Pericardial Diseases

Pericarditis

Introduction

Pericarditis refers to **inflammation of the pericardium**, a fibrous sac surrounding the heart.

Prevalence

Pericarditis is more prevalent in men, predominantly in **young adults**. It is the most common disease of the pericardium seen in clinical practice. Pericarditis makes up **0.1%** of all hospital admissions and **5%** of emergency department admissions for chest pain.

Anatomy

The pericardium is the outer lining of the heart and comprises of two parts, an **outer fibrous pericardium** and **inner serous pericardium**.

The fibrous pericardium surrounds the heart with tough **connective tissue** but remains unattached to the heart itself.

The serous pericardium consists of an **outer parietal layer**, which sticks to the inner surface of the fibrous pericardium, and an **inner visceral layer** that attaches to the heart and forms the heart's outer epicardium layer.

A small space exists between the parietal and visceral layers of the serous pericardium, called the **pericardial cavity**, where a small volume of fluid separates the heart from its surroundings, reducing friction and enabling a degree of freedom in heart movement and changes in shape.

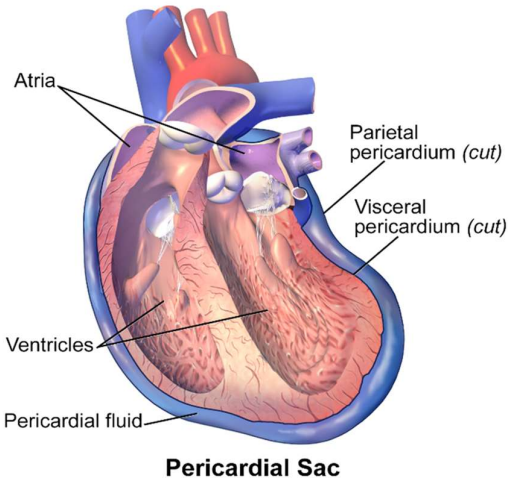

Figure: The pericardium

Causes of pericarditis/Aetiology

Acute pericarditis has several potential causes, although in most cases it is **idiopathic**, and an underlying cause is not found.

However, **potential underlying causes** of pericarditis include:

- **Infections**: viruses (e.g. coxsackievirus and HIV), bacteria (e.g. staphylococcus and *Mycobacterium tuberculosis*) and fungi (e.g. histoplasmosis)
- **Acute myocardial infarction**: pericarditis occurs 1-3 days after an infarction involving the full thickness of the ventricular wall (transmural). This is believed to be the result of the healing necrotic heart tissue interacting with the pericardium.
- **Dressler's syndrome**: this form of pericarditis tends to occur weeks to months after myocardial infarction. It is an autoimmune response triggering systemic inflammation, affecting other serous membranes as well such as the pleura.
- **Cancer**: primary tumours (e.g. mesotheliomas) or metastatic (e.g. from breast or lung cancers)
- **Autoimmune**: collagen or vascular disorders (e.g. rheumatoid arthritis, systemic lupus erythematosus)
- **Drug-induced** (e.g. hydralazine)
- **Uraemic**: from the accumulation of toxic metabolites and nitrogenous waste in the blood as seen with end-stage renal disease

Risk factors

Risk factors for **pericarditis** include:

- **Age**: the average age of patients with acute pericarditis is 41-60 years and advanced age is a risk factor for bacterial pericarditis
- **Sex**: males have a higher risk for developing acute pericarditis Seasons: idiopathic pericarditis has been found to occur most often in the spring and fall
- **Steroids**: recurrent pericarditis occurs more often in patients being treated with steroids

Additional risk factors for **bacterial pericarditis** include:

- Diabetes
- Extensive burn injuries
- Systemic infections
- Immunosuppression
- Heart surgery
- Chest trauma
- Pre-existing pericardial effusion

Diagnosis

History & clinical findings

Typical **symptoms** of pericarditis include:

- **Chest pain (>90%)**: typically, retrosternal but can be left-sided, radiating to the neck, shoulders and arms. Radiation to the trapezius ridge is a classic sign. It can be exacerbated by deep inspiration (pleuritic) and when lying down (supine), typically relieved by sitting or leaning forwards.

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  - Dyspnoea

Other **important areas to cover** in the history include:

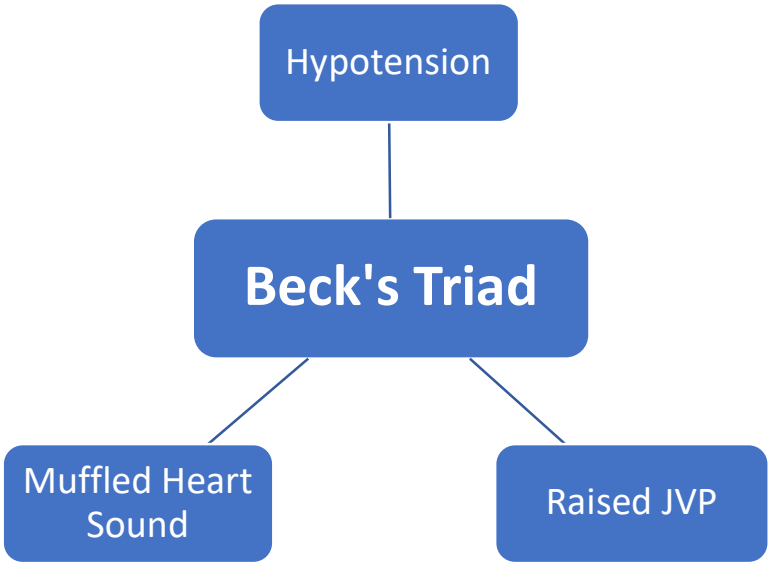
- **Systems review**: can identify clues related to the causative diagnoses such as recent infective symptoms or a known autoimmune disorder
- Drug history (e.g. chemotherapy drugs)
- Travel history: may reveal recent travel to countries endemic for certain infectious diseases

Clinical examination

A thorough **cardiovascular examination** should be performed to look for features of pericardial effusion and cardiac tamponade.

Typical **clinical findings** in pericarditis include:

- **Pericardial rub**: due to friction between the pericardial layers, typically loudest at the left lower sternal border, best heard with the patient leaning forward
- **Evidence of pericardial effusion**: usually not symptomatic unless large, may hear soft/distant heart sounds, tubular breath sounds in the left axilla/base due to bronchial compression, obscured apex beat
- **Beck's triad indicative of cardiac tamponade**: hypotension, muffled heart sounds & a raised JVP



Differential diagnoses

It is important to differentiate acute pericarditis from **other causes of chest pain** such as acute coronary syndrome, pneumonia with pleurisy, pulmonary embolism, gastro oesophageal reflux disease and costochondritis.

A detailed history is important to make this distinction as well as a thorough systems review. Investigations such as ECGs and chest X-rays are also important for the exclusion of other differential diagnoses.

Other **less common differentials** include:

- Aortic dissection
- Intra-abdominal pathology
- Pneumothorax

Investigations

Bedside investigations

Relevant **bedside investigations** include:

- **Basic observations (vital signs)**: to check for signs of shock such as hypotension and tachycardia
- **12-lead ECG**: typical findings are widespread 'concave/saddle shaped' ST-elevation except in aVR and often V_1, PR segment depression; low voltage QRS complexes/ 'electrical alternans' indicates significant pericardial effusion. These ECG changes reflect myocardial involvement as the pericardium is electrically inert.

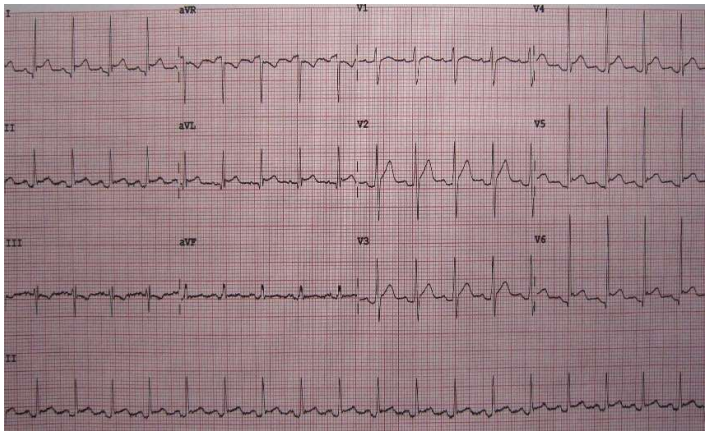


Figure 2. ECG demonstrating the typical PR depression and concave shaped ST elevation in pericarditis

ECG changes in chronological order in pericarditis:

- **Stage I**: generalized (which implies that occurs in most ECG leads both limb & precordial) & widespread concave STE & PR depression (occurs during the first 2 weeks). Except lead aVR & V1. The magnitude of STE is typically <4 mm high.
- **Stage II**: normalisation of ST changes; generalized T wave flattening (1 to 3 weeks)
- **Stage III**: flattened T waves become inverted (3 to several weeks)
- **Stage IV**: ECG returns to normal (several weeks onwards)

Laboratory investigations

There is no single diagnostic laboratory test for acute pericarditis. However, blood tests can help exclude other causes or may give clues to the underlying aetiology or potential precipitating factors.

Relevant **laboratory investigations** include:

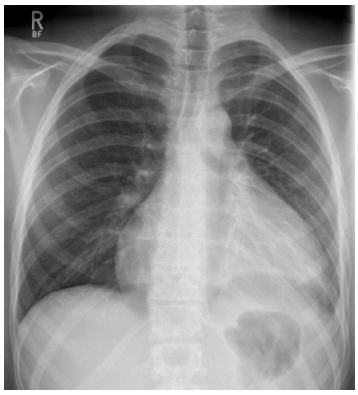
- **Full blood count**: raised white blood cell count is a common finding
- **Inflammatory markers**: a raised CRP/ESR is a common finding
- **Troponin**: may be elevated if there is co-existent myocarditis
- **Urea and electrolytes**: for renal dysfuncti
- **Liver function tests**: for liver dysfunction

Additional testing would be done if suspecting a **specific cause**, for example measuring anti-nuclear antibody in a young woman if there is suspicion of systemic lupus erythematosus.

Imaging

Relevant **imaging investigations** include:

- **Chest X-ray**: often normal in acute pericarditis, a raised cardiothoracic ratio is typically associated with a pericardial effusion of over 300mls and there may be a globular appearance to the cardiac silhouette (Figure).
- **Transthoracic echocardiography**: performed to check for any evidence of effusion. If there is an effusion, it is important to look for any signs of haemodynamic compromise as it the haemodynamic effects of the effusion rather than the size of the effusion which predicts if the patient may need the effusion draining and decisions on whether they need to stay in as an inpatient or if they can be managed as an outpatient.
- **Cardiac CT or MRI**: may be performed in atypical presentations to look for pericardial thickening and inflammation. An MRI may be performed in suspected myopericarditis as these patients have poorer long-term outcomes and require additional drug treatment including ACE inhibitors or beta-blockers as well as follow up.



Management

After confirming the diagnosis, assessing for an underlying cause, and looking for evidence of pericardial effusion, treatment is usually directed at **alleviation of symptoms** as acute idiopathic pericarditis is typically **self-limiting** in **70-90%** of patients.

If an underlying cause of pericarditis is found, management should involve treating the underlying condition.

General **lifestyle advice** for all patients includes **restricting physical activity** until symptoms have resolved and, for athletes, it is recommended to return to sports after **three months**, only after symptoms have fully resolved and investigation findings have normalised. As with all presentations, **safety netting** for symptoms of deterioration is important.

Symptomatic management

- **Non-steroidal anti-inflammatories** such as ibuprofen are first-line for symptomatic treatment. The choice of drug is based on the patient's history (e.g., allergies, contraindications or co-morbidities). For example, aspirin would be favoured if it is already needed for antiplatelet treatment and patient preferences. Gastroprotection with a **proton pump inhibitor** should be given as well.
- **Colchicine** is recommended as an adjunct for three months. It has been shown to improve the response to medical therapy and reduce recurrences by approximately 50% during follow-up.
- **Corticosteroids** are **second-line**, for example, if there is a contraindication to or failure of NSAID and colchicine therapy. Low doses are recommended to prevent complications and colchicine is given concurrently.

Recurrent or chronic pericarditis

Approximately 15-30% of patients develop a **recurrence of symptoms**. This can be termed 'incessant' with symptoms lasting for more than 4-6 weeks or 'chronic', lasting for more than 3 months. This rate of recurrence may rise to 50% in patients not given colchicine, especially if treated with steroids.

Novel treatment options now exist for refractory recurrent pericarditis, including i**mmunosuppressants** (such as azathioprine), **intravenous immunoglobulins** and **IL-1 antagonists** (such as anakinra).

A potential alternative to giving further medical treatment is **pericardiectomy** (surgically removing part or all of the pericardium).

Predictors of poor prognosis

Major risk factors identified suggestive of a **poor prognosis** include:

- Fever >38^{o}C
- Subacute onset
- Large pericardial effusion

- Cardiac tamponade
- Failure of response to NSAIDs after a week of therapy

Complications

1. Pericardial effusion

Any disease leading to pericarditis can cause **pericardial effusion**.

- 200mL acutely, normally pericardial space is filled with 15-50mL with fluid
- >1L if accumulates slowly

Causes/Etiology

- (See causes of pericarditis)

Symptoms

- Small effusion may be asymptomatic unless associated with pericarditis
- Large effusions may cause symptoms of cardiac tamponade, even if effusion occurs rapidly (see symptoms of cardiac tamponade)

Diagnosis

Fluid is taken by pericardiocentesis*

- **If fluid looks bloody with RBCs > 100,000/mm^3**
  - Trauma
  - Malignancy
  - Pulmonary embolism
- **Fluid looks chylous**
  - Injury to thoracic duct e.g., trauma during surgery
  - Leukemic infiltration
- **Fluid looks purulent**
  Look for WBC count, gram statin culture, cytology, glucose, protein & LDH levels
  - Increase WBC:
    - Inflammatory or infectious
  - Protein >6.0 g/dL & Glucose <60mg/dL:
    - Bacterial or tuberculous infection
    - Inflammatory process or malignancy
  - Isolated increased fluid & LDH >300U/dL:
    - Malignancy

Treatment

- Small → resorbed by themselves
- >20 mm & persist >month → Drained
- Recurrent small effusion with no symptoms with no evidence of hemodynamic compromise → regular follow-up with echocardiography

- Rapid & large effusion → emergency drainage via pericardiocentesis using echo/fluoroscopic guidance
- Hypotensive patient → volume expansion with IV fluids & blood products

2. Cardiac tamponade

Tamponade: pressure which obstruct blood flow

Cardiac tamponade is a life-threatening condition characterised by accumulation of fluid in the pericardial space.

- Compress all chambers
- Impairs venous return to heart
- Decrease cardiac output

Etiology

- **Pericardial effusion**: it can develop into cardiac tamponade depends upon – how much & how quickly it occurs

- **Ruptured myocardium after MI**: accumulation of blood in pericardial sac followed by ruptured myocardium after MI.
- **Aortic dissection/Aortic root rupture**: through fibrous pericardium blood pools in sac.
- **Trauma**: blunt chest trauma or procedure related trauma rupture blood vessels or myocardium
- **Surgery**: post cardiac surgeries lead to weakened myocardium that may rupture & leads to cardiac tamponade

- **Infections**: viruses (e.g. coxsackievirus and HIV), bacteria (e.g. staphylococcus and *Mycobacterium tuberculosis*) and fungi (e.g. histoplasmosis)
- **Radiation**
- **Malignancy/tumour**: primary tumours (e.g. mesotheliomas) or metastatic (e.g. from breast or lung cancers)
- **Autoimmune disease**: SLE, sarcoidosis
- **Uremic pericarditis**: increased urea in blood due to kidney problems irritates serous pericardium
- **Hyperthyroidism**
- **Chronic inflammation**
- **Medications**: cyclosporine, hydralazine, isoniazid

Signs

- **Impaired RV Filling**
  - Raised JVP
  - Pedal oedema
  - Ascites

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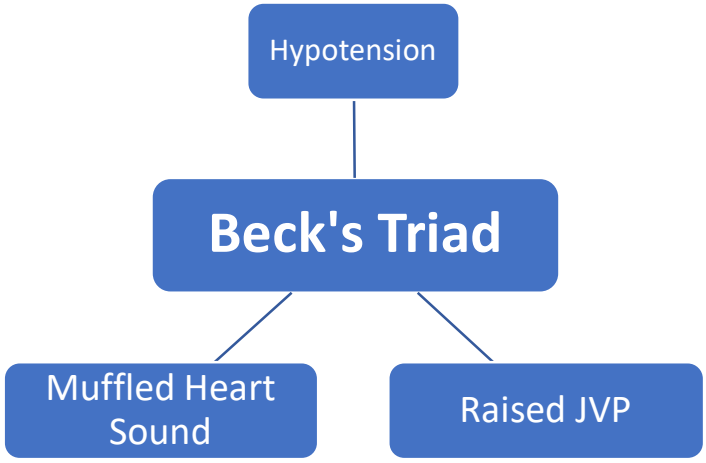
  - **Impaired LV Filling**
    - Decreased Cardiac output
    - Hypotension
    - Dyspnoea
    - Increased Heart Rate
  - **Muffled Heart Sound**
  - **Tachycardia**
  - **Tachypnoea**
  - **Kussmaul's sign:** neck veins distended during inspiration instead of collapsing. Usually seen in constrictive pericarditis
  - **Pericardial rub:** usually seen in pericarditis
  - **Pulses paradoses:** a decrease in systolic blood pressure of >10 mmHg during inspiration
  - Larger Effusion → Ewart's Sign: Dullness to percussion over left subscapular area from Compression of the left lung base

During inspiration negative pressure build up in the thoracic cavity leads to increase venous return to the right side of the heart. But heart can't expand properly because of external pressure from the fluiddue to cardiac temponade. Extra volume pushes the IVS to the left leads to compression of LV & reduce its filling (paradoxical movement of IVS on echo). this leads to reduced filling decrease in stroke volume & a subsequent drop in SBP



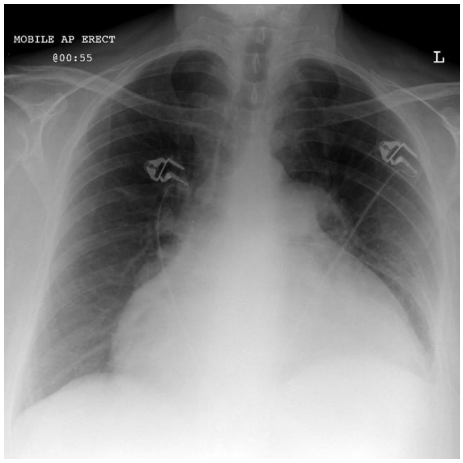
Specifically used to describe acute cardiac tamponade, for chronic cardiac Tamponade it includes ascites

Investigations

Chest X-ray

- Enlarged, globe-shaped heart

- >200mL fluid→Cardiomegaly with or without an epicardial fat pad sign
- A massive bottle-shaped cardiac silhouette
- A sudden decrease in the cardiac diameter of >2cm



ECG

- **Low Voltage:** large amounts of pericardial fluid will diminish the QRS amplitude

- **Electrical Alternans:** the amplitude of the QRS complexes vary from one beat to another (in the same lead). This is due to the swinging back & forth of the heart in the pericardial space.
- **PQ segment depression**
- **Sinus tachycardia**

ECHO

- **Pericardial effusion** is seen on 2D echocardiography as an echolucent space surrounding the heart.
  The size of the effusion can be estimated in the PLAX, A4C & subcostal views. Measurements are taken in diastole & the effusion is generally classified as:
  - Small: if <1.0cm or 10mm from the LV wall → 50-100mL fluid volume
  - Moderate: if 1.0-2.0 cm or 10-20mm from the LV wall → 100-500mL fluid volume
  - Large: if ≥2 cm or >20mm from the LV wall → >500mL

- **RA inversion (collapse)** is best visualized in the A4C & subcostal views. Normally right atrium contracts with atrial systole but in tamponade the RA wall remains collapsed throughout ventricular diastole. RA inversion manifest when intrapericardial pressure is higher than in the right atrium. This presents **prior to the hemodynamic changes** that lead to RV diastolic collapse.

- **RV diastolic collapse:** M-mode shows a characteristic “dipping” of the anterior RV free wall during diastole. As in atrial collapse, this occurs when intrapericardial

- pressure exceeds RV pressure. Patients with PHTN & RVH may not have RV diastolic collapse.
  - **Septal bounce:** “septal bounce” or exaggerated septal motion can be seen due to ventricular interdependence. This is due to during inspiration negative intrathoracic pressure leads to increase venous return but heart can’t expand due to external pressure from the pericardial fluid. Extra volume pushes the IVS to the left LV & LV volume decreases. However, during expiration RV filling volume decreases but LV filling volume increases. Leads septum to move from left to right. Best seen in A4C
  - In the subcostal view, visualization of a dilated IVC >2.1 cm with <50% collapse during inspiration as well as dilated hepatic veins with expiratory diastolic flow reversal suggest increased RA pressure, lending support to the diagnosis of elevated intracardiac pressures secondary to pericardial disease.
  - In Doppler echocardiography the increase in blood flow entry into the RV during inspiration corresponds to an increase in tricuspid valve inflow velocity of approximately 40% or greater. Reciprocally, a decrease in mitral inflow velocity of approximately 25% or greater is seen.

Cardiac Catheterization: measure pressure inside cardiac chambers. In tamponade pressure in all 4 chambers is equal.

Cardiac tamponade can be confused with conditions that cause shock, low blood pressure, raised JVP, including:

- Decompensated heart failure
- Conditions causing pulmonary hypertension such as pulmonary embolism, chronic lung disease, coronary artery disease, liver cirrhosis
- Right ventricular myocardial infarction

Treatment

- Treatment involves the expedient drainage of the pericardial collection and, where feasible, repair, or treatment of the underlying cause. This can be performed percutaneously with either landmark or ultrasound-guided pericardiocentesis, via open sternotomy, or increasingly with a balloon pericardiotomy.

3. Constrictive pericarditis

Inflammation in pericardium leads to fibrous scarring & calcification, with adhesions of the parietal and visceral pericardium. This scarring tends to be symmetric and if the pericardium becomes inelastic to a point where it hinders diastolic filling of the cardiac chambers, this is termed **constrictive pericarditis**.

Limits heart’s ability to expand & function normally

This can be considered the **final stage of the inflammation** involving the pericardium. The risk of progression is particularly linked to the aetiology with the risk being highest in

bacterial pericarditis. The most prevalent cause reported in developed countries is idiopathic, viral, post-cardiac surgery or post-radiation.

These represent chronic changes; therefore, it enables to body to compensate and is therefore not imminently life threatening like cardiac tamponade.

Causes

- (see causes of pericarditis)

Diagnosis

- **Classic Findings**
  - Kussmaul's Sign
  - Increase CVP
    - Hepatic congestion
    - Pitting Oedema
    - Portal HTN → Ascites
- **Auscultation**
  - Pericardial knock during diastole:
  - Sudden termination of ventricular inflow by the incasing pericardium
- **ECG**
  - No specific findings
  - Non-specific ST & T wave changes & tachycardia are common
  - Low voltage
  - Advanced cases → atrial fibrillation due to stretching of atrial walls
- **ECHO**
  - Thickened Pericardium with calcification but it is severe to be recognised on 2D echocardiographic images.
  - Nonspecific bi-atrial enlargement represents elevated filling pressures
  - Abrupt cessation of left ventricular & right ventricular diastolic filling
  - Intraventricular septal shift/bounce with flattening & left sided deviation
  - Pulmonary pressures are often normal in patients with constrictive pericarditis as opposed to restrictive cardiomyopathy, where pulmonary pressure >60mmHg are commonly seen. Premature pulmonic valve opening which is a subtle finding.
  - IVC dilation
  - Increased hepatic doppler flow reversal during expiration
  - Significant atrioventricular valve inflow with respiratory variations
  - Mitral septal annular velocity (e') may be higher than the lateral annulus secondary to:
    - Tethering of the lateral wall from the adjacent thickened, adherent pericardium
    - Exaggerated motion of the unencumbered septal wall ("annulus reverses")

- **Cardiac Magnetic Resonance**

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  - Differentiate a small pericardial effusion from pericardial thickening

Treatment

- For the majority of patients, the definitive treatment for chronic constrictive pericarditis is **surgical pericardiectomy** (resection of the pericardium).

Differentiating Constrictive Pericarditis Vs Restrictive Cardiomyopathy		
	Constrictive Pericarditis	**Restrictive Cardiomyopathy**
Physical Exam	Kussmaul's Sign Pericardial Knock	Kussmaul's Sign
ECHO	Thick Pericardium Septal Bounce Abrupt ↓ in Ventricular Filling	Bi-atrial Enlargement Diastolic Dysfunction
Cardiac CT/MRI	Thick Pericardium	Normal Pericardium
Cardiac Catheterization	Discordance of EDP	Concordance of EDP

Treatment of Pericardial Disease	
Pericardial Disease	**Treatment**
Acute Pericarditis	– NSAIDS + Colchicine (Viral) – ASA + Colchicine (Post MI) – Dialysis (Uraemia)
Constrictive Pericarditis	– Pericardiectomy
Pericardial Effusion	– Observation (serial TTE) – Pericardial window (if recurrent effusions)
Cardiac Tamponade	– Stabilize Hemodynamics – Pericardiocentesis (non-hemopericardium) – Surgical Drain + Repair (hemopericardium)