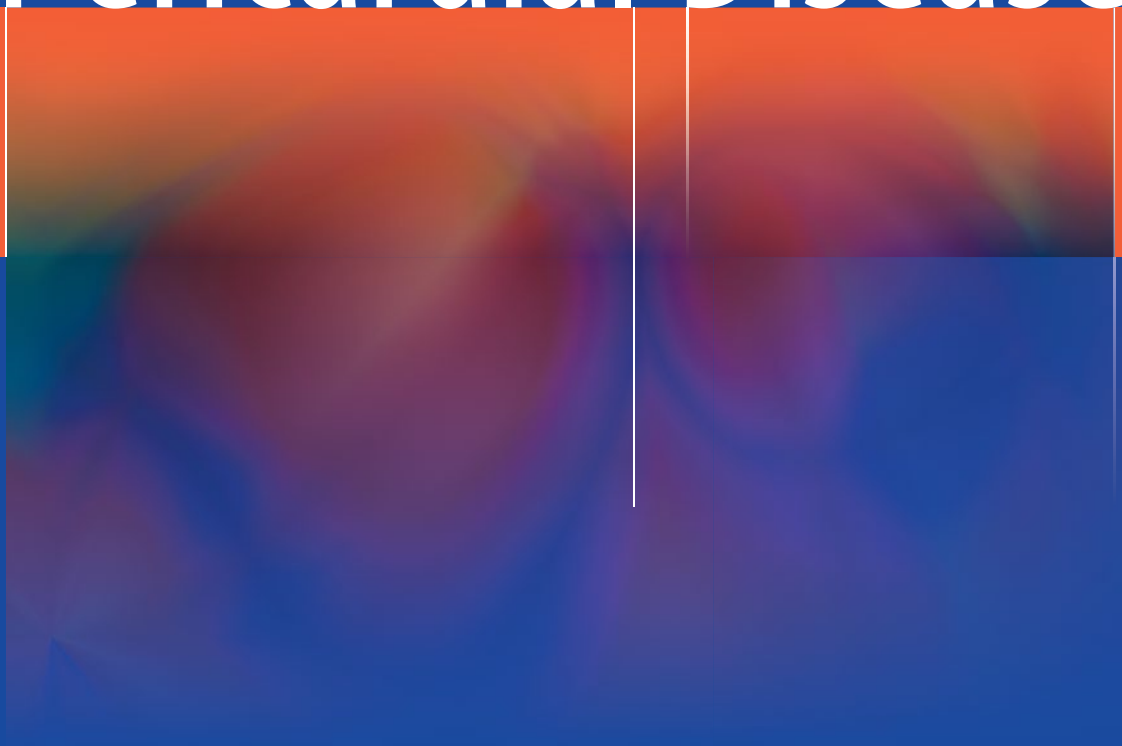
Eyal Herzog
*Editor*

# Management of Pericardial Disease



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Editor

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# Preface

Over the past 20 years, I have been teaching cardiology to physicians and other health care professionals. When I ask my trainees to provide me with a disease that they are not comfortable managing, they almost always have the same reply: pericardial disease. The realization of this gap in training has motivated me to create this book which is specifically devoted to Pericardial Disease.

Pericardial disease is a broad term that describes a wide range of pathologies. The clinical aspects of pericardial disease encompass acute and recurrent pericarditis, pericardial effusion and pericardial tamponade, constrictive pericarditis, and effusive-constrictive pericarditis. These disorders differ not only in clinical presentation but also in the timeline of their development. Thus, management of pericardial disease can be challenging for many clinicians. To assist medical professionals with this often complex area, this book provides an extensive review of pericardial disease evaluation and management using a unique stepwise pathway-based approach.

*Management of Pericardial Disease* contains a selection of defining clinical images for guiding the identification and management of pericardial disease. Fellows, residents, cardiologists, thoracic medicine physicians, cardiothoracic surgeons, radiologists, and intensive care and emergency medicine physicians alike will find this book to be an essential resource for developing the skills and knowledge applicable to managing pericardial disease in patients.

Because pericardial disease is often life threatening, it is my hope that this book will serve as an instrumental guide for helping physicians to save the lives of patients with pericardial disease.

New York, NY, USA — Eyal Herzog, MD

# Contents

# Part I

# Evaluation of Pericardial Disease

# Anatomy and Physiology of the Pericardium

1

Martin Y. Tabaksblat, Dan G. Halpern, Edgar Argulian, and Eyal Herzog

## Anatomy

### Pericardium

The pericardium is a membranous sac surrounding the heart and the roots of the great vessels that is composed of both fibrous and serosal layers (Fig. 1.1). The fibrous layer of pericardium forms a conical-like sac surrounding the heart; superiorly, the fibrous pericardium is attached to and is continuous with the adventitia of the great vessels as well as with the pretracheal fascia. The pericardium is attached anteriorly to the manubrium and xiphoid process by the sternopericardial ligaments, posteriorly to the vertebral column and inferiorly to central tendon of the diaphragm. The pericardium is separated from the anterior thoracic wall by the lungs and pleura but is in direct contact with it at the lower left half of the sternum and the sternal abutments of the left fourth and fifth costal cartilages [1]. The phrenic nerves contained within the pericardiophrenic bundles pass laterally along each side of the heart between the fibrous pericardium and mediastinal pleura. The serosal pericardium consists of two layers, a serous visceral layer (epicardium) that is adherent to the heart and epicardial fat and a serous layer which lines the internal surface of the fibrous pericardium together forming the parietal pericardium.

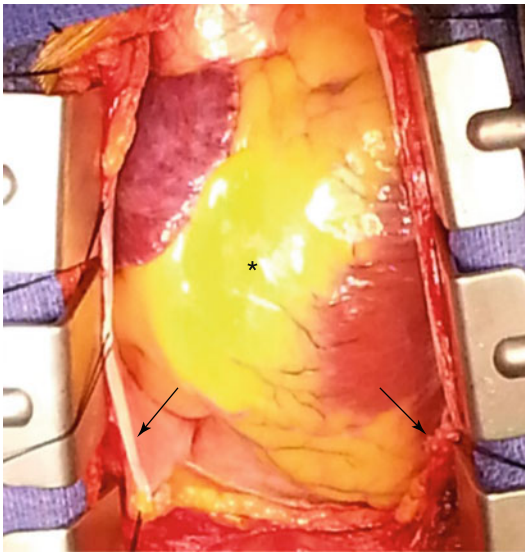


**Fig. 1.1** Human heart with pericardium splayed (*black arrows*) revealing epicardial fat (*asterisk*)

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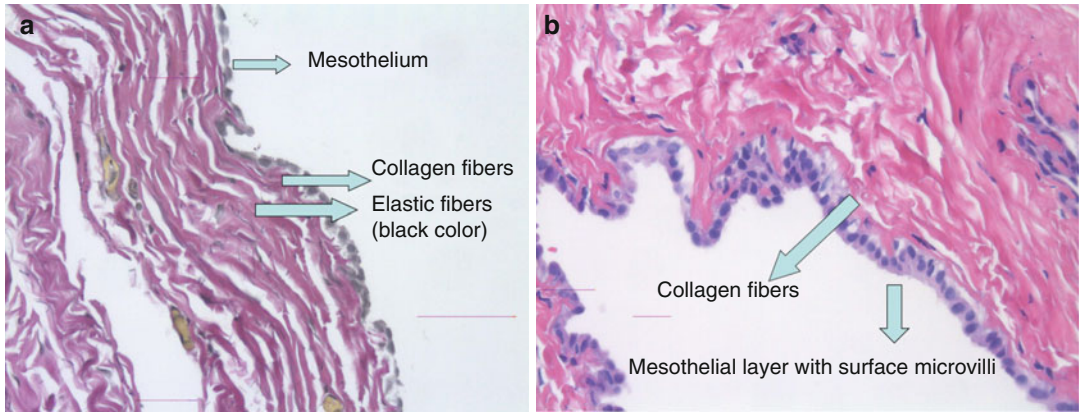


**Fig. 1.2** Parietal pericardium. (**a**) EVG stain of parietal pericardium displaying the serosal (mesothelial) layer and fibrous layers composed of collagen and elastic fibers. (**b**) H&E stain of parietal pericardium displaying serosal (mesothelial) layer and collagen fibers (Courtesy of Dr. Shweta Gera and Dr. Pushpa Kancherla, Mt. Sinai St. Luke's Pathology Department, New York, NY)

The normal pericardial thickness is less than 2 mm as seen on imaging studies and less than 1 mm on anatomical studies [2]. The pericardial space between the visceral and parietal layers normally contains less than 50 ml of serous fluid which in normal hearts is contained in the pericardial recesses and sinuses mostly over the atrial-ventricular and inter-ventricular grooves [3] (Fig. 1.1).

## Serosal Pericardium

The serosal layer is composed of a surface layer of flattened mesothelial cells whose luminal surface is completely lined with surface microvilli and few cilia which are thought to serve as both specialized friction-bearing surfaces as well as to increase the cell surface area available for fluid transport [4]. Histologic examination of the serosal pericardium suggests the capability of the luminal surface to modify its configuration as well as the ability to permit both transport through intercellular spaces and across the cytoplasm by vesicular transport [4].

## Fibrous and Parietal Pericardium

The parietal pericardium is composed of the serosal and fibrosal layers as well as an outer layer of epipericardial tissue. The fibrous pericardium is composed of connective tissue cells, microvasculature, lymphatics, collagen fibers, and small elastic fibers. The epipericardial layer is composed of connective tissue as well as neural elements and blood vessels [4]. Coarse collagenous bundles in the epipericardial layer form the sternopericardial ligaments. Mast cells, lymphocytes, and histiocytes can be found in both the fibrosal and epipericardial layers [4]. The varied orientation and the wavy arrangement of the collagen fibers in the fibrous layer are such that they allow for some degree of multidirectional stretch to occur. However, given the inextensible nature of collagen fibrils, once the collagen fibrils are straightened out, further stretching of the fibrous layer is limited [4]. It has also been shown that the waviness of the pericardial collagen is maximal in young adulthood and decreases thereafter with age [4] (Fig. 1.2).

## Pericardial Sinuses and Recesses

The visceral pericardium envelopes the heart and its attached vessels and is reflected into the parietal pericardium forming a sac around the heart. This reflection creates two invaginations one enclosing the aorta and pulmonary trunk and the other enclosing the venae cavae and

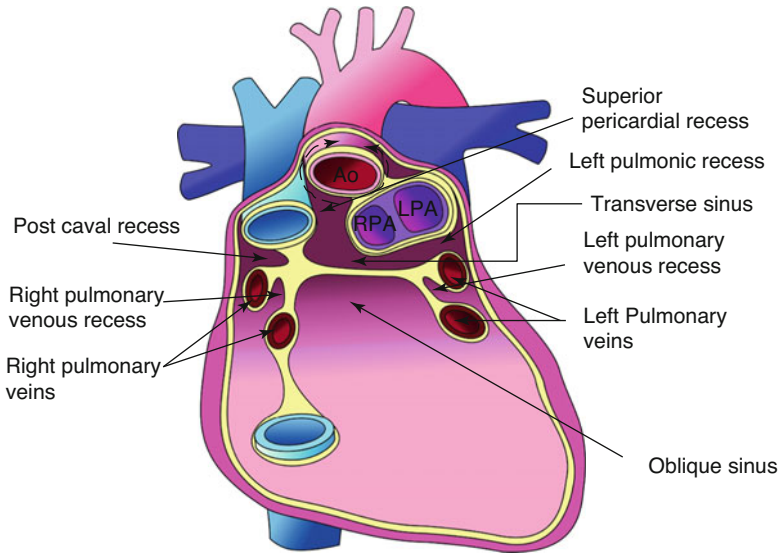


**Fig. 1.3** Anatomic locations of the pericardial recesses and sinuses. *Ao* aorta, *LPA*, *RPA* left and right pulmonary arteries respectively, *SVC*, *IVC* superior and inferior venae cavae respectively (Courtesy of Adult Congenital Heart group, Boston Children's Hospital and Brigham and Women's Hospital, Harvard Medical School, Boston, MA)

pulmonary veins. At these reflections about the vessels the pericardial cavity forms the pericardial sinuses and recesses which are continuous with the pericardial cavity. Normally, much of the pericardial fluid is contained within these sinuses and recesses. Familiarity with the anatomy of the sinuses and recesses may prove helpful in diagnostic and therapeutic procedures. For example, for patients requiring physiologic (atrial-ventricular) pacing who have limited venous access, placement of epicardial pacemaker leads through the pericardial reflections has been shown to be effective [5].

The transverse sinus is a passage between these two invaginations with the aorta and pulmonary trunk anteriorly and the atria and veins posteriorly. Bachmann's bundle, a source of certain atrial arrhythmias, lines the floor of the transverse sinus (roof of the left atrium) and can be a target for radiofrequency ablation (RFA) [6]. The oblique sinus is a cul-de-sac like space that lies behind the left atrium and formed about the pulmonary veins and the inferior vena cava. The oblique vein of Marshall, also a potential source of arrhythmia, lies within the oblique sinus and is amenable to RFA via an epicardial approach [6].

Smaller spaces formed by reflections of pericardium between adjacent structures are called pericardial recesses. These recesses are named according to the structures that delineate them. The superior (aortic) pericardial recess is an extension of the transverse sinus that lies anteriorly, posteriorly and to the right of the ascending aorta and is bordered posteriorly by the superior vena cava. The superior pericardial recess can be misinterpreted as an aortic dissection, lymphadenopathy, or a cystic mediastinal mass on computed tomography (CT) imaging [7]. The inferior aortic recess is an extension of the transverse sinus that lies between the lower part of the ascending aorta and the right atrium. The anterior left ventricular outflow tract (LVOT) and proximal aorta (and aortic valve cusps) can be accessed for RFA via the inferior aortic recess [6]. The post caval recess lies behind the superior vena cava and is separated from the transverse sinus above by the right pulmonary artery and below by the right upper pulmonary vein. The left and right pulmonic recesses are lateral extensions of the transverse sinus that lie inferior to the left and right pulmonary arteries respectively. The left and right pulmonary venous recesses lie behind the left atrium between the upper and lower pulmonary veins (Fig. 1.3).

## Pericardial Fat

Fat deposits are found around the heart as epicardial fat (Fig. 1.1) covered by the visceral

pericardial layer and as fat deposits on the outer surface of the fibrous pericardium. The epicardial fat predominantly overlies the atrioventricular and interventricular grooves and the right ventricle and contains the coronary arteries and veins, lymphatics, and nervous tissue. The epicardial fat serves as both a mechanical and immune barrier for the heart, a regulator of vascular flow by vasocrine mechanisms and as a local source of fatty acids during periods of high myocardial demand. Epicardial fat is associated with cardiovascular disease [8] which may be mediated by its paracrine effects, locally secreting cytokines which can accelerate the atherosclerotic process by means of endothelial dysfunction, smooth muscle proliferation, and oxidative stress [9].

## Lymphatic Drainage

The pericardium has an extensive network of lymphatics providing active turnover of protein and various other substances from within the pericardial space. This turnover is mediated by lymphatics in both the epicardium and parietal pericardium. The lymphatic vessels of the anterior pericardium either travel upwards along the phrenic nerves terminating in the anterior right and left mediastinal nodes or travel downwards terminating at the diaphragm or prepericardial lymph nodes. The lymphatics of the lateral pericardium drain into the anterior mediastinal, tracheobronchial, lateropericardial, prepericardial and paraesophageal lymph nodes. The lymphatics of the posterior pericardium drain into the paraesophageal and tracheobronchial lymph nodes. Lymphatics of the inferior or diaphragmatic part of the pericardium drain into the right lateropericardial, right prepericardial, paraesophageal, and tracheobronchial lymph nodes [10] (Fig. 1.4).

## Vascular Supply

The pericardium receives its blood supply from branches of the internal thoracic (mammary) and musculophrenic arteries and the descending thoracic aorta [11]. The pericardial veins vary in number and drain into the left innominate, azygous, and internal thoracic veins. The lymphatic system is also thought to play an important role in venous drainage of the myocardium.

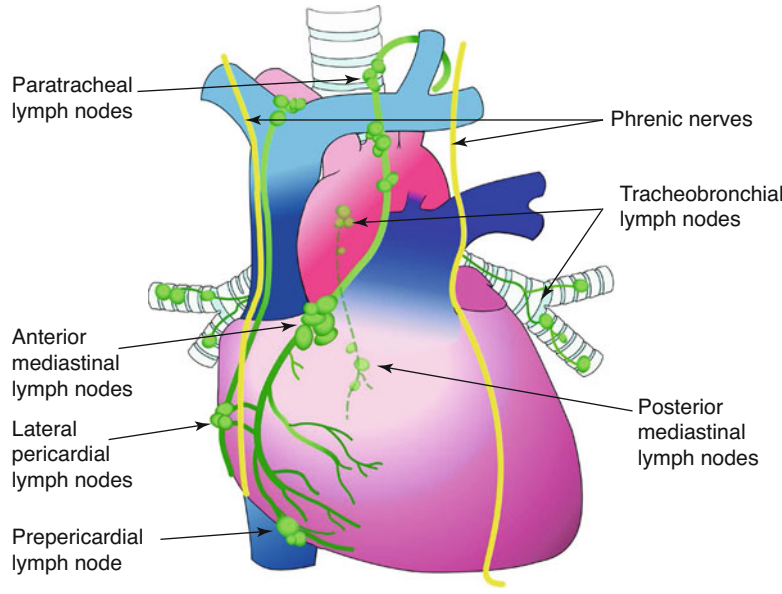


**Fig. 1.4** Lymphatic drainage of the pericardium (Courtesy of Adult Congenital Heart group, Boston Children's Hospital and Brigham and Women's Hospital, Harvard Medical School, Boston, MA)

## Innervation

Parasympathetic nerve fibers branching from the vagus, left recurrent laryngeal, and esophageal plexus innervate the pericardium. Sympathetic innervation is supplied from the first dorsal ganglion, stellate ganglion, and the aortic, cardiac, and diaphragmatic plexuses [11]. Additionally, the pericardium secretes prostaglandins with which increased levels have been shown to modulate sympathetic nerve effects and potentially suppress the development of arrhythmias in various situations [12].

## Physiology of the Pericardium

The pericardium serves several functions for the heart which includes shielding the heart from physical and biologic insults, promotion of efficient cardiac function, and limitation of excessive cardiac displacement (Table 1.1). Despite these beneficial functions of the pericardium, those without a pericardium either due to congenital [complete] absence of the pericardium or surgical removal of the pericardium (pericardiectomy) suffer minimal consequences.

As mentioned above, the fibrous pericardium is capable of stretching but, once the collagen fibrils that compose it are straightened out, further stretching of the fibrous layer is limited [4]. This limited degree of stretch translates into a non-linear pressure-volume relation of the pericardium. Initially an increase in pericardial fluid volume minimally affects the pericardial pressure until the reserve volume of the pericardium is exceeded and a critical pressure is met at which point small increases in pericardial fluid volume result in significantly greater changes in pressure (Fig. 1.5 curve a). On the other hand, when the pericardium is removed the pressure-volume curve is less steep and the heart is capable of dilating approximately 50 percent greater than it would with an intact pericardium (Fig. 1.5 curve b) [11]. The pericardium thus acts as a relatively inelastic envelope which serves to limit excessive acute cardiac dilatation, protect against excessive ventriculoatrial regurgitation, and maintains normal and uniform ventricular function and compliance relationships [15]. Since the right heart is thin-walled and less resistant compared to the left ventricle, the pericardium affects right heart hemodynamics to a greater degree than the left side. At least 50 % of the normal right-sided diastolic pressures are due to the pericardial influence [16]. In acute right ventricular dilation, the effect of pericardial constraint can affect left-sided filling pressures due to ventricular interdependence. In chronic volume overload states the pericardium adapts to these higher volumes and pressures and the pericardial pressure-volume curve shifts to the right and flattens to a small degree, allowing for greater increases in fluid volume with attenuated increases in pressure (Fig. 1.5 curve c) [13]. Similar changes and shift of the pressure-volume curve can be seen

**Table 1.1** Functions of the pericardium

| |
|---|
| Mechanical |
| Limits excessive acute cardiac distention |
| Protects against excessive ventriculoatrial regurgitation |
| Maintains ventricular function and compliance relationships |
| Reduces friction to the heart |
| Serves as a barrier to infection |
| Biologic |
| Secretes immunologic factors protecting the heart |
| Fibrinolytic activity of the mesothelial layer |
| Modulates sympathetic tone |
| Aids venous and lymphatic drainage of the heart |

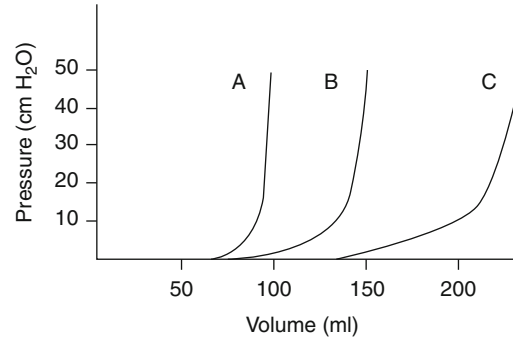


**Fig. 1.5** Pressure-volume curves of canine hearts. (*A*) Isolated canine heart with intact pericardium. (*B*) Isolated canine heart after pericardiectomy. (*C*) Chronically dilated canine heart with intact pericardium (Adapted from Freeman and LeWinter [13] and Hort [14])

with slowly enlarging pericardial effusions and explains why tamponade physiology is not observed in many cases of large, slowly accumulating pericardial effusions.

The relatively inelastic nature of the pericardium enhances ventricular interaction, wherein changes in pressure or volume of the right heart influence pressure-volume characteristics of the left heart. Sudden distention of the left ventricle increases pericardial pressure which in turn increases right ventricular resistance, and reduces right ventricular stroke volume thereby reducing venous return to the left ventricle and left ventricular stroke volume. In the absence of the pericardium, this interventricular relationship is diminished. An example of this physiologic relationship can be seen with positive end-expiratory pressure (PEEP) and intermittent positive pressure breathing. Both of these ventilation modalities typically increase the pulmonary artery transmural pressure, resulting in increased right ventricular size. Because of the interventricular relationship which is enhanced by the pericardium, left ventricular chamber size and compliance subsequently decrease in-turn decreasing cardiac output. It is for this reason that PEEP and positive pressure ventilation is contraindicated in cardiac tamponade [15].

Normal intrapericardial pressure is usually subatmospheric and is nearly equal to intrapleural pressure (pericardial transmural pressure of zero), whereas intracardiac pressures are normally supraatmospheric. Intrapleural pressure varies depending on the location within the thorax. Given that the heart is enclosed by the pericardium the two are intimately related; that is, fluctuations in intracardiac pressure reflect on intrapericardial pressure and visa versa. Therefore, intrapericardial pressure is greatest at end diastole and falls during systole. Myocardial transmural pressure (distending pressure) which is closely related to preload, is equivalent to the intrapericardial cavity pressure subtracted from the cavity or chamber pressure [15, 17].

Since the intrapericardial pressure is affected by intrapleural pressure, respiration affects cardiac hemodynamics. Inspiration reduces intrapleural pressure thereby reducing pericardial, right atrial, right ventricular, pulmonary capillary wedge, and systemic pressures. With inspiration the pericardial pressure decreases more than atrial pressure, the right atrial transmural pressure increases thereby increasing right heart filling and hence right ventricular preload. Also, there is a physiologic fluctuation in systolic blood pressure explained by phasic variation in the filling of the right- and left-sided cardiac chambers related to intrathoracic pressure changes with respiration. Normally, this fluctuation does not exceed 10 mmHg but it can be exaggerated by accumulating pericardial effusion that restricts cardiac filling and makes the respiratory variation in the right and left ventricular filling more pronounced and interdependent. This phenomenon of 'pulsus paradoxus' is one of the clinical correlates of pericardial tamponade.

## References


1. Standring S, Gray H. Gray's anatomy: the anatomical basis of clinical practice. 40th ed. Edinburgh: Churchill Livingstone, Elsevier, 2008.
2. Peebles CR, Shambrook JS, Harden SP. Pericardial diseas–natomy and function. Br J Radiol. 2011;84(3): S324–37.
3. Little WC, Freeman GL. Pericardial disease. Circulation. 2006;113(12):1622–32.
4. Ishihara T, Ferrans VJ, Jones M, Boyce SW, Kawanami O, Roberts WC. Histologic and ultrastructural features of normal human parietal pericardium. Am J Cardiol. 1980;46(5):744–53.
5. Costa R, Scanavacca M, da Silva KR, Martinelli Filho M, Carrillo R. Novel approach to epicardial pacemaker implantation in patients with limited venous access. Heart Rhythm. 2013;10(11):1646–52.
6. Lachman N, Syed FF, Habib A, Kapa S, Bisco SE, Venkatachalam KL, Asirvatham SJ. Correlative anatomy for the electrophysiologist, part I: the pericardial space, oblique sinus, transverse sinus. J Cardiovasc Electrophysiol. 2010;21(12):1421–6.
7. Basile A, Bisceglie P, Giulietti G, Calcara G, Figuera M, Mundo E, Granata A, Runza G, Privitera C, Privitera G, Patti MT. Prevalence of "high-riding" superior pericardial recesses on thin-section 16-MDCT scans. Eur J Radiol. 2006;59(2):265–9.
8. Mahabadi AA, Massaro JM, Rosito GA, Levy D, Murabito JM, Wolf PA, O'Donnell CJ, Fox CS, Hoffmann U. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. Eur Heart J. 2009;30(7):850–6.

9. Bertaso AG, Bertol D, Duncan BB, Foppa M. Epicardial fat: definition, measurements and systematic review of main outcomes. Arq Bras Cardiol. 2013;101(1):e18–28.
10. Eliskova M, Eliska O, Miller AJ. The lymphatic drainage of the parietal pericardium in man. Lymphology. 1995;28(4):208–17.
11. Holt JP. The normal pericardium. Am J Cardiol. 1970;26(5):455–65.
12. Miyazaki T, Pride HP, Zipes DP. Prostaglandins in the pericardial fluid modulate neural regulation of cardiac electrophysiological properties. Circ Res. 1990;66(1):163–75.
13. Freeman GL, LeWinter MM. Pericardial adaptations during chronic cardiac dilation in dogs. Circ Res. 1984;54(3):294–300.
14. Hort W. Herzbeutel und herzgrosse. Arch Kreislaufforsch. 1964;44:21–35.
15. Spodick DH. The normal and diseased pericardium: current concepts of pericardial physiology, diagnosis and treatment. J Am Coll Cardiol. 1983;1(1):240–51.
16. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, Hung J, Garcia MJ, Kronzon I, Oh JK, Rodriguez ER, Schaff HV, Schoenhagen P, Tan CD, White RD. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013;26(9):965–1012.e15.
17. Shabetai R, Mangiardi L, Bhargava V, Ross Jr J, Higgins CB. The pericardium and cardiac function. Prog Cardiovasc Dis. 1979;22(2):107–34.

## Anatomy and Physiology of the Pericardium-For Patients and their Families

The pericardium is a sac-like covering around the heart and the attachments of the blood vessels to the heart (Fig. 1.1). The pericardium serves several functions for the heart which include shielding the heart from physical and biologic insults, promotion of efficient cardiac function, and limitation of excessive movement of the heart. Despite these beneficial functions of the pericardium, those without a pericardium either due to congenital [complete] absence of the pericardium or surgical removal of the pericardium (pericardiectomy) suffer minimal consequences.

The pericardium has attachments to surrounding structures within the chest cavity (mediastinum) and is bordered by the sternum, spine, diaphragm, and lungs. The pericardium is in direct contact with the chest wall at the lower left part of the sternum where it is connected to the left fourth and fifth ribs. This area is important as it is a common area to perform a pericardiocentesis, or sampling of the pericardial fluid with a needle. The phrenic nerves, which send and receive signals to and from the diaphragms, pass along the right and left sides of the heart.

The pericardium folds about the blood vessels attached to the heart forming the pericardial space. At the locations where the pericardium folds or reflects there are small pockets of space called sinuses and recesses that are connected to the pericardial cavity. Normally, much of the pericardial fluid is contained within these sinuses and recesses (Fig. 1.3). Familiarity with the anatomy of the sinuses and recesses may prove helpful to doctors in both diagnostic and therapeutic procedures. It is also important for doctors to be familiar with the normal anatomy so as not to confuse these sinuses or recesses with other important structures or dangerous findings.

The pericardium is composed of specialized cells that serve as friction bearing surfaces as well as to transport certain substances across the pericardium. Collagen fibers within the pericardium are wavy in appearance and straighten out when stretched (Fig. 1.2). The orientation and structure of the pericardial tissue components allow for the pericardium to stretch to some degree before it reaches a limit at which point small increases in stretch result in significantly higher pressures within the pericardial space. When the pericardium is absent due to congenital absence or surgical removal the heart is capable of expanding more than it can with an intact pericardium. When the heart is chronically overloaded the heart slowly dilates and the pericardium adapts to the higher pressures. It is for this reason that slowly enlarging pericardial effusions (excessive pericardial fluid volume) do not necessitate an emergency whereas, rapidly growing effusions can potentially be life threatening.

# Etiologies of Pericardial Diseases

2

Dan G. Halpern, Vikram Agarwal,
and Leonard S. Lilly

## Introduction

There is a wide spectrum of conditions that affect the pericardium, including congenital defects and cysts, infectious, immune-mediated, metabolic, traumatic, neoplastic and drug-related causes [1] (Table 2.1). Most of these disorders result from an extrapericardial process (e.g., viral infections, uremia, chest radiation therapy), whereas a minority are isolated to the pericardium itself (e.g., cysts). Pathologically, the two most common disease processes are pericarditis (i.e., inflammation) and pericardial effusion. A less frequent development is pericardial constriction, a consequence of inflammatory insults that results in thickening, fibrosis and calcification [2]. Clinically, the presentation of pericardial disease is primarily determined by the degree and chronicity of the inflammatory process, the rate and amount of effusion accumulation, and the degree of pericardial thickening and fibrosis. The etiology of most cases of acute pericarditis is deemed "idiopathic" as no specific diagnosis is actively sought [3, 4]. The majority of such episodes are believed to be of viral origin.

Important questions in the history of patients with suspected pericardial diseases should focus on recent febrile illnesses, prior pericarditis episodes, recent procedures involving the chest, myocardial infarction (MI), the medication history (e.g., those associated with drug-induced lupus), tuberculosis exposure, travel history, a history of malignancy, previous radiation exposure, renal function, thyroid disease and the patient's immune status.

## Infectious Pericardial Diseases

### Viral Pericarditis

Viruses are the most common infectious agents that cause pericarditis. They may invade the pericardium directly, or may indirectly elicit an immune response. The most common viruses to cause pericarditis are echovirus and coxsackieviruses. Other important viral causes in the adult population include cytomegalovirus (CMV), herpesvirus (HSV), human immunodeficiency virus (HIV), and Ebstein-Barr virus (EBV). CMV pericarditis is more common in immune-compromised individuals including post-transplant and HIV patients [5]. In viral pericarditis, there is

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**Table 2.1** Etiologies of diseases of the pericardium

| | |
|---|---|
| 1. | **Idiopathic** (acute and recurrent pericarditis) |
| 2. | **Infectious** |
| | (i) **Viral** – Coxsackie A/B, echovirus, CMV,EBV, HSV, HBV, HCV, HIV/AIDS, Influenza, adenovirus, varicella, rubella, mumps, parvovirus, B19, HHV6 |
| | (ii) **Bacterial** – Staphylococci, Streptococci, *Coxiella burnetti*, *Borrelia burgdorferi*, *Haemophilus influenzae,* meningococci, Chlamydia, Mycoplasma, Legionella, Leptospira, Legionella, Listeria, rickettsiae |
| | (iii) **Mycobacterial** – *Mycobacterium tuberculosis, Mycobacterium avium-intracellulare complex (*MAIC) |
| | (iv) **Fungal** – histoplasmosis, coccidioidosis, aspergillosis, blastomycosis, candidiasis |
| | (v) **Parasitic** – Chagas disease, African tripanosomiasis, echinococcosis, toxoplasmosis, amebiasis, schistosomiasis |
| 3. | **Systemic inflammatory and autoimmune diseases** |
| | (i) **Connective tissue diseases –** systemic lupus erythematosus, rheumatoid arthritis, scleroderma, ankylosing spondylitis, mixed connective tissue disease, dermatomyositis |
| | (ii) **Vasculitides** – Takayasu arteritis, polyarteritis nodosa, Kawasaki disease, temporal arteritis, Churg-Strauss disease, Wegener granulomatosis |
| | (iii) **Rheumatic fever** |
| | (iv) **Granulomatous disease –** sarcoidosis |
| | (v) **Autoinflammatory diseases** – Familial Mediterranean Fever, inflammatory bowel diseases, TNF receptor-1 associated periodic syndrome (TRAPS) |
| 4. | **Pericardial diseases secondary to diseases of surrounding organs** – pericarditis early after myocardial infarction, congestive heart failure, myocarditis, aortic aneurysm, pulmonary embolism, pulmonary hypertension, pneumonia, esophageal disease, paraneoplastic |
| 5. | **Post cardiac injury syndrome** – Dressler syndrome (late post myocardial infarction syndrome), post-pericardiotomy syndrome, post heart transplant, pulmonary embolism |
| 6. | **Neoplastic** |
| | (i) **Primary tumors** – mesothelioma, angiosarcoma |
| | (ii) **Secondary tumors** – metastatic or by direct extension e.g., lung cancer, breast cancer, Hodgkin's lymphoma, mesothelioma, gastric and colon cancer, melanoma and sarcoma |
| 7. | **Mediastinal radiation therapy** |
| 8. | **Hemopericardium and pericardial trauma** |
| | (i) Direct injury – penetrating thoracic injury, procedure related trauma (e.g., pacemaker, ablation, PCI, device placement), esophageal perforation |
| | (ii) Indirect injury – cardiopulmonary resuscitation, blunt trauma (e.g., automobile chest impact) |
| 9. | **Aortic dissection** |
| 10. | **Renal Disease** – uremic and dialysis pericarditis |
| 11. | **Metabolic/Endocrine** – hypothyroidism (myxedema), scurvy, ovarian hyperstimulation syndrome |
| 12. | **Congenital** – pericardial cysts, absence of pericardium |
| 13. | **Drug induced pericarditis** – procainamide, hydralazine, isoniazid, methyldopa, phenytoin, penicillin, doxorubicin, daunorubicin, tetracyclines |
| 14. | **Miscellaneous** – cholesterol pericardium, chylopericardium |

commonly an upper respiratory tract infection prodrome preceding evidence of pericarditis. Assessment for rising serum viral titers has a limited role in diagnosis as it does not prove causality and most patients will have recovered before the results of such testing is available. Viral pericarditis is usually self- limiting, but may involve the myocardium (myopericarditis), or may lead to effusive or constrictive physiology.

## HIV-Related Pericardial Disease

HIV may act on the pericardium by direct invasion, by related opportunistic pathogens, by an indirect immune response and by associated neoplastic involvement (e.g., Kaposi sarcoma and lymphoma). The most common pericardial presentation in HIV patients is simple pericardial effusion, which is present in 10–20 % of cases

and has been linked to shorter survival and lower CD4 counts [1–3]. The effusions are usually small, asymptomatic and non-progressive.

Pericardial effusion in HIV patients can also result from severe hypoalbuminemia due to AIDS related cachexia or capillary leak syndrome. The latter results from elevated cytokines (IL-2 and tumor-necrosis factor) that cause a systemic inflammatory response syndrome. HIV treatments, including nucleoside reverse transcriptase inhibitors (e.g., abacavir, lamivudine, zidovudine) and protease inhibitors (e.g., saquinavir, ritonavir) may additionally cause lipodystrophy; manifested by increased pericardial fatty tissue, visualized by echocardiography or MRI.

## Bacterial Pericarditis

The most common pyogenic bacterial pathogens to invade the pericardium are staphylococci and streptococcal species [4–6] (Fig. 2.1). Less commonly implicated are *Haemophilus influenzae, Salmonella enteritidis, Niesseria meningitidis, Legionella pneumophila, Chlamydia pneumoniae, Coxiella burnetii, Treponema pallidum, Borrelia burgdorferi, Mycoplasma pneumoniae,* gram negative bacteria and rarely anaerobes. Bacterial pericarditis typically results in the accumulation of purulent fluid in the pericardial sac ranging from a thin layer to large quantities of frank pus. It is a life-threatening condition that presents as an acute febrile illness commonly complicated by tamponade. Though its prevalence has decreased since the advent of antibiotics, purulent pericarditis may result from local extension of suppurative pneumonia or cardiac ring abscess from endocarditis, following chest surgery or trauma, esophageal perforation, subdiaphragmatic abscess, or from hematogenous or lymphatic spread from a distant focus. In the developing world, tuberculous pericarditis remains the most common cause of chronic pericardial purulence. Patients with uremia, connective tissue disease and immune deficiency are more prone to this condition.

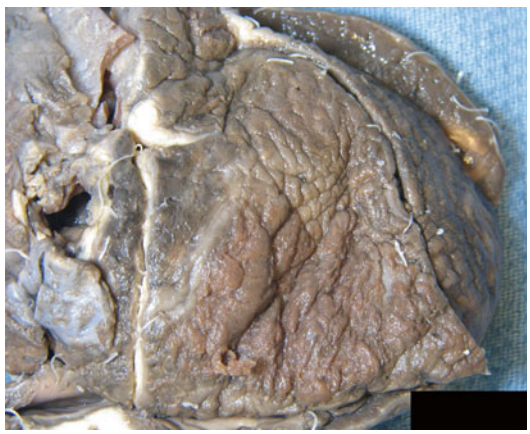

**Fig. 2.1** Purulent pericarditis. The parietal pericardium has been removed to expose the purulent material covering the visceral pericardium (Courtesy of Dr. Stephen Sanders, Boston Children's Hospital, Harvard Medical School, Boston, MA)

The most common organism cultured in bacterial pericarditis is *Staphylococcus aureus* and its route of spread is typically hematogenous. *Streptococcus pneumoniae* is the most common organism causing purulence by direct extension from an adjacent pneumonia with empyema. Although suppurative foci complicating endocarditis may infiltrate the pericardial space, sterile pericardial effusion is more common in this situation. *Salmonella enteritidis* has been reported as a cause of purulent pericarditis in patients with HIV, lupus, malignancy and cirrhosis [7]. Esophageal perforation or mediastinal extension of peritonitis is associated with gram negative bacterial pericarditis, and penetrating trauma to the chest (e.g., knife wound) is often polymicrobial. The diagnosis of bacterial pericarditis is confirmed via pericardiocentesis and identification of the responsible pathogen by microscopy and culture. Effusion characteristics are exudative with high protein and low glucose concentrations. Treatment includes drainage of the purulent effusion and systemic antimicrobial therapy. Pericardiocentesis may serve both diagnostic and therapeutic purposes, but a thick effusion with fibrin stranding may prevent the complete drainage of purulent material [6]. Irrigation of the pericardial space with fibrinolytic agents such as urokinase or streptokinase may aid in drainage [8]. The creation of a window via the subxiphoid approach allows a surgeon to mechanically lyse

adhesions and more completely evacuate the effusion. In rare instances, a complete open pericardiectomy is required to disrupt adhesions and loculations to allow complete drainage.

## Mycobacterial Pericardial Disease

Tuberculous pericarditis arises in approximately 4 % of patients with pulmonary tuberculosis (TB), and while now uncommon in the developed world, it remains an important cause of constrictive pericarditis in developing countries [9], where it is commonly diagnosed in association with AIDS. *Mycobacterium tuberculosis* infects the pericardium by direct invasion from adjacent tissues (primarily the lungs and the tracheobronchial tree), by hematogenous spread, or from reactivation from an extra-cardiac source. Pathologically four stages of development of pericardial disease occur: (1) granuloma formation with fibrinous exudation containing high concentrations of tuberculous bacilli; (2) serosanguinous effusion with a low concentration of bacilli, high protein and lymphocytic predominant exudate; (3) caseation of granulomas with early pericardial constriction including fibrosis and thickening; and (4) full pericardial constriction, scarring and calcification [10]. Progression among the stages is variable and generally the acute pericardial phase lasts between 2 to 4 weeks and the constriction component may take several years to develop.

Classically patients with tuberculous pericarditis present with fever, weight loss, night sweats and symptoms of right heart failure in the chronic phase, but at any stage may experience chest discomfort, cough and shortness of breath. Constrictive pericarditis can be dry or effusive and subsequently its presentation may vary from right-sided heart failure to tamponade, respectively.

Suspicion of mycobacterial disease starts by recognizing a history of TB exposure or HIV infection. Screening testing (e.g., tuberculin skin test or interferon gamma) may disclose exposure, but does not prove active disease. The diagnosis of TB pericarditis [11, 12] requires the identification of acid-fast bacilli (AFB) by stain or culture (40–60 % sensitive), a positive polymerase chain reaction for the DNA of *Mycobacterium tuberculosis* in the pericardial effusion, or demonstration of caseating granulomas in biopsied pericardial tissue (80–90 % sensitivity). The diagnostic yield is highest during the effusive stage. An increased level of adenosine deaminase (ADA) >40 units/l in pericardial effusion is 88 % sensitive and 83 % specific for TB. Imaging studies of the chest with CT or MRI may help detect pulmonary and other organ involvement. The mainstay of treatment is multidrug antituberculous therapy, which should be empirically administered when clinical suspicion is high in endemic areas of TB while awaiting conclusive diagnosis. Corticosteroid therapy for tuberculous pericarditis is controversial [13]. While such therapy may shorten the duration of symptoms, there has been no demonstrated survival benefit or prevention of progression to constriction. Surgical treatment of constrictive pericarditis with pericardiectomy is reserved for patients who exhibit persistent hemodynamic findings of constriction.

## Fungal Pericarditis

Fungal pericarditis in the immune-competent patient is seen in endemic areas for *Histoplasma capsulatum* and *Coccidioides immitis*. Conversely, in the immunocompromised patient, candidiasis, aspergillosis and blastomyces infections are major fungal pathogens. Other patients predisposed to fungal infections are those who have chronic indwelling catheters, dialysis patients, alcoholics, burn victims and in individuals after prolonged antimicrobial therapy [14]. Diagnosis is made by fungal staining, positive cultures from pericardial effusion or tissue, and by measurement of serum titers of anti-fungal antibodies. Other than uncomplicated localized histoplasmosis, treatment usually requires antifungal antimicrobial therapy [15].

## Parasite-Related Pericardial Disease

Protozoans and helminthes may affect the pericardium during their migration in the body, or as

a target organ [16]. The most common parasitic infection that involves the heart is Chagas disease (American trypanosomiasis) caused by *Trypanosoma cruzi,* which is endemic to central and south America. It causes myopericarditis acutely and cardiomyopathy in the chronic phase. Conversely, the African form of trypanosomiasis ("sleeping sickness") caused by *T. gambiense or T. rhodesiense* may incite pericarditis even months to years following the initial infection. *Toxoplasma gondii* may result in acute pericarditis in the immune-compromised and progress to constrictive pericarditis. Other rare parasitic causes of pericarditis include *Entamoeba histolytica* (amebiasis), *Echinococcus granulosus*, *Trichinella spiralis* and *Schistosoma* species.

## Pericardial Involvement in Systemic Inflammatory Diseases

Systemic inflammatory diseases encompass rheumatogic diseases, vasculitides, granulomatous conditions, and autoinflammatory diseases. Although pericardial involvement is not uncommon in these disorders, only rarely do patients present with primary cardiac symptoms. Pericardial conditions that can arise during the course of these systemic diseases include acute and recurrent pericarditis and pericardial effusions. Usual screening tests include antinuclear antibodies (ANA) and rheumatoid factor. The overall prognosis of pericardial involvement in systemic inflammatory diseases is good, and only rarely is there progression to cardiac tamponade or constrictive pericarditis.

### Rheumatologic Diseases (Connective Tissue Diseases)

#### Systemic Lupus Erythematosus

Cardiac involvement in systemic lupus erythematosus (SLE) can occur in multiple forms, including premature and accelerated coronary atherosclerosis, venous thromboembolism and cardiac inflammation [17]. Pericardial involvement is common and usually benign. Although pericardial effusion develops in >40 % of patients during the course of disease, symptoms of pericarditis occur only occasionally, usually when the systemic disease involves other serosal surfaces (e.g., pleuritis) [18].

#### Rheumatoid Arthritis

Clinical acute pericarditis arises in approximately 25 % of patients with rheumatoid arthritis (RA) [19]. When present, pericarditis usually occurs with active rheumatoid disease and other extra-articular manifestations. Symptoms typically respond to high dose aspirin and other NSAIDs.

#### Systemic Sclerosis

Systemic sclerosis is characterized by the excess production of collagen, which results in fibrosis of involved organs. Although the most common cardiac manifestations are the development of systemic or pulmonary hypertension, it can also directly affect the myocardium, pericardium and conduction system. Symptomatic pericarditis occurs in up to 20 % of patients with systemic sclerosis, while evidence of pericardial involvement is found in >50 % of patients at autopsy [20]. Late constrictive pericarditis can also occur.

#### Acute Rheumatic Fever

Although rarely seen in the developed world, acute rheumatic fever remains prevalent in developing countries. Acute pericarditis is commonly seen in the first week of acute rheumatic fever, and is a sign of active rheumatic carditis. It usually manifests with a loud pericardial rub, and although pericardial effusion is commonly seen, pericardial tamponade is rare.

### Other Rheumatologic Conditions

In patients with polymyostitis and dermatomyositis, pericardial involvement is not as common as other connective tissue disorders, occuring in <10 % of patients [21]. Pericarditis is more common (10–30 %) in patients with mixed connective tissue disorder, but complications such as pericardial tamponade are unusual [21].

### Vasculitides

Vasculitides are characterized by inflammation and damage of vessel walls. Large vessel vasculitides include Takayasu arteritis and giant cell arteritis, while medium vessel vasculitis includes polyarteritis nodosa and Kawasaki disease. Small vessel vasculitides includes Churg-Strauss syndrome and Wegener's disease. Pericardial involvement is rare in the large vessel disorders compared to those with medium and small vasculitides [21].

### Granulomatous Diseases

Sarcoidosis is the predominant granulomatous disease with clinically significant pericardial involvement. Although mild to moderate pericardial effusions are commonly detected, symptomatic pericarditis is rare [22].

### Autoinflammatory Diseases

Familial Mediterranean fever (FMF) is an autosomal recessive disorder that occurs in specific ethnic groups of Mediterranean countries and presents with recurrent attacks of serositis, including pericarditis. TNF receptor-1 associated periodic syndrome (TRAPS) is a rare autosomal dominant disorder that arises from mutations in the gene that codes for a TNF alpha receptor. Protracted fever, eye, muscle, and pericardial inflammation are clinical manifestations [23].

## Pericardial Diseases Secondary to Diseases of Surrounding Organs

Pericardial abnormalities may result from conditions that arise in adjacent structures such as the myocardium (e.g., heart failure, myocardial infarction, myocarditis), the great vessels (e.g., aortic dissection), the lungs (pneumonia and pulmonary embolism), the thoracic duct (e.g., chylopericardium) and the esophagus.

### Congestive Heart Failure

Both pericardial and pleural effusions are commonly present in congestive heart failure and myocarditis. Pericardial effusions are related to increased right atrial pressure promoting transudation into the pericardial space [24].

### Post Myocardial Infarction Pericarditis

Post myocardial infarction (MI) pericarditis exists in two forms. The first form presents in the first few days after a transmural infarction as a direct extension of inflammation to the pericardium [11, 25]. The incidence of post-infarction pericarditis has decreased to <5 % since the introduction of reperfusion therapies and limitation of infarct size. The classic ECG changes of pericarditis are usually not apparent and the diagnosis is based on clinical suspicion, fever, pleuritic chest pain, and the presence of an effusion by echocardiography. Recommended treatment is aspirin, as other nonsteroidal anti-inflammatory agents and steroids have been associated with delayed infarct healing [26]**.** The second form of pericarditis after MI occurs later and is known as Dressler syndrome. When present, it arises weeks after the MI and is presumed to have an autoreactive immune mechanism similar to the post-cardiac injury syndrome described later.

### Pulmonary Hypertension

Pericardial effusion arises in up to 25 % of patients with group I pulmonary hypertension (i.e., idiopathic or primary). Larger effusions are associated with right heart failure, elevated right atrial pressures, poor hemodynamic status and worse prognosis [27–29]. These effusions are rarely of hemodynamic significance. Treatment should focus on the primary process and not on the pericardial effusion.

## Post Cardiac Injury Syndrome (PCIS)

In addition to Dressler syndrome, pericarditis may occur weeks to months after other forms of cardiac injury including patients who have undergone cardiac surgery (postpericardiotomy syndrome), percutaneous cardiac procedures (e.g., percutaneous coronary interventions, pacemaker lead insertion, electrophysiology ablation procedures), or who have sustained chest trauma [25, 30, 31]. It is presumed that these conditions share a common pathway in which cardiac injury (ischemic, traumatic or iatrogenic) exposes myocardial antigens which incites a systemic inflammatory response. PCIS presents with fever, acute pleuritic chest pain, pericardial effusion and pleural infiltrates and effusions, with elevated inflammatory markers. Of note, colchicine was shown to prophylactically reduce the incidence of PCIS after cardiac surgery in the prospective randomized Colchicine for Post-Pericardiotomy Syndrome (COPPS) trial [32].

## Pericardial Trauma

Injury to the pericardium can occur from blunt trauma (e.g., steering wheel impact during a motor vehicle accident or cardiopulmonary resuscitation) or penetrating trauma (e.g., stab or bullet wound, or iatrogenic during medical procedures). In such cases blood accumulates rapidly within the pericardial space such that a small volume of effusion can result in tamponade physiology (as little as 100–200 ml) [33]. In direct injuries to the pericardium with hemodynamic compromise, thoracotomy with surgical exploration is required for survival. As with all types of pericardial injury, PCIS may develop later in the course, and constriction may develop following an organized intra-pericardial hematoma.

Iatrogenic injuries to the pericardium have risen in frequency as the number and complexity of percutaneous interventions increase [11, 33]. Transseptal puncture to access the left heart appears to hold a high risk of wall perforation (1–3 %), especially if not performed under biplane fluoroscopy or intra-cardiac echocardiogram guidance. Other procedures or hardware that may traumatize the pericardium include pacemaker leads (0.3–3.1 %), guidewires for stent or other hardware placement (0.1–3 %), rotablation (0.1–5.4 %), atherectomy (0–2 %), high pressure stenting (<2 %), mitral valvulopasty (1–4 %), pulmonary artery catheters, endomyocardial biopsies (0.3–5 %), atrial fibrillation ablation (1–6 %) and atrial septal occluder (1.8–3 %). Rescue pericardiocentesis in these situations has a very high success rate (95 %) and the mortality rate is low (<1 %).

## Aortic Dissection and Hemopericardium

Hemopericardium is a life-threatening complication of ascending aortic dissection (type A) and pre-operative tamponade is a leading cause of mortality in this condition. A presentation of acute aortic regurgitation with pericardial effusion should raise the suspicion of an ascending aortic dissection, the presence of which can be confirmed by CT or transesophageal echocardiography [34]. Prompt surgical repair of the dissection is required. Preoperative pericardiocentesis with control of intravascular volume has been performed successfully in patients who could not otherwise survive awaiting surgical intervention [35].

# Neoplastic Pericardial Disease

Pericardial tumors are uncommon, with metastatic involvement occurring more frequently than primary neoplasms. Neoplastic effusions tend to be large and hemorrhagic. In general autopsy studies of cancer patients, malignant involvement of the pericardium is detected in up to 20 % [36] (Fig. 2.2).

## Primary Tumors of the Pericardium

Mesothelioma is the most common primary malignant neoplasm of the pericardium, accounting for ~50 % of all primary pericardial tumors.

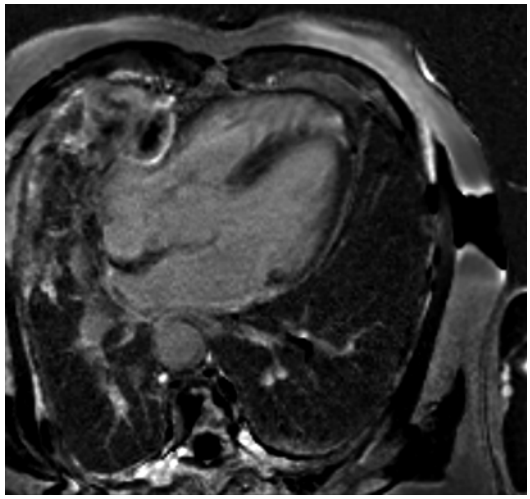

**Fig. 2.2** Metastatic disease. MRI delayed enhancement image demonstrating mesothelioma penetrating the pericardium through a pericardial patch (Courtesy of Dr. Michael L. Steigner, Brigham and Women's Hospital, Harvard Medical School, Boston, MA)

As compared to pleural mesothelioma, no definite association with asbestos exposure has been established. It may arise in children or adults, with a preponderance for males (2:1 male: female ratio) [37]. Typically at presentation, patients present with diffuse pericardial involvement and signs and symptoms of constrictive pericarditis may be present. Other primary malignant pericardial tumors include sarcomas (fibrosarcoma and liposarcoma), lymphoma and malignant teratomas. These malignancies usually present as large masses with hemorrhagic pericardial effusion. Benign pericardial tumors include lipomas, teratomas, and fibromas.

## Secondary or Metastatic Malignant Pericardial Disease

Metastases to the heart and pericardium are far more common than primary tumors and portend a poor prognosis. Noncardiac tumors may invade the heart and pericardium by means of lymphatic or hematogenous dissemination or local extension. Pulmonary primary tumors are the most common source of pericardial neoplastic disease, accounting for approximately 40 % of malignant effusions [38, 39]. Other primary tumors that spread to the pericardium include breast, melanoma, and hematologic malignancies, including lymphoma and leukemia. Tumors below the diaphragm, such as from the gastrointestinal tract and the renal system, rarely extend to the pericardium. Pericardial Kaposi sarcoma or lymphoma may appear in patients with HIV disease.

## Radiation Pericarditis

Therapeutic radiation for malignancy is an important cause for acute pericarditis, pericardial effusion and constrictive pericarditis (Fig. 2.3). Most cases are secondary to irradiation of the chest for Hodgkin lymphoma, breast or lung cancer [40]. Pericardial inflammation may present during acute radiation treatment or findings of constrictive pericarditis may arise many years thereafter. Constriction related to radiation therapy increases the surgical risks of pericardiectomy and worsens post-operative outcomes.

## Renal Related Pericardial Disease

Pericardial involvement in advanced renal disease includes uremic pericarditis (6–10 % of patients, prior to initiation of dialysis), dialysis-related pericarditis, large pericardial effusions and rarely constrictive pericarditis [11, 41]. The incidence of pericarditis rises with greater levels of azotemia and uremic pericarditis is an indication for acute initiation of dialysis. Pericarditis arising in patients already on dialysis may result from inadequate intensity of dialysis treatments. Pathologically, there are adhesions bridging a thickened pericardium in a "bread and butter" appearance. The pericardial effusion may range from serous fluid to hemorrhagic. Although most patients present with pleuritic chest pain and fever, others may remain asymptomatic and afebrile. Clinically, the hemodynamic response to cardiac compression may be blunted (i.e., absence of tachycardia) in patients with renal failure, due to accompanying autonomic dysfunction [42]. Pericardial rubs are common but

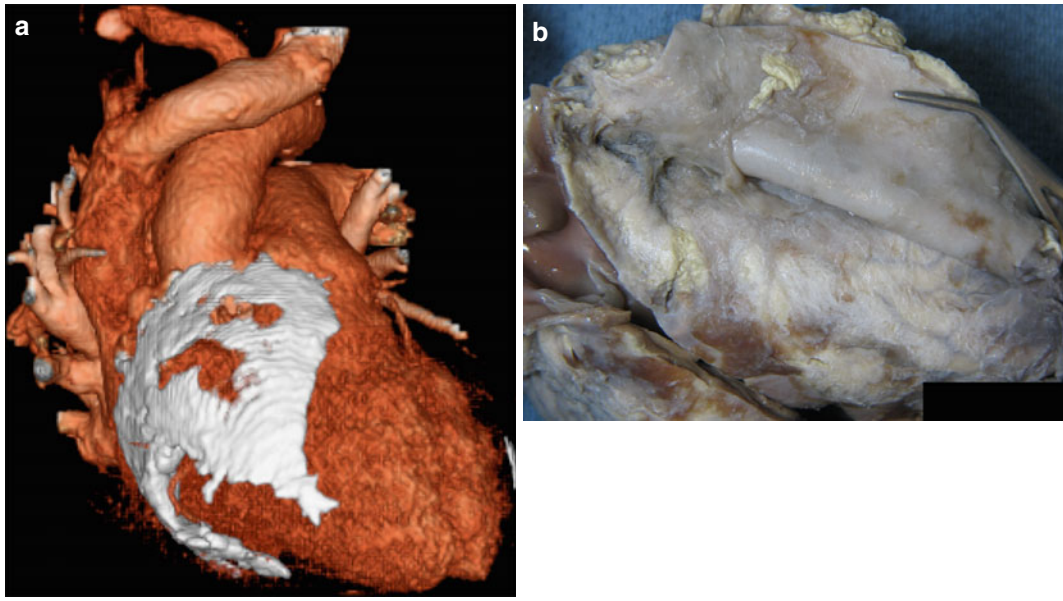


**Fig. 2.3** Radiation pericarditis. (**a**) CT 3D volume rendering of substantial calcification of the pericardium in a patient with radiation induced constrictive pericarditis. (**b**) Radiation induced constrictive pericarditis in a patient with Hodgkin's disease. The thickened and calcified parietal pericardium is artificially folded outward to demonstrate an elaborate network of adhesions and thickening between the parietal and visceral pericardium (Image **a**: Courtesy of Dr. Michael L. Steigner, Brigham and Women's Hospital, Harvard Medical School, Boston, MA. Image **b**: Courtesy of Dr. Stephen Sanders, Boston Children's Hospital, Harvard Medical School, Boston, MA)

are often transient. Pericardial effusions are found by imaging in the majority of patients and may be accompanied by pleural effusions. Typical ECG findings of pericarditis are often absent. Treatment requires intensive dialysis, which typically results in rapid improvement of symptoms and size of the effusion. However, vigorous dialysis should not be initiated until cardiac compression has been ruled out, as a rapid decrease in intravascular volume could result in tamponade physiology in that setting. Furthermore, it is preferable to consider non-heparinized hemodialysis, or peritoneal dialysis, in the setting of a significant pericardial effusion to avoid the possibility of intrapericardial hemorrhage. NSAIDS and systemic corticosteroids have been used in cases of dialysis failure with limited efficacy.

Subxiphoid pericardiotomy is reserved for non-resolving effusions, and at some centers is accompanied by instillation of a nonabsorbable steroid. Full pericardiectomy is rarely needed for refractory cases.

In renal transplant patients [43], CMV pericarditis should be excluded as a cause of pericardial effusion. An effusion may also appear as a rare side effect of sirolimus immunosuppressant therapy in this population (≤2 % of patients).

## Congenital Anomalies of the Pericardium

### Total and Partial Absence of the Pericardium

Congenital defects of the pericardium are rare (1/10,000 of autopsies), and are divided into total absence of the pericardium (heart and lung in the same cavity) and partial absence (Fig. 2.4). The defects are the result of failure of the pleuropericardial membranes to fuse in utero. The pericardium develops during the third to seventh weeks of embryonic life from the lateral mesodermal plate that lines the pleural, pericardial

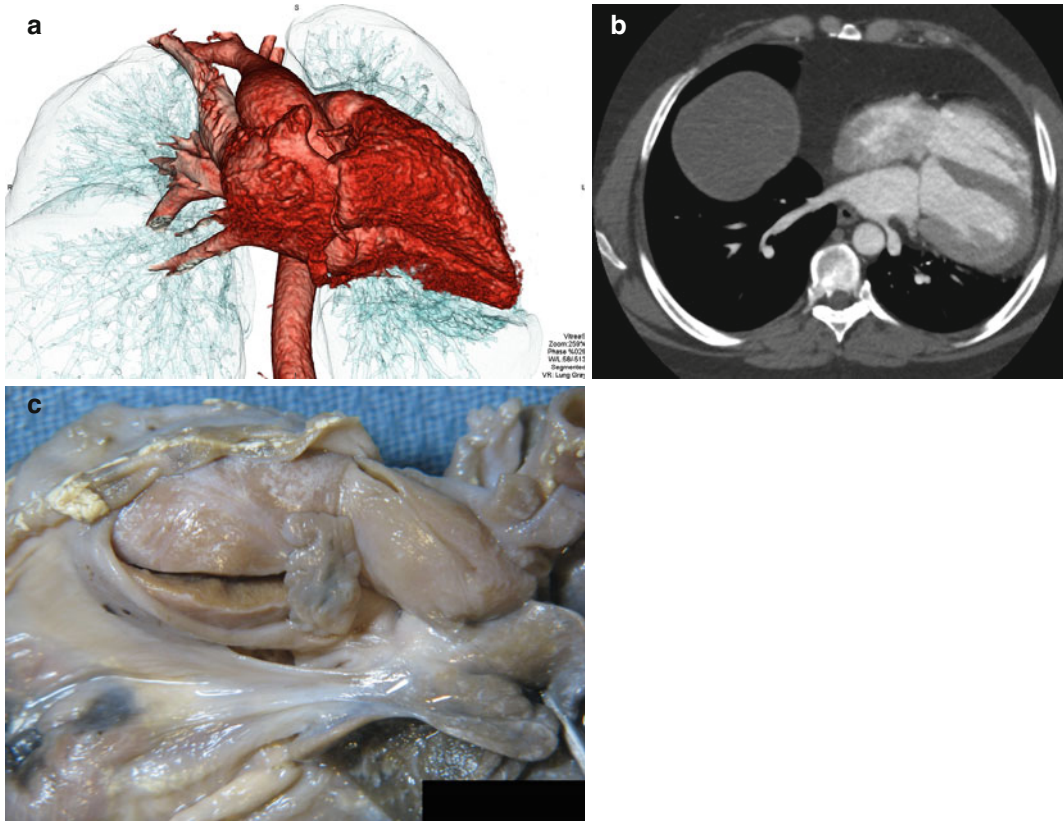


**Fig. 2.4** Partial absence of the pericardium. (**a**) CT 3D volume rendered image depicting the lateral displacement of the heart to the left. The exposed great vessels cause the lung to abnormally occupy the space between the aorta and pulmonary artery (*arrow*). (**b**) Axial CT image depicting the extreme lateral rotation of the heart with its apex pointing posteriorly. (**c**) Pathological specimen – the pericardium is missing over the lateral left border of the heart and the proximal great vessels. The existing pericardium has a thickened and smooth edge (Images **a**, **b**: Courtesy of Dr. Michael L. Steigner, Brigham and Women's Hospital, Harvard Medical School, Boston, MA. Image **c**: Courtesy of Dr. Stephen Sanders, Boston Children's Hospital, Harvard Medical School, Boston, MA)

and peritoneal spaces. There is predominance of such defects of the left side (70 %) versus the right (17 %) or bilateral partial absence (13 %) [44, 45]. Two theories have been raised to explain this phenomenon. Perna et al. suggested that premature atrophy of the left duct of Cuvier that gives rise to the left superior vena cava (connecting the left innominate vein to the coronary sinus) may cause absorption of the pericardium on the left because of decreased blood supply. Alternatively, Sunderland et al. proposed that defects are the consequence of dyssynchrony between growth of the heart and the enveloping pericardium, especially on the left side where structures increase to a greater volume [46]. Associated congenital abnormalities exist in approximately 30 % of patients, including patent ductus arteriosus, bronchogenic cysts, tricuspid insufficiency, atrial septal defects, left diaphragmatic hernia and pulmonary sequestration. Although most patients with total absence of the pericardium are asymptomatic, torsion and increased stress between the base of the heart and the great vessels might explain reports of chest pain and dyspnea. This is in contrast to partial defects of the pericardium that may pose clinical risk because of displacement or herniation of heart structures (e.g., atria or partial ventricle). There is also an increased risk of traumatic aortic dissection due to increased structure mobility.

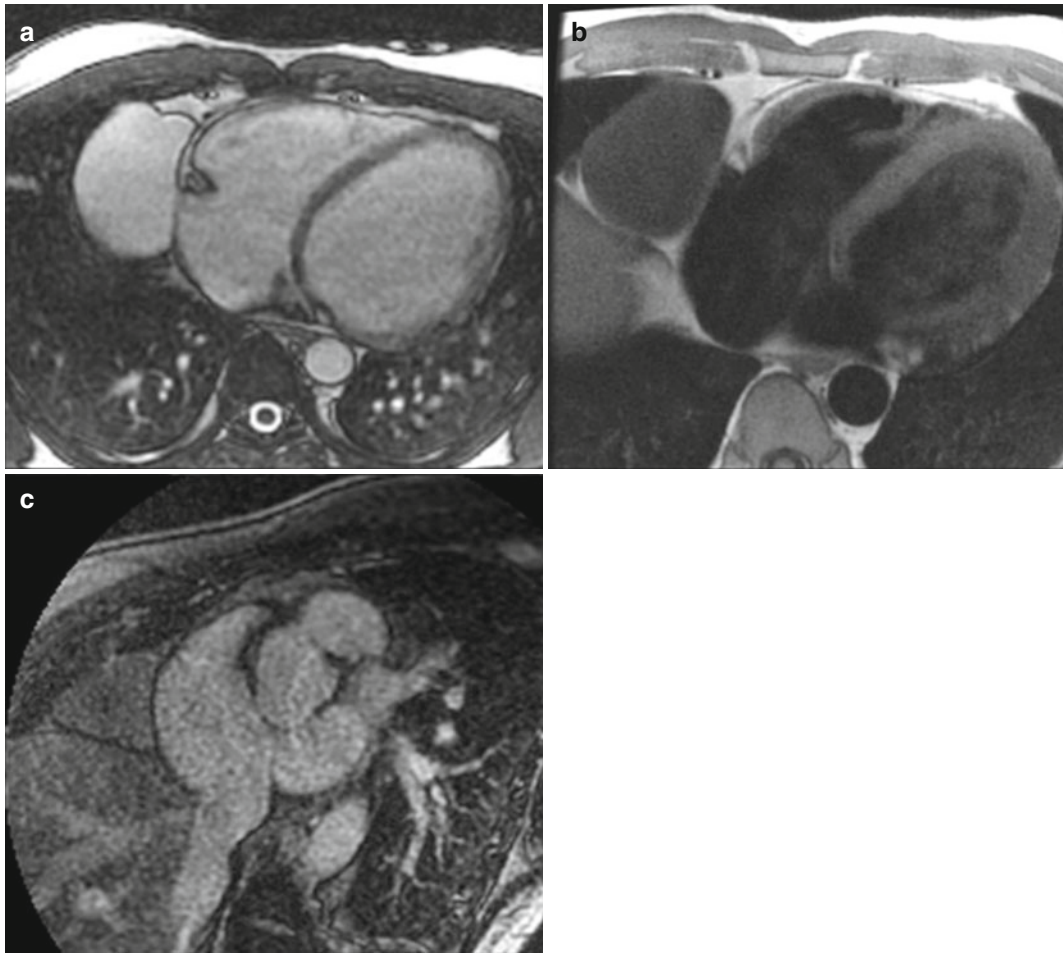


**Fig. 2.5** Pericardial cyst. (**a**) Steady state free procession (SSFP) acquisition showing bright fluid filled cyst adherent to the lateral wall of the right ventricle (**b**). T1 weighted double inversion recovery sequence demonstrating hypointense fluid. (**c**) Delayed enhancement image showing no uptake of gadolinium in the cyst (Courtesy of Dr. Michael L. Steigner, Brigham and Women's Hospital, Harvard Medical School, Boston, MA)

Diagnostically, most cases are detected incidentally (during imaging or surgery).

In congenital absence of the pericardium, the heart's apex may shift to the mid-axillary line with cardiomegaly on chest X-ray and the ECG exhibits rightward axis and incomplete right bundle branch block. On echocardiography, the lateral apical shift causes right-sided predominance on the apical long-axis view (and may be incorrectly interpreted as right ventricular enlargement). MRI is the modality of choice for the detection of pericardial defects and possible herniation of heart structures [47]. Surgical pericardioplasty is indicated when there is a high risk of mechanical complication.

## Pericardial Cysts

Pericardial cysts may be congenital or acquired; with an incidence of 1/100,000 individuals (Fig. 2.5). Congenital cysts are usually benign, asymptomatic and incidentally discovered [48, 49]. They are usually located at the right costophrenic angle (51–70 %) or left costophrenic angle (28–38 %) and rarely elsewhere in the mediastinum. Histologically they contain a single layer of mesothelial cells surrounded by connective tissue. Acquired types of cysts include inflammatory (e.g., rheumatic, post-cardiotomy or traumatic) and infectious (e.g., bacterial, echinococcal or

tuberculous). They can be divided into unilocular or multilocular types, with a diameter typically ranging from 1 to 5 cm. Symptomatology of chest pain, cough and dyspnea may arise from the mass effect of a cyst and in rare cases from hemorrhagic eruption of the cyst into the pericardial space causing tamponade. On echocardiography a cyst is imaged as a hypoechoic structure with distal acoustic enhancement because of its fluid content. Calcification of the cyst and pericardial effusion are rare. CT and MRI can distinguish cysts from other entities such as hematoma, a prominent fat pad, a large left atrial appendage or tumor [50]. Congenital cysts are usually treated conservatively unless there is evidence of structural compression. When treatment is necessary, percutaneous aspiration and ethanol sclerosis can be attempted prior to thoracotomy and surgical excision. Hydatid cysts are aspirated and the cyst is injected with ethanol or silver nitrate after pre-treatment with albendazole.

## Hypothyroidism Related Pericardial Effusion

Pericardial effusion in clinical hypothyroidism is seen in up to 30 % of patients, is often large, but rarely progresses to tamponade due to its slow accumulation [51, 52]. Other cardiac manifestations of hypothyroidism include impaired ventricular contractility, bradycardia, and non-pitting edema. The ECG typically demonstrates sinus bradycardia, decreased voltage and mild prolongation of the QT interval. Therapy consists of thyroid hormone replacement therapy, and the degree of hypothyroidism determines the route of administration (i.e., intravenous versus oral). Thyroid hormone enhances the absorption of the pericardial effusion and thus unless hemodynamically compromising, there is no urgency to drain hypothyroid-induced effusions.

## Drug/Toxin Induced Pericarditis

Many drugs and toxins may precipitate pericardial inflammation and effusion [11] (Table 2.2). The mechanisms by which the pericardium is affected include drug-induced lupus reactions, hypersensitivity, "serum sickness", foreign substance reaction and immunopathy. Procainamide, hydralazine, anti-tumor necrosis factor (TNF)- α therapies, isoniazid, reserpine, methyldopa and phenytoin are examples of drugs that may induce a lupus-like response with manifestations that include pericardial effusion. Penicillin, L-tryptophan and cromolyn sodium can induce hypersensitivity reactions. Minoxidil, amiodarone, cyclosporine, and anthracyclines (e.g., doxorubicin) may result in idiosyncratic pericardial reactions. "Serum sickness" may arise after administration of blood products and foreign antisera (e.g., anti-tetanus). Venomous scorpion fish sting is an example of a toxin that has been reported to cause pericarditis. Additional foreign-substance reactions can occur from direct contact with the pericardium by talc, asbestos, silicones, tetracycline and inhalation of Teflon (polytetrafluoroethylene).

**Table 2.2** Drug and toxin induced pericardial disease

| |
|---|
| 1. D**rug induced lupus erythematosus (positive anti-nuclear antibody (ANA) and anti-histone antibody)** – Procainamide, hydralazine, methyldopa, isoniazid, reserpine, anti-tumor-necrosis factor (TNF)-alpha agents, phenytoin, tocainide, mesalazine |
| 2. H**ypersensitivity reactions (eosinophilic)** – penicillin, L-tryptophan, cromolyn sodium |
| 3. I**diosyncratic reaction** – amiodarone, minoxidil, streptokinase, cyclophosphamide, cyclosporine, thiazides, streptomycin, thiouracils, sulfa, GM-CSF, vaccines, 5-fluorouracil, bromocriptine, polymer fume inhalation, cytarabine, p-Aminosalicylic acid, mesalazine, practolol, psicofuranine, methylsergide |
| 4. A**nthracycline derivatives** – doxorubicin, daunorubicin |
| 5. S**erum sickness** – blood products, foreign antisera (antitetanus) |
| 6. V**enom** – scorpion venom |
| 7. F**oreign body reaction** – Talc (Mg silicate), tetracycline, asbestos, sclerosant, Iron |
| 8. H**emopericardium** – anticoagulants and thrombolytic agents |

## Cholesterol Pericarditis

Cholesterol pericarditis is an uncommon condition manifested by elevated cholesterol levels in the pericardial effusion, with crystal formation in chronic cases. It most often results from a chronic pericardial effusion as may occur in rheumatoid arthritis, tuberculosis infection, hypothyroidism and rarely with pericardial trauma [53, 54]. Classically the associated effusion is large, has a "gold paint" hue and the cholesterol concentration is high (>500 mg/dl) with a cholesterol to triglyceride ratio >1. Crystal formation does not usually develop in myxedema. The pathophysiology of the disease is unknown, but is presumed to be related to cholesterol debris accumulation from lysed pericardial or red blood cells with thickening and scarring of the pericardial tissue. Therapy is based on treating the underlying systemic disease, and when needed for chronic scarring, pericardiectomy.

## Chylopericardium

Chylopericardium is a rare condition that arises from an abnormal communication between the thoracic duct and the pericardial space [11, 55]. This may occur by direct injury to the thoracic duct from chest trauma or surgery, or indirectly by congenital malformations or tumors (lymphangiomas, aplasia of the cisterna chyli, lymphangiomatous hamartomas, lymphangiectasis and Gorham's disease) as well as acquired conditions that cause obstruction (subclavian vein thrombosis, pancreatitis, infections (e.g., TB) and mediastinal tumors). Chylous pericardial effusions appear milky-opaque on aspiration, and have a high concentration of triglycerides (>500 mg/dl), protein (>3 g/dl), a high specific gravity (1.010–1.021) and a cholesterol to triglyceride ratio <1. There is usually lymphocytic predominance and the effusion is positive for Sudan III stain for fat globules. A diet devoid of triglycerides would cause the effusion to lose its milky appearance. CT lymphangiography may identify the responsible thoracic duct abnormality. Radionuclide imaging with 99mTechnicium labeled red blood cells 24 hours after oral administration of 131-I-triolein has been shown to identify chylous effusions.

The clinical presentations of chylopericardium include acute pericarditis, a large pericardial effusion with or without tamponade physiology, or constrictive pericarditis. The first line of treatment is pericardiocentesis (which is typically required for diagnosis) and dietary modification with a medium chain enriched triglyceride diet. If the effusion reaccumulates, surgical correction or shunt placement between the pericardium and the peritoneum (where the chyle can be reabsorbed) is required [56].

## Pericardial Diseases During Pregnancy

Pericardial effusions are common during pregnancy, occurring in up to 20 % of women in the first and second trimester and up to 40 % in the third trimester [57]. Such effusions are usually small in size and are almost always clinically silent. Effusions during pregnancy have been associated with increased weight (fluid retention), hypertension and nonspecific ST-T abnormalities on the ECG. The effusion usually resolves spontaneously by 2 months after delivery.

Acute pericarditis during pregnancy is similar in etiology and outcomes to the general population, but its treatment requires caution as aspirin and other NSAIDs may cause premature closure of the ductus arteriosus and can compromise fetal renal function after the 20th week of gestation. Generally, colchicine treatment is avoided during pregnancy because of demonstrated teratogenicity in animals. If needed, low-dose corticosteroids are considered safe during pregnancy (e.g., prednisone <25 mg/day, with a downward taper).

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## References


1. Blanchard DG, Hagenhoff C, Chow LC, McCann HA, Dittrich HC. Reversibility of cardiac abnormalities in human immunodeficiency virus (hiv)-infected individuals: a serial echocardiographic study. J Am Coll Cardiol. 1991;17:1270–6.
2. Chen Y, Brennessel D, Walters J, Johnson M, Rosner F, Raza M. Human immunodeficiency virus-associated pericardial effusion: report of 40 cases and review of the literature. Am Heart J. 1999;137:516–21.
3. Heidenreich PA, Eisenberg MJ, Kee LL, Somelofski CA, Hollander H, Schiller NB, Cheitlin MD. Pericardial effusion in aids. Incidence and survival. Circulation. 1995;92:3229–34.
4. Sagrista-Sauleda J, Barrabes JA, Permanyer-Miralda G, Soler-Soler J. Purulent pericarditis: review of a 20-year experience in a general hospital. J Am Coll Cardiol. 1993;22:1661–5.
5. Klacsmann PG, Bulkley BH, Hutchins GM. The changed spectrum of purulent pericarditis: an 86 year autopsy experience in 200 patients. Am J Med. 1977;63:666–73.
6. Augustin P, Desmard M, Mordant P, Lasocki S, Maury JM, Heming N, Montravers P. Clinical review: intrapericardial fibrinolysis in management of purulent pericarditis. Crit Care. 2011;15:220.
7. Hsu RB, Lin FY. Risk factors for bacteraemia and endovascular infection due to non-typhoid salmonella: a reappraisal. QJM. 2005;98:821–7.
8. Defouilloy C, Meyer G, Slama M, Galy C, Verhaeghe P, Touati G, Ossart M. Intrapericardial fibrinolysis: a useful treatment in the management of purulent pericarditis. Intensive Care Med. 1997;23:117–8.
9. Fowler NO. Tuberculous pericarditis. JAMA. 1991;266:99–103.
10. Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. Circulation. 2005;112:3608–16.
11. Maisch B, Seferovic PM, Ristic AD, Erbel R, Rienmuller R, Adler Y, Tomkowski WZ, Thiene G, Yacoub MH. Guidelines on the diagnosis and management of pericardial diseases executive summary; the task force on the diagnosis and management of pericardial diseases of the european society of cardiology. Eur Heart J. 2004;25:587–610.
12. Reuter H, Burgess L, van Vuuren W, Doubell A. Diagnosing tuberculous pericarditis. QJM. 2006;99:827–39.
13. Ntsekhe M, Wiysonge C, Volmink JA, Commerford PJ, Mayosi BM. Adjuvant corticosteroids for tuberculous pericarditis: promising, but not proven. QJM. 2003;96:593–9.
14. Kraus WE, Valenstein PN, Corey GR. Purulent pericarditis caused by candida: report of three cases and identification of high-risk populations as an aid to early diagnosis. Rev Infect Dis. 1988;10:34–41.
15. Wheat J. Histoplasmosis. Experience during outbreaks in indianapolis and review of the literature. Medicine (Baltimore). 1997;76:339–54.
16. Hidron A, Vogenthaler N, Santos-Preciado JI, Rodriguez-Morales AJ, Franco-Paredes C, Rassi Jr A. Cardiac involvement with parasitic infections. Clin Microbiol Rev. 2010;23:324–49.
17. Mandell BF. Cardiovascular involvement in systemic lupus erythematosus. Semin Arthritis Rheum. 1987;17:126–41.
18. Tincani A, Rebaioli CB, Taglietti M, Shoenfeld Y. Heart involvement in systemic lupus erythematosus, anti-phospholipid syndrome and neonatal lupus. Rheumatology (Oxford). 2006;45 Suppl 4:iv8–13.
19. Grossman LA, Kaplan HJ, Ownby FD, Grossman M. Acute pericarditis with subsequent clinical rheumatoid arthritis. Arch Intern Med. 1962;109:665–72.
20. Byers RJ, Marshall DA, Freemont AJ. Pericardial involvement in systemic sclerosis. Ann Rheum Dis. 1997;56:393–4.
21. Imazio M. Pericardial involvement in systemic inflammatory diseases. Heart. 2011;97:1882–92.
22. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. Am J Respir Crit Care Med. 1999;160:736–55.
23. Rigante D, Cantarini L, Imazio M, Lucherini OM, Sacco E, Galeazzi M, Brizi MG, Brucato A. Autoinflammatory diseases and cardiovascular manifestations. Ann Med. 2011;43:341–6.
24. Natanzon A, Kronzon I. Pericardial and pleural effusions in congestive heart failure-anatomical, pathophysiologic, and clinical considerations. Am J Med Sci. 2009;338:211–6.
25. Imazio M, Hoit BD. Post-cardiac injury syndromes. An emerging cause of pericardial diseases. Int J Cardiol. 2013;168:648–52.
26. Hammerman H, Alker KJ, Schoen FJ, Kloner RA. Morphologic and functional effects of piroxicam on myocardial scar formation after coronary occlusion in dogs. Am J Cardiol. 1984;53:604–7.
27. Fenstad ER, Le RJ, Sinak LJ, Maradit-Kremers H, Ammash NM, Ayalew AM, Villarraga HR, Oh JK, Frantz RP, McCully RB, McGoon MD, Kane GC. Pericardial effusions in pulmonary arterial hypertension: characteristics, prognosis and role of drainage. Chest. 2013;144:1530–8.
28. Hinderliter AL, Willis PWT, Long W, Clarke WR, Ralph D, Caldwell EJ, Williams W, Ettinger NA, Hill NS, Summer WR, de Biosblanc B, Koch G, Li S, Clayton LM, Jobsis MM, Crow JW. Frequency and prognostic significance of pericardial effusion in primary pulmonary hypertension. Pph study group. Primary pulmonary hypertension. Am J Cardiol. 1999;84:481–4, A410.
29. Raymond RJ, Hinderliter AL, Willis PW, Ralph D, Caldwell EJ, Williams W, Ettinger NA, Hill NS, Summer WR, de Boisblanc B, Schwartz T, Koch G, Clayton LM, Jobsis MM, Crow JW, Long W. Echocardiographic predictors of adverse outcomes in

primary pulmonary hypertension. J Am Coll Cardiol. 2002;39:1214–9.
30. Khan AH. The postcardiac injury syndromes. Clin Cardiol. 1992;15:67–72.
31. Imazio M, Brucato A, Rovere ME, Gandino A, Cemin R, Ferrua S, Maestroni S, Barosi A, Simon C, Ferrazzi P, Belli R, Trinchero R, Spodick D, Adler Y. Contemporary features, risk factors, and prognosis of the post-pericardiotomy syndrome. Am J Cardiol. 2011;108:1183–7.
32. Imazio M, Trinchero R, Brucato A, Rovere ME, Gandino A, Cemin R, Ferrua S, Maestroni S, Zingarelli E, Barosi A, Simon C, Sansone F, Patrini D, Vitali E, Ferrazzi P, Spodick DH, Adler Y. Colchicine for the prevention of the post-pericardiotomy syndrome (copps): a multicentre, randomized, double-blind, placebo-controlled trial. Eur Heart J. 2010;31:2749–54.
33. Holmes Jr DR, Nishimura R, Fountain R, Turi ZG. Iatrogenic pericardial effusion and tamponade in the percutaneous intracardiac intervention era. JACC Cardiovasc Interv. 2009;2:705–17.
34. Erbel R, Engberding R, Daniel W, Roelandt J, Visser C, Rennollet H. Echocardiography in diagnosis of aortic dissection. Lancet. 1989;1:457–61.
35. Hayashi T, Tsukube T, Yamashita T, Haraguchi T, Matsukawa R, Kozawa S, Ogawa K, Okita Y. Impact of controlled pericardial drainage on critical cardiac tamponade with acute type a aortic dissection. Circulation. 2012;126:S97–101.
36. vasanth. 2013.
37. Nilsson A, Rasmuson T. Primary pericardial mesothelioma: report of a patient and literature review. Case Rep Oncol. 2009;2:125–32.
38. Thurber DL, Edwards JE, Achor RW. Secondary malignant tumors of the pericardium. Circulation. 1962;26:228–41.
39. Chiles C, Woodard PK, Gutierrez FR, Link KM. Metastatic involvement of the heart and pericardium: CT and MR imaging. Radiographics. 2001;21:439–49.
40. Groarke JD, Nguyen PL, Nohria A, Ferrari R, Cheng S, Moslehi J. Cardiovascular complications of radiation therapy for thoracic malignancies: the role for non-invasive imaging for detection of cardiovascular disease. Eur Heart J. 2014;35:612–23.
41. Gunukula SR, Spodick DH. Pericardial disease in renal patients. Semin Nephrol. 2001;21:52–6.
42. Alpert MA, Ravenscraft MD. Pericardial involvement in end-stage renal disease. Am J Med Sci. 2003;325:228–36.
43. Sever MS, Steinmuller DR, Hayes JM, Streem SB, Novick AC. Pericarditis following renal transplantation. Transplantation. 1991;51:1229–32.
44. Abbas AE, Appleton CP, Liu PT, Sweeney JP. Congenital absence of the pericardium: case presentation and review of literature. Int J Cardiol. 2005;98:21–5.
45. Nasser WK. Congenital absence of the left pericardium. Am J Cardiol. 1970;26:466–70.
46. Cuccuini M, Lisi F, Consoli A, Mancini S, Bellino V, Galanti G, Capaccioli L. Congenital defects of pericardium: case reports and review of literature. Ital J Anat Embryol. 2013;118:136–50.
47. Gatzoulis MA, Munk MD, Merchant N, Van Arsdell GS, McCrindle BW, Webb GD. Isolated congenital absence of the pericardium: clinical presentation, diagnosis, and management. Ann Thorac Surg. 2000;69:1209–15.
48. Satur CM, Hsin MK, Dussek JE. Giant pericardial cysts. Ann Thorac Surg. 1996;61:208–10.
49. Hynes JK, Tajik AJ, Osborn MJ, Orszulak TA, Seward JB. Two-dimensional echocardiographic diagnosis of pericardial cyst. Mayo Clin Proc. 1983;58:60–3.
50. Maksimovic R, Dill T, Seferovic PM, Ristic AD, Alter P, Simeunovic DS, Markovic Z, Bachmann GF, Maisch B. Magnetic resonance imaging in pericardial diseases. Indications and diagnostic value. Herz. 2006;31:708–14.
51. Kerber RE, Sherman B. Echocardiographic evaluation of pericardial effusion in myxedema. Incidence and biochemical and clinical correlations. Circulation. 1975;52:823–7.
52. Kabadi UM, Kumar SP. Pericardial effusion in primary hypothyroidism. Am Heart J. 1990;120:1393–5.
53. Brawley RK, Vasko JS, Morrow AG. Cholesterol pericarditis. Considerations of its pathogenesis and treatment. Am J Med. 1966;41:235–48.
54. Barcin C, Yalcinkaya E, Kabul HK. Cholesterol pericarditis associated with rheumatoid arthritis: a rare cause of pericardial effusion. Int J Cardiol. 2013;166:e56–8.
55. Yokusoglu M, Savasoz BS, Baysan O, Erinc K, Gunay C, Isik E. Primary chylopericardium. Thorac Cardiovasc Surg. 2005;53:386–8.
56. Chan BB, Murphy MC, Rodgers BM. Management of chylopericardium. J Pediatr Surg. 1990;25:1185–9.
57. Imazio M, Brucato A, Rampello S, Armellino F, Trinchero R, Spodick DH, Adler Y. Management of pericardial diseases during pregnancy. J Cardiovasc Med (Hagerstown). 2010;11:557–62.

## Etiologies of Pericardial Diseases- For Patients and their Families

Pericardial diseases commonly present as pericarditis (inflammation of the pericardium) or as pericardial effusions (fluid accumulation within the pericardial space). Rarely, repeated bouts of pericarditis may result in scarring and thickening of the pericardium, a condition termed constrictive pericarditis. While there are many possible causes of pericarditis, it is often hard to identify the exact cause. On the other hand, in case of a significant pericardial effusion, a sample of fluid can be withdrawn through a needle and analyzed to aid in the diagnosis. When no definite diagnosis for pericarditis is made, it is termed idiopathic pericarditis. Most of the idiopathic cases of pericarditis are presumed to be secondary to a viral infection.

Other infections which can cause pericarditis include bacterial infections, tuberculosis, fungal, and parasitic infections. Patients with underlying AIDS frequently develop infections which can produce pericarditis as well as pericardial effusions. Pericarditis can also develop in association with underlying autoimmune diseases (diseases in which the body attacks itself), including but not restricted to rheumatoid arthritis, systemic lupus erythematosus, scleroderma, sarcoidosis and various vasculitides (e.g., Takayasu arteritis, Kawasaki disease). Some medications, like procainamide, hydralazine, phenytoin, and isoniazid, can also produce pericarditis, although this is not very common.

Also, there is a higher risk of developing pericarditis after a major heart attack. This appears in two forms, the first is early on and in conjunction with the acute infarct and a later form that involves a whole body inflammatory response (Dressler syndrome). In addition, there is a greater risk of developing pericarditis after invasive procedures of the heart and this is termed post-cardiac injury syndrome (PCIS). PCIS may be seen after heart surgery or percutaneous intervention, such as cardiac catheterization or radiofrequency ablation for rhythm disorders. Occasionally blood may accumulate in the pericardial space (hemopericardium) due to a tear in the large blood vessel leaving the heart (aortic dissection), after injury to the chest (e.g., motor vehicle accident or knife wound) or when procedures are performed on the heart, including open heart surgery, insertion of devices in the heart and other interventional procedures to the heart.

In addition, the pericardium can be involved when a disease process affects the heart muscle or the surrounding organs. Pericardial effusions are commonly seen in heart failure and lung diseases such as pneumonia or chronic disease of the lung with elevated lung pressures. Cancer may also infiltrate the pericardium and is one of the leading causes of pericardial effusion development. Occasionally pericardial effusions could be detected during pregnancy, usually without clinical significance. Additional causes of pericardial diseases include kidney disease, thyroid disease, after radiation exposure to the chest and genetic diseases such as Familial Mediterranean Fever. Rarely, a cyst (sac filled with fluid) may develop in the pericardial space, which may be present from birth (congenital) or at a later stage (acquired). Very rarely, the pericardium may either be completely or partially absent, causing the heart to shift its position inside the chest.

# 3 History and Physical Examination of a Patient with Pericardial Disease

Suhash Patel and Itzhak Kronzon

## Acute Pericarditis

### Background

Acute pericarditis as its name indicates is a fairly sudden inflammation of the pericardial sac that encases the heart. It accounts for 5 % of non-ischemic chest pain visits to the Emergency Department annually [1, 2].

The diagnosis and treatment for acute pericarditis is mostly empirical and one that needs a systematic approach, so that one does not overlook a more serious, life-threatening condition.

### History and Presentation

The clinical presentations of acute pericarditis may vary depending on the underlying etiology with the majority (85–90 %) of cases being idiopathic [3–5]. Many patients will endorse having a nonspecific antecedent respiratory or gastrointestinal infection.

A history of viral or bacterial infection, neoplasm, autoimmune disorder, previous chest radiation, recent myocardial infarction and certain medications (such as hydralazine, isoniazid, phenytoin, doxorubicin, procainamide) may predispose the patient to an increased risk of acute pericarditis [6].

Nonspecific symptoms may include malaise, cough, and fever [7]. As seen in cases of pleurisy, the respirations may be shallow and rapid due to the pain, causing a sensation of shortness of breath. Fever >38 °C is rare and one should be suspicious for purulent pericarditis necessitating the need for an emergent echocardiogram [6].

Most patients present with chest pain (>98 %) that is sharp, sudden in onset, retrosternal and pleuritic in nature that is exacerbated by coughing or inspiration and can be quite severe and incapacitating [5, 8]. In some cases, however, there may be absence of pain, as often seen in those with rheumatologic diseases [8]. The chest pain of pericarditis may radiate to the arms, neck or left shoulder similar to those patients having an acute coronary syndrome. However, if the dull, overbearing pain radiates to one or both of the trapezius muscle ridges, it is likely irritation of the phrenic nerve, which traverses the pericardium and also innervates this muscle group [6, 8]. Patients may also report relief of chest discomfort when sitting up and leaning forward as this decreases pressure on the parietal pericardium and worsens when lying supine.

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This chapter will primarily focus on the patient's history and key physical examination findings that will allow clinical recognition of the diagnosis.

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## Physical Examination

On initial evaluation, low grade fever and tachycardia may be present.

Upon auscultation, the pathognomonic finding in acute pericarditis is a pericardial friction rub that is heard at some point in the course of 85 % of cases [3]. Friction rubs are thought to be generated by the contact between the inflamed parietal and visceral pericardium. However, it is important to note that they can still be heard in the presence of a pericardial effusion [8].

Friction rubs can be localized or widespread in location but typically best heard as the patient leans forward with the diaphragm of the stethoscope using firm pressure at the left sternal border or apex. While friction rubs are audible throughout the respiratory cycle, they are heard best when respiration is suspended. This is done to avoid confusion with a concomitant pleural or pleuropericardial friction rub, which are absent when respirations are suspended [6].

The classic friction rub often sounds like a high-pitched squeaky or scratchy quality. Frequently, it has three components (about 50 % of the time) which corresponds to the movement of the heart [1, 2]. As seen in Fig. 3.1, there is a presystolic or atrial rub that precedes S1 (which is not heard in patients with atrial fibrillation), ventricular systolic rub that occurs between S1 and S2, and the faintest and most difficult early diastolic rub from the rapid ventricular filling after S2. Biphasic rubs are present a third of the time and are due to atrial and diastolic rubs. The rarest is the monophasic rubs which are due to ventricular systole and can occur in those with atrial fibrillation [1, 2, 6, 7]. The rubs are dynamic and can disappear and reappear in the same day so it is prudent to perform multiple examinations to confirm its presence if initially absent [6, 7].

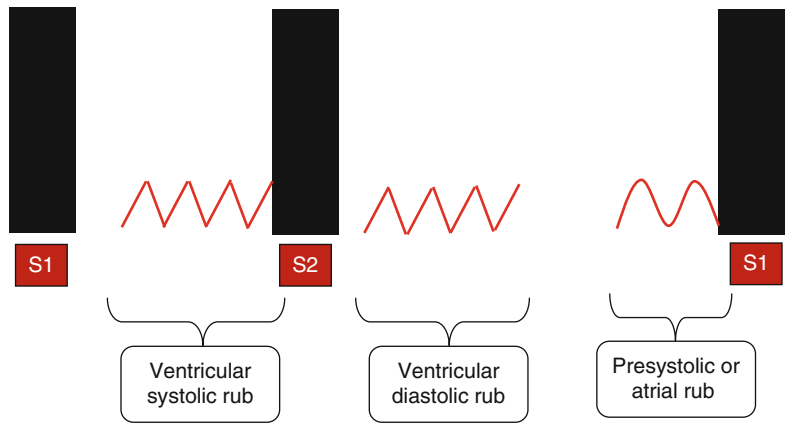


**Fig. 3.1** A classic three component friction rub and its timing within the cardiac cycle

## Pericardial Effusion Without Compression

### Background

Pericardial effusion is an accumulation of fluid in the pericardial space between the visceral and parietal pericardium that is in excess of what is normally present (15–50 mL) [6].

### History and Presentation

Pericardial effusions have various etiologies but it is typically suspected based n history and physical exam, supported by an electrocardiogram and chest x-ray and confirmed by an imaging modality such as an echocardiogram. They are often found incidentally on evaluation of suspected cardiopulmonary disease.

Most patients, unless there is cardiac tamponade, characteristically are asymptomatic even with large (≥1 liters), slow developing pericardial effusions [7]. If symptoms do develop, they usually arise from the compression of surrounding structures such as the stomach, lung and

phrenic nerve and include dysphagia, nausea, abdominal fullness, dyspnea and orthopnea [6, 9]. Those with fever are often related to the underlying cause such as pericarditis.

### Physical Examination

The exam is often unremarkable with a small effusion. However, those with a large effusion can have distant or muffled heart sounds on auscultation. There is also dullness beyond the point of maximal impulse upon percussion in the absence of lung disease to the left lower lobe.

While it is not routinely performed today, the combination of dullness to percussion, bronchial or tubular breath sounds and egophany in a triangular area at the tip of the left scapula is known as the Ewart's or Bamberger-Pins-Ewart sign described in 1896 [10].

## Cardiac Tamponade

### Background

Cardiac tamponade is a medical emergency that occurs with the collection of material such as fluid, blood, pus, or clots due to various etiologies such as infection, malignant disease, renal failure, radiation therapy, anticoagulant therapy, invasive cardiac procedures with perforation, cardiovascular surgery, chest trauma and aortic dissection. This leads to increased intrapericardial pressure causing compression of all cardiac chambers and ultimately hemodynamic collapse [9].

### History and Presentation

Cardiac tamponade can be the consequence of any etiology of pericardial disease and most symptoms are nonspecific, therefore tamponade is an elusive clinical diagnosis.

The clinical presentation and hemodynamic effect of patients with cardiac tamponade principally depends upon the volume of the effusion, rapidity of accumulation and the clinical circumstances. Acute cardiac tamponade typically occurs within minutes in patients with mechanical complication of the heart or great vessels such as cardiac or aortic rupture, trauma, or complication of an invasive procedure and present with the characteristic Beck's triad of hypotension, elevated jugular venous pressure (JVP) in addition to dyspnea, tachypnea and chest pain [9]. It is a clinical syndrome in which there is impairment of diastolic filling leading to low cardiac output from the rapid accumulation of fluid in a relatively stiff pericardium that can be life-threatening if not quickly recognized and treated.

In subacute cardiac tamponade, the rate of growth of the pericardial effusion tends to be slower, filling the pericardial space up to 2 liters and allowing pericardial stretch and compensatory mechanisms to take place with a gentler rate of increase in pericardial pressures [6]. Early in their course, patients lack symptoms but as the pericardial reserve volume is met, there is poor organ perfusion causing confusion, cool extremities and worsening renal function. They also develop fatigue, chest pressure, peripheral edema and dyspnea progressing to orthopnea until it reaches the critical point causing life-threatening tamponade [9, 11, 12].

Low-pressure cardiac tamponade is a phenomenon that occurs in patients with severe hypovolemia due to hemorrhage, overdiuresis, or hemodialysis with intracardiac diastolic pressures that are only 6–12 mmHg [9, 13]. Most common symptoms include weakness and dyspnea on exertion.

Large pericardial effusions can lead to atypical presentations by means of localized compression. There can be compression of the phrenic nerve as it traverses the pericardium leading to hiccups, diaphragm causing nausea, esophagus producing dysphagia, and left recurrent laryngeal nerve triggering atypical Ortner's Syndrome causing hoarseness [7].

### Physical Examination

Physical examination is crucial in patients with cardiac tamponade as it is considered a clinical diagnosis.

The combination of the classic Beck's triad of hypotension, elevated JVP and distant heart sounds is infrequently present (10–40 %) in acute cardiac tamponade. Patients with cardiac tamponade can be hypotensive, normotensive or even hypertensive [9, 14–16]. Hypotension is not universally seen in patients with subacute or low-pressure cardiac tamponade. In fact, hypertension (even over 200 mmHg) with characteristic features of tamponade, while infrequent, is not rare and has been described as a tamponade variant due to excessive sympathetic activation in the setting of subacute cardiac tamponade and is typical in patients with preexisting hypertension [9, 14]. One of the key physical findings is jugular venous distension (JVD) that is almost always present and with clear lungs to distinguish it from left-sided heart failure. While it may be difficult to appreciate, it is important to detect abnormality in the waveforms of the jugular pulsations. In normal patients, jugular pressure falls twice, first during ventricular ejection (*x* descent) and again during early rapid ventricular filling (*y* descent). The two descents are parallel with two peaks in venous return. In cardiac tamponade, the *x* descent is preserved because cardiac size diminishes during ventricular ejection, which is more rapid than cardiac filling allowing the lowering of intrapericardial pressure causing the venous return to peak. However, due to the abnormally elevated intrapericardial constraint from the effusion, there is reduced diastolic compliance leading to the lack of the *y* descent. The *y* descent is diminished in mild cases and absent in moderate or severe cases of cardiac tamponade [8, 9]. However, there can be a normal or low JVP in cases of rapidly developing cardiac tamponade, particularly with hemorrhagic cardiac tamponade because of the shortage of time for compensatory increase in venous pressure [8].

Traditionally, most patients (77 %) will exhibit sinus tachycardia (a heart rate of more than 90 beats per minute) to partially maintain cardiac output and tachypnea (80 %) [9, 16, 17]. Furthermore, tachycardia may not be seen in patients with early cardiac tamponade despite evidence of hemodynamically significant effusion. However, exceptions to the rule include those with hypothyroidism and uremia that can be bradycardic [7, 9]. It is also important to note that patients with sudden accumulation of fluid in the pericardial space can also lead to bradycardia due to increased vagal tone. Contrary to common belief, an audible friction rub may be heard especially in patients with inflammatory pericarditis [7].

### Pulsus Paradoxus

The hallmark physical examination finding of cardiac tamponade is a paradoxical pulse, which is found in over three-quarters of moderate to severe cardiac tamponade cases [16–18]. Pulsus paradoxus is an inspiratory decline in systolic blood pressure of more than 10 mmHg resulting from two physiologic phenomenons that reduces left ventricular stroke volume on inspiration. First, there is compression and poor filling of the left ventricle caused by increased venous return to the right side of the heart referred to as ventricular interdependence. In addition, inspiratory drop in blood pressure is due to the incomplete transmission of negative intrathoracic pressures to the left side of the heart (left ventricular diastolic pressure) while maintaining this decrease in the pulmonary capillary bed and pulmonary veins, thus decreasing the gradient between the pulmonary veins and the left atrium and the left ventricular diastolic pressure. On physical examination, the pulsus paradoxus can be appreciated as a decreased force of the pulse synchronous with inspiration. In extremely severe cases, the pulse dissipates completely during inspiration. A regular heartbeat but an irregular peripheral pulse is the paradox. Using a sphygmomanometer, it is typically the first audible blood pressure sound during expiration but disappears with inspiration. As the cuff pressure is deflated, blood pressure sounds are audible throughout the respiratory cycle. The difference in pressure between the two sounds allows an estimation of the severity of pulsus paradoxus. Essentially this can be best illustrated, as seen in Fig. 3.2, with an arterial line showing a decreased blood pressure on inspiration. This finding can be difficult to recognize in severe shock in the radial pulse but will still be apparent in the femoral or carotid

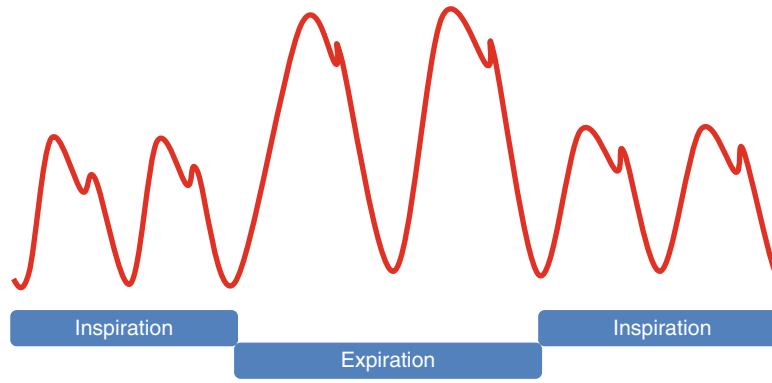


**Fig. 3.2** *Pulsus paradoxus* demonstrating an exaggerated decline in systolic blood pressure during inspiration, resulting from an increase in negative intrathoracic pressure

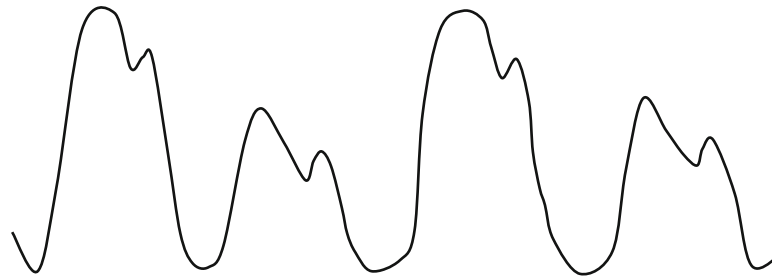

**Fig. 3.3** *Pulsus alternans* illustrating beat-to-beat alternation that is seen more commonly with severe left ventricular dysfunction but can also be seen in cardiac tamponade

pulse. Pulsus paradoxus may be absent in cardiac tamponade in patients with chronic hypertension leading to elevated ventricular diastolic pressures, low-pressure tamponade, atrial septal defects or aortic insufficiency [9, 17–19]. This phenomenon can also be seen in extracardiac diseases such as pulmonary embolism and intrinsic lung disease such as chronic obstructive pulmonary disease and severe asthma. While more commonly associated with severely impaired left ventricular function, there may be the presence of *pulsus alternans*, a fluctuation of a weak pulse and a strong pulse in the presence of a regular rhythm as seen in Fig. 3.3. This is primarily thought to be due to alteration in end-diastolic pressure that affects the efficiency of the Frank-Starling mechanism.

A physical examination finding of decreased tactile fremitus, diminished breath sounds, and dullness to percussion of lung fields with clinical signs of cardiac tamponade but without a pericardial effusion suggests a large pleural effusion causing cardiac tamponade which will resolve after thoracentesis [20].

## Constrictive Pericarditis

### Background

Constrictive pericarditis is a clinical and pathoanatomical syndrome associated with global compressive disease of the heart due to a non-compliant, chronically inflamed, thickened and often calcific pericardium restricting diastolic filling and leading to biventricular heart failure.

### History and Presentation

Obtaining important history of any illness commonly linked with pericarditis such as radiation therapy (typically many years after treatment), post-cardiac surgery (may occur as early as 2 weeks or as late as several years after surgery, the majority appearing 3–12 months postoperatively), autoimmune disorder (systemic lupus erythematosus, rheumatoid arthritis), infections, malignancy, and uremia is greatly important in

considering this diagnosis [21]. The constrictive process is usually gradual, and most patients, by the time they visit a physician, have had established and incapacitating disease [22]. Therefore, the diagnosis is typically made in the chronic phase of the disease and patients classically present with debilitating chronic right-heart failure [21]. The symptoms include dyspnea on exertion, fatigue, palpitations as well as signs of volume overload manifesting as weight gain, increased abdominal girth, ascites, pleural effusions, peripheral edema and anasarca [7, 20]. Not uncommonly, patients with clinical symptoms of constriction are misdiagnosed with liver or gastrointestinal diseases, often undergoing extensive workup [23]. While right-heart failure predominates over left, patients may develop left-sided systolic dysfunction as a major complication of chronic constrictive pericarditis due to myocardial fibrosis/atrophy [7]. A key differential diagnosis with a similar clinical presentation that needs to be ruled out is restrictive cardiomyopathy that is often due to an infiltrative process.

## Physical Examination

There are several physical examination clues to the clinical diagnosis of constrictive pericarditis, most importantly JVD. The jugular venous pressure can be ≥20 cm $H_2O$ in severe cases and often needs to be examined with the patient sitting upright due to dampening of jugular pulsations if in the semi recumbent position. As seen with tamponade, the *x* descent is preserved. However, the *y* descent (early diastolic filling) becomes steeper, sharper and deeper with inspiration [21]. The prominent *y* descent is due to the faster than normal early rapid decline in the ventricular diastolic pressure allowing early diastolic filling. Verification of this finding can be performed by palpating the contralateral carotid artery allowing confirmation of an inward venous pulsation that is asynchronous with the carotid pulse. In 50 % of cases, the sudden interruption of the early diastolic filling by a rigid pericardium leads to an accentuated heart sound (like a high-pitched $S_3$) called a pericardial knock. The timing of pericardial knock correlates to the nadir of the *y* descent illustrated in Fig. 3.4 [23]. While less commonly seen in constriction, pulsus paradoxus (seen in Fig. 3.2) can be present in one-third of cases.

The lack of expected inspiratory decline in JVP due to the failure of transmitting the negative intrathoracic pressure to the intrapericardial chambers that leads to the failure of caval and right atrial pressures to decline is known as Kussmaul's sign seen in Fig. 3.5 [7, 23]. In severe cases, the JVP increases with inspiration. It is important to note that Kussmaul's sign is not diagnostic of constrictive pericarditis as it can be seen in restrictive cardiomyopathy, right heart failure and severe tricuspid regurgitation.

In most cases of constrictive pericarditis, there is greater systemic than pulmonary congestion. Peripheral edema can be extensive in severe and chronic cases, leading to scrotal edema and anasarca but less frequently pulmonary edema. There is greater presence of right-heart than left-heart failure due to the equalization of diastolic pressures as well as that of right and left atrial pressures. The abdominal examination will demonstrate hepatic congestion with jaundice (differentiated from cirrhosis by the presence of JVD and hepatomegaly), ascites and in severe cases, hepatomegaly with pulsatile liver synchronized with the jugular pulse.

# Effusive-Constrictive Pericarditis

## Background

Effusive-constrictive pericarditis (ECP) is defined as the presence of pericardial disease that is consistent with constrictive pericarditis while simultaneously having a pericardial effusion. The constrictive physiology persists with an elevated right atrial pressure despite drainage or disappearance of the effusion and decreased intrapericardial pressure [8, 24]. The constriction seen in ECP is that of the visceral pericardium, unlike chronic constrictive pericarditis that is due to the parietal pericardium [8]. ECP had been relatively uncommon from limited published data; however, it has now become a more widely documented clinical condition [24, 25].

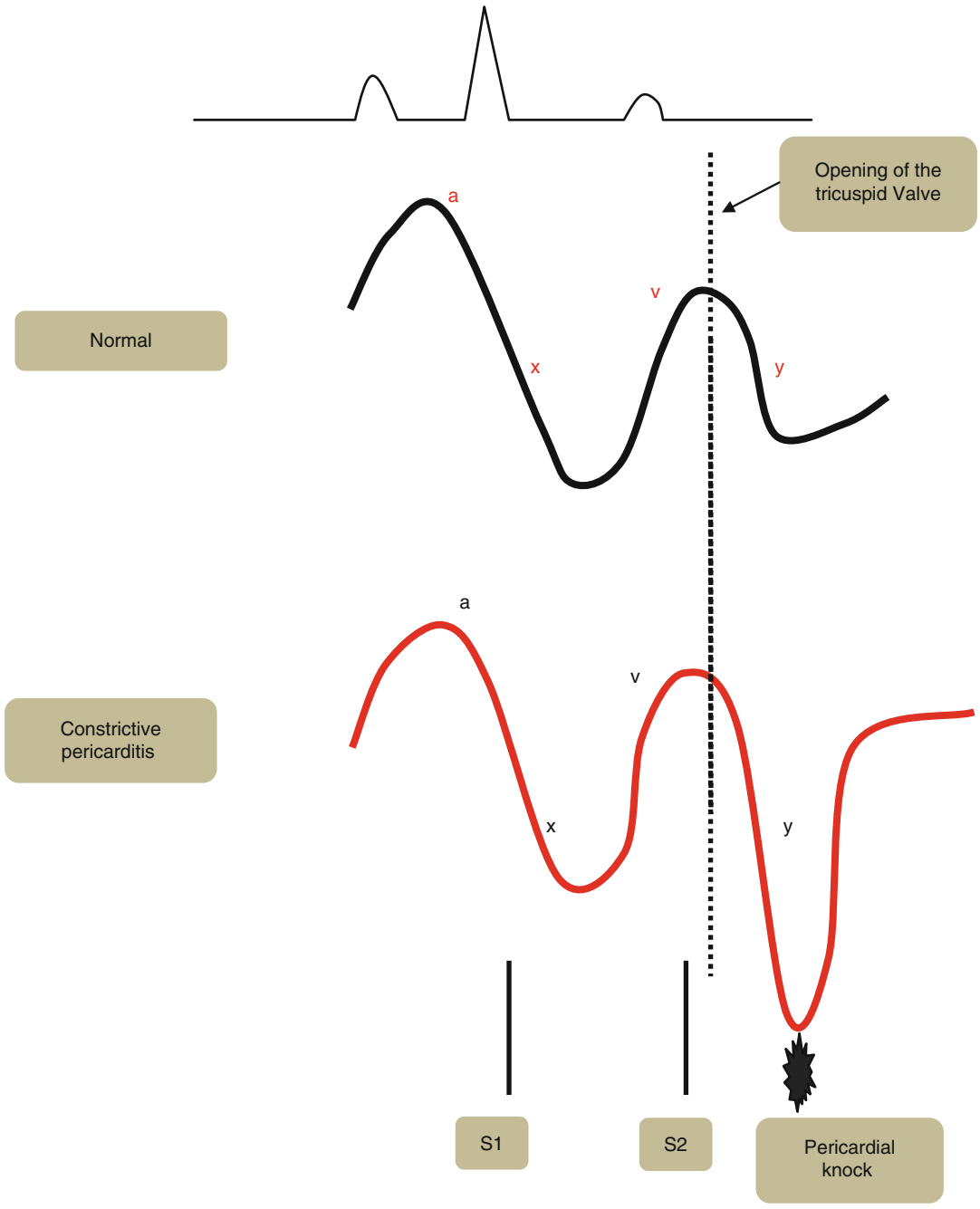


**Fig. 3.4** Constrictive pericarditis central venous pressure tracing with an ECG and phonocardiogram illustrating rapid *y* descent after opening of the tricuspid valve with a "dip and plateau" appearance and a pericardial knock

## History and Presentation

Patients with ECP initially present with the hemodynamic profile of cardiac tamponade. After pericardiocentesis, the hemodynamic profile demonstrates a reduction in intrapericardial pressure but the disturbance now resembles constriction. Patients will therefore display clinical features of pericardial effusion, constriction or both.

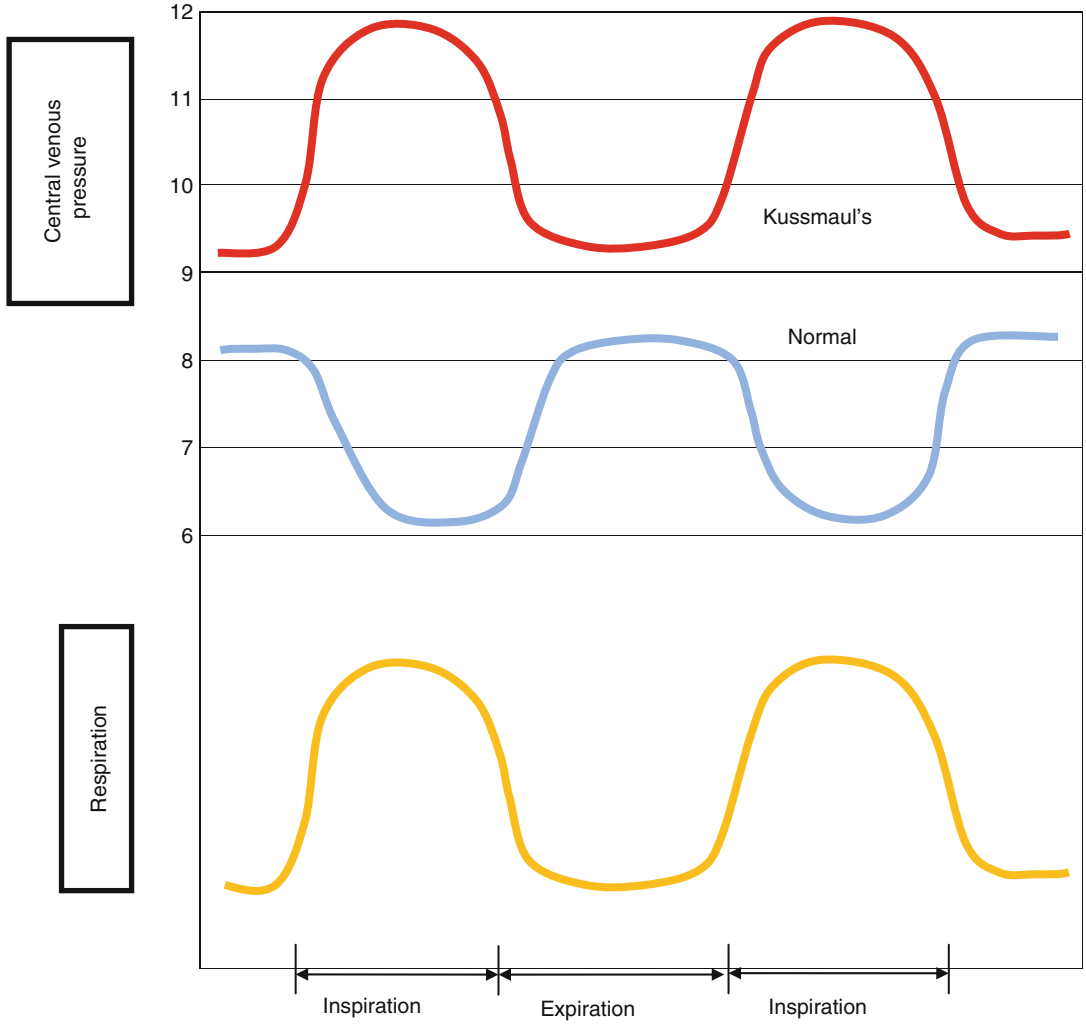


**Fig. 3.5** Kussmaul's sign in constrictive pericarditis

## Physical Examination

There are several clinical signs that suggest that a patient with suspected constrictive pericarditis may have ECP. These include pulsus paradoxus (an unusual finding in constriction), absent pericardial knock, less striking *y* descent, and the absence of Kussmaul's sign [24].

## References

1. Lorrell BH. Pericardial diseases. In: Braunwald E, editor. Heart disease: a textbook of cardiovascular medicine. 5th ed. Philadelphia: W.B. Saunders; 1997. p. 1478–534.
2. Launbjerg J, Fruergaard P, Hesse B, Jorgensen F, Elsborg L, Petri A. Long-term risk of death, cardiac events and recurrent chest pain in patients with acute

chest pain of different origin. Cardiology. 1996;87: 60–6.
3. Zayas R, Anguita M, Torres F, et al. Incidence of specific etiology and role of methods for specific etiologic diagnosis of primary acute pericarditis. Am J Cardiol. 1995;75:378–82.
4. Permanyer-Miralda G, Sagrista-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. Am J Cardiol. 1985;56:623–30.
5. Little WC, Freeman GL. Pericardial disease. Circulation. 2006;113:1622–32.
6. Lange RA, Hillis LD. Clinical practice. Acute pericarditis. N Engl J Med. 2004;351:2195.
7. Seferovic P, Ristic A, Maksimovic R, et al. Pericardial syndromes: an update after the ESC guidelines 2004. Heart Fail Rev. 2013;18:255–66.
8. Imazio M, Demichelis B, Parrini I, et al. Day-hospital treatment of acute pericarditis: a management program for outpatient therapy. J Am Coll Cardiol. 2004;43:1042.
9. Spodick DH. Acute cardiac tamponade. N Engl J Med. 2003;349:684–90.
10. Ewart W. Practical aids in the diagnosis of pericardial effusion in connection with the question as to surgical treatment. Br Med J. 1896;1:717–21.
11. Spodick DH. Threshold of pericardial constraints the pericardial reserve volume and auxiliary pericardial functions. J Am Coll Cardiol. 1985;6:296–7.
12. Reddy PS, Curtiss EI, O'Toole JD, Shaver JA. Cardiac tamponade: hemodynamic observations in man. Circulation. 1978;58:265–72.
13. Cooper JP, Oliver RM, Currie P, Walker JM, Swanton RH. How do the clinical findings in patients with pericardial effusions influence the success of aspiration? Br Heart J. 1995;73:351–4.
14. Ramsaran EK, Benotti JR, Spodick DH. Exacerbated tamponade deterioration of cardiac function by lowering excessive arterial pressure in hypertensive cardiac tamponade. Cardiology. 1995;86:77–9.
15. Shabetai R. Diseases of the pericardium. In: Hurst JW, Schlant RC, Alexander RW, editors. The heart: arteries and veins. 8th ed. New York: McGraw-Hill; 1994. p. 1654–62.
16. Guberman BA, Fowler NO, Engel PJ, Gueron M, Allen JM. Cardiac tamponade in medical patients. Circulation. 1981;64:633–40.
17. Bilchick KC, Wise RA. Paradoxical physical findings described by Kussmaul: pulsus paradoxus and Kussmaul's sign. Lancet. 2002;359:1940–2.
18. Swami A, Spodick DH. Pulsus paradoxus in cardiac tamponade: a pathophysiologic continuum. Clin Cardiol. 2003;26:215–7.
19. Winer HE, Kronzon I. Absence of paradoxical pulse in patients with cardiac tamponade and atrial septal defects. Am J Cardiol. 1979;44(2):378–80.
20. Traylor JJ, Chan K, Wong I, et al. Large pleural effusions producing signs of cardiac tamponade resolved by thoracentesis. Am J Cardiol. 2002;89:106.
21. Troughton RW, Asher CR, Klein AL. Pericarditis. Lancet. 2004;363:717–27.
22. Maisch B. Pericardial diseases with a focus on etiology, pathogenesis, pathophysiology, new diagnostic imaging methods, and treatment. Curr Opin Cardiol. 1994;9:379–88.
23. Ling L, Oh J, Schaff H, et al. Constrictive pericarditis in the modern era. Evolving clinical spectrum and impact on outcome after pericardiectomy. Circulation. 1999;100:1380–6.
24. Syed FF, Ntsekhe M, Mayosi BM, Oh JK. Effusive-constrictive pericarditis. Heart Fail Rev. 2013;18: 277–87.
25. Cameron J, Oesterle SN, Baldwin JC, Hancock EW. The etiologic spectrum of constrictive pericarditis. Am Heart J. 1987;113:354.

# EKG in Pericardial Disease

4

Eric M. Bader, Edgar Argulian, Emad F. Aziz,
Eyal Herzog, and Henry Greenberg

Since Willem Einthoven coined the term electrocardiogram (EKG) at the turn of the twentieth century [1], the EKG has become an increasingly central tool in the clinician's armamentarium.

The goal of this chapter is to examine the role of the EKG in the diagnosis and staging of pericarditis. Additionally, we will address the pathophysiology of the findings behind the EKG changes in pericardial disease which allows for a more complete understanding of the processes involved and leads to a more flexible approach to interpreting the EKG.

A reflection of the electrical activity of the heart, the measured EKG is influenced by the electrical rhythm of the heart, its conductive properties and the nature of its depolarization and repolarization [2]. Contributing significantly to this picture are the conductive or insulating properties of the thorax in which the heart sits. In acute pericarditis there are a number of simultaneously occurring processes, depending on the etiology of the condition. This may result in changes in the heart's rhythm, its conductive properties as well as the degree of conduction or insulation in the surrounding thorax.

The similarity of symptoms and the nature of presentation make it imperative to differentiate acute pericarditis from acute coronary syndromes. A correct diagnosis prevents unnecessary interventions with their associated risks, misallocation of resources and ensures timely, appropriate intervention when necessary (Fig. 4.1).

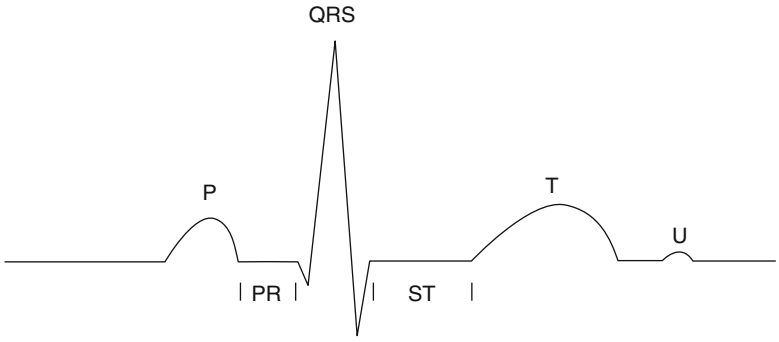


**Fig. 4.1** The EKG complex: individual components are identified here and will be discussed in the main text

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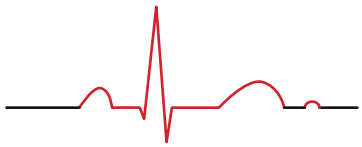
## EKG Findings in Acute Pericarditis

The pericardium is a fibrous sac that is composed of both a visceral and parietal layer that surrounds the heart and extends onto the proximal great vessels. When inflamed, be it as part of an infectious, inflammatory or oncologic process, pericarditis is present. At times, the underlying myocardium may be involved as well and this leads to a condition termed myopericarditis. This inflammatory process causes changes in the tissue of the pericardium and, when involved, the myocardium. Additionally, it may increase the amount of fluid present in the pericardial space.

## Low Voltage EKG Signal



One of the hallmarks of acute pericarditis is the pericardial effusion. While it may be of varying size and hemodynamic significance, the short-circuiting effect of this effusion, as well as the electrically insulating properties of the contained fibrin are thought by many to result in low voltage recordings on the EKG. Others suggest that the low voltage seen in pericarditis is specifically a marker of cardiac tamponade [3]. Electrocardiographically, low voltage is defined as an amplitude of less than 0.5 mv (or 5 mm) on the limb leads and less than 1 mv on the precordial leads (10 mm) [4]. Anatomically, there is a larger amount of space available for fluid to collect around the anterior heart structures, as the pericardial reflections behind the atria limit the posterior potential space. This results in a low amplitude QRS complexes, while the P wave amplitude will be spared in the limb leads due to the relative paucity of fluid around the posterior atria.

While the finding of low voltage occurs in many patients with pericardial disease, it is neither a sensitive nor a specific finding and occurs in any condition in which the amplitude of the ventricular signal is decreased. The differential diagnosis of low voltage therefore includes systemic conditions including myxedematous involvement of myocardium as seen in hypothyroidism, even in absence of effusion [5], cardiac amyloidosis, scleroderma, and in chronic ischemic heart disease. Other conditions such as obesity, chronic obstructive pulmonary disease, a pneumothorax or pleural effusions may also increase the impedance across the chest wall, decreasing the EKG amplitude (Table 4.1, Fig. 4.2).

**Table 4.1** Differential diagnosis of the low voltage EKG

| |
|---|
| Hypothyroidism – myxedematous involvement of myocardium |
| Chronic obstructive pulmonary disease |
| Infiltrative heart disease: ex. amyloidosis, scleroderma |
| Chronic ischemic heart disease |
| Pleural effusion |
| Pneumothorax |
| Obesity |

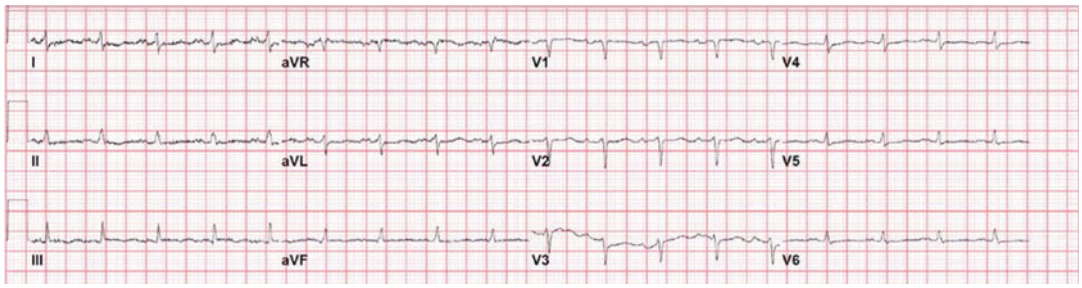
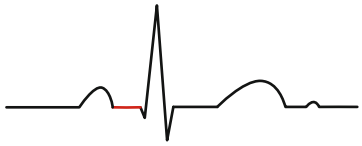



**Fig. 4.2** Low voltage EKG: note the low amplitude of the signal in both the limb and precordial leads relative to normal gain signal at the beginning of the tracing

## PR Deviation



Changes in the PR segment are present in approximately 80 % of patients with acute pericarditis, PR deviation is a particularly sensitive sign of pericardial effusion [6], and often persists after the ST segment changes have resolved and are not subject to the same confounding variables that affects ST segments. It is of diagnostic utility even in the presence of existing bundle branch block, acute myocardial infarction and LVH [7, 8]. Typically, in pericardial disease PR depressions are seen in both the limb and precordial leads. Particularly suggestive of pericarditis is PR elevation, occasionally in V1, but most commonly in AVR. These findings are thought to represent pressure mediated atrial injury of a mechanism similar to the ventricular injury associated ST elevations [9]. Measuring PR deviation can be challenging particularly due to the need for an appropriate electrocardiographic isoelectric reference baseline to measure against. This is evidenced by the fact that the persistent PR depression is often confused with continued ST segment elevation in these patients [6].

The differential diagnosis of PR deviation is more limited; in addition to pericarditis, it is rarely seen in patients with early ventricular repolarization (Fig. 4.3).

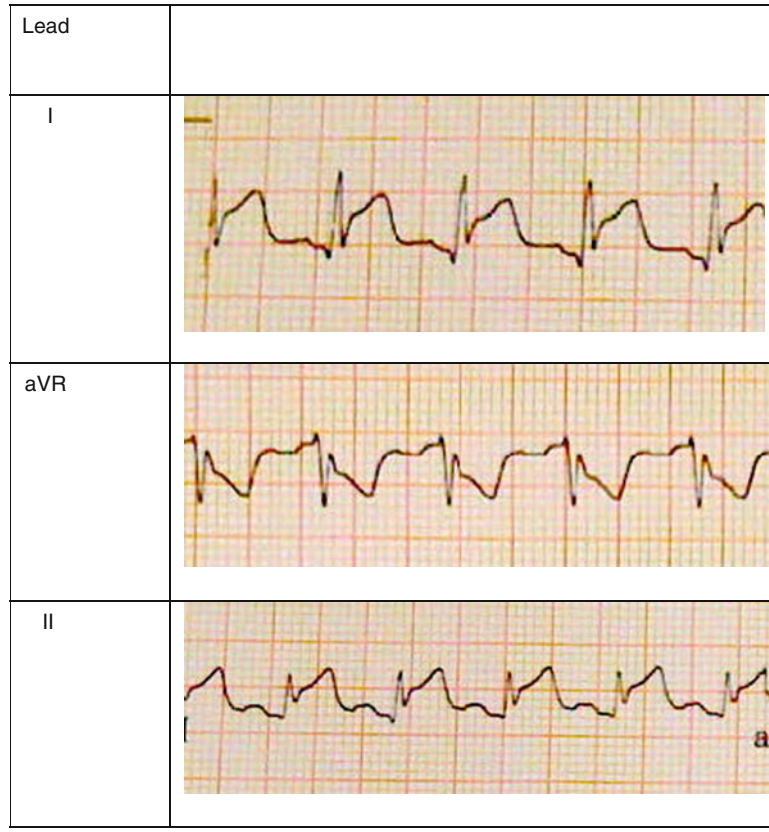
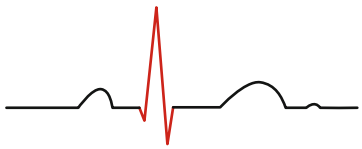



**Fig. 4.3** PR deviation in acute pericarditis: note the depression of the PR segment below the baseline in leads I and II, and the PR elevation in aVR

## Electrical Alternans



The accumulation of fluid around the heart releases the heart from its usual anatomic constraints and allows the heart free range to oscillate in the chest cavity. Typically, this will cause a varying QRS amplitude and vector, alternating from beat to beat, known as electrical alternans. In addition, in the presence of a pericardial effusion, respiratory variation in axis becomes more pronounced. This change is not seen from beat to beat, but rather gradually over a series of QRS complexes. It is important to note however, that while complete alternans of all components of the EKG is suggestive of cardiac tamponade, it is a specific but not highly sensitive sign [9]. Other conditions that can cause electrical alternans include [10] alternating bundle branch blocks causing differential patterns of myocardial depolarization, atrio-ventricular reentry utilizing an accessory pathway, ventricular bigeminy, where every alternate beat is ventricular in origin, alternans pre-excitation in which a supraventricular rhythm is alternately conducted via the atrioventricular node and via an accessory pathway, and the presence of a severe ventricular cardiomyopathy. Bidirectional ventricular tachycardias, as seen in patients with digitalis toxicity, catecholaminergic polymorphic ventricular tachycardia and Anderson-Tawil, or long QT seven syndrome, may also mimic electrical alternans [11, 12] (Table 4.2, Fig. 4.4).

**Table 4.2** Differential diagnosis of electrical alternans on EKG

| |
|---|
| Differential patterns of conduction caused by varying block |
| AV reentry with accessory pathway |
| Ventricular bigeminy |
| Alternans pre-excitation |
| Alternans bundle branch block |
| Severe cardiomyopathy |
| Bidirectional ventricular tachycardia |

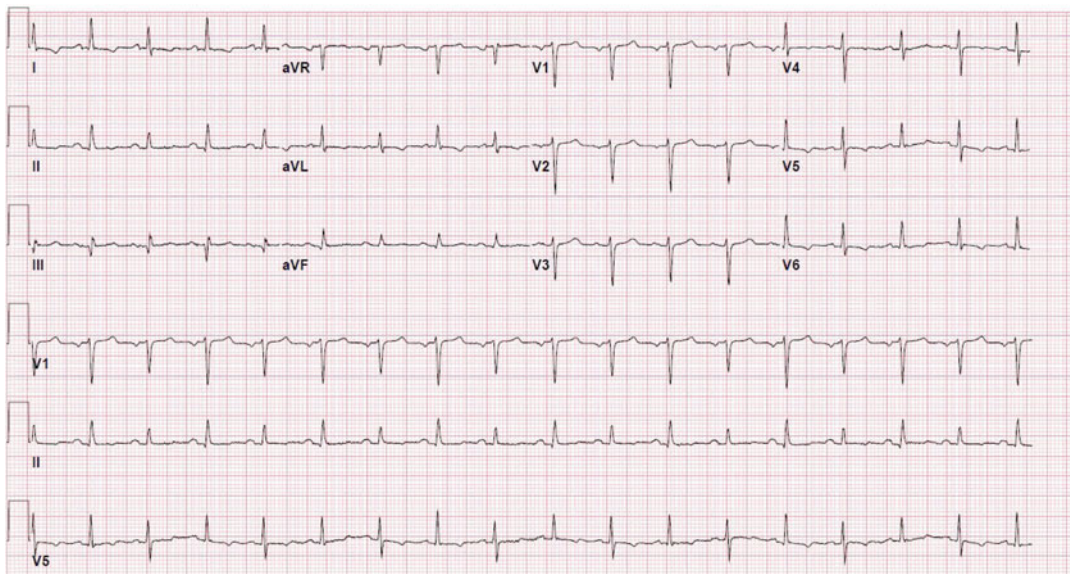
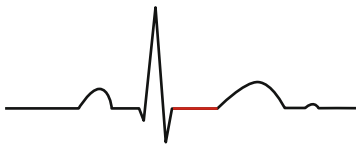



**Fig. 4.4** Electrical alternans in acute pericarditis: note the alternating amplitude and axis of consecutive beats in the inferior and lateral leads

## ST Segment Deviation



Deviation of the ST segment, specifically ST elevation, is present in approximately 90 % of patients with acute pericarditis. This is thought to represent myocardial injury, similar to that seen when direct pressure is applied to the myocardium when placing a pacing wire, and is termed a "current of injury". The axis of these changes is predominantly inferior and anterior, very rarely involving the right sided leads or V1. The mechanism of this injury is multifactorial and is postulated to be due to the increased pressure exerted by the pericardial fluid on the epicardial aspect of the myocardium as well as inflammation of the myocardium. It is important to note the possibility of generating transient ST elevation in patients with pericarditis who exercise, and therefore the ST segment changes seen in these patients may vary based on heart rate. The differential diagnosis for ST elevation is quite broad as ST elevation is seen in a large number of normal and pathological processes.

## Normal Variant

There is a normal variant of repolarization which is common in younger males, a demographic frequently affected by pericarditis. To differentiate this from pericardial disease, it is important to note that normal variant ST elevation is usually only present in the precordial leads and not in the limb leads. Additionally the QRS amplitude in the left lateral leads is greater in the "normal variant" than in pericarditis [13, 14].

## Early Repolarization

The pattern of early ventricular repolarization has similar changes to the first stage of pericarditis [14]. Early studies suggested that in patients with early repolarization, these changes vanish or greatly diminish with the administration of isoproterenol or with exercise, while the changes get worse with the same maneuvers in patients with pericarditis. However, it is important to note that exercising patients with pericarditis has been shown to worsen outcomes [15]. Additionally, a report by Saviolo et al. demonstrates that these findings are not universally true [16].

## Neurological Injury

Spinal cord injury, specifically damage to the C5 and C6 segments which provide sympathetic innervation to the heart can also cause elevation of the ST segment. Significantly however, these changes reverse with the administration of isoproterenol, demonstrating how sympathetic tone modulates ventricular repolarization [17].

## Cardioversion

ST elevations may be seen in patients immediately after direct current cardioversion. These changes will resolve with time.

## Acute Coronary Syndrome

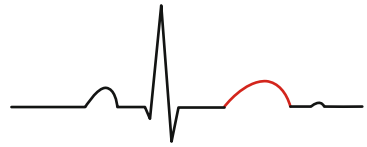
Among the many conditions that mimic acute pericardial disease, it is perhaps most important to differentiate between pericardial disease and acute myocardial injury. Typically, the changes seen in acute myocardial injury are confined to the distribution of individual coronary arteries, while the changes of pericarditis are more global, reflecting the global pressure of the surrounding fluid on the chambers of the heart. Additionally, the terminal component of the QRS may merge directly into the ST segment elevation in acute ischemia, as opposed to pericardial disease, where the QRS morphology remains unchanged, but is followed

by an elevated ST segment. Most importantly, perhaps is the morphology of the ST segment which in acute coronary syndrome is convex, with effacement of the T wave, while in pericardial disease the ST segment is concave and preserves the morphology of the T wave [18] (Table 4.3, Fig. 4.5).

**Table 4.3** Partial list of differential diagnosis of etiologies of ST segment elevation

| |
|---|
| Normal variant |
| Early repolarization |
| Acute ischemia |
| Spinal cord injury |
| Post cardioversion |
| Channelopathies ex: brugada syndrome |
| Ventricular aneurysm |

## T Wave Changes



Acute myocarditis, that may be superficial – sub-epicardial or, less commonly, transmural is often associated with pericarditis. These changes are reflected in the pattern of ventricular repolarization demonstrated in the T wave. As opposed to the vector generated in the ST segment, the vector generated in the T wave is rightward, upward and posteriorly oriented. One

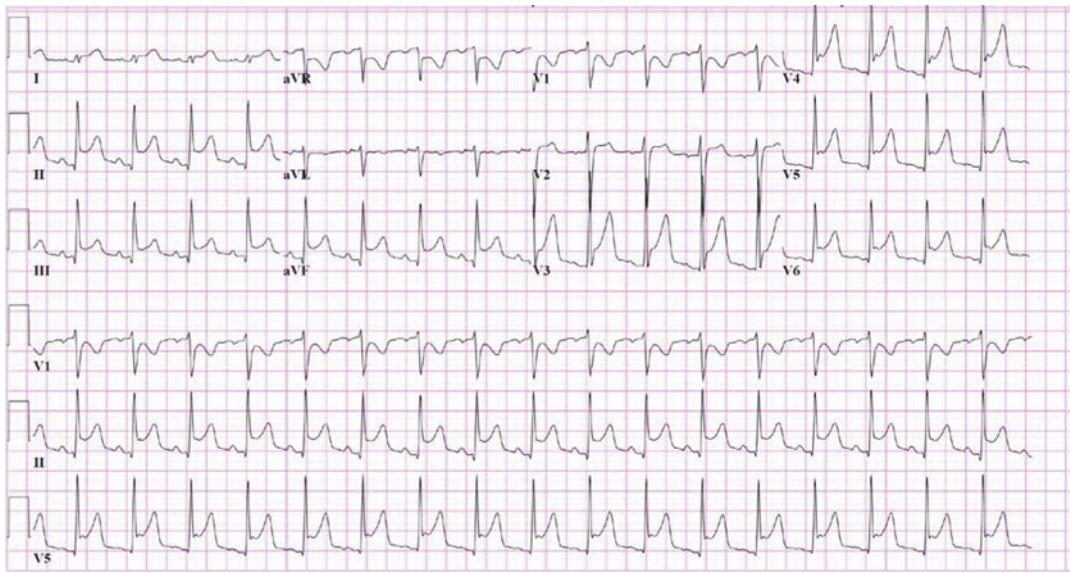



**Fig. 4.5** ST elevation in acute pericarditis: note the diffuse, concave elevations in the ST segment, not respecting the distribution of any single coronary artery

of the challenges of differentiating myocarditis from myocardial ischemia is the similarity between the T wave changes of the two entities. Significantly however, the changes seen in myopericarditis, tend to be lower amplitude, are more global and do not respect the territories of individual coronary arteries. Classically these T waves will be incompletely inverted, with only terminal T wave inversion. Additionally, in approximately 40 % of cases demonstrate a small negative inflection at the peak of the T wave [18]. In contrast the T wave changes in myocardial ischemia are of greater amplitude, are more completely inverted and typically localize to the distribution of a single artery (Fig. 4.6).

## Evolution of EKG Changes

The evolution of EKG changes described above in acute pericarditis has been classically described to take place in four stages [18]. In this scheme, the leads are divided into "epicardial" leads representing epicardial electrical activity and "cavity" leads such as aVR that represent endocardial activation [19]. In stage 1, there is diffuse ST-segment elevation in the epicardial leads, with corresponding depression in the "cavity" leads. In Stage 2, the ST segments return to baseline and the T wave amplitude decreases, either simultaneously with the decrease in ST-segment normalization or subsequently. At this point the PR changes should be evident as

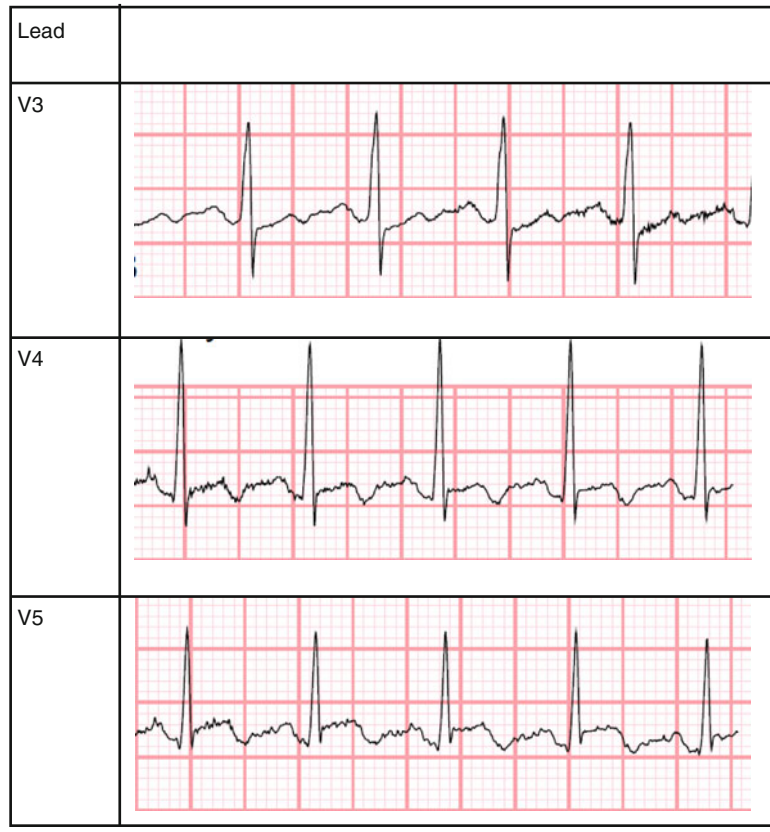



**Fig. 4.6** T wave changes in acute myopericarditis: note terminal inversion of T waves

well. In Stage 3, the T waves begin to invert, either forming shallow or completely inverted T waves. In Stage 4, the EKG returns to baseline. While the patient's EKG may transition directly from stage 1 to stage 3 or 4, this is thought generally to represent a sampling error in a rapidly progressing or resolving process. Patients who so progress are said to have "typical variant" patterns [6] (Table 4.4, Figs. 4.7, 4.8, 4.9, and 4.10).

## Cardiac Arrhythmias in Pericardial Disease

Cardiac arrhythmias are uncommon in acute pericarditis, with an incidence of 7 %. These arrhythmias, when seen, are most commonly supraventricular in origin, predominantly atrial fibrillation/flutter. These arrhythmias typically occur in patients with underlying structural heart disease [20].

**Table 4.4** Stages of evolution of EKG changes [19]

| Stage | All leads except for V1 and AVR | | | V1 and AVR | | |
|---|---|---|---|---|---|---|
| | PR segment | ST segment | T waves | PR segment | ST segment | T waves |
| 1 | Depressed or isoelectric | Elevated | Upright | Elevated or isoelectric | Depressed | Inverted |
| 2 | Depressed or isoelectric | Isoelectric | Upright | Elevated or isoelectric | Isoelectric | Inverted |
| 2 (Late) | Depressed or isoelectric | Isoelectric | Decreased or inverted | Elevated or isoelectric | Isoelectric | Upright, possibly decreased |
| 3 | Isoelectric | Isoelectric | Inverted | Isoelectric | Isoelectric | Upright |
| 4 | Isoelectric | Isoelectric | Upright | Isoelectric | Isoelectric | Inverted |

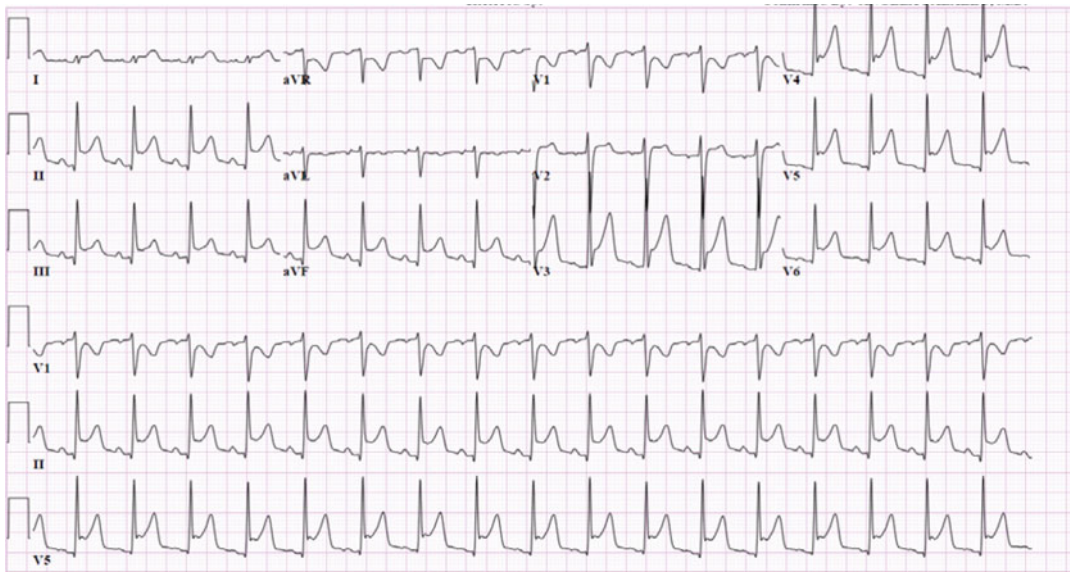



**Fig. 4.7** Stage 1 pericarditis: for description of evolution of EKG changes please refer to the main text and Table 4.4.

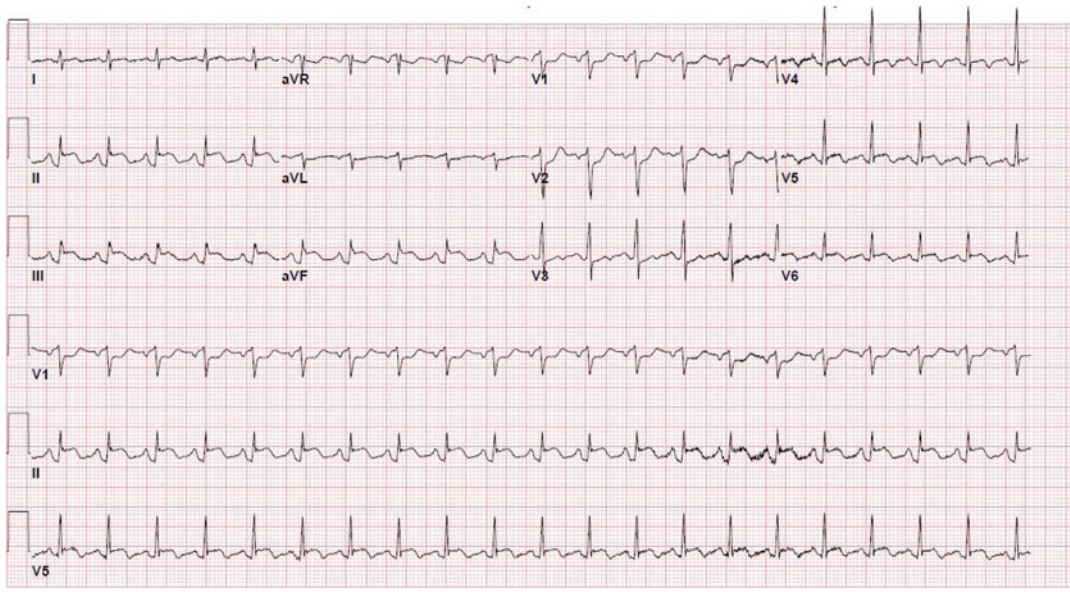



**Fig. 4.8** Stage 2 pericarditis: for description of evolution of EKG changes please refer to the main text and Table 4.4

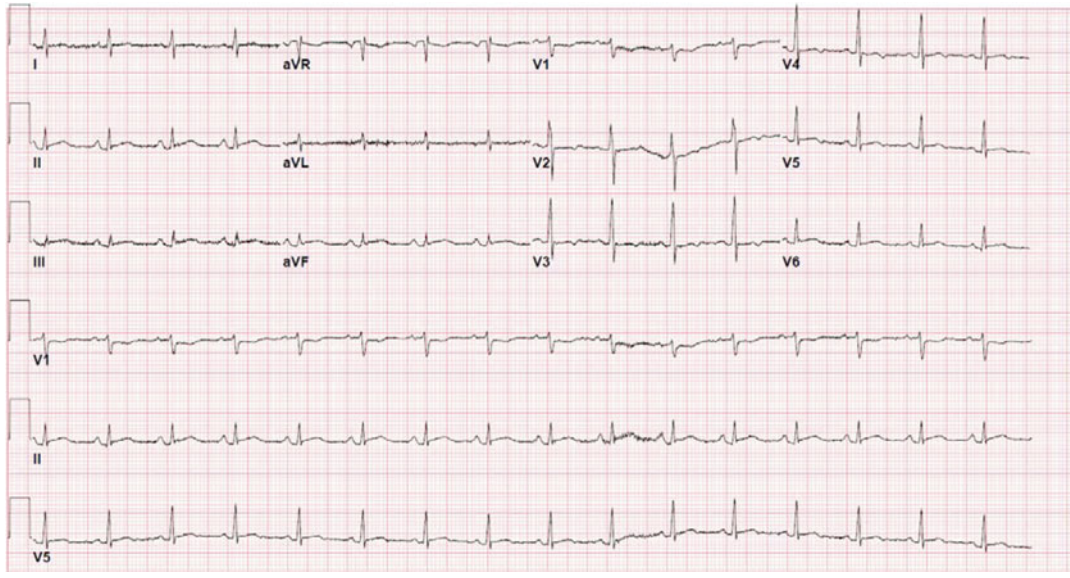



**Fig. 4.9** Stage 3 pericarditis: for description of evolution of EKG changes please refer to the main text and Table 4.4

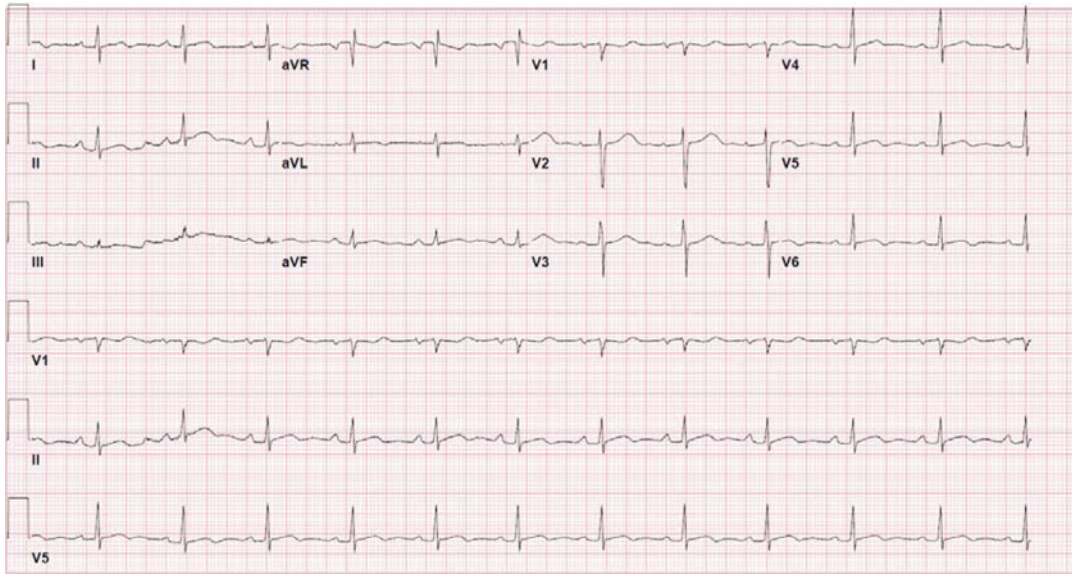



**Fig. 4.10** Stage 4 pericarditis: for description of evolution of EKG changes please refer to the main text and Table 4.4

## Chronic Pericardial Disease

Chronic pericarditis may be caused by many pathological processes. Any of the EKG manifestations of acute pericarditis described above may be present in patients with chronic pericarditis. It has been suggested that a normal EKG excludes the presence of chronic constrictive pericarditis. In this condition, common findings include low voltage, present in the majority of patients, which is thought to be caused by a combination of myocardial atrophic and fibrotic involvement as well as the previously described short circuiting insulating properties of the effusion [21, 22]. Additionally, flattening, notching and or inversion of the T waves are present in more than 90 % of patients [23, 24].

Conduction abnormalities within the atrium are common in patients with chronic pericarditis, leading to a widened P wave mimicking a left atrial abnormality. Similarly, the presence of myocardial fibrosis can lead to abnormalities of ventricular myocardial depolarization, typified by seemingly pathological Q waves [21]. RV dysfunction is suggested by a right ventricular hypertrophy pattern. Right axis deviation is also seen in constrictive pericarditis [25].

As opposed to acute pericarditis where arrhythmias are uncommon, in chronic pericarditis atrial arrhythmias are common, being present in up to 50 % of patients, most frequently atrial fibrillation, followed by atrial flutter [24].

## References

1. Barold SS. Willem Einthoven and the birth of clinical electrocardiography a hundred years ago. Card Electrophysiol Rev. 2003;7(1):99–104.
2. Fye WB. A history of the origin, evolution, and impact of electrocardiography. Am J Cardiol. 1994;73(13):937–49.
3. Bruch C, et al. Changes in QRS voltage in cardiac tamponade and pericardial effusion: reversibility after pericardiocentesis and after anti-inflammatory drug treatment. J Am Coll Cardiol. 2001;38(1):219–26.
4. Kadish AH, et al. ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography. A report of the ACC/AHA/ACP-ASIM task force on clinical competence (ACC/AHA committee to develop a clinical competence statement

on electrocardiography and ambulatory electrocardiography). J Am Coll Cardiol. 2001;38(7):2091–100.
5. Tajiri J, et al. The cause of low voltage QRS complex in primary hypothyroidism. Pericardial effusion or thyroid hormone deficiency? Jpn Heart J. 1985;26(4):539–47.
6. Spodick DH. Diagnostic electrocardiographic sequences in acute pericarditis. Significance of PR segment and PR vector changes. Circulation. 1973;48(3):575–80.
7. Kudo Y, et al. Clinical correlates of pr-segment depression in asymptomatic patients with pericardial effusion. J Am Coll Cardiol. 2002;39(12):2000–4.
8. Porela P, et al. PR depression is useful in the differential diagnosis of myopericarditis and ST elevation myocardial infarction. Ann Noninvasive Electrocardiol. 2012;17(2):141–5.
9. Charles MA, Bensinger TA, Glasser SP. Atrial injury current in pericarditis. Arch Intern Med. 1973;131(5): 657–62.
10. Goyal M, Woods KM, Atwood JE. Electrical alternans: a sign, not a diagnosis. South Med J. 2013;106(8):485–9.
11. Kummer JL, Nair R, Krishnan SC. Bidirectional ventricular tachycardia caused by digitalis toxicity. Circulation. 2006;113(7):e156–7.
12. Priori SG, et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. Circulation. 2002;106(1): 69–74.
13. Ginzton LE, Laks MM. The differential diagnosis of acute pericarditis from the normal variant: new electrocardiographic criteria. Circulation. 1982; 65(5):1004–9.
14. Spodick DH. Differential characteristics of the electrocardiogram in early repolarization and acute pericarditis. N Engl J Med. 1976;295(10):523–6.
15. Imazio M, Trinchero R. Myopericarditis: etiology, management, and prognosis. Int J Cardiol. 2008; 127(1):17–26.
16. Saviolo R, Spodick DH. ELectrocardiographic responses to maximal exercise during acute pericarditis and early repolarization. Chest J. 1986;90(3):460–2.
17. Lehmann KG, et al. Altered ventricular repolarization in central sympathetic dysfunction associated with spinal cord injury. Am J Cardiol. 1989;63(20): 1498–504.
18. Surawicz B, Lasseter KC. Electrocardiogram in pericarditis. Am J Cardiol. 1970;26(5):471–4.
19. Spodick DH. Electrocardiogram in acute pericarditis. Distributions of morphologic and axial changes by stages. Am J Cardiol. 1974;33(4):470–4.
20. Spodick DH. Arrhythmias during acute pericarditis: a prospective study of 100 consecutive cases. JAMA. 1976;235(1):39–41.
21. Levine HD. Myocardial fibrosis in constrictive pericarditis. Electrocardiographic and pathologic observations. Circulation. 1973;48(6):1268–81.
22. Dines DE, Edwards JE, Burchell HB. Myocardial atrophy in constrictive pericarditis. Proc Staff Meet Mayo Clin. 1958;33(4):93–9.
23. Wood P. Chronic constrictive pericarditis. Am J Cardiol. 1961;7:48–61.
24. Chambliss JR, et al. Chronic cardiac compression (chronic constrictive pericarditis); a critical study of sixty-one operated cases with follow-up. Circulation. 1951;4(6):816–35.
25. Chesler E, Mitha AS, Matisonn RE. The ECG of constrictive pericarditis–pattern resembling right ventricular hypertrophy. Am Heart J. 1976;91(4): 420–4.

## EKG in Pericardial Disease-For Patients and their Families

Pericarditis is a condition when the pericardium, a tissue layer that envelopes the outer, or epicardial surface of the heart becomes inflamed. This may cause fluid to build up around your heart. In some cases, this inflammation may extend into the heart muscle as well. In this case the condition is termed myocarditis.

There are many ways to diagnose pericarditis. Your doctor will first develop a careful understanding of your symptoms and the progression of your illness. Symptoms of pericarditis include chest pressure, chest pain, and shortness of breath. You may recently have had an influenza like illness with aches and fevers. After gathering the history of your condition, one of the first diagnostic steps is to have a test called an electrocardiogram, or EKG. The EKG measures the electrical activity of your heart and can help your doctor differentiate pericarditis from other conditions.

Patients with pericarditis may have irregular heart rhythms, as well as changes in the way the electrical system in the heart functions. By recording your heart's electrical activity, your doctor may be able to assess for inflammation, as well as the presence of fluid around your heart, and the pressure that the fluid exerts on your heart. While your doctor will be able to interpret the EKG on the spot, in many medical systems the EKG will be subsequently reviewed by a specialist to confirm its findings. EKG's are often stored in your secure medical record. This allows your doctor to compare changes over time.

In order to obtain your EKG, your healthcare provider will attach 10 leads by means of stickers placed in pre-defined standardized locations. These leads connect to a small computer that analyzes the signal and graphs it both on the screen and on calibrated paper. As the EKG does not apply any electrical current to you, and is completely passive, you should not experience any discomfort.

The EKG complex is divided into a number of components, or segments that begin with the P wave and conclude with a U wave. Your physician will be paying special attention to your PR segment, the height and axis of your QRS component, as well as the shape of your ST segment and T wave. The inflammatory changes caused by pericarditis can cause depression of the PR segment, elevation of the ST segment and a low voltage QRS signal, among other changes.

There are classically defined changes seen in pericarditis. These changes typically involve four "stages", representing the underlying processes affecting your heart. Typically, when pericarditis has resolved, the EKG will return to normal. If however, your doctor tells you that your EKG remains abnormal, it is advisable to retain a copy to carry around on your person. This assures that in an emergency, a copy of your EKG is available for your next medical provider to assess and compare to your current EKG.

It is important to note that while the EKG is very helpful in diagnosing pericardial disease, it may be the first of several tests that your doctor orders. Based on the findings of your EKG, your doctor may subsequently order an echocardiogram, CT scan, or MRI.

# Echocardiography in Pericardial Disease

5

Muhamed Saric

## For Physicians and Other Health Care Professionals

### Introduction

Echocardiography is used extensively in the diagnosis and management of all forms of pericardial disease spanning from congenital anomalies of the pericardium to acute pericarditis, pericardial effusion, tamponade, constrictive pericarditis and pericardial tumors.

Due to its widespread availability, portability, safety, and ability to provide both anatomic and hemodynamic data, echocardiography is typically the initial imaging modality of choice for visualization of pericardial disorders as well as for guidance of pericardiocentesis. Additional imaging with computed tomography (CT) and cardiac magnetic resonance (CMR) may be necessary in selected cases, typically to overcome limitations of echocardiography as in patients with difficult echocardiographic windows, when there is a need for more precise measurement of pericardial thickness or when tissue characterization and/or relationship to structures surrounding the pericardium is required.

Dedicated guidelines of the European Society of Cardiology (ESC) [1] and the American Society of Echocardiography (ASE) [2] provide in-depth recommendations on proper use of echocardiography in pericardial disorders. Echocardiography is also an integral part of the CHASER pathway for the management of pericardial disease [3].

### Normal Echocardiographic Appearance of the Pericardium

A brief overview of pericardial anatomy as it specifically relates to echocardiography is provided below.

**Pericardial Thickness**: Pericardium is a sac-like structure consisting of a parietal and a visceral (epicardial) layer. Normal pericardial wall thickness is approximately 1–2 mm. Unfortunately, transthoracic echocardiography (TTE) does not have sufficient image resolution and therefore is not recommended for measurements of pericardial thickness. In contrast, pericardial thickness can be measured by transesophageal echocardiography (TEE) [4] and such measurements approach the gold standard of CT and CMR.

**Pericardial Fluid**: Normally there is only a very small amount of physiologic pericardial fluid (<50 mL) and separation between parietal and visceral layers is either imperceptible on echocardiography or occurs only during ventricular systole, when a slit like echo lucent area between the two layers may be seen.

**Pericardial Fat**: A variable amount of fat may accumulate in and around the pericardial sac.

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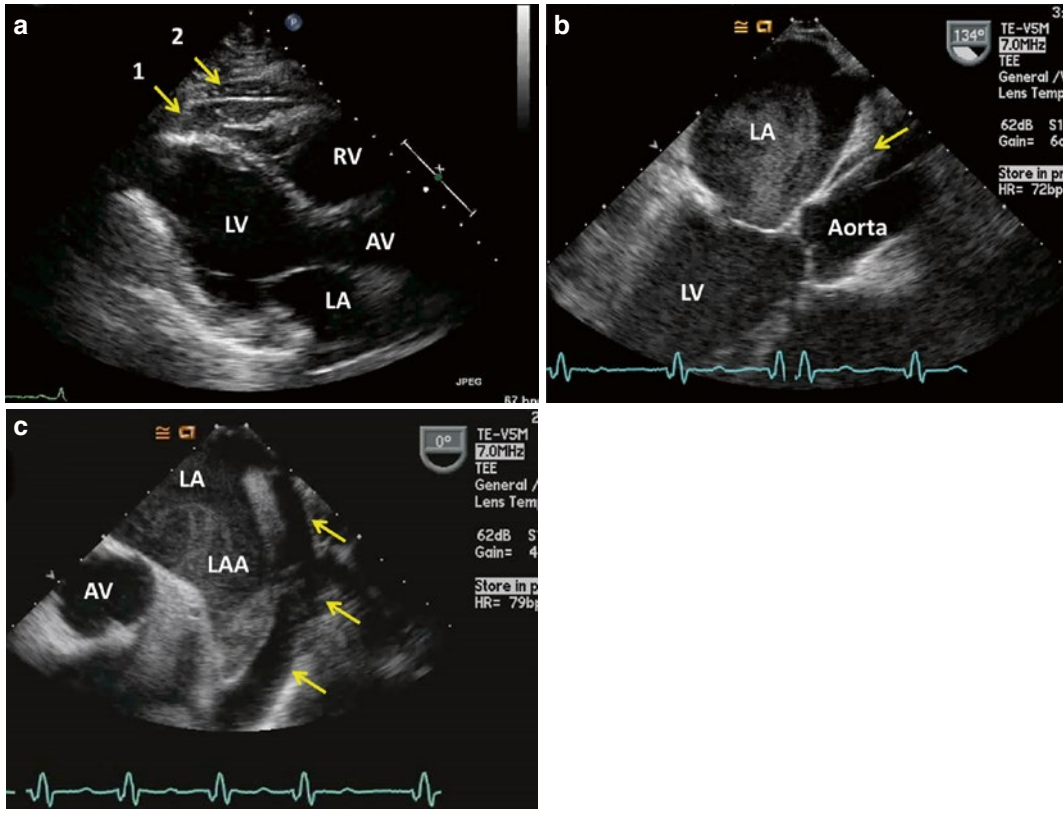


**Fig. 5.1** Pericardial anatomy. Panel **a**: Pericardial fat pad on transthoracic echocardiogram in the parasternal long-axis view. Note the heterogeneous appearance of the two layers of pericardial fat (*arrows*); one layer is intrapericardial (epicardial; #1), and the other is extrapericardial (mediastinal; #2). Panel **b**: Transesophageal echocardiogram demonstrates effusion in the transverse sinus (*arrow*) of the pericardium adjacent to the ascending aorta. This finding should not be mistaken for a type A aortic dissection. Panel **c**: Transesophageal echocardiogram demonstrates effusion in the transverse sinus (*arrows*) of the pericardium adjacent to the left atrial appendage which is filled with dense spontaneous echo contrast ('smoke') in this patient with atrial fibrillation. Abbreviations: *AV* aortic valve, *LA* left atrium, *LAA* left atrial appendage, *LV* left ventricle, *RV* right ventricle

Intrapericardial (epicardial), fat tends to accumulate in the atrioventricular groove and along the coronary arteries. Additional fat tissue is seen extrapericardially in the surrounding mediastinum, especially anterior to the right heart. The epicardial and mediastinal fat layers should not be mistaken for a loculated pericardial effusion (Fig. 5.1, Panel a). Echocardiographically, pericardial fat is heterogeneous, non-circumferential and moves in concert with the heart. In contrast, pericardial effusion is typically echo lucent, stationary and circumferential rather than restricted to the region around the right heart.

**Intra vs Extrapericardial Structures**: For a full understanding of pericardial physiology and pathology, it is important to recognize which cardiac structures are within and which are outside the pericardial sac. The proximal portions of the great vessels (the ascending aorta and the main pulmonary artery) are within the pericardial sac. Thus injuries or dissections of proximal portions of these vessels may lead to pericardial effusion. In contrast, superior portion of the left atrium and the ostia of the pulmonary veins are not within the pericardial sac. This anatomic fact contributes to exaggerated respiratory variations in tamponade and constrictive pericarditis as further discussed in appropriate sections of this chapter.

**Pericardial Extensions**: The main pericardial space communicates with several extensions referred to as sinuses and recesses. Transverse sinus (Fig. 5.1, Panels b, c) is located around

the origins of the great vessels and the left atrial appendage while the oblique sinus surrounds the ostia of the pulmonary veins. Pericardial effusion may occasionally be restricted to one or more of these sinuses and recesses. These localized pericardial effusions should not be mistaken for other pathologies such as the type A aortic dissection in the case of fluid accumulation in the transverse sinus.

## Congenital Absence of the Pericardium

Partial or complete absence of the pericardium is a rare congenital disorder that could not reliably be diagnosed in vivo prior to advent of modern cardiac imaging. Congenital absence of the pericardium was first undoubtedly described in 1793 on autopsy by the Scottish physician and pathologist Matthew Baillie (1761–1823) [5] although an earlier and likely erroneous description might have been made by the Italian anatomist Realdo Colombo (1516–1559) [6]. The reported occurrence of congenital absence of the pericardium is 1 per 14,000 autopsies [7].

### Key Anatomic Features

Since partial absence of the pericardium surrounding the left heart is the most common form, excessive displacement of the cardiac apex to the left (levoposition and levorotation of the heart) is the key anatomic feature.

### Echocardiography Indications

Congenital absence of the pericardium may be an incidental finding or the patient may present with nonspecific symptoms such as chest pain, palpitations or shortness of breath.

### Echocardiography Findings

Echocardiographically, congenital absence of the pericardium cannot be visualized per se but is rather deduced from indirect signs. Because the cardiac apex is displaced laterally in the partially absent left-sided pericardium, standard echocardiographic imaging windows provide unusual images of the heart. In the parasternal views, the right ventricle, although typically normal in size, appears enlarged. Additionally, there is increased cardiac motion due to absence of pericardial constraint and paradoxical interventricular septal motion (Fig. 5.2, Panel a). On the apical 4-chamber view the cardiac apex is displaced to the left and the heart has an unusual tear-drop shape.

Patients in whom the pericardium was surgically removed (Fig. 5.2, Panel b) may have echocardiographic findings similar to those in patients with congenitally absent pericardium (e.g. patients post pericardiectomy for constrictive pericarditis).

### Alternative Imaging

Congenital absence of the pericardium may be suspected from an unusual shape to the cardiac silhouette on chest X ray (Fig. 5.2, Panel c). Definitive diagnosis of congenitally absent pericardium is usually established by CT or CRM.

## Pericardial Cysts and Diverticula

Congenital pericardial cysts and diverticula may be considered as accessory pericardial spaces. Pericardial cysts are thin-walled unilocular structures filled with clear, watery fluid; they do not communicate with the pericardial sac. In contrast, pericardial diverticula are abnormal extensions that communicate with the main pericardial space.

In general, pericardial cysts are rare, typically benign and congenital in nature with a prevalence of 1 per 100,000 cases [8]. Congenital pericardial cysts arise from the primitive coelum, the progenitor of pericardial, pleural and peritoneal cavities. Their exact embryogenesis is uncertain. Acquired cysts, such as pericardial hydatid cysts, may be seen in parts of the world where parasitic infections with *Echinococcus* species are common. Like congenital cysts, hydatid cysts are filled with a watery fluid, thus the name (from Greek *ὑδατίς*; stem *ὑδατιδ-* meaning ‘a drop of water’).

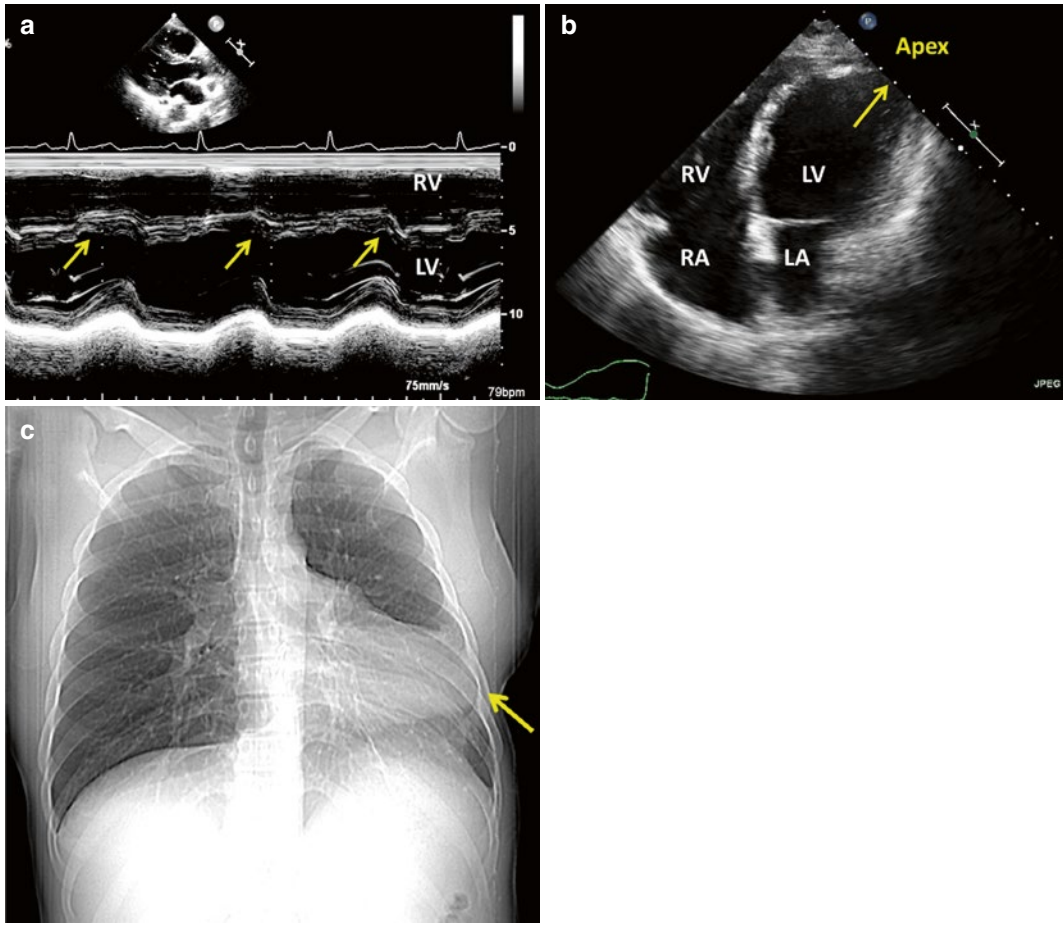


**Fig. 5.2** Absence of the pericardium. Panel **a**: M mode recording shows paradoxical interventricular septal motion (*arrow*) in a patient with congenital absence of the pericardium. Panel **b**: Transthoracic echocardiogram in the apical 4-chamber view demonstrates characteristic lateral displacement of the cardiac apex (*arrow*) in a patient with absent pericardium after surgical stripping (pericardiectomy). Panel **c**: Chest X ray demonstrates an unusual cardiac silhouette with lateral and cranial displacement of the cardiac apex (arrow) in a patient with congenital absence of the pericardium (Courtesy of Dr. Robert Donnino, Department of Radiology and Division of Cardiology, New York University Langone Medical Center). Abbreviations: *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

## Key Anatomic Features

Congenital pericardial cysts are typically located in one of the cardiophrenic angles, more often in the right than the left cardiophrenic angle. Their size varies from small fluid collection in the cardiophrenic angle to large masses filling the mediastinum.

## Echocardiography Indications

Pericardial cysts and diverticula may be an incidental finding or the patient may present with nonspecific symptoms such as chest pain, palpitations or shortness of breath.

## Echocardiography Findings

On ultrasound imaging, pericardial cysts were first characterized by M mode echocardiography in 1975 [9], and then by 2D echocardiography in 1983 [10]. The key echocardiographic findings of a pericardial cyst include an echo lucent, thin-walled structure located adjacent to the heart and above the diaphragm (most often in and around the right atrioventricular groove), filled with clear, stationary fluid and without obvious communications to any of the surrounding structures (Fig. 5.3, Panel a).

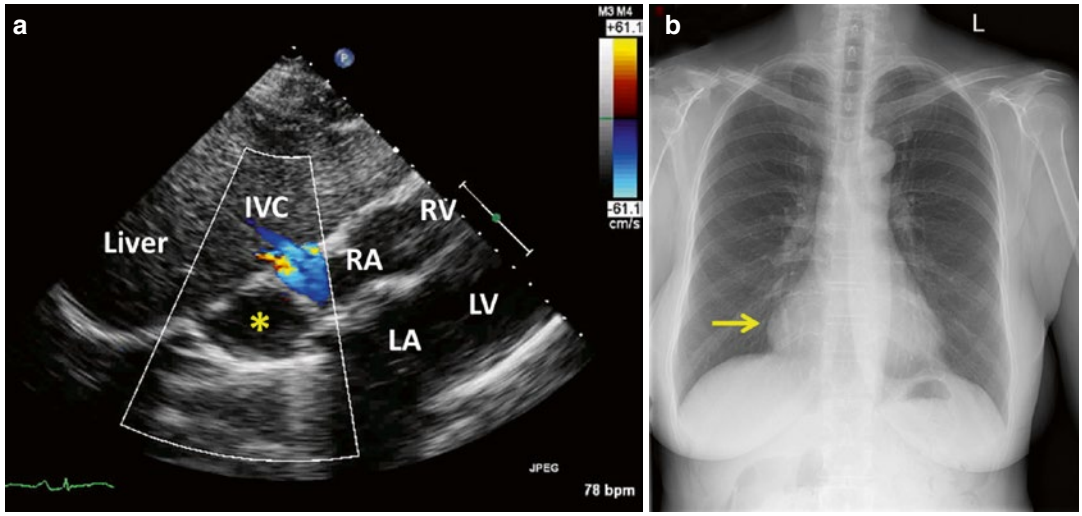


**Fig. 5.3** Pericardial cyst. Panel **a**: Transthoracic echocardiogram in the subcostal view demonstrates a small pericardial cyst (*asterisk*) adjacent to the right atrium (*RA*). Abbreviations: *IVC* inferior vena cava, *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle. Panel **b**: Chest X ray demonstrates a pericardial cyst in the right cardiophrenic angle (*arrow*). Panel **b**: Chest X ray demonstrates a pericardial cyst in the right cardiophrenic angle (*arrow*) (Courtesy of Dr. Robert Donnino, Department of Radiology and Division of Cardiology, New York University Langone Medical Center)

### Differential Diagnosis

Other echo lucent structures adjacent to the heart such as pericardial and pleural effusion or ascites may be mistaken for a pericardial cyst. Pericardial effusions tend to be circumferential and often show signs of organization. Unlike pericardial cysts, left and right pleural effusions follow the anatomic boundaries of respective pleural spaces.

Vascular anomalies (especially in and around atrioventricular grooves) such as coronary artery aneurysms, coronary artery fistulas and enlarged coronary sinus may be differentiated from pericardial cysts with the intravenous administration of echocardiographic contrast agents. Unlike vascular anomalies, pericardial cysts do not communicate with the vascular pool and thus they do not opacify after echocardiographic contrast administration. To differentiate pericardial cysts from coronary artery aneurysms and coronary artery fistulas, microbubble contrast agents (such as perflutrane) should be used while agitated saline can be used for the diagnosis of enlarged coronary sinus due to persistence of the left superior vena cava.

### Alternative Imaging

The diagnosis of a pericardial cyst is often suspected on a chest X ray as a mass like density, typically located in the right cardiophrenic angle (Fig. 5.3, Panel b). The definitive diagnosis of pericardial cysts and diverticular is usually established by CT or CMR.

## Pericardial Effusion

Pericardial effusion is an accumulation of fluid in the pericardial sac between the visceral and parietal layer of the pericardium. There are numerous causes of pericardial effusions including infectious, metabolic, rheumatologic, traumatic, neoplastic and idiopathic etiologies. In the developed countries, the predominant causes of pericardial effusion are idiopathic and traumatic (especially iatrogenic following surgical or percutaneous procedures).

The hemodynamic spectrum of a pericardial effusion spans from asymptomatic to tamponade, cardiovascular collapse and death.

### Key Anatomic and Hemodynamic Features

The pericardial sac envelopes the entire heart except the cranial portion of the left atrium around the ostia of the pulmonary veins. The

proximal portions of the ascending aorta and the main pulmonary artery are also within the pericardial sac. In contrast, the descending thoracic aorta lies outside the pericardial sac; this anatomic feature helps differentiate a pericardial effusion from a left pleural effusion (see below).

The primary determinant of hemodynamic significance of a pericardial effusion is not the volume of intrapericardial fluid per se but rather the intrapericardial pressure exerted by that volume. This is further discussed in the Tamponade section below.

## Echocardiography Indications

Pericardial effusion may be an incidental finding on an echocardiogram ordered for a different reason, or the patient may present with chest pain, shortness of breath or hypotension and shock.

## Echocardiography Findings

Here the general echocardiographic features of pericardial effusions will be discussed (Fig. 5.4). Tamponade findings are described separately in a section below.

Pericardial effusions are typically circumferential (around the entire heart) but not necessarily

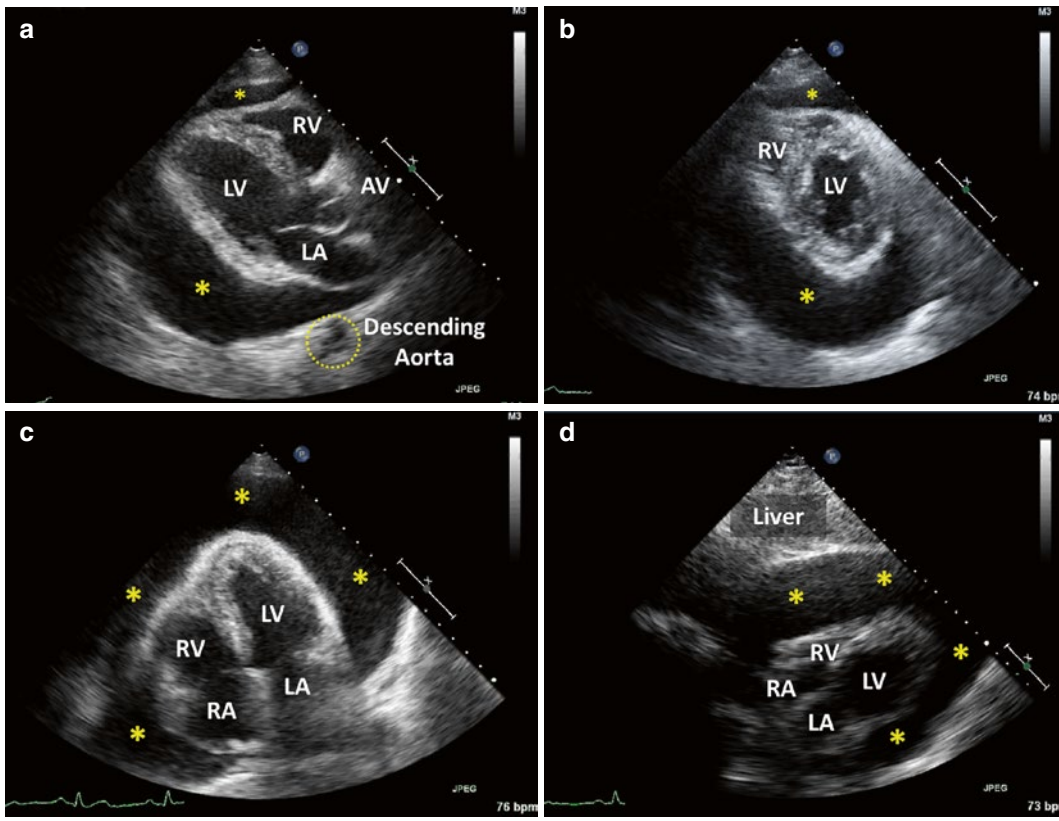


**Fig. 5.4** Pericardial effusion. Transthoracic echocardiogram demonstrates a large pericardial effusion (*asterisks*) in a 47-year-old woman with breast cancer. Panel **a**: Parasternal long axis view demonstrates typical interposition of the pericardial effusion (*asterisks*) between the heart and the descending thoracic aorta. This finding differentiates a pericardial effusion from a left pleural effusion in which there is no such interposition between the heart and the descending thoracic aorta. Panel **b**: Parasternal short axis at the level of the papillary muscles demonstrates that the pericardial effusion (*asterisks*) is larger posterior to the left ventricle that anterior to the right ventricle. This is due to gravity in this supine patient. Panel **c**: In the apical 4-chamber view, note that the pericardial effusion (*asterisks*) surrounds the cardiac apex. This feature helps distinguish a pericardial effusion from a pleural effusion. Panel **d**: Subcostal view demonstrates a large pericardial effusion (*asterisks*). Abbreviations: *AV* aortic valve, *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

symmetrical; a larger amount of fluid tends to occur in more dependent areas compared to less dependent ones. In a supine patient, circumferential pericardial effusions tend to be larger posterior to the left heart than anterior to the right heart. Loculated pericardial effusions may occur in any portion of the pericardial sac.

The consistency of pericardial fluid varies from clear, water like collections to partly organized (with strands spanning the two layers of the pericardium) to fully organized, tumor like densities (as in the case of hemorrhagic effusion).

On an echocardiography report, the size, location (circumferential vs. loculated) and fluid characteristics (clear vs. organized) should be described. The size of a circumferential pericardial effusion may be expressed and the end-diastolic effusion thickness (the distance between epicardial and parietal layers of the pericardium). Small pericardial effusions have end-diastolic thickness of <1 cm; moderate between 1 and 2 cm; and large >2 cm as described in the latest ASE guidelines [2].

The volume of pericardial fluid can roughly be estimated using the so-called cube rule which assumes that the heart is a prolate ellipsoid and that a volume of a cardiac chamber is the cube of its short-axis diameter [11]. In practical terms, one obtains 2D echocardiographic images of the heart in the parasternal long or short axis and then measures the end-diastolic thickness of the pericardial fluid (PF), end-diastolic diameters of the left (LV) and right ventricles (RV), and end-diastolic thickness of the right ventricular free wall (RVF), interventricular septum (IVS) and inferolateral wall (IL).

The end-diastolic diameter of the heart is RVF + RV + IVS + LV + IL; this diameter cubed gives the volume of the heart. The end-diastolic diameter of the pericardial sac is the sum of anterior and posterior pericardial effusion thickness plus the end-diastolic diameter of the heart; the cube of the end-diastolic pericardial sac diameter represents the volume of the pericardial sec. The volume of pericardial effusion is then the difference between the pericardial sac volume and the volume of the heart.

Example:
The patient has a pericardial effusion that measures 1.0 cm both anterior to the right heart and posterior to the left heart at end diastole; RVF = 0.3 cm; RV = 1.7 cm; IVS = 0.7 cm; LV = 3.9 cm; IL = 0.6 cm.

*Heart*:

$$\text{End}-\text{diastolic diameter of the heart} = 0.3+1.7+0.7+3.9+0.6 = 7.2\,\text{cm}$$

$$\text{End}-\text{diastolic volume of the heart} = (7.2)^3 = 373\,\text{mL}$$

*Pericardial sac*:

$$\text{End}-\text{diastolic diameter of the pericardial sac} = 1.0+1.0+7.2 = 9.2\,\text{cm}$$

$$\text{End}-\text{diastolic volume of the pericardial sac} = (9.2)^3 = 779\,\text{mL}$$

*Pericardial effusion*:

$$\text{Pericardial effusion} = 779-373 = 405\ \text{mL}.$$

It must be emphasized that this calculation method gives only a rough estimate of pericardial effusion volume and might overestimate effusion volume especially if cardiac diameters are large.

When pericardial effusions are very large, one may observe a swinging motion of the heart with the cardiac apex moving toward and then away from the anterior chest wall. In such instances, one may notice the electrical alternans (a change in QRS voltage) on simultaneous EKG tracings which should accompany any echocardiographic recording. Additionally, overall EKG voltage may be diminished [12].

## Differential Diagnosis

Typically, the differential diagnosis of pericardial effusion includes pericardial fat, pericardial cyst, pleural effusion and ascites.

Pericardial fat is typically non-circumferential and most prominent along the right heart border; it is heterogeneous in appearance, and moves in concert with the heart (Fig. 5.1, Panel **a**). In contrast, pericardial effusion is typically echo lucent, immobile and circumferential with the largest amount of fluid in dependent areas closest to the ground.

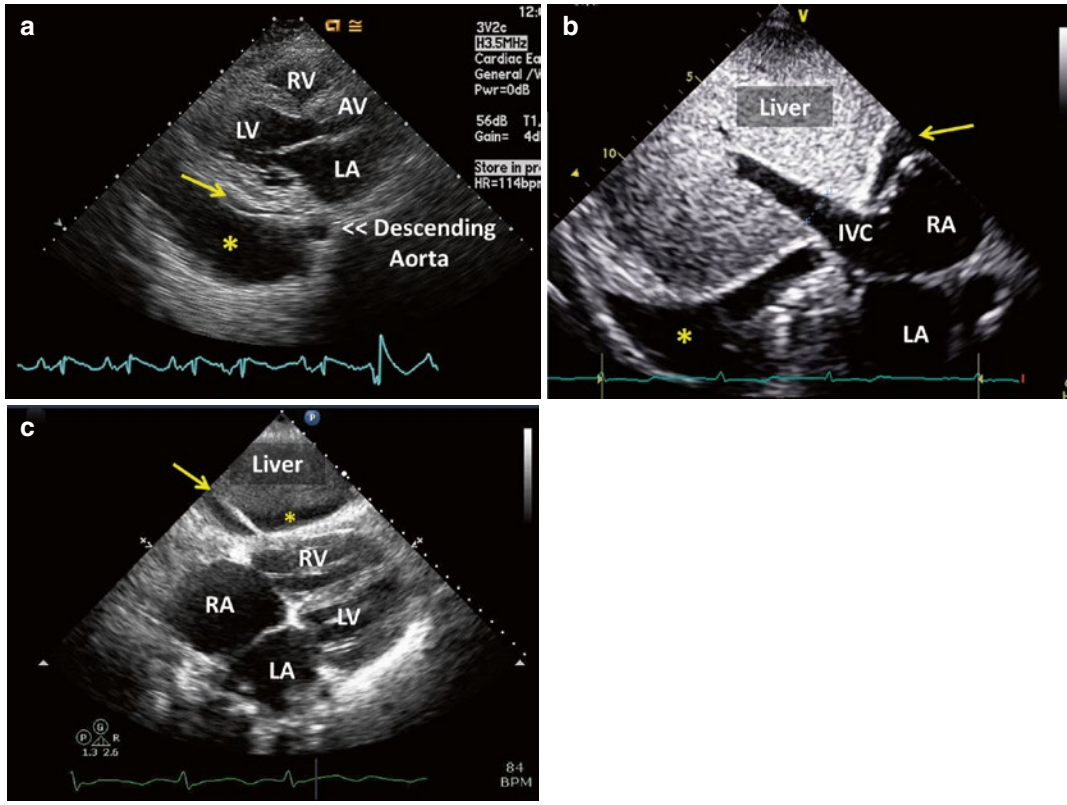


**Fig. 5.5** Differential diagnosis of a pericardial effusion. Panel **a**: Left pleural effusion – Transthoracic echocardiogram in the parasternal long axis view demonstrates a left pleural effusion (*asterisk*) and a very small pericardial effusion (*arrow*). Note that unlike the pericardial effusion, the left pleural effusion does not create an echo lucent area of separation between the descending thoracic aorta and the heart. Panel **b**: Right pleural effusion – Transthoracic echocardiogram in the subcostal view demonstrates a left pleural effusion (*asterisk*) and a pericardial effusion (*arrow*). Note that the right pleural effusion follows the contours of the diaphragm which lies just cranial to the liver boundary. Panel **c**: Ascites – Transthoracic echocardiogram in the subcostal view demonstrates ascites (*asterisk*) between the liver and the heart. The presence of the falciform ligament (*arrow*) helps differentiate ascites from a pericardial effusion. Abbreviations: *AV* aortic valve, *IVC* inferior vena cava, *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

Pericardial cysts are thin-walled structures containing clear, stationary fluid; they tend to occur in the right atrioventricular groove and have no direct communication with any surrounding structure (Fig. 5.3, Panel a).

Left pleural effusion is located posterior to the left ventricle on parasternal views or lateral to the left ventricle on apical views (Fig. 5.5, Panel a). To differentiate a left pleural effusion from a pericardial effusion, one should pay a special attention to the relationship between the descending thoracic aorta and the left heart border on e.g., parasternal views. The larger the pericardial effusion, the more separation between the descending thoracic aorta and the left heart border there is. In contrast, left pleural effusion does not create an echo lucent area of separation between the descending thoracic aorta and the heart. Because there is no communication between the left and right pleural spaces at the cardiac apex, periapical fluid collection seen on apical views are more likely to be pericardial than pleural in origin.

Right pleural effusion is best differentiated from the pericardial effusion in the subcostal view; a right pleural effusion follows the contours of the diaphragm (Fig. 5.5, Panel b).

Ascites is a subdiaphragmatic fluid collection containing the falciform (sickle-shaped) ligament

which anchors the liver to the diaphragm (Fig. 5.5, Panel c).

### Alternative Imaging

Echocardiography is typically sufficient to establish the diagnosis and hemodynamic significance of a pericardial effusion.

Imaging with CT and CMR may provide additional anatomic details; particularly related to extracardiac structures and their relationship to pericardial effusion (e.g. type A aortic dissection, mediastinal hematoma post cardiac surgery, thoracic tumor extension into the pericardial space etc.).

EKG has low sensitivity for detection of pericardial effusion; low voltage and electrical alternans are seen only infrequently [12].

## Tamponade

Tamponade, originally a French word meaning 'plugging', refers to a clinical syndrome of impaired cardiac filling due to elevation of intrapericardial pressure in the setting of a pericardial effusion. As a clinical entity, cardiac tamponade resulting from a pericardial effusion was first described in the 1930s [13].

Cardiac tamponade is a form of diastolic heart failure. It is important to emphasize that tamponade is not a discrete point in time but rather a process of progressive impairment in cardiac filling extending from an asymptomatic phase to exercise intolerance to hypotension, shock and death. An increase in intracardiac pressures and tachycardia are compensatory mechanisms that delay the progression of tamponade physiology.

### Key Anatomic and Hemodynamic Features

The primary determinant of hemodynamic significance of a pericardial effusion is not the size of a pericardial effusion but rather the magnitude of intrapericardial pressure. Cardinal features of tamponade are cardiac chamber collapse (due to extrinsic compression of cardiac walls by pericardial effusion), ventricular interdependence (manifested as exaggerated respiratory variations in cardiac filling), and frequently intracardiac pressure elevation including right atrial pressure elevation leading to a plethoric inferior vena cava.

A normal intrapericardial pressure is close to 0 mmHg or even negative (subatmospheric). In tamponade, intrapericardial pressure exceeds intracardiac pressures for at least part of the cardiac cycle.

The intrapericardial pressure (P) is a product of intrapericardial volume (V) and pericardial stiffness ($\Delta P/\Delta V$):

$$P = V * \frac{\Delta P}{\Delta V}$$

Pericardial stiffness, an inverse of pericardial compliance, is the slope of the intrapericardial pressure-volume curve; it demonstrates a nonlinear relationship between the volume of pericardial effusion and the intrapericardial pressure.

At low effusion volumes, the slope if rather flat; initial increases in the size of pericardial effusion lead to only a modest rise in intrapericardial pressure. However, the slope becomes subsequently very steep; at this portion of the curve even a small increase in the size of pericardial effusion leads to marked increases in intrapericardial pressure which, in turn, may precipitate tamponade physiology. Conversely, in a patient with tamponade, even removal of a relatively small amount of pericardial effusion, may promptly relieve signs and symptoms of tamponade.

The location of this pressure-volume curve relative to the x axis (pericardial effusion volume) is dependent on the rate of pericardial fluid accumulation. With acute pericardial effusion (such as with a hemorrhagic effusion in a patient with type A aortic dissection) the curve and the inflection point occur at low volumes; in other words, a relatively small amount of acute pericardial effusion may lead to tamponade physiology. In contrast, with chronic effusion, pericardial stiffness is lower because pericardium has time to adapt to slowly increasing amounts of pericardial fluid and the pressure-volume curve is shifted to the right.

Once the intrapericardial pressure exceeds the intracardiac pressure, extrinsic compression

by the pericardial fluid leads to invagination of a cardiac wall into its respective chamber (chamber collapse). Aside from chamber collapse, tamponade physiology is also characterized by exaggeration of normal respiratory variations in cardiac filling. Normally, left and right ventricle fill during diastole away from each other and not at the expense of each other; consequently, the interventricular septum stays in the middle during inspiration and expiration.

Pericardial fluid, like any other fluid, is uncompressible. Thus, pericardial effusion constrains ventricular filling and forces the two ventricles to fill at each other's expense; the impact on each ventricle is dependent on the respiratory phase. During inspiration, the right ventricle fills at the expense of the left ventricle while during expiration the opposite is true. These respiratory variations in cardiac filling are the cardinal feature of tamponade physiology and together with signs of chamber collapse they provide the basis for echocardiographic diagnosis of tamponade.

## Echocardiography Indications

Primary indications for echocardiography imaging in a patient with tamponade include clinical signs and symptoms of heart failure, hypotension and shock. Heart failure, when present, is typically diastolic with predominance of signs and symptoms of right heart failure (clear lungs, hepatomegaly, ascites, and lower extremity edema).

## Echocardiography Findings

Echocardiographic diagnosis of tamponade is based on visualization of the three cardinal features of tamponade physiology in the setting of a pericardial effusion: chamber collapse, respiratory variations and elevation of right atrial pressure. Chamber collapse is relatively specific for tamponade physiology, while respiratory variations are also seen in constrictive pericarditis and several other conditions such as labored breathing, pulmonary embolism, obesity and chronic obstructive lung disease (COPD). Because an increase in intracardiac pressures is a compensatory mechanism in both tamponade and constriction, plethora of the inferior vena cava, a sign of right atrial pressure elevation, is frequently seen in tamponade and constriction.

Chamber collapse: Free walls of cardiac chambers invaginate into the chamber when intrapericardial pressure exceeds intracardiac pressure. Because intracardiac pressures are lower in diastole and since the right heart has thinner walls the left heart, it is the collapse of the right ventricular and right atrial free wall that is typically seen is tamponade. Because in cardiac timing ventricular events are used, the ventricular wall collapse is said to occur during ventricular diastole and the atrial wall collapse during ventricular systole [14].

Right atrial collapse: Right atrial collapse (Fig. 5.6, Panels a, b) is more sensitive but less specific than right ventricular collapse for the diagnosis of tamponade. When clinically significant, the right atrial collapse typically lasts at least 1/3 of ventricular systole; this finding was first described in 1983 on 2D transthoracic echocardiography [15].

Right ventricular collapse: Right ventricular collapse (Fig. 5.6, Panels c, d) is more specific but less sensitive than right atrial collapse for the diagnosis of pericardial effusion. Historically, this echocardiographic finding was described earlier than right atrial collapse. It was first reported in 1979 on M mode echocardiography [16] and then in 1982 on 2D transthoracic echocardiography [17].

Because right ventricular diastolic pressures are lowest at the onset of diastole, early diastolic collapse of the right ventricular free wall is an echocardiographic sign of tamponade physiology. The longer the duration of right ventricular collapse, the more pronounced tamponade physiology is.

Left heart collapse: Because the left ventricular wall is the thickest of all cardiac walls its invagination is not commonly seen in tamponade. Because only the distal portion of the left atrium is intrapericardial, it is only this portion that can be involved in tamponade-related collapse. When compression of the extrapericardial portions of the left atrium around the ostia of the pulmonary veins is seen, an alternative diagnosis should be considered.

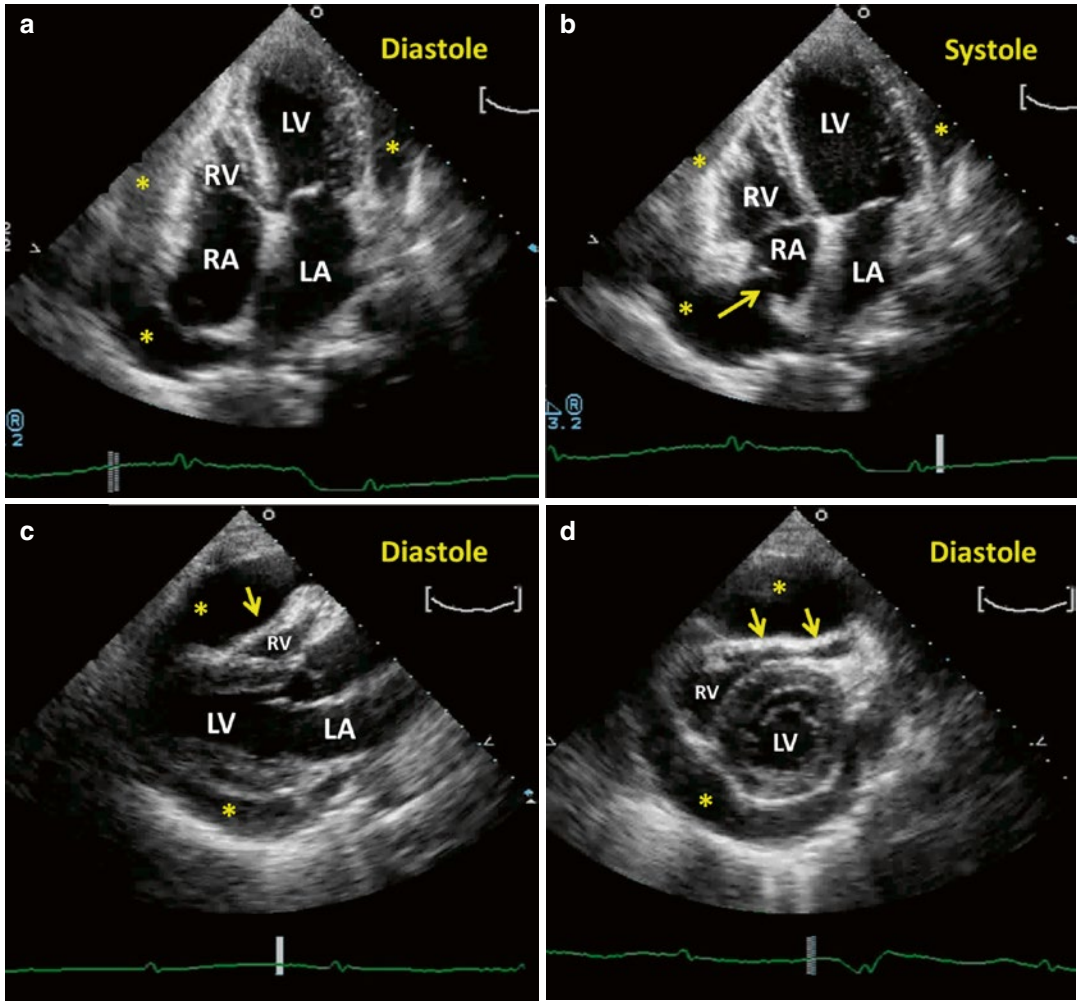


**Fig. 5.6** Tamponade: 2D echocardiographic findings. Transthoracic echocardiogram demonstrates tamponade physiology in a young woman with metastatic breast cancer and a large pericardial effusion (*asterisks*). Panels **a**, **b**: Apical 4-chamber views demonstrate right atrial physiology in tamponade. Characteristic bucking (collapse) of the right atrial free wall occurs during ventricular systole (Panel **b**) but not during ventricular diastole (Panel **a**). Note that the mitral and tricuspid valves are closed when right atrial buckling occurs. Panels **c, d**: Parasternal views demonstrate right ventricular physiology in tamponade. Characteristic buckling (collapse) of the right ventricular wall occurs during ventricular diastole. Note that the mitral valve is open when right ventricular buckling occurs. Abbreviations: *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

Respiratory variations: Changes in filling patterns that are phasic with respiration can be observed by both 2D and Doppler echocardiography. All modern ultrasound systems are capable of recording respiratory cycles (respirometry), typically by measuring chest impedance from existing EKG leads used during echocardiography. Alternatively, an add-on respirometer clipped to the nasal orifice and connected to the ultrasound system may be used. It is important to emphasize that respiratory variations described below refer to normal breathing (negative pressure ventilation) and cannot be applied when patients are intubated and mechanically ventilated (positive pressure).

On 2D, one observes the location of the interventricular septum relative to the respiratory

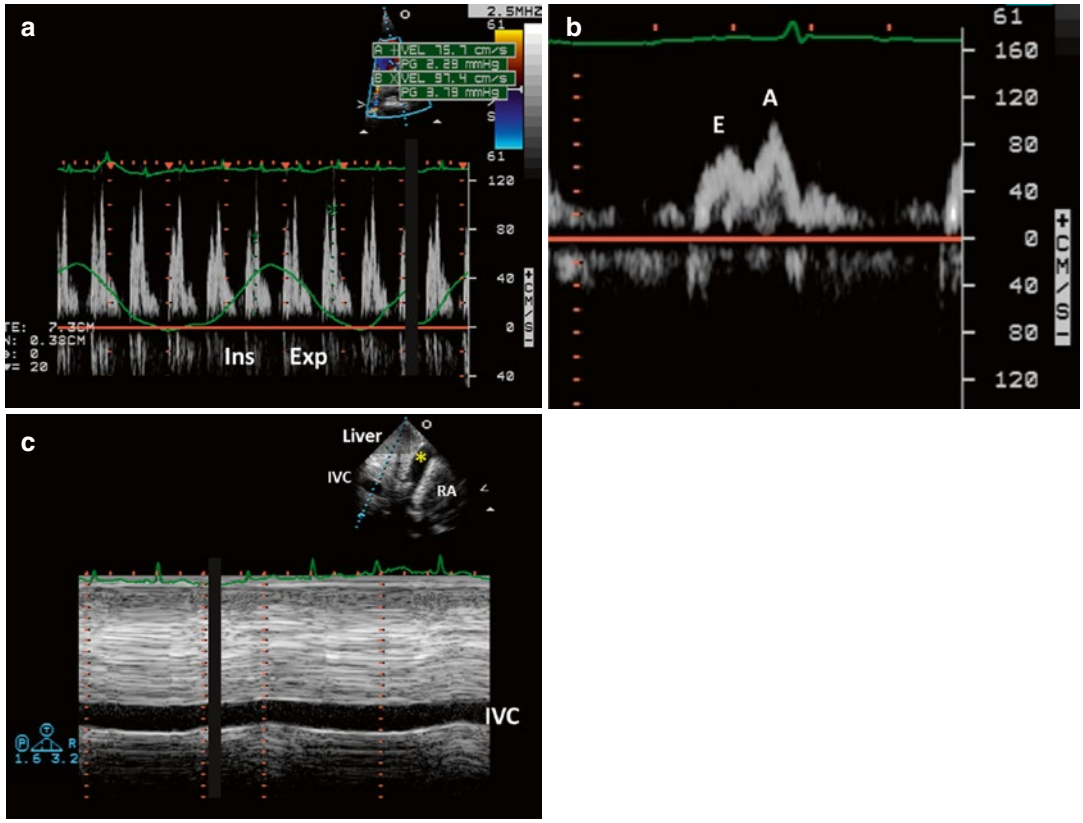


**Fig. 5.7** Tamponade: Doppler and M mode findings. Transthoracic echocardiogram demonstrates tamponade physiology in a young woman with metastatic breast cancer. Panel **a**: Mitral inflow – Spectral Doppler recordings at the level of mitral leaflet tips with simultaneous respirometry demonstrates marked respiratory variations in the peak velocity of the mitral E wave. Note that the E wave velocity is lower during inspiration (Ins) than during expiration (Exp). Panel **b**: Mitral inflow – Spectral Doppler tracings at faster sweep rate demonstrates morphology of individual mitral inflow flow velocity pattern. Note the abnormal relaxation filling pattern in this young woman; this is consistent with the diagnosis of tamponade as tamponade impedes early diastolic filling of the left ventricle. Panel **c**: Plethora of the inferior vena cava – M mode recording through the inferior vena cava (*IVC*) demonstrates an almost completer absence of respiratory variations in the IVC diameter; this is indicative of an elevated right atrial pressure in this patient with tamponade

cycle. In tamponade, there is a marked movement of the interventricular septum toward the left ventricle during inspiration. In contrast, the septum moves toward the right ventricle during expiration. Because respiratory rate is typically lower than the heart rate, this septal shift phasic with respiration does not occur with each cardiac beat.

Doppler recordings of mitral and tricuspid inflow, left ventricular outflow, as well as pulmonary and hepatic vein flow may be used to demonstrate respiratory variations in tamponade.

Mitral inflow: Flow velocity recording at the level of mitral valve may be obtained by either pulsed or continuous wave Doppler. Continuous wave Doppler is preferred when there is excessive translational movement of the heart in large pericardial effusions. On mitral inflow recordings one pays particular attention to the changes in the peak E wave velocity that are phasic with respiration (Fig. 5.7, Panel a) as well as to the overall mitral filling pattern of individual cardiac cycles. It tamponade, the peak E wave velocity is the lowest at the first inspiratory beat and the

highest at the first expiratory beat. The percent respiratory variation in the peak mitral E wave in calculated as follows:

$$\textit{Mitral Respiratory Variation} = \frac{E_{expiration} - E_{inspiration}}{E_{expiration}} * 100\,\%$$

Arbitrarily, a respiratory variation of >30 % is considered significant and consistent with tamponade physiology. It is important to emphasize that these respiratory variations are indicative of ventricular interdependence; thus they may be seen in both tamponade and constrictive pericarditis.

One common explanation for these respiratory variations in mitral inflow in based on the anatomic fact that pulmonary veins are outside the pericardial sac. In normal individuals, inspiration is mediated by a drop in intrathoracic pressure. This drop in pressure affects equally the pulmonary veins and the left heart; thus there is no net change in the pulmonary vein to left heart pressure gradient, and no significant change in peak E wave velocities.

In tamponade and constriction, there is still normal drop in pulmonary vein pressures during inspiration. However, there is no concomitant lowering of intracardiac pressures during inspiration because either pericardial fluid (in tamponade) or inelastic pericardium (in constriction) isolates the heart from the intrathoracic pressure changes. This results in a decreased pulmonary vein to left heart pressure gradient and lower E wave velocities during inspiration. Decreased filling of the left ventricle then facilitates the shift of the interventricular septum toward the left ventricle during inspiration.

In addition to respiratory variations in the peak velocity of the mitral E wave, one should also pay attention to the overall mitral filling pattern. In tamponade, the impediment to left ventricular filling occurs in early diastole. In constriction, on the other hand, the impediment is in late diastole. Consequently, tamponade (Fig. 5.7, Panel b) is characterized by an impaired relaxation filling pattern (prolonged isovolumic relaxation time, E/A <1 and prolonged deceleration time). In contrast, constriction is characterized by a restrictive filling pattern (short isovolumic relaxation time, E/A >2; short deceleration time, typically <150 ms).

Left ventricular outflow tract: Respiratory variations in peak LVOT velocities are also seen in conditions of ventricular interdependence including tamponade. Just as with mitral inflow recordings, the highest LVOT velocity is observed with the first expiratory beat and the lowest LVOT velocity with the first inspiratory beat. Although there are respiratory variations in LVOT velocities, no specific cutoff value is given in current guidelines.

Tricuspid Inflow: Respiratory variations in the tricuspid inflow are more pronounced and opposite of those in mitral inflow. The highest tricuspid E wave velocity typically occurs with the first inspiratory beat and the lowest with the first expiratory beat. The percent respiratory variation in the peak tricuspid E wave in calculated as follows:

$$\textit{Tricuspid Respiratory Variation} = \frac{E_{expiration} - E_{inspiration}}{E_{expiration}} * 100\,\%$$

Arbitrarily, a respiratory variation with an absolute value of >60 % is indicative of cardiac tamponade. Note that the above tricuspid respiratory variation formula results in negative numbers, while the mitral formula results in positive numbers.

Hepatic veins: A normal hepatic flow velocity pattern consists of two antegrade and two retrograde waves. The two antegrade waves are S (systolic) and D (diastolic) waves. Between S and D, there is a small ventricular retrograde (VR) wave. After the D wave and concomitant with the atrial contraction, there an atrial reversal wave (AR) wave. With inspiration, there is augmentation of both S and D waves.

In conditions of ventricular interdependence such as tamponade and constriction, there is a drop in systemic vein to right heart pressure which results in (1) diminished augmentation of antegrade waves during inspiration; D wave is especially affected and may disappear

completely in advanced tamponade; and (2) there is an enhancement of diastolic flow reversal that is most prominent on the first expiratory beat (expiratory flow reversal).

Right atrial pressure elevation: As cardiac compression by pericardial effusion progresses, there is a compensatory increase in all diastolic pressures in the heart (this is referred to as equalization of diastolic pressures on invasive intracardiac pressure recordings). Plethora of the inferior vena cava (IVC) is the primary echocardiographic manifestation of this phenomenon (Fig. 5.7, Panel c). In advanced tamponade, IVC is dilated (>2.1 cm) and collapses less than 50 % with inspiration; this is indicative of elevated right atrial pressure (≥15 mmHg).

### Differential Diagnosis

Differential diagnosis of tamponade includes other conditions with either chamber collapse or ventricular interdependence. Chamber collapse may be seen when there is extrinsic compression of a cardiac chamber by a surrounding structure (such as tumor or aortic aneurysm). Unlike tamponade, these extrinsic compressions occur throughout the cardiac cycles. Ventricular interdependence with respiratory variations is a feature of both tamponade and constriction. Pericardial effusion is present in tamponade but absent in pure constrictive pericarditis. Respiratory variations may also be seen in conditions of labored breathing such as pulmonary embolism, obesity and COPD. IVC plethora is a nonspecific finding and is observed in any condition that leads to right atrial pressure elevation (including right heart failure, constriction and significant tricuspid stenosis or regurgitation).

### Alternative Imaging

Echocardiography is the imaging modality of choice for the diagnosis of tamponade and for guidance of pericardiocentesis [18]. There is typically no role for either CT or CMR in the diagnosis of acute cardiac tamponade since echocardiography is usually the fastest way to diagnose tamponade and identify the need for prompt and potentially lifesaving pericardiocentesis.

## Acute Pericarditis

Acute pericarditis is an inflammatory disorder with numerous etiologies including infections (especially viral), connective tissue disorders and malignancies; it may be idiopathic or may occur after myocardial infarction, cardiac surgery and radiation therapy to the chest. Acute pericarditis is characterized by a combination of chest pain, abnormal auscultatory findings, EKG changes and pericardial effusion. Chest pain is positional and worsens with inspiration ('pleuritic' in nature). On auscultation, there is pericardial rub. EKG may demonstrate diffuse ST segment elevations and PR depressions (Fig. 5.8, Panel a).

### Echocardiography Indications

Patients with acute pericarditis are referred for echocardiography primarily because of chest pain.

### Echocardiography Findings

Primary echocardiographic finding of acute pericarditis is pericardial effusion which may vary from trace to large. There may be fibrin strands or other signs of organization in the pericardial space (Fig. 5.8, Panel b).

### Differential Diagnosis

Differential diagnosis of acute pericarditis is essentially the differential diagnosis of pericardial effusion.

### Alternative Imaging

CT and CMR may demonstrate not only the presence of pericardial effusion but they may also show active inflammation in thickened and noncalcified walls of the pericardium.

## Constrictive Pericarditis

Constrictive pericarditis (often simply referred to as constriction) is a form of chronic pericarditis that leads to impaired cardiac filling due progressive thickening and calcification of the pericardial wall. Worldwide, tuberculosis is the leading

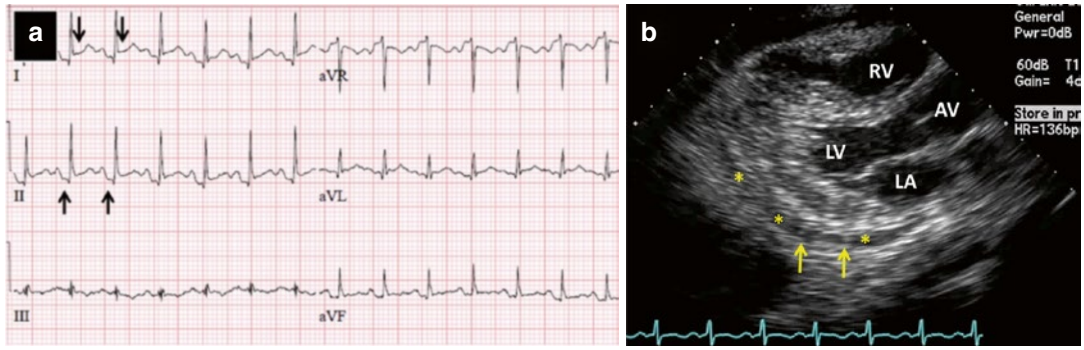


**Fig. 5.8** Acute pericarditis. Panel **a**: Electrocardiogram (EKG) of a patient with acute pericarditis demonstrates diffuse PR depressions and ST elevations (*arrows*). Panel **b**: Transthoracic echocardiogram in the parasternal long-axis view demonstrates a small pericardial effusion (*asterisks*) that contain fibrin strands (*arrows*). Abbreviations: *AV* aortic valve, *LA* left atrium, *LV* left ventricle, *RV* right ventricle

cause; however, in the developed countries most cases are either idiopathic or related to prior cardiac surgery. Like tamponade, constrictive pericarditis presents clinically as diastolic heart failure with predominance of signs and symptoms of right heart failure (clear lungs, hepatomegaly, ascites, and lower extremity edema).

With respect to concomitant presence of pericardial effusion, constrictive pericarditis may be either noneffusive or effusive. Noneffusive constrictive pericarditis is much more common; thus the terms 'constrictive pericarditis' and 'noneffusive constrictive pericarditis' are often used interchangeably.

## Noneffusive Constrictive Pericarditis

### Key Anatomic and Hemodynamic Features

Thickened and calcified pericardium with fusions between the visceral and parietal layers of the pericardium is the key anatomic features of constrictive pericarditis. Free walls of the ventricles which are adjacent to the abnormal pericardium are more constrained in their movement than the interventricular septum which anatomically is not covered by the pericardium.

Hemodynamically, in both tamponade and constrictive pericarditis the heart is constrained by the pericardium which then leads to ventricular interdependence and respiratory variations in cardiac flows. The major hemodynamic difference between tamponade and constrictive pericarditis is the mechanism and the timing of maximum pericardial constraint.

In tamponade the constraint is due to pericardial fluid, while in constrictive pericarditis is due to inelastic pericardium. In tamponade, the constraint is most prominent during early diastole leading to an abnormal relaxation filling pattern. In constrictive pericarditis, the impediment occurs during late diastole resulting in the so-called restrictive filling pattern. Both tamponade and constrictive pericarditis are characterized by intracardiac pressure elevations.

Another difference between the two is the presence or absence of chamber collapse. In tamponade, the effusion leads to chamber collapse while in constrictive pericarditis the inelastic pericardium does not.

### Echocardiography Indications

Patient with constrictive pericarditis are referred for echocardiography primarily because they presents with signs and symptoms of heart failure.

### Echocardiography Findings

The role of echocardiography is to demonstrate the cardinal anatomic and hemodynamic features of constrictive pericarditis: a thickened and calcified pericardium, ventricular interdependence

with respiratory variations in cardiac flows, the so-called restrictive mitral filling pattern, elevated right atrial pressure leading to inferior vena cava plethora, and regional differences in myocardial motion and deformation.

Pericardial thickness & calcifications: As previously noted, transthoracic echocardiography does not have sufficient image resolution to allow for reliable measurements of pericardial wall thickness. In contrast, transesophageal echocardiography may provide measurements of pericardial thickness that are comparable to reference techniques of CT and CMR.

Ventricular interdependence & Respiratory variations: Marked respiratory variations resulting from ventricular interdependence is a cardinal feature of constrictive pericarditis. As described above in the Tamponade section, ventricular interdependence and respiratory variations are not pathognomonic for constrictive pericarditis as they also occur in tamponade. Furthermore, respiratory variation may also occur in several conditions of labored breathing such as COPD, asthma, obesity and pulmonary embolism.

On M mode and 2D imaging, there is characteristic interventricular septal motion phasic with respiration (Fig. 5.9, Panels a, b). As described in details in the Tamponade section above, the interventricular septum moves

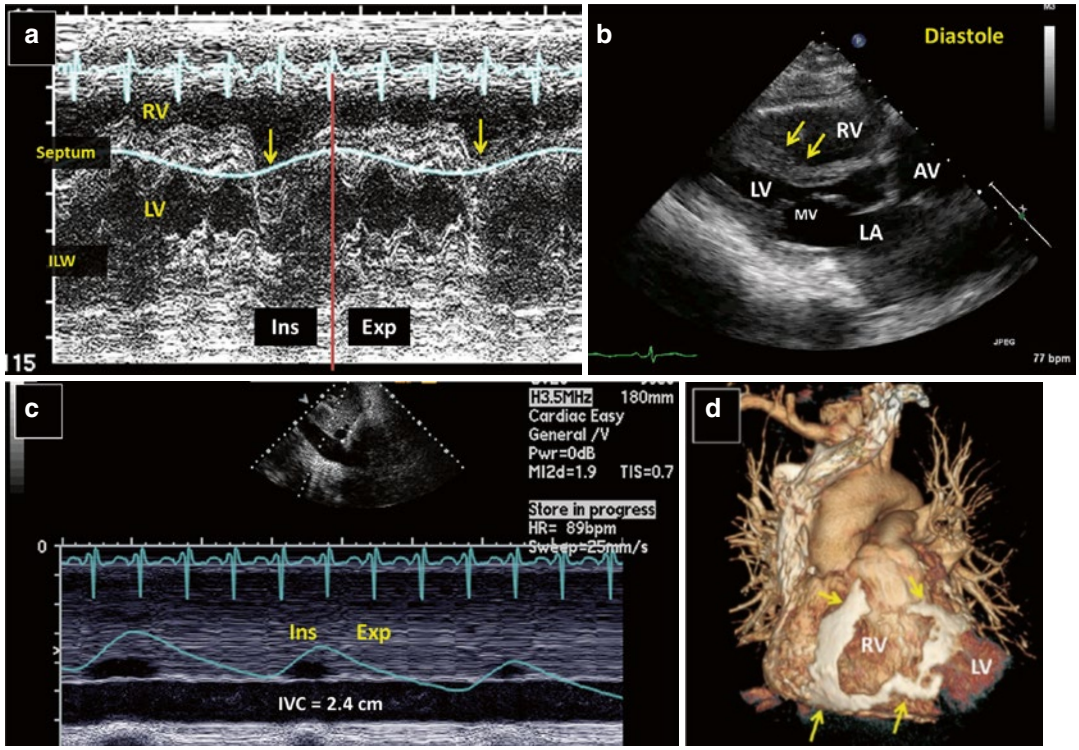


**Fig. 5.9** Constrictive pericarditis: echocardiographic & CT findings. Panel **a**: M mode recording in a patient with constrictive pericarditis demonstrates characteristic respiratory variations in the right and left ventricular chamber sizes due to abnormal interventricular septal motion phasic with respiration. Note that interventricular septum bounces (*arrow*) toward the left ventricle (*LV*) during inspiration (*Ins*) and toward the right ventricle (*RV*) during expiration (*Exp*). Panel **b**: Transthoracic echocardiogram in the parasternal long-axis view demonstrates characteristic diastolic septal bounce of the interventricular septum (*arrows*) toward the left ventricle during inspiration. Panel **c**: M mode recordings through a dilated inferior vena cava (*IVC*) demonstrate complete absence of respiratory variations in the IVC diameter; this is indicative of an elevated right atrial pressure and consistent with the diagnosis of constriction. Panel **d**: 3D CT rending of the heart demonstrates large area of pericardial calcifications (*arrows*) (Courtesy of Dr. Pierre Maldjian, Department of Radiology, University of Medicine and Dentistry, Newark, NJ). Abbreviations: *AV* aortic valve, *Exp* expiration, *ILW* inferolateral wall, *Ins* inspiration, *LA* left atrium, *LV* left ventricle, *MV* mitral valve, *RV* right ventricle

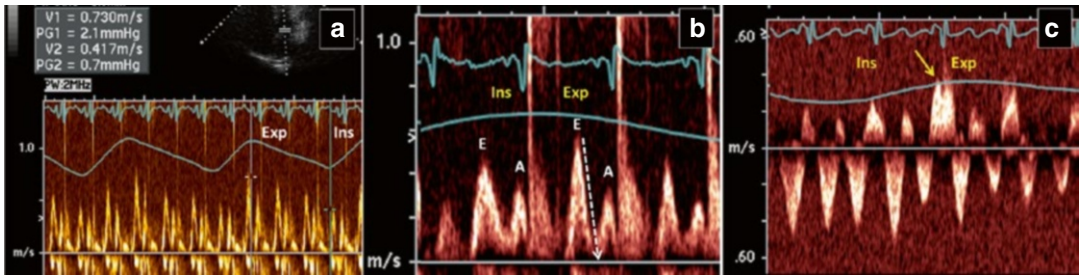


**Fig. 5.10** Constrictive pericarditis: Doppler findings. Panel **a**: Mitral inflow – Spectral Doppler recordings at the level of mitral leaflet tips with simultaneous respirometry demonstrates marked respiratory variations in the peak velocity of the mitral E wave. Note that the E wave velocity is lower during inspiration (*Ins*) beat than during expiration (*Exp*). Panel **b**: Mitral inflow – Spectral Doppler tracings at faster sweep rate demonstrates morphology of individual mitral inflow flow velocity pattern. Note the restrictive filling pattern (E/A >2; rapid E wave deceleration time (*arrow*)) as well as respiratory variations in the peak velocity of the mitral E wave which is higher during expiration (Exp) than during inspiration (Ins)). This is consistent with the diagnosis of constriction as constriction impedes preferentially the late diastolic filling of the left ventricle. Panel **c**: Hepatic vein spectral Doppler tracing demonstrates pronounced expiratory (Exp) flow reversal

toward the left ventricle during inspiration and toward the right ventricle during expiration. This then results in cyclical changes in the size of the two ventricles phasic with respiration (the right ventricle is largest and the left ventricle is the smallest at the first inspiratory beat; the opposite occurs in expiration).

On Doppler recordings, respiratory variations in the peak velocity of the E wave of at least 25 % at the level of the mitral valve and at least 40 % at the level of the tricuspid valve, and are consistent with the diagnosis of constrictive pericarditis (Fig. 5.10, Panel a).

Restrictive mitral filling pattern: In constrictive pericarditis, the overall mitral filling pattern is restrictive (short isovolumic relaxation time; E/A >2; short deceleration of the E wave [typically less than 150 ms]) as shown in Fig. 5.10, Panel b. The short deceleration time of the mitral E wave is the Doppler equivalent of the rapid *y* decent on central venous pressure recordings.

Inferior vena cava plethora: In both tamponade and constriction, there is a compensatory increase in all diastolic pressures in the heart (this is referred to as equalization of diastolic pressures on invasive intracardiac pressure recordings). Plethora of the inferior vena cava (IVC) is the primary echocardiographic manifestation of this phenomenon (Fig. 5.9, Panel c). In advanced constrictive pericarditis, IVC is dilated (>2.1 cm) and collapses less than 50 % with inspiration; this is indicative of elevated right atrial pressure (≥15 mmHg). IVC plethora is consistent with but not pathognomonic for constrictive pericarditis as it may occur whenever the right atrial pressure is elevated (such as tamponade, significant tricuspid stenosis or regurgitation and right heart failure).

Hepatic vein flow velocities: In constrictive pericarditis, there is enhancement of expiratory flow reversal in spectral Doppler tracings of hepatic vein flows (Fig. 5.10, Panel c).

Abnormal mitral annular velocities: In constrictive pericarditis, one pays attention to the ratio between the lateral and medial peak e′ velocities as well as to absolute mitral annular tissue e′ velocities.

Tissue Doppler e′ ratio (Annulus reversus): Normally, the peak velocity of the mitral annular tissue Doppler e′ wave is higher at the lateral compared to the medial (septal) annulus. In other words:

$$\text{Normal individual}: \text{Lateral } e' > \text{Medial } e'$$

In constrictive pericarditis, pericardial adhesions to the underlying myocardium typically lead to decreased mobility of the lateral annulus; this then leads to lowering of lateral e′ velocity below those of the medial e′. Since this is reversed from what is normally seen, the phenomenon is referred to as annulus reversus [19]:

Constrictive pericarditis : Lateral e′ < Medial e′
[Annulus reversus]

Absolut e′ velocities: It is important to note that despite lowering of lateral e′ velocities, both lateral and medical e′ velocity may still be within normal limits in constrictive pericarditis. This is in contrast to restrictive cardiomyopathy where mitral annular velocities are low.

Abnormal left ventricular strain: Normally, subendocardial fibers are primarily responsible for the left ventricular longitudinal strain, while subepicardial layers are primarily responsible for the circumferential strain. Given that pericardial adhesions in constrictive pericarditis lead to relative immobilization of epicardial layers of the left ventricle while leaving the subendocardial layers unaffected, the typical strain pattern of constrictive pericarditis consists of (1) diminished circumferential strain; and (2) preserved longitudinal strain. This is in contrast to restrictive cardiomyopathy where longitudinal strain is preferentially affected [20].

### Differential Diagnosis

Differential diagnosis of constrictive pericarditis includes tamponade, restrictive cardiomyopathy, other forms of respiratory variations in cardiac flows, and other causes of heart failure. Constrictive pericarditis shares marked respiratory variations with tamponade, obesity, pulmonary embolism, COPD and asthma. Lack of pericardial effusion differentiates noneffusive constrictive pericarditis from tamponade. Furthermore, constrictive pericarditis has a restrictive mitral filling pattern while tamponade has an abnormal relaxation pattern.

Restrictive cardiomyopathy typically does not demonstrate respiratory variations in mitral inflow. Furthermore, mitral annular tissue Doppler velocities are low in restrictive cardiomyopathy but normal in constrictive pericarditis. Unlike constrictive pericarditis, restrictive cardiomyopathy is not characterized by annulus reversus. The E/e′ ratio is typically elevated in restrictive cardiomyopathy (indicative of elevated left atrial pressure) but frequently normal in constrictive pericarditis. With respect to left ventricular strain, restrictive cardiomyopathy typically shows diminished longitudinal strain while constrictive pericarditis typically demonstrates diminished circumferential strain.

### Alternative Imaging

CT and CMR are the gold standard for measuring pericardial thickness. CT is the gold standard for detection of pericardial calcifications (Fig. 5.9, Panel d).

## Effusive Constrictive Pericarditis

Effusive constrictive pericarditis is a rare form of constrictive pericarditis in which there is presence of both pericardial effusion and increased pericardial thickness. The patient presents initially with pericardial effusion. After removal of pericardial fluid via pericardiocentesis or surgical drainage, the patient remains symptomatic and echocardiography demonstrates findings typical of constrictive physiology described above.

## Pericardial Tumors

Primary pericardial tumors are rare and typically benign. Most common benign tumors of the pericardium are lipomas, fibromas, hemangiomas, lymphangiomas and teratomas. Primary malignancies of the pericardium include mesothelioma and various forms of sarcoma.

Secondary tumors of the pericardium are much more common than the benign tumors; metastatic seeding of the pericardium may be seen with lymphomas and melanomas as well as with malignancies of the breast, lung, stomach or colon.

### Echocardiography Indications

Pericardial tumors may be an incidental finding or the patient may present with nonspecific symptoms such as chest pain, palpitations or shortness of breath.

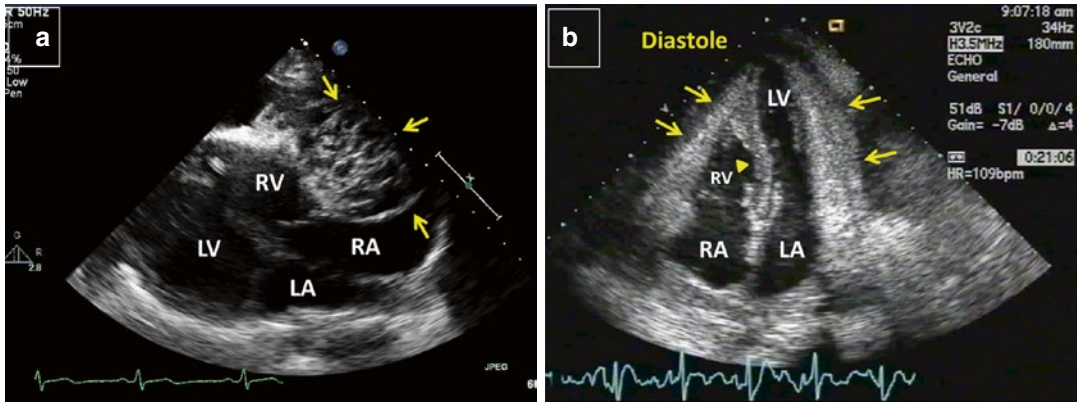


**Fig. 5.11** Pericardial tumors. Panel **a**: Benign lymphangiomas of the pericardium – Transthoracic echocardiogram in an off-axis parasternal view demonstrate a large cystic tumor (*arrows*). The findings are consistent with but not pathognomonic for lymphangiomas (Courtesy from Dr. Adam Skolnick , Division of Cardiology, New York University Langone Medical Center). Panel **b**: Malignant metastatic adenocarcinoma of the pericardium – Note the diffuse infiltration of the pericardium (*arrows*) by adenocarcinoma. This resulted in pericardial constriction as demonstrated by the diastolic interventricular septal bounce toward the left ventricle during inspiration. Abbreviations: *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

### Echocardiography Findings

Benign pericardial tumors typically present as circumscribed masses adherent to the pericardium. Lipomas and fibromas are typically solid in appearance while teratomas, hemangiomas and lymphangiomas may demonstrate cysts and septations (Fig. 5.11, Panel a).

Malignant pericardial tumors are often diffuse and typically present with pericardial effusion that demonstrates signs of organization. These tumors typically are confined to the pericardium and do not infiltrate the myocardium. Melanomas are a notable exception as they demonstrate widespread myocardial involvement.

Circumscribed pericardial tumors may cause extrinsic compression of surrounding cardiac chambers while diffuse tumors may lead to constrictive physiology (Fig. 5.11, Panel b) [21].

### Differential Diagnosis

Pericardial tumors need to be differentiated from other mediastinal masses; identification of points of mass attachment to the pericardium is an important clue that may differentiate pericardial from mediastinal tumors. Differential diagnosis of pericardial malignancies often includes pericardial effusion, tamponade and constrictive pericarditis.

### Alternative Imaging

CT and CMR provide incremental value in localization and tissue characterization of pericardial tumors.

## References

1. Maisch B, Seferović PM, Ristić AD, Erbel R, Rienmüller R, Adler Y, Tomkowski WZ, Thiene G, Yacoub MH, Task Force on the Diagnosis and Management of Pricardial Diseases of the European Society of Cardiology. Guidelines on the diagnosis and management of pericardial diseases executive summary; The Task force on the diagnosis and management of pericardial diseases of the European society of cardiology. Eur Heart J. 2004;25(7):587–610.
2. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, Hung J, Garcia MJ, Kronzon I, Oh JK, Rodriguez ER, Schaff HV, Schoenhagen P, Tan CD, White RD. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013;26(9):965–1012.e15. doi:10.1016/j.echo.2013.06.023.
3. Argulian E, Halpern DG, Aziz EF, Uretsky S, Chaudhry F, Herzog E. Novel "CHASER" pathway for the management of pericardial disease. Crit Pathw Cardiol. 2011;10(2):57–63.

4. Ling LH, Oh JK, Tei C, Click RL, Breen JF, Seward JB, Tajik AJ. Pericardial thickness measured with transesophageal echocardiography: feasibility and potential clinical usefulness. J Am Coll Cardiol. 1997;29(6):1317–23.
5. Baillie M. On the want of a pericardium in the human body. Tr Soc Improve Med Chir Knowl. 1793;1:91.
6. Columbus R. De re anatomica. Venice: Nicola Bevilacqua; 1559, page 265.
7. Southworth H, Stevenson CS. Congenital defects of the pericardium. Arch Intern Med. 1938;61:223–40.
8. Patel J, Park C, Michaels J, Rosen S, Kort S. Pericardial cyst: case reports and a literature review. Echocardiography. 2004;21:269–72.
9. Felner JM, Fleming WH, Franch RH. Echocardiographic identification of a pericardial cyst. Chest. 1975;68(3):386–7.
10. Hynes JK, Tajik AJ, Osborn MJ, Orszulak TA, Seward JB. Two-dimensional echocardiographic diagnosis of pericardial cyst. Mayo Clin Proc. 1983;58(1):60–3.
11. Horowitz MS, Schultz CS, Stinson EB, Harrison DC, Popp RL. Sensitivity and specificity of echocardiographic diagnosis of pericardial effusion. Circulation. 1974;50(2):239–47.
12. Eisenberg MJ, de Romeral LM, Heidenreich PA, Schiller NB, Evans Jr GT. The diagnosis of pericardial effusion and cardiac tamponade by 12-lead ECG. A technology assessment. Chest. 1996;110(2):318–24.
13. Bigger IA. Wounds of the heart and pericardium. South Med J. 1932;25(8):785–94.
14. Mercé J, Sagristà-Sauleda J, Permanyer-Miralda G, Evangelista A, Soler-Soler J. Correlation between clinical and Doppler echocardiographic findings in patients with moderate and large pericardial effusion: implications for the diagnosis of cardiac tamponade. Am Heart J. 1999;138(4 Pt 1):759–64.
15. Gillam LD, Guyer DE, Gibson TC, King ME, Marshall JE, Weyman AE. Hydrodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. Circulation. 1983;68(2):294–301.
16. Shiina A, Yaginuma T, Kondo K, Kawai N, Hosoda S. Echocardiographic evaluation of impending cardiac tamponade. J Cardiogr. 1979;9:555–63.
17. Armstrong WF, Schilt BF, Helper DJ, Dillon JC, Feigenbaum H. Diastolic collapse of the right ventricle with cardiac tamponade: an echocardiographic study. Circulation. 1982;65(7):1491–6.
18. Tsang TS, Enriquez-Sarano M, Freeman WK, Barnes ME, Sinak LJ, Gersh BJ, Bailey KR, Seward JB. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. Mayo Clin Proc. 2002;77(5):429–36.
19. Reuss CS, Wilansky SM, Lester SJ, Lusk JL, Grill DE, Oh JK, Tajik AJ. Using mitral 'annulus reversus' to diagnose constrictive pericarditis. Eur J Echocardiogr. 2009;10(3):372–5.
20. Sengupta PP, Krishnamoorthy VK, Abhayaratna WP, Korinek J, Belohlavek M, Sundt 3rd TM, Chandrasekaran K, Mookadam F, Seward JB, Tajik AJ, Khandheria BK. Disparate patterns of left ventricular mechanics differentiate constrictive pericarditis from restrictive cardiomyopathy. JACC Cardiovasc Imaging. 2008;1(1):29–38.
21. Anis A, Narayan RL, Kapa S, Klapholz M, Saric M. Metastatic signet ring adenocarcinoma: an unusual cause of cardiac constriction. Mt Sinai J Med. 2006;73(6):898–901.

## Echocardiography in Pericardial Disease-For Patients and their Families

Information regarding the echocardiographic exam in general as well as regarding the findings specific to individual disorders is provided below.

Echocardiogram: You doctor may order an echocardiogram to examine the heart and the envelope that surrounds the heart called the pericardium. Echocardiogram uses ultrasound wave to create an image of the heart. Ultrasound wave are similar to regular sound waves except that human ears cannot hear them. Ultrasound imaging has been performed for more than 50 years and diagnostic ultrasound waves have not been shown to cause any harm to humans.

Typical echocardiogram is called transthoracic echocardiogram, often abbreviated as TTE. During TTE you will be lying on a bed. A technologist or a physician will apply a small amount of nontoxic gel to your skin and then place a small probe to various points of your chest. The exam is not painful.

If TTE imaging is not sufficient, your doctor may order a different type of echocardiogram called transesophageal echocardiogram, often abbreviated as TEE. During a TEE, you will be lying on a bed. First you will be given medications through your veins; these medications will make you sleepy and will numb the pain. You will then be asked to swallow a small ultrasound camera mounted on a cable that is attached to the ultrasound machine. After swallowing, the camera will be placed into your food pipe (also called esophagus) and the stomach. Overall, TEE is considered a safe procedure and complications are unusual.

TTE and TEE may demonstrate a completely normal pericardium or may demonstrate one of the abnormal findings described below.

Congenital absence of the pericardium: Normally, the heart is surrounded by a protective envelope called pericardium. Very rarely, a person may be born without some or all parts of the pericardium. Doctors and other medical professionals call this condition 'congenital absence of the pericardium'. With this condition you may not feel anything unusual and the absent pericardium is often detected by chance, for instance on a pre-employment chest X ray or on an echocardiogram ordered for a different reason (heart murmur, for instance). Based on echocardiogram and other forms of heart imaging, your doctor will be able to tell you if any treatment is necessary.

Pericardial cyst: Echocardiogram may show that you were born with a pouch filled with clear fluid called pericardial cyst. It is located near the heart. This is a rare condition and often causes no harm. Occasionally, people who have a pericardial cyst may notice shortness of breath, chest pain or abnormal heartbeat. If your discomfort is significant, your doctor may consider referring you to a surgeon who may need to perform a surgery to remove the cyst.

Pericardial effusion: Normally there is no significant amount of fluid inside the pericardial sac, the space between the heart and the envelope of the heart called pericardium. When fluid accumulates inside the pericardial sac, doctors and other medical professionals refer to that fluid as pericardial effusion. There are many causes of pericardial effusion; medical professionals taking care of you will tell you what the most likely cause of your pericardial effusion is. Sometimes, if you have a pericardial effusion you may feel nothing unusual (doctors would say that your pericardial effusion is asymptomatic). In other instances, pericardial effusion may lead to shortness of breath, chest pain, rapid heartbeat and low blood pressure.

It is important that you consult your doctor when you are diagnosed with a pericardial effusion; although you may originally feel nothing unusual, pericardial effusion is some instances may lead to a more serious condition called tamponade.

Tamponade: Tamponade is a very serious condition in which the fluid around the heart called pericardial effusion (see above) interferes significantly with your heart function. In tamponade, you may feel your heart racing or your blood pressure may be low and you even may pass out. If you are diagnosed with tamponade, please take that finding very seriously as you may die

without prompt treatment. To treat tamponade, doctors may need to remove the pericardial fluid promptly from your chest. Fluid removal can be accomplished by placing a needle through the chest into the pericardial sac; this procedure is called pericardiocentesis. If pericardiocentesis is not successful, you may need to undergo chest surgery to create a hole in the pericardium; this is called a pericardial window procedure.

Acute pericarditis: After undergoing an echocardiogram you may be told that you might have pericarditis. This condition has many causes and in many instances it resolves with no lasting effects.

Constrictive pericarditis: Your echocardiogram may show that you have constrictive pericarditis. This condition develops over months or even years and leads to thickening and calcium deposits in the pericardium. You may have been referred for an echocardiogram because you experienced swelling of your legs, fatigue and shortness of breath. If your echocardiogram showed findings of constrictive pericarditis, you doctors may decide to wait and watch or they may refer you to surgeon who will consider surgical removal of diseased pericardium during an open heart surgery.

Pericardial tumor: Your echocardiogram may demonstrate a mass inside the envelope of the heart called the pericardium. Such a mass could be a benign tumor or may represent a malignancy. Sometimes your echocardiogram will show abnormal fluid around the heart called pericardial effusion. In other instances, the echocardiogram may show thickening of the pericardium called constrictive pericarditis. Pericardial effusion and constrictive pericarditis are described in more detail above.

# Cardiac Catheterization Evaluation of a Patient with Pericardial Disease

6

Brandon M. Jones and Samir R. Kapadia

## For Physicians and Other Healthcare Providers

### Introduction

Differentiating between pericardial constriction and restrictive myocardial disease can be extremely difficult, and the cardiac catheterization laboratory provides a number of powerful ways in which pericardial disease can be evaluated, or in which a suspected diagnosis can be confirmed. In fact, all cath lab operators should be well versed in the interpretation of invasive hemodynamic data. While a comprehensive constriction study involves several measurements that are made using simultaneous (duel-transducer) left and right heart catheters, it is equally important to be alert to the signs and symptoms of acute pericardial disease, which may be noticed during other, routine cath lab procedures. Cardiac tamponade can rarely but rapidly develop during different procedures in the catheterization laboratory like coronary artery perforation during a percutaneous intervention (PCI), right ventricular injury during a myocardial biopsy or pacing wire insertion, or an injury during transseptal catheterization or electrophysiology procedures like ablation or lead extraction. Failure to quickly make a diagnosis may potentially delay otherwise life saving interventions. Thus, this section will focus on the normal hemodynamic relationships of the heart and pericardium, the steps required to perform a dedicated study to differentiate pericardial constriction from restrictive myocardial disease, and the hemodynamic findings of acute cardiac tamponade.

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### Indications for Catheterization

The most common indication for diagnostic referral to the catheterization laboratory is to differentiate constrictive pericardial disease from restrictive myocardial disease. In the process, it is also possible to exclude other conditions that may enter into the differential diagnosis of such patients, including coronary artery disease, pulmonary arterial hypertension, or congestive heart failure. Some patients may come to the cath lab with a suspected diagnosis of pericardial disease based on other imaging modalities such as echocardiography or MRI, but require confirmatory data before deciding on an open-chest, pericardial stripping procedure. Others simply require coronary angiography to exclude the need for concurrent coronary artery bypass grafting (CABG) during surgery.

Patients will also be referred to the cardiac catheterization laboratory for the management of acute cardiac tamponade. Although each medical center will have its own procedures in place

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for performing pericardiocentesis, in many centers this is a procedure that is done primarily in the cardiac catheterization lab (please see section on management of pericardial effusion and tamponade). It is important to recognize that cardiac tamponade is a clinical diagnosis that can be confirmed by echocardiography or right heart catheterization. Echocardiography is primarily used in most situations except in patients decompensating fast in the cardiac catheterization laboratory with suspected tamponade, where right heart catheterization can be very useful for making a quick diagnosis.

## Contraindications

There are several relative contraindications to cardiac catheterization. Most importantly, as a general rule, patients with correctible medical conditions should be stabilized prior to any elective procedure. Coagulopathies or platelet disorders should be corrected, and anti-coagulant medications should be discontinued at an appropriate interval prior to the procedure. There are no firm guidelines for anticoagulation management during elective catheterization procedures, and bleeding complications will vary based on body habitus and vascular access strategy. In general, an INR <1.8 and platelet count >50,000 are often used as minimum, safe values. Radial access for the artery and brachial or even femoral access for the veins can be safely performed in therapeutically anticoagulated patients. In elective patients with no contraindication to stopping anticoagulation, warfarin is usually discontinued 3–5 days prior to the procedure. Heparin infusions should be discontinued >2 h prior to the procedure. The newer, oral, direct thrombin inhibitors (dabigatran, rivaroxaban, apixaban) should be discontinued at least 48 h prior to the procedure, but there is limited experience with these agents and some would consider a longer drug free interval.

Impaired renal function and contrast allergies must be considered if coronary angiography is planned, although a full hemodynamic study can be completed without contrast dye. Various protocols for pre-procedural hydration or contrast allergy pre-medication can be employed. Many studies have evaluated strategies for minimizing the risk of contrast-induced nephropathy in patients who are thought to be at risk. These include using iso-osmotic contrast agents, prehydration with saline or sodium bicarbonate, or administration of N-acetylcystine prior to the procedure [1,2]. Much of the data surrounding this topic has been controversial, and is beyond the scope of this chapter, but in general we feel that minimizing the use of contrast along with appropriate peri-procedural hydration are the most effective ways to limit injury [3].

## Prior to Catheterization

A careful history should be obtained with special attention to conditions that may impact the ability to perform the procedure safely, including respiratory problems such as COPD, inability to lay flat due to orthopnea, and detailed review of allergies and current medications.

A physical exam should include cardiopulmonary evaluation to exclude decompensated heart failure, and a careful study of the vascular structures. The femoral pulses should be palpated and auscultated for bruits, and distal pulses should be documented. If the radial artery approach is considered, the Allen's test or Barbeau test should be completed to confirm adequate collateral circulation from the ulnar artery [4]. A brief airway inspection can identify patients at risk for difficult intubation in case of respiratory emergencies, and in some cases should prompt more careful preparation.

Routine pre-procedural testing should include creatinine, hemoglobin, platelet count, and in patients with history of bleeding or on anticoagulant medications, a PTT and/or INR. A 12-lead EKG should be completed recently enough to be an adequate comparison in the case of suspected ischemic or arrhythmic complications during the procedure. Special attention should be paid to bundle branch blocks as a patient with a LBBB could develop complete heart block if the right bundle becomes irritated by the

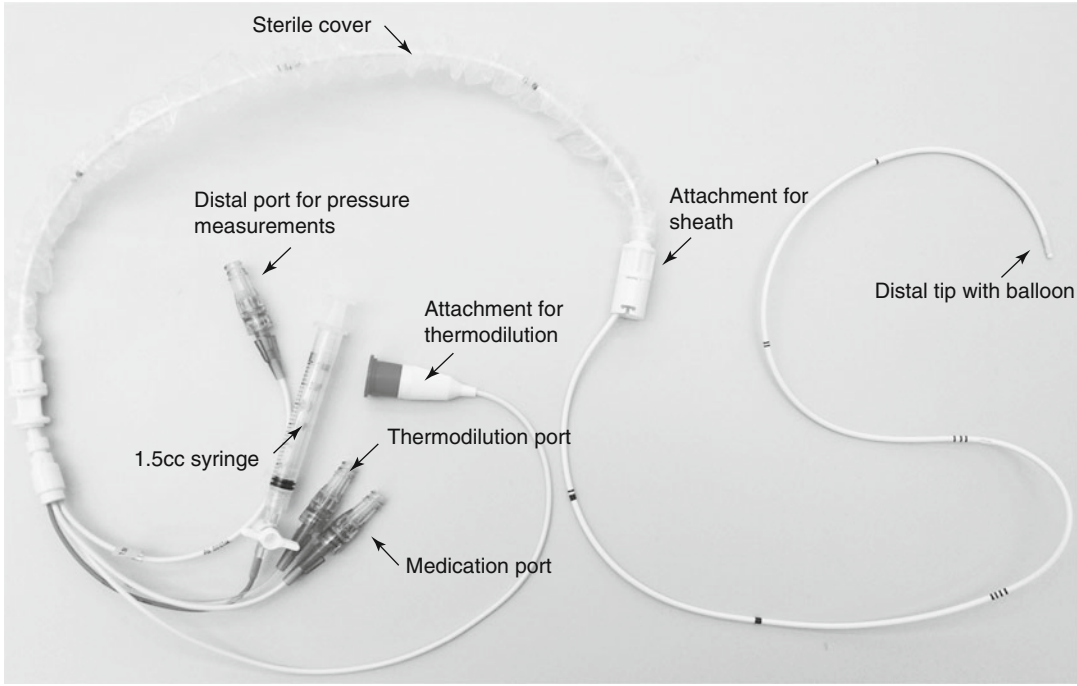


**Fig. 6.1** Pulmonary artery or "Swan-Ganz" catheter

pulmonary artery catheter. Conversely, given the fact that there is an anterior and posterior branch of the left bundle, the LV catheter is less likely to induce complete heart block in a patient with pre-existing RBBB.

Informed consent should be obtained in all patients before administration of procedural sedation. This should include a discussion of the purpose of the study, what the patient should expect, methods used for ensuring patient safety and comfort, and the potential risks of the procedure.

## Hemodynamic Assessment by Right Heart Catheterization

A right heart catheterization is completed with a balloon tipped catheter termed a pulmonary artery catheter or a "Swan-Ganz" catheter [5]. The catheter has multiple lumens and ports. The distal port is used to connect to a pressure transducer and obtain hemodynamic waveforms. Proximal ports are used for administration of medications, or for injection of cold saline as is used to measure cardiac output by the thermodilution technique (Fig. 6.1).

Once venous access is obtained, the catheter is advanced with the balloon inflated to the right atrium, then the right ventricle, the pulmonary artery, and finally into a pulmonary capillary wedge position. Advancing the catheter can be done under fluoroscopy, or by simply watching the pressure tracings as they transition from each chamber of the heart until an appropriate wedge tracing is identified. Pulmonary artery catheters are frequently placed in ICU settings where fluoroscopy equipment is not available, but fluoroscopy can be especially helpful in situations where the cardiac anatomy or valvular pathology make passage of the catheter into the pulmonary artery difficult, such as is frequently the case with severe tricuspid regurgitation. The careful use of a guidewire (0.018–0.025 in.) under fluoroscopy is sometimes needed to augment stiffness and achieve correct placement of the catheter in the pulmonary artery.

As the catheter passes first into the right atrium, a normal pressure waveform should be identified (Fig. 6.2). The a-wave represents atrial contraction, followed by the x-descent as the atrium relaxes. The c-wave represents the period of brief, isovolumetric contraction of the right ventricle where the tricuspid valve briefly bows upward under RV systolic pressures, prior to the opening of the pulmonic valve, at which point the RV empties and the tricuspid pulls away from the RA allowing the x-decent to continue. The v-wave represents venous return to the RA as the pressure gradually rises. Finally, the y-decent represents passive filling of the RV due to opening of the tricuspid valve, just prior to atrial contraction. The easiest way to correctly identify the a-wave is to note that it occurs slightly after the p-wave on the EKG.

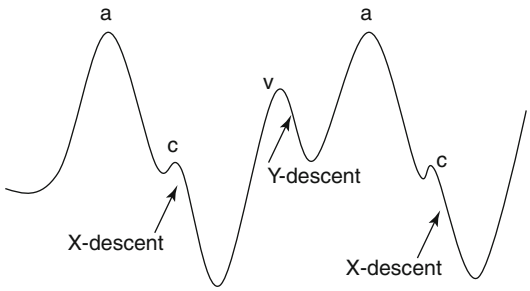


**Fig. 6.2** Normal right atrial pressure

As the catheter passes into the RV, an obvious change in the pressure tracing will be noted as systolic pressures rise (Fig. 6.3). RV end-diastolic pressure should closely approximate the mean RA pressure, and should be measured at the end of diastole, just prior to isovolumetric contraction.

Just like the pressure waveform that is measured in the systemic arterial circulation, the pulmonary artery waveform will have a rise in pressure during systole, followed by a gradual decrease in pressure during diastole (Fig. 6.4). Systolic pressure should closely approximate RV systolic pressure. A dicrotic notch during diastole occurs at the time of closure of the pulmonic valve, and interrupts the otherwise smooth descent of the pressure tracing. This is analogous to the dicrotic notch seen in an arterial line tracing due to closure of the aortic valve.

Once the balloon passes distally enough in the pulmonary artery to completely occlude the vessel, the pressure transducer will no longer be able to measure the normal pulmonary artery pressures waveforms behind it. At this point, a continuous column of blood exists between the tip of the catheter, through the pulmonary capillaries, and all the way through the pulmonary veins. Thus, once in correct wedge position, the hemodynamic tracing will approximately transduce the pressure waveform of the left atrium. Understanding this phenomenon will help one to troubleshoot when the waveform does not appear

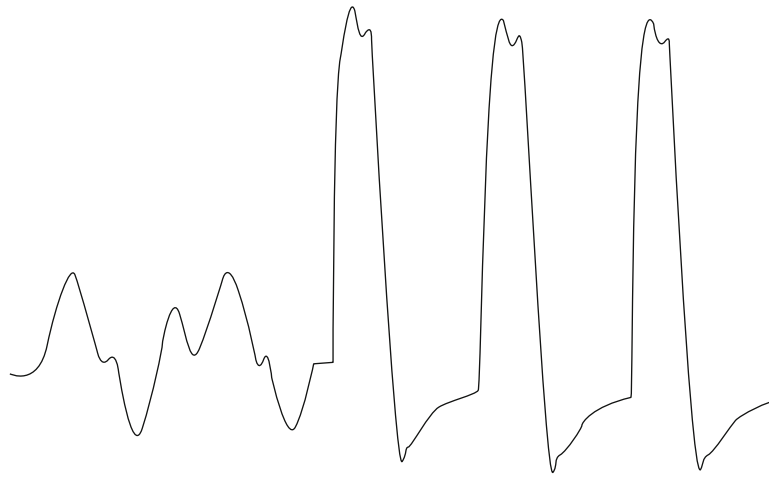

**Fig. 6.3** Normal right atrial to right ventricular pressure

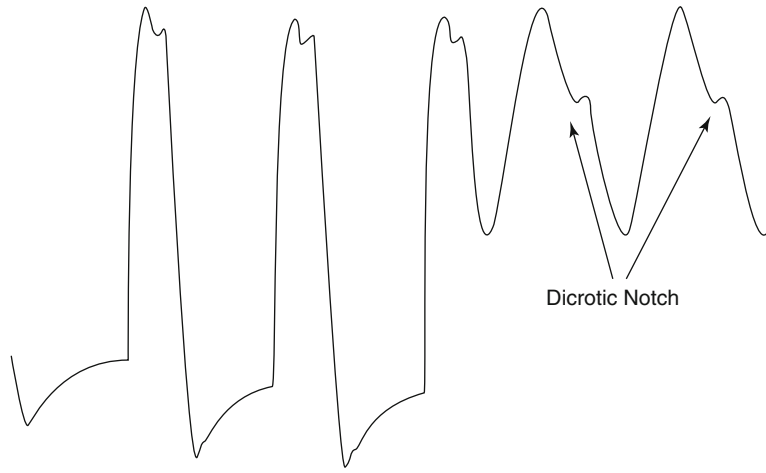


**Fig. 6.4** Normal right ventricular to pulmonary arterial pressure

as would be expected. One common mistake is made when the catheter is incompletely in a fixed position, and the tracing represents partial wedge and partial pulmonary artery pressures. When this happens, it can be helpful to wedge the catheter under fluoroscopy, as the normal systolic and diastolic movement of the balloon will terminate, and the balloon will hold its position when correctly wedged. Another way to confirm that the catheter is in a correct position (although it is very rarely required) is by the very slow and careful drawing back of blood from a wedged catheter. Checking the oxygen saturation of this blood should reveal a normal arterial concentration (as it is drawn back across the capillaries from the pulmonary veins). Pressure tracings of the left atrium will appear similar to that of the right atrium, other than being somewhat higher. A PCWP tracing will differ somewhat from a directly measured left atrial pressure due to the column of fluid that separates the two, and this often leads to dampening of the waveform and a larger delay between events seen on the EKG and events measured on the pressure waveform (i.e. the delay between the p-wave and a-wave will be shorter on the RA tracing and longer on the PCWP tracing).

Given that all of the measurements made during a right and left heart catheterization are done within the thoracic cavity, it is important to remember the normal relationship between intra-thoracic pressures and the respiratory cycle. Frequently, the pressure tracings will rise and fall by a substantial amount during the respiratory cycle, and it is often confusing to decide the correct point to make measurements. The key is to understand that pressures in the thoracic cavity always return to "normal" at the end of expiration. In a person breathing independently, inspiration causes a small amount of negative pressure within the thoracic cavity, and this returns to normal during expiration. In a patient on a positive pressure ventilator though, the opposite will occur, and the pressure will rise as air is forced into the lungs during inspiration, and return to normal during expiration. Thus, measurements should always be taken at the end of expiration, which is the point at which the pressure in the lungs is equal to the pressure in the atmosphere, and is also referred to as the Functional Reserve Capacity (FRC) of the lungs. In patients who are on ventilators with substantial positive end expiratory pressure (PEEP), the measured pressure at end-expiration may slightly over-estimate the patient's normal physiologic pressures.

## Hemodynamic Assessment by Left Heart Catheterization

Routine pressure measurements can also be made in the arterial circulation and in the left ventricle.

Systemic arterial blood pressure can be measured peripherally at the site of an arterial sheath or a dedicated arterial line. Pressure can also be measured at the tip of the cardiac catheter as it is placed in the aorta. There are several techniques for crossing the aortic valve with a catheter, but for the purpose of a dedicated hemodynamic study, a pigtail catheter will give the most accurate data.

Using a 0.035 in J-wire, the pigtail catheter is advanced to the aortic valve level. Using a 30° RAO projection, the pigtail should be oriented so that it forms a "6" and faces the aortic valve. From this position, the J-wire should be placed just inside the distal orifice of the catheter, and the catheter advanced. At this point, the catheter may fall easily into the ventricle. More commonly though, the catheter bends upwards until it forms a "9" in the ascending aorta. At this time, slowly withdrawing the catheter may allow it to fall forward through the open valve during systole. In some cases, the catheter may prolapse into the ventricle but the pigtail portion remains above the valve. This can usually be corrected by pushing the J-wire forward briefly, which will stiffen the distal portion of the catheter and advance it. Crossing a stenotic or prosthetic valve will provide additional challenges that may require different catheters and wires, but once successfully inside the left ventricle, a pigtail can typically be placed over an exchange-length wire. Crossing a mechanical valve is rarely attempted.

## Normal Pericardial Physiology

In a normal heart the pericardium is relatively non-compliant, and functions to prevent distention of the ventricles, and to couple the ventricles throughout the cardiac cycle. Normally, inspiration leads to a decrease in intra-thoracic pressure, which in turn leads to a decrease in the pressures in the cardiac chambers. Given that the majority of the systemic venous system remains outside the thorax, this leads to a corresponding increase in pressure difference between the vena cavae and the right atrium, and blood return to the heart is augmented. The same is not true for the blood return to the left atrium however as the pulmonary veins are located within the thoracic cavity, so left sided filling remains fairly stable throughout the respiratory cycle. The right ventricle is very compliant, so the increase in volume does not affect the reduction in pressure that is experienced during inspiration, but it does cause the septum to bow slightly toward the LV, causing a small reduction in LV filling and systolic pressure. This normal phenomenon is called a pulsus. Under normal conditions, the effect is small though, and the difference between the highest and lowest recorded systolic pressure over several respiratory cycles should be less than 12 mmHg. Thus, a normal patient will experience a slight decrease in right atrial pressure during inspiration, and the RV and LV pressures should move in concert with each other, demonstrating a slight reduction during inspiration, and rise with expiration.

## Hemodynamic Findings of Pericardial Constriction

Many of the hemodynamic findings of pericardial constriction are similar to those found in cardiac tamponade and/or restrictive myocardial disease, so it is important to understand where the differences can be noted. The following section will focus mainly on the hemodynamic changes that are characteristic of pericardial constriction, but will also describe which findings are similar to or different from those seen in other disease processes.

As the pulmonary artery catheter is floated towards the right atrium, the pressure tracing will demonstrate elevated pressures. In the case of cardiac tamponade, external compression of the right ventricle will lead to blunting of the y-descent, as the right atrium is unable to empty quickly during tricuspid valve opening. In severe or late tamponade, there may be loss of normal RA waveforms entirely. This is distinct from the pattern seen in constrictive pericardial disease, characterized by an underfilled RV and a non-compliant atrium, leading

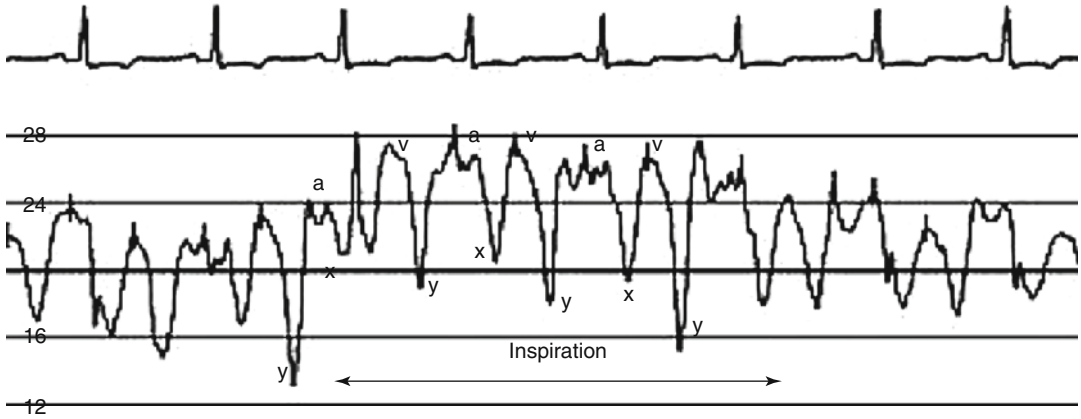


**Fig. 6.5** RA Tracing in a patient with pericardial constriction demonstrating a steep y-descent and a positive Kussmaul's sign

to a steep y-decent as the atrium rapidly empties into the RV. Also in constriction, a Kussmaul's sign can be seen, where there is a paradoxical increase in RA pressure and JVP with inspiration. Engorged abdominal veins empty into the right atrium due to increased abdominal pressure during inspiration, but the constricted heart is unable to accommodate the increase in volume, which results in elevated pressures. This phenomenon is not specific for constriction and may be seen in cases of RV hypertrophy or failure, but is not present in the majority of patients with cardiac tamponade where abdominal veins are not chronically engorged. In general, the hemodynamic findings of restrictive heart disease as measured in the right atrium will be indistinguishable from those of pericardial constriction (Fig. 6.5).

Next, pass the catheter into the RV. In patients with pericardial constriction, there is early rise of the diastolic pressure as the constricted ventricle quickly fills, then a plateau, followed by a normal, sharp rise during systole. This pattern is often referred to as a "square-root sign" because diastole resembles the mathematic symbol ($\surd$) for the square root. Also, the RV-end diastolic pressure (mmHg) is usually more than one third of the RV-systolic pressure in the setting of constriction. Tamponade will present with RV diastolic pressures that are elevated, closely approximate the RA and PA diastolic pressures, and the RV pulse pressure may be reduced due to depressed cardiac output. The hemodynamic findings of restrictive heart disease are indistinguishable from constriction in the right ventricle. In general, any condition that leads to impaired diastolic filling of the right ventricle can present with a "square-root" sign (Fig. 6.6).

A pulmonary artery and pulmonary capillary wedge pressure should be measured in order to have a complete hemodynamic study. In tamponade, there can be equalization of diastolic pressures across all chambers of the heart, so RA, RV diastolic, PA diastolic, and wedge pressures may all be nearly equal.

The cardiac output and index should be measured while the catheter is in the pulmonary artery. It is important to verify that the cardiac output and index are normal prior to a study to evaluate for pericardial constriction because low output states may interfere with the study. Cardiac output and index may be measured by thermodilution or by the Fick formula for calculating cardiac output:

$$\text{Cardiac Output}\left(\text{ml}/\text{min}\right) = \frac{\text{Oxygen consumption}\left(\text{VO2}\right)}{\text{AVO2 difference}}$$

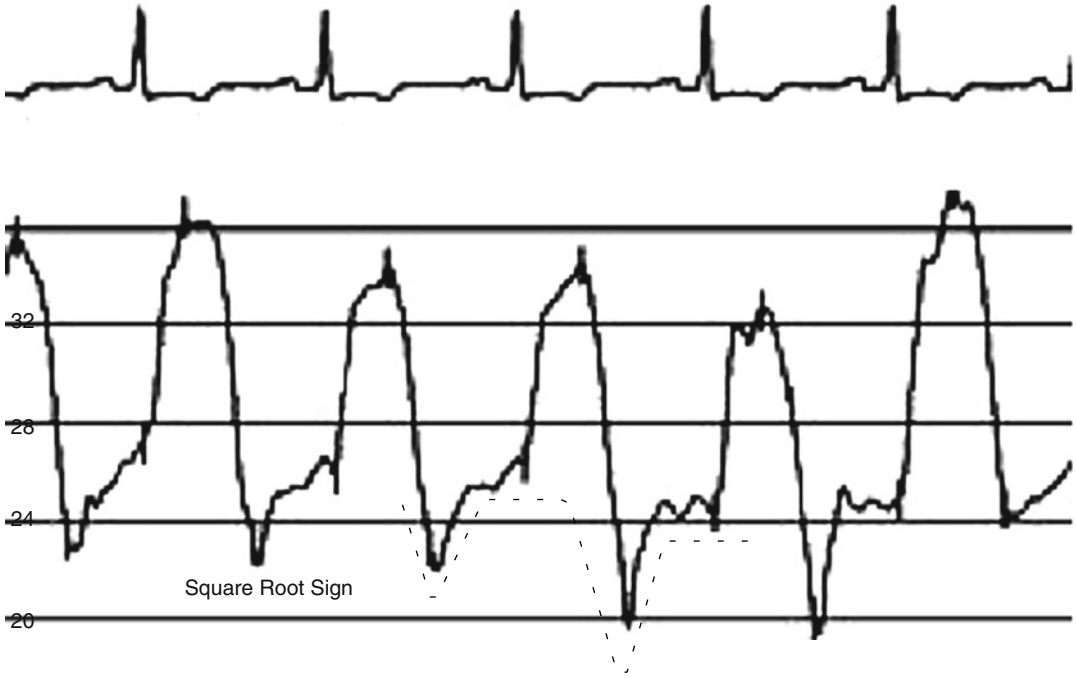


**Fig. 6.6** RV Tracing in a patient with pericardial constriction showing the characteristic dip-and-plateau or "square-root" sign

An accurate Fick calculation requires an accurate measurement of oxygen consumption (VO2), which can be completed in many catheterization laboratories using a metabolic or respiratory analyzer. If a measured VO2 is not available, it can be estimated, but this can result in substantial error. Some of the most simplified methods for estimating VO2 include using the patient's weight in kg and multiplying by 3, or taking the BMI and multiplying by 125 to give a value that is reported in mL O2/min. The AV O2 difference is the oxygen content in arterial blood (mL O2/mL blood) minus the oxygen content in the pulmonary artery. As most of the oxygen content is bound to hemoglobin, the full formula for AV O2 difference can be simplified, resulting in the following, simplified calculation:

$$\text{Cardiac Output (L/min)} = \frac{\text{VO2}}{\left(\begin{pmatrix}\text{Arterial O2 sat}\\ -\text{PA O2 sat}\end{pmatrix} \times \text{Hgb}\left(\text{g/dl}\right) \times 13.4\right)}$$

$$\text{Cardiac Index}\left(\text{L/min/m}^2\right) = \frac{\text{Cardiac Output}\left(\text{L/min}\right)}{\text{BSA}\left(\text{m}^2\right)}$$

Once the basic right heart measurements have been made, advance the pigtail catheter into the left ventricle, and bring the swan-ganz catheter back into the right ventricle. At this time, both catheters should be carefully flushed with normal saline, and each should be connected to a separate and dedicated pressure transducer. Be careful to re-zero both catheters before making any measurements. The first finding that will be noted is that there is elevation and equalization of the LV and RV end-diastolic pressures, which can be seen in constriction, restriction, or tamponade. To best appreciate this, put pressure waveforms on 40-scale and focus on diastolic pressures (Fig. 6.7).

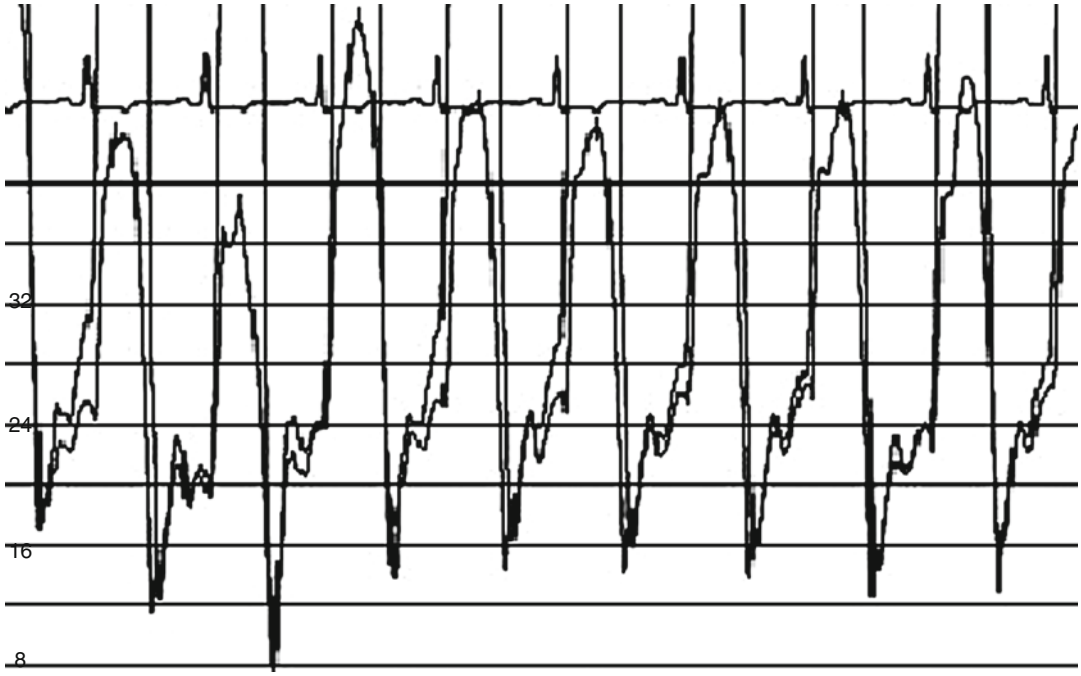


**Fig. 6.7** Simultaneous LV and RV tracings in a patient with pericardial constriction showing elevation and equalization of LV and RV end-diastolic pressure

Ventricular interdependence is the cardinal feature of pericardial constriction that differentiates it from restrictive myocardial disease. This is the phenomenon by which inspiration leads to paradoxically elevated RV systolic pressures with a simultaneous decrease in LV systolic pressures. Thus, to distinguish between constrictive and restrictive disease, the pressure scale should be changed to include the entire systolic waveform (usually 100- or 200-scale), and several respiratory cycles will be measured to determine ventricular interdependence based on calculating the Systolic Area Index (SAI) as described by Dr. Nishimura and colleagues (Mayo Clinic, Rochester MN) [6]. Per Dr. Nishimura's protocol, patients need to be in a regular rhythm, and patients in atrial fib require overdrive ventricular pacing for an accurate study. Patients with RA pressures <15 mmHg were given 1 L normal saline so as not to miss ventricular interdependence due to inadequate filling of the right ventricle. At this point, several waveforms were recorded during exaggerated respiration. It should be noted that PVC's are not uncommon due to catheter irritation of the ventricle, and respiratory cycles should only be sampled if they are free of premature beats. An example of one such tracing follows (Fig. 6.8):

Note that the first arrow represents the highest LVEDP during expiration and the subsequent beat is thus selected. The second arrow represents the lowest LVEDP during inspiration and the subsequent beat is thus selected. Visually, in this case, it seems quite obvious that the area under the curve (AUC) for the RV pressure tracing (lightly shaded) increases substantially during inspiration, and this correlates with the increased RV volume and pressure that is seen in patients with pericardial constriction during inspiration. Similarly, it is visibly obvious that the LV volume and pressure as represented by the darkly shaded AUC decreases substantially during this same inspiratory cycle. Thus, it would be concluded that the patient has clear signs of ventricular interdependence consistent with constriction.

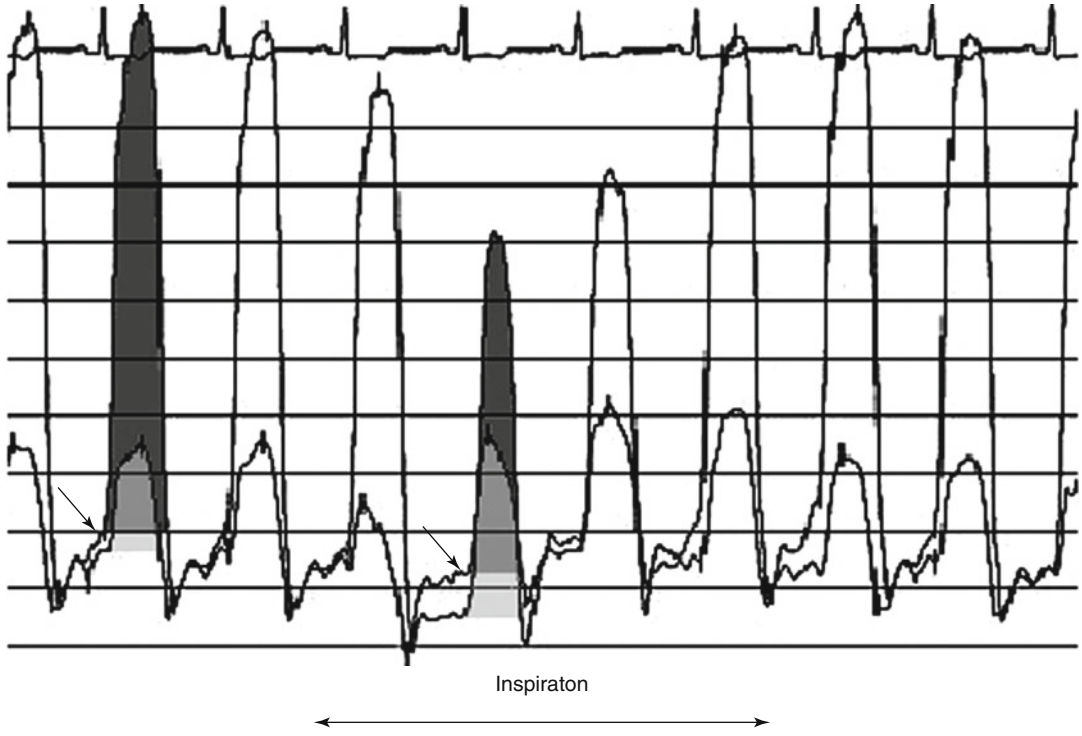


**Fig. 6.8** Calculation of the systolic area index

Rarely however is the result as obvious as this example, and thus, computer software can be used to calculate the systolic area index by the following formula.

$$\text{SAI} = \begin{pmatrix} \text{Inspiratory} \\ \text{RV AUC} \\ /\text{LV AUC} \end{pmatrix} / \begin{pmatrix} \text{Expiratory} \\ \text{RV AUC} \\ /\text{LV AUC} \end{pmatrix}$$

A positive study for constriction is one in which the calculated SAI ratio is greater than 1.1 as averaged over at least three high fidelity tracings. The example above yielded a calculated SAI of 2.08 and is highly consistent with pericardial constriction. Dr. Nishimura and his colleagues reported a 97 % sensitivity and 100 % predictive accuracy of their technique in correctly identifying constrictive pericarditis vs. restrictive myocardial disease using the systolic area index.

## Hemodynamic Findings Specific to Tamponade

Several changes will occur when the heart becomes constrained by an acute, hemodynamically significant pericardial effusion. The most obvious initial changes can also be noted on clinical exam, and include elevation of right sided pressures (jugular vein distention), tachycardia, and hypotension. In addition to hypotension, the arterial pulse pressure (difference between systolic and diastolic pressure) may narrow as the stroke volume decreases. A right heart catheterization will demonstrate elevation and equalization of end diastolic pressures across chambers of the heart reflecting the transmission of intrapericardial pressures.

The most characteristic hemodynamic finding of cardiac tamponade is the exaggerated inspi-

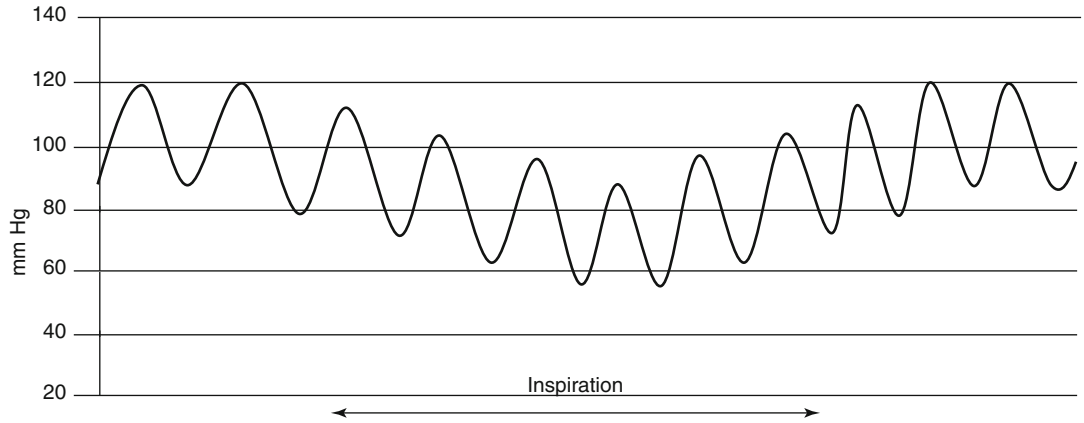


**Fig. 6.9** Pulsus paradoxus, as could be seen in cardiac tamponade

ratory pulsus. Although better known for the sign that bears his name, this phenomenon was first described by Adolf Kussmaul, who noticed "Diminution or complete absence of the radial pulse during inspiration." It was felt to be a paradox because heart sounds could still be auscultated despite the loss of a radial pulse, and hence Kussmaul termed this the "pulsus paradoxus." The finding of a pulsus paradoxus can be challenging to confirm with only a stethoscope and blood pressure cuff, but is very easy to assess with a continuous arterial waveform. Observe the arterial line tracing through several normal respiratory cycles. The difference between the highest systolic pressure (seen during expiration) and the lowest systolic pressure (seen during inspiration) is the "pulsus," and values >12 mmHg are considered positive. A pulsus paradoxus is not specific for tamponade, and can sometimes be observed in constrictive disease (~50 % of patients), emphysema, bronchial asthma, hypovolemic shock, pulmonary embolism, pregnancy, or severe obesity. Other conditions may cause the pulsus to be absent such as severe LV dysfunction, positive pressure ventilation, severe aortic regurgitation, atrial septal defect, or a regionalized pericardial effusion as could be seen in postoperative cardiac surgery patients (Fig. 6.9).

## Coronary Artery Disease in Patients with Pericardial Disease

It is not uncommon to find other cardiac abnormalities in patients with pericardial disease. Patients with radiation heart disease for example represent a population that is at particularly high risk for having valvular dysfunction, arrhythmias or heart block, and coronary artery disease. A full catheterization procedure should almost always include cine coronary angiography, as there is rarely a compelling reason to omit this step. Even patients with relative contraindications to contrast administration such as moderate renal insufficiency or contrast allergies can be safely investigated given adequate preparation. Patients with radiation heart disease will more often present with proximal vessel or left main disease than the general population.

## Radiographic Findings

While most patients presenting to the cath lab will already have a dedicated chest x-ray or CT study, some features of chronic pericardial disease may be noted on simple fluoroscopy of the cardiac silhouette. Calcific deposition of the

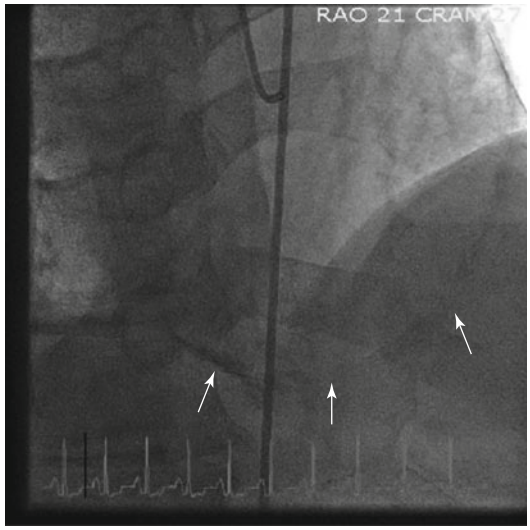


**Fig. 6.10** Calcium deposition of the pericardium surrounding the RV

pericardium can be frequently seen. Patients may also have mitral annular calcifications or calcification of other valve structures, which would be equally easy to identify, and should be commented upon in the catheterization report (Fig. 6.10).

## Conclusion

Cardiac catheterization, especially a dedicated hemodynamic investigation, can be a very useful tool for diagnosing or confirming pericardial disease. Pericardial constriction and restrictive heart disease have very similar physiology in many respects, but can be distinguished in most cases by demonstrating ventricular interdependence. The most sensitive and specific way to demonstrate ventricular interdependence is to calculate a systolic area index (SAI) greater than 1.1 as averaged over at least three exaggerated respiratory cycles. Finally, cardiac tamponade is a true emergency that requires immediate treatment, so it is important to be attentive to the clinical and hemodynamic characteristics of tamponade, and make a rapid diagnosis (Table 6.1).

**Table 6.1** Hemodynamic response to inspiration in different pericardial disease conditions

| | Normal heart | Cardiac tamponade | Pericardial constriction | Restrictive heart disease |
|---|---|---|---|---|
| Right atrium | Decrease in RA pressure | Usually no change given blunting of RA waveform | Increase in pressure, "Kussmal's sign" | Increase in pressure, "Kussmal's sign" |
| Right ventricle systolic pressure | ↓ | ↓ | ↑ | ↓ |
| Left ventricle systolic pressure | ↓ | ↓ | ↓ | ↓ |
| Systolic area index | ≤1.1 | ≤1.1 | >1.1 | ≤1.1 |
| Arterial pressure | Normal pulsus ≤12 mmHg | Pulsus paradoxus >12 mmHg | Pulsus may be abnormal up to 50 % of patients | Normal pulsus ≤12 mmHg |

## References

1. Maioli M, Toso A, Leoncini M, Micheletti C, Bellandi F. Effects of hydration in contrast-induced acute kidney injury after primary angioplasty: a randomized, controlled trial. Circ Cardiovasc Interv. 2011;4:456–62.
2. Acetylcysteine for prevention of renal outcomes in patients undergoing coronary and peripheral vascular angiography: main results from the randomized acetylcysteine for contrast-induced nephropathy trial (act). Circulation. 2011;124:1250–9.
3. Tepel M, Aspelin P, Lameire N. Contrast-induced nephropathy: a clinical and evidence-based approach. Circulation. 2006;113:1799–806.
4. Barbeau GR, Arsenault F, Dugas L, Simard S, Lariviere MM. Evaluation of the ulnopalmar arterial arches with pulse oximetry and plethysmography: comparison with the allen's test in 1010 patients. Am Heart J. 2004;147:489–93.
5. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283:447–51.
6. Talreja DR, Nishimura RA, Oh JK, Holmes DR. Constrictive pericarditis in the modern era: novel criteria for diagnosis in the cardiac catheterization laboratory. J Am Coll Cardiol. 2008;51:315–9.

## Other Selected References

Griffin BP. Manual of cardiovascular medicine. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2013.
Ragosta M. Textbook of clinical hemodynamics. Philadelphia: Saunders, Elsevier, Inc.; 2008.

## Cardiac Catheterization Evaluation of a Patient with Pericardial Disease-For Patients and their Families

### Introduction

Patients who are suspected of having pericardial disease are sometimes asked to have a procedure in the cardiac catheterization laboratory. Usually, this test is requested after your doctor has already developed a strong suspicion of pericardial disease based on taking a detailed history, completing a physical exam, and perhaps having obtained other imaging tests such as an x-ray, CT scan, or cardiac MRI. Usually, the reason for the test is to confirm a diagnosis of pericardial disease, and to exclude other diseases that may have similar features. Patients who are very symptomatic from their pericardial disease are sometimes considered for open-heart surgery to remove the pericardium, and thus a catheterization procedure is sometimes requested in order to confirm the diagnosis. Also, most patients who are going to have open-heart surgery will need to first have their coronary arteries evaluated with a catheterization procedure to ensure that they won't need any coronary artery bypass grafts at the time of surgery. The catheterization laboratory is very similar to an operating room with regards to how it is set up, and this will be explained in detail below.

### Prior to Your Procedure

Before you are scheduled to come to the catheterization laboratory, your doctor will complete a detailed review of your current symptoms and other medical conditions, and perform a physical examination. Notify your doctor of any bleeding disorders or if you are taking any blood thinning medications. Notify your doctor of any allergies you have, especially allergies to contrast dye, narcotic medications (morphine, fentanyl, etc.), or benzodiazepines (lorazepam, midazolam, etc.). Notify your doctor of any problems with your breathing, or inability to lay flat. In most cases, it is required that you have some simple blood work done prior to the procedure to ensure that you have adequate kidney function and blood counts. Also, if you are on blood thinning medications, it is common to check the level of these medications on the day of the procedure.

In general, warfarin (also called Coumadin) is discontinued 5 days prior to the procedure. The newer, oral anti-coagulation medications (dabigatran, rivaroxaban, apixaban) should be discontinued at least 48 h prior to the procedure, but some doctors may request that you stop these even earlier. Depending on the reason why you are taking a blood thinner, your doctor may ask that you substitute another medication for a few days while your oral blood thinners clear out of your system. Most often, this involves taking injections of a heparin product called enoxaparin (also called Lovenox), which is given as an injection under the skin every 12 h.

Your doctor will ask about any other medications you are taking, and advise you if you should stop any of them prior to the procedure. Generally speaking, there is no reason to stop taking aspirin, clopidogrel (also called Plavix), or any other routine medications. Some doctors may ask that you not take one type of blood pressure medication called an ACE-inhibitor (lisinopril (Zestril), ramipril (Altace), enalapril (Vasotec), Benazepril (Lotensin), Captopril, etc.) on the morning of your procedure. If you take medications for diabetes, you should ask how to manage your insulin or your diabetes pills on the day of your procedure. In some cases, your doctor will ask you to reduce the amount of insulin you take in the morning because you will be asked not to eat breakfast. Also, it is not uncommon for doctors to ask you to skip taking Metformin on the morning of the procedure, and perhaps for a few days after.

### The Day of Your Catheterization

Usually, your doctor will ask that you not have any food or drink after midnight on the night before your procedure. Sometimes, if the procedure is scheduled for the afternoon, a light breakfast is permitted. Medications can be taken with

small sips of water. Once you arrive to the laboratory, you will be asked to change into a medical gown. One or more IV lines will need to be started so that you can be given fluids or other medications during the procedure as needed. Your normal vital signs (blood pressure, heart rate, etc.) will be documented. If your doctor has not gone over the procedure in the clinic, someone will discuss it with you at this time. This conversation should include the reason for the procedure, what the doctors intend to do, how it will be done, and what the risks and expected benefits are of having the procedure. Generally speaking, a diagnostic cardiac catheterization procedure is felt to be very safe, but given that the doctor will be placing small instruments near to, and in some cases inside your heart, there are several important risks to discuss.

The most common complication of having the catheterization procedure is bruising or minor bleeding at the site where the catheters enter the blood vessel. This is slightly more common if the groin vessels are used as compared to the wrist or the neck. Up to 5 % of patients may experience enough bleeding to cause swelling which is called a hematoma and this may lead to discomfort that persist for a few days. Bleeding that is serious enough to require a blood transfusion is rare, and occurs less than 1 % of the time. There is a small risk of infection due to introducing instruments through the skin, but the use of sterile technique limits this risk substantially. As the catheters are placed inside the aorta, there is the potential that they may come into contact with atherosclerotic "plaques" which are abnormal areas in the walls of blood vessels, which may contain calcium or fat molecules. Some people have small areas of blood clot that adhere to the wall of the arteries as well. If any of these plaques become disrupted by the catheter, they may break loose and flow into smaller blood vessels that are "down-stream" from the larger aorta, potentially causing a small artery to become blocked. This is very uncommon, but could be potentially serious if it occurred near the head or the heart, where it could cause a stroke or heart attack. Fortunately, this type of complication occurs in less than 1 in 1,000 procedures. When the catheters enter the chambers of the heart, it is very common to induce several extra heartbeats, and the patient may notice a fluttering sensation or palpitations. It is very uncommon to have serious or persistent heart rhythm problems during a catheterization procedure. The risk of death from a diagnostic catheterization procedure is less than 1 in 2,000.

After the doctor explains the procedure, and you have had a chance to ask questions, you will likely be asked to sign a form giving your informed consent to undergo the procedure.

## How a Catheterization Is Done

A catheterization procedure is done by a cardiologist with specific training. Not all cardiologists do these procedures, and you may be referred to a different doctor to have the procedure completed, than the one who you see in the clinic. In simple terms, the procedure involves placing a small, flexible, plastic tube called a "catheter" inside your blood vessel. The doctor will get access to the blood vessels by placing a needle through the skin, very similar to how an IV line is placed. For the purpose of a pericardial constriction study, the doctor will need to place one catheter in the artery and one in the vein. Usually, this is done by gaining access to the femoral artery and femoral vein, which pass right next to each other as they course through the groin just next to the hip. Some cardiologists may choose to use the artery in the wrist or the elbow, and may choose to use the large vein in the neck called the Jugular Vein. Regardless of the location used to place the catheter, the doctor will give plenty of numbing medication at that location so as to minimize discomfort.

A catheterization procedure will initially seem very similar to the process of having outpatient surgery to those who have had any simple surgical procedure, but you shouldn't be concerned, as it does not involve any cutting into the skin. Once you arrive in the procedure room, you will notice that it appears similar to an operating room. There is a table in the middle of the room for the patient, a table with sterile equipment for the doctor, several television screens and moni-

tors, and several nurses, technicians, and doctors. The main difference is the x-ray equipment that is present in the catheterization laboratory, and you will notice a large robot that is controlled by the doctor. Also, you may notice that some of the staff are sitting behind a large window in a control room. Initially, you will be asked to lie on your back on the table in the middle of the room. Usually the pubic hair is then shaved on each side of the groin, and the appropriate areas are carefully cleaned with antiseptic solution. A large sterile drape is then placed over the patient, and at this time it is very important to remain still so as not to contaminate the sterility of the procedure room. At this time, the x-ray machine is brought over the table, and you will notice that it moves in all directions to give the doctor different views of the catheters as they pass inside your blood vessels. The x-ray machine may at times move near your head, but will not touch it.

Typically, the patient is given some medication for light sedation prior to beginning. This will usually be a combination of an opioid pain medication such as fentanyl, and a benzodiazepine such as midazolam (versed). Once you are comfortable and the doctor is ready, he/she will give numbing medication under the skin. The numbing medication will initially sting for approximately 30 s (varies) but once it has taken effect, you shouldn't feel any more pain. The doctor will place a needle into the blood vessel, then pass a wire into the vessel through the needle. The needle will then be taken out, and a short "sheath" which is a small, short, plastic tube, will be placed into the vessel. It is through this sheath that the longer catheters that reach up to the heart are placed. There are no nerves inside the blood vessels, so you will not feel anything as the catheters pass up to the heart.

Once the catheters are in place, the doctor will take several pictures with the x-ray machine, and take several measurements of the pressures inside your heart from the tip of the catheters. During the procedure, you may be asked to hold your breath, or do certain breathing exercises such as taking several deep breaths in and out. Sometimes, the doctors or nurses will ask you to cough. In rare cases, the catheter may irritate the heart's electrical system which can lead to extra heart beats, missed heart beats, or other rhythm problems. Coughing can sometimes help to return your heart rhythm to normal in these cases.

## Once the Procedure Is Over

When the procedure is done, all the catheters will be removed from the sheaths. These sheaths will next need to be removed. The veins have relatively low pressure, so the sheath in the vein can be removed and bleeding will usually stop fairly easily with several minutes of holding light pressure over the site. Arteries however have high pressure, and require slightly more attention at the time of sheath removal. If the arterial sheath was placed in the radial artery in the wrist, the doctor will frequently place a type of "bracelet" around the wrist. This bracelet has a balloon that inflates with air to put pressure over the site where the artery was punctured. It stays in place over approximately 2 h while the air is slowly let out. Once the air is completely removed and there is no bleeding noted, the patient is usually able to go home. If the femoral artery in the groin is used, there are several options. The doctor may elect to remove the sheath and hold pressure over the site until there is no bleeding noted. This may take as little as 5 min or sometimes more than 30 min depending on the diameter of the catheter and the tendency of the patient to bleed. Once bleeding is controlled, the patient is usually asked to remain flat in bed for between 3 and 4 h (sometimes more) to make sure that there are no bleeding complications. Bending the leg, coughing, laughing, or raising the head or torso (sitting up) in the bed all put pressure on the artery in the groin, and may cause the artery to start bleeding again.

In some cases, the doctor may elect to put a "closure device" in the artery at the end of the procedure. There are several types of closure devices. Some involve putting an absorbable plug under the skin, just over the top of the hole in the artery. Some involve placing a stich or suture in

the artery to tie the hole closed. In general, the types of devices used will depend on several factors including where in the artery the needle went in, and which devices the cardiologist feels most comfortable using. Each have their benefits and possible complications, but in general, the overall benefit to the patient is that you will be able to get out of bed and ambulate considerably sooner than if you have your sheath removed and simple pressure held. The doctor may not be able to know until the procedure is complete if you are a good candidate for a closure device.

Finally, the doctor will discuss the findings of the procedure with you, and/or with your family if you so choose. The results will also be discussed or reported to the doctor that asked you to have the procedure. Usually, patients are allowed to go home the same day as the procedure, assuming there are no complications that would require more prolonged observation in the hospital.

# Multimodality Imaging (X-Ray, CT, and MRI) in Pericardial Disease

7

Vikram Agarwal, Seth Uretsky, and Amgad N. Makaryus

## Introduction

The accurate diagnosis of pericardial diseases is frequently challenging, and requires an integration of medical history, physical examination, imaging, invasive hemodynamic measurements, hematological testing, pericardial fluid evaluation, and characterization of pericardial biopsy specimens. With the rapid advances in technology, multimodality noninvasive cardiac imaging has assumed a central role in the diagnosis and management of various pericardial conditions, particularly when the clinical findings are equivocal.

Echocardiography is often the initial cardiac imaging modality because of its low cost, wide availability, portability, and lack of ionizing radiation. The role of transthoracic echocardiography (Fig. 7.1) to help diagnose and manage pericardial disease is well established. However, under certain conditions, the utility of echocardiography may be limited by suboptimal acoustic windows. Such conditions include, but are not limited to obesity, obstructive lung disease, chest wall deformities, and post-surgical changes. Pericardial effusions in unusual locations, especially loculated pericardial effusions may be difficult to detect on echocardiography. In addition, echocardiography is highly operator dependent, has a narrow field of view, and has limited tissue characterization.

In spite of the ever increasing armamentarium of more detailed and sophisticated imaging modalities, chest x-ray (CXR) remains a simple, easy, and inexpensive imaging modality which invariably provides valuable information as the crucial first step in the differential diagnosis of pericardial diseases. Often, incidental pericardial findings are found on chest x-rays performed for unrelated reasons which spur further investigations. Occasionally, it is also useful in following the progression of the disease, and with its wide field of view may reveal additional mediastinal and pulmonary pathology.

Cardiac CT (CCT) has good spatial and temporal resolution, a wide field of view, and images that can be reconstructed for a particular view during post processing. It is the ideal technique for the evaluation of pericardial calcification and is very useful in preoperative planning. Although recent advances in scanner technology and software have significantly decreased the radiation exposure to patients undergoing CCT, the use of CCT exposes patients to ionizing radiation and iodinated contrast medium. In addition, functional evaluation is limited unless a retrospective

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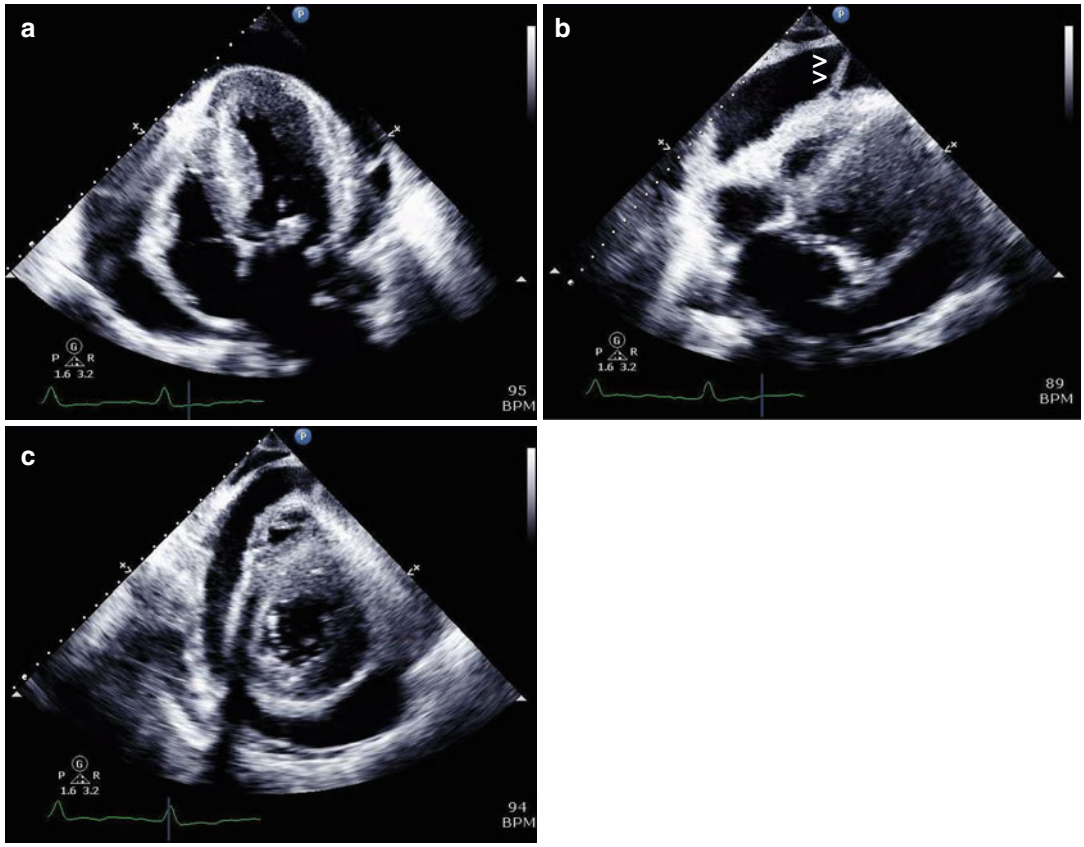


**Fig. 7.1** (**a**) Apical four chamber echocardiographic view in a 37 year old man with pericarditis revealing a large circumferential pericardial effusion. (**b**) Subcostal echocardiographic view in the same patient as in (**a**) with pericarditis again revealing a large circumferential pericardial effusion. Intrapericardial effusion stranding is noted (*arrowheads*). (**c**) Parasternal short axis echocardiographic view revealing the same large circumferential pericardial effusion

study is performed, which is associated with a higher radiation dose than CCT studies acquired with prospective ECG gating. The newer generation CT scanners can now perform retrospective ECG gated cardiac studies using radiation doses lower than a typical dose of conventional chest CT. Performing CCT can be challenging in patients with irregular heart rates or those who are unable to lay flat or hold their breath.

Cardiovascular MR (CMR) is a valuable imaging tool—for both morphologic and functional assessments—to evaluate pericardial abnormalities. CMR has the advantages of being noninvasive and not exposing patients to ionizing radiation. In addition, CMR has good spatial resolution; can differentiate among types of soft tissue; has a wide field of view; and multiplanar imaging capabilities. These characteristics of CMR are useful in the evaluation of the pericardium, particularly for tissue characterization, assessment of inflammation, and to evaluate processes that may affect the myocardium. CMR is ideally suited for evaluation of small or loculated pericardial effusions, pericardial inflammation, and functional abnormalities caused by pericardial constriction and for characterization of pericardial masses. The wide field of view enables assessment of surrounding structures as well. However, acquiring good quality CMR images can be challenging, with prolonged study times, in patients with underlying cardiac arrhythmias and inability to co-operate during prolonged breath holding maneuvers. In the presence of significant arrhythmias, nongated CMR images

can still provide valuable information about the underlying morphological and structural abnormalities. Until recently, CMR was contraindicated in patients with implanted cardiac devices. However, with newer devices and protocols based on device selection, appropriate programming, and monitoring, CMR can be performed in a safe fashion [1]. CMR is also not ideally suitable for the detection of calcifications [2, 3].

## Normal Pericardial Anatomy

### Pericardial Anatomy

The pericardium is an avascular flask-shaped fibrous sac which surrounds the heart and the origin of the large blood vessels, the ascending aorta, pulmonary artery, left pulmonary veins, and superior vena cava. It consists of two layers: the inner serosal layer and the outer fibrous pericardium. The inner serosal layer is further comprised of a visceral and parietal pericardium [4]. The parietal layer lines the inner surface of the fibrous pericardium to which it adheres, whereas the visceral layer envelops the epicardial surface of the heart, separated from it only by a layer of epicardial fat that contains the coronary vessels. In autopsy studies, the normal pericardium measures 0.4–1.0 mm in thickness [4]. A potential space separates the visceral and the parietal serosal layers and normally contains up to 50 ml of serous fluid distributed mostly over the atrioventricular and interventricular grooves. Like visceral abdominal fat, the thickness of the epicardial fat is generally increased in obesity. This epicardial fat distribution is typically asymmetric, with three to four times more epicardial fat present along the right ventricle (RV) than along the left border of the heart [5].

## Appearance on Cardiac Imaging of the Normal Pericardium

### CXR (Fig. 7.2)

The normal pericardium is frequently identified on a lateral plain chest radiograph as a thin, linear opacity between the anterior subxiphoid mediastinal fat and subepicardial fat [6]. In the postero-anterior (PA) view, the pericardium may be seen along the left heart border.

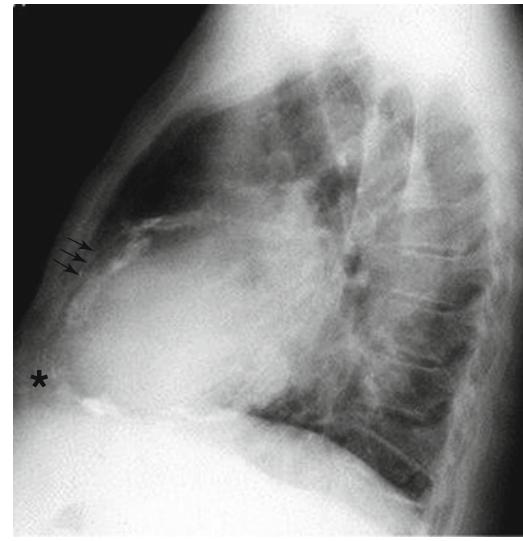

**Fig. 7.2** Radiographic view from a lateral chest roentgenogram revealing calcified pericardium (*arrows*) on the anterior portion above the apex of the heart (*asterisk*)

### CCT (Figs. 7.3, 7.4, and 7.5)

For pericardial imaging by means of CT equipped with multidetector technology, use of high-resolution volumetric acquisition with a section thickness >3 mm generally yields excellent anatomic depiction of the pericardium [7]. With CCT, the normal pericardium is best imaged in systole and appears as a line with an average thickness of 1.3–2.5 mm (almost always <4 mm; Fig. 7.3). The pericardium is a bright, linear structure that is easily detectable in both contrast- and noncontrast enhanced CCT examinations because of its visibility against the low attenuation of the surrounding epicardial fat [8–11]. Hence, visualization of the pericardium varies with location and amount of pericardial fat. It is sometimes difficult to visualize the pericardium against the lateral, posterior, and inferior left ventricular wall. Although dynamic evaluation of the ventricular septum to evaluate constrictive physiology is theoretically possible with ECG gated

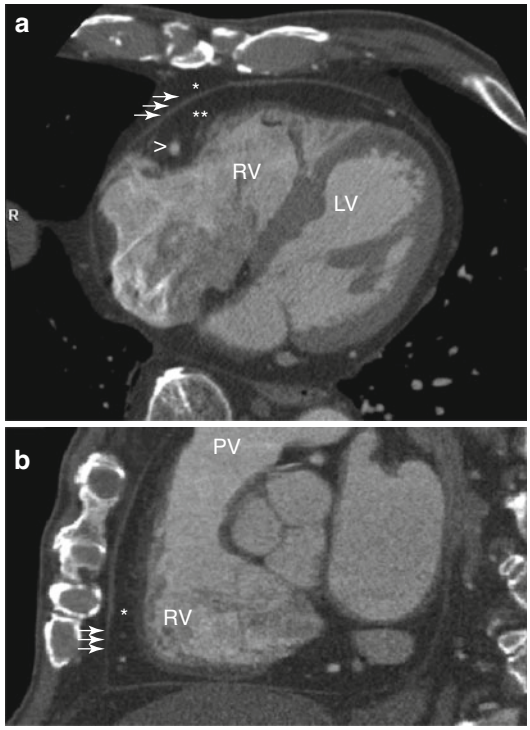


**Fig. 7.3** (**a**) Transaxial CT tomogram of the heart in the horizontal long axis of the left ventricle (*LV*) at a level halfway between the cranial and caudal ends of the heart. Pericardium of normal thickness (*arrows*) is noted in the typical location over the free wall of the right ventricle (*RV*) between the subpericardial (*double asterisk*) and mediastinal (*asterisk*) layers of fat. Also noted in this image is the right coronary artery which courses within the subpericardial fat layer (*arrowhead*). (**b**) Sagittal CT tomogram of the heart in the short axis at the level of the mid portion of the RV. Normal thickness pericardium (*arrows*) is seen extending from near the diaphragm over the RV to above the level of the pulmonary valve (*PV*). The normal subpericardial layer of fat is also noted adjacent to the right ventricle (*asterisk*)

CT, real time functional imaging is much easier and more accurately assessed by using echocardiography or CMR [3].

### CMR (Figs. 7.6, 7.7, 7.8, 7.9, and 7.10 and Table 7.1)

Normal pericardium is seen as a smooth, curvilinear structure that is surrounded by high-signal epicardial and mediastinal fat. The normal pericardium, composed primarily of fibrous tissues,

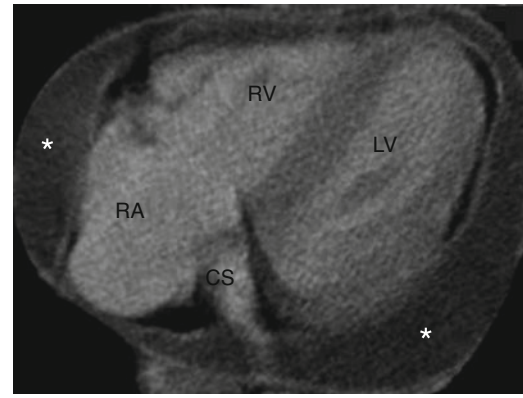


**Fig. 7.4** Transaxial CT tomogram image of the heart at the level of the coronary sinus (*CS*). Water-density fluid (*asterisk*) is present posterior to the left ventricle (*LV*) and adjacent to the right atrium (*RA*) and right ventricle (*RV*), consistent with pericardial effusion separating the external fibrous and serous inner layers of the pericardium

has intermediate-to-low signal on T1- and T2-weighted black blood fast spin-echo (FSE) and steady-state free precession (SSFP) sequences [12] (Fig. 7.6). The two pericardial layers are not separately discerned. The presence of fat and fluid makes visualization of pericardium easier. Although the pericardium is prominently seen adjacent to the right ventricular free wall, right atrioventricular groove, inferior aspect of the left ventricle, and left ventricular apex, it is visualized less clearly adjacent to the lateral left ventricular wall because of the paucity of fat and low signal from adjacent lungs. On CMR, the normal pericardium measures 1.2 mm in diastole and 1.7 mm in systole [2]. The higher thickness of normal pericardium on MRI results from a combination of cardiac motion, low spatial resolution with partial volume averaging, and chemical-shift artifact. The normal pericardium does not have early or delayed contrast enhancement [2, 13].

## Pericardial Pathology and Its Appearance on Cardiac Imaging

### Pericardial Effusion

Asymptomatic pericardial effusions may be initially detected by chest radiography performed for other reasons. To augment the cardiac silhouette

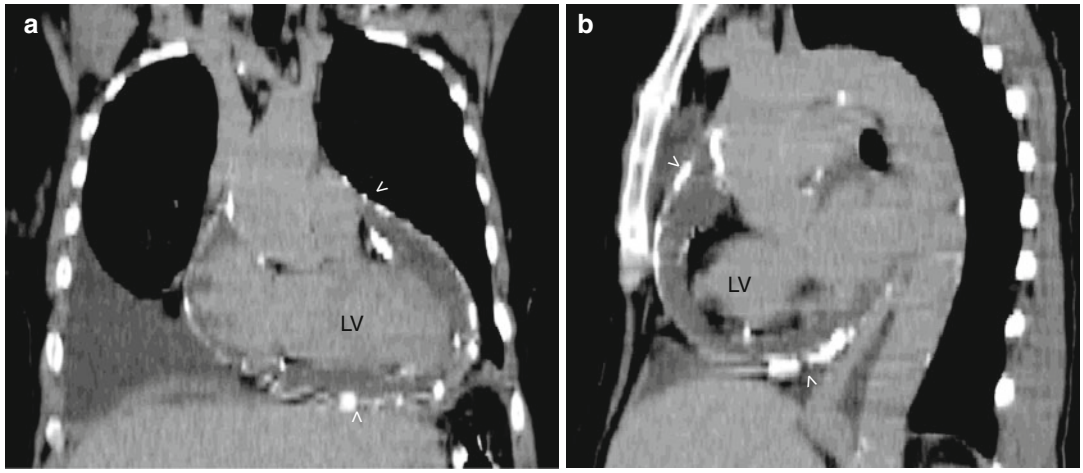


**Fig. 7.5** Noncontrast CT tomogram in the coronal view (**a**) and sagital view (**b**) showing the left ventricle (*LV*). These views shows extensive calcification (*arrowheads*) of the pericardium in a patient with constrictive pericarditis

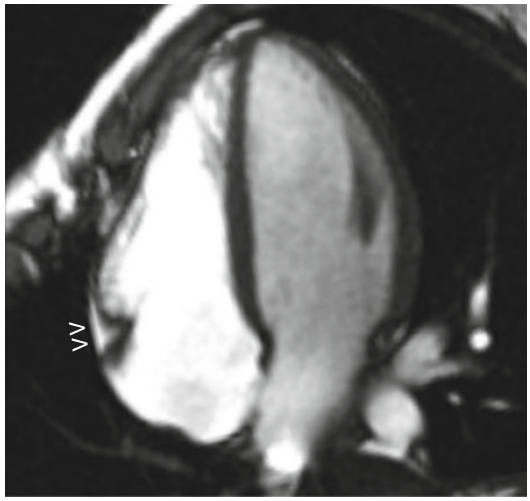

**Fig. 7.6** Gradient echo MRI sequence in the horizontal long axis of the heart showing normal pericardium and minimal subpericardial fat in the right atrioventricular groove (*arrowheads*). Note that fat appears bright in this MRI sequence

on chest x-ray, a minimum of about 250 ml of fluid collection is required, and consequently smaller effusions may be occult [14]. On CXR, a water-bottle configuration with generalized symmetric cardiac enlargement with increased cardiothoracic ratio may be seen [15]. However, on CXR, it may be difficult to distinguish this from cardiomyopathy. Occasionally, in patients with pericardial effusion, the "fat pad" sign, a soft tissue stripe >2 mm between the epicardial fat and the anterior mediastinal fat can be seen anterior to the heart on the lateral view [16]. Occasionally, serial studies can be done to aid in the diagnosis, especially if rapid changes in the size of the heart shadow are observed. Transthoracic echocardiography is the first line imaging modality to evaluate pericardial effusion (Fig. 7.1), based on some of the reasons mentioned earlier. However, CCT and CMR imaging are useful adjuncts to transthoracic echocardiography especially since they provide a wider field of view and facilitate a more comprehensive evaluation of pericardial effusions. These modalities are useful in detection of small loculated effusions, especially those in anterior locations. When echocardiography findings are inconclusive, CCT (Fig. 7.4) and CMR (Fig. 7.8) can better localize the effusions, and also help quantify the amount of accumulated fluid [2, 17, 18]. Although varying degrees of fluid collections can have certain characteristic patterns of fluid accumulation, since fluid does not spread homogeneously, there is no direct correlation between the thickness of the pericardial cavity and the actual volume of the accumulated fluid [19]. The volume of pericardial fluid can be quantified similar to quantification of ventricular volumes. In

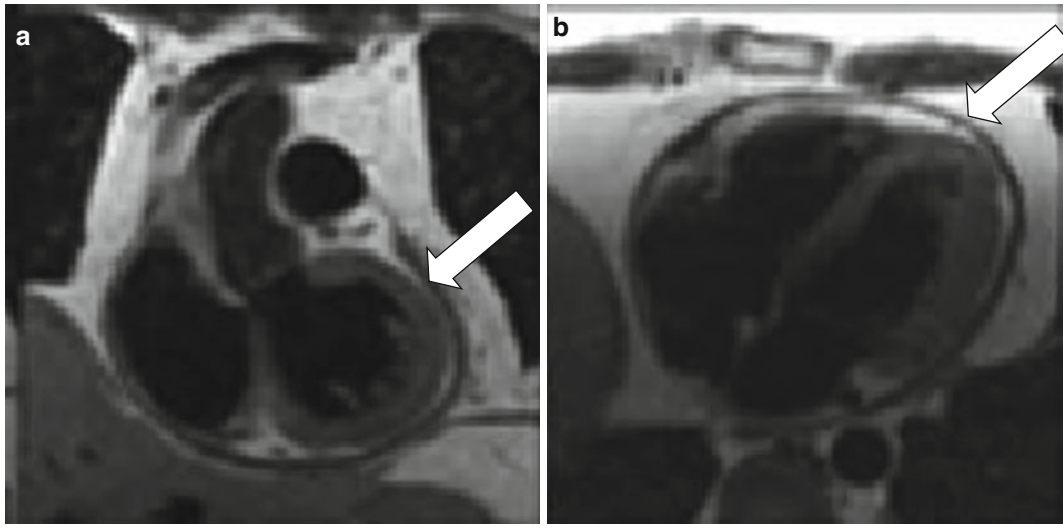


**Fig. 7.7** Coronal (**a**) and axial (**b**) double inversion recovery spin echo MRI images of a patient with a history of pericarditis 4 months prior during a trip to Asia. The pericardial effusion was treated with anti-inflammatories and decreased in size, but the patient continued to have dyspnea on exertion and peripheral edema. The MRI shown revealed a remaining small pericardial effusion and diffusely thickened pericardium (*arrows*)

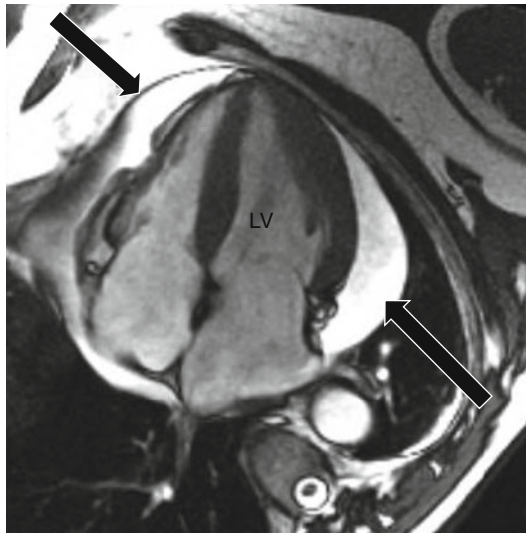


**Fig. 7.8** Gradient echo MRI image of the heart in the horizontal long axis of the left ventricle (*LV*) noting a large predominately posteriorly-located pericardial effusion (*arrows*)

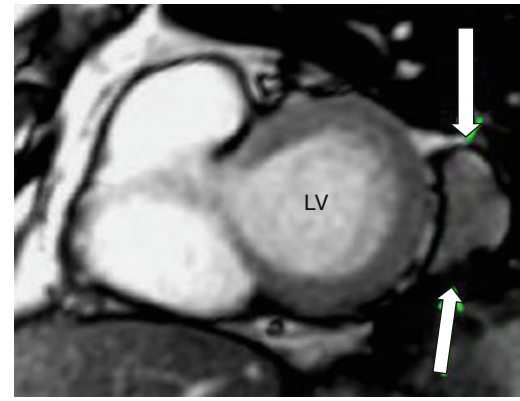


**Fig. 7.9** Gradient echo MRI image of the heart in the short axis view of the left ventricle (*LV*) noting a loculated pericardial effusion adjacent to the lateral portion of the LV (*arrows*)

addition, epicardial fat is readily identified on CCT and CMR, which is especially useful when fibrin is adherent to the cardiac surface.

A limited characterization of pericardial fluid can be achieved on CCT by measuring attenuation values and on CMR by measuring signal intensity on MR images. CCT and CMR can also readily identify hemopericardium when it complicates aortic dissection, and thereby prevent inappropriate and potentially catastrophic pericardiocentesis [13, 20]. On CCT, pericardial fluid with attenuation close to that of water (<10 Hounsfield units) is likely to be a simple effusion, while attenuation value greater than that of water is more likely to be due to purulent exudate, malignancy, or related to hypothyroidism (20–60

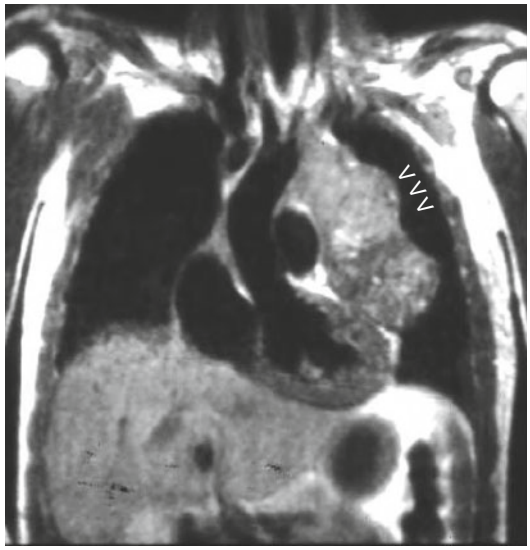

**Fig. 7.10** Coronal MRI spin-echo sequence revealing a mass (*arrowheads*) contained within the pericardial space with a disordered and multi-signal appearance which was diagnosed as a pericardial fibrosarcoma

Hounsfield units). Hemorrhagic collections have higher attenuation values (>60 Hounsfield units). Effusions with attenuation less than water have been reported with cases of chylopericardium (−60 to −80 Hounsfield units) [8, 9, 11]. On CMR, simple transudative effusions manifest with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Complex effusions, such as exudative effusions with high protein and cell content, and hemorrhagic fluid, have high signal intensity on T1-weighted and intermediate signal on T2-weighted images [2, 8, 13]. However, sometimes because of motion artifacts, the characterization of the pericardial fluid is not always possible. Often, the use of bright-blood dynamic cine MR imaging facilitates the better visualization of intrapericardial contents, including coagulated blood and fibrinous strands, which are often found in loculated pericardial effusions.

**Table 7.1** Assessment of the pericardium with MR imaging [2, 8, 10, 12, 13]

| Target | MR sequences |
|---|---|
| Pericardial width/localization/extent | T1 and T2 weighted imaging, cine imaging |
| Pericardial delineation | T1 and T2 weighted imaging, cine imaging, gadolinium enhanced imaging |
| Pericardial layer and fluid characterization | T1 and T2 weighted imaging, cine imaging, contrast agent enhanced T1-weighted or late gadolinium enhanced imaging |
| Pericardial function | Cine imaging, myocardial tagging (to assess fusion of pericardial layers and adherence to myocardium) |
| Pericardial masses | T1 and T2 weighted imaging, double inversion recovery with fat saturation, triple inversion recovery, cine imaging, late gadolinium enhanced imaging |
| Cardiac morphology<br>Ventricular size and shape<br>Myocardial morphpology | T1 weighted imaging, cine imaging |
| Cardiac systolic function<br>Regional and global systolic ventricular function | Cine imaging |
| Cardiac filling (diastolic function) | Phase contrast |
| Ventricular coupling<br>Ventricular septal shape<br>Septal motion patterns<br>Respiratory-related septal shift | Real-time cine, phase contrast |
| Other findings<br>Myocardial processes (myocarditis, myocardial infarction, myocardial infiltrative or storage disease)<br>Vena caval size<br>Mediastinal and pulmonary processes<br>Ascites and pleural fluid | T1 and T2 weighted imaging, cine imaging, late gadolinium enhanced imaging |

**Table 7.2** CCT and CMR features that differentiate thickening and effusion [2, 8, 11–13]

| Features | Effusion | Thickening |
|---|---|---|
| Location | Follows distribution typical of effusion | Does not follow typical distribution, usually anteriorly located |
| Decubitus position | Change in configuration with change in posture | No change in configuration with change in posture |
| Margins | Smooth | Irregular or nodular with increased attenuation |
| Contrast enhancement | Absent | May be present if associated with inflammation |
| Tagging | Loss of tags with cardiac cycle | Myocardial tags persist throughout cardiac cycle |
| **CMR** | | |
| Dynamic changes | Mobility of fluid and changes in the regional dimension of the pericardial sac throughout the cardiac cycle | No mobile component and no changes in the regional dimension of the pericardial sac |
| T1- and T2-weighted imaging | Signal void | Gray/dark (except in calcification) |
| Steady state free precision imaging and gradient-echo sequences | High | Low |

Both CCT and CMR (Table 7.2) provide additional assessment of the pericardial layers, including thickness, composition and inflammation. In conditions like pericardial effusion secondary to malignancy, an irregularly thickened pericardium or pericardial nodularity may be seen on CMR images, further allowing the differentiation between simple pericardial effusions from inflammatory effusive pericarditis or malignant pericardial diseases [8, 10]. Sometimes, on CCT and CMR, differentiating a small pericardial effusion from a thickened pericardium can be difficult. However, certain features can help differentiate the two pathologies (Table 7.2). Additionally, since almost the entire chest is visualized during CCT or CMR, associated mediastinal and pulmonary abnormalities can also be detected during the examination.

## Cardiac Tamponade

The diagnosis of acute life threatening cardiac tamponade is a clinical diagnosis, which is usually confirmed by emergent transthoracic echocardiography. Chest x-rays have a very limited role in the assessment of cardiac tamponade. Performing hemodynamic evaluation on imaging modalities such as CMR, which require relatively prolonged imaging times and patient cooperation, may not be appropriate for clinically unstable patients with suspected cardiac tamponade. However, when a loculated or complex effusion causes a subacute cardiac tamponade, CCT can provide valuable information to assess the feasibility of percutaneous versus surgical drainage. CMR can provide information regarding associated pericardial pathology, but is not the initial modality of choice in a clinically unstable patient. On CCT and CMR, the typical findings of cardiac tamponade include superior vena cava, inferior vena cava, and hepatic vein dilation, "diastolic inversion", i.e. collapse of the right ventricle free wall in early diastole and collapse of the right atrium free wall during late diastole and early systole, "flattened heart" sign i.e. diminished anteroposterior diameter, and bowing or inversion of the interventricular septum, which correlates with the inspiratory septal bulge or bounce seen on echocardiography [2, 3, 8, 13]. Careful attention should be paid to differentiate cardiac tamponade from effusive-constrictive pericarditis. In effusive-constrictive pericarditis with associated effusion at presentation, the com-

plaints are caused by a pathologic noncompliant pericardium rather than by the effusion itself. Thus, it is important to look for features of constriction, which can occur transiently in the resolution phase, after pericardiocentesis or with organized effusions.

## Pericarditis

While the most common manifestation of pericarditis is its acute presentation, it may also present in subacute, recurrent, and chronic forms. The clinical symptoms depend on the severity of inflammation. In acute pericarditis, other than highlighting significant pericardial effusion, the chest x-ray may be fairly unremarkable. In chronic pericarditis, the x-ray may show any underlying pericardial calcification if present. While echocardiography is considered as the initial modality of choice to guide further diagnostic and therapeutic procedures, CCT and CMR can provide invaluable additional information, especially with regards to better pericardial tissue visualization and characterization. Delayed enhancement imaging using gadolinium can also assess for myocardial damage if associated myocarditis is suspected.

On CCT, noncalcified pericardial thickening associated with pericardial effusion is suggestive of acute pericarditis. With chronic forms of pericarditis, pericardial layers tend to be irregularly thickened and effusions may be loculated owing to the presence of adhesions. On contrast-enhanced CCT, diffuse enhancement of the thickened pericardium indicates inflammation [8, 11]. As discussed above, the CCT can also help characterize the associated pericardial effusion if present.

Similar to CCT, T1-weighted and bright-blood sequences can be used to identify underlying pericardial morphological features, associated pericardial effusion and adhesions. In addition, in equivocal cases, T2-weighted images and delayed gadolinium enhancement can be used to identify edema and inflammation of the inflamed pericardial layers [2, 8, 13]. This underlying edema and inflammation may extend to the adjacent myocardium or epicardial fat, and may be focal or diffuse. This pericardial enhancement on histological examination reflects inflammation, including edema, neovascularization, and granulation tissue formation [21]. It also correlates with elevated markers of inflammation [22, 23]. On T2-weighted images, the pericardial thickening has a grayish signal, while the effusion has a low signal. However, it is important to interpret the delayed gadolinium pericardial enhancement in the appropriate clinical context as this enhancement is nonspecific [2, 13, 24]. Sometimes, the pericardial and associated myocardial (myopericarditis) or epicardial fat enhancement may occur in the absence of associated pericardial thickening. In chronic pericarditis, the pericardium may be irregularly thickened and on delayed gadolinium enhancement variable contrast enhancement may be seen [2, 13, 22].

Although the role of CCT in the management and diagnosis of patients with acute and chronic pericarditis remains uncertain, CMR has become a vital tool for assessing patients with underlying pericarditis especially with associated myocardial involvement (myopericarditis). This is especially important to guide management in patients with pericarditis with associated poor prognostic signs, including lack of response to standard treatment, worsening hemodynamic instability, and chronic indolent course of disease. CMR is not only the most sensitive test to detect pericardial involvement (Sensitivity—94–100 %) [25, 26], but it is also useful to diagnose associated constrictive pericarditis. In addition, CMR can also be used to monitor and follow up response to treatment of patients with chronic and recurrent pericarditis.

## Constrictive Pericarditis

Although acute and subacute forms of pericardial constriction have been occasionally described, constrictive pericarditis usually represents the end stage of a chronic inflammatory process involving the pericardium, which results in thickening, dense fibrosis, calcification, and adhesions

of the parietal and visceral pericardium. While constrictive pericarditis typically affects the parietal pericardium, occasionally this process can only involve the visceral layer. The underlying pathophysiology is related to the constriction of the heart which impairs cardiac filling, especially diastolic filling of the ventricle. Since the total cardiac volume is restricted by the rigid and fixed pericardial volume, there is equalization of end-diastolic pressures in all four cardiac chambers, and increased ventricular coupling which is strongly influenced by respiration. This results in elevated systemic venous pressures and low cardiac output [17, 27].

The diagnosis of pericardial constriction can be challenging. Constrictive pericarditis is difficult to diagnose on chest x-ray. However, certain findings on chest x-ray suggest the existence of constrictive pericarditis. In the classical form of the disease, the cardiac silhouette is neither enlarged nor reduced, whereas in other forms, pericardial effusion may contribute to enlarged cardiac size. Signs of pericardial calcification are suggestive of constrictive pericarditis while pericardial calcification by itself is not diagnostic of constriction. A lateral chest X-ray (Fig. 7.2) may reveal pericardial calcification over the right atrium and ventricle, as well as atrioventricular grooves. Clinically, it is difficult to differentiate between constrictive pericarditis and restrictive cardiomyopathy. However, it is of paramount importance to differentiate the two entities as patients with constrictive pericarditis might benefit from pericardial stripping. Both these entities are characterized by similar clinical manifestations and may exhibit similar findings at regular echocardiography and hemodynamic cardiac catheterization. In such cases, other imaging modalities, especially CMR can play a vital role in not only assessing hemodynamic status, but to also exclude other causes of right heart failure, such as pulmonary hypertension, shunts, and right ventricle dysplasia or infarction. In addition, CMR can determine if the pericardium—thickened, inflamed, or without thickening, is causing constriction; and simultaneously evaluate if the patient will benefit from pericardial stripping [2, 8, 13].

## Morphological Abnormalities

There are two important morphological characteristics of the pericardium which are evaluated when considering a diagnosis of constrictive pericarditis—pericardial thickening and presence of associated pericardial calcification. Traditionally, pericardial thickness has been used as an important criterion for the diagnosis of constrictive pericarditis. Pericardial thickening of >4 mm is an indicator suggestive of constriction in patients with the appropriate symptoms and signs of right heart failure; while >5–6 mm is highly specific for constriction [2, 8, 28]. This thickening is most pronounced over the right heart (right ventricle and anterior atrioventricular groove), usually associated with irregular pericardial delineation. However, recently this concept of pericardial thickening has been debated, as occasionally constriction can be seen without associated pericardial thickening [29]. Also, it has now been shown that toward the end-stages of an irreversible chronic fibrosing pericarditis, there is thinning of the chronically inflamed pericardium [2]. In addition, as seen with conditions like acute pericarditis and cardiac surgeries, pericardial thickening may occur without signs and physiological changes associated with pericardial constriction [27]. Pericardial calcification is the second important morphological abnormality visualized on imaging studies to aid the diagnosis of constrictive pericarditis. Pericardial calcifications, however, are less common nowadays than in the past, which is probably related to the decrease in rates of tuberculosis and the increase in iatrogenic causes of constriction [13]. Recent studies report pericardial calcifications in 27–28 % of patients with histologically confirmed diagnosis of constrictive pericarditis [11, 30]. In these studies, as underlying tuberculosis was ruled out in nearly all cases, the pericardial calcification most likely represent nonspecific response to chronic inflammation. Although pericardial calcification may only be present in approximately one third of the patients with constrictive pericarditis, when present in the appropriate clinical scenario, it is highly suggestive of the diagnosis of constrictive pericarditis.

CCT (Fig. 7.5) plays an important role in the diagnosis and management of constrictive pericarditis as it is a very reliable method to evaluate pericardial thickness. It is also the most accurate method to detect even minute amounts of pericardial calcification. Pericardial enhancement on postcontrast CCT indicates inflammation, which can be useful in patients without pericardial thickening or lack of pericardial calcification. In addition, CCT can help visualize associated complications such as the intramyocardial extent of the fibrocalcific process, which can affect the success of a planned surgical pericardiectomy. By identifying critical vascular structures with a detailed depiction of both the severity of thickening and the presence and location of calcifications, preoperative CCT facilitates better surgical planning and stratification of procedural risk.

Since the pericardium is outlined by fat and lung tissue, CMR (Fig. 7.7) can provide an accurate measurement of pericardial thickness with a reported accuracy of 93 % when the pericardium is >4 mm thick. CMR has also been shown to be better than CCT at differentiating between pericardial fluid and thickened pericardium [2, 9]. The thickened fibrotic and/or calcified pericardium appears as a dark, low signal intensity signal stripe with occasional focal or diffuse, irregular, fibrocalcific changes on T1-weighted and T2-weighted CMR images and at cine imaging [2, 8, 13]. In healthy persons, the pericardium moves synchronous with the cardiac cycle, whereas in patients with underlying constriction, there is tethering and restricted ventricular expansion adjacent to the thickened pericardial areas [8, 13]. Consequently, the pericardial motion with the cardiac cycle may be reduced or even absent, while the systolic myocardial contraction is usually normal. These findings can be easily visualized using tagging. In healthy persons, because of the free motion of the pericardium during the cardiac cycle, the tag lines are typically displaced, whereas in patients with pericardial constriction, the tag lines are stretched and fail to break because of restricted motion between the pericardial layers. Commonly during gadolinium contrast–enhanced CMR of the pericardium in patients with constrictive pericarditis, there is delayed gadolinium enhancement suggestive of residual inflammation [2, 21]. However, this is not a universal finding, as during the end stages of chronic fibrosing forms of constrictive pericarditis, there is no enhancement after contrast material administration [2]. When residual inflammation is visualized, there is likelihood that these patients will respond to anti-inflammatory treatment and may not be good candidates for pericardiectomy [2, 13, 30].

## Functional and Hemodynamic Consequences

The encasement of the heart by a noncompliant, rigid pericardium leads to multiple functional abnormalities, including, dissociation between intrathoracic and intracardiac pressures which isolates the heart from normal respiratory changes in intrathoracic pressures. This leads to increased cardiac filling pressures with equalization of end-diastolic pressures in all four cardiac chambers, increased ventricular coupling influenced by respiration, elevated systemic venous pressures, and low cardiac output. The underlying cardiac cavities may be constricted by the abnormal pericardium, having a flattened or tubular-shaped appearance with distortion of the ventricular septum. The septum itself becomes flattened or sigmoid in shape during diastole and can exhibit the phenomenon of septal bounce. With long-standing constriction, the ventricles may appear conical. As a result of the increased cardiac filling pressures, there may be unilateral or bilateral atrial enlargement, dilatation of the superior- and inferior vena cavae and hepatic veins, pleural effusion, and ascites. In the superior vena cava and inferior vena cava, the systolic flow is decreased, absent, or reversed, but in diastole, forward flow is increased with increased late backflow. The tricuspid valve inflow may show a restrictive filling pattern of enhanced early filling and decreased or absent late filling, depending on the degree of pericardial constriction and increased filling pressures. While only a limited amount of functional and hemodynamic information can be obtained from CCT, CMR is an

excellent functional modality which allows the detection of hemodynamic features of constriction on real-time cine sequences.

## Effusive Constrictive Pericarditis

Effusive constrictive pericarditis is a rare syndrome in which there is tamponade caused by tense effusion and constriction caused by an inflamed and noncompliant visceral pericardium. It is believed that effusive-constrictive pericarditis most likely represents an intermediate transition from acute pericarditis with pericardial effusion to pericardial constriction [27]. Consequently, it is a distinct entity with transitional and overlapping pathophysiologic features of acute effusive pericarditis with associated cardiac tamponade and chronic constrictive pericarditis. In effusive constrictive pericarditis, even after the removal of pericardial fluid, the constriction is not relieved [2]. The diagnosis of effusive-constrictive pericarditis is often challenging because the morphologic abnormalities, even at visual inspection, are not impressive. The findings on CCT and CMR represent an overlap of acute pericardial effusion and constrictive pericarditis. These include thickening of the pericardium, associated pericardial effusion, pericardial inflammation, ventricular interdependence and associated flattening or inversion of septum. These patients report improvement of symptoms, either spontaneously or respond to anti-inflammatory drugs.

## Tuberculous Disease of the Pericardium

While the incidence of tuberculous pericarditis has dramatically decreased in the developed world, its incidence is still very high in the developing world [31]. It is a serious condition because of the high incidence of progression to constrictive pericarditis and high mortality rates. Tuberculous involvement of pericardium can manifest in various forms including, pericardial effusion, constrictive pericarditis, pericardial tamponade as a complication of constrictive pericarditis, and pericardial abscess [19]. Based on the underlying manifestation, the chest x-ray may show pericardial fluid collection, pericardial calcification, and associated lung and mediastinal involvement. However, thinning of the pericardium is not commonly observed with tuberculosis. CCT demonstrate pericardial thickening, pericardial fluid collection, or concurrent tuberculosis in the lungs or mediastinum. CCT can also help identify constrictive pericarditis, by depicting the constellation of findings, including, pericardial thickening, effusion, lymphadenopathy and calcification. This calcification tends to be irregular, thick, amorphous and occurs predominantly in the AV grooves [11]. On T1-weighted images of CMR, the pericardium may show signal intensity similar to the myocardium while low signal intensity lesions can be seen on the inner surface of the thickened pericardium. These low signal intensity signals are the combination of residual ferromagnetic elements after hemorrhage in the pericardial space with fibrosis of the pericardium. On delayed gadolinium enhancement studies, uniform tramline-like hyperenhancement was noted at the site of fibrous hypertrophic parietal and visceral pericardium [32].

## Pericardial Masses

Pericardial masses represent a heterogeneous group of cystic lesions, hematomas, complex organized effusions, masslike structures, and primary and secondary malignancies that affect or involve the pericardium. CT and MR imaging are often necessary in the diagnostic workup, because they provide an accurate description of the pericardial abnormalities and the relationship to the surrounding structures and facilitate understanding of the underlying cause, establishment of the differential and final diagnosis, and assessment of complications such as cardiac tamponade.

## Cysts and Diverticula

Pericardial cysts are uncommon and generally benign lesions. While most pericardial cysts are

congenital defects, rarely they may also be acquired e.g. hydatid cyst. Congenital pericardial cysts are the most common benign pericardial mass [12]. Pericardial cysts are developmental abnormalities caused by the pinching-off of a blindly ending parietal pericardial recess. The right cardiophrenic angle is the most common location (80 %) [33]. Pericardial cysts usually have thin, smooth walls without internal septations. They attach to the pericardium directly or by a pedicle [12]. A pericardial diverticulum has an origin similar to that of a pericardial cyst, but unlike a cyst, a pericardial diverticulum communicates with the pericardial cavity; as a result, the wall is incomplete on the medial aspect [34, 35]. Pericardial diverticula are clinically identical to cysts, and if present in an unusual location, can be hard to distinguish from bronchogenic or thymic cysts [36]. A pericardial cyst may be initially suspected because of an abnormal chest x-ray. On chest x-ray, cysts are typically seen as a mass at the cardiophrenic sulcus [36]. They can be variable size and shape and may not always be round or oval. In addition, they may change in shape and size with respiratory maneuvers and change in position. CCT can confirm the diagnosis of a pericardial cyst and diverticula by demonstrating the position and extent of the lesion; fluid density and characterization of the mass. Their attenuation is slightly higher than water (30–40 Hounsfield units), with no enhancement after the administration of intravenous contrast [36]. CMR demonstrates well-defined and sharply marginated, homogeneous unilocular cyst or diverticula, with low signal on T1-weighted images and homogeneously high signal on T2-weighted images with no contrast enhancement with intravenous gadolinium. Rarely, if the cystic fluid has a high proteinaceous content, the T1 weighted images may have a high signal, and very rarely a loculated margin may be seen [2, 8].

## Hematomas

Pericardial hematoma is rare and typically follows cardiac surgery, pericardiocentesis, chest trauma, or epicardial injury. On CXR, there may be paracardiac enlargement and if the hematoma is old and organized, calcifications may be visualized. The CCT and CMR imaging characteristics of a pericardial hematoma depend on the age of the blood collection. On CCT, initially, the hematoma is of high attenuation. Over a period of time this attenuation decreases, and gradually organizes and can become fibrotic with calcification. Hematomas do not enhance with intravenous contrast [11]. On CMR imaging, in the acute phase, the hematoma has a homogeneously high signal, while in the subacute phase, it has heterogeneous high signal on T1- and T2-weighted sequences [37]. In the chronic phase, a low signal with a dark rim is seen [38, 39]. No delayed contrast enhancement is seen with gadolinium administration. This lack of delayed enhancement can help distinguish coronary or ventricular pseudoaneurysm from hematomas. Additionally, internal flow in pseudoaneurysms can be detected using velocity-encoded cine MR imaging [40].

## Neoplasms

Primary pericardial tumors are very rare and, when found, are more often benign. Benign pericardial primary tumors include lipoma, teratoma, fibroma, hemangioma, and lymphangioma. Malignant mesothelioma is the most common malignant primary pericardial lesion [41, 42]. Other primary malignant tumors include malignant fibrosarcoma (Fig. 7.10), angiosarcoma, and malignant teratoma. Secondary pericardial tumors due to either local invasion from neighboring organs or metastases are much more common. Secondary pericardial tumors most frequently occur from lymphoma, melanoma, as well as lung and breast carcinoma [43].

The chest x-ray may show mediastinal widening, hilar masses and concomitant mediastinal and pulmonary masses with pleural effusions. CCT and CMR can provide valuable information about the morphology, location, and extent of a pericardial neoplasm. Benign pericardial masses may grow to sizable lesions before they produce compression of cardiac chambers or displacement

of mediastinal structures. Benign tumors can be found in both the parietal pericardium and epicardium as discrete pedunculated or sessile masses. Malignant neoplasms are usually characterized by the presence of pericardial masses, nodular lesions or plaques, or by a variable amount of a complex hemorrhagic effusion that is disproportionally greater than the size of the solid lesion [44].

CCT is superior to CMR in identifying other thoracic lesions, including primary lung cancer, pulmonary metastases, and mediastinal lymph nodes. On CCT, benign tumors of the pericardium including lipomas, usually demonstrate low-attenuation fat (i.e., negative Hounsfield units), and teratomas present as masses containing both fat and high-attenuating calcium. On the other hand, pericardial malignancy may appear as a mass in the pericardium, an irregular, thickened nodular pericardium with a complex pericardial effusion; and/or pericardial enhancement after intravenous contrast administration. Also, certain imaging features like disruption of the pericardial sac; presence of hemorrhagic effusion; invasion into the epicardial fat tissue, myocardium, or a cardiac chamber; and mediastinal adenopathy, can help identify aggressive malignancies [10, 44].

Similar to CCT, CMR can help accurately delineate the tumor implantation and determine its relation to contiguous anatomical structures. Although tissue characterization in pericardial tumor evaluation by CMR is superior to that of echocardiography and CCT, the tissue characterization of pericardial tumor is often difficult as they usually have intermediate signal on T1-weighted images and high signal on T2-weighted images. However, there are certain exceptions, including lipoma and liposarcoma which appear with high signal intensity due to their fatty content. With contrast administration, hemangiomas exhibit enhancement which is heterogeneous and intense except in low-flow lesions. Pericardial metastases are usually seen as a large hemorrhagic pericardial effusion with irregular or nodular pericardial thickening, and associated nodules or masses. Melanoma metastases can be characterized because they have high signal on T1-weighted images. Increased tissue edema in malignant pericardial tumors is typically manifested by increased signal on either T2-weighted images or Short T1 inversion recovery images [10].

## Miscellaneous

In patients with a prior cardiac surgery, the differential diagnoses of a pericardial gossypiboma or foreign body granuloma (e.g., surgical sponge) should always be considered [45]. Pericardial fat necrosis is a benign entity of unknown cause which typically manifests with sudden onset of chest pain. On CCT, the lesion appears as an encapsulated region of fat attenuation with dense strands surrounded by the increased attenuation of the anterior mediastinal paracardiac fat and thickening of the adjacent pericardium [46]. The CMR findings are variable and depend on the pathologic stages of fat necrosis. On the T1- and T2-weighted images, in the acute stage, there may be a peripheral rim and central dot-and-line of low signal intensity, while the postgadolinium T1-weighted fat suppression images show increased enhancement of the rim. In the chronic stage, both central globular and peripheral rim enhancements may be observed [47].

## Congenital Absence of Pericardium (Fig. 7.11)

Congenital absence of the pericardium is a rare anomaly. It encompasses a range of congenital pericardial defects from a small foramen in the pericardium to a complete absence of the entire pericardium. Congenital absence is typically partial, but occasionally it is complete. It may be associated with other congenital cardiac malformations such as atrial septal defect; tetralogy of Fallot; patent ductus arteriosus; mitral stenosis; and malformations of the lung, chest wall, and diaphragm [48]. Cardiac structures or portions of the lung can herniate through these defects. On chest radiographs, a left-sided pericardial defect causes typical levodisplacement of the heart and aortic knob, with the trachea remaining at the midline.

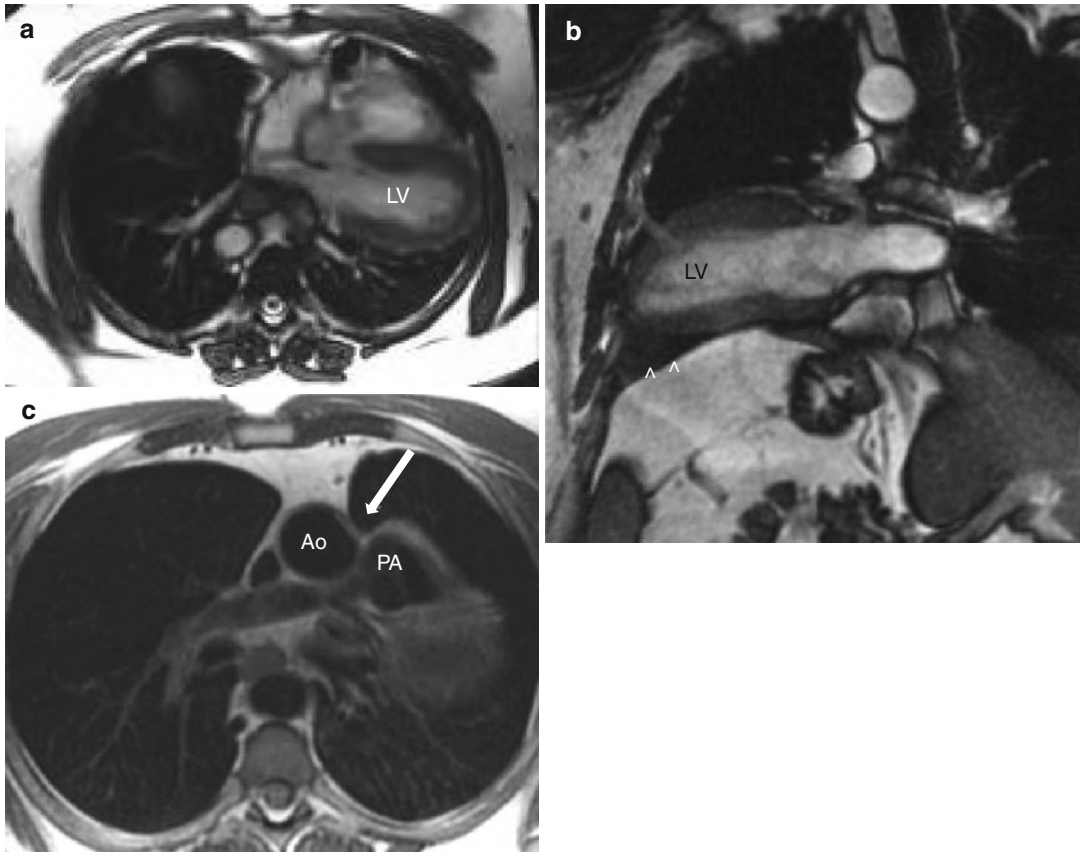


**Fig. 7.11** (**a**) Transaxial gradient echo MRI images of the heart in the horizontal long axis of the left ventricle (*LV*) with the patient in the supine position show a prominent leftward shift of the heart in this patient found to have congenital absence of the pericardium. (**b**) Sagittal gradient echo MRI image of the patient in Fig. 7.11a showing interposition (*arrowheads*) of the lung between the inferior portion of the left ventricle (*LV*) and the diaphragm as seen in patients with congenital absence of the pericardium. (**c**) Transaxial spin-echo MRI sequence of the patient in Fig. 7.11a showing interposition (*arrow*) of the lung between the aorta (*Ao*) and the pulmonary artery (*PA*) as seen in patients with congenital absence of the pericardium

At CCT and CMR (Fig. 7.11), there may be absence of the entire pericardium or a portion of it. However, either finding alone is not sufficient to make a diagnosis of congenital absence because in patients with minimal epicardial and pericardial fat, the pericardium lies almost immediately on the myocardium, and differentiation between myocardium and pericardium can be challenging [49]. The diagnosis therefore usually relies on several indirect morphologic signs such as an abnormal location of cardiac structures with excessive levorotation or cardiac indentation at the location of the defect [50, 51]. The interposition of lung tissue in spaces typically covered by the pericardium, including, aorta and pulmonary artery or between the diaphragm and the base of the heart is a very specific sign [52]. A diagnosis of congenital absence should not be made without mediastinal shift or regional bulging. Since herniation is often intermittent in time, positional changes such as to positioning the patient in the left lateral decubitus can be helpful in diagnosing pericardial defects.

## Conclusion

Accurate diagnosis of pericardial diseases is challenging and requires an integration of medical history, physical examination, laboratory testing and integrally, imaging. With the rapid advances in cardiac imaging, especially CCT and CMR, multimodality noninvasive cardiac imaging has earned a central role in the diagnosis and management of various pericardial conditions particularly when the clinical findings are equivocal or nondiagnostic.

## References


1. Jung W, Zvereva V, Hajredini B, Jackle S. Safe magnetic resonance image scanning of the pacemaker patient: current technologies and future directions. Europace. 2012;14:631–7.
2. Bogaert J, Francone M. Cardiovascular magnetic resonance in pericardial diseases. J Cardiovasc Magn Reson. 2009;11:14.
3. Wang ZJ, Reddy GP, Gotway MB, Yeh BM, Hetts SW, Higgins CB. CT and MR imaging of pericardial disease. Radiographics. 2003;23 Spec No:S167–80.
4. Spodick DH. Macrophysiology, microphysiology, and anatomy of the pericardium: a synopsis. Am Heart J. 1992;124:1046–51.
5. Rabkin SW. Epicardial fat: properties, function and relationship to obesity. Obes Rev. 2007;8:253–61.
6. Hsu YM, Yao NS, Liu JM. Steroid-induced mediastinal lipomatosis with radiographic features of pericardial effusion. Am J Emerg Med. 2000;18:346–8.
7. Bull RK, Edwards PD, Dixon AK. CT dimensions of the normal pericardium. Br J Radiol. 1998;71:923–5.
8. Klein AL, Abbara S, Agler DA, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013;26:965–1012.e15.
9. Verhaert D, Gabriel RS, Johnston D, Lytle BW, Desai MY, Klein AL. The role of multimodality imaging in the management of pericardial disease. Circ Cardiovasc Imaging. 2010;3:333–43.
10. O'Donnell DH, Abbara S, Chaithiraphan V, et al. Cardiac tumors: optimal cardiac MR sequences and spectrum of imaging appearances. AJR Am J Roentgenol. 2009;193:377–87.
11. O'Leary SM, Williams PL, Williams MP, et al. Imaging the pericardium: appearances on ECG-gated 64-detector row cardiac computed tomography. Br J Radiol. 2010;83:194–205.
12. Smith WH, Beacock DJ, Goddard AJ, Bloomer TN, Ridgway JP, Sivananthan UM. Magnetic resonance evaluation of the pericardium. Br J Radiol. 2001;74:384–92.
13. Cardiac RP. Cardiac MRI: part 2, pericardial diseases. AJR Am J Roentgenol. 2011;197:W621–34.
14. Merce J, Sagrista-Sauleda J, Permanyer-Miralda G, Evangelista A, Soler-Soler J. Correlation between clinical and Doppler echocardiographic findings in patients with moderate and large pericardial effusion: implications for the diagnosis of cardiac tamponade. Am Heart J. 1999;138:759–64.
15. DeCamp Jr MM, Mentzer SJ, Swanson SJ, Sugarbaker DJ. Malignant effusive disease of the pleura and pericardium. Chest. 1997;112:291S–5.
16. Eisenberg MJ, Dunn MM, Kanth N, Gamsu G, Schiller NB. Diagnostic value of chest radiography for pericardial effusion. J Am Coll Cardiol. 1993;22:588–93.
17. Troughton RW, Asher CR, Klein AL. Pericarditis. Lancet. 2004;363:717–27.
18. Sun JS, Park KJ, Kang DK. CT findings in patients with pericardial effusion: differentiation of malignant and benign disease. AJR Am J Roentgenol. 2010;194:W489–94.
19. Roberts WC. Pericardial heart disease: its morphologic features and its causes. Proc (Bayl Univ Med Cent). 2005;18:38–55.
20. Meziane MA, Fishman EK, Siegelman SS. CT diagnosis of hemopericardium in acute dissecting aneurysm of the thoracic aorta. J Comput Assist Tomogr. 1984;8:10–4.
21. Zurick AO, Bolen MA, Kwon DH, et al. Pericardial delayed hyperenhancement with CMR imaging in patients with constrictive pericarditis undergoing surgical pericardiectomy: a case series with histopathological correlation. JACC Cardiovasc Imaging. 2011;4:1180–91.
22. Hoey ET, Gulati GS, Ganeshan A, Watkin RW, Simpson H, Sharma S. Cardiovascular MRI for assessment of infectious and inflammatory conditions of the heart. AJR Am J Roentgenol. 2011;197:103–12.
23. Feng D, Glockner J, Kim K, et al. Cardiac magnetic resonance imaging pericardial late gadolinium enhancement and elevated inflammatory markers can predict the reversibility of constrictive pericarditis after antiinflammatory medical therapy: a pilot study. Circulation. 2011;124:1830–7.
24. Cummings KW, Bhalla S, Javidan-Nejad C, Bierhals AJ, Gutierrez FR, Woodard PK. A pattern-based approach to assessment of delayed enhancement in nonischemic cardiomyopathy at MR imaging. Radiographics. 2009;29:89–103.
25. Young PM, Glockner JF, Williamson EE, et al. MR imaging findings in 76 consecutive surgically proven cases of pericardial disease with CT and pathologic correlation. Int J Cardiovasc Imaging. 2012;28:1099–109.
26. Taylor AM, Dymarkowski S, Verbeken EK, Bogaert J. Detection of pericardial inflammation with late-enhancement cardiac magnetic resonance imaging: initial results. Eur Radiol. 2006;16:569–74.

27. Little WC, Freeman GL. Pericardial disease. Circulation. 2006;113:1622–32.
28. Oh KY, Shimizu M, Edwards WD, Tazelaar HD, Danielson GK. Surgical pathology of the parietal pericardium: a study of 344 cases (1993–1999). Cardiovasc Pathol. 2001;10:157–68.
29. Talreja DR, Edwards WD, Danielson GK, et al. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. Circulation. 2003; 108:1852–7.
30. Ling LH, Oh JK, Schaff HV, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. Circulation. 1999;100:1380–6.
31. Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. Circulation. 2005;112:3608–16.
32. Hayashi H, Kawamata H, Machida M, Kumazaki T. Tuberculous pericarditis: MRI features with contrast enhancement. Br J Radiol. 1998;71:680–2.
33. Breen JF. Imaging of the pericardium. J Thorac Imaging. 2001;16:47–54.
34. Akiba T, Marushima H, Masubuchi M, Kobayashi S, Morikawa T. Small symptomatic pericardial diverticula treated by video-assisted thoracic surgical resection. Ann Thorac Cardiovasc Surg. 2009;15: 123–5.
35. Sechtem U, Tscholakoff D, Higgins CB. MRI of the abnormal pericardium. AJR Am J Roentgenol. 1986;147:245–52.
36. Jeung MY, Gasser B, Gangi A, et al. Imaging of cystic masses of the mediastinum. Radiographics. 2002;22 Spec No:S79–93.
37. Seelos KC, Funari M, Chang JM, Higgins CB. Magnetic resonance imaging in acute and subacute mediastinal bleeding. Am Heart J. 1992;123: 1269–72.
38. Brown DL, Ivey TD. Giant organized pericardial hematoma producing constrictive pericarditis: a case report and review of the literature. J Trauma. 1996; 41:558–60.
39. Ferguson ER, Blackwell GG, Murrah CP, Holman WL. Evaluation of complex mediastinal masses by magnetic resonance imaging. J Cardiovasc Surg (Torino). 1998;39:117–9.
40. Higgins CB, Sakuma H. Heart disease: functional evaluation with MR imaging. Radiology. 1996;199: 307–15.
41. Restrepo CS, Vargas D, Ocazionez D, Martinez-Jimenez S, Betancourt Cuellar SL, Gutierrez FR. Primary pericardial tumors. Radiographics. 2013;33: 1613–30.
42. Kaul TK, Fields BL, Kahn DR. Primary malignant pericardial mesothelioma: a case report and review. J Cardiovasc Surg (Torino). 1994;35:261–7.
43. Luk A, Ahn E, Vaideeswar P, Butany JW. Pericardial tumors. Semin Diagn Pathol. 2008;25:47–53.
44. van Beek EJ, Stolpen AH, Khanna G, Thompson BH. CT and MRI of pericardial and cardiac neoplastic disease. Cancer Imaging. 2007;7:19–26.
45. Coskun M, Boyvat F, Agildere AM. CT features of a pericardial gossypiboma. Eur Radiol. 1999;9: 728–30.
46. Pineda V, Caceres J, Andreu J, Vilar J, Domingo ML. Epipericardial fat necrosis: radiologic diagnosis and follow-up. AJR Am J Roentgenol. 2005;185:1234–6.
47. Lee HH, Ryu DS, Jung SS, Jung SM, Choi SJ, Shin DH. MRI findings of pericardial fat necrosis: case report. Korean J Radiol. 2011;12:390–4.
48. Van Son JA, Danielson GK, Schaff HV, Mullany CJ, Julsrud PR, Breen JF. Congenital partial and complete absence of the pericardium. Mayo Clin Proc. 1993;68:743–7.
49. Schiavone WA, O'Donnell JK. Congenital absence of the left portion of parietal pericardium demonstrated by nuclear magnetic resonance imaging. Am J Cardiol. 1985;55:1439–40.
50. Topilsky Y, Tabatabaei N, Freeman WK, Saleh HK, Villarraga HR, Mulvagh SL. Images in cardiovascular medicine. Pendulum heart in congenital absence of the pericardium. Circulation. 2010;121:1272–4.
51. Psychidis-Papakyritsis P, de Roos A, Kroft LJ. Functional MRI of congenital absence of the pericardium. AJR Am J Roentgenol. 2007;189:W312–4.
52. Gatzoulis MA, Munk MD, Merchant N, Van Arsdell GS, McCrindle BW, Webb GD. Isolated congenital absence of the pericardium: clinical presentation, diagnosis, and management. Ann Thorac Surg. 2000; 69:1209–15.

## Multimodality Imaging (X-Ray, CT, and MRI) in Pericardial Disease-For Patients and their Families

Assessing the diseases of the pericardium can be a challenging task, and non-invasive imaging modalities (not requiring introduction of instruments inside the body) of testing have gradually become an important part of assessing the pericardium. The imaging modalities include, echocardiogram, chest x-ray, cardiac CT scan and cardiac MRI. It is important to realize that most of these tests provide information complimentary to each other, and depending upon the acuity of illness, one or more tests may be performed to provide adequate care to the patient.

Chest x-rays are often the initial imaging test performed on most patients, to get an overall assessment of the heart and lungs. It is often findings on the chest x-ray, which raise the suspicion of underlying pericardial involvement.

The chest x-ray has multiple advantages, including easy availability, low cost, and low radiation exposure. Although more detailed tests need to be undertaken to evaluate the underlying extent and cause of pericardial involvement, distinct findings on chest x-ray can help identify pericardial conditions, including, pericardial effusion (collection of fluid in the pericardial space), and pericardial masses. In patients with underlying pericardial masses, (e.g. collection of blood (hematoma), benign and malignant tumors, and cysts), while the x-ray can occasionally provide clues about some underlying abnormality, cardiac CT and cardiac MR are utilized to provide more detailed information, including size and composition of these masses.

Cardiac CT (cardiac computed tomography) is a type of x-ray which takes detailed pictures of the heart and pericardium. It combines a series of x-ray views taken from many different angles, and these images are processed by the computer to make a three-dimensional (3D) picture of the whole heart. As compared to routine chest x-ray, the images obtained from cardiac CT are of superior quality and provide more detailed information, especially about the structure of the heart and pericardium. In addition, since it also acquires pictures of the surrounding structures, including the lungs, it can also visualize any disease process or changes in these structures.

During the cardiac CT scan, a doughnut-shaped x-ray machine moves around the body in a circle. Occasionally an iodine-based dye (contrast dye) is injected into one of the veins (contrast CT scan), which highlights the coronary arteries and the pericardium under certain conditions. Because an x-ray machine is used, cardiac CT involves radiation. However, the amount of radiation used is considered small, which is similar to the amount of radiation you are naturally exposed to over 1–5 years, depending upon the type of cardiac CT performed.

In patients with underlying involvement of the pericardium, the cardiac CT scan is especially useful to detect increased pericardial thickness and calcification. In pericardial effusion, cardiac CT can provide an estimate of the amount of accumulated fluid, and also help characterize the accumulated fluid, which can occasionally help identify the underlying cause of fluid accumulation. In patients with inflammation of the pericardium (pericarditis), the cardiac CT can identify the underlying thickening of the pericardium, especially with contrast cardiac CT.

Similar to cardiac CT, cardiac MRI (magnetic resonance imaging) is a non-invasive diagnostic tool, which is being increasingly utilized for the diagnosis of diseases involving the pericardium. MRI uses powerful magnets and radio waves to create a magnetic field. This magnetic field is produced by passing an electric current through wire coils. Simultaneously, other coils, located in the machine and in some cases, placed around the part of the body being imaged, send and receive radio waves, producing signals that are detected by the coils. Under the influence of this magnetic field, the body produces a weak signal, which is produced by the redirection of the axes of spinning protons, which are the nuclei of hydrogen atoms. While initially these signals are weak, these signals are recorded by the coils, and subsequently processed to provide detailed images of the heart. To visualize the heart and pericardium

better, a small amount of MRI dye (gadolinium) is occasionally injected into a vein.

As compared to cardiac CT which provides information mainly about the structure of the heart and pericardium, the cardiac MR not only provides more detailed information about the structure of the heart and pericardium, but also invaluable information about the physiology (mechanism of working) of the heart.

Although cardiac MRI is a painless and non-invasive test which provides valuable information, it is relatively expensive and may not be readily available at all centers.

Similar to cardiac CT, cardiac MRI can help characterize the pericardial fluid and help identify the cause of fluid accumulation. By providing valuable information about the cardiac physiology, it can help identify if the accumulated fluid is putting pressure on the heart (cardiac tamponade). In pericarditis, by using various imaging sequences, especially with the help of gadolinium, cardiac MRI provides information about the thickening of pericardium, associated inflammation, and helps distinguish between acute inflammation as compared to chronic inflammation. In patients with constrictive pericarditis, the cardiac MRI also provides a non-invasive method of identifying the physiological and hemodynamic effect of the pericardium on the functioning of the heart.

# Part II

# Management of Pericardial Disease

# Acute and Recurrent Pericarditis

8

Massimo Imazio

## For Physicians and Healthcare Providers

### Epidemiology and Impact

Acute and recurrent pericarditis are the most common disorders involving the pericardium. There are few available epidemiological data and the exact incidence and prevalence of acute and recurrent pericarditis are unknown. However, acute pericarditis is recorded in about 0.1 % of hospitalized patients and 5 % of patients admitted to the Emergency Department for non-ischemic chest pain [1, 2]. In an observational study from an urban area in Northern Italy the incidence of acute pericarditis was 27.7 cases per 100,000 persons per year [3].

Recurrences affect about one third of patients with a first attack of acute pericarditis and one half of those with a first recurrence when treated with conventional anti-inflammatory therapy without colchicine [4, 5].

### Definitions

Acute pericarditis is the acute inflammation of the pericardium that may be due to infectious or non-infectious causes. Recurrent pericarditis is the recurrence of symptoms and/or signs of pericarditis after the remission of the first attack of pericarditis and an arbitrary symptom-free interval of 6 weeks [5, 6]. The term "incessant pericarditis" is adopted for cases without resolution of signs and symptoms of pericarditis and a symptom-free interval of less than 6 weeks [5, 6]. The term "chronic" pericarditis is considered, as for pericardial effusions, with a disease persisting for >3 months [7].

### Etiology

Pericarditis may be caused by infectious or non-infectious agents (Table 8.1). The etiology of pericarditis is varied and pericarditis can occur as isolated disease or a manifestation of a systemic disease (i.e. a systemic inflammatory disease). The etiology that can be found in a specific setting depends on the epidemiological background. Tuberculosis is the leading cause of pericardial diseases as well as pericarditis all over the world, being the most important etiology in developing countries where tuberculosis is endemic and often associated with HIV infection [8]. On the contrary, tuberculosis is reported in <5 % of cases in Western Europe and North America [9, 10]. Nevertheless immigration may contribute to a future increase of cases related to tuberculosis.

Current diagnostic criteria do not allow the identification of the cause in more than two thirds of patients in Western Europe and North America.

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**Table 8.1** Etiology of pericarditis

| |
|---|
| **Infectious causes (>2/3 of cases)** |
| ***Viral*** (especially enteroviruses, adenoviruses, EBV, CMV, parvovirus, HCV, HIV) |
| ***Bacterial*** (especially tuberculosis) |
| Other (rare): fungal (rare; histoplasma more likely in immunocompetent patients; aspergillosis, blastomycosis, candida more likely in immunosuppressed host). Parasitic (very rare; echinococcus, toxoplasma) |
| **Non-infectious causes (about 1/3 of cases)** |
| ***Systemic inflammatory diseases*** (especially: systemic lupus erythematosus, Rheumathoid arthritis, scleroderma, Sjogren syndrome, Behcet syndrome) |
| Autoinflammatory diseases (especially familial mediterranean fever, TRAPS) |
| ***Post-cardiac injury syndromes*** (post-pericardiotomy syndrome, post-myocardial infarction, post-traumatic following any kind of interventional cardiovascular procedure, irradiation or accidental trauma) |
| ***Neoplastic diseases*** (especially secondary to lung and breast cancer or lymphomas, rarely as primary tumours of the pericardium, especially pericardial mesothelioma) |
| ***Drugs or toxic agents*** (rare): procainamide, hydralazine, isoniazid, and phenytoin (lupus-like syndrome), penicillins (hypersensitivity pericarditis with eosinophilia), doxorubicin, and daunorubicin (often associated with a cardiomyopathy; may cause a pericardiopathy) |

In developed countries such cases are supposed to be viral or post-viral and named as "idiopathic".

## Diagnosis and Workup

The diagnosis of acute pericarditis is based on clinical criteria. Patients with an infectious etiology may present with signs and symptoms of systemic infection such as fever and leukocytosis. Viral etiologies in particular may be preceded by "flu-like" respiratory or gastrointestinal symptoms. Patients with a known autoimmune disorder or malignancy may present with signs or symptoms specific to their underlying disorder.

The major clinical manifestations of acute pericarditis include:

- Chest pain in >90 % of cases – typically sharp and pleuritic, improved by sitting up and leaning forward
- Pericardial friction rub in 25–33 % of cases – a superficial scratchy or squeaking sound best heard with the diaphragm of the stethoscope over the left sternal border
- Electrocardiogram (ECG) changes – new widespread ST elevation or PR depression in 50–60 % of cases
- Pericardial effusion in >60 % of cases

The diagnosis of acute pericarditis is reached with at least two of four of these clinical manifestations [1, 5].

Criteria for the diagnosis of recurrent pericarditis [4] include a documented first attack of acute pericarditis, according to previously stated diagnostic criteria; a symptom-free interval of 6 weeks or longer; and evidence of subsequent recurrence of pericarditis. Patients with persistent pericarditis or those with a symptom-free interval of less than 6 weeks should be given the diagnosis of incessant pericarditis [5, 6].

Recurrence is documented by recurrent pain and one or more of the following signs:

- a pericardial friction rub,
- changes on electrocardiography (ECG),
- echocardiographic evidence of pericardial effusion, and
- an elevation in the white-cell count, erythrocyte sedimentation rate, or C-reactive protein level

Specific features at presentation suggest an increased risk of a non-idiopathic, non-viral etiology and possible complications during follow-up [11]. These features include: fever >38 °C, subacute course, large effusion or cardiac tamponade, and failure of aspirin or of nonsteroidal anti-inflammatory drugs. Patients without high risk features may be managed as outpatient (Fig. 8.1) [12–14].

Initial evaluation of an patient with a acute or recurrent pericarditis include first, the initial history and physical examination – This evaluation should consider disorders that are known to involve the pericardium, such as prior malignancy, autoimmune disorders, uremia, recent myocardial infarction, and prior cardiac surgery. The examiner should pay particular attention to

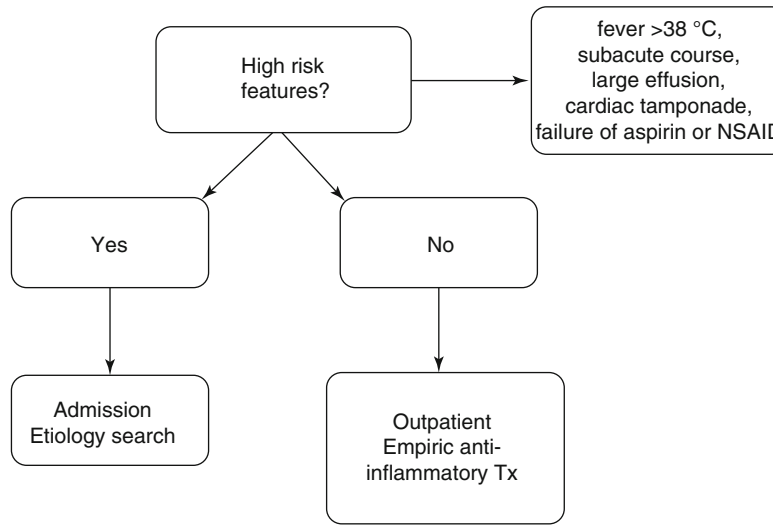


**Fig. 8.1** Triage of pericarditis (see text for explanation)

auscultation for a pericardial friction rub and the signs associated with tamponade.

Subsequent testing [12, 13] should include:

- Complete blood count, troponin level, erythrocyte sedimentation rate or serum C-reactive protein level, an electrocardiogram, echocardiography, and chest x-ray in all cases.
- Blood cultures if fever higher than 38 °C (100.4 °F) or signs of sepsis.
- Tuberculin skin test or an interferon-gamma release assay (e.g, QuantiFERON TB assay) if not recently performed. The interferon-gamma release assay is most helpful in immunocompromised or HIV positive patients and in regions where tuberculosis is endemic.
- Antinuclear antibody (ANA) titer in selected cases (eg, young women, especially those in whom the history suggests a rheumatologic disorder). Rarely, acute pericarditis is the initial presentation of a systemic inflammatory disease (SID), i.e. systemic lupus erythematosus (SLE). It is important to recognize that a positive ANA is a non-specific test. A rheumatology consult should be sought in patients with pericarditis in whom a diagnosis of a SID is suspected.
- HIV serology
- Computed tomography (CT) may be useful to confirm the diagnosis and especially evaluate concomitant pleuropulmonary diseases and lymphadenopathies, thus suggesting a possible etiology of pericarditis (i.e. TB, lung cancer). Non-calcified pericardial thickening with pericardial effusion is suggestive of acute pericarditis. Moreover, with the administration of iodinated contrast media, enhancement of the thickened visceral and parietal surfaces of the pericardial sac confirms the presence of active inflammation. Computed tomographic attenuation values can help in the differentiation of exudative fluid (20–60 Hounsfield units), as found with purulent pericarditis, and simple transudative fluid (<10 Hounsfield units).
- Cardiac magnetic resonance imaging may be performed if the echocardiogram is unrevealing but the diagnosis of acute pericarditis is suspected, especially in patients with ongoing fever, poor response to treatment, or suspicion of hemodynamic compromise [15].

Echocardiography should be performed in all cases, with urgent echocardiography if cardiac tamponade is suspected. Even a small effusion can be helpful in confirming the diagnosis of pericarditis, although the absence of an effusion does not exclude the diagnosis. In addition, echocardiography can be particularly helpful if purulent pericarditis is suspected, if there is concern about myocarditis, or if there is radiographic evidence of cardiomegaly, particularly if this is a new finding.

The 2003 American College of Cardiology/American Heart Association/American Society of Echocardiography (ACC/AHA/ASE) guidelines for the clinical application of echocardiography stated that evidence and/or general agreement supported the use of echocardiography for the evaluation of all patients with suspected pericardial disease [16]. Similarly, a 2013 expert consensus statement from the ASE recommends echocardiography for all patients with acute pericarditis [15].

Multimodality imaging is an integral part of modern management for pericarditis and pericardial diseases. Among multimodality imaging tests, echocardiography is most often the first-line test, followed by CMR and/or CT [15].

Viral studies are not cost-effective, since the yield is low and management is not altered [17].

Pericardiocentesis should be performed for therapeutic purposes in patients with cardiac tamponade and diagnostic purposes when a bacterial or neoplastic etiology is suspected and not assessed by other diagnostic means. In fact, the definite diagnosis of such etiologies relies on the demonstration of the etiological agent in the pericardial fluid or tissue [13]. Persistent symptomatic disease >3 weeks may warrant a pericardial biopsy.

## Management

Medical treatment of pericarditis should be targeted at the cause as much as possible. For bacterial causes, specific antibiotic therapies are the key for successful management. The same applies for neoplastic pericarditis where oncologic therapies provide causative treatment [18, 19]. Nevertheless if the cause is unknown or viral there are no specific therapies available and we may provide successful treatments for patients as we do for other medical conditions when the cause cannot be known (i.e. primary hypertension). The mainstay of the medical therapy of acute and recurrent pericarditis is aspirin or a non-steroidal anti-inflammatory drug (generally ibuprofen or indomethacin) (Class I indication, LOE A) [20]. The choice of the specific drug should be based on previous history in order to select a drug that has been efficacious in previous attacks of pericarditis, concomitant diseases (i.e. favoring aspirin on patients who already are or need an antiplatelet agent), and last, but not least, physician experience [21]. An attack dose is recommened for 7–10 days till symptoms resolution and C-reactive protein normalization [18–23]. Colchicine may help to hasten symptoms resolution, improve remission rates at 1 week, and reduce recurrence by 50 % at 18 months (Class I indication, LOE A) [4, 5].

Corticosteroids should be used as second choice for patients refractory to more than 1 NSAID plus colchicine, contraindications or intolerance to aspirin or NSAID, specific indications (i.e. SID, pregnancy). Low to moderate doses (i.e. prednisone 0.2–0.5 mg/kg/day) should be favored instead of high doses (i.e. prednisone 1.0 mg/kg/day) to decrease the risk of severe side effects, chronicization, and disease-related hospitalizations (class IIa, LOE B) [24]. Additional immunosuppressive therapies are based on less evidence based data and should be considered only for true refractory cases also after failure of combined therapies with aspirin or a NSAID, colchicine and a corticosteroid [21, 23].

A summary of current first and second line therapies for acute and recurrent pericarditis is provided in Table 8.2.

Surgical therapies are the last option in cases with recurrent cardiac tamponade or symptomatic pericardial effusions [21]. Pericardiectomy is also available in experienced centres and may provide better event-free survival in patients' refractory to multiple medical therapies [25].

Hospitalization is recommended in patients with high risk features that warrant an etiology search and may be at risk of complications (i.e. cardiac tamponade, constriction) requiring monitoring and long term follow-up (Fig. 8.1) [14].

## Prognosis

The prognosis of acute and recurrent pericarditis is related to the etiology and not to the number of recurrences [26, 27]. Large pericardial effusions

**Table 8.2** Current first and second line therapies for acute and recurrent pericarditis

| Drug | Attack dose | Tapering | Class and LOE |
|---|---|---|---|
| Aspirin | 750–1,000 mg every 8 h | Every week in 3–4 weeks | I, LOE A |
| Ibuprofen | 600 mg every 8 h | Every week in 3–4 weeks | I, LOE A |
| Indomethacin | 25–50 mg every 8 h | Every week in 3–4 weeks | I, LOE A |
| Colchicine | 0.5 mg BID (>70 kg), otherwise 0.5 mg once daily for 3–6 months | No tapering recommended | I, LOE A |
| Prednisone | 0.2–0.5 mg/kg/day for 2–4 weeks | Taper slowly 2.5–5 mg every 2–4 weeks | IIa, LOE B |

*LOE* level of evidence, *A* meta-analysis or multiple RCTs, *B* a single RCT or non-randomised studies, *C* case reports or experts opinion

and cardiac tamponade are more common in bacterial and neoplastic etiologies [11]. The same also applies to the risk of evolution towards constrictive pericarditis. The risk is low (<1 %) in idiopathic and viral pericarditis, intermediate for systemic inflammatory diseases, post-cardiac injury syndromes, neoplastic pericardial disease and high (20–30 %) for tuberculous and purulent pericarditis [26]. Idiopathic recurrent pericarditis has a very low risk (<1 %) of evolution towards constriction [27].

## References


1. Imazio M. Contemporary management of pericardial diseases. Curr Opin Cardiol. 2012;27(3):308–17.
2. Lilly LS. Treatment of acute and recurrent idiopathic pericarditis. Circulation. 2013;127(16):1723–6.
3. Imazio M, Cecchi E, Demichelis B, Chinaglia A, Ierna S, Demarie D, Ghisio A, Pomari F, Belli R, Trinchero R. Myopericarditis versus viral or idiopathic acute pericarditis. Heart. 2008;94(4):498–501.
4. Imazio M, Brucato A, Cemin R, Ferrua S, Belli R, Maestroni S, Trinchero R, Spodick DH, Adler Y, CORP (Colchicine for Recurrent Pericarditis) Investigators. Colchicine for Recurrent Pericarditis (CORP): a randomized trial. Ann Intern Med. 2011; 155(7):409–14.
5. Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, Beqaraj F, Demarie D, Forno D, Ferro S, Maestroni S, Belli R, Trinchero R, Spodick DH, Adler Y, The ICAP Investigators. A randomized trial of colchicine for acute pericarditis. N Engl J Med. 2013; 369:1522–28.
6. Soler-Soler J, Sagristà-Sauleda J, Permanyer-Miralda G. Relapsing pericarditis. Heart. 2004;90(11): 1364–8.
7. Imazio M, Adler Y. Management of pericardial effusion. Eur Heart J. 2013;34(16):1186–97.
8. Syed FF, Sani MU. Recent advances in HIV-associated cardiovascular diseases in Africa. Heart. 2013;99(16):1146–53.
9. Imazio M, Spodick DH, Brucato A, Trinchero R, Adler Y. Controversial issues in the management of pericardial diseases. Circulation. 2010;121(7):916–28.
10. Imazio M, Brucato A, Trinchero R, Adler Y. Diagnosis and management of pericardial diseases. Nat Rev Cardiol. 2009;6(12):743–51.
11. Imazio M, Cecchi E, Demichelis B, Ierna S, Demarie D, Ghisio A, Pomari F, Coda L, Belli R, Trinchero R. Indicators of poor prognosis of acute pericarditis. Circulation. 2007;115(21):2739–44.
12. Imazio M, Trinchero R. Triage and management of acute pericarditis. Int J Cardiol. 2007;118(3):286–94.
13. Imazio M, Brucato A, Derosa FG, Lestuzzi C, Bombana E, Scipione F, Leuzzi S, Cecchi E, Trinchero R, Adler Y. Aetiological diagnosis in acute and recurrent pericarditis: when and how. J Cardiovasc Med (Hagerstown). 2009;10(3):217–30.
14. Spodick DH. Risk prediction in pericarditis: who to keep in hospital? Heart. 2008;94(4):398–9.
15. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, Hung J, Garcia MJ, Kronzon I, Oh JK, Rodriguez ER, Schaff HV, Schoenhagen P, Tan CD, White RD. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013; 26(9):965–1012.e15.
16. Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 Guideline for the clinical application of echocardiography. www.acc.org/qualityandscience/clinical/statements.htm. Accessed on 24 Aug 2006.
17. Lazaros G, Vlachopoulos C, Stefanadis C. Extensive infectious panel testing for acute pericarditis: a ghost hunt? Cardiology. 2011;119(3):131–3.
18. Imazio M, Brucato A, Mayosi BM, Derosa FG, Lestuzzi C, Macor A, Trinchero R, Spodick DH, Adler Y. Medical therapy of pericardial diseases: part I: idiopathic and infectious pericarditis. J Cardiovasc Med (Hagerstown). 2010;11(10):712–22.

19. Imazio M, Brucato A, Mayosi BM, Derosa FG, Lestuzzi C, Macor A, Trinchero R, Spodick DH, Adler Y. Medical therapy of pericardial diseases: part II: noninfectious pericarditis, pericardial effusion and constrictive pericarditis. J Cardiovasc Med (Hagerstown). 2010;11(11):785–94.
20. Imazio M, Adler Y. Treatment with aspirin, NSAID, corticosteroids, and colchicine in acute and recurrent pericarditis. Heart Fail Rev. 2013;18(3):355–60.
21. Imazio M. Treatment of recurrent pericarditis. Expert Rev Cardiovasc Ther. 2012;10(9):1165–72.
22. Imazio M, Brucato A, Maestroni S, Cumetti D, Dominelli A, Natale G, Trinchero R. Prevalence of C-reactive protein elevation and time course of normalization in acute pericarditis: implications for the diagnosis, therapy, and prognosis of pericarditis. Circulation. 2011;123(10):1092–7.
23. Imazio M, Brucato A, Trinchero R, Spodick D, Adler Y. Individualized therapy for pericarditis. Expert Rev Cardiovasc Ther. 2009;7(8):965–75.
24. Imazio M, Brucato A, Cumetti D, Brambilla G, Demichelis B, Ferro S, Maestroni S, Cecchi E, Belli R, Palmieri G, Trinchero R. Corticosteroids for recurrent pericarditis: high versus low doses: a nonrandomized observation. Circulation. 2008;118(6):667–71.
25. Khandaker MH, Schaff HV, Greason KL, Anavekar NS, Espinosa RE, Hayes SN, Nishimura RA, Oh JK. Pericardiectomy vs medical management in patients withbrelapsing pericarditis. Mayo Clin Proc. 2012;87(11):1062–70.
26. Imazio M, Brucato A, Maestroni S, Cumetti D, Belli R, Trinchero R, Adler Y. Risk of constrictive pericarditis after acute pericarditis. Circulation. 2011;124(11):1270–5.
27. Imazio M, Brucato A, Adler Y, Brambilla G, Artom G, Cecchi E, Palmieri G, Trinchero R. Prognosis of idiopathic recurrent pericarditis as determined from previously published reports. Am J Cardiol. 2007;100(6):1026–8.

## Acute and Recurrent Pericarditis- For Patients and their Families

### Epidemiology and Impact

Pericarditis is the most common disease affecting the pericardium, that is, the double-layer membrane protecting the outer portion of the heart. Specific data on the frequency of the disease are scarce. However pericarditis is reported as cause of about 5 % of non-ischemic chest pain admissions at the Emergency Department. After a first attack of pericarditis recurrences of pericarditis are common and involve about one third of patients.

### Definitions

Different definitions are commonly used in medical records. "***Acute pericarditis***" is the first acute episode of inflammation of the pericardium regardless of the cause, that may be infectious or non infectious. "***Recurrent pericarditis***" is the recurrence of pericarditis after a symptom-free interval of 6 weeks. "***Incessant pericarditis***" is pericarditis either acute or recurrent with prolonged symptoms and without a recognizable symptom-free interval of at least 6 weeks. "***Chronic pericarditis***" is pericarditis persisting for >3 months.

### Etiology

The etiology of pericarditis is varied and most cases are due to infections. Viral infection are considered the most important cause in developed countries while tuberculosis is the most important cause in developing countries, where it is commonly associated with HIV infection. Additional causes include autoimmune diseases (especially Systemic Lupus Erythematosus and Rheumatoid Arthritis), post-traumatic (also after cardiovascular interventions such as percutaneous coronary interventions, pacemaker implantation, ablation of atrial fibrillation), neoplastic involvement in lung or breast cancer or lymphomas.

### Diagnosis and Workup

The diagnosis of pericarditis is based on clinical criteria that consider the most common features at presentation (pleuritic chest pain, pericardial rub due to increased attrition between inflamed pericardial layers, pericardial effusion, and electrocardiographic changes). Testing is especially directed to exclude specific causes that may require a targeted therapy (i.e. tuberculous or bacterial pericarditis, neoplastic pericarditis).

### Management

Medical therapy is directed as much as possible to the cause. Unfortunately the cause remains unknown for most cases that are labeled as "idiopathic" (that is without a known cause). Mainstay of empiric antinflammatory therapy for these cases include aspirin or a non-steroidal anti-inflammatory drug (i.e. ibuprofen or indomethacin). Colchicine is added to fasten symptoms resolution and halve the risk of recurrences. Corticosteroids may promote chronicization and are reserved for cases refractory to first line therapies and for specific indications (i.e. pregnancy, systemic inflammatory diseases). Surgery with removal of the pericardium (pericardiectomy) is the last option after failure of medical therapies.

### Prognosis

The overall prognosis depends on the etiology. It is benign and self-limiting for viral and idiopathic pericarditis, while bacterial and neoplastic etiologies or autoimmune forms are associated with an increased risk of complications during follow-up. Thus a long term follow-up is recommended in these cases.

# Constrictive Pericardial Heart Disease

9

Patrick Collier and Allan Klein

## For Physicians and Other Health Care Professionals

### Introduction

Constrictive pericarditis occurs when cardiac filling is excessively constrained by the pericardium. In this setting, the pericardium is usually thickened (>2 mm in 80 % of such cases) and often calcified (in around 50 % of cases often at the base or at the AV groove) [1]. Etiology of constriction can be for many reasons including prior cardiac surgery (most common cause in the US), viral pericarditis, no known cause (idiopathic), prior chest radiotherapy, connective tissue disease, HIV infection and tuberculosis [2].

The constraining pericardium is responsible for "ventricular interaction / interdependence" – a term used to describe a critical pathophysiological feature of constriction, namely that filling of one side of the heart can only occur at the expense of the other side. For example, interaction means that expansion of the right ventricle volume due to increased venous return to the right heart during inspiration can only occur by shifting of the inter-ventricular septum towards the left ventricle. In addition, a further reduction in left ventricular volume occurs during inspiration because of "dissociation of intracardiac and intra-thoracic pressures" whereby pressures within the pulmonary veins (extrapericardial) but not the left ventricle (intrapericardial) decline during inspiration resulting in an adverse trans-pulmonary gradient. Early ventricular filling is rapid but once mid-diastole is reached ventricular volumes become compressed by the noncompliant diseased pericardium. As per Starling's law, a reduction in end diastolic volume limits subsequent stroke volume. Compensatory elevations in systemic and pulmonary venous pressures are a consequence of attempts to maintain cardiac filling in the setting of a fixed volume circuit. The increase in cardiac volume required with exercise quickly results in high filling pressures so that exercise limitation is an early feature of constriction.

Constrictive pericarditis is an important specific cause of "heart failure with preserved ejection fraction", and in particular may present as a right-predominant heart failure syndrome [3]. Elevated venous pressures as a consequence of constriction result in fluid overload, (ranging from peripheral edema, ascites, pulmonary/pericardial effusion, congestive liver disease, anasarca, pulmonary edema) while reduced cardiac output contributes to symptoms of fatigue and

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excessive tiredness. Shortness of breath during exertion progresses to orthopnea and shortness of breath at rest. Bi-atrial enlargement as a result of elevated filling pressures leads to a propensity for atrial arrhythmia such as atrial fibrillation.

## Diagnosis

Classic signs of constrictive physiology, though not always present, include a pericardial knock (due to abrupt cessation of mid-diastolic filling due to pericardial constraint), Kussmaul's sign (the lack of an inspiratory reduction in JVP due to impaired cardiac filling) and the misleadingly named pulsus paradoxus (a greater than normal inspiratory drop in systemic blood pressure, specifically >10 mmHg). Detailed examination of the neck reveals an elevated mean jugular venous pulse along with a rapid Y descent consistent with rapid early filling and corresponding to the high E wave seen in trans-mitral Doppler flow during echo.

Alternative conditions that may mimic constrictive pericarditis (or that may even sometimes coexist) are numerous and make the diagnosis of constriction even more difficult. Such confounders include atrial fibrillation, restrictive cardiomyopathy, pericardial effusion, severe tricuspid regurgitation and right heart failure all of which can cause (or contribute to) elevated venous pressures and low cardiac output. For example, beat-to-beat variation in heart function due to rapidly changing R-R intervals during atrial fibrillation makes detection of respiro-phasic variation difficult. Distinguishing constrictive pericarditis pathophysiology from that of restrictive cardiomyopathy can be difficult because a stiff ventricle can mimic a stiff pericardium. Indeed, many different parameters attempting to distinguish both conditions have been the subject of many publications of years. The most successful parameter to emerge in this regard seems to be the systolic area index measured via heart catheterization. Using simultaneous LV and RV high fidelity manometer pressure traces during expiration and inspiration, the systolic area index is defined as the ratio of the area under the curve for the right versus the left ventricle during inspiration versus expiration and a value greater than 1.1 was found to be diagnostic for constriction [4]. In the setting of a large pericardial effusion, the diagnosis of constriction may only be apparent following drainage of the effusion. Equally, if symptoms don't improve following drainage of a large pericardial effusion, constriction should be considered.

The degree of constrictive physiology present can range along a spectrum between different patients so that all of the classical features may not all be present from the outset particularly with milder forms of constriction. Finally, it is also worth pointing out that the degree of constrictive physiology present is highly related to the particular fluid status of an individual at the time of assessment – for example, constriction may be very difficult to detect in the setting of hypovolemia. For the same reason, holding diuretic therapy for several days prior to cardiac catheterization may help unmask the underlying physiology.

## Testing

Pericardial constriction clearly can be a difficult diagnosis to detect and often requires multiple different forms of testing.

Blood tests such as the inflammatory markers ESR and CRP can give an indication as to the presence of ongoing inflammation. Autoantibodies may help with assessment for the presence of underlying connective tissue disease. On the other hand, because brain natriuretic peptide (BNP) is produced mainly by the left ventricle in response to wall stretch which is constrained by the pericardium in the setting of constriction, high level of BNP may points to an alternative diagnosis such as restriction.

Electrocardiography findings in constriction are nonspecific and include increased heart rate, low-voltage QRS, repolarization abnormalities with atrial fibrillation present in over one-fifth of patients [1].

Echocardiography is the first-line imaging modality of choice to assess for constriction (see Fig. 9.1) because of availability, utility and cost. With good echocardiographic windows, a comprehensive transthoracic echocardiogram with respirometry recording may be diagnostic so that additional imaging modalities may not be necessary.

Expected echocardiographic findings in constriction include a restrictive filling pattern of diastolic trans-atrioventricular valve flow with high E wave velocity and a short E wave deceleration time (reflecting rapid early filling) with respiro-phasic variation (reflecting both ventricular interdependence and dissociation) (see Fig. 9.2).

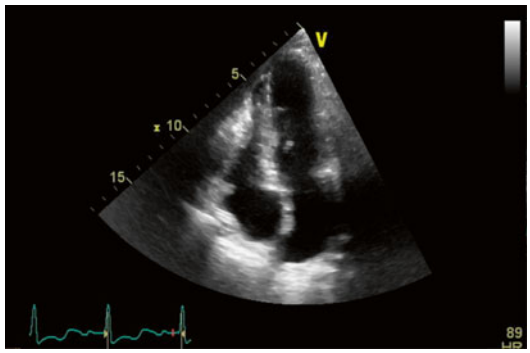


**Fig. 9.1** Tubular deformity of the left ventricle in pericardial constriction

Motion of the inter-ventricular septum in constriction is complex. A septal bounce can be seen with every cardiac cycle and relates to abrupt mid-diastolic cessation filling of both the left and right ventricles due to pericardial restraint. This is discrete from septal shift which varies with each respiratory cycle. During inspiration, the inter-ventricular septum shifts to the left due to increased right ventricular filling (via ventricular interdependence) and reduced left ventricular filling (via dissociation of intra-cardiac and intra-thoracic pressures). The opposite leftward motion of the inter-ventricular septum during expiration accounts for the large reversals seen in diastolic hepatic vein flow during expiration. In clinically unsuspected cases, echocardiographic findings of abnormal ventricular septal motion along with increased pericardial thickness may often be the first alerts that constrictive physiology is present.

Color M-mode demonstrates increased propagation velocity of early diastolic trans-mitral flow (reflecting rapid early filling). Both ejection fraction and tissue Doppler assessment of longitudinal function are typically preserved with constrictive physiology. While E/e' theoretically increases with worsening diastolic function, this is not necessary the case with constriction as e' is preserved (annulus paradoxus). Tethering of the lateral

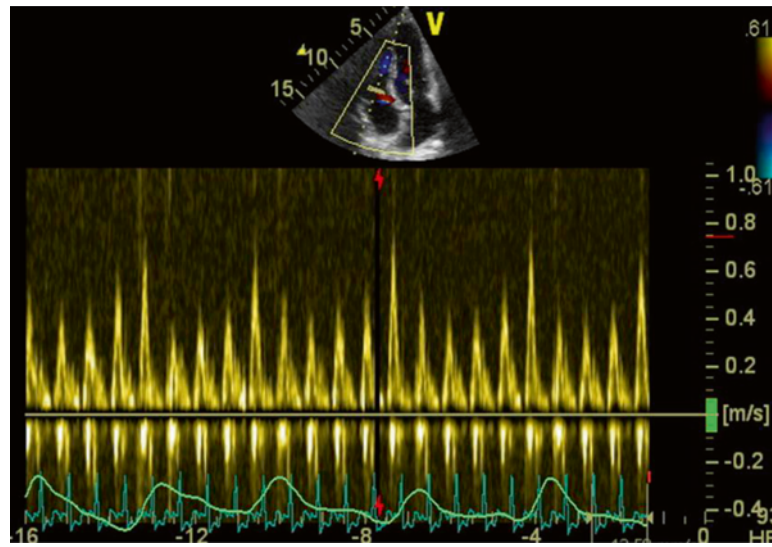


**Fig. 9.2** Respiro-phasic variation due to ventricular interaction in constriction

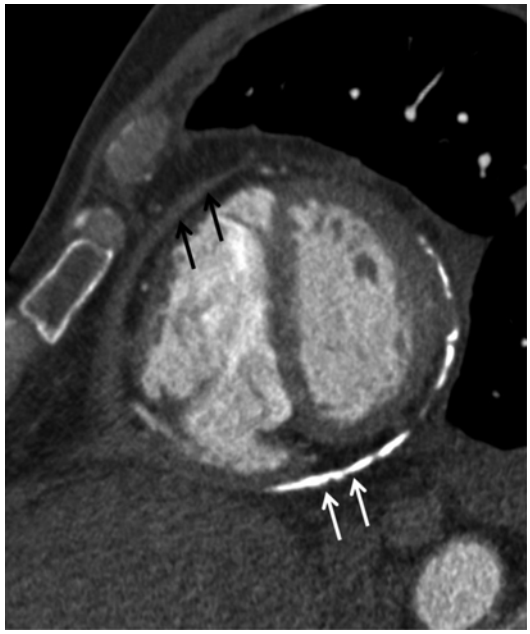

**Fig. 9.3** Pericardial thickening (*black arrows*) and calcification (*white arrows*) as demonstrated by CT

end is thickened pericardium may mean that e' is lower measured laterally compared to the mobile inter-ventricular septum (annulus reversus). Marked dilation and absent or diminished collapse of the IVC and hepatic veins is a common finding in constriction (reflecting elevated systemic venous pressures).

For more detailed anatomic assessment of pericardial and associated structures, there is perhaps no more useful noninvasive imaging modality than cardiac CT. This is the most sensitive modality to detect pericardial thickening and pericardial calcification (see Fig. 9.3) which as mentioned already are suggestive but not necessary for the diagnosis of constriction. Indirect anatomical finding such as tubular deformation of the ventricles with prominent venous dilation and accumulation of third space fluid would be expected findings in constriction. Radiation exposure with cardiac CT continues to decrease via increasing use of more optimal CT techniques such as EKG synchronization, perspective triggering as well as reduced tube voltage where appropriate.

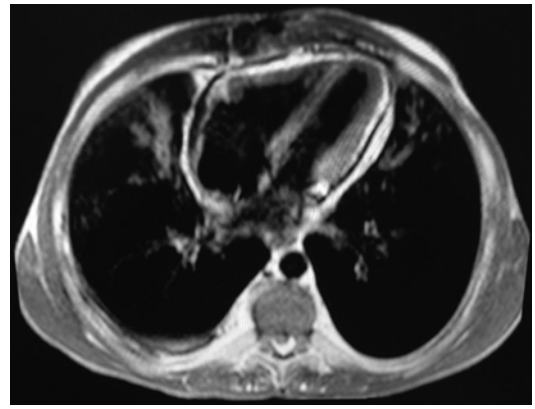

**Fig. 9.4** Pericardial enhancement and circumferential thickening by MRI

Cardiac MRI can provide exquisite anatomical and physiological detail in the setting of constriction (see Fig. 9.4) with cine sequences capable of demonstrating all of the functional changes detailed above by echocardiography and with phase encoding velocimetry capable of obtaining information sooner to Doppler echo. Furthermore, MRI sequences designed to assess for the presence of inflammation (T2 weighted sequences and delayed gadolinium enhancement) may provide useful information with regard to potential reversibility of constrictive features [5]. These findings suggest that role of cardiac MRI may prove to be particularly useful for patients with increased inflammatory biomarkers or for those with a short duration of constrictive symptoms in whom intensive medical therapy may have a higher likelihood of success. Patients with constrictive pericarditis that demonstrated pericardial late gadolinium enhancement were noted to have greater fibroblast proliferation, chronic inflammation, pericardial thickening and neovascularization [6].

## Management

As mentioned, the mechanical effects of the pericardium on the heart are diminished by avoiding fluid overload. Not surprisingly, diuretics are used as an initial temporizing preoperative therapy as well as primary therapy for those patients

who are not surgical candidate. Early stages of pericardial constriction (recent onset) might have an inflammatory component and might respond to anti-inflammatory therapy. Regimens involve triple therapy with a non-steroidal anti-inflammatory agent such as ibuprofen, colchicine as well as a slowly tapering course of high-dose oral glucocorticoid have been used [7]. Emergent data suggesting that early forms of constriction may be reversible introduces a new concept of transient constrictive pericarditis. For some patients, the possibility of prevention of constriction may be a new goal of treatment particularly for those with an early diagnosis. It has been suggested that such use of anti-inflammatory therapies for early constriction may mean that pericardiectomy may be avoided in up to 20–30 % of patients with acute or subacute constriction [8]. Such treatment may also potentially act in an adjuvant manner by treating the inflammation and reducing adhesion formation which theoretically might result in more optimal surgical outcomes. The use of colchicine to reduce recurrence rates of pericarditis may impact the natural history of pericardial disease and thereby serve to limit the likelihood of chronic downstream sequelae such as constriction [9]. As an etiology for constriction, tuberculosis is rare in the developed world but if found would warrant a specific and extensive course of appropriate antimicrobial therapy.

Pericardiectomy is the definitive standard of care for constrictive pericarditis with the aim of resecting as much of the diseased pericardium as is possible while attempting to prevent injury to the underlying myocardium and adjacent structures such as phrenic nerve [10]. Most patients have relief of symptoms early after pericardiectomy. Indeed, an immediate and dramatic hemodynamic improvement maybe apparent to the surgical team even before the patient has left the operating room. Operative outcomes are dependent on patient selection as those with "end-stage disease", pre-operative myocardial dysfunction, renal dysfunction or mixed constrictive restrictive disease have worse outcomes. Operative outcomes are also influenced by etiology of the pericardial disease with better outcomes found in those with idiopathic or postsurgical constriction as opposed to radiation induced disease. Persistent heart failure symptoms may necessitate continued medical therapy particularly in the presence of post-operative left ventricular systolic dysfunction. Lastly, recurrent constriction is rare but may indicate incomplete pericardial resection or possibly epicarditis.

## References


1. Talreja DR, Edwards WD, Danielson GK, Schaff HV, Tajik AJ, Tazelaar HD, et al. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. Circulation. 2003;108(15):1852–7. Epub 2003/10/01.
2. Ling LH, Oh JK, Schaff HV, Danielson GK, Mahoney DW, Seward JB, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. Circulation. 1999; 100(13):1380–6. Epub 1999/09/29.
3. Argulian E, Halpern DG, Aziz EF, Uretsky S, Chaudhry F, Herzog E. Novel "CHASER" pathway for the management of pericardial disease. Crit Path Cardiol. 2011;10(2):57–63. Epub 2011/10/13.
4. Talreja DR, Nishimura RA, Oh JK, Holmes DR. Constrictive pericarditis in the modern era: novel criteria for diagnosis in the cardiac catheterization laboratory. J Am Coll Cardiol. 2008;51(3):315–9. Epub 2008/01/22.
5. Feng D, Glockner J, Kim K, Martinez M, Syed IS, Araoz P, et al. Cardiac magnetic resonance imaging pericardial late gadolinium enhancement and elevated inflammatory markers can predict the reversibility of constrictive pericarditis after antiinflammatory medical therapy: a pilot study. Circulation. 2011;124(17): 1830–7. Epub 2011/10/05.
6. Zurick AO, Bolen MA, Kwon DH, Tan CD, Popovic ZB, Rajeswaran J, et al. Pericardial delayed hyperenhancement with CMR imaging in patients with constrictive pericarditis undergoing surgical pericardiectomy: a case series with histopathological correlation. JACC Cardiovasc Imaging. 2011;4(11): 1180–91. Epub 2011/11/19.
7. Haley JH, Tajik AJ, Danielson GK, Schaff HV, Mulvagh SL, Oh JK. Transient constrictive pericarditis: causes and natural history. J Am Coll Cardiol. 2004;43(2):271–5. Epub 2004/01/23.
8. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic

Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013;26(9):965–1012 e15. Epub 2013/09/04.
9. Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, Beqaraj F, et al. A randomized trial of colchicine for acute pericarditis. New Engl J Med. 2013;369(16):1522–8. Epub 2013/09/03.
10. Maisch B, Seferovic PM, Ristic AD, Erbel R, Rienmuller R, Adler Y, et al. Guidelines on the diagnosis and management of pericardial diseases executive summary; the task force on the diagnosis and management of pericardial diseases of the European society of cardiology. Eur Heart J. 2004;25(7):587–610. Epub 2004/05/04.

## Constructive Pericardial Heart Disease-For Patients and their Families

### Introduction

Constrictive pericarditis or "constriction" is a disease involving scarring or thickening of the sac-like covering of the heart (the pericardium) that has become so severe that it interferes with the ability of the heart to fill with blood.

Constriction usually occurs in adults and may be life threatening if untreated. It is most commonly caused by conditions associated with inflammation of the pericardium such as prior cardiac surgery (most common cause in the US), viral pericarditis, no known cause (idiopathic), prior chest radiotherapy, connective tissue disease and tuberculosis.

In order for the heart muscle pump to work properly, it first has to be able to expand adequately and fill up with blood. However, with constriction, pericardial scarring prevents this from happening. Eventually, blood is only able to return to the right side of the heart (the venous side of the circulation) under high pressure. Veins under high pressure become leaky and that is why constriction is associated with long-term swelling of the ankles and legs (edema). This may progress to swelling of the abdomen (ascites) and abnormal liver function. With limited heart filling comes limited heart pumping (low cardiac output) which may cause patients with constriction to complaint of fatigue, excessive tiredness, weakness and difficulty breathing. Such symptoms typically develop slowly and get worse without treatment.

Constriction may limit the amount of exercise that a patient is able to do. As the heart normally expands with exercise (total cardiac volume increases), the compressive effect of the pericardium in constriction will be even more apparent during any attempts to exercise. However, because the disease process happens gradually, the patient may not recognize themselves "slowing down" and may put this symptom down to "being unfit" or "getting older".

### Diagnosis

Constrictive pericarditis can be a very difficult diagnosis to make. This is because the signs and symptoms are non-specific and may develop slowly. Also, there is not simply one test that can make the diagnosis and say that constriction is present or not. It requires physicians to have a high level of clinical suspicion particularly in patients who have risk factors for constriction such as prior cardiac surgery, viral pericarditis or radiotherapy for example.

If other conditions are present (for example, one fifth of patients may have an irregular heart rhythm such as atrial fibrillation), this may make it even harder to make the diagnosis. It is worth pointing out that constriction exists along s spectrum of severity, so that all of the classical features may not be present from the outset. For these reasons, it is not uncommon for a diagnosis of constriction to be delayed especially outside specialist centers.

Sometimes the possibility of constriction may be raised after patients undergo routine cardiac imaging tests such as echocardiography. Specialist assessment with more sophisticated non-invasive imaging techniques such as cardiac CT or MRI and/or invasive testing with cardiac catheterization may be required to establish a diagnosis.

### Testing

The history and physical exam of a patient with pericardial disease is covered in more detail in Chap. 3 while the different forms of testing to evaluate pericardial disease have already been mentioned in Chaps. 4, 5, 6 and 7. Multiple different forms of testing may be required to establish a diagnosis of constric-

tion which, as mentioned, can be a difficult diagnosis to make.

Lab testing may help exclude rarer causes of pericarditis such as connective tissue diseases and tuberculosis which are important to recognize as specific additional treatments for such patients may be required.

An echocardiogram test can help establish a diagnosis of constriction by using sound waves to create a moving picture of the heart. This test does not involve any radiation exposure and is usually carried out by a trained sonographer by placing a probe on the chest wall (transthoracic echo). Even more detailed pictures can be obtained by a physician if a special echo probe is passed down a patient's throat (transesophageal echo). These techniques allow two-dimensional and 3-dimensional pictures to be obtained as well as very detailed information about filling of the heart.

A cardiac MRI uses radio waves and powerful magnets to image the heart and can provide the clinician with excellent images to assess not just the pericardium but the entire heart. Like echocardiography, it does not involve ionizing radiation such as X-rays. However, not all patients will be able to undergo cardiac MRI for safety reasons. Patients are screened prior to the test and those with metallic foreign bodies including aneurysm clips, pacemakers and certain types of implants for example are prohibited. Cardiac MRI is demanding for patients who are required to be able to lie still usually within a narrow tube for up to 30–60 min as well as to be able to follow careful breathing instructions. However, the advantage of this test is that it can provide very useful information regarding what the structure ("anatomy") of the heart looks like, as well as how the heart is functioning ("physiology").

A cardiac CT scan is a non-invasive imaging test involving X-rays that provides excellent anatomical detail of the pericardium as well as the entire chest cavity. Advantages include the fact that it is a quick test (scanning time lasts seconds). Also, unlike MRI, cardiac CT can detect calcification which makes a diagnosis of constriction more likely (although constriction can still be present in the absence of calcification). With cardiac MRI and cardiac CT, a special dye (contrast) is often given before the test through a vein (IV) in your hand or forearm in order to allow the radiologist see certain areas more clearly. Before such contrast agents can be safely administered, it is necessary to confirm that a patient's kidney function is satisfactory using a blood test.

For some patients, noninvasive imaging may not be sufficient to make a diagnosis of constriction and an invasive test called a cardiac catheterization may be considered. Such testing is usually performed as a day case procedure using local anesthetic and mild sedation. This test involves passage of a small hollow tube called a catheter through a blood vessel in the arm or groin from where it can be then be moved up to the heart in order to measure pressures within the heart chambers.

## Management

Once a diagnosis has been made, the goal of treatment is to improve heart function by relieving the constriction. The initial treatment for constriction is usually conservative (treated with medications). For example, the mechanical effects of the pericardium on the heart in constriction are diminished by avoiding fluid overload. A low-sodium diet may also be recommended to limit fluid accumulation, while diuretic medications ("water pills") are often prescribed to enable the body remove excess fluid more easily. For patients with constrictive pericarditis that are suspected to have residual active inflammation, non-steroidal anti-inflammatory medication, colchicine and/or steroid medications may be considered. It is increasingly recognized that a portion of patients may have "transient" constrictive pericarditis that may resolve with medical therapy in the first instance. Occasionally, the underlying explanation for the constrictive pericarditis may be discovered to be due to rarer causes such as connective tissue diseases and tuberculosis that warrant additional regimes such as immunosuppressive or anti-tuberculosis medications.

The definitive treatment of constrictive pericarditis is a type of surgery called a pericardiectomy which involves cutting out or removing the scarred pericardium overlying the constricted heart muscle. This surgery is complex, requiring hospital admission including admission to intensive care unit for at least immediate postoperative care. For some patients, they may have a history of prior or multiple cardiac surgeries. Therefore, pericardiectomy surgery is generally reserved for those who have not gotten better with medical therapy and have persistent severe symptoms. Seeking referral to a surgeon with considerable sub-specialist expertise in this area is advisable (Figs. 9.1, 9.2, 9.3, and 9.4).

**Further patient information is available at:**
www.nlm.nih.gov/medlineplus/healthtopics.html
www.nhlbi.nih.gov
www.americanheart.org

# Pericardial Effusion and Tamponade

10

Edgar Argulian, Harikrishna Makani, and Eyal Herzog

The general approach to pericardial effusion once it is recognized includes establishing the cause of pericardial disease and assessing its hemodynamic significance.

## Recognizing the Presence of Pericardial Effusion

Pericardial effusion can be recognized based on clinical suspicion or it can be an incidental finding on chest or cardiac imaging [1]. The following clinical settings may indicate the need to specifically evaluate for the presence of pericardial effusion:

1. Cardiac arrest with pulseless electrical activity or asystole;
2. Chest discomfort and/or any signs of hemodynamic instability in chest trauma, recent cardiac surgery or percutaneous cardiac intervention;
3. Any of the following when otherwise unexplained: chest pain, fever, dyspnea, and elevated cardiac biomarkers;
4. Physical and electrocardiographic findings attributable to pericardial disease; the latter includes tachycardia, low voltage and electrical alternans (please refer to the corresponding electrocardiography chapter);
5. Enlarged cardiac siluette or pleural effusions on chest X-ray;
6. Any patient with ascending aortic dissection, severe pulmonary hypertension, renal failure, use of some medications, rheumatic diseases, malignancy, or other systemic conditions when pericardial effusion is thought to contribute to presentation or have prognostic significance [2].

## Establishing the Cause of Pericardial Effusion

A structured approach helps to establish the cause of pericardial effusion in most cases [1, 3]. A very aggressive approach as used in some studies has a high diagnostic yield but low clinical relevance, especially for small effusions [4, 5]. Routine sampling of pericardial fluid is unnecessary [2, 6]. History and physical examination often provide clues to the etiology of pericardial effusion. For example, pericardium can be involved in patients with active systemic malignancy and malignant effusion should be strongly considered in these patients [7]. Active or recent infection, radiation therapy, rheumatic disease, and recent acute coronary syndrome, cardiac surgery or percutaneous cardiac procedure, all provide relevant clues to etiology [2]. A typical clinical presentation, physical findings and electrocardiographic changes commonly confirm the diagnosis of acute idiopathic pericarditis [8].

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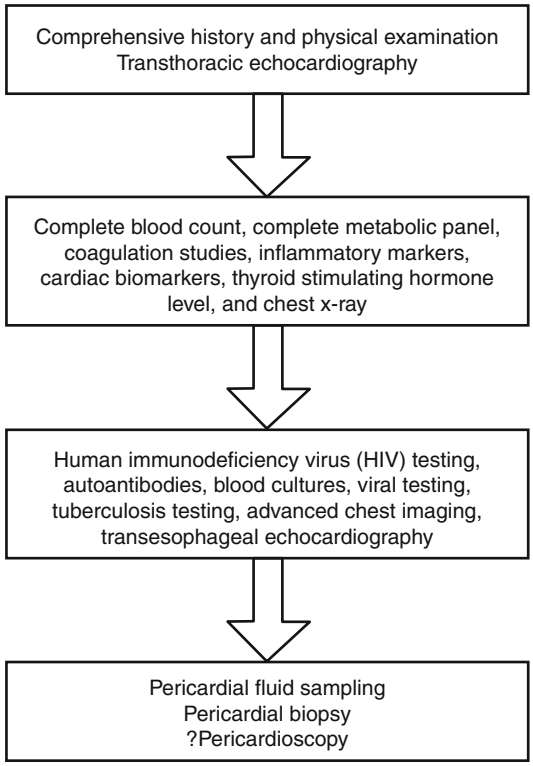


**Fig. 10.1** Stepwise parsimonious approach to diagnosing the etiology of pericardial effusion

In one study, presence of 'inflammatory' signs (characteristic chest pain, pericardial friction rub, fever, and/or diffuse ST-segment elevation) in patients with pericardial effusion was strongly associated with acute idiopathic pericarditis [9].

We use parsimonious stepwise approach to laboratory testing and imaging in patients with pericardial effusion at our institution (Fig. 10.1) [1]. Transthoracic echocardiography is the standard test in establishing the presence of pericardial effusion, quantifying the size of the effusion and assessing its hemodynamic impact [2]. The initial tier of testing includes complete blood count, complete metabolic panel, coagulation studies, inflammatory markers (erythrocyte sedimentation rate, C-reactive protein), cardiac biomarkers, thyroid stimulating hormone (TSH) level, and chest X-ray [1]. In appropriate clinical settings, human immunodeficiency virus (HIV) testing, autoantibodies, and blood cultures are obtained. Advanced chest imaging (CT scan, positron emission tomography and magnetic resonance imaging) can be helpful in certain clinical situations, especially when malignancy is suspected [10]. Besides, CT scan and cardiac magnetic resonance can be used as adjunct imaging modalities for assessing pericardial effusion in some patients. They offer precise effusion localization, quantification and tissue characterization which is especially important for loculated and complex effusions [11]. Tuberculosis testing should also be considered in the right epidemiologic and clinical settings. Viral cultures have little clinical significance and should not be routinely obtained but they may be useful in some patients (e.g., cytomegalovirus infection in transplant patients) [2]. Transesophageal echocardiography (TEE) can diagnose loculated effusion when transthoracic echocardiography is limited (e.g., postoperative patients) and regional tamponade is considered.

Simple clinical assessment has been shown to assist in establishing the diagnosis: large effusion without 'inflammatory' signs or clinical signs of tamponade (jugular venous distention, hypotension, and/or pulsus paradoxus) commonly signifies chronic idiopathic pericardial effusion (likelihood ratio = 20, $P < 0.001$) whereas large effusions with clinical signs of tamponade and without 'inflammatory' signs should raise the suspicion for malignancy (likelihood ratio = 2.9, $P < 0.001$) [9]. Pericardial effusion sampling for diagnostic purposes and occasionally pericardial biopsy should be considered in following settings:

1. Concern for purulent and tuberculous pericarditis;
2. Clinical suspicion of neoplastic pericardial effusion;
3. Moderate to large pericardial effusion in patients with advanced HIV and/or immune suppression;
4. Moderate to large or progressive pericardial effusion in patients that are not responding to initial therapy or when the tiered work-up is inconclusive.

Pericardial fluid analysis can include Gram and acid-fast bacilli stains and cultures, polymerase chain reaction, tuberculosis-specific testing (e.g., adenosine deaminase, lysozyme, and gamma-interferon), tumor markers, and cytology [2]. Contrary to common practice and unlike pleural effusion work-up, cell count, lactate dehydrogenase

and protein and glucose levels have not been shown to be particularly useful in differential diagnosis and management of patients with pericardial effusion [12]. Pericardioscopy allows a targeted pericardial biopsy and it can potentially increase the diagnostic accuracy of sampling (e.g., neoplastic pericardial effusion) [13].

## Assessing Hemodynamic Significance of Pericardial Effusion

When evaluating the hemodynamic impact of pericardial effusion one should take into account the acuity of presentation. Acute accumulation of fluid (within minutes to hours) rapidly exceeds the pericardial stretch limit and commonly presents as cardiogenic shock [14]. This dramatic presentation is called acute or surgical tamponade and it requires immediate intervention. Chamber perforation during a percutaneous procedure is a good example of acute tamponade. Blunt chest trauma and ascending aortic dissection resulting in blood accumulation within pericardium require prompt surgical intervention and percutanous pericardial effusion drainage is relatively contraindicated [2]. When pericardial fluid accumulates slowly (within days to weeks) a large amount of fluid can be present without dramatic lowering of the cardiac output [14]. This can lead to subacute or medical tamponade which requires careful assessment of both clinical and imaging data to establish the need for pericardial effusion drainage [15]. The following discussion will elaborate the assessment for subacute (medical) tamponade.

### History and Physical Examination

Although many refer to pericardial tamponade as a "clinical diagnosis," the existing evidence suggests that subacute tamponade is a difficult diagnosis to make on mere clinical grounds. Dyspnea is the cardinal symptom of subacute pericardial tamponade, but it is very nonspecific [16]. Other symptoms such as fever, cough, and chest pain can occur and typically reflect the underlying cause (i.e., pericarditis) rather than pericardial fluid accumulation. Clinical findings of pericardial tamponade include tachycardia, jugular venous distention, pulsus paradoxus, and diminished heart sounds and all lack both sensitivity and specificity. Tachycardia is common in hospitalized patients for many reasons and it could be blunted by medications such as beta-blockers. In a systematic review, the jugular venous distention had a pooled sensitivity of 76 % for cardiac tamponade [16]. Assessment of jugular venous distention is limited by the experience of the observer; it can be difficult in some patients, even for experienced clinicians [17, 18]. Besides, jugular venous distention is associated with other conditions causing shortness of breath such as pulmonary hypertension and congestive heart failure. While patients with acute (surgical) tamponade rapidly progress to cardiogenic shock, hypotension is rather uncommon in patients with subacute tamponade who accumulate pericardial effusion within days to weeks. On the contrary, many patients are hypertensive due to high levels of circulating catecholamines in response to hemodynamic stress [19, 20]. In studies of pericardial tamponade, the mean systolic blood pressure ranged from 127–144 mmHg [19]. According to a recent review, hypertensive tamponade is seen in 27–43 % of patients [19]. Systolic blood pressure commonly decreases in these patients after pericardial effusion drainage, and treating the hypertensive response without draining the effusion can be dangerous [19, 21].

### Pulsus Paradoxus

Pulsus paradoxus is considered the cornerstone of the clinical diagnosis of pericardial tamponade [14]. Interestingly, it is not a "paradoxical" phenomenon but an exaggeration of the physiologic decrease in systolic arterial pressure with inspiration. Under normal conditions, the decrease in blood pressure is <10 mmHg, and it is explained by phasic variation in the filling of the right- and left-sided cardiac chambers related to intrathoracic pressure changes with respiration. With tamponade, the accumulating pericardial effusion restricts cardiac filling and makes the respiratory variation in the right and left ventricular filling more pronounced and interdependent [14]. Pulsus paradoxus

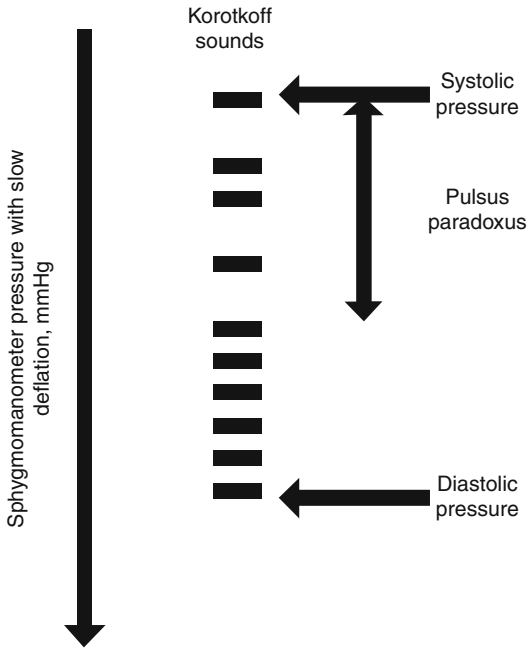


**Fig. 10.2** Obtaining pulsus paradoxus as the difference between intermittent and persistent Korotkoff sounds during normal respiration

is measured by manual sphygmomanometer as the difference between intermittent and persistent Korotkoff sounds during normal respiration, not with deep breathing (Fig. 10.2) [16]. A wide variation in the incidence of pulsus paradoxus has been reported in patients with pericardial tamponade, ranging from 12 to 75 % [22]. According to one study, approximately 20 % of tamponade patients had "low-pressure" cardiac tamponade defined as low intrapericardial pressure and low post-drainage right atrial pressure [23]. In "low-pressure" tamponade patients, the incidence of jugular venous distention was 22 % and pulsus paradoxus was reported in only 7 % of patients [23]. Besides limited sensitivity for pericardial tamponade, pulsus paradoxus is not very specific. A myriad of conditions have been reported to be associated with pulsus paradoxus; a short list includes asthma, right ventricular infarction, severe hypovolemia, constrictive pericarditis, restrictive cardiomyopathy, pneumothorax, chronic obstructive lung disease, and pulmonary embolism [15]. Some of these conditions can also cause jugular venous distention and tachycardia, common associated findings of pericardial tamponade.

## Invasive and Imaging Data

Before the widespread use of echocardiography invasive data using cardiac catheterization were commonly obtained to confirm the diagnosis of tamponade. Cardiac catheterization in tamponade demonstrates equilibration of diastolic intracardiac pressures and respiratory variation in right and left-sided cardiac pressures corresponding to pulsus paradoxus [2].

Echocardiography is currently the cornerstone of hemodynamic evaluation of pericardial effusion [2]. Normally, intrapericardial pressure is lower than the central venous pressure. As pericardial fluid accumulates the intrapericardial pressure equilibrates first with the right sided filling pressures and then left-sided filling pressures [16]. During tamponade, intrapericardial pressure may temporarily exceed intracavitary pressure in various chambers during cardiac cycle and result in chamber collapse. Certain pitfalls should be kept in mind when interpreting echocardiographic findings. Transient buckling of the right atrium is commonly seen in patients with pericardial effusion and it is not specific [24]. A more sustained collapse of the right atrium lasting at least one third of the cardiac cycle appears to be more specific for cardiac tamponade [24]. Right ventricular early diastolic collapse is a less sensitive finding but has a high specificity. Right ventricular outflow tract should be inspected carefully for the signs of collapse since it is the thinnest area of the right ventricle and M-mode echocardiography should be used for precise timing. Left-sided chamber collapse is much less sensitive but highly specific for tamponade [2]. Importantly, a study by Merce et al. showed that 34 % of patients with pericardial effusion but without clinical features of pericardial tamponade had at least one chamber collapse on echocardiography [25]. Therefore, in patients with pericardial effusion who have chamber collapse, one should carefully document respiratory flow variation across valves as a sign of ventricular interdependence and interrogate the inferior vena cava size and collapsibility as a sign of elevated right-sided filling pressures (Fig. 10.3) [26]. An abnormal filling pattern in the superior vena cava with a markedly diminished diastolic flow can also be observed. We define respiratory

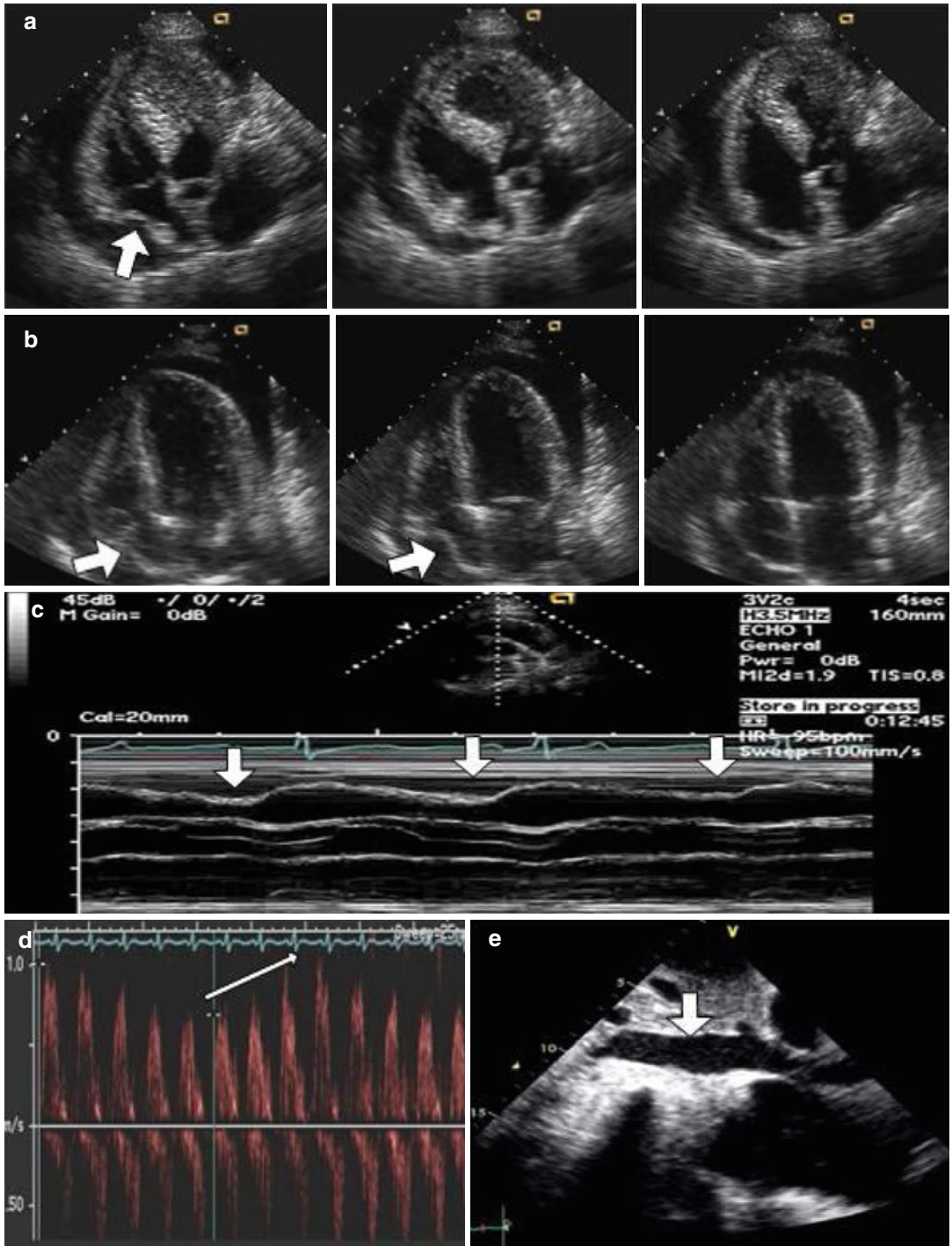


**Fig. 10.3** Echocardiographic findings in pericardial tamponade. (**a**) Transient inward motion of the right atrium (*arrow*) is commonly seen in patients with pericardial effusion and it is not specific for tamponade. (**b**) A sustained collapse of the right atrium (*arrows*) lasting at least one third of the cardiac cycle is specific for tamponade. (**c**) M-mode echocardiography showing diastolic collapse of the right ventricular outflow tract (*arrows*) is specific for tamponade. (**d**) Respiratory variation in the mitral inflow velocities (*arrow*) and (**e**) vena cava engorgement (*arrow*) are supportive signs for cardiac tamponade

variation in the inflow velocities conservatively as >30 % across mitral valve and >60 % for tricuspid valve [11]. These echocardiographic signs, when present, increase the specificity of diagnosis [26]. Finally, the size of pericardial effusion seems to be an important but frequently underappreciated part of the echocardiographic assessment. In one study of hospitalized patients with pericardial effusion, the size of the effusion was the only independent predictor of adverse in-hospital outcomes in a multivariate model, but not chamber collapse or inferior vena cava plethora [27]. We define a moderate pericardial effusion as the largest pocket between 1 and 2 cm at the end diastole and a large effusion as >2 cm [1].

The diagnosis of cardiac tamponade may be particularly difficult in patients with pulmonary hypertension and right ventricular failure because they commonly accumulate pericardial effusion. Pericardial effusion in these patients is a marker of adverse outcomes [28]. Common clinical findings of pericardial tamponade such as tachycardia and jugular venous distention may not be helpful in differential diagnosis for shortness of breath and progressive right-sided heart failure. Collapse of the left-sided cardiac chambers has been described as an important echocardiographic clue to the presence of cardiac tamponade in these settings [29]. Conversely, more common findings of tamponade such as right atrial and ventricular collapse can be masked by elevated right-sided filling pressures. Poor outcomes have been reported with routine draining of pericardial effusion in these patients [30].

## Integrative Approach to Pericardial Drainage

The diagnosis of subacute pericardial tamponade can be challenging because most patients are not hypotensive and can actually be hypertensive. An integrative approach that includes careful consideration of both clinical and imaging data helps clinicians to assess the hemodynamic impact of pericardial effusion and the need for drainage [1, 3, 15]. The decision making should include the following factors:

1. Presence and timeline for symptoms (commonly dyspnea);
2. Supportive physical findings (jugular venous distention, tachycardia, and pulsus paradoxus);
3. Etiology of pericardial effusion and response to initial treatment;
4. Size of pericardial effusion;
5. Evidence of chamber collapse on echocardiography;
6. Supporting signs for pericardial tamponade on echocardiography (respiratory variation in velocities and flows, superior vena cava flow pattern, engorgement of the inferior vena cava).

Percutaneous pericardiocentesis guided by echocardiography is the intervention of choice in many cases when pericardial drainage is desired. Emergency pericardiocentesis in acute (surgical) tamponade can be life-saving. A study summarizing 21 year experience from Mayo Clinic showed that echo-guided approach is rapid, safe and effective with major complication rate of 1.2 % [31]. Extended catheter drainage has been used in certain scenarios including neoplastic pericardial effusion when intrapericardial treatment is also occasionally employed [2]. Stepwise drainage of pericardial effusion is reasonable in very large effusions and patients with pulmonary hypertension to avoid acute right ventricular dilation (‘decompression syndrome’) [2]. Surgical drainage is generally preferred in traumatic pericardial effusion, aortic dissection, small effusions, recurrent effusions, and purulent pericarditis [2]. In loculated (typically post-surgical) effusions surgical approach or video-assisted thoracoscopic pericardiectomy can be used. Pericardial biopsy when necessary can be done using surgical procedure or pericardioscopy [2]. Post-drainage echocardiography is important in assessing the efficacy of the procedure, possible complications and fluid re-accumulation, and diagnosing constriction physiology.

## Supportive Care

Promptly instituted treatment for presumed etiology of pericardial effusion (i.e., anti-inflammatory therapy in acute pericarditis) can result in

improvement and defer the need for pericardial drainage. The response should be monitored by serial echocardiographic examinations. Endotracheal intubation with positive pressure ventilation requires great caution since it can markedly reduce cardiac preload and result in rapid hemodynamic deterioration [32]. Fluid resuscitation should also be used cautiously. In a hemodynamic study by Sagrista-Sauleda et al., 49 patients with pericardial tamponade were given 500 mL of intravenous normal saline before pericardiocentesis [33]. Increase in cardiac index >10 % from baseline was observed in 47 % of patients. The improvement in cardiac index was modest and only patients with systolic blood pressure <100 mmHg got the benefit. Actually, 31 % of patients experienced decrease in the cardiac output as the result of volume expansion. Intravenous saline infusion also consistently caused a significant increase in intrapericardial pressure, right atrial pressure, and left ventricular end-diastolic pressure [33].

## References


1. Argulian E, Halpern DG, Aziz EF, Uretsky S, Chaudhry F, Herzog E. Novel "CHASER" pathway for the management of pericardial disease. Crit Pathw Cardiol. 2011;10:57–63.
2. Maisch B, Seferovic PM, Ristic AD, et al. Guidelines on the diagnosis and management of pericardial diseases executive summary; the task force on the diagnosis and management of pericardial diseases of the European society of cardiology. Eur Heart J. 2004; 25:587–610.
3. Halpern DG, Argulian E, Briasoulis A, Chaudhry F, Aziz EF, Herzog E. A novel pericardial effusion scoring index to guide decision for drainage. Crit Pathw Cardiol. 2012;11:85–8.
4. Levy PY, Corey R, Berger P, et al. Etiologic diagnosis of 204 pericardial effusions. Medicine (Baltimore). 2003;82:385–91.
5. Corey GR, Campbell PT, Van Trigt P, et al. Etiology of large pericardial effusions. Am J Med. 1993;95: 209–13.
6. Permanyer-Miralda G, Sagrista-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. Am J Cardiol. 1985;56:623–30.
7. Porte HL, Janecki-Delebecq TJ, Finzi L, Metois DG, Millaire A, Wurtz AJ. Pericardoscopy for primary management of pericardial effusion in cancer patients. Eur J Cardiothorac Surg. 1999;16:287–91.
8. Zayas R, Anguita M, Torres F, et al. Incidence of specific etiology and role of methods for specific etiologic diagnosis of primary acute pericarditis. Am J Cardiol. 1995;75:378–82.
9. Sagrista-Sauleda J, Merce J, Permanyer-Miralda G, Soler-Soler J. Clinical clues to the causes of large pericardial effusions. Am J Med. 2000;109:95–101.
10. Sagrista-Sauleda J, Merce AS, Soler-Soler J. Diagnosis and management of pericardial effusion. World J Cardiol. 2011;3:135–43.
11. Klein AL, Abbara S, Agler DA, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr. 2013;26:965–1012. e15.
12. Ben-Horin S, Bank I, Shinfeld A, Kachel E, Guetta V, Livneh A. Diagnostic value of the biochemical composition of pericardial effusions in patients undergoing pericardiocentesis. Am J Cardiol. 2007;99:1294–7.
13. Seferovic PM, Ristic AD, Maksimovic R, Tatic V, Ostojic M, Kanjuh V. Diagnostic value of pericardial biopsy: improvement with extensive sampling enabled by pericardioscopy. Circulation. 2003;107:978–83.
14. Spodick DH. Acute cardiac tamponade. N Engl J Med. 2003;349:684–90.
15. Argulian E, Messerli F. Misconceptions and facts about pericardial effusion and tamponade. Am J Med. 2013;126:858–61.
16. Roy CL, Minor MA, Brookhart MA, Choudhry NK. Does this patient with a pericardial effusion have cardiac tamponade? JAMA. 2007;297:1810–8.
17. Cook DJ. Clinical assessment of central venous pressure in the critically ill. Am J Med Sci. 1990;299: 175–8.
18. Davison R, Cannon R. Estimation of central venous pressure by examination of jugular veins. Am Heart J. 1974;87:279–82.
19. Argulian E, Herzog E, Halpern DG, Messerli FH. Paradoxical hypertension with cardiac tamponade. Am J Cardiol. 2012;110:1066–9.
20. Brown J, MacKinnon D, King A, Vanderbush E. Elevated arterial blood pressure in cardiac tamponade. N Engl J Med. 1992;327:463–6.
21. Rowan SB, Krantz MJ. Paradoxical decrease in blood pressure after relief of cardiac tamponade: the role of sympathetic activity. Med Sci Monit. 2006;12:CS16–9.
22. Spodick DH. Acute pericarditis: current concepts and practice. JAMA. 2003;289:1150–3.
23. Sagrista-Sauleda J, Angel J, Sambola A, Alguersuari J, Permanyer-Miralda G, Soler-Soler J. Low-pressure cardiac tamponade: clinical and hemodynamic profile. Circulation. 2006;114:945–52.
24. Gillam LD, Guyer DE, Gibson TC, King ME, Marshall JE, Weyman AE. Hydrodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. Circulation. 1983;68:294–301.
25. Merce J, Sagrista-Sauleda J, Permanyer-Miralda G, Soler-Soler J. Should pericardial drainage be

performed routinely in patients who have a large pericardial effusion without tamponade? Am J Med. 1998;105:106–9.
26. Merce J, Sagrista-Sauleda J, Permanyer-Miralda G, Evangelista A, Soler-Soler J. Correlation between clinical and Doppler echocardiographic findings in patients with moderate and large pericardial effusion: implications for the diagnosis of cardiac tamponade. Am Heart J. 1999;138:759–64.
27. Eisenberg MJ, Oken K, Guerrero S, Saniei MA, Schiller NB. Prognostic value of echocardiography in hospitalized patients with pericardial effusion. Am J Cardiol. 1992;70:934–9.
28. Benza RL, Miller DP, Gomberg-Maitland M, et al. Predicting survival in pulmonary arterial hypertension: insights from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL). Circulation. 2010;122:164–72.
29. Frey MJ, Berko B, Palevsky H, Hirshfeld Jr JW, Herrmann HC. Recognition of cardiac tamponade in the presence of severe pulmonary hypertension. Ann Intern Med. 1989;111:615–7.
30. Hemnes AR, Gaine SP, Wiener CM. Poor outcomes associated with drainage of pericardial effusions in patients with pulmonary arterial hypertension. South Med J. 2008;101:490–4.
31. Tsang TS, Enriquez-Sarano M, Freeman WK, et al. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. Mayo Clin Proc. 2002;77:429–36.
32. Little WC, Freeman GL. Pericardial disease. Circulation. 2006;113:1622–32.
33. Sagrista-Sauleda J, Angel J, Sambola A, Permanyer-Miralda G. Hemodynamic effects of volume expansion in patients with cardiac tamponade. Circulation. 2008;117:1545–9.

## Pericardial Effusion and Tamponade-For Patients and their Families

Pericardial effusion refers to fluid accumulation in the double-membrane pericardial sack which surrounds the heart. Normally, there is little amount of fluid that allows the heart to expand and receive blood. Abnormal fluid or blood accumulation in the pericardial sack can occasionally compress the heart and impair normal filling of heart chambers and therefore normal heart functioning. This is referred to as 'tamponade', a potentially life-threatening condition. Pericardial effusion can develop suddenly, e.g., during a cardiac procedure when even a small amount of accumulated blood around the heart can cause compression; immediate intervention is necessary in that case to relieve the compression. Sometimes pericardial fluid accumulates slowly, over day and weeks as a result of infection, cancer spread, renal failure, or some other causes. In those cases the symptoms are less dramatic but commonly include shortness of breath. Other symptoms may include tiredness, chest pain, and fever. Certain findings on physical examination and changes on electrocardiogram and chest X-ray can be suggestive of pericardial effusion. Ultrasound of the heart (also called echocardiogram) is the most commonly used diagnostic test to establish the presence of pericardial effusion and to assess the degree of heart compression. To establish the cause of pericardial effusion the physician will typically order certain diagnostic tests which may include blood tests and occasionally advanced imaging tests (such as CT scan). Draining the pericardial fluid can be considered in some patients for two reasons: (1) establishing the diagnosis if the other tests are inconclusive; and (2) relieving compression of the heart. It is performed either by a needle or surgery. During the former, a needle is introduced into the pericardial sack commonly under the guidance of ultrasound or X-ray. The physician may decide to leave a tube (called a 'drain') in the pericardial sack for several days to avoid re-accumulation. The tube can be pulled out easily once the amount of drainage from the pericardial sack decreases significantly.

# Echocardiography-Guided Pericardial Drainage

11

Mark V. Sherrid

The clinical scenario of a patient who presents with symptomatic large pericardial effusion is relatively common in hospital-based practice [1]. Two management questions usually emerge: (1) should this effusion be drained?; (2) how should we do it? Percutaneous drainage of pericardial effusions with echocardiographic guidance has emerged as a commonly employed therapeutic and diagnostic option for these patients [2].

Echocardiographic guided pericardial drainage is a less invasive technique than subxiphoid surgical pericardial window [3, 4]. Moreover analysis of the pericardial fluid removed, especially with the advanced techniques now available will most often yield specific diagnostic information. It is indicated for diagnosis and symptomatic management of large pericardial effusions both with and without tamponade.

Echocardiographic guidance of pericardial drainage improves its safety. A first report came from Callahan and coworkers at the Mayo Clinic [3] which demonstrated the value of 2D echo-guidance for pericardiocentesis in 117 patients. Kopecky and colleagues then followed [4] with description of pericardial catheter drainage in 42 patients; it was noteworthy that only six patients (14 %) required subsequent surgical pericardiectomy. More recent review described 1,127 patients from a 21 year experience [5, 6]. The most common etiologies for the effusion were malignant 25 %, post operative 28 %, and cardiac perforation from prior invasive procedure 14 %. Virtually all of the patients had either tamponade clinically or echocardiographic tamponade (84 %). The recurrence rate was only 14 % for the patients who had extended drainage. The major complication rate was 1.2 %. Echo-guided drainage has been extended to the pediatric population [7].

Others have detailed their experience with percutaneous echo-guided pericardial drainage [8–23]. Comparison of surgical subxiphoid pericardiostomy and percutaneous drainage has been described [22, 23] though there has not been a randomized trial. In these series, pericardial drainage has generally performed well with little advantage shown by the surgical technique. Allen and colleagues found higher complication rates with the percutaneous technique, but pericardial drainage was not echocardiographically guided [23]. A similar comparison was reported by McDonald and coworkers [22]. This series was retrospective and not randomized; moreover, echocardiographic guidance was not universal. Hospital mortality and effusion recurrence was higher in the percutaneous group, but this could be due to selection of patients [20]. Regardless, if symptomatic pericardial effusion recurs, a repeat drainage procedure can be performed or surgical pericardiectomy may be selected at this time.

Surgery requires anesthesia and, often intubation. Risks of pneumonia and infection are

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increased. In the weakened patient this can result in prolonged intubation, pulmonary infection, morbidity (i.e., tracheostomy) and mortality. In patients with hypotension or hemodynamic instability, induction of anesthesia may be complicated by cardiac arrest. Surgical subxiphoid pericardiectomy and drainage often requires prolonged hospitalization and it is more painful. Also, in patients with pericardial malignancy, potentially prognosis-improving chemotherapy may be started sooner with the percutaneous technique.

## Anticoagulation During Pericardial Drainage

Anticoagulation does not preclude performing echo-guided pericardial drainage. A higher frequency of late post-operative pericardial effusion was thought to be due to anticoagulation. The average INR in patients on anticoagulation was 2.28 at the time of percutaneous drainage; ongoing anticoagulation is not a contraindication to percutaneous drainage [22]. In contrast, systemic anticoagulation would generally be reversed before open windown pericardiectomy and drainage.

## Exudate vs. Transudate, and Conventional Microbiology

Analyses of the pericardial fluid specific gravity (>1.015), protein level (>3.0 g/dL), fluid/serum ratio >0.5, LDH >200 mg/dL, serum/fluid >0.6, and low glucose can separate exudates from transudates, but are not directly diagnostic [15]. Purulent effusions with positive cultures have significantly lower fluid glucose levels <60–80 mg/dl, than non-infectious effusions. White cell count is highest in inflammatory and infectious diseases, and lowest in myxedema. In suspected bacterial infections, gram stain and at least three cultures of pericardial fluid for aerobes and anaerobes as well as the blood cultures are mandatory.

## Diagnostic Yield for Malignancy

History of prior malignancy particularly those in the chest, or in lymphatic continuity with the mediastinum will lead to a high suspicion of malignant effusion. The chest CT scan offers invaluable insight as to the likely etiology of pericardial effusion. Whenever a large pericardial effusion is found, chest CT with contrast should be performed, before pericardial drainage, if time allows. Fluid cytology should be performed on the fluid in all cases and yield is high. For patients with high suspicion of malignancy tumor markers (carcinoembryonic antigen, alpha-fetoprotein, and carbohydrate antigens) are also done. Concerning cytology, yield is higher with more fluid sent for analysis. It is our practice to send to cytology all the fluid remaining after the basic analyses. In the study of McDonald and coworkers, in patients with previously known malignancy, there was no difference in the frequency that malignancy was confirmed with cytology in the percutaneous group vs the open pericardiostomy group, 59 % vs. 62 %. The lack of incremental yield occurred despite pathological examination of the pericardial specimens. Of 52 patients with open drainage only four (7 %) had negative cytology and positive pathology. Their conclusion was that this makes "selection of the open procedure for enhanced diagnostic purposes a questionable strategy" [22]. High frequency for finding malignant cells in patients with malignant effusions has also been reported by others [10, 15]. In patients suspected of having malignant effusions, Lindenberger and colleagues found malignant cells in 82 % of cases and suspicious cells in 7 % [10]. These investigators recommend percutaneous drainage for the wider spectrum of large effusions, including late postoperative effusions (median 12 days post-op), uremia, inflammatory disease, idiopathic as well as malignant disease. Indeed, they would only exclude immediate post-operative hemorrhagic effusions.

## Specific Diagnosis of Tuberculosis from Fluid Analysis

A definite diagnosis of tuberculous effusion requires the demonstration of tuberculosis bacilli in pericardial fluid or tissue. However, the diagnosis is probable in patients with the diagnosis of active tuberculosis elsewhere in the body, most commonly in the lung. In this regard the chest CT scan with scrutiny for typical tuberculous involvement is invaluable. Pericardial fluid with a lymphocytic pericardial exudate with elevated adenine deaminase (ADA) levels is highly suggestive even if bacteria are not seen or grown.

Because of the relatively low yield of finding tuberculous bacilli in fluid and because of slow growth of the organism, serologic and DNA diagnosis from the fluid has lately received considerable attention [2, 24, 25]. Adenosine deaminase is an enzyme particularly found in T lymphocytes; it is a marker of enhanced cellular immunity and thus elevated in tuberculous infections and pericardial effusions [24] (Fig. 11.1). Various levels of ADA were tested as the cutoff level for the diagnosis of TB, and using ≥30 U/L was found to yield a sensitivity, specificity, PPV, and NPV of 94, 68, 80, and 80 % respectively [24]. However, elevated levels also occur with rheumatoid arthritis, sarcoidosis, and in some empyemas and a level of ≥40 is recommended by Imazio [1].

Interferon-γ (IFNγ, or type II interferon) is a cytokine that is critical for innate and adaptive immunity against viral and intracellular bacterial infections. IFNγ is an important activator of macrophages. The key association between

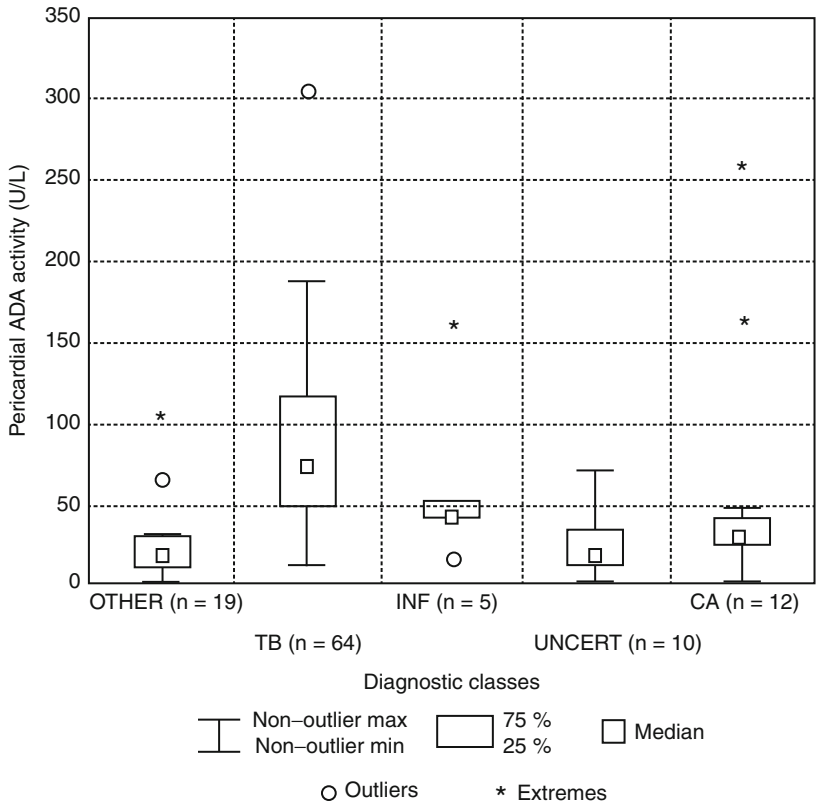


**Fig. 11.1** Pericardial adenosine deaminase activity in various causes of effusion: A box and whisker plot of the distribution of pericardial ADA activity in the various diagnostic classes. *OTHER* other pericardial effusions, *INF* infective, *UNCERT* pericardial effusions of unknown origin, *CA* malignancy (Reproduced by permission from Burgess et al. [24])

interferon-γ and granulomas is that interferon-γ activates macrophages so that they become more powerful in killing intracellular organisms. Using a cutoff level for IFNγ of 200 pg/L as being diagnostic for tuberculous pericarditis resulted in a 100 % sensitivity and 100 % specificity for TB in the study of Burgess et al. [24]. In a subsequent publication this group found that a much lower level, IFN γ ≥50 pg/ml, concentration had 92 % sensitivity, 100 % specificity and a positive predictive value (PPV) of 100 % for the diagnosis of tuberculous pericarditis; in this study pericardial fluid ADA ≥40 U/l had 87 % sensitivity and 89 % specificity [26].

Improved specificity is found with the polymerase chain reaction (PCR) that detects the presence of tuberculous DNA in the effusion. Lee et al. found a sensitivity of 75 % and a specificity of 100 % [25]. Others have reported much lower sensitivity in documented tuberculous pericarditis [26].

Thus, in suspected tuberculosis acid-fast bacilli staining, mycobacterium culture or, adenosine deaminase (ADA), interferon γ (IFN γ), PCR analyses, pericardial lysozyme, or radiometric growth detection for tuberculosis can be performed on fluid depending on local availability of analyses. Diagnosis of neoplastic effusion can be made confidently with low levels of ADA and high levels of CEA. In addition, high ADA levels may predict the evolution towards pericardial constriction.

## Complications of Pericardiocentesis and Drainage

Pericardiocentesis with echocardiography guidance is more often feasible when the effusion extends to the anterior pericardial space with >1 cm thickness of the effusion. Cases of loculated effusion or purely posterior effusion are best referred for surgery if drainage is necessary. In pericardial drainage appropriate case selection decreases complications. The most feared complication of 2-D echo guided catheter drainage is chamber perforation, which occurs infrequently, 16 patients (1.4 %) in the largest experience of 1,127 patients. Of these five (0.4 %) had lacerations that required surgery and one patient died postoperatively [5]. This complication may be avoided by careful selection of patients. Avoid patients without a clear target, a >1 cm anterior effusion under the needle. Moreover, the >1 cm clearance should be maintained throughout the cardiac cycle. Avoid patients with just posterior effusions. Monitor the ECG and if ventricular arrhythmias occur withdraw the needle. If perforation does occur and the catheter is placed in the right ventricle, the best course of action is to insert another catheter correctly into the pericardial space. Once its correct position is assured, withdraw the first catheter. Generally the right ventricular puncture will seal. If hemopericardium recurs after drainage at any time surgery should be done. Pneumothorax is also a possible complication of echo-guided pericardial drainage occurring in 1.1 % of patients. Of these five (0.4 %) of the patients required chest tube for lung re-expansion. This may be avoided by selecting an interspace that is directly over a large, clearly visualized, pericardial effusion, with minimal distance for the needle to traverse.

Another serious complication of pericardiocentesis is laceration or perforation of the coronary vessels. In addition, patients can experience air embolism, pneumothorax, arrhythmias (usually vasovagal bradycardia), and puncture of the peritoneal cavity or abdominal viscera. Internal mammary artery fistulas, acute pulmonary oedema, and purulent pericarditis are rarely reported.

Safety has been improved with echocardiographic or fluoroscopic guidance. Recent large echocardiographic series reported an incidence of major complications of 1–1.6 %. In contrast, in a large series of fluoroscopy-guided percutaneous pericardiocenteses, cardiac perforations occurred in <1 %, serious arrhythmias in 0.6 %, arterial bleeding in 1.1 %, pneumothorax in 0.6 %, infection in 0.3 %, and a major vagal reaction in 0.3 % [2, 27].

## Additional Intrapericardial Therapy for Malignant Effusions

Malignant pericardial effusion and tamponade may complicate breast cancer, lung cancer, lymphomas, Kaposi's sarcoma and leukemias. For many of these patients life expectancy is measured in weeks not years. Returning these patients home as soon as possible is an important goal. Reducing symptoms and improving the quality of life are the primary goals of treatment. Additional treatment besides drainage should be selected based on prognosis, and success rates. Oncologists, radiotherapists, and palliative care physicians should be consulted. For long-term prevention of recurrences, extended catheter drainage for several days seems to allow the two pericardial surfaces to adhere, decreasing the likelihood of fluid re-accumulation. Local installation of chemotherapeutic agents into the pericardial space is a reasonable approach for patients with overall expected shortened survival. Systemic chemotherapy or radiation therapy should be started as soon as possible for sensitive tumors. Therapeutic approaches vary for different tumor types. Use of 'pure' sclerosing agents like tetracycline has been replaced by agents with both sclerosing and antineoplastic activity (bleomycin or thiotepa), effective in breast cancer, at least when associated with systemic chemotherapy. Local chemotherapy with platinum, mitoxantrone, and other agents may have a role for local control, but beginning or resuming systemic chemotherapy may be the most important goal. Surgical window pericardiectomy is appropriate for patients with recurrent symptomatic re-accumulation.

## Technique [3, 6, 28]

The patient is placed in a shallow right anterior decubitus position by placing a pillow or wedge underneath the right shoulder. Two-dimensional echocardiography is performed, specifically searching for the area of the chest wall where the pericardial fluid is closest to the skin [3, 4] (Fig. 11.2a). Our preferred location is at the apex of the left ventricle. As pericardial fluid accumulates, the lung is pushed out of the way and the apex becomes completely occupied by the pericardial effusion (Fig. 11.2). An excellent ultrasound window offers assurance that one is not over the lung. This window often extends as far as the left anterior axillary line in very large effusions. The pericardial fluid is generally 2–3 cm below the skin in this location. Other sites of entry are possible, including the parasternal spaces and the traditional subxiphoid entry. The subxiphoid route always requires a longer needle track with associated discomfort and demands a more precise direction of needle angle. The parasternal spaces, while completely accessible, require one to avoid the internal thoracic artery [29]. We have generally required an effusion >1 cm in the AP direction. Attempting to place the needle in a smaller effusion risks hitting the heart.

The ideal interspace is chosen and a mark is made there with an indelible marker. With the transducer showing a "straight shot" into pericardial fluid one observes the transducer angle relative to the center of the chest: both medial-lateral and #2 cranio-caudad. Note also how far from the skin the fluid would be expected, and also the distance to the heart. Next, the ultrasound gel is cleaned off and the patient is prepped and draped.

The site of entry is just over the top of the rib. Local anesthesia is instilled, including both the skin and the intercostal muscle. The patient is lightly sedated. A ½cm incision is made with a #14 scalpel blade.

The pericardiocentesis needle is gently inserted through the incision with the precise angle that had been indicated by the echo probe (Fig. 11.2b). The trocar is left in place until the needle is almost at the depth where fluid might be expected. It is then removed and gentle aspiration is applied using a 3 cc syringe. The pericardium is usually entered with a small pop. Once pericardial fluid is found, it is important to keep the needle still to avoid lacerating the heart. One advantage of the apical route is that the coronary arteries are small at the apex and there is less danger of lacerating a major coronary artery. Such a complication is more likely from the parasternal entry.

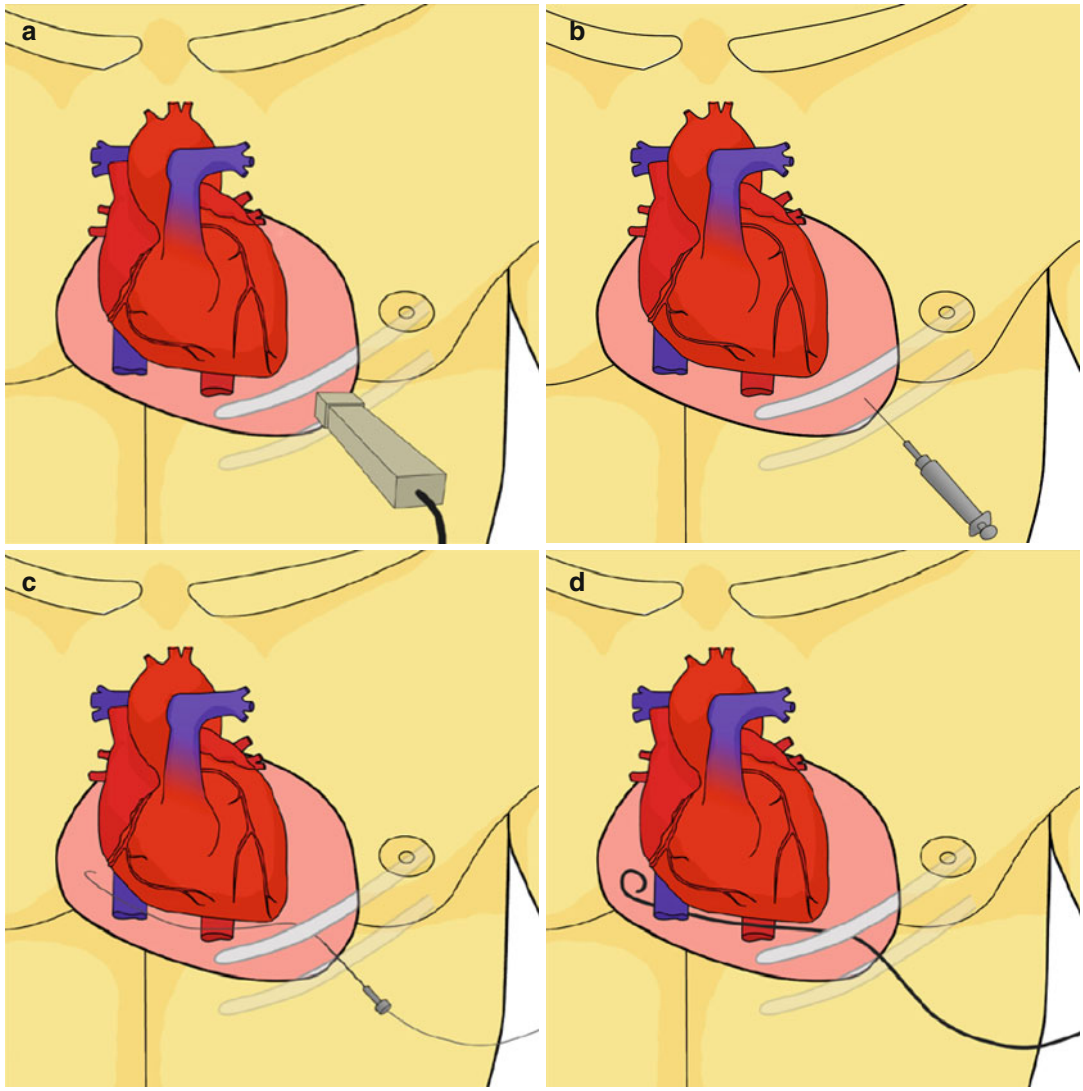


**Fig. 11.2** The technique of echocardiographic guided pericardial drainage: (**a**) Using the 2D echocardiographic transducer the physician searches for the interspace location on the chest wall with the closest access to the large pericardial effusion. Generally the fluid will be 2–3 cm from the transducer. The transducer angle, cranio-caudad and medial-lateral from the center of the chest is noted. The interspace location is marked with a marker. The patient is prepped and draped. (**b**) Local anesthesia and low dose sedation is administered. Using the same position and angle noted above, the pericardial needle is gently advanced over the top of the rib into the pericardial space. (**c**) A J wire is advanced though the needle and into the pericardial space. If fluoroscopy is available the J wire is noted to course from the left side into the right without any intervening boundaries. This is a good confirmer that the wire is in the pericardial space and not in the heart. A sheath is placed over the wire, using standard Seldinger technique. Agitated saline may be injected at this point. (**d**) The pigtail catheter is then advanced into the pericardial space and evacuation of the fluid is begun (Reproduced with permission from Sherrid et al. [28])

Bloody fluid is often aspirated in patients who have malignant effusions or post-surgical cases. However, on close inspection or after spinning, the fluid is serosanguineous not frank blood. Throughout the insertion of the needle and the sheath, a nurse observer watches the

electrocardiogram; the occurrence of ventricular tachycardia, indicates that the heart has been hit and the needle should be withdrawn.

A guide wire with a small J is placed through the needle into the pericardial space (Fig. 11.2c). If the procedure has been done in the cardiac catheterization laboratory, typically the wire is seen to pass from the left chest into the right chest on fluoroscopy, as there are no intracardiac borders to confine it. This is a good marker of entry into the pericardial space. The needle is removed and then, using standard Seldinger technique, a sheath and introducer are inserted into the pericardial space and the guide wire and introducer are removed, leaving just the sheath.

At this point agitated saline may be injected into the sheath to confirm location during echocardiography recording. This may also be done earlier, when just the needle is in place. It is not necessary to record the echocardiographic transit of the needle and sheath because the needle and sheath are rarely clearly seen. A pigtail catheter 6–8 F is inserted through the sheath and the sheath is withdrawn (Fig. 11.2d).

## Removal of the Fluid

The first aliquot should go for bacterial and fungal culture, Gram stain, AFB smear and AFB culture. The next aliquot should go for cells, protein, sugar and LDH. The last aliquot, the largest, should be sent in its entirety to the cytology laboratory. If tamponade had been present, after removal of 200 cc, the patient's vital signs will often improve. The catheter is then sewn to the chest wall with three restraining sutures and taped thoroughly. The need for multiple restraining sutures and a loop cannot be overemphasized, to avoid inadvertent removal of the catheter. The fluid is collected by gravity drainage or attachment to a Hemovac collector.

The catheter is left for at least 3 days until fluid drainage is <30 cc/day. This allows for apposition of the two layers of the pericardium with each other. This apposition fosters fibrous adhesions to form between the two layers of the pericardium and prevents new fluid accumulation. Adhesions are also the mechanism whereby surgical window pericardiostomy works, as well. After surgical pericardiostomy, the window closes after several days. To avoid clotting of the catheter, 3 cc of heparinized saline should be injected, using sterile technique, and left in the pericardial tube every 8 h.

There may be oozing of pericardial fluid around the catheter through the insertion site. This is not of concern, and we have not seen infections. It is managed by sterile dressing changes. If there is suspicion of malignancy, we generally wait until the cytology returns. If cytology is positive, in many cases, after consultation with the oncology service, we will inject intrapericardial bleomycin 30 units diluted in 50 cc normal saline, or thiotepa may be indicated. This is done to foster adhesions between the visceral and parietal pericardium. However, others indicate that bleomycin is not necessary to prevent recurrence [5].

When the catheter is removed the sutures are cut and the catheter is simply pulled back. Gentle pressure is placed on the entry site for a minute and then a small dressing is placed. Chest x-ray is obtained afterwards.

## References

1. Imazio M, Adler Y. Management of pericardial effusion. Eur Heart J. 2013;34:1186–97.
2. Maisch B, Seferovic PM, Ristic AD, et al. Guidelines on the diagnosis and management of pericardial diseases executive summary; the task force on the diagnosis and management of pericardial diseases of the European society of cardiology. Eur Heart J. 2004;25:587–610.
3. Callahan JA, Seward JB, Nishimura RA, et al. Two-dimensional echocardiographically guided pericardiocentesis: experience in 117 consecutive patients. Am J Cardiol. 1985;55:476–9.
4. Kopecky SL, Callahan JA, Tajik AJ, Seward JB. Percutaneous pericardial catheter drainage: report of 42 consecutive cases. Am J Cardiol. 1986;58:633–5.
5. Tsang TS, Enriquez-Sarano M, Freeman WK, et al. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. Mayo Clin Proc. 2002;77:429–36.
6. Tsang TS, Freeman WK, Sinak LJ, Seward JB. Echocardiographically guided pericardiocentesis:

evolution and state-of-the-art technique. Mayo Clin Proc. 1998;73:647–52.
7. Tsang TS, El-Najdawi EK, Seward JB, Hagler DJ, Freeman WK, O'Leary PW. Percutaneous echocardiographically guided pericardiocentesis in pediatric patients: evaluation of safety and efficacy. J Am Soc Echocardiogr. 1998;11:1072–7.
8. Vaitkus PT, Herrmann HC, LeWinter MM. Treatment of malignant pericardial effusion. JAMA. 1994;272:59–64.
9. Wei JY, Taylor GJ, Achuff SC. Recurrent cardiac tamponade and large pericardial effusions: management with an indwelling pericardial catheter. Am J Cardiol. 1978;42:281–2.
10. Lindenberger M, Kjellberg M, Karlsson E, Wranne B. Pericardiocentesis guided by 2-D echocardiography: the method of choice for treatment of pericardial effusion. J Intern Med. 2003;253:411–7.
11. Kabukcu M, Demircioglu F, Yanik E, Basarici I, Ersel F. Pericardial tamponade and large pericardial effusions: causal factors and efficacy of percutaneous catheter drainage in 50 patients. Tex Heart Inst J. 2004;31:398–403.
12. Selig MB. Percutaneous transcatheter pericardial interventions: aspiration, biopsy, and pericardioplasty. Am Heart J. 1993;125:269–71.
13. Maisch B, Ristic AD. Practical aspects of the management of pericardial disease. Heart. 2003;89:1096–103.
14. Gibbs CR, Watson RD, Singh SP, Lip GY. Management of pericardial effusion by drainage: a survey of 10 years' experience in a city centre general hospital serving a multiracial population. Postgrad Med J. 2000;76:809–13.
15. Meyers DG, Meyers RE, Prendergast TW. The usefulness of diagnostic tests on pericardial fluid. Chest. 1997;111:1213–21.
16. Wang PC, Yang KY, Chao JY, Liu JM, Perng RP, Yen SH. Prognostic role of pericardial fluid cytology in cardiac tamponade associated with non-small cell lung cancer. Chest. 2000;118:744–9.
17. de la Gandara I, Espinosa E, Gomez Cerezo J, Feliu J, Garcia Giron C. Pericardial tamponade as the first manifestation of adenocarcinoma. Acta Oncol. 1997;36:429–31.
18. Girardi LN, Ginsberg RJ, Burt ME. Pericardiocentesis and intrapericardial sclerosis: effective therapy for malignant pericardial effusions. Ann Thorac Surg. 1997;64:1422–7; discussion 1427–8.
19. Celermajer DS, Boyer MJ, Bailey BP, Tattersall MH. Pericardiocentesis for symptomatic malignant pericardial effusion: a study of 36 patients. Med J Aust. 1991;154:19–22.
20. Zipf RE Jr, Johnston WW. The role of cytology in the evaluation of pericardial effusions. Chest. 1972;62:593–6.
21. Salem K, Mulji A, Lonn E. Echocardiographically guided pericardiocentesis - the gold standard for the management of pericardial effusion and cardiac tamponade. Can J Cardiol. 1999;15:1251–5.
22. McDonald JM, Meyers BF, Guthrie TJ, Battafarano RJ, Cooper JD, Patterson GA. Comparison of open subxiphoid pericardial drainage with percutaneous catheter drainage for symptomatic pericardial effusion. Ann Thorac Surg. 2003;76:811–5; discussion 816.
23. Allen KB, Faber LP, Warren WH, Shaar CJ. Pericardial effusion: subxiphoid pericardiostomy versus percutaneous catheter drainage. Ann Thorac Surg. 1999;67:437–40.
24. Burgess LJ, Reuter H, Carstens ME, Taljaard JJ, Doubell AF. The use of adenosine deaminase and interferon-gamma as diagnostic tools for tuberculous pericarditis. Chest. 2002;122:900–5.
25. Lee JH, Lee CW, Lee SG, et al. Comparison of polymerase chain reaction with adenosine deaminase activity in pericardial fluid for the diagnosis of tuberculous pericarditis. Am J Med. 2002;113:519–21.
26. Reuter H, Burgess L, van Vuuren W, Doubell A. Diagnosing tuberculous pericarditis. QJM. 2006;99:827–39.
27. Sagrista Sauleda J, Almenar Bonet L, Angel Ferrer J, et al. The clinical practice guidelines of the Sociedad Espanola de Cardiologia on pericardial pathology. Rev Esp Cardiol. 2000;53:394–412.
28. Sherrid MV, Sherrid G, Uretsky S. Echocardiography-guided pericardial drainage. In: Herzog E, Chaudhry F, editors. Echocardiography in acute coronary syndromes from prevention to diagnosis and treatment. London: Springer; 2009. p. 333–40.
29. Kronzon I, Glassman LR, Tunick PA. Avoiding the left internal mammary artery during anterior pericardiocentesis. Echocardiography. 2003;20:533–4.

## Echocardiography-Guided Pericardial Drainage-For Patients and their Families

Your doctor has told you that there is fluid accumulating in the sac that surrounds your heart. This sac is called the pericardial space. The fluid is called a pericardial effusion. It may be compressing your heart and causing you symptoms of shortness of breath, chest pain or weakness or you may have mild chronic symptoms. Regardless, your doctor has recommended that the fluid should be removed to improve your symptoms, and that the fluid should be analyzed to determine the cause of the fluid collection. How then should this be done?

There are two choices. Either you doctor will recommend a small surgical procedure called a pericardial window, or the fluid can be drained through the skin using a catheter guided by echocardiography- ultrasound of the heart. The judgment of which of these two techniques to use is guided by a variety of issues: size of the effusion, presumed cause of the effusion, results of xrays and CT scans you may have had, other illness you have had, and local expertise of the doctors caring for you. If your doctor recommends echocardiography-guided pericardial drainage here is what you can expect.

The whole procedure should take 60–90 min. It may be done in your regular hospital bed, or in the echocardiography or catheterization laboratory. You may be sedated, but general anesthesia is usually not needed. First, echocardiography cardiac ultrasound will be performed, you probably have had this before, but this exam will be focused on finding the specific place on your chest wall where a catheter (thin tube) can be safely inserted into your chest wall and into the pericardial sac to drain the fluid. Once the site is determined the physician operator will inject some local anesthesia into the skin and subcutaneous tissues. This may hurt a bit. Then he/she will use a longer needle to find the fluid, insert a sheath, and then a catheter into the sac. He may ask for echocardiography or fluoroscopic (xray) pictures at this point to assure that the catheter has gone to the right spot. You will feel some tugging and pressure in your chest wall during this period. You might feel more severe discomfort. If you do, please ask for intravenous pain medication to ease the pain.

After the tube is well positioned drainage of the fluid begins. The physician will send samples in bottles to various laboratories for analysis. The catheter usually is hooked up to a removal device called a Hemovac, though sometimes only gravity bag is used to drain the sac. The catheter is sutured to your chest wall to prevent you from accidentally pulling it out. A dressing is applied. Your doctors may inject a blood thinner into the catheter to keep it from clotting.

Back on the hospital floor the collecting bag is emptied and measured. Almost always the volume of fluid draining decreases over time. The duration the tube remains in is a judgment that will be made by your doctors, but it can stay in for 5–7 days if necessary. Generally it comes out at 4 days, after the tests have returned. There is a benefit to the days of drainage: the two surfaces of the pericardium tend to adhere during this period which may prevent recurrence of fluid. Removal of the catheter is generally painless, though there might be a short burst of discomfort as it is removed.

In the vast majority of patients this sort of drainage is definitive and all that is needed. However, in ~15 % of patients fluid reaccumulates along with symptoms and another procedure needs to be done. This could be another echocardiography-guided pericardial drainage procedure or a surgical window. On occasion, a surgical procedure may be needed for another reason: to establish a diagnosis of why the fluid has collected if the diagnosis has not been established by the first drainage procedure.

# Surgical Management of Pericardial Disease

12

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## For Physicians and Health Care Providers

### Introduction

The pericardium is an important structure of unique interest to the cardiac surgeon who routinely encounters its elegant design. The pericardium itself is a lubricated compartment that protects the heart by maintaining its position in the chest and limiting dilation from volume overload. It is <2 mm thick and composed of collagen and elastin [1]. The visceral and parietal layers are contiguous with each other at the origins of the great vessels. Entry into the pericardium for surgery reveals not only the heart but also other structures of anatomic significance. Openings are present at the superior vena cava, inferior vena cava, pulmonary artery, and aorta. The phrenic nerves adhere to the pericardium laterally and are critical for preservation of respiratory function [2].

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The pericardium has the unique quality of passive noncompliance [2]. Surgery of the pericardium is mainly required for hemodynamic effects of a pressurized sac around the heart that can occur with the presence of fluid or constriction.

### Resection of Pericardial Cysts, Tumors, and Congenital Defects

Rare conditions of the pericardium occasionally require surgical intervention. Pericardial cysts are fluid-filled sacs that are often located at the pericardiophrenic angle, more commonly on the right side [3]. Generally, these are of little clinical significance. These cysts may form as a result of inflammation, bacterial infection, trauma, or cardiac surgery. Most cysts are discovered incidentally. Symptoms can occur and may include chest pain, dyspnea, cough, or palpitations [4]. If symptomatic, surgical excision is indicated and may be performed in an open or minimally invasive fashion [5].

Cardiac neoplasms are also rare, found in 1–3 % of patients at autopsy [6]. The pericardium itself may have primary or metastatic tumors that require resection [7]. Mesothelioma is the most common primary malignancy of the pericardium [7]. Symptoms such as chest pain, constrictive pericarditis, or cardiac tamponade have been described [7]. Malignant pericardial effusion is most often caused by metastatic cancer.

Congenital defects of the pericardium occur in 1/10,000 autopsy specimens, with 70 % of

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these defects occurring on the left side [8, 9]. A partial defect may be symptomatic and can be complicated by herniation and strangulation of the heart through the defect. Total deficit of the pericardium occurs in 1/14,000 births and these patients are usually asymptomatic [9]. They are at risk for traumatic type A aortic dissection [10]. Patch replacement of the pericardium (pericardioplasty) has been described with good success [11, 12].

## Mediastinal Exploration

Exploration of the mediastinum and opening of the pericardium are required in a variety of clinical settings. These include trauma, iatrogenic injury, postoperative cardiac surgery, and aortic dissection.

### Trauma

Traumatic pericardial effusion after blunt or penetrating injury is a rare but clear indication for drainage and possibly exploration [13–15]. In the current era, diagnosis of a traumatic injury may still be difficult despite rapid ultrasound, echocardiography, and computerized tomography scans. Prompt drainage is important regardless of method and early identification of injury is the key [16]. Traumatic cardiac rupture requiring repair has been found in up to 5.7 % of patients who require drainage [16].

### Iatrogenic Injury

Iatrogenic injury to the heart can occur after catheter-based procedures and may require surgical intervention. Percutaneous cardiac procedures are complex and rapidly advancing in the current era. Transseptal puncture to access the left heart takes place during electrophysiology procedures on the left atrium. Percutaneous transaortic valve replacement and valve dilations involve complex vascular access and imaging techniques. Guide wires, sheaths, dilators, balloons, leads, or ablation techniques may result in cardiac injury [17]. The incidence of perforation in atrial fibrillation ablation is reported as 6 % [18]. Pacemakers have an incidence of perforation of 1.7 % [19]. When fluid accumulates in the pericardial space after catheter-based procedures, it is usually a result of cardiac perforation [17]. It is important to remember that in traumatic situation <100 cc of fluid in the pericardial space can cause hemodynamic compromise [20, 21]. Similar to traumatic injury, prompt recognition is the key. These injuries are routinely treated by percutaneous drainage alone. However, depending on the location and size of injury, median sternotomy and exploration may be required [17].

### Postoperative Tamponade

Cardiac surgeons open the pericardium in order to access the heart. Although drainage tubes are left within the mediastinum after surgery, coagulopathy and postoperative bleeding can occur. This is more common after long cardiopulmonary bypass times and complex procedures. Strict criteria for reoperation for bleeding are maintained in order to prevent complications and organ dysfunction in the postoperative period. In addition, surgeons must carry a high suspicion of tamponade in patients with significant or persistent high-volume bleeding initially who have a sudden drop in output with corresponding hemodynamic changes. These may include: equalization of right and left heart pressures, low cardiac index, low mixed venous saturation, tachycardia, hypotension requiring increased pressors, and elevated central venous pressure. A stat chest x-ray (CXR) or echocardiogram may confirm tamponade but this is ultimately a clinical diagnosis. Patients are promptly returned to the operating room for evacuation of hematoma and exploration through the previous sternotomy incision.

Postpericardiotomy syndrome is another situation in which inflammatory fluid accumulates in the pericardial space after surgery. This syndrome occurs in a delayed fashion after cardiac surgery and has been documented in up to 1.5 % of patients [22] (Fig. 12.1).

Despite over 70 years experience of cardiac surgery, the question of pericardial closure after cardiac procedures has not been definitively answered [23]. Some surgeons close the pericardium, others do not, and many believe that neither is of clinical significance. There has been little

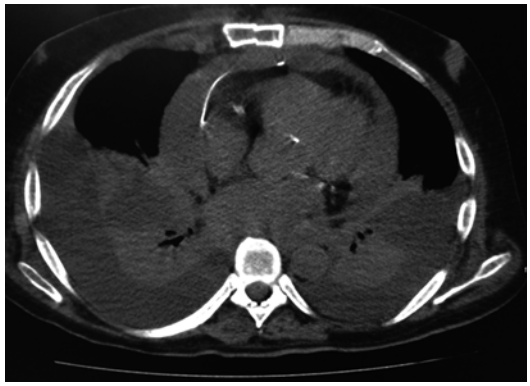

**Fig. 12.1** Computerized tomography scan of the chest demonstrating a patient with delayed pericardial effusion after cardiac surgery resulting in hypotension, low cardiac output, and bilateral pleural effusions with atelectasis

scientific study and no clinical randomized trials. What is known is that the pericardium maintains compliance and the integrity of the Starling curve as it limits hypertrophy with exercise. It is structurally protective with mechanical membranous and ligamentous function. Benefits of closing the pericardium include making potential reoperation safer with fewer adhesions, return of the mediastinum back to the original setting, and the possibility of improved hemodynamics [23]. Others are concerned that closure results in increased risk of tamponade, negative hemodynamics, increased use of inotropes, and possible graft compromise [23]. Tension- free substitutes do exist but come with financial cost and possible infectious complications [23].

### Aortic Dissection

Pericardial effusion and tamponade may occur in the setting of Type A aortic dissection. In this setting, surgery for the dissection should be performed immediately rather than drainage of the hemopericardium, which may result in further bleeding [4].

## Pericardial Window

The etiology of pericardial fluid causing compression varies and includes infections, post-irradiation sequelae, collagen vascular diseases, myocardial infarction, and malignancy [24–30] (Table 12.1). Medical therapy may be started initially but large effusions associated with pericarditis may be unresponsive to non-steroidal anti-inflammatory drugs, corticosteroids, or colchicine [29]. The diagnosis of a large pericardial effusion can be made from CXR, computerized tomography (CT) scan or echocardiography (Fig. 12.2). The definitive treatment for large pericardial effusions or cardiac tamponade is

**Table 12.1** Etiology of pericardial disease [25]

| |
|---|
| **Congenital** |
| Congenital anomalies and defects |
| Pericardial cysts |
| **Acute and chronic pericarditis** |
| **Effusive +/– tamponade** |
| Idiopathic |
| Uremic |
| Infectious |
| Pyogenic |
| Tuberculosis |
| Viral |
| Neoplastic |
| Associated with systemic disease (connective tissue disease) |
| Traumatic |
| Radiation |
| **Constrictive +/– effusion** |
| Idiopathic |
| Infectious |
| Previous cardiac surgery |

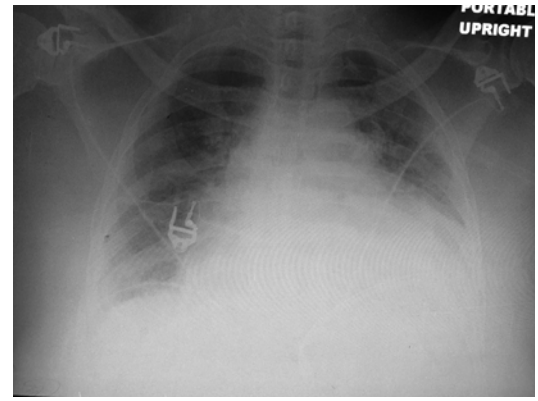


**Fig. 12.2** Chest x-ray of a patient with a large pericardial effusion from idiopathic pericarditis. Note the marked cardiomegaly and obscured left diaphragm

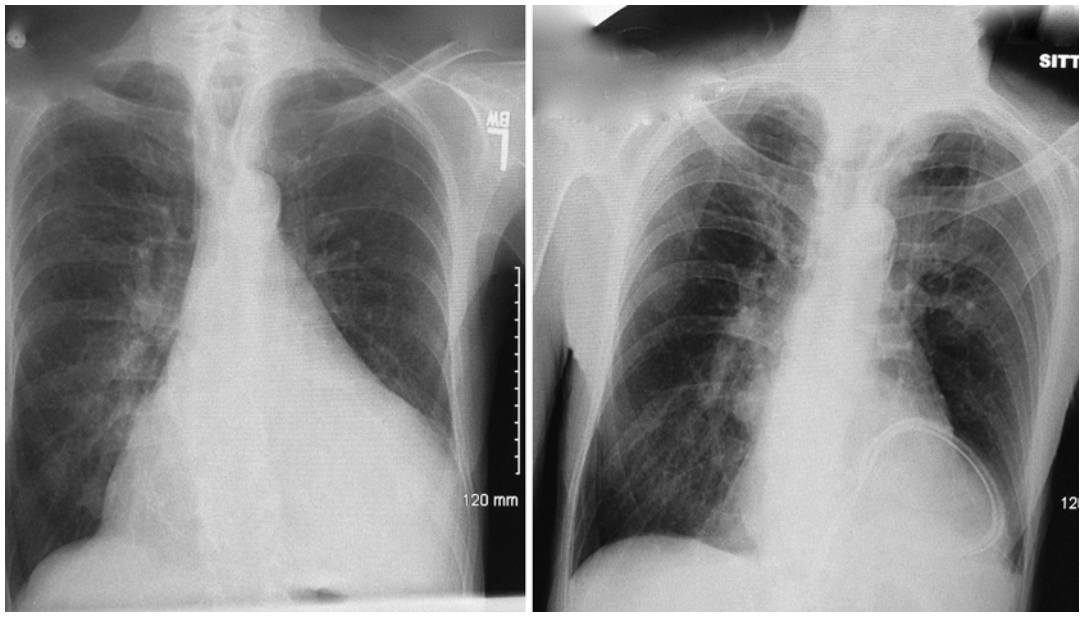


**Fig. 12.3** Example of pre- and post-operative chest x-rays in a patient who underwent open surgical drainage via sub-xiphoid pericardial window. Note the position of the long flexible drain lying behind the heart and marked decrease in the large cardiac silhouette

pericardial drainage. If hemodynamic compromise has occurred, medical treatment has failed, or a diagnosis is needed, then intervention is required. The specific presence of purulent pericardial fluid may have a distinct effect separate from tamponade physiology and has a characteristically high mortality without drainage [31].

An open surgical procedure offers several advantages. Firstly, complete drainage can be achieved. There is ample access to pericardial tissue for histopathological and microbiological diagnoses. Loculated or mixed effusions can be evacuated (Fig. 12.3). There is little risk of traumatic injury as there is direct visualization of the pericardial space.

## Sub-Xiphoid Pericardial Window

Sub-xiphoid pericardial window, or subxiphoid pericardiostomy, is a common approach to pericardial drainage [25–29, 32]. General anesthesia is preferred for this procedure, but it may be performed with monitored or local anesthesia [33]. Rapid induction can proceed with careful attention to blood pressure throughout the process. The patients are placed supine during the procedure. If the patient is suspected to be in true cardiac tamponade, the patient's chest is often prepared and draped for surgery while he remains awake. In case of hemodynamic collapse upon induction, rapid evacuation of fluid may be performed. Sub-xiphoid drainage under local anesthesia is also an acceptable choice for patients who are unstable.

### Technique

A midline incision is made from the xiphisternal junction to below the tip of the xiphoid. Alternatively a 5 cm transverse incision can be made at the tip of the xiphoid [1]. The upper linea alba is divided in the midline and the xiphoid is incised or completely resected. The tissue plane between the posterior wall of the sternum and the anterior pericardium is developed by blunt finger dissection. The distal sternum is then elevated for visualization of the pericardium. The anterior pericardium is grasped directly and incised to drain the fluid. Culture swabs, fluid analysis, and cytology specimens

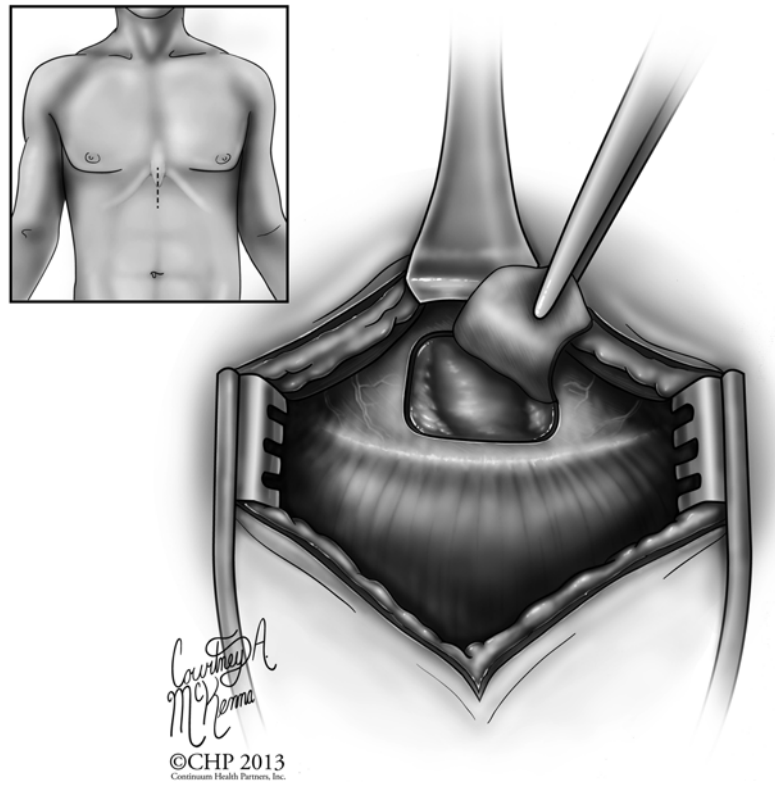


**Fig. 12.4** Diagram of the incision site and technique for performing a sub-xiphoid pericardial window. Direct visual access of the pericardium and pericardial space is available

are collected. Pericardial fluid is analyzed for hematocrit and cell count, amylase, lactate dehydrogenase, protein, glucose, culture, and cytology. The pericardial space is then evaluated by direct vision, digital exam, and echocardiographic visualization if needed. The pericardium may be explored digitally to identify adhesions or tumor deposits. The optional use of intraoperative transesophageal echocardiography may facilitate removal of complex loculated collections and can insure complete drainage. A piece of pericardium is excised, typically 4–5 cm in size (Fig. 12.4). A single chest tube is placed through the pericardiotomy, exiting the body through a separate incision. Both firm large bore and soft flexible drains may be used to insure optimal drainage, particularly in the case of a bloody effusion. The chest tube is left in place for several days after the operation until the drainage is minimal, usually <50 cc/day. This time period is the key to this procedure. The irritative nature of the chest tubes within the space can help form adhesions between the pericardium and epicardium to help prevent recurrence. The chest incision is closed in two layers and covered with sterile dressings.

## Outcomes

Multiple retrospective studies over the past 25 years have reviewed outcomes of subxiphoid pericardial window, after its initial success in providing drainage and preventing recurrent effusion. Early studies, however, reported 30-day mortality rates of up to 20 %, with deaths due to associated cancer rather than the procedure itself [34]. Current studies show 30-day mortality of 0.8–4.8 % [27, 35, 36] and a recurrence rate of 2–10 % [35–37].

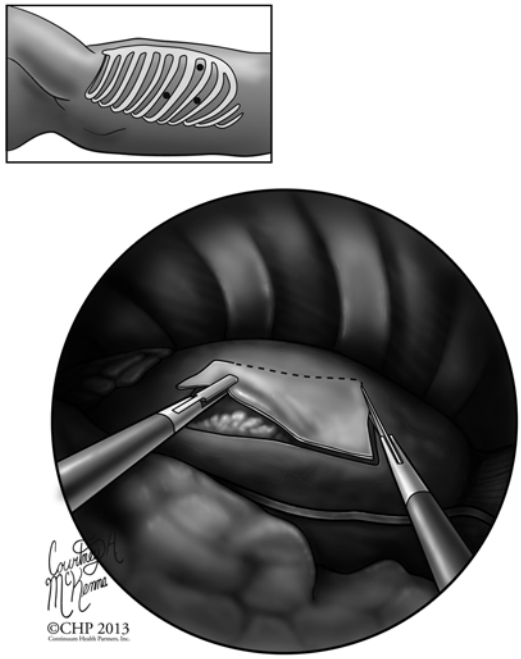


**Fig. 12.5** Diagram of the incision sites and technique for performing a video-assisted thoracoscopic pericardial window. Note the visualization of the pericardium within the chest cavity and the area of pericardium available for resection

Risk factors for short-term mortality include the occurrence of postoperative low cardiac output syndrome (PLCOS). This syndrome is early and rapid cardiac failure after relief of tamponade and can occur in up to 4.8 % of patients [36]. It accounted for all the postoperative deaths (0.8 %) in a recent study [27]. The mechanism for this complication is not completely clear but is likely due to chronic external support of the heart by pericardial fluid. When this support is removed, the heart may immediately overdilate, resulting in systolic dysfunction and failure. These patients need close monitoring, as the mortality from this syndrome is very high.

Complications of the procedure include recurrence and transient arrhythmias [36]. Constrictive pericarditis develops in up to 3 % of patients who survive after 1 year, most commonly in those patients with tuberculous pericarditis or nontuberculous bacterial pericarditis [27]. Direct injury to the heart may occur in 0.8 % and requires median sternotomy for treatment [27]. Wound infections may occur in up to 5 % of patients [27].

Underlying disease, specifically malignancy, is an important risk factor for decreased survival after subxiphoid pericardiostomy [28]. The presence of malignant pericardial effusion leads to limited life expectancy; better survival is found in those patients who have malignant cells but no tumor in the pericardium [38]. The type of malignancy also plays a role: patients with hematologic malignancy were found to have significantly longer survival when compared with patients with other malignancies [36]. Metastatic lung cancer to the pericardium has been shown to have a very poor survival rate, particularly when compared to other cancers [28, 39]. Detectable malignant invasion of the thorax on CT scan and positive echocardiographic findings compatible with tamponade are two independent risk factors for poor outcome [28].

### Comparison with Percutaneous Drainage

The optimal management for pericardial effusions with acute pericardial tamponade remains controversial. The two most commonly performed techniques include subxiphoid window and percutaneous catheter drainage (Table 12.2). Percutaneous catheter drainage may be performed with local anesthesia and requires a needle to be placed in the pericardial space, usually under echocardiographic guidance. A guide wire can be inserted and a drainage catheter is passed over the wire [40].

Multiple studies have directly compared these two techniques (Table 12.3). Allen et al. performed a direct comparison of the two procedures in 1999 [35]. The mortality, complication, and recurrence rates were significantly higher for percutaneous drainage (4.3, 17.3, and 33.3 %, respectively) than for subxiphoid drainage (0, 1.1, and 1.1 % respectively) [35]. This same study combined published collected data from 1977 to 1999 and found 560 patients undergoing subxiphoid pericardial window for pericardial tamponade. These patients had a mortality rate of 0.6 %, a complication rate of 1.5 %, and a recurrence rate of 3.2 % [35]. Percutaneous catheter drainage (331 patients) demonstrated increased

**Table 12.2** Advantages and disadvantages of subxiphoid pericardial window vs. percutaneous catheter drainage [24–28, 35, 37, 41]

| | Advantages | Disadvantages |
|---|---|---|
| Subxiphoid pericardial window | • Direct visualization<br>• Access to pericardial tissue for histopathological and microbiological diagnoses<br>• Evacuation of loculated or mixed effusions<br>• Less risk of traumatic injury | • General anesthesia (or local anesthesia with sedation for unstable patients)<br>• More invasive |
| Percutaneous catheter drainage | • Local anesthesia<br>• Less invasive<br>• Immediate relief of symptoms | • Higher complication rate (blind needle placement)<br>• Higher recurrence rate |

**Table 12.3** Outcomes data of surgical subxiphoid window vs. percutaneous drainage of pericardial effusions [35, 37, 41]

| | Date | Patient number | Mortality (%) | Morbidity (%) | Recurrence (%) |
|---|---|---|---|---|---|
| *Subxiphoid* | | | | | |
| Combined (Allen) [35] | 1977–1995 | 560 | 0.6 | 1.5 | 3.2 |
| Allen [35] | 1999 | 94 | 0 | 1.1 | 1.1 |
| McDonald [37] | 2003 | 150 | 10.7 | 0.1 | 4.7 |
| Saltzman [41] | 2012 | 72 | 19.8 | 26.4 | 2.8 |
| *Percutaneous* | | | | | |
| Combined (Allen) [35] | 1984–1999 | 331 | 4.3 | 10.6 | 13.9 |
| Allen (included in combined) [35] | 1999 | 23 | 4.3 | 17.3 | 33.3 |
| McDonald [37] | 2003 | 96 | 22.9 | 3.1 | 15.6 |
| Saltzman [41] | 2012 | 121 | 18.1 | 4.9 | 28.9 |

mortality, morbidity and effusion recurrence of 4.3, 10.6, and 13.9 %, respectively [35]. Subxiphoid pericardiostomy is a safe and durable technique for chronic effusion despite the less invasive nature of the percutaneous drain.

Others studies concur that recurrent effusion is more frequent in the percutaneous versus the open group, (28.9 % vs. 2.8 %), [41] and (15.6 and 4.7 %) [37]. Mortality rates that are higher in the percutaneous group are difficult to extract from data as variable comorbid conditions and hemodynamic states leading to percutaneous drainage are confounding factors. It has been shown that extended catheter drainage may help decrease this rate of recurrence in percutaneous techniques, likely secondary to the inflammatory/adhesion forming qualities of the drains themselves [42].

Ultimately, an individualized, patient-centered approach is necessary in making decisions about percutaneous versus open procedures. Patients with positive cytology on previous pericardiocentesis or a limited lifespan where recurrence is unlikely may benefit from percutaneous drainage. Effusions that are loculated, posterior, or of mixed density, may be better served with an open subxiphoid window. The presence of malignancy, direct invasion of the pericardium, poor long term prognosis, and clinical conditions all play a role in this decision process.

## Thoracoscopic Pericardial Window

An alternative technique to subxiphoid window is video-assisted thoracoscopic surgery (VATS) drainage of pericardial fluid into the pleural space. Anesthesia preparation is more complicated and

time-intensive. It requires bronchoscopic-directed placement of a double-lumen endotracheal tube to achieve single lung ventilation. Lateral decubitus positioning is also required. Thoracoscopy is performed through a 10-mm camera port placed in the seventh intercostal space in the mid-axillary line. The pericardial resection and any additionally procedures are completed through one or two working incisions. A section of pericardium approximately 4–5 cm in diameter is resected anterior to the phrenic nerve, which creates a window into the pleural space [43] (Fig. 12.5). A flexible chest tube may be placed into the pericardial space along with a pleural tube. Alternatively, a single chest tube may be placed into the pleural space for drainage of both cavities.

This procedure has specific advantages and disadvantages. One benefit of the thoracoscopic approach is that it allows simultaneous access to the pleural and pericardial spaces, which is helpful in the setting of large pleural effusion or concomitant pleural disease. Thoracoscopy affords better visualization of the pleural cavity and pericardium, which allows for more direct sampling of suspicious sites [43, 44]. The entry into another body cavity is a potential disadvantage depending on the co-morbidities of the patient. Generally, sub-xiphoid windows are preferred in a setting in which the patient is unstable to avoid the prolonged anesthetic and preparation time that is associated with VATS.

In a study of 71 patients directly comparing sub-xiphoid and VATS, O'Brien et al. found significant differences in complication rates [44]. The sub-xiphoid group had a 2 % morbidity rate while the VATS group had a 27 % morbidity rate [44]. Complications included pneumothoraces, an on-going air leak requiring discharge with a Heimlich valve, and readmission for self-limited drainage from the chest tube site. The 30-day mortality rate was 13 and 0 % for subxiphoid and VATS, respectively, but all mortalities were non-specific to the procedure and were attributed to advancing malignancy or worsening of underlying medical illness in the absence of recurrent effusion [44]. Patients with greater comorbidities were selected for sub-xiphoid drainage. Recurrence was similar in both groups (10 % of the sub-xiphoid group and 8 % of the VATS). Malignant effusions were found to have a greater risk of recurrence [44].

A recent study found that limited survival is not a contraindication for VATS pericardial window as selected patients could achieve improvement through palliation [45]. Prognostic factors of poor survival included pericardial cytology with metastatic involvement of the pericardium, similar to other studies [44, 28]. Others have found that there are few differences in recurrences or complications, but that operative time is longer for VATS [46].

In summary, the sub-xiphoid approach is simpler, faster, and slightly less morbid. This is the preferred approach if the patient's life expectancy is likely to be limited due to major comorbidities or extensive metastatic disease. In contrast, those patients with benign disease, malignancy that has not metastasized extensively or is responsive to chemotherapy, and those who require concomitant intrapleural procedures, would benefit from VATS [44] (Table 12.4).

## Pericardiectomy

### Indications

Constrictive pericarditis is a rare but severely disabling condition of the pericardium leading to impaired filling of the ventricles and reduced ventricular function [4]. The majority of cases of constrictive pericarditis are idiopathic [4, 47].

**Table 12.4** Advantages and disadvantages of thoracoscopic pericardial window [43, 44]

| Advantages | Disadvantages |
|---|---|
| • Simultaneous access to pericardial and pleural spaces | • Prolonged anesthesia time |
| • Better visualization of pericardium and pleural cavity | – Double lumen tube placement for single lung ventilation |
| • More direct sampling of suspicious sites | – Lateral decubitus positioning |
| • Concomitant thoracoscopic procedures | • Increased morbidity in presence of comorbid conditions or extensive metastatic disease |

Patients present with symptoms such as dyspnea, orthopnea, jugular venous distention, or ascites. CXR or CT scan may confirm a thickened or calcified pericardium, a classic diagnostic feature of constrictive pericarditis [4]. However constriction may present in up to 18 % of patients with normal pericardial thickness [48]. True constrictive physiology is best defined at cardiac catheterization with findings as described in previous chapters. The hallmarks of constrictive physiology are equalization of diastolic pressures in the ventricles and a dip plateau pattern (square root sign) of the ventricular filling pressure curves [1]. Pericardiectomy for constrictive pericarditis corrects hemodynamic abnormalities and can produce dramatic clinical improvement [47].

Pericardiectomy is indicated once the diagnosis of constrictive pericarditis has been established. Constrictive pericarditis is irreversible and surgical resection is the only effective treatment. Surgeons are sometimes consulted to evaluate patients for pericardiectomy who have frequent and highly symptomatic recurrences that are refractory to medical therapy [4]. Recurring pericarditis management relies on exercise restriction and is treated medically with NSAIDS, colchicine, and/or corticosteroids [4]. Patients who are deemed candidates for surgery should be on a steroid-free regimen for several weeks prior to surgery. Patients with little physiologic effects and significant comorbidities should be delayed until more significant symptoms occur. This is especially true in the case of radiation-induced pericarditis, in which the myocardial tissue is affected [1, 49].

## Technique

Pericardiectomy is performed under general anesthesia. Anesthetic considerations are similar to other routine cardiac procedures except for the use of short acting muscle relaxants. It is helpful to have minimal paralysis during dissection near the phrenic nerve. TEE is used routinely to evaluate changes in cardiac size and function and, specifically, to assess the tricuspid valve which may require repair for severe regurgitation and chronic right heart failure [50].

Cardiopulmonary bypass is usually on standby and surgeons will reserve it for extremely difficult dissections, reoperations, or concomitant required cardiac surgery. Pericardiectomy is most commonly approached through a median sternotomy, which provides excellent exposure. Left thoracotomy or bilateral anterior thoracotomy approaches have also been used. Finding the proper plane can be very difficult; the plane between the parietal and visceral layers is avascular. Serious bleeding and/or injury can result if the epicardium is penetrated. Sometimes the parietal layer may be very densely adhered to the epicardium with heavily calcified spicules. These areas can be rongeured, but total removal is often hazardous. The dissection plane in a post-radiated heart provides further challenges to complete decortication [50, 51].

A key step in this procedure is that resection should begin with the left ventricle first. Specific right ventricular dilatation and failure can result when the right ventricle is freed from its pericardial restraints before the left ventricle is freed. This would allow for increased filling of the right ventricle in the setting of persistently increased right ventricular afterload. Pulmonary edema and right ventricular failure due to outflow obstruction can occur if the right ventricle is released first [1]. Ultimately the goal is to do as complete a resection as safely possible, with decortications of both ventricles, both atria, and both cava (Fig. 12.6). Care should be taken to visualize and preserve both phrenic nerves. Hemostasis should be achieved and chest tubes left in place. Utilizing a pulmonary artery catheter, the adequacy of the pericardial resection can be evaluated by measuring mean arterial pressures and RV end-diastolic pressures before and after completion of the operation. Perioperative low output cardiac failure can usually be managed with inotropic medications and occasionally the use of an intra-aortic balloon pump if needed.

Manipulation of the heart can lead to hemodynamic instability in these patients. The need for cardiopulmonary bypass (CPB) must be considered during this procedure and initiated if necessary. This is straightforward in the setting of median sternotomy in which the aorta and right

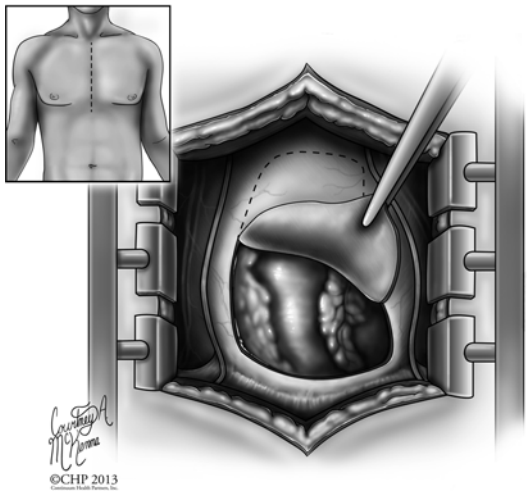


**Fig. 12.6** Diagram of the incision site (median sternotomy) allowing access to the entire heart for pericardiectomy for constrictive pericarditis. The anterior, lateral, and inferior pericardium should be excised to allow for complete release of the constrictive process

atrial appendage are available for cannulation. The femoral artery and vein are also sites of potential cannulation for bypass. It must be remembered that cardiopulmonary bypass empties the heart and may make dissection of the pericardium more difficult. However, it prevents hemodynamic shifts with lifting and dissection that can cause poor organ perfusion and postoperative dysfunction. CPB requires full anticoagulation with heparin and can increase bleeding, coagulopathy, and a generalized systemic inflammatory response.

This surgery is often technically demanding and tedious. There is potential for myocardial injury, phrenic nerve injury, and coronary artery injury. With longstanding disease there can be remodeling of myocardial anatomy. Changes in filling can also contribute to failure. These patients require intensive care monitoring postoperatively with constant hemodynamic assessment and early cardiac support if needed. This may include vasopressors and inotropic medications.

## Outcomes

In the current era, pericardiectomy for constrictive pericarditis has a mortality rate of 6–14 % [48, 50–57]. The complete normalization of cardiac hemodynamics can be expected in about 60 % of patients [58, 59]. In a recent study, George et al. found that a 5–7.6 % morality with 1, 5, and 10-year survival of 82, 64, and 49 %, respectively [54] (Table 12.5).

**Table 12.5** Outcomes data for pericardiectomy for constrictive pericarditis

| Author | Years | N | Mortality | Long-term survival |
|---|---|---|---|---|
| Bertog | 1977–2000 | 163 | 6 | 88 % 7-year |
| Ling | 1936–1990 | 313 | 14 % | N/A |
| Szabo | 1988–2012 | 89 | 7 | 6 % 2-year |
| George | 1995–2010 | 98 | 7.1 | 82 %1-year<br>64 % 5-year<br>49 % 10-year |
| Gopaldas | 1998–2008 | 13, 593 | 7.5 % | N/A |
| Tokuda | 2008–2012 | 346 | 10 % | N/A |

Several factors have been found to be risk factors for poor outcome, including high NYHA class, female sex, and the underlying etiology of the effusion [53]. Inflammatory and idiopathic etiologies have the best outcome, while postradiation patients fare the worst [53]. The need for CPB is also associated with increased mortality [54]. Poor prognosis has been associated with increased age, decreased left ventricular systolic dysfunction, elevated pulmonary artery pressure, and increased creatinine [52]. Other studies have confirmed that age [50], preop NYHA class [58, 60–62], and hepatic [62] and renal dysfunction [61] are important. Recently, diabetes mellitus and high early diastolic inflow velocity have been shown to predict high mortality [63]. In 2013, Gopaldas et al. published a nationwide outcomes study of over 13,000 pericardiectomy patients [55]. He found that after risk adjustment, age, female gender, comorbidity index, and primary diagnosis were significant predictors of in-hospital mortality and complications [55].

Complications of pericardiectomy include direct myocardial injury during dissection which can lead to cardiac failure and bleeding. Failure to achieve complete resection may result in suboptimal hemodynamic changes. Low cardiac output syndrome (LCOS) is the most significant

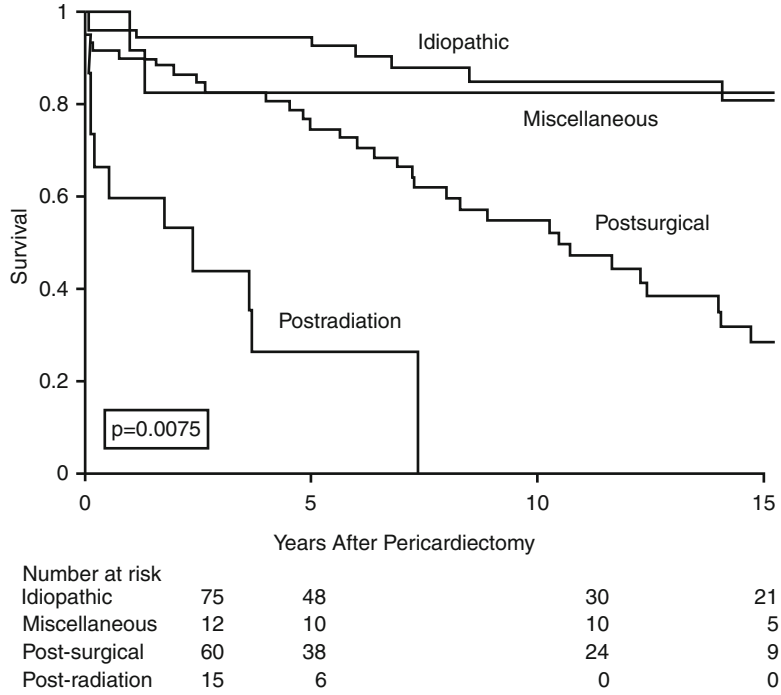


**Fig. 12.7** Kaplan-Meier curves showing a significant difference (log-rank test, p = 0.0075) in overall survival of patients after pericardiectomy, based on the presumed cause of constrictive pericarditis (Permission obtained from Elsevier Ltd. [52])

complication. It is likely due to myocardial atrophy as the heart is chronically externally supported; once released the heart is subject to over dilation and failure [64]. However, this is not the only issue as it does not explain why patients with constrictive idiopathic disease have much better outcomes after surgery than other groups. LCOS occurs in 14–28 % of patients after pericardiectomy [64]. It is rapid, and can lead to systemic heart failure and death [64]. The treatment is supportive care [64].

Although complete pericardiectomy is technically challenging and can cause significant hemodynamic compromise, it has been found that smaller operations are more poorly tolerated and that a less aggressive pericardiectomy is a risk factor of overall survival [65]. Furthermore, reoperative pericardiectomy has a significant and nearly prohibitive early mortality. Cho et al. showed in 41 patients who presented for reoperative pericardiectomy had a 30 day morality of 12 % with a 5 year survival of only 4 % [66]. Risk factors for these patients included high NYHA class 3 or 4 and less than 1 year between operations [66]. It is clear that a simple anterior pericardiectomy is not sufficient release to normalize cardiac function. Those who survive total pericardiectomy do better in the long term. Patients with underlying restrictive cardiomyopathy and pulmonary hypertension can have a more complicated course.

The etiology of the constriction relates directly to survival (Fig. 12.7). Patients with constrictive pericarditis due to radiation injury have markedly reduced late survival [51]. Many post radiation patients have myocardial fibrosis, restrictive cardiomyopathy, coronary artery disease, and valvular heart disease [58]. If pericarditis is secondary to radiation, it is important to consider that the underlying cardiomyopathy is still present even after release of the heart. Postoperative recovery for patients with previous radiation is complicated by poor lung function and chest wall fibrosis. Long-term survival

of these patients demonstrates 40 % 5- year survival and 11 % 10- year survival [54].

Overall survival is also related to the duration of symptoms. If the indication for surgery was established early, long-term survival after pericardiectomy may correspond to that of the general population [50].

## References


1. Harken AH, Hall AW, Hammond FL. In: Baue AE, editor. The pericardium in Glenn's thoracic and cardiovascular surgery. 6th ed. Stamford: Appleton and Lange; 1996. p. 2299–310.
2. Spodick DH. Macrophysiology, microphysiology, and anatomy of the pericardium: a synopsis. Am Heart J. 1992;124:1046–51.
3. Stoller JK, Shaw C, Matthay RA. Enlarging atypically located pericardial cyst: recent experience ad literature review. Chest. 1986;89(3):402–6.
4. Maisch B, Seferovic PM, Ristic AD, et al. Guidelines on the diagnosis and management of pericardial diseases. Executive summary. Eur Heart J. 2004;25: 587–610.
5. Weder W, Klotz HP, Segesser LV, Larguader F. Thoracoscopic resection of a pericardial cyst. J Thorac Cardiovasc Surg. 1994;107:313.
6. Burke A, Virmani R. Tumors of the heart and great vessels. In: Atlas of tumor pathology, third Series, Fascicle 16. Washington DC, Armed Forces Institute of Pathology, 1995;181–207.
7. Luk A, Ahn E, Vaideeswar P, Butany III JW. Pericardial tumors. Semin Diagn Pathol. 2008;25: 47–53.
8. Cottrill CM, Tamaren J, Hall B. Sternal defects associated with congenital pericardial and cardiac defects. Cardiol Young. 1998;8(1):100–4.
9. VanSon JAM, Danelson GK, Callahan JA. Congenital absence of the pericardium: displacement of the heart associated with tricuspid insufficiency. Ann Thorac Surg. 1993;56:1405.
10. Meunier JP, Lopez S, Teboul J, et al. Total pericardial defect: risk factor for traumatic aortic type A dissection. Ann Thorac Surg. 2002;74(1):266.
11. Risher WH, Rees AD, Oschner JL, McFadden PM. Thoracoscopic resection of pericardium for symptomatic congenital pericardial defect. Ann Thorac Surg. 1993;56:1390.
12. Loebe M, Meskhishvili V, Weng Y, et al. Use of polytetrafluoroetylene surgical membrane as a pericardial substitute in the correction of congenital heart defects. Tex Heart Inst J. 1993;20(3):213–7.
13. Arom KV, Richardson JD, Webb G, Grover FL, Trinkle JK. Subxiphoid pericardial window in patients with suspected traumatic pericardial tamponade. Ann Thorac Surg. 1977;23(6):545–9.
14. Andrade-Alegre R, Mon L. Subxiphoid pericardial window in the diagnosis of penetrating cardiac trauma. Ann Thorac Surg. 1994;58(4):1139–41.
15. Brewster SA, Thirlby RC, Syder 3rd WH. Subxiphoid pericardial window and penetrating cardiac trauma. Arch Surg. 1988;123(8):937–41.
16. Huang YK, Lu MS, Liu KL, Liu EH, Chu JJ Tsai FC, Lin PJ. Traumatic pericardial effusion: impact of diagnostic and surgical approaches. Resuscitation. 2010;81(12):1682–6.
17. Holmes Jr DR, Nishimura R, Fountain R, Turi ZG. Iatrogenic pericardial effusion and tamponade in the percutaneous intracardiac intervention era. JACC Cardiovasc Interv. 2009;2(8):705–17.
18. Hsu LF, Jais P, Hocini M, et al. Incidence and prevention of cardiac tamponade complicating ablation for atrial fibrillation. Pacing Clin Electrophysiol. 2005;28 Suppl 1:S106–9.
19. Mahapatra S, Bybee KA, Bunch TJ, et al. Incidence and predictors of cardiac perforation after permanent pacemaker placement. Heart Rhythm. 2005;2: 907–11.
20. Spodick DH. Acute cardiac tamponade. N Engl J Med. 2003;349:684–90.
21. Holt JP, Rhode EA, Kines H. Pericardial and ventricular pressure. Circ Res. 1960;8:1171–80.
22. Ashikhmina EA, Schaff HV, Sinak LJ, Li Z, Dearani JA, Suri RM, Park SJ, Orszulak TA, Sundt RM. Pericardial effusion after cardiac surgery: risk factors, patient profiles, and contemporary management. Ann Thorac Surg. 2010;89:112–8.
23. Boyd WD, Tyberg JV, Cox JL. A review of the current status of pericardial closure following cardiac surgery. Expert Rev Cardiovasc Ther. 2012;10(9): 1109–18.
24. Hoit BD. Management of effusive and constrictive pericardial heart disease. Circulation. 2002;105: 2939–42.
25. Chen EP, Miller JI. Modern approaches and use of surgical treatment for pericardial disease. Curr Cardiol Rep. 2002;4:41–6.
26. Cho YH, Schaff HV. Surgery for pericardial disease. Heart Fail Rev. 2013;18:375–87.
27. Becit N, Unlu Y, Ceviz M, Kocogullari CU, Kocak H, Gurlertop Y. Subxiphoid pericardiostomy in the management of pericardial effusions: case series analysis of 368 patients. Heart. 2005;91:785–90.
28. Mirhosseini SM, Fakhri M, Mozaffary A, Lotfaliany M, Behzadnia N, Aval ZA, Ghiasi SMS, Boloursaz MR, Masjedi MR. Risk factors affecting the survival rate in patients with symptomatic pericardial effusion undergoing surgical intervention. Intract Cardiovasc Thorac Surg. 2013;16:495–500.
29. Azam S, Hoit BD. Treatment of pericardial disease. Cardiovasc Ther. 1999;1(1):79–89.
30. Palacios IF. Pericardial effusion and tamponade. Curr Treat Options Cardiovasc Med. 1999;1(1):79–89.
31. Rubin RH, Moellering RC. Clinical, microbiological and therapeutic aspects of purulent pericarditis. Am J Med. 1975;59:68.

32. Mills SA, Julian S, Holliday RH, Vinten-Johansen J, Case LD, Hudspeth AS, Tucker WY, Cordell AR. Subxiphoid pericardial window for pericardial effusive disease. J Cardiovasc Surg (Torino). 1989;30(5): 768–73.
33. O'Connor CJ, Tuman KJ. The intraoperative management of patients with pericardial tamponade. Anesthesiol Clin. 2010;28(1):87–96.
34. Moores DWO, Allen KB, Faber LP, Dziuban SW, Gillman DJ, Warren WH, Ilves R, Lininger L. Subxiphoid pericardial drainage for pericardial tamponade. J Thorac Cardiovasc Surg. 1995;109: 546–52.
35. Allen KB, Faber LP, Warren WH, Shaar CJ. Pericardial effusion: subxiphoid pericardiostomy versus percutaneous catheter drainage. Ann Thorac Surg. 1999;67:437–40.
36. Dosios T, Theakos N, Angouras D, Asimacopoulos P. Risk factors affecting the survival of patients with pericardial effusion submitted to subxiphoid pericardiostomy. Chest. 2003;124:242–6.
37. McDonald JM, Meyer BF, Guthrie TJ, Battafarano RJ, Cooper JD, Patterson GA. Comparison of open subxiphoid pericardial drainage with percutaneous catheter drainage for symptomatic pericardial effusion. Ann Thorac Surg. 2003;76:811–6.
38. Wang HJ, Hsu KL, Chiang FT, Tseng CD, Tseng YZ, Liau CS. Technical and prognostic outcomes of double-balloon pericardiotomy for large malignancy-related pericardial effusions. Chest. 2002;122: 893–9.
39. Cullinane CA, Paz IB, Smith D, Carter N, Grannis Jr FW. Prognostic factors in the surgical management of pericardial effusion in the patient with concurrent malignancy. Chest. 2004;125:1328–34.
40. Roberts JR, Kaiser LR. Pericardial procedures. In: Kaiser LR, Kron IR, Spray TL, editors. Mastery of cardiothoracic surgery. 2nd ed. Philadelphia: Lippincott Williams and Wilkins; 1998. p. 221–9.
41. Saltzman AJ, Paz YE, Rene AG, Green P, Hassanin A, Argenziano MG, Rabbani L, Dangas G. Comparision of surgical pericardial drainage with percutaneous catheter drainage for pericardial effusion. J Invasive Cardiol. 2012;24(11):590–3.
42. Rafique AM, Patel N, Biner S, Eshaghian S, Mendoza F, Cercek B, Siegel RJ. Frequency of recurrence of pericardial tamponade in patients with extended versus nonextended pericardial catheter drainage. Am J Cardiol. 1820–1825;2011: 108.
43. Georghiou GP, Stamler A, Sharoni E, Fichman-Horn S, Berman M, Vidne BA, Saute M. Video-assisted thoracoscopic pericardial window for diagnosis and management of pericardial effusions. Ann Thorac Surg. 2005;80:607–10.
44. O'Brien PKH, Kucharczuk JC, Marshall B, Friedberg JS, Chen Z, Kaiser LR, Shrager JB. Comparative study of subxiphoid versus video-thoracoscopic pericardial "Window". Ann Thorac Surg. 2005;80: 2013–9.
45. Neragi-Miandoab S, Linden PA, Ducko CT, Bueno R, Richards WG, Sugarbaker DJ, Jaklitsch MT. VATS pericardiotomy for patients with known malignancy and pericardial effusion: survival and prognosis of positive cytology and metastatic involvement of the pericardium: a case control study. Int J Surg. 2008;6:110–4.
46. Muhammad MIA. The pericardial window: is a video-assisted thoracoscopy approach better than a surgical approach? Interact Cardiovasc Thorac Surg. 2011;12:174–8.
47. Harken AH, Hammond GL, Edmunds Jr LH. Pericardial diseases in cardiac surgery in the adult. New York: McGraw Hill; 1997. p. 1303–17.
48. Talreja DR, Edwards WD, Danielson GK, et al. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. Circulation. 2003;108:1852–7.
49. Karram T, Rinkevitch D, Markiewicz W. Poor outcome in radiation- induced constrictive pericarditis. Int J Radiat Oncol Biol Phys. 1993;25(2):329–31.
50. Ling LH, Oh JK, Schaff HV, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. Circulation. 1999;100(13):1380–6.
51. Ufuk Y, Kestelli M, Yilik L, et al. Recent surgical experience in chronic constrictive pericarditis. Tex Heart Inst J. 2003;30(1):27–30.
52. Bertog SC, Thambidorai SK, Parakh K, Schoenhagen P, Ozduran V, Houghtaling PL, et al. Constrictive pericarditis: etiology and cause-specific survival after pericardiectomy. J Am Coll Cardiol. 2004;43: 1445–52.
53. Szabó G, Schmack B, Bulut C, Soós P, Weymann A, Stadtfeld S, Karck M. Constrictive pericarditis: risks, aetiologies and outcomes after total pericardiectomy: 24 years of experience. Eur J Cardiothorac Surg. 2013;44(6):1023–8.
54. George TJ, Arnaoutakis GJ, Beaty CA, Kilic A, Baumgartner WA, Conte JV. Contemporary etiologies, risk factors, and outcomes after pericardiectomy. Ann Thorac Surg. 2012;94(2):445–51.
55. Gopaldas RR, Dao TK, Caron NR, Markley JG. Predictors of in-hospital complications after pericardiectomy: a nationwide outcomes study. J Thorac Cardiovasc Surg. 2013;145:1227–33.
56. Tokuda Y, Miyata H, Motomura N, Araki Y, Oshima H, Usui A, Takamoto S, Japan Adult Cardiovascular Database Organization. Outcome of pericardiectomy for constrictive pericarditis in Japan: a nationwide outcome study. Ann Thorac Surg. 2013;96(2):571–6.
57. Lin Y, Zhou M, Xiao J, Wang B, Wang Z. Treating constrictive pericarditis in a chinese single-center study: a five-year experience. Ann Thorac Surg. 2012;94(4):1235–40.
58. DeValeria PA, Baumgartner WA, Casale AS, et al. Current indications, risks, and outcome after pericardiectomy. Ann Thorac Surg. 1991;52(2):219–24.
59. Senni M, Redfield MM, Ling LH, et al. Left ventricular systolic and diastolic function after pericardiec-

tomy in patients with con- strictive pericarditis: doppler echocardiographic findings and correlation with clinical status. J Am Coll Cardiol. 1999;33(5): 1182–8.
60. Seifert FC, Miller DC, Oesterle SN, Oyer PE, Stinson EB, Shumway NE. Surgical treatment of constrictive pericarditis: analysis of outcome and diagnostic error. Circulation. 1985;72:II264–73.
61. Nataf P, Cacoub P, Dorent R, et al. Results of subtotal pericardiectomy for constrictive pericarditis. Eur J Cardiothorac Surg. 1993;7:252–5; discussion: 255–6.
62. Aagaard MT, Haraldsted VY. Chronic constrictive pericarditis treated with total pericardiectomy. Thorac Cardiovasc Surg. 1984;32:311–4.
63. Kang SH, Song JM, Kim M, Choo SJ, Chung CH, Kang DH, Song JK. Prognostic predictors in pericardiectomy for chronic constrictive pericarditis. J Thorac Cardiovasc Surg. 2014;147(2): 598–605.
64. Sunday R, Robinson LA, Bosek V. Low cardiac output complicating pericardiectomy for pericardial tamponade. Ann Thorac Surg. 1999;67:228–31.
65. Chowdhury UK, Subramaniam GK, Kumar AS, Airan B, Singh R, Talwar S, et al. Pericardiectomy for constrictive pericarditis: a clinical, echocardiographic, and hemodynamic evaluation of two surgical techniques. Ann Thorac Surg. 2006;81:522–9.
66. Cho YH, Schaff HV, Dearani JA, Daly RC, Park SJ, Li Z, Oh JK. Completion pericardiectomy for recurrent constrictive pericarditis: importance of timing of recurrence on late clinical outcome of operation. Ann Thorac Surg. 2012;93(4):1236–40.

## Surgical Management of Pericardial Disease-For Patients and their Families

The pericardium is a double-layered membrane that covers the heart. Excess fluid in the space between the pericardium and the heart is referred to as a pericardial effusion. This can result from a variety of illnesses including bacterial infections, cancer, a reaction to radiation, or a heart attack. The initial management of pericardial effusions is usually with medicines such as NSAIDs or steroids; however, if the effusion is not controlled with medicine or a diagnosis is needed, surgery is required.

Too much fluid in the cavity can also lead to compression of the heart called 'pericardial tamponade'. This is a potentially dangerous condition as it prevents the heart from beating normally and providing enough blood flow to the body.

The definitive treatment for large pericardial effusions or pericardial tamponade is drainage with a surgical procedure. These procedures open up the pericardium and allow complete drainage of the fluid, thereby relieving the pressure on the heart. The surgical procedures allow for sampling of the pericardial tissue for biopsy and less risk of injury to the heart when compared with placing a needle or thin catheter into the pericardial space. Pericardial fluid is sent to the laboratory for analysis of its contents and to try and determine what caused the fluid to accumulate.

### Sub-Xiphoid Pericardial Window

General anesthesia is usually preferred for this procedure. However, a sub-xiphoid pericardial window can be performed with local anesthesia and adequate sedation if the patient is unstable.

The patient is placed lying on his back during the procedure. The procedure is as follows: a small incision is either made vertically over the xiphoid (a bone that hangs off the bottom of the ribcage in the center of the chest) or horizontally right below where the xiphoid ends. The surgeon will then use his fingers to gently dissect down to the heart. The pericardium is cut and the fluid is drained and sent for culture and analysis. The pericardium is then explored for adhesions or tumor deposits before cutting out a small piece, creating a "window". A chest tube is placed through the window and through a separate skin incision, exiting the body. The chest tube is left in place for several days after the operation until the drainage is minimal, at which time it is removed.

Possible complications from this procedure include developing air between the lung and chest cavity (pneumothorax), irregular heart rhythms (arrhythmia), or damage to the heart muscle. Recurrence of the effusion is also possible, although the rates of this are very low with this technique.

Another commonly performed technique for pericardial fluid drainage is percutaneous catheter drainage. Percutaneous catheter drainage is performed under local anesthesia and is achieved with either blind placement of a needle into the pericardial space using anatomical landmarks or with an ultrasound. A wire is passed through the needle and a drainage catheter is passed over the wire. The wire and needle are removed and the catheter is secured. There are more complications with this procedure when compared with the sub-xiphoid pericardial window such as damage to the heart and a higher chance of recurrence of the effusion. However, very unstable patients may have more benefit from this procedure.

### Thoracoscopic Pericardial Window

Another procedure that is used for drainage of pericardial effusions is thoracoscopic drainage of pericardial fluid into the spaces surrounding the lungs (pleural space) and out through a chest tube. General anesthesia must be used in these cases and the time of the procedure is longer because of positioning and other simultaneous lung procedures. Thoracoscopy, or visualizing the lung and heart through a small camera, is achieved with two to three small incisions allowing a camera and small instruments into the chest cavity. A piece of pericardium approximately 4 cm in diameter is cut away and a chest tube is placed in the pleural space. Post-operative

management is similar to that of the sub-xiphoid technique.

Advantages of this procedure include simultaneous access to both the pleural and pericardial spaces, better visualization of the pericardium and more direct sampling of anything that looks suspicious (for example, cancer). However, entry into two cavities is also potentially a disadvantage, especially in patients who have many medical problems or those who are unstable. Again, sub-xiphoid pericardial window is the preferred procedure in the setting of an unstable patient.

## Total Pericardiectomy

Constrictive pericarditis is a rare but severely disabling disease of the pericardium. The pericardium is a membrane that forms the cavity in which the heart lives. Normally this cavity is filled with a small amount of fluid and the pericardium is usually soft and pliable allowing the heart to expand when filling with blood and contract when ejecting the blood out to the rest of the body. In constrictive pericarditis, there has been some insult to the heart leading to a stiffening of the pericardium and this does not allow the heart to move properly. Most importantly, it leads to an impaired filling of the ventricles and a reduced ventricular function. The majority of cases of constrictive pericarditis are of unknown cause (idiopathic). When a cause can be identified, it is most commonly seen in patients who have had open-heart surgery. Patients may have symptoms such as shortness of breath with activity; some may be short of breath with lying down. When these symptoms are present, patients need a thorough evaluation. CXR and CT scans are some of the initial tests which may be used. Constrictive physiology is best diagnosed by measuring specific heart pressures using a catheter placed through the groin into the heart (cardiac catheterization).

Pericardiectomy, or removal of the pericardium, is indicated once the diagnosis of constrictive pericarditis has been established. True constrictive pericarditis is irreversible and surgical resection is the only effective treatment. The management of recurring pericarditis relies on exercise restriction and medicines such as NSAIDS, colchicine, and/or corticosteroids. Patients with little physiologic effects and significant comorbidities should be delayed until more significant symptoms occur. This is especially true in the case of radiation-induced pericarditis. Unfortunately, the radiation effects do not stop at the pericardium. The myocardium, the heart muscle itself, is often affected as well. The chest wall and lungs can also be damaged with radiation. In the 20 % of patients that develop constrictive pericarditis secondary to radiation therapy, the operative mortality is high (21 %) and the postoperative 5-year survival is very low (1 %).

## Pericardiectomy Technique and Outcomes

Pericardiectomy for constrictive pericarditis corrects the hemodynamic abnormalities and can produce dramatic clinical improvement. Pericardiectomy is performed under general anesthesia. The technique is still an area of considerable controversy. The heart-lung machine is usually on standby and surgeons will reserve it for extremely difficult dissections, reoperations, or if concomitant intracardiac surgery is required. The two main incisions are either through a median sternotomy, which is an incision going through the middle of the sternum, or a thoracotomy (i.e., left thoracotomy or bilateral anterior thoracotomies), which is an incision on either side through the rib spaces. Most commonly the median sternotomy is used. Ultimately the goal is to do as complete a resection as safely possible, with removal of the pericardium covering both ventricles, both atria, and both vena cava. Chest tubes are left in place after surgery to drain residual fluid.

Pericardiectomy for constrictive pericarditis has a mortality rate of 6–12 %. Overall survival is related to the duration of symptoms. If the indication for surgery was established early, long-term survival after pericardiectomy corresponds to that of the general population. Several factors have been found to be independent predictors of overall survival. These include: constriction

caused by radiation, age, congestive heart failure, and kidney function.

Complications of pericardiectomy include direct myocardial injury during dissection, which can lead to cardiac failure and bleeding. Failure to achieve complete resection may result in suboptimal hemodynamic changes, but the extent of dissection heavily depends on being able to safely remove the pericardium. A serious condition called low cardiac output syndrome can develop after the dense covering is removed from the surface of the heart. This can cause the heart to overfill and lead to poor blood flow out of the heart and organ dysfunction of the kidneys and liver. This syndrome may be treated with intravenous medications or more significant cardiac support systems.

# Pathway for the Management of Pericardial Disease

13

Eyal Herzog, Dan G. Halpern, Farooq A. Chaudhry, Emad F. Aziz, and Edgar Argulian

Pericardial disease is a broad term that describes a wide range of pathologies. The clinical aspects of pericardial disease encompass acute pericarditis, pericardial tamponade, pericardial effusion, constrictive pericarditis and effusive-constrictive pericarditis. These disorders differ not only in clinical presentation but also in the timeline of disease development; e.g., pericardial tamponade is commonly an acute, life-threatening event, whereas constrictive pericarditis is a chronic process developing over months to years. Therefore, pericardial disease management is challenging for most clinicians. The evidence base in the field is relatively scarce compared with other disease entities in cardiology. European Society of Cardiology released guidelines for the diagnosis and management of pericardial diseases [1]. Currently, there are no guidelines from American cardiology societies to help clinicians in managing pericardial disease. In this chapter we outline a unified, stepwise pathway-based approach for the management of pericardial disease [2] (Fig. 13.1).

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## The Advanced Cardiac Admission Program

The "Advanced Cardiac Admission Program (ACAP)" was launched at St Luke's Roosevelt Hospital Center in New York, in 2004. It consists of a series of projects which have been developed to bridge the gap between published guidelines and implementation during "real world" patient care (available at: www.nycardiology-pathways.org). The pericardial disease management pathway is the ninth project of the ACAP program [2].

## How to Use the Pathway

### Entering the Pathway

Despite the broad range of pericardial pathologies, there is a limited number of clinical presentations that would make a clinician suspect pericardial disease (Fig. 13.2). We assigned each clinical presentation a certain pathway which starts with patient's complaints and

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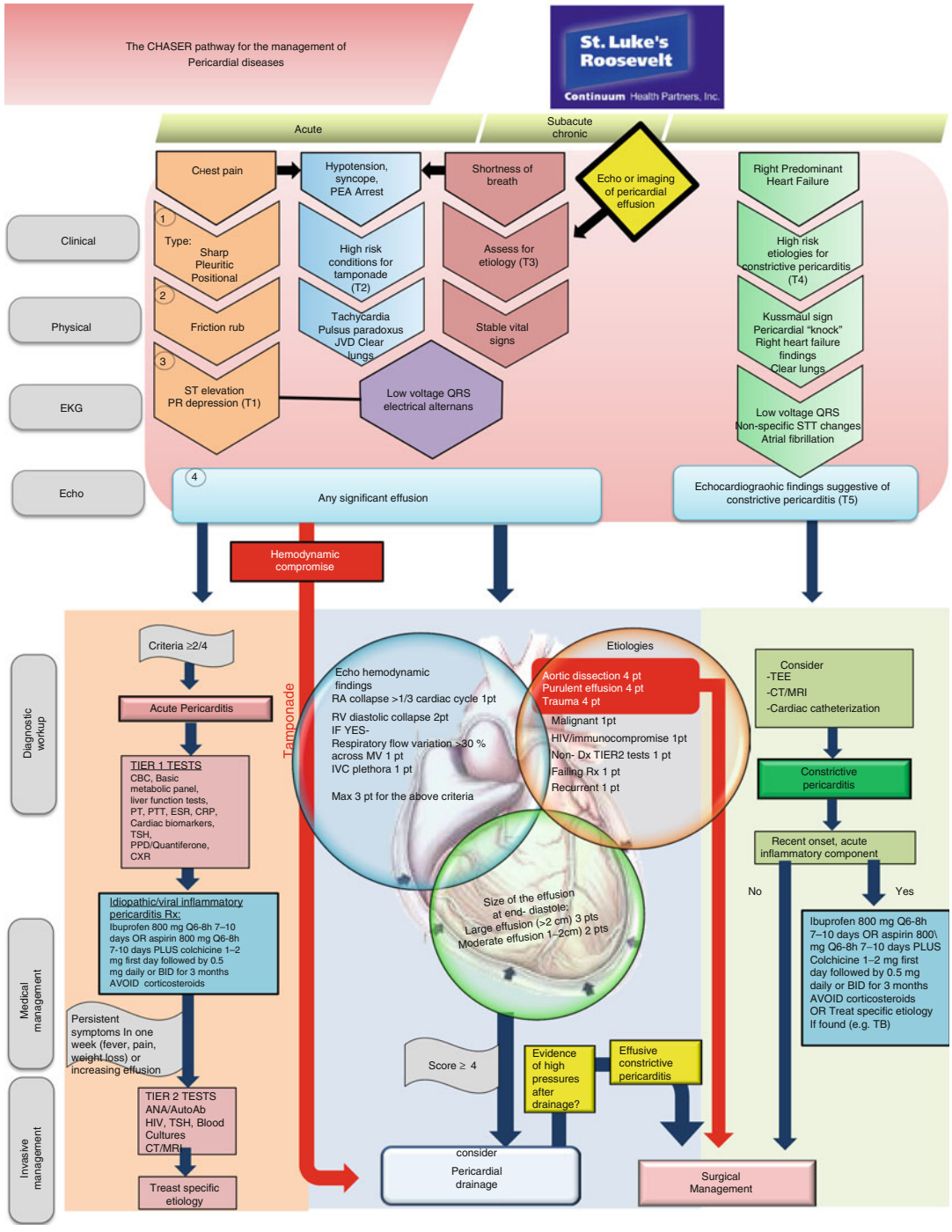


**Fig. 13.1** Novel "CHASER" pathway for the management of pericardial disease. The figure outlines a unified, step-wise pathway-based approach to pericardial disease management

continues along the lines of further work-up, diagnosis, and management. Typical clinical presentations in patients with pericardial disease include chest pain, hypotension/arrest, dyspnea, and right-predominant heart failure. Incidental finding of pericardial effusion during imaging

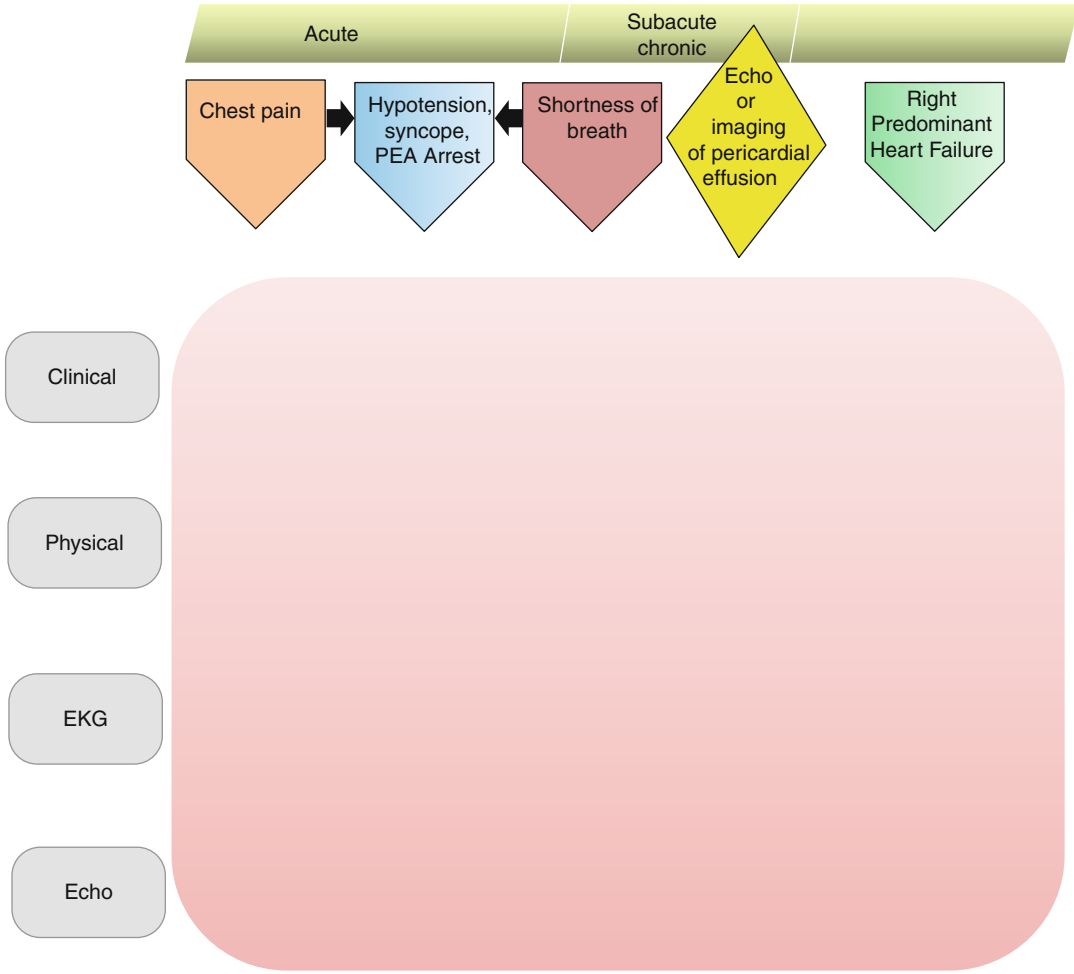


**Fig. 13.2** Entry points into the pericardial disease pathway. The entry points based on the initial clinical presentation form "CHASER" acronym

study is also a common clinical scenario. Figure 13.2 outlines the entry points into the pericardial disease management pathway. The timeline of symptom development is a continuum ranging from acute, immediate presentation to subacute and chronic symptoms. A systematic approach to patients with suspected pericardial disease starts with the chief presenting complaint and is followed by a history taking, physical examination, electrocardiogram (EKG), and echocardiography. Further diagnostic testing is tailored to the initial findings.

The following are the five entry points:

1. **Chest Pain**

   Acute pericarditis should be considered in the differential diagnosis of any patient presenting with chest pain along with other etiologies. The chest pain algorithm of the pathway is outlined in Fig. 13.3. The diagnosis of acute pericarditis relies on the following four cardinal features: characteristic chest pain which is pleuritic and positional, friction rub on physical examination, characteristic evolving EKG changes (Table 13.1), and pericardial

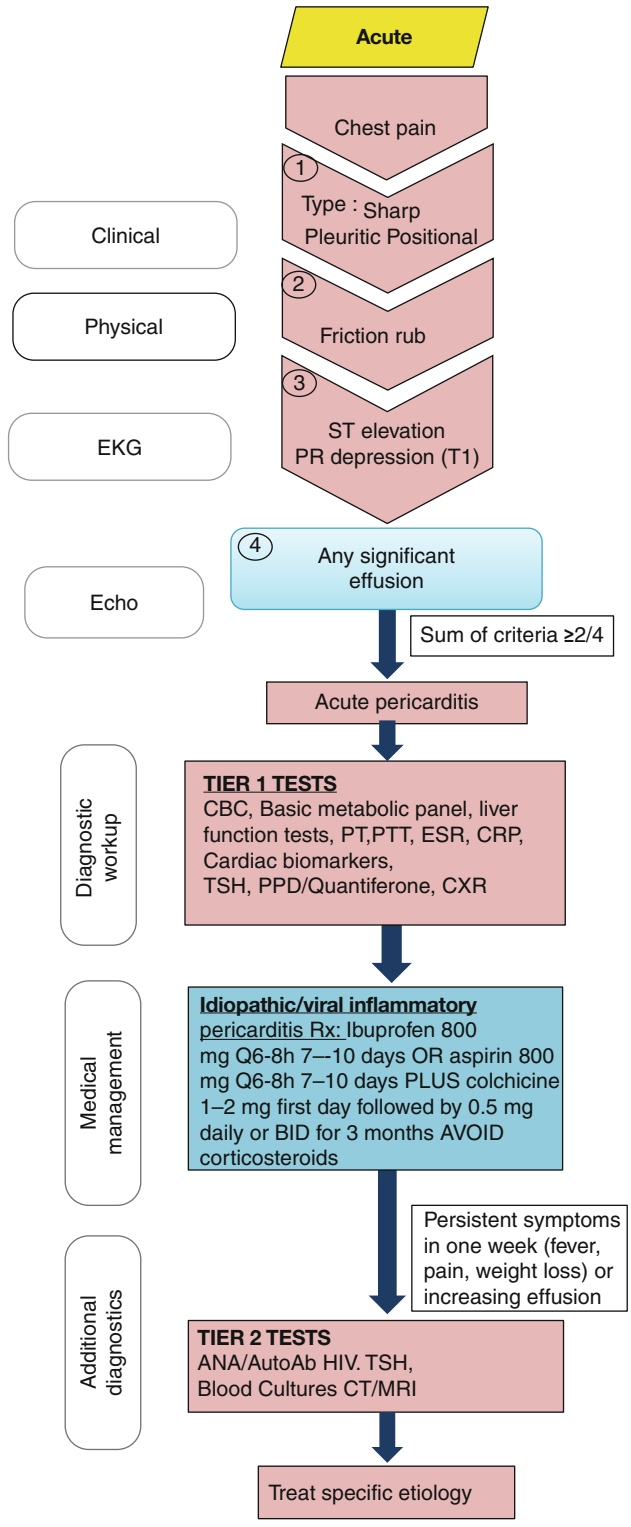


**Fig. 13.3** Evaluation of chest pain in patient with possible acute pericarditis. A stepwise algorithm outlines evaluation and management of chest pain patients suspected to have acute pericarditis

**Table 13.1** EKG features of acute pericarditis

| |
|---|
| Stage 1: diffuse ST segment elevation and PR segment depression |
| Stage 2: normalization of ST segment changes |
| Stage 3: diffuse T wave inversion |
| Stage 4: normalization of T wave changes |

EKG indicates electrocardiogram

effusion demonstrated by echocardiography [3–5]. Presence of at least two of these features is usually diagnostic of acute pericarditis. Most cases of acute pericarditis in the western world are idiopathic or viral but other causes should also be considered [6]. Initial testing in all patients with acute pericarditis should include tier 1 testing (Fig. 13.3) [7]. Positive cardiac biomarkers indicate myocardial involvement. Inflammatory markers such as C-reactive protein can be followed sequentially to monitor disease progression and response to treatment. Typical treatment includes nonsteroidal anti-inflammatory agents at full doses for 7–10 days [1]. We recommend the following doses: ibuprofen 600–800 mg every 6–8 h for 7–10 days or aspirin 800 mg every 6–8 h for 7–10 days. In post-myocardial infarction pericarditis, aspirin is preferred. In patients without contraindications, colchicines at a dose of 1–2 mg first day followed by 0.5 mg daily or twice daily for 3 months should be given as it reduces the rate of recurrence substantially [5, 8].

Corticosteroids increase the likelihood of relapse and should be avoided unless specifically indicated (e.g., in patients with connective tissue disease) [5, 9]. Patients with idiopathic or viral pericarditis usually respond promptly to treatment. Patients with persistent symptoms or with atypical clinical features are more likely to have other causes of pericarditis such as connective tissue disease and should undergo tier 2 testing as seen in Fig. 13.3 [10]. Those tests include imaging studies such as computed tomography scan of the chest or magnetic resonance imaging [1]. Corticosteroids can be used as a last resort for those patients if no specific cause was found [1].

2. **Hypotension, Syncope, or Pulseless Electrical Activity Arrest**

Patients with tamponade can have an acute, dramatic presentation like patients with acute ascending aortic dissection involving the pericardial sac, or these patients can present with subacute symptoms of chest pain, dyspnea, and syncope like patients with neoplastic pericarditis. Cardiac tamponade should be suspected in any patients with hypotension, collapse, and pulseless electrical activity arrest (Fig. 13.4), and high-risk conditions commonly associated with tamponade should be specifically thought (Table 13.2) [11]. These include blunt chest trauma, recent procedure/intervention (e.g., electrophysiology procedures and coronary interventions), chest surgery, and aortic dissection. Neoplastic pericardial effusion, tuberculous pericarditis, and uncommonly idiopathic pericarditis can progress to tamponade. Physical examination findings should focus on pulsus paradoxus, jugular vein pressure, and lung auscultation. EKG findings may include low voltage QRS complex size and finding of electrical alternans. Echocardiography is essential in diagnosing pericardial effusion and confirming tamponade by the echocardiographic signs of hemodynamic compromise (Fig. 13.5). Echocardiography is also commonly used for guiding the intervention. Pericardiocentesis can be life-saving in these patients.

3. **Dyspnea**

Patients with significant pericardial effusion often present with dyspnea, poor exercise tolerance, chest discomfort, and fatigue. Although the differential diagnosis of dyspnea is broad, it should include pericardial effusion (Fig. 13.6). The pericardium can be the primary focus for the disease as in most cases of acute pericarditis or it can be involved in a systemic process such as malignancy, endocrine diseases, or rheumatic diseases. In every patient with suspected pericardial disease, a systematic approach and consideration of possible etiologies are important parts of clinical reasoning (Table 13.3). These patients are hemodynamically stable and have no clinical

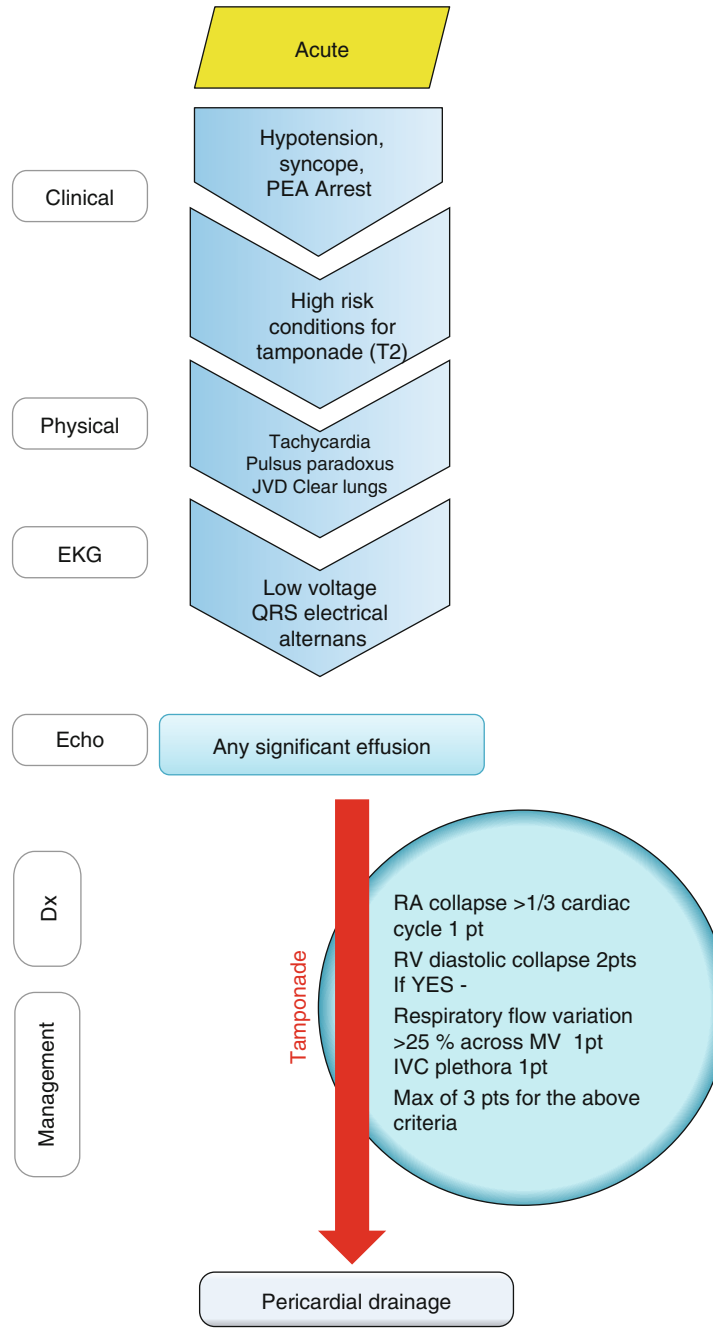


**Fig. 13.4** Approach to a patient with hypotension, syncope or pulseless electrical activity (*PEA*) arrest with possible pericardial tamponade. Initial clinical evaluation of patients suspected to have cardiac tamponade is outlined in the figure

signs of tamponade. EKG characteristics commonly include low voltage QRS complex size. Pulsus alternans is occasionally seen with large effusions without tamponade [11]. Echocardiography is an effective and inexpensive tool in diagnosing pericardial effusion.

4. **Incidental Finding of Pericardial Effusion** Sometimes, pericardial effusion is found as an incidental finding in patients worked-up for other causes. Although it is important to search systematically for possible etiologies of pericardial disease in each individual

**Table 13.2** High-risk conditions for tamponade

| |
|---|
| Advanced renal failure |
| Aortic dissection |
| Chest trauma |
| Connective tissue disease |
| Malignancy |
| Purulent infection |
| Recent acute coronary syndrome |
| Surgery/intervention |
| Suspected tuberculosis |

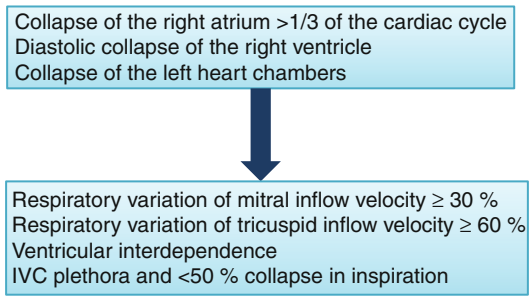


**Fig. 13.5** Echocardiographic signs of hemodynamic compromise. The findings of heart chamber collapse are presented in order of decreasing sensitivity and increasing specificity. Confirmatory signs include respiratory variation across the atrioventricular valves, ventricular interdependence, and inferior vena cava (*IVC*) plethora

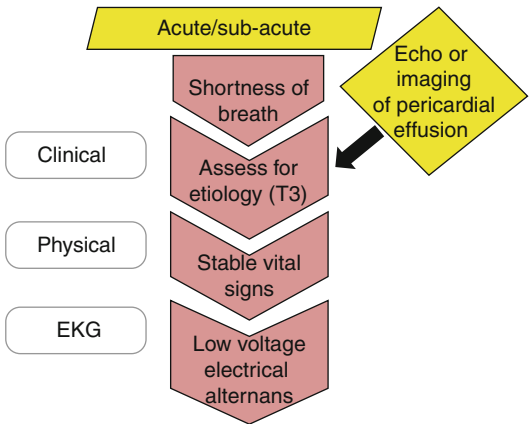


**Fig. 13.6** Approach to a patient with dyspnea and possible pericardial effusion. Initial clinical evaluation of patients suspected to have pericardial effusion is outlined in the figure. Some patients are diagnosed with incidental pericardial effusion during imaging study done for other indications

**Table 13.3** Causes of pericardial disease

| |
|---|
| Endocrine |
| Hemopericardium (trauma, procedure, aortic dissection) |
| Idiopathic |
| Infectious (including viral, tuberculosis, and purulent) |
| Medications |
| Neoplastic |
| Perimyocardial infarction |
| Postcardiotomy syndrome |
| Radiation |
| Renal failure |
| Rheumatic/autoimmune diseases |

patient (Table 13.3), a substantial number of these cases remain unexplained [12, 13]. In patients with moderate to large effusion, tier 1 and tier 2 testing seem reasonable [12]. If a specific cause is found, it should be addressed. In patients with no obvious clue to the cause of the effusion and no evidence of hemodynamic compromise, elevated inflammatory markers suggest acute idiopathic pericarditis and trial of nonsteroidal anti-inflammatory agents is justified. If inflammatory markers are within normal limits and there is no evidence of hemodynamic compromise, idiopathic pericardial effusion is high on the list of differential diagnosis [12]. Some patients with pericardial effusion have elevated right-sided pressures after pericardial drainage and they might have effusive-constrictive pericarditis [14].

5. **Right-sided Heart Failure**

Patients with constrictive pericarditis typically present with right-predominant heart failure (Fig. 13.7). Careful review of medical history for high-risk conditions associated with constrictive pericarditis is necessary (Table 13.4) [15]. Peripheral edema, hepatomegaly, jugular venous distention, and ascites are prominent findings on physical examination. Lungs are typically clear although pleural effusion may be present. EKG findings, especially repolarization abnormalities are nonspecific. Atrial fibrillation is present in over one-fifth of patients [16]. Echocardiography is essential in patients suspected to have constriction; these

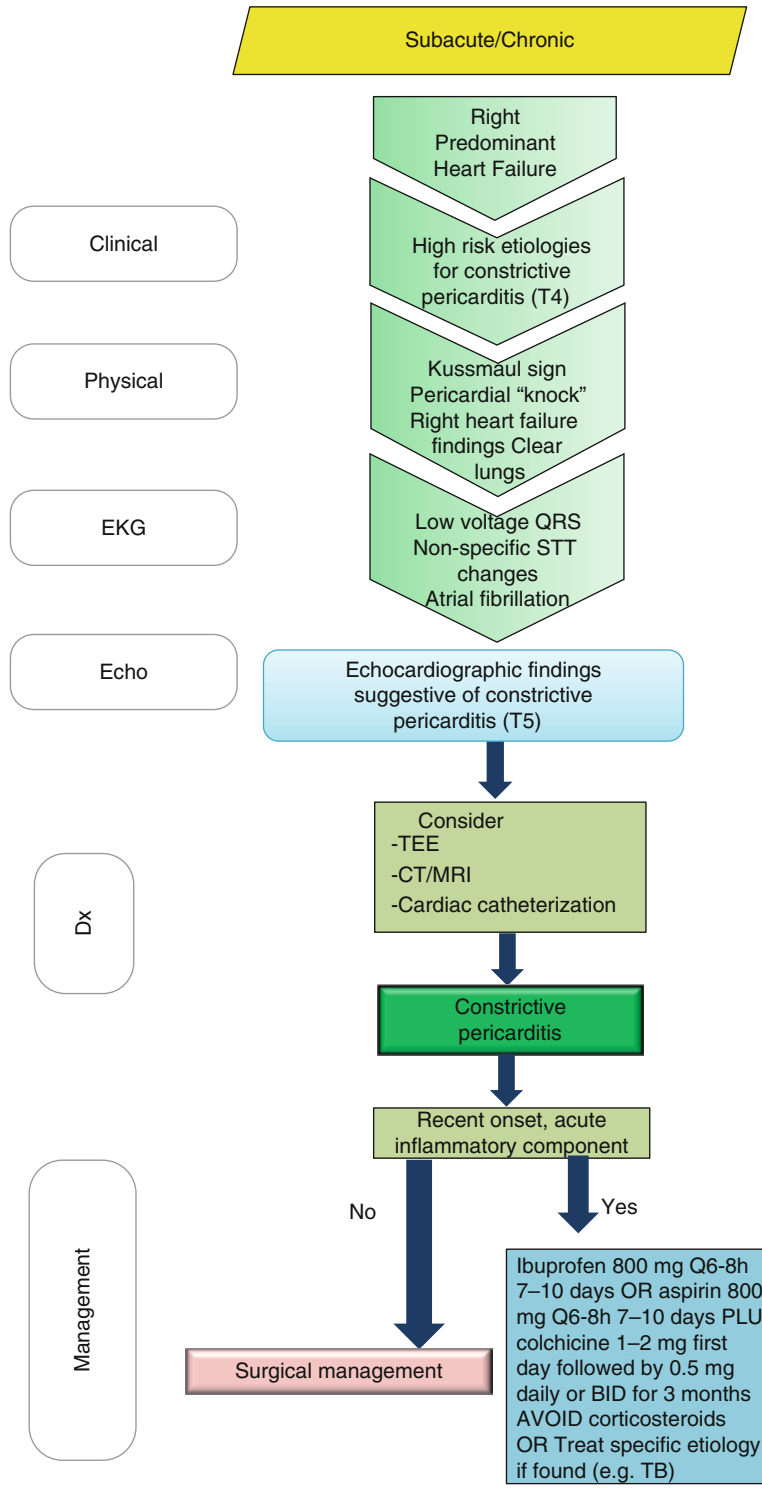


**Fig. 13.7** Evaluation of right-predominant heart failure in a patient with possible constrictive pericarditis. A stepwise algorithm outlines evaluation and management of patients with right-predominant heart failure suspected to have constrictive pericarditis

**Table 13.4** High-risk conditions for constrictive pericarditis

| |
|---|
| Cardiac surgery |
| Connective tissue disease |
| HIV infection |
| Previous pericarditis |
| Radiation therapy to the chest |
| Tuberculosis |

HIV indicates human immunodeficiency virus

**Table 13.5** Echocardiographic findings of constrictive pericarditis

| |
|---|
| Normal left ventricular ejection fraction |
| Normal left ventricular wall thickness |
| Thickened pericardium (>2 mm) and/or pericardial calcifications |
| Restrictive filling pattern (E >> A wave, high E wave velocity, short E wave deceleration time) |
| Respiratory flow variations across atrioventricular valves |
| Displacement of interventricular septum |
| Rapid flow propagation (>100 cm/s) |
| Normal tissue Doppler findings (E' >8 cm/s) |
| Expiratory hepatic veins flow reversal |

patients typically have normal left ventricular ejection fraction. Other echocardiographic findings include biatrial enlargement and restrictive filling pattern on the mitral inflow Doppler recording (Table 13.5) [14]. Further studies to confirm the diagnosis and differentiate it from restrictive cardiomyopathy include imaging studies (like magnetic resonance imaging) and cardiac catheterization. Pericardial thickness as measured by transesophageal echocardiography may be helpful in making the diagnosis [17]. Early stages of pericardial constriction due to idiopathic pericarditis may have an inflammatory component and may respond to anti-inflammatory therapy [18]. Surgical therapy is otherwise the standard of care.

## Pericardial Effusion Score

Acute cardiac tamponade necessitates immediate pericardiocentesis. The decision to drain the pericardium in patients with slowly accumulating and subacute tamponade is often challenging. We proposed a score approach to decision-making in clinically stable patients with pericardial effusion as outlines in Fig. 13.8. The score is composed of the following three major parameters: the etiology of the effusion, the size of the effusion, and the echocardiographic assessment of hemodynamic parameters. Etiologic factors favoring drainage of the effusion include traumatic effusion, aortic dissection, and purulent effusion. These effusions typically require surgical drainage as opposed to pericardiocentesis [1]. In malignant effusions, drainage should be considered to relieve symptoms and confirm neoplastic involvement of pericardium [19]. Pericardial effusion in patients with advanced human immunodeficiency virus and immunosupression, as well as unexplained and progressive effusion should also be considered for drainage because some of the neoplastic and infectious causes in these patients are treatable [20, 21]. The size of the pericardial effusion as assessed by echocardiography at the end of diastole is a very important variable [22]. It should be viewed in the context of disease progression (the rate of fluid accumulation).

Chronic large effusions present for more than 3 months are less likely to cause hemodynamic compromise as opposed to recent effusion (<1 month) [14]. Echocardiographic signs of hemodynamic compromise provide important evidence in favor of drainage because they may indicate early or impending tamponade. Of note, right atrial collapse is the earliest sign of hemodynamic compromise but has a low specificity if only buckling is present. Right atrial collapse lasting more than one-third of cardiac cycle seems to be both specific and sensitive [23]. Right ventricular diastolic collapse is a specific sign of hemodynamic compromise but is less sensitive than right atrial collapse [24]. In patients with significant pulmonary hypertension and right ventricular hypertrophy, the sensitivity of this finding is even lower. Left-sided chamber collapse is a late finding in tamponade, and therefore lacks sensitivity [25]. Confirmatory findings should be specifically looked for once a chamber collapse is present. These include respiratory variation in flow velocity across the atrioventricular

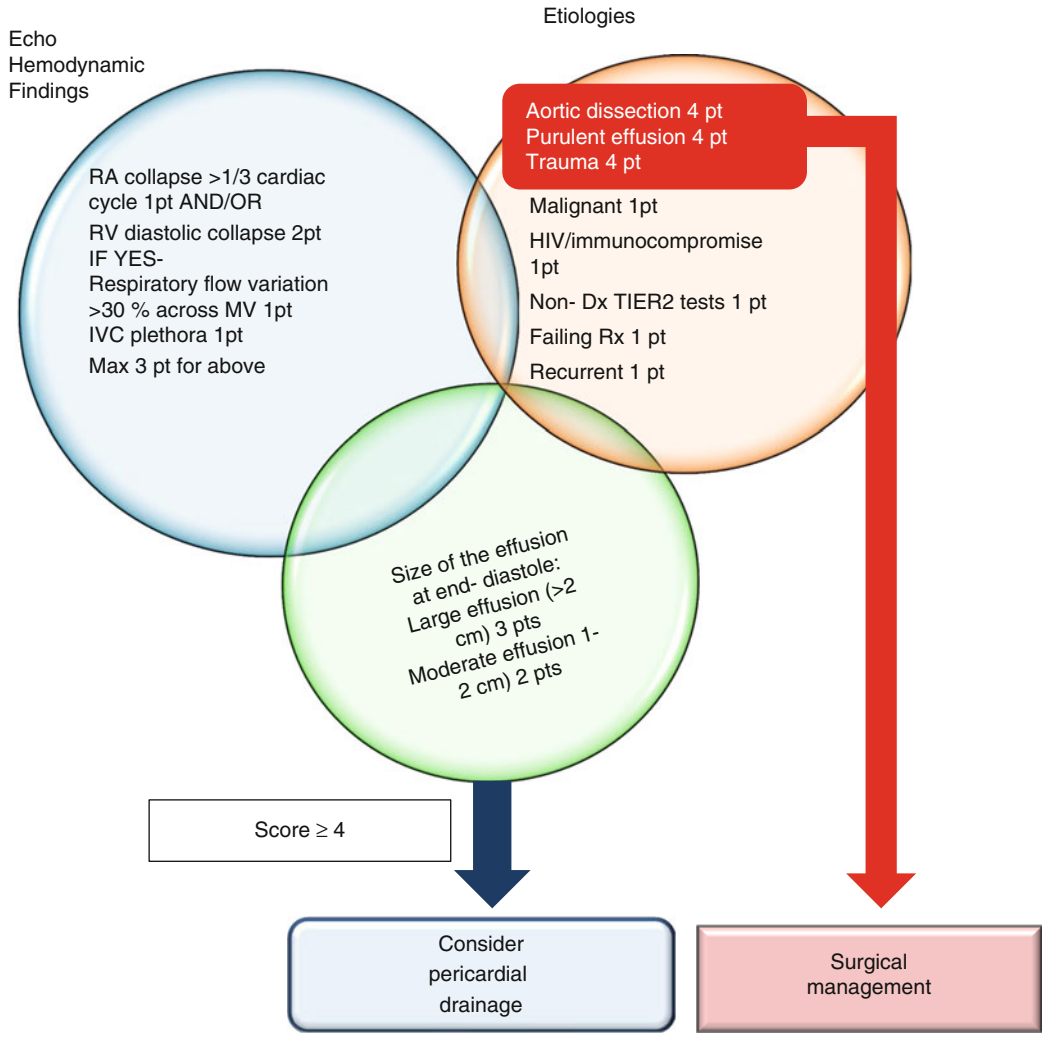


**Fig. 13.8** Pericardial effusion score. The pericardial effusion score which has three components (etiology of the effusion, effusion size, and echocardiographic evidence of hemodynamic compromise) helps to guide clinical decision making in clinically stable patients with pericardial effusion

valves (the mitral and the tricuspid valves) implying ventricular interdependence and engorgement of inferior vena cava with reduced respiratory collapse. Any chamber collapse combined with a confirmatory finding has a very high sensitivity and specificity for tamponade [26]. In general, score of 4 or more provides strong evidence in favor of draining the effusion. It should not be viewed as an absolute indication for drainage but rather as a qualitative measure to support decision-making. Importantly, the score may change over time as the variables change. Patients with a borderline score may need frequent reassessment in terms of effusion size progression and echocardiographic evidence of hemodynamic compromise.

We conducted a case–control study in consecutive hospitalized patients with moderate-to-large pericardial effusion who had no evidence of hemodynamic compromise upon admission. Patients with pericardial effusion drained for diagnostic and/or therapeutic purpose served as cases, and patients who were not drained served as controls. Our conclusion was that the pericardial

effusion scoring index obtained at the initial presentation in patients without immediate hemodynamic compromise showed a high accuracy in identifying patients who required pericardial effusion drainage downstream [27].

## Pericardial Drainage

In patients who need pericardial drainage, echocardiographically guided pericardiocentesis appears to be safe [28]. Depending on the pericardial fluid accumulation pattern, parasternal, subxiphoid, and apical approaches are all acceptable. As mentioned above, the surgical drainage of pericardial effusion is more appropriate in certain patient groups such as in patients with aortic dissection, traumatic hemopericardium, purulent pericarditis, and loculated effusions [1].

### Conclusions

A stepwise, pathway-based approach to the management of pericardial disease is intended to provide guidance for clinicians in decision-making and a patient-tailored evidence-based approach to medical and surgical therapy for pericardial disease.

## References


1. Maisch B, Seferovic PM, Ristic AD, et al. Guidelines on the diagnosis and management of pericardial diseases executive summary; The Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology. Eur Heart J. 2004;25:587–610.
2. Argulian E M.D., M.P.H., Halpern DG M.D., Aziz EF M.D., et al. Novel "CHASER" pathway for the management of pericardial disease. Crit Pathw Cardiol. 2011;10:57–63.
3. Troughton RW, Asher CR, Klein AL. Pericarditis. Lancet. 2004;363:717–27.
4. Spodick DH. Acute pericarditis: current concepts and practice. JAMA. 2003;289:1150–3.
5. Imazio M, Bobbio M, Cecchi E, et al. Colchicine in addition to conventional therapy for acute pericarditis: results of the COlchicine for acute PEricarditis (COPE) trial. Circulation. 2005;112:2012–6.
6. Zayas R, Anguita M, Torres F, et al. Incidence of specific etiology and role of methods for specific etiologic diagnosis of primary acute pericarditis. Am J Cardiol. 1995;75:378–82.
7. Permanyer-Miralda G. Acute pericardial disease: approach to the aetiologic diagnosis. Heart. 2004;90:252–4.
8. Imazio M, Bobbio M, Cecchi E, et al. Colchicine as first-choice therapy for recurrent pericarditis: results of the CORE (COlchicine for REcurrent pericarditis) trial. Arch Intern Med. 2005;165:1987–91.
9. Lange RA, Hillis LD. Clinical practice. Acute pericarditis. N Engl J Med. 2004;351:2195–202.
10. Imazio M, Demichelis B, Parrini I, et al. Day-hospital treatment of acute pericarditis: a management program for outpatient therapy. J Am Coll Cardiol. 2004;43:1042–6.
11. Spodick DH. Acute cardiac tamponade. N Engl J Med. 2003;349:684–90.
12. Sagrista-Sauleda J, Merce J, Permanyer-Miralda G, et al. Clinical clues to the causes of large pericardial effusions. Am J Med. 2000;109:95–101.
13. Levy PY, Corey R, Berger P, et al. Etiologic diagnosis of 204 pericardial effusions. Medicine (Baltimore). 2003;82:385–91.
14. Little WC, Freeman GL. Pericardial disease. Circulation. 2006;113:1622–32.
15. Ling LH, Oh JK, Schaff HV, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. Circulation. 1999;100:1380–6.
16. Talreja DR, Edwards WD, Danielson GK, et al. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. Circulation. 2003;108:1852–7.
17. Ling LH, Oh JK, Tei C, et al. Pericardial thickness measured with transesophageal echocardiography: feasibility and potential clinical usefulness. J Am Coll Cardiol. 1997;29:1317–23.
18. Haley JH, Tajik AJ, Danielson GK, et al. Transient constrictive pericarditis: causes and natural history. J Am Coll Cardiol. 2004;43:271–5.
19. Maisch B, Ristic A, Pankuweit S. Evaluation and management of pericardial effusion in patients with neoplastic disease. Prog Cardiovasc Dis. 2010;53:157–63.
20. Chen Y, Brennessel D, Walters J, et al. Human immunodeficiency virus associated pericardial effusion: report of 40 cases and review of the literature. Am Heart J. 1999;137:516–21.
21. Gowda RM, Khan IA, Mehta NJ, et al. Cardiac tamponade in patients with human immunodeficiency virus disease. Angiology. 2003;54:469–74.
22. Eisenberg MJ, Oken K, Guerrero S, et al. Prognostic value of echocardiography in hospitalized patients with pericardial effusion. Am J Cardiol. 1992;70:934–9.
23. Gillam LD, Guyer DE, Gibson TC, et al. Hydrodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. Circulation. 1983;68:294–301.
24. Leimgruber PP, Klopfenstein HS, Wann LS, et al. The hemodynamic derangement associated with right

ventricular diastolic collapse in cardiac tamponade: an experimental echocardiographic study. Circulation. 1983;68:612–20.
25. Fusman B, Schwinger ME, Charney R, et al. Isolated collapse of left-sided heart chambers in cardiac tamponade: demonstration by two-dimensional echocardiography. Am Heart J. 1991;121:613–6.
26. Merce J, Sagrista-Sauleda J, Permanyer-Miralda G, et al. Correlation between clinical and Doppler echocardiographic findings in patients with moderate and large pericardial effusion: implications for the diagnosis of cardiac tamponade. Am Heart J. 1999;138:759–64.
27. Halpern DG, Argulian E, Briasoulis A, et al. A novel pericardial effusion scoring index to guide decision for drainage. Crit Pathw Cardiol. 2012;11(2):85–8.
28. Tsang TS, Freeman WK, Sinak LJ, et al. Echocardiographically guided pericardiocentesis: evolution and state-of-the-art technique. Mayo Clin Proc. 1998;73:647–52.

# Index



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