List of Abbreviations

ACEI	**Angiotensin converting enzyme inhibitor**
ADA	**Adenosine deaminase**
AF	**Atrial fibrillation**
ANA	**Antinuclear antibody**
AP	**Acute pericarditis**
BB	**Beta blockers**
BNP	**Brain natriuretic peptide**
BP	**Blood pressure**
BUN	**Blood urea nitrogen**
CA	**Coronary angiography**
CABG	**Coronary artery bypass graft**
CAD	**Coronary artery disease**
CEA	**Carcinoembryonic antigen**
CKD	**Chronic kidney disease**
CK	**Creatine kinase**
CMR	**Cardiac magnetic resonance imaging**
CMV	**Cytomegalovirus**
COPD	**Chronic obstructive airway disease**
COPE	**Colchicine for acute pericarditis trial**
CORE	**Colchicine for recurrent pericarditis trial**
CP	**Constrictive pericarditis**
CRP	**C-reactive protein**
CT	**Computed tomography**
CTDs	**Connective tissue diseases**
CTR	**Cardiothoracic ratio**
CXR	**Chest X-ray**
DM	**Diabetes mellitus**
DT	**Deceleration time**
ECG	**Electrocardiogram**
EF	**Ejection fraction**
ESC	**European society of cardiology**
ESR	**Erythrocyte sidementation rate**
ESRD	**End stage renal disease**
HB	**Haemoglobin**
HF	**Heart failure**
HIV	**Human immunodeficiency virus**

IE	**Infective endocarditis**
IFN	**Interferon**
INR	**International normalized ratio**
IVC	**Inferior vena cava**
JVP	**Jugular venous pressure**
LA	**Left atrium**
LDH	**Lactate dehydrogenase**
LGE	**Late gadolinium enhancement**
LV	**Left ventricle**
MR	**Mitral regurge**
MRI	**Magnetic resonance imaging**
NHL	**Non Hodgkin lymphoma**
NSAIDs	**Non steroidal anti-inflammatorydrugs**
PCR	**Polymerase chain reaction**
PE	**Pericardial effusion**
PP	**Pulsus paradoxus**
RA	**Right atrium**
RHD	**Rheumatic heart disease**
RV	**Right ventricle**
RWMAs	**Regional wall motion abnormalities**
SK	**Streptokinase**
SLE	**Systemic lupus erythematosus**
STEMI	**ST elevation myocardial infarction**
TB	**Tuberculosis**
TEE	**Trans oesophageal echocardiography**
TLC	**Total leucocytic count**
TSH	**Thyroid stimulating hormone**
TTE	**Trans thoracic echocardiography**
VT	**Ventricular tachycardia**

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Introduction

Pericardial diseases are common in clinical practice, having multiple aetiologies, however they may be under or misdiagnosed and in sometimes improperly managed. The general management of pericardial diseases is largely empirical because of the relative lack of randomized trials in patients with pericardial diseases compared with other cardiovascular diseases and lack of specific updated guidelines being ESC guideline on pericardial diseases[1] published in 2004 is the last specific guidelines.

The pericardium consists of two sacs;[2] the outer, fibrous pericardium and the inner, serous or visceral pericardium (epicardium). The pericardium prevents friction between the heart and surrounding structures, acts as a mechanical and immunological barrier and limits distention of the heart which maintains a relatively fixed maximal heart volume. In normal hearts, these functions are achieved by the presence of a small amount of pericardial fluid (15–50 ml) produced by the visceral pericardium.[3]

Pericardial diseases can manifest as acute pericarditis, isolated pericardial effusion with or without cardiac tamponade or constrictive pericarditis.

Acute pericarditis is inflammation of the pericardial layers which is usually caused by infection (viral causes are more common than bacterial), but can also have a noninfectious aetiology.[4] Chronic inflammation with fibrosis and calcification can lead to a rigid, usually thickened and calcified pericardium, with possible progression to pericardial constriction.[5]

Pericardial effusion may be mild, moderate or severe according to grading by echocardiography.[6] Cardiac tamponade occurs when intrapericardial pressure exceeds intracavitary pressure within cardiac chambers. In most severe cases of cardiac tamponade, hemodynamic compromise occurs in the form of hypotension, tissue hypoperfusion and death if left untreated.[7]

Constrictive pericarditis may follow any inflammatory condition in the pericardium. The pericardium becomes thick, rigid, fibrotic and may be calcified. This rigid inelastic pericardium limits the diastolic filling of the heart, thus it results in systemic venous congestion and decreasing forward cardiac output.[8]

The treatment of pericardial diseases includes the use of anti-inflammatory drugs, aspiration of excess pericardial fluid either percutaneously (percutaneous pericardiocentesis) or surgically and performing pericardial window, and pericardiectomy.

Multiple observational studies had included patients with pericardial diseases, but they either focus on certain entity of pericardial diseases (pericarditis, pericardial effusion, cardiac tanponade or constrictive pericarditis), include certain aetiologies and exclude others, or study only certain variable(s) eg: **Massimo imazio et al 2011** study[9] which evaluated the role of Hs-CRP in follow up of patients with acute pericarditis. To our knowledge, there is lack in large registry studies that include patients with different pericardial diseases of multiple aetiologies and following them over long period of time.

Aim of The Work

1- Description of demographic and clinical characteristics of patients with pericardial diseases admitted to our hospital being a large tertiary care center.

2- Detection of the predictors of inhospital morbidity and mortality among patients with pericardial diseases.

Chapter (1)

Anatomy and Physiology of the Pericardium

- ## Anatomy of the pericardium

The pericardium encloses the heart and the great vessels origin, and consists of two layers:[2]

1-**The visceral pericardium**:

A monolayer membrane of mesothelial cells and associated collagen and elastin fibers that is adherent to the epicardial surface of the heart. It reflects back near the origins of the great vessels, becoming continuous with and forming the inner layer of the parietal pericardium. The reflection lines of the serous pericardium between the great vessels at the base of the heart are arranged around two complex connected tubes; the transverse and oblique sinuses, and include other several smaller recesses (Figure 1).[3] These are not separated compartments but extensions of the pericardial cavity. These sinuses have a reserve function and may strategically accumulate fluid in the presence of increased fluid content, thus creating pocket like structures (the so called pericardial reserve volume).

2-**The parietal pericardium:**

A fibrous layer which is about 1 to 2 mm thick in normal humans and surrounds most of the heart. It is largely acellular and also contains both collagen and elastin fibers. It has ligamentous attachments to the diaphragm, sternum, and other structures which ensure that the heart occupies a fixed position within the thoracic cavity regardless of respiration and body position.

Between these two layers, the pericardial cavity is formed and normally contains up to 50 mL of serous fluid which is distributed mostly over the atrioventricular and interventricular grooves and is often seen, particularly within the pericardial recesses which are parts of pericardial cavity.

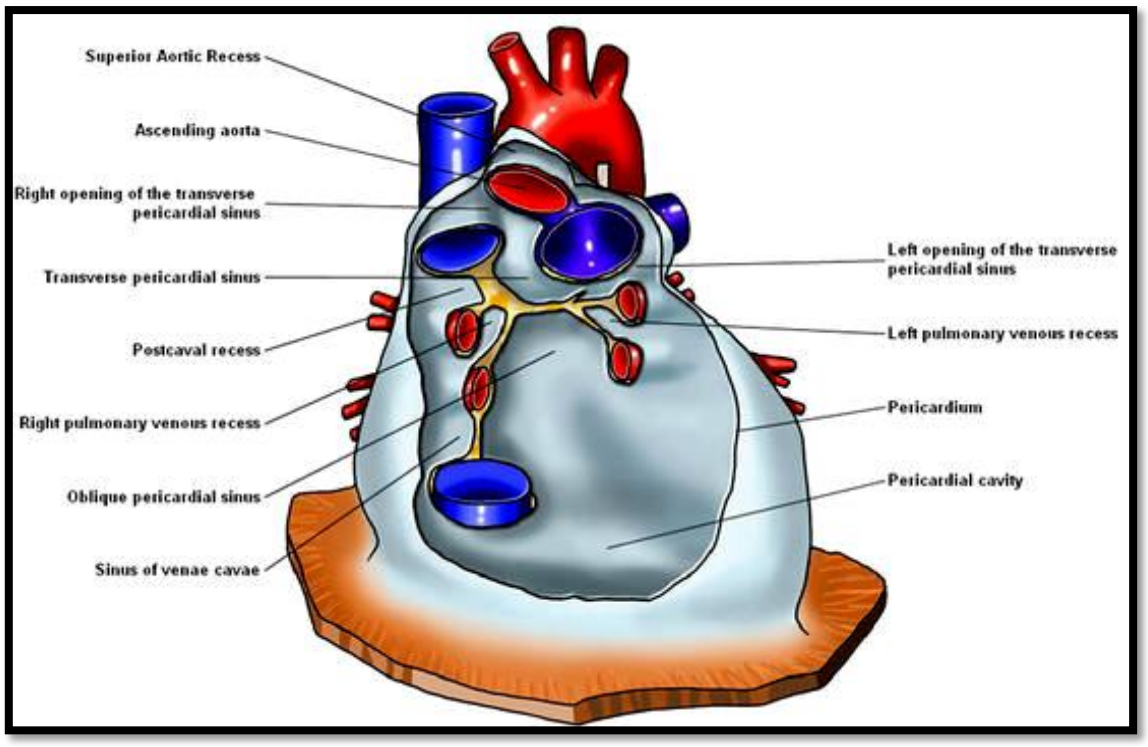

Figure 1: Schematic draw showing the normal pericardial anatomy and pericardial sinuses

- **Functions of the pericardium:**[10]

I-Mechanical Functions:

A. Relatively inelastic cardiac envelope:

1. Limitation of excessive acute dilation.
2. Protection against excessive ventriculoatrial regurgitation.
3. Maintenance of normal ventricular compliance (volume-elasticity relation).
4. The pericardium plus pericardial fluid act as hydrostatic system distributing hydrostatic forces over epicardial surfaces which:
    a. Favours equality of transmural end-diastolic pressure throughout ventricle, therefore uniform stretch of musclefibers (preload).
    b. Constantly compensates for changes in gravitational and inertial forces by distributing them evenly around the heart.

5. Ventricular interaction (aided by relative pericardial stiffness):
    a. Reduces ventricular compliance with increased pressure in the opposite ventricle (e.g: limits right ventricular stroke work during increased impedance to left ventricular outflow).
    b. Provides mutually restrictive chamber favoring balanced output from right and left ventricles integrated over several cardiac cycles.

B. Provision of closed chamber with slightly subatmospheric pressure in which:

1. The level of transmural cardiac pressures will be low relative to even large increases in filling pressures.
2. Pressure changes aid atrial filling via more negative pericardial pressure during ventricular ejection.

II-Membranous Function (Shielding the Heart):

A. Reduction of external friction due to heart movements.

B. Barrier to inflammation from contiguous structures.

C. Buttressing of thinner portions of the myocardium:

1. Atria.
2. Right ventricle.

D. Fibrinolytic activity in mesothelial lining.

III-Ligamentous Function:

Limitation of undue cardiac displacement.

IV-Neurohormonal functions:

A. The pericardium is well innervated with mechanoreceptors and chemoreceptors and phrenic afferents. The roles of these receptors are incompletely understood, but they probably participate in reflexes arising from the pericardium and epicardium (e.g., the Bezold-Jarisch reflex) as well as in transmission of pericardial pain.

B. The mesothelium of the pericardium is metabolically active and produces prostaglandin E_2, eicosanoids, and prostacyclin; these substances modulate sympathetic neurotransmission and myocardial contractility and may influence epicardial coronary arterial tone. Epicardial mesothelial cells may modulate myocyte

structure and function and gene expression. The level of brain natriuretic peptide (BNP) in the pericardial fluid is a more sensitive and accurate indicator of ventricular volume and pressure than is either plasma BNP or atrial natriuretic factor; it may play an autocrine-paracrine role in heart failure.[11]

- ## Imaging of the pericardium[5,12,13,14]

The normal pericardium is seen as a very thin linear density surrounding the heart, typically, the pericardium is best visualized along the right ventricle, and often not visualize over the left ventricle because of a sparseness of epicardial fat and the vicinity of pulmonary parenchyma. Normal pericardial thickness ranges from 0.7 to 2.0 mm on CT images. These values slightly overestimate those obtained in anatomic cadaveric studies (0.4-1.0mm). Differences can be explained by the intrinsically limited spatial and temporal resolutions of CT, which do not allow one to fully discriminate between pericardial layers and fluid component. It can be difficult to differentiate fluid from thickened pericardium in CT imaging and MR imaging is usually superior.

Discrimination of the pericardium from the myocardium requires the presence of epicardial fat or pericardial fluid. The higher-attenuation is distinguished in relation to the low-attenuation mediastinal fat anteriorly and epicardial fat posteriorly. Epicardial fat normally increases with age, and is common to find excessive fat accumulation in older, obese, diabetic, or patients with steroid excess.

Pericardial sinuses and recesses can be identified as areas of water attenuation around the great mediastinal vessels. Most recesses are linear when not filled with fluid and band shaped as the fluid content increases. However, they may also present as crescent, triangle, spindle, ovoid, hemisphere, or irregular shapes. Pericardial recesses are commonly described as lymph nodes, but they can also simulate other conditions, including aortic pathology. However they are distinguished by being sharply outlined structures with uniform water-equivalent attenuation without walls or rims in their expected anatomic location. They can be divided according to the part of the pericardial cavity from which they arise. The three main sites of origin are the transverse sinus, the oblique sinus and the pericardial cavity proper (Table 1).[15]

Table 1: Origin of different pericardial recesses

Related sinus/space	Recesses
Pericardial cavity proper	Right and left pulmonic vein recesses Postcaval recess
Transverse pericardial sinus	Superior aortic recess Right and left pulmonary artery recesses Inferior aortic recess
Oblique pericardial sinus	Posterior pericardial recess

I-Pericardial cavity proper:

A-Right and left pulmonic vein recesses:

They are located between the superior and inferior pulmonary veins on both sides, where the pericardium is attached to the venous adventitia, projecting superiorly and medially, indenting the side walls of the oblique sinus. They are usually small, with a diameter up to 1cm. At CT, the left pulmonic vein recess is identified more frequently than the right pulmonic vein recess, however, the latter is usually deeper than the former. As the pulmonary veins penetrate the fibrous pericardium to enter the left atrium, a serosal sleeve of pericardium invests the veins. At the level of the inferior pulmonary vein, pericardial fluid in the sleeve can be misinterpreted as adenopathy.

B-Postcaval recess:

The postcaval recess is a diverticulum of the pericardial cavity proper, extends behind and along the right lateral aspect of the superior vena cava. It is bounded by the right pulmonary artery and the right superior pulmonary vein.

II-Transverse pericardial sinus:

This space is located posterior and inferior to the ascending aorta and pulmonary trunk and above to the left atrium. It connects with the pericardial cavity between the ascending aorta and superior vena cava, but this connection is not always clearly seen. It has a linear-shaped virtual cavity that should not be misinterpreted, when filled with fluid, as a focal aortic dissection or as an enlarged mediastinal lymph node on CT images. Several minor recesses take origin from this space:

A. Superior aortic recess:

The superior aortic recess is a superior extension of the transverse sinus that extends anterior to the ascending aorta. This recess may simulate aortic dissection or thrombus on non enhanced CT. This recess can be divided the superior aortic recess in anterior, posterior and right lateral portions.

B. Right and left pulmonary artery recesses:

They form the lateral extent of the transverse sinus and are located below the right and left pulmonary arteries, respectively:

1) The right pulmonary recess is inferior to the proximal right pulmonary artery. This recess is bounded by the reflection of serous pericardium extending from the right pulmonary artery to the superior vena cava.
2) The left pulmonary recess is bounded superiorly by the left pulmonary artery, inferiorly by the left superior pulmonary vein and medially by the ligament of Marshall, a vestigial fold of the remnant left superior vena cava.

C. Inferior aortic recess:

The inferior aortic recess is a crescentic diverticulum between the right lateral aspect of the ascending aorta and the right atrium. It is a caudal extension from the transverse sinus found between the ascending aorta and the superior vena cava or the right atrium and extends down to the level of the aortic valve.

III- Oblique pericardial sinus

The oblique pericardial sinus is the most posterior pericardial space .It has an inverted U-shaped pericardial reflection located behind the left atrium and is inferior to the transverse sinus, from which it is separated by a double reflection of serous pericardium. In CT images the oblique sinus is usually clearly separated from the transverse sinus by a fat plan. Fluid in the oblique sinus can simulate abnormalities in the esophagus, descending thoracic aorta, and subcarinal and bronchopulmonary lymph nodes. The oblique sinus extends superiorly behind the right pulmonary artery and medial to the bronchus intermedius, where it is called **the posterior pericardial recess**. Fluid in the posterior pericardial recess may be mistaken for peribronchial or subcarinal lymph nodes.