment (level of evidence B, class IIb).
- **Corticosteroids** should be used only in patients with poor general condition or in frequent crises (level of evidence C, class IIa). The recommended regimen is: prednisone 1-1.5 mg/kg, for at least one month. If patients do not respond adequately, azathioprine (75-100 mg/day) or cyclophosphamide can be added.
- **Pericardiectomy** - only in frequent and highly symptomatic recurrences resistant to medical treatment (level of evidence B, class IIa).

# Pericardial Effusion and Cardiac Tamponade

## Indications for Pericardiocentesis

### Class I

- Cardiac tamponade
- Effusions >20 mm in echocardiography (diastole)
- Suspected purulent or tuberculous pericardial effusion

### Class IIa

- Effusions 10-20 ml in echocardiography in diastole for diagnostic purposes other than purulent pericarditis or tuberculosis (pericardial fluid and tissue analyses, pericardioscopy, and epicardial/pericardial biopsy)
- Suspected neoplastic pericardial effusion

# Pericardial Effusion and Cardiac Tamponade

## Indications for Pericardiocentesis

### Class IIb

- Effusions <10 ml in echocardiography in diastole for diagnostic purposes other than purulent, neoplastic or tuberculous pericarditis.

### Class III (contraindications)

- Aortic dissection
- Relative contraindications include uncorrected coagulopathy, anticoagulant therapy, thrombocytopenia  $<50000/\text{mm}^3$ , small, posterior, and loculated effusions.
- If the diagnosis can be made otherwise or the effusions are small and resolving under anti-inflammatory treatment.

# Pericardial Effusion and Cardiac Tamponade

## How to Perform Pericardiocentesis

- Obtain current and reliable echocardiography findings before the procedure.
- Pericardiocentesis guided by fluoroscopy is performed in the cardiac catheterization laboratory in local anaesthesia.
- The subxiphoid approach has been used most commonly, with a long needle directed towards the left shoulder at a 30° angle to the skin.

# Pericardial Effusion and Cardiac Tamponade

## How to Perform Pericardiocentesis

Pericardiocentesis guided by echocardiography is performed in intensive care unit or in operating theatre.

- Echocardiography should identify the shortest route where the pericardium can be entered intercostally (usually in the sixth or seventh rib space in the anterior axillary line).
- Intercostal arteries should be avoided.



# Pericardial Effusion and Cardiac Tamponade

## How to Perform Pericardiocentesis

- Strict aseptic conditions, ECG, and blood pressure monitoring have to be provided.
- Direct ECG monitoring from the puncturing needle is not an adequate safeguard.
- Right-heart catheterization can be performed simultaneously, allowing exclusion of constriction.

# Pericardial Effusion and Cardiac Tamponade

## How to Perform Pericardiocentesis

- The needle approaches pericardium slowly.
- Steady manual aspiration is essential.
- Stop the needle as soon as the effusion is aspirated.
- Exchange for soft J-tip guidewire and after dilatation for a multi-holed pigtail catheter.
- Drain the fluid in  $<1$  l steps to avoid the acute right-ventricular dilatation.
- Perform prolonged pericardial drainage (several days) until  $<25$  ml/day.

# Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

## CLASS I

- Suspected malignant effusion: CYTOLOGY
- Suspected tuberculous effusion: ACID-FAST BACILLI STAINING, mycobacterium CULTURE (preferably with radiometric growth detection e.g., BACTEC-460), adenosine deaminase, IFN-gamma, pericardial lysozyme, PCR analyses.
- Suspected bacterial infection: at least three cultures of pericardial fluid for aerobes and anaerobes as well as three blood cultures. Positive cultures should be followed by sensitivity tests for antibiotics.

# Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

## CLASS IIa

- **Viral vs. autoreactive pericarditis:** PCR analyses for cardiotropic viruses.
- **Suspected neoplastic pericarditis:** Tumour markers (CEA, AFP, CA 125, CA 72-4, CA 15-3, CA 19-9, CD-30, CD-25...).
- **Benign reactive mesothelial cells vs. adenocarcinoma:** Combination of epithelial membrane antigen, CEA, and vimentin immunocytochemical staining.

# Pericardial Effusion Analyses

Should be ordered according to the clinical presentation

## CLASS IIb

### Exudate vs transudate:

- Pericardial fluid specific gravity ( $>1015$ )
- Protein level ( $>3.0$  g/dl; fluid/serum ratio  $>0.5$ )
- LDH ( $>200$ mg/dl; serum/fluid  $>0.6$ ), and
- Glucose (exudates vs. transudates =  $77.9 \pm 41.9$  vs.  $96.1 \pm 50.7$  mg/dl)

# Constrictive pericarditis vs. Restrictive cardiomyopathy

## Diagnostic Procedure

- Clinical presentation
- ECG
- Chest X-ray
- M-mode/2D echocardiogram
- Doppler
- TEE
- CT/MRI
- Cardiac catheterization
- RV/LV angiography
- Coronary angiography

# Constrictive pericarditis vs. Restrictive cardiomyopathy

## Methods

- Physical findings
- ECG
- Chest radiography
- 2D-echocardiography
- Doppler studies

**Mitral inflow, pulmonary vein, tricuspid inflow, hepatic veins,  
inferior vena cava, colour M-mode, mitral annular motion**

- Tissue Doppler, echocardiography
- Cardiac catheterization
- EMB
- CT/MRI

# Management of Constrictive Pericarditis

- **Pericardiectomy** is the only treatment for permanent constriction.
- The indications are based upon clinical symptoms, echocardiography findings, CT/MRI, and heart catheterization.
- **Antero-lateral thoracotomy**
- **Median sternotomy** (faster access to the aorta and right atrium for extracorporeal circulation).
- **Primary installation of cardiopulmonary bypass is not recommended** (diffuse bleeding following systemic heparinisation).
- Areas of strong calcification or dense scarring may be left as islands to avoid major bleeding.



# Pericardiectomy for Constrictive Pericarditis

## Major complications

- Acute perioperative cardiac insufficiency (should be treated by fluid substitution and catecholamines, high doses of digitalis, and intraaortic balloon pump in most severe cases).
- Ventricular wall rupture.
- Mortality (in properly selected cases 6-12%, but >40% in unselected patients).

## Long term results

- If indication for surgery was established early, long-term survival after pericardiectomy corresponds to that of the general population.

# Pathoanatomical forms of Constrictive Pericarditis



Annular form



Left-sided form



Right sided form



Global form



Global form with  
MYOCARDIAL ATROPHY



Global form with  
MYOCARDIAL FIBROSIS

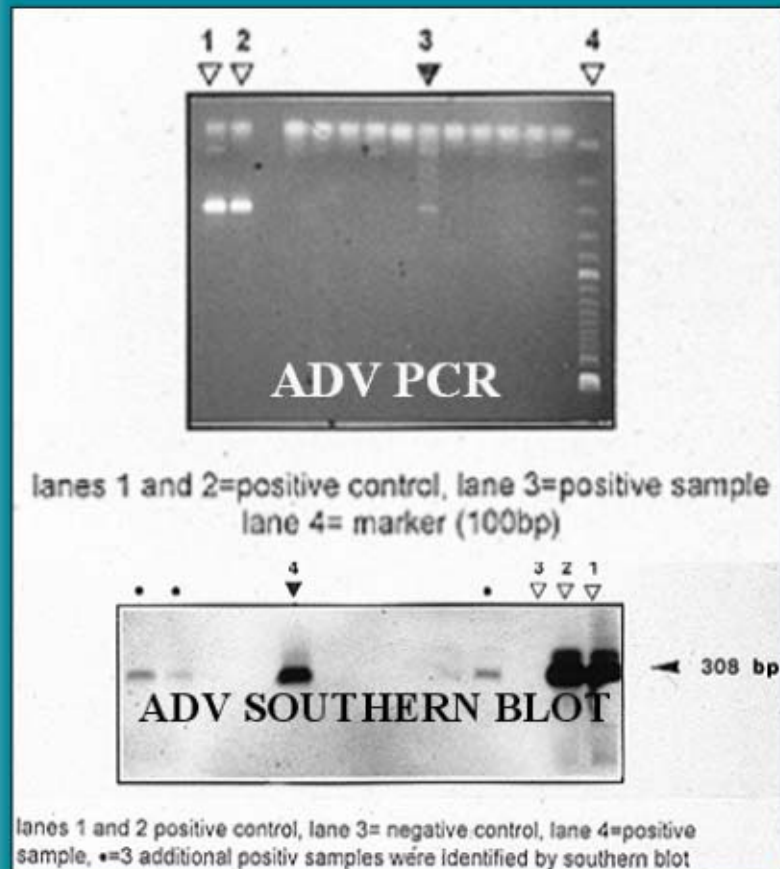
**Very high mortality in pericardiectomy**

Rienzi et al. J Thorac Imaging 1993

- Cardiac mortality and morbidity at pericardiectomy is mainly caused by the pre-surgically unrecognised presence of myocardial atrophy or myocardial fibrosis.

- Exclusion of patients with **extensive myocardial fibrosis and/or atrophy** significantly reduce the mortality rate for pericardiectomy.

# Diagnosis of Viral Pericarditis



- The diagnosis of viral pericarditis is not possible without the evaluation of pericardial effusion and/or pericardial/epicardial tissue, preferably by PCR or in-situ hybridisation (level of evidence B, class IIa).
- A four-fold rise in serum antibody levels (two samples within 3-4 weeks) is suggestive but not diagnostic for viral pericarditis (level of evidence B, class IIb).

# Management of Viral Pericarditis

- In most cases the disease is self-limiting and no specific treatment is necessary.
- Symptomatic treatment for chest pain, and eventual rhythm disorders and congestive heart failure is indicated.
- In patients with chronic or recurrent symptomatic pericardial effusion and confirmed viral infection the following specific treatment is under investigation:
  - **CMV pericarditis**: hyperimmunoglobulin - 1 time per day 4ml/kg on day 0, 4, and 8; 2 ml/kg on day 12 and 16;
  - **Coxsackie B pericarditis**: Interferon alpha or beta 2,5 Mio. IU/m<sup>2</sup> surface area s.c. 3 x per week;
  - **Adenovirus and parvovirus B19 pericarditis**: immunoglobulin treatment: 10 g intravenously at day 1 and 3 for 6-8 hours.

# Management of Viral Pericarditis

- Treatment is **symptomatic**, while in large effusions and cardiac tamponade pericardiocentesis is necessary.
- Persons with HIV infection and tuberculosis usually can be treated with standard anti-tuberculous regimens with good results, although in some cases, prolonged therapy may be warranted.
- Since treatment of HIV may require protease inhibitors or non-nucleoside reverse transcriptase inhibitors use of **rifampicin may be precluded**.
- The use of **corticoid therapy as an adjunct to tuberculostatic treatment is allowed** (level of evidence A, class I).

# Diagnosis of Bacterial Pericarditis

- Percutaneous pericardiocentesis must be promptly performed if bacterial pericarditis is suspected.
- Pericardial fluid should undergo Gram, acid-fast, and fungal staining, followed by cultures for aerobes, anaerobes, and *M. tuberculosis* (preferably with radiometric growth detection).
- **Drug sensitivity testing is essential for treatment selection.**
- PCR analyses, increased levels of adenosine deaminase (>40 IU/L), interferon-gamma (>200 pg/L), or pericardial lysozyme (>6.5 microg/dL) are highly sensitive and specific for diagnosis of tuberculous effusion, but are **cost-effective only if the pre-test probability is high** (populations with high incidence of tuberculosis).

# Management of Bacterial Pericarditis

- Urgent pericardial drainage, combined with intravenous antibiotic therapy (e.g. vancomycin 1 g bid, ceftriaxone 1-2 g bid, and ciprofloxacin 400 mg/day) is mandatory in purulent pericarditis.
- In selecting antimicrobial therapy the ability of potential agents to kill the causative organism as well as the minimum inhibitory concentration (**MIC** - the lowest concentration that inhibits growth) and minimum bactericidal concentration (**MBC** - the lowest concentration that decreases a standard inoculum of organisms 99.9% during 24 hours) need to be considered.
- Irrigation with **urokinase** or **streptokinase**, using large catheters, may liquefy the purulent exudate, but open surgical drainage is preferable.

# Management of Tuberculous Pericarditis

- **The initial treatment:**
  - Isoniazid 300 mg/day
  - Rifampicin 600 mg/day
  - Pyrazinamide 15-30 mg/kg/day
  - Ethambutol 15-25 mg/kg/day
  - Prednisone (1-2 mg/kg/day) may be given simultaneously with antituberculous therapy for 5-7 days and progressively reduced to discontinuation in 6-8 weeks.
- **After two months** most patients can be **switched to two-drug regimen** (isoniazid and rifampicin) for the **total of six months**.



# Management of Tuberculous Pericarditis

- **Respiratory isolation** if active pulmonary or laryngeal tuberculosis is also suspected.
- Patients are considered to be noninfectious if they have a **clinical response to anti-tuberculous chemotherapy and three consecutive smear-negative sputum samples** that were collected on different days.
- **Pericardiectomy** is reserved for recurrent effusions or continued elevation of central venous pressure after 4-6 weeks of antituberculous and corticosteroid therapy.

# Pericarditis in Renal Failure

## Diagnosis

Chest pain, pericardial friction rub and pericardial effusion in a patient with advanced renal failure (acute or chronic) before dialysis has been instituted or in patients on maintenance chronic haemodialysis or peritoneal dialysis.

- Due to autonomic impairment in uremic patients, heart rate may remain slow (60–80 beats/min) during tamponade, despite fever and hypotension.
- The ECG does not show the typical diffuse ST/T wave elevations observed with other causes of acute pericarditis due to the lack of the myocardial inflammation.

# Pericarditis in Renal Failure

## Management

Frequent (heparin-free) haemodialyses.

- **Peritoneal dialysis**, which does not require heparinisation, may be therapeutic in pericarditis resistant to haemodialysis, or if heparin-free haemodialysis cannot be performed.
- NSAIDs and systemic corticosteroids have limited success when intensive dialysis is ineffective.
- Cardiac tamponade and large chronic effusions resistant to dialysis must be treated with **pericardiocentesis** (level of evidence B, class IIa).
- Large, non-resolving symptomatic effusions should be treated with **intrapericardial instillation of corticosteroids** (triamcinolone hexacetonide 50 mg every 6 hours for 2 to 3 days).
- **Pericardiectomy** is indicated only in refractory, severely symptomatic patients.

# Autoreactive Pericarditis

## Diagnosis

Pericardial effusion with  $>5000/\text{mm}^3$  lymphocytes and mononuclear cells (autoreactive lymphocytic), or antibodies against heart muscle tissue (autoreactive antibody-mediated).

- Inflammation in epicardial/endomyocardial biopsies by  $\geq 14$  cells/ $\text{mm}^2$ .
- Exclusion of active viral infection both in pericardial effusion and endomyocardial/epimyocardial biopsies (no virus isolation, no IgM-titer against cardiotropic viruses in pericardial effusion, and negative PCR for major cardiotropic viruses).
- TBC, *B. burgdorferi*, *C. pneumoniae*, and other bacterial infection excluded by PCR and/or cultures.
- Neoplastic infiltration absent in pericardial effusion and biopsy samples.
- Exclusion of systemic, metabolic disorders, and renal failure.

# Autoreactive Pericarditis and Pericardial Involvement in Systemic Autoimmune Diseases

## Management

- Intrapericardial treatment with triamcinolone plus colchicine per os 0.5 mg bid for six months is highly efficient with rare side effects (level of evidence B, class IIa).
- In systemic autoimmune diseases intensified treatment of the underlying disease and symptomatic management are indicated (evidence level B, class I).
- For tapering of prednisone, ibuprofen or colchicine should be introduced early.

# Postpericardiotomy Syndrome

## Diagnosis

- Chest pain, pericardial friction rub, ECG changes, PE within days to months after cardiac, pericardial injury or both.

## Management

- Symptomatic treatment as in acute pericarditis.
- In refractory forms long term (3-6 months) oral corticoids or preferably pericardiocentesis and intrapericardial instillation of triamcinolone (300 mg/m<sup>2</sup>).
- Redo surgery and pericardiectomy are very rarely needed.
- Primary prevention with short-term perioperative steroid treatment or colchicine is under investigation.
- Warfarin administration in pts with early postoperative PE imposes greatest risk.

# Postinfarction Pericarditis

(Pericarditis epistenocardica and Dressler's syndrome)

## Diagnosis

- Detection of PE after acute myocardial infarction.
- ECG changes are often overshadowed by myocardial infarction changes.
- Postinfarction PE >10 mm is most frequently associated with haemopericardium, and two thirds of these patients may develop tamponade/free wall cardiac rupture.

# Postinfarction Pericarditis

(Pericarditis epistenocardica and Dressler's syndrome)

## Management

- **Hospitalisation** to observe for tamponade, differential diagnosis, and adjustments of treatment is needed.
- **Ibuprofen**, which increases coronary flow, is the agent of choice.
- **Aspirin**, up to 650 mg every 4 hours for 2 to 5 days has also been successfully applied (other nonsteroidal agents risk thinning the infarction zone).
- **Corticosteroid therapy** can be used for refractory symptoms only but could **delay myocardial infarction healing**.
- In cardiac rupture, **urgent surgical treatment** is life saving. However, if the immediate surgery is not possible **pericardiocentesis and intrapericardial fibrin-glue instillation** could be an alternative.



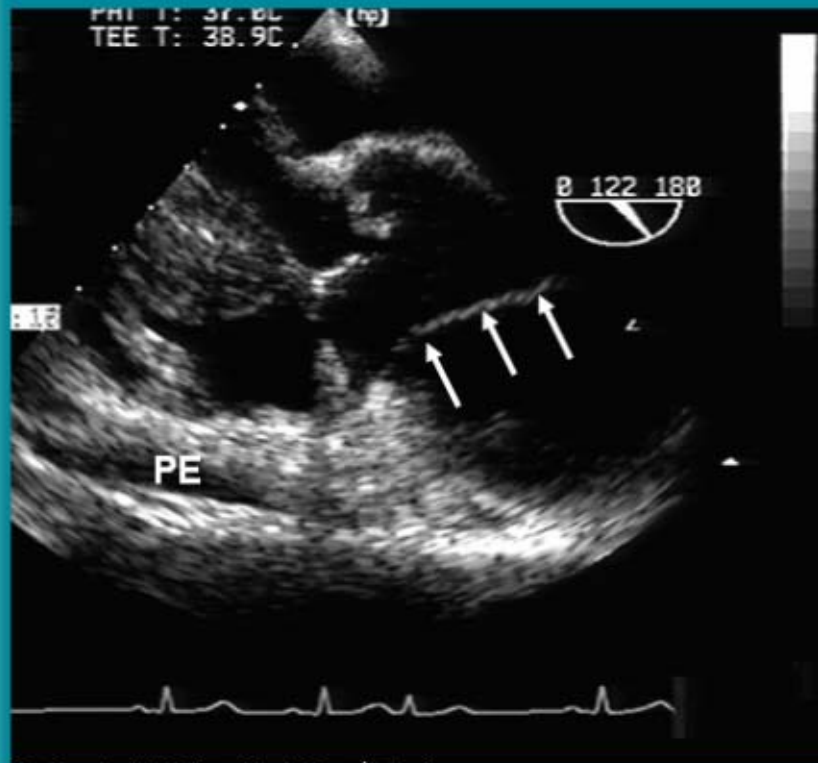
# Traumatic Pericardial Effusion

## Management

- Urgent echocardiography, if available TEE
- Rescue pericardiocentesis
- Autotransfusion
- Urgent thoracotomy and surgical repair

# Haemopericardium in Aortic Dissection

## Diagnosis



- Echocardiography (both TTE and TEE)
- CT or MRI in complex cases
- Angiography (only in stable patients)

# Haemopericardium in Aortic Dissection

## Management

- Pericardiocentesis is contraindicated, due to the risk of intensified bleeding and extension of the dissection.
- Surgery should be performed immediately (evidence level B, class I).

# Neoplastic Pericarditis

## Diagnosis

- Confirmation of the malignant infiltration within the pericardium (cytology, histology, if available tumour markers) (level of evidence B, class I).
- Of note, in up to 2/3 of the patients with documented malignancy pericardial effusion is caused by non-malignant diseases, e.g. radiation pericarditis, or opportunistic infections.

# Neoplastic Pericarditis

## Management

- Systemic antineoplastic therapy whenever possible (prevents recurrences in up to 67% of cases).
- Pericardiocentesis to relieve symptoms and establish diagnosis (level of evidence B, class IIa).
- Intrapericardial instillation of a cytostatic/sclerosing agent (level of evidence B, class IIa).
  - Cisplatin (single instillation of 30 mg/m<sup>2</sup>) is preferred for pericardial metastases of the lung cancer and
  - Intrapericardial instillation of thiotepa (15 mg on days 1,3, and 5) for breast cancer.

# Neoplastic Pericarditis

## Management (cont.)

- **Prolonged pericardial drainage** is recommended, in all patients with large effusions because of the high recurrence rate (40-70%)(level of evidence B, class I).
- In resistant cases **percutaneous balloon pericardiotomy** or rarely pericardiectomy may be indicated (repeated pericardiocentesis and/or intrapericardial therapy were not successful).
- **Radiation therapy** is very effective (93%) in controlling malignant effusion (level of evidence B, class IIa) in patients with radiosensitive tumours (e.g. lymphomas and leukemias). However, radiotherapy of the heart can cause myocarditis and pericarditis by itself.

# Pericardial Effusion in Pregnancy

## Diagnosis

- Many pregnant women develop a minimal to moderate clinically silent hydropericardium by the third trimester. Cardiac compression is rare.
- ECG changes of acute pericarditis in pregnancy should be distinguished from the slight ST-segment depressions and T-wave changes seen in normal pregnancy.
- Occult constriction becomes manifest in pregnancy due to the increased blood volume.

# Pericardial Effusion in Pregnancy

## Procedures

- Pulsus paradoxus
- Electrocardiogram
- Chest radiography
- Echocardiography
- Magnetic resonance imaging
- Swan-Ganz catheterization
- Cardiac catheterization
- Pericardiocentesis
- Pericardioscopy and epicardial/pericardial biopsy



# Pericardial Effusion in Pregnancy

## Management

- Most pericardial disorders are managed as in nonpregnant.
- Caution is necessary while high-dose aspirin may prematurely close the ductus arteriosus.
- Colchicine is contraindicated in pregnancy.
- Pericardiotomy and pericardiectomy can be safely performed if necessary and do not impose a risk for subsequent pregnancies.

# Foetal Pericardial Effusion



- Foetal pericardial fluid can be detected by echocardiography after 20 weeks' gestation and is normally 2 mm or less in depth.
- More fluid should raise questions of hydrops foetalis, Rh disease, hypoalbuminemia, and immunopathy or maternally transmitted mycoplasmal or other infections, and neoplasia.

# Drug- and Toxin-related Pericardial Disease

## A. Drug-induced lupus erythematosus

- Procainamide
- Tocainide
- Hydralazine
- Methyldopa
- Mesalazine
- Reserpine
- Isoniazid
- Hydantoins

## B. Hypersensitivity reaction

- Penicillins
- Tryptophan
- Cromolyn sodium

## C. Idiosyncratic reaction or hypersensitivity

- Methysergide
- Minoxidil
- Practolol
- Bromocriptine

## C. Idiosyncratic reaction or hypersensitivity

- Psicofuranine
- Polymer fume inhalation (Teflon)
- Cytarabine
- Phenylbutazone
- Amiodarone
- Streptokinase
- p-Aminosalicylic acid
- Thiazides
- Streptomycin
- Thiouracils
- Sulfa drugs
- Cyclophosphamide
- Cyclosporine
- Mesalazine
- 5-Fluorouracil
- Vaccines (Smallpox, Yellow fever)
- GM-CSF

## D. Anthracyclines

- Doxorubicin
- Daunorubicin

## E. Serum sickness

- Foreign antisera (e.g., antitetanus)
- Blood products

## F. Venom

- Scorpion fish sting

## G. Foreign-substance reactions (direct pericardial application)

- Talc (Mg silicate)
- Silicones
- Tetracycline/other sclerosants
- Asbestos
- Iron in  $\beta$ -thalassemia

## H. Haemopericardium

- Anticoagulants
- Thrombolytic agents