Pericarditis and Pericardial Effusions

Ho H. Phan, Amanda Phares, Gustavo P. Fraga,
and Lindemberg M. Silveira-Filho

Acute Pericarditis

Epidemiology

Pericarditis is the most common disease of the pericardium worldwide. It most commonly affects young adults and middle aged people. The actual incidence of pericarditis is unknown as many cases are mild and resolve without a diagnosis. A few population-based studies in Europe and North America estimate the incidence of pericarditis to range from 3.32 to 27.7 cases per 100,000 person-years [1–3]. The incidence of pericarditis among hospitalized patients is 1.5–2 times more common in men than women. While the highest incidence is in young adults, in-hospital mortality is highest in the elderly population.

H. H. Phan (✉)
Trauma and Acute Care Surgery, Department of Surgery, University of California, Davis, Sacramento, CA, USA
e-mail: hhphan@ucdavis.edu

A. Phares
Department of Surgery, University of California Davis, Sacramento, CA, USA
e-mail: anphares@ucdavis.edu

G. P. Fraga
Department of Surgery, Division of Trauma Surgery, School of Medical Sciences (SMS), University of Campinas (Unicamp), Campinas, São Paulo, Brazil

L. M. Silveira-Filho
Cardiovascular Surgery Unit, Department of Surgery, School of Medical Sciences, State University of Campinas, Campinas, São Paulo, Brazil
e-mail: lmsf@fcm.unicamp.br

J. M. Galante, R. Coimbra (eds.), *Thoracic Surgery for the Acute Care Surgeon*,
Hot Topics in Acute Care Surgery and Trauma,
https://doi.org/10.1007/978-3-030-48493-4_6

Etiology

Acute pericarditis is characterized by polymorphonuclear infiltration, increase in vascularity, and formation of fibrous pericardial adhesions. The pathogenesis of acute pericarditis is still unclear, but more data are suggesting an immune-mediated process.

In developed countries, 80% of the cases of acute pericarditis are determined to be idiopathic [4, 5]. Most of these cases are presumed to be due to a viral etiology. Tuberculosis is still a common cause of acute pericarditis worldwide due to its high prevalence in developing countries. Pericarditis can present with either infectious or non-infectious etiologies. Infectious etiologies include viral, bacterial, fungal, and parasitic. Non-infectious etiologies include neoplasms (most commonly lung, breast, lymphoma, mesothelioma), autoimmune diseases, pericardial injury syndromes (trauma, radiation, post-pericardiotomy syndrome, transmural myocardial infarction), metabolic syndromes (uremia, myxedema, anorexia nervosa), and drugs (particularly hydralazine and procainamide).

Clinical Presentation and Diagnosis

According to the European Society of Cardiology (ESC) guidelines, acute pericarditis is diagnosed when two out of the following four clinical features are present: pericardial chest pain, pericardial rub on clinical examination, characteristic EKG changes, and new or worsening pericardial effusion on echocardiography [6, 7]. According to ESC, incessant pericarditis is defined as pericarditis lasting for more than 4–6 weeks but less than 3 months without remission. Recurrent pericarditis is when pericarditis occurs after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer. Chronic pericarditis is defined as pericarditis lasting more than 3 months.

The most common symptom of pericarditis is the substernal chest pain that may radiate to the left shoulder, arm, and/or jaw. This chest pain often worsens with inspiration, coughing, or lying supine, and may improve with sitting up and leaning forward. This characteristic chest pain is present in 90% of the cases and may have other associated symptoms such as fever, chills, dyspnea, and weakness. The pericardial rub, generally heard best over the left sternal border, louder at inspiration and leaning forward, is highly specific for acute pericarditis. However, it is present in only 1/3 of the cases. Electrocardiographic (EKG) changes, typically widespread ST-segment elevation or PR interval depression, are present in about 60% of patients. These characteristic findings are more common in younger patients and are associated with concomitant myocarditis [5]. As EKG changes naturally evolve throughout the course of pericarditis, the presence of characteristic of EKG findings depends on the timing of diagnosis along the course of disease. Early in the disease course, PR depression or ST elevation may be present. Later in the disease course and in chronic pericarditis, T-wave inversion may be present. In patients who respond rapidly to treatment, there may not be any EKG changes. Thus, the absence

of EKG changes does not exclude the diagnosis of pericarditis. Pericardial effusions can be seen on echocardiography in approximately 60% of the cases. Most of the effusions are small or moderate. The presence of large effusions (>20 mm) is a poor prognostic indicator. Because of the similarity in clinical presentation, pericarditis should always be a differential diagnosis in patients being evaluated for acute coronary syndromes.

Other markers of inflammation such as C-reactive protein (CRP) and white blood count (WBC) can also be used as supporting evidence and to follow response to therapy. White blood count is only modestly elevated in patients with idiopathic pericarditis. Highly elevated WBC suggests infectious etiology. C-reactive protein is elevated in about 75% of patients with acute pericarditis and normalizes 1–2 weeks later. Thus, its level is useful for treatment response follow-up [8]. Approximately 30% of patients have concomitant myocarditis, thus assessing markers of myocardial injury such as troponin or creatine kinase is recommended [7]. Although chest X-ray is usually normal in patients with pericarditis, it is routinely recommended to evaluate for pleural involvement. In patients with large pericardial effusions, an enlarged cardiac silhouette on chest X-ray can be seen.

In cases where pericarditis is suspected but not confirmed, cardiac computed tomography (CT) and cardiac magnetic resonance imaging (CMR) might be useful in supporting the diagnosis of pericarditis. The presence of pericardial thickening, contrast-enhanced pericardium on CT, or enhanced pericardial gadolinium uptake on CMR supports the diagnosis of pericarditis. Besides their supportive role, CT and CMR are also useful in evaluating neoplastic disease, congenital abnormality, and calcification in constrictive pericarditis.

Biochemical and cell-count analyses of pericardial fluid do not bring useful information in the majority of patients diagnosed with acute pericarditis. If purulent, tuberculosis, or neoplastic etiologies are suspected, pericardiocentesis should be done and pericardial fluid sent for cell count, biochemical analysis, cytology, culture, and molecular analysis (polymerase chain reaction).

The majority of cases are idiopathic or viral in nature. Specific clinical features may be present at the time of diagnosis that would increase the likelihood of having an etiology other than viral or idiopathic. These predictors are fever >38 °C, subacute onset (symptoms over several days without a clear-cut acute onset), large pericardial effusion (>20 mm on echocardiography), cardiac tamponade, and failure to respond to non-steroidal anti-inflammatory medications within 7 days [7, 9]. These features also increase the likelihood of subsequent complications (recurrence, tamponade, constriction).

Management

Post-Cardiac Injury Syndrome

Post-cardiac injury syndromes (PCIS) are syndromes that include post-traumatic pericarditis, post-myocardial infarction pericarditis, and post-pericardiotomy syndrome (after cardiac surgery). The pathogenesis of PCIS is thought to be an

immune-mediated reaction against the injured pericardium. PCIS usually manifests 2–4 weeks after the initial injury. In addition to the typical signs and symptoms of pericarditis, systemic inflammatory indicators such as fever and elevated CRP are also present. Concomitant pleural involvement (pleuritis and pleural effusions) is also common. It is sometimes difficult to differentiate PCIS from post-operative pericardial or pleural effusions. The demonstration of inflammation is critical in differentiating PCIS from post-operative effusions. The main treatment for PCIS is anti-inflammatory therapy (NSAIDs +colchicine).

It is important to differentiate the post-pericardiotomy syndrome from post-operative pericardial effusion after cardiac surgery, as this has treatment implications. Post-operative pericardial effusions are very common after cardiac surgery, and they usually disappear after 7–10 days. Many patients are asymptomatic and NSAIDs' treatment is not indicated as they are ineffective and may be associated with an increased risk of side effects. A small number of patients with large post-operative pericardial effusions may progress to cardiac tamponade and may need pericardial drainage.

Idiopathic, Viral and Immune-Mediated Acute Pericarditis

The treatment for acute pericarditis is non-steroidal anti-inflammatory drugs (NSAIDs). The most common agents used are aspirin, ibuprofen, and indomethacin. The 2015 ESC guidelines provide an outline of recommended dose schedules for these commonly used NSAIDs [7]. Although there is no randomized control trial that would guide the duration of therapy, most experts recommend that NSAID treatment should be maintained until resolution of symptoms and normalization of C-reactive protein [7]. This usually takes 7–10 days, after which tapering of the medications should be considered. To date, there is no randomized controlled trial comparing the efficacy of different NSAIDs used. Proton pump inhibitor during NSAID treatment is recommended for gastric protection [4].

There are strong data to support the use of colchicine in combination with NSAIDs for the treatment of acute pericarditis. The combination of colchicine with NSAIDs has been shown to reduce treatment failure and recurrence compared to treatment with NSAIDs alone [10, 11]. Colchicine is given at the weight-adjusted dose for the duration of 3 months. A loading dose for colchicine is not necessary and should be avoided to minimize adverse events. The most common side effect associated with colchicine is gastrointestinal intolerance, which is reported in up to 10% of patients. Tapering of colchicine is not required but can be considered.

Corticosteroids are recommended as a second-line treatment for patients who have contraindications to NSAIDs or have failed combined therapy with NSAIDs and colchicine as long as infectious etiologies have been excluded. Corticosteroids should be considered as the initial treatment for patients with connective tissue or immune-mediated disorders as etiology for pericarditis. If corticosteroids are considered, they should be given in low to moderate doses (Prednisone 0.2–0.5 mg/kg/day or equivalent) rather than high doses (1.0 mg/kg/day or equivalent) as high doses are associated with higher rate of recurrences and adverse events [7]. Corticosteroids should be continued until resolution of symptoms and normalization of C-reactive protein, after which it can be slowly tapered.

Recurrent Pericarditis

Twenty to 30% of patients treated for acute pericarditis will have recurrent or chronic pericarditis. Treatment of these patients should be targeted at the underlying etiology if there is an identifiable cause (see below). The first-line treatment for recurrent disease remains anti-inflammatory therapy. NSAIDs and colchicine at the dosage used for the initial therapy should be reinstituted. If only NSAIDs were used at the initial episode, then colchicine should be added for the recurrent episode as it has been shown to reduce future recurrence and evolution into chronic disease. Most patients with recurrent disease will have a good response with combination of NSAIDs and colchicine treatment. If the patients have multiple recurrences, the treatment should be maintained as long as the therapy is still effective and the symptoms are not too disabling. If patients no longer have a good response to NSAIDs and colchicine or have disabling symptoms, low-dose corticosteroids can be added. For patients who do not respond to combination treatment and/or corticosteroid treatment, alternative therapies such as azathioprine, intravenous immunoglobulins, and biologic agents (IL-1R inhibitor Anakinra) have been proposed [4].

For patients who present with recurrent refractory disease and no response to any medical therapy, pericardiectomy can be considered as a last treatment option. To date, pericardiectomy as a treatment option for persistent relapsing pericarditis is supported only by retrospective series [12–14]. In the series reported by Khandaker et al., patients with relapsing pericarditis who underwent pericardiectomy were found to have markedly lower relapses compared to patients continuing with medical treatment at 5-year follow-up [13].

Uremic Pericarditis

Pericardial manifestations of end-stage renal failure are pericarditis and chronic pericardial effusion. Uremic pericarditis frequently begins before renal replacement therapy. Up to 30% of patients do not have chest pain, and EKG findings are absent in most patients. The pathogenesis of uremic pericarditis may be related to retention of toxic metabolites and fluid overload. The preferred treatment is dialysis, either peritoneal or hemodialysis. Patients with uremic pericarditis respond rapidly to dialysis, and the majority of the patients will have resolution of chest pain and pericardial effusion [15]. As the pericardial effusions are often hemorrhagic, systemic anticoagulation should be avoided to prevent bleeding into the pericardial space. Some patients with renal failure may develop pericarditis after initiation of dialysis, even with normal BUN and creatinine levels. This condition is called dialysis-associated pericarditis. Increasing the intensity of dialysis in these patients will result in resolution of pericarditis within a couple of weeks. The development of tamponade is a concern, and these patients should undergo careful hemodynamic and echocardiographic monitoring during intensive dialysis. Pericardiocentesis and pericardial drainage are indicated in patients with tamponade or impending tamponade. Anti-inflammatory therapy particularly with indomethacin has been tried with limited success. Indomethacin has been shown to reduce fever without changing the course of pericardial inflammation or effusion [16]. High-dose corticosteroids may be beneficial, but their use is limited due

to high risk of recurrence and side effects. In patients who have large effusions or who do not respond to dialysis, pericardiotomy for drainage may be considered, even in the absence of tamponade physiology. Intrapericardial treatment with triamcinolone hexacetonide (50 mg every 6 h for 3 days) can be effective in resolving effusions [17]. In patients with recurrent disease or with constrictive pericarditis, pericardiectomy may be required.

Purulent Pericarditis

Purulent pericarditis is caused by bacterial contamination of the pericardial space after cardiac/thoracic surgery through hematogenous spread or by direct extension of intrathoracic and subdiaphragmatic infections (Fig. 1). It is rare nowadays and is more common in immunosuppressed patients. The most common causative organism is *Staphylococcus aureus*. Other common organisms include *Streptococcus pneumonia*, *Haemophilus influenza*, gram-negative bacteria, and *Candida species*. Clinical features typical of pericarditis are usually present in addition to fever (in virtually all patients) and leukocytosis (in most patients). Accumulation of pus in the pericardial sac can lead to tamponade, and pericardiocentesis helps establish the diagnosis along with pericardial fluid culture. A low pericardial-to-serum glucose ratio and elevated pericardial fluid WBC help differentiate purulent from tuberculous or neoplastic pericarditis.

The treatment for purulent pericarditis involves targeted antibiotic therapy and drainage of the pericardial sac. Drainage of the pericardial sac can be achieved by repeated pericardiocentesis, but thick fluid may drain poorly resulting in loculation of the pericardial space. Better drainage can be achieved by subxiphoid pericardiotomy with placement of drainage catheter. The pericardial catheter can also be used for irrigation and/or for instillation of fibrinolytic therapy. Intrapericardial fibrinolysis therapy has been proposed as an alternative to pericardiectomy [18].

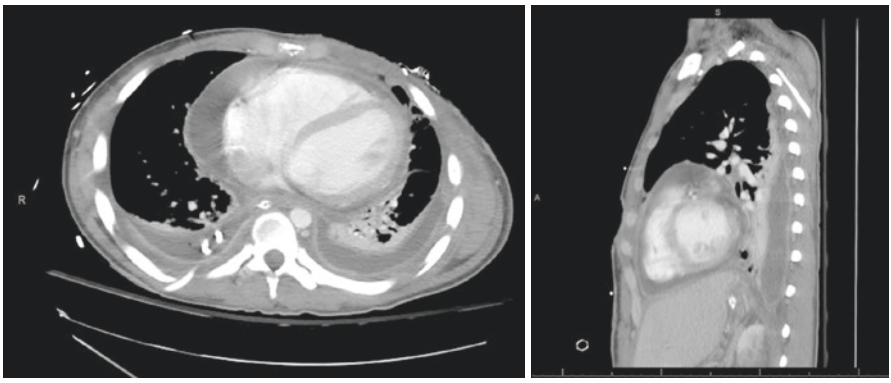

Fig. 1 Purulent pericarditis and bilateraly empyema in a patient who underwent resuscitative thoracotomy, pericardiotomy, repair of left hemidiaphragm, and bowel resection associated with blunt trauma. Microbiological studies revealed *Staphylococcus* and *Candida* species

If drainage is insufficient, infection is persistent or constriction develops, pericardiectomy may be required. Purulent pericarditis is a far more severe disease than other types of pericarditis and frequently demands early, aggressive treatment with pericardiotomy for drainage to avoid complications. Prognosis for purulent pericarditis is poor with reported mortality rate between 20 and 30%.

Tuberculous Pericarditis

Tuberculous pericarditis is rare in the United States due to the low prevalence of tuberculosis but remains the leading cause of pericarditis where tuberculosis is endemic. Pericardial infection may occur via hematogenous spread or via direct extension from lung, bronchial tree, pleura, or adjacent lymph nodes. Tuberculous pericarditis can present in three stages: acute, subacute, and chronic. In the acute phase, serosanguineous effusion and lymphocytic infiltration are present. Protein concentration is high, and tubercle bacilli concentration is low. As the bacilli concentration is low in this phase, the tuberculosis etiology is seldom confirmed. In the subacute phase, granulomatous inflammation with or without caseation and pericardial thickening are present. The chronic stage is characterized by fibrosis, calcification, and constriction.

Clinical presentation varies depending on the phase at diagnosis. The onset of disease may be abrupt, resembling idiopathic pericarditis, or insidious, resembling congestive heart failure. The latter is more common. Pericardiocentesis is recommended for routine evaluation of suspected tuberculous pericarditis. In cases where pericardial fluid analysis is uncertain, pericardial biopsy may be required. In general, the diagnosis of tuberculous pericarditis is established by the detection of tubercle bacilli in smear, culture, or PCR analysis of pericardial fluid and/or detection of tubercle bacilli or caseating granulomas on histological examination of the pericardium. Pericardial fluid high in protein content, increase in leukocyte count with predominance of lymphocyte, elevated adenosine deaminase level, or elevated interferon-gamma level is highly suggestive of tuberculous pericarditis.

The primary treatment for tuberculous pericarditis is multidrug antibiotic treatment, same as the regimen used for pulmonary tuberculosis. The regimen usually consists of rifampin, isoniazid, pyrazinamide, and ethambutol for 2 months followed by isoniazid and rifampin, for a total of 6 months of therapy. Improvement of symptoms is expected within 2–3 weeks of treatment. Adjuvant corticosteroid therapy in patients with tuberculous pericarditis may reduce the incidence of constrictive pericarditis and possibly reduce the need for pericardiectomy [19]. However, the risk of Kaposi sarcoma may increase with use of adjuvant corticosteroid in patients with concomitant HIV infections [20]. In patients with chronic constrictive pericarditis, pericardiectomy may be the only treatment.

Without effective tuberculosis treatment, up to 50% of patients with tuberculous pericarditis will progress to constriction. Timely and effective anti-tuberculosis chemotherapy is the key to reducing the risk of constriction.

Pericardial Neoplasms

Primary pericardial neoplasms are very rare. The most common malignant primary tumor of the pericardium is mesothelioma. It is usually a diffuse disease, encasing the heart and invading the myocardium leading to constriction. Benign tumors of the pericardium include teratoma, lipomas, and fibromas. Benign tumors are not invasive or infiltrative, but they can cause compressive symptoms. Metastatic pericardial neoplasms are more common than primary neoplasms. The most common metastatic malignant tumors of the pericardium are lung cancer, breast cancer, melanoma, lymphomas, and leukemias. Patients with documented malignancy who develop pericardial effusion should raise suspicion for pericardial tumor involvement. However, it is important to note that, in 2/3 of these patients, the pericardial effusions are caused by non-neoplastic etiologies [7]. Imaging studies such as CT, CMR, and PET may be helpful in revealing pericardial tumor involvement. Pericardial fluid analysis and pericardial biopsies are necessary for confirmation of malignant pericardial disease.

The primary treatment for pericardial neoplasms should be directed at the underlying malignancy. Patients with symptomatic effusions or tamponade should undergo pericardial drainage. Reaccumulation of effusions can occur up to 60% of patients. In most of these patients, pericardial and cardiac tumor involvement indicates advanced disease, and management should focus on palliation. Intrapericardial treatment with chemotherapeutic agents (cisplatin for lung cancer, thiotepa for breast cancer) and sclerosing agents (tetracyclines) may reduce recurrences. In patients with radiosensitive tumors such as lymphomas and leukemias, radiation treatment can be effective in controlling malignant pericardial effusions. However, radiation can also cause pericardial and myocardial damage. To reduce reaccumulation of malignant effusions, pericardial windows to allow drainage into the peritoneal or pleural cavity can be created. This option should be considered in advanced neoplastic disease patients with poor prognosis as palliative treatment.

Prognosis

The overall prognosis is very good for patients with idiopathic pericarditis. Approximately 70–80% of patients will be successfully treated with complete resolution during the initial episode. In about 20–30% of patients, incessant or recurrent pericarditis may develop [5]. Cardiac tamponade is rare in idiopathic pericarditis, and it generally occurs at the beginning of the disease process. Constrictive pericarditis as a sequela of viral/idiopathic pericarditis is exceedingly rare (<1%), even in patients with repeated recurrences [7]. In patients diagnosed with specific etiologies, the risk for development of constrictive pericarditis is much higher. The risk of constrictive pericarditis is 3–4% in patients with autoimmune disease and neoplasms, while the risk is as high as 20–35% in patients with tuberculous or purulent pericarditis [8].

Constrictive Pericarditis

Constrictive pericarditis is a condition caused by a reduction in elasticity of the pericardium due to scarring from an inflammatory or infectious process. This loss of elasticity leads to limitations in cardiac filling and cardiac function. Physiologic changes associated with constrictive pericarditis include enhanced ventricular interdependence, early rapid diastolic filling, and reductions in ventricular volumes and stroke volume. Patients usually present with symptoms of right heart failure. Diagnosis is based on signs and symptoms along with characteristic findings on echocardiography, computed tomography, cardiac magnetic resonance, and/or cardiac angiography. Transient forms may be effectively treated using anti-inflammatory medications. The only effective treatment for chronic constrictive pericarditis is pericardiectomy.

Etiology

Constrictive pericarditis can result from a variety of pericardial disorders including viral and bacterial pericarditis and can occur following cardiac surgery or radiation treatment [7]. In a prospective trial in Israel and Italy, 500 patients with acute pericarditis were followed and, overall, less than 2% developed constrictive pericarditis. Only 0.5% of patients with idiopathic or viral pericarditis progressed to constrictive pericarditis, while 3% of patients with connective tissue diseases, 4% of patients with neoplastic processes, 20% of patients with tuberculosis, and 33% of patients with purulent pericarditis progressed to constrictive pericarditis [21]. The time between the predisposing condition and developing constrictive pericarditis is variable. The primary causes differ between developed and developing countries. In developed countries, the most common causes are idiopathic or viral, post-cardiac surgery, and post-radiation therapy. In developing countries, infectious causes are more common with the major cause being tuberculosis [7, 22].

Clinical Presentation and Diagnosis

The most common symptoms of constrictive pericarditis are those of right heart failure such as peripheral edema and hepatomegaly, fluid overload, and dyspnea on exertion. Physical examination findings associated with constrictive pericarditis are elevated jugular venous distension (JVD), pulsus paradoxus, Kussmaul's sign, and a pericardial knock. JVD is the most common physical finding (90% of patients) followed by pericardial knock (50%). Pulsus paradoxus and Kussmaul's sign are uncommon. A pericardial knock is an additional heart sound heard during early diastole. It is usually heard best in the left sternal border and is a result of sudden cessation of ventricular filling. Pulses paradoxus is defined as a decrease in systolic blood pressure more than 10 mmHg with inspiration. It is related to a compensatory

decrease in left ventricular volume in response to an increase in right ventricular volume during inspiration. This is a result of enhanced ventricular interdependence from having a fixed overall cardiac volume. Kussmaul's sign is referred to the loss of inspiratory decline in JVD caused by increased atrial pressures. Frequently, patients present with other associated systemic physical findings, especially peripheral edema, ascites, hepatomegaly, and cachexia [22, 23]. Occasionally, patients with idiopathic constrictive pericarditis are referred for diagnosis from gastroenterologists, as the hepatic decompensation may be the first notable sign that prompts investigation.

Constrictive pericarditis is diagnosed by the presenting symptoms of right heart failure and evidence of impaired diastolic filling due to pericardial constriction. Patients presenting with signs and symptoms of constrictive pericarditis should undergo electrocardiography, chest X-ray, and echocardiography [7]. EKG findings seen in constrictive pericarditis include non-specific ST and T wave changes, tachycardia, low voltage, and atrial fibrillation (late sign due to atrial distension) (see Fig. 2) [7, 23]. These EKG findings are seen in 20–40% of patients, and none of them are specific to constrictive pericarditis. Chest X-ray may reveal a ring of calcification around the heart in about 1/3 of patients [7]. This finding is fairly specific for constrictive pericarditis. Echocardiography can identify increased pericardial thickness, bilateral atrial enlargement, and dilated inferior vena cava and hepatic veins. Echocardiographic findings that favor constriction physiology include the characteristic ventricular septal motion abnormality, respiratory variation in mitral inflow velocity, respiratory variation in pulmonary venous flow velocity, preserved or increased mitral annulus velocity, and hepatic vein flow reversal that is more prominent during expiration [7]. The characteristic septal motion abnormality seen in constriction is generally referred to as "septal bounce".

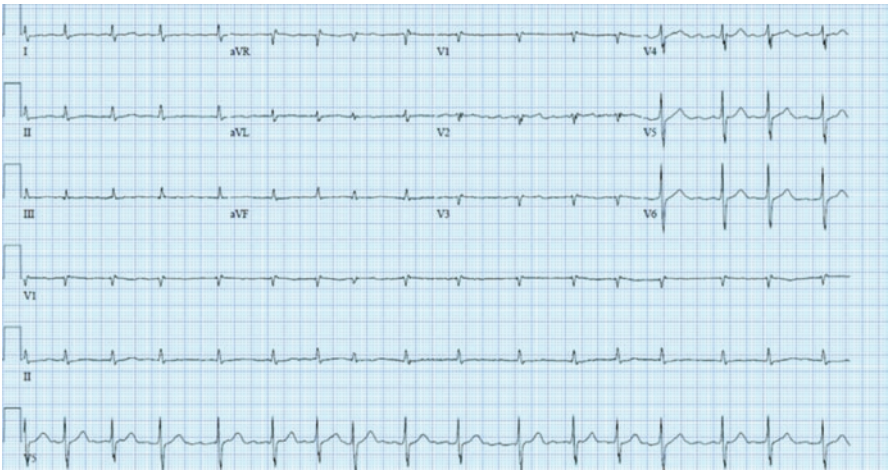

Fig. 2 Electrocardiographic findings of low electrical voltage and atrial fibrillation in a patient with constrictive pericarditis

It is the paradoxical motion of the interventricular septum that deviates toward and then away from the left ventricle during diastole. This is a sign of enhanced ventricular interdependence.

If initial workup is suggestive but not diagnostic for constrictive pericarditis, additional imaging using CT or CMR is recommended. CT findings associated with constrictive pericarditis include increased pericardial thickness, pericardial calcification, bilateral atrial dilation, abnormal shape of the interventricular septum, and dilation of the inferior vena cava (IVC) (see Fig. 3). Sometimes, reversal of contrast flow can be seen in hepatic veins or vena cava. CMR findings include increased pericardial thickness, increased ventricular interdependence, and dilation of the IVC. In addition to their role in supporting the diagnosis, CT and CMR are also very useful for operative planning.

If CT and CMR do not confirm the diagnosis of constrictive pericarditis, cardiac angiography may be needed. Cardiac angiography provides hemodynamic information that can aid in the diagnosis. The key findings seen in cardiac angiography are elevation and equalization of end-diastolic pressures in all chambers, increased right atrial pressure with associated prominent X and Y descents, early diastolic dip followed by a high diastolic plateau (square root sign) on right and left ventricular pressure curves, and enhanced ventricular interdependence seen as mirror-image discordance in systolic pressures between the right and left ventricles during inspiration [7].

The signs and symptoms of constrictive pericarditis overlap with other cardiac disorders, mainly restrictive cardiomyopathy and cardiac tamponade. Medical history is key to differentiating between constrictive pericarditis and restrictive cardiomyopathy as the predisposing conditions are very different between the two. Poor

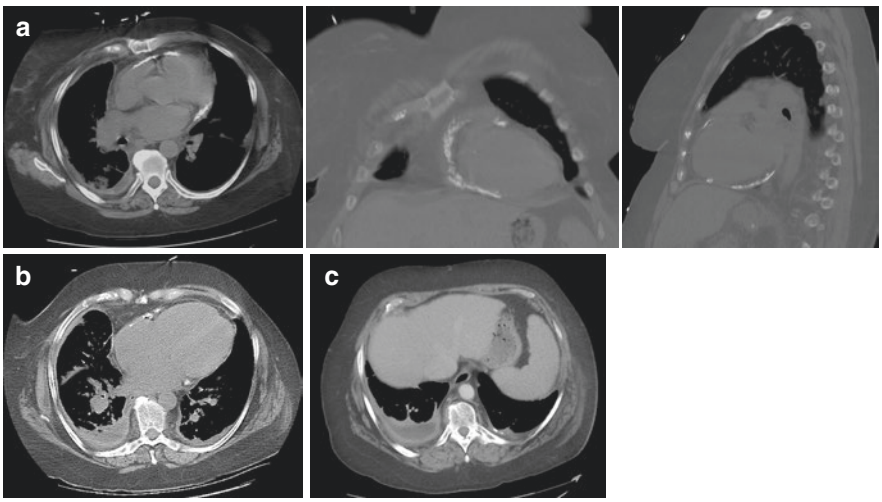

Fig. 3 Computed Tomography showing pericardial calcification (**a**), bilateral atrial enlargement (**b**), and dilation of the inferior vena cava (**c**) in a patient with constrictive pericarditis

Table 1 Diagnosis of constrictive pericarditis and cardiac tamponade

	Constrictive pericarditis	Cardiac tamponade
Presentation	Peripheral edema, hepatomegaly, dyspnea on exertion	Fatigue, dyspnea, syncope, shock
Physical exam	Jugular venous distension, pulses paradoxus, Kussmaul's sign, precordial knock	Tachycardia, hypotension, jugular venous distension, distant heart sounds, pulses paradoxus
EKG	Tachycardia, low voltage, non-specific ST changes, atrial fibrillation	Tachycardia, low voltage, electrical alternans
Chest X-ray	Pericardial calcifications	Normal or enlarged cardiac silhouette
Echocardiogram	Pericardial thickening, bilateral atrial enlargement, dilated IVC and hepatic veins, septal motion abnormality, respiratory variation in mitral inflow velocity and pulmonary venous flow velocity	Pericardial effusion, early diastolic collapse of right ventricle, late diastolic collapse of right and left atria, respiratory variation with mitral and tricuspid flow velocities
CT/MR	Pericardial thickening, pericardial calcifications, bilateral atrial dilation, dilated IVC	Pericardial effusion
Cardiac angiography	Elevation and equalization of end-diastolic pressures in all chambers, increased right atrial pressure, enhanced ventricular interdependence	Elevation and equalization of diastolic pressures in all chambers

filling in restrictive cardiomyopathy is caused by myocardial stiffness leading to poor relaxation and compliance, whereas myocardial relaxation is normal in constrictive pericarditis. On imaging, pericardial thickening supports a diagnosis of constrictive pericarditis, while myocardial thickening supports a diagnosis of restrictive cardiomyopathy. In constrictive pericarditis, the right and left ventricular end-diastolic pressures are equal, while the left ventricular end-diastolic pressure is greater than the right in restrictive cardiomyopathy [7]. The diagnosis of constrictive pericarditis as compared to cardiac tamponade is summarized in Table 1.

Management

Constrictive pericarditis can be divided into three forms, each with a different recommended treatment. Transient constrictive pericarditis is a temporary form of constrictive pericarditis resulting after acute pericarditis and can be treated with anti-inflammatory medications. The constriction ceases after the inflammation resolves, usually after several weeks of anti-inflammatory treatment. Patients diagnosed with early constrictive pericarditis should initially have the underlying disease process treated to reverse the constriction and prevent progression to chronic constrictive pericarditis.

Another form of constrictive pericarditis is effusive–constrictive pericarditis. In this form, cardiac function is limited by both pericardial fluid and the scarred pericardium. Patients are typically misdiagnosed as having cardiac tamponade, and,

once the effusion is drained, continue to have signs and symptoms of constrictive pericarditis. A diagnosis of effusive–constrictive pericarditis can be made when the right atrial pressure fails to fall by 50% or to a level below 10 mmHg after pericardiocentesis. Following pericardiocentesis, medical therapy can be targeted to treat the inflammation. Patients with persistent disease should be considered for pericardiectomy.

Chronic constrictive pericarditis, the third form, is treated by pericardiectomy. Pericardiectomy is indicated in patients who have persistent and significant symptoms. The procedure is performed by removing as much pericardium as technically possible, most commonly through a median sternotomy. Operative mortality ranges from 2.5 to 10% depending on the series. Pericardiectomy is technically challenging and should be performed by specialists. In patients with very mild disease, the operative risk outweighs the potential benefit. In patients with advanced disease and long-term history of the constrictive pericarditis, little benefit is seen, and the operative risks are likely higher. These patients might not be offered pericardiectomy due to the high operative risk and are managed instead with medical therapy targeted at symptom reduction. The exact criteria used for selection of patients for pericardiectomy have not been well described.

Cardiac Tamponade

Pericardial tamponade is a condition where the accumulation of pericardial fluid (effusion, pus, or blood) causes compression of cardiac chambers leading to an increase in intracardial pressure, reduced ventricular filling, and decreased cardiac output. The severity of the clinical symptoms and hemodynamic abnormalities depends on the speed of fluid accumulation, the volume of the pericardial fluid, and the compliance of the pericardium. A small amount of fluid can cause tamponade if it accumulates rapidly and the pericardium does not have enough time to distend. A classic example of this is myocardial injury from penetrating trauma resulting in rapid accumulation of blood in the pericardium and compression of the cardiac chambers. In contrast, slowly accumulating effusions, such as those associated with pericarditis, autoimmune conditions, and renal failure, can get very large before hemodynamic instability becomes evident. Regardless of etiology or effusion size, cardiac tamponade is a life-threatening condition that demands prompt and effective treatment.

Etiology

Almost any cause of pericardial effusion can result in tamponade. Etiologies related to a more acute development of tamponade are post-injury (trauma or iatrogenic), post-pericardiotomy syndromes, cardiac rupture (post-myocardial infarction), aortic dissection, idiopathic pericarditis, neoplasms, and granulomatous diseases.

Large volume effusions that develop insidiously over time can evolve into cardiac tamponade, especially when the underlying etiology of pericarditis has not been diagnosed. In these cases, the development of tamponade is less dramatic and less acute. These patients may have pericardial effusions over the period of days to weeks without cardiovascular symptoms. As their effusions continue to develop and the pericardial pressures reach a critical threshold, the patients begin to manifest signs and symptoms of decreased cardiac output. Autoimmune diseases, neoplasms, renal failure, idiopathic pericarditis, granulomatous diseases, and myxedema are some conditions that can present with subacute onset of tamponade.

Clinical Presentation and Diagnosis

Patients with pericardial tamponade may present with symptoms of fatigue and dyspnea. In more severe cases, syncope and shock are the presenting symptoms. A number of findings may be present on physical examination, but none of them alone are highly sensitive or specific. Tachycardia is the result of adrenergic response due to the declining stroke volume and is present in almost all patients. In contrast, the presence of hypotension is more variable. Jugular venous distension is common but may be absent in patients who are severely hypovolemic. Thus, the lack of this finding does not rule out tamponade. Muffled or distant heart sounds due to the damping effect of the pericardial effusion may be present. *Pulsus paradoxus* (a decrease in systolic blood pressure more than 10 mm of Hg during inspiration) is a common finding. It is a sign of exaggerated ventricular interdependence related to a fixed pericardial volume. Inspiratory increase in venous return and right ventricular volume results in compensatory decrease in left ventricular volume, leading to reduced stroke volume and systemic blood pressure. The classic Beck's triad (jugular venous distension, hypotension, and muffling of heart sounds) is only present in 10% of patients [24].

Electrocardiogram may show sinus tachycardia, abnormalities related to pericarditis, and/or low voltage. Electrical alternans refers to beat-to-beat variation in the QRS complexes due to the swinging of the heart within the pericardial fluid. It is a relatively specific indicator of tamponade, but it is rarely seen. Chest X-ray is usually normal, especially in those with acute onset of tamponade. In cases of slowly developing tamponade, the cardiac silhouette can be enlarged with a "water bottle" configuration.

Echocardiography can reliably identify and characterize pericardial effusions and can help differentiate cardiac tamponade from other potential causes of similar clinical presentations. Echocardiographic findings most suggestive of cardiac tamponade are early diastolic collapse of the right ventricle and late diastolic collapse of the right and left atria. Other echocardiographic findings are respiratory variation with reciprocal changes in right and left ventricular volumes and respiratory variation in mitral and tricuspid flow velocities. Cardiac catheterization is usually not used to diagnose cardiac tamponade. If it is performed, it usually demonstrates elevation and equalization of diastolic pressures in all chambers. Inspiratory increase

in right-sided pressures with associated reduction in left-sided pressures (*pulsus paradoxus*) may also be observed. The diagnosis of cardiac tamponade as compared to constrictive pericarditis is summarized in Table 1.

Management

Cardiac tamponade is a life-threatening condition that demands prompt and effective treatment. Drainage of the pericardial fluid can be done either by pericardiocentesis or by surgical pericardiotomy. Pericardiocentesis should be performed under echocardiographic guidance to minimize complications and to target the appropriate collection. A drainage catheter should be inserted for ongoing drainage. Pericardiocentesis is generally preferred in hemodynamically unstable patients as it can be performed at bedside and can be achieved quickly. Open surgical drainage has the advantage of allowing direct visualization of the epicardium and manual break-up of loculations for better evacuation of pericardial contents. Open surgical drainage also permits access for pericardial biopsy. Open drainage is generally preferred for hemopericardium due to trauma and purulent pericarditis.

Once tamponade is relieved with drainage, the underlying cause for tamponade must be identified and treated. For trauma victims and patients with aortic dissection or myocardial rupture, emergent surgical intervention is required. It is important to note that general anesthesia and positive pressure ventilation can worsen venous return and hemodynamic collapse. For this reason, these patients should be prepped and ready for incision prior to induction under general anesthesia.

Pericardial Procedures

Pericardiocentesis

Pericardiocentesis is usually performed to investigate the etiology of pericarditis/effusion or to relieve symptoms of cardiac tamponade. The procedure should be accomplished under fluoroscopic or echocardiographic guidance. The latter is preferred and is more commonly employed. Blind pericardiocentesis is very risky and should not be done, except in very rare, immediately life-threatening situations. If blind pericardiocentesis must be done, the subxiphoid approach is recommended. If clinically feasible, the patient should be positioned semi-upright and rotated slightly toward the left. This allows the fluid to concentrate more in the inferior and anterior portion of pericardial space. A long needle is advanced below the xiphoid process and angled 30–45° below the skin surface, aiming slightly toward the left, while the operator aspirates the syringe until pericardial fluid is observed. To help with blind aspiration, a precordial EKG electrode can be attached to the needle to transduce the signal during aspiration. If the needle contacts the cardiac surface, ST changes or negative deflection will appear on the EKG tracing, and this should signal the operator to withdraw the needle slightly (see Fig. 4).

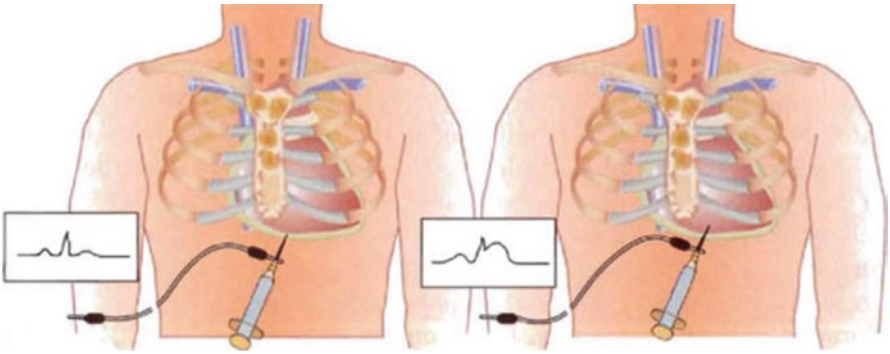

Fig. 4 EKG monitoring showing the change in tracing if the myocardium is contacted with the needle. (From Sadiq, A and Wall, M: Chapter 9 Pericardiocentesis. *In* Falter, F [Ed.], *Bedside Procedures in the ICU*, DOI https://doi.org/10.1007/978-1-4471-2259-3_9, Springer-Verlag London Limited 2012)

For ultrasound-guided pericardiocentesis, echocardiographic evaluation is used to determine the optimal needle entry site, which should be the point on the body that is closest to the transducer probe and where the fluid collection is the largest. With the patient semi-upright and left tilted, the ideal spot is identified using echocardiography, and it is marked as the intended site of entry. This spot is typically found along the left parasternal axis away from the left internal thoracic artery. Insertion of the needle into the fluid collection can either be guided by continuous echocardiographic visualization or guided based on the trajectory of the transducer probe and depth as memorized by the operator. Once the needle is inserted, the extracardiac position can be confirmed by injecting a few milliliters of agitated saline infusion and visualization of bubbles in the pericardial space on echocardiography. Once intrapericardial position is confirmed, the needle is then exchanged over a guidewire with a pigtail catheter, which is left in place for continued drainage. For fluoroscopic guided pericardiocentesis, the needle is usually inserted via the subxiphoid approach toward the heart shadow, while the operator alternates between suction and injection of small amount of diluted contrast, until pericardial fluid is aspirated. The location of the needle is confirmed by injecting contrast medium into the pericardial space prior to exchanging with a guidewire. Multiple fluoroscopic projections should be used to confirm the position of the guidewire prior to placement of the pigtail catheter.

In cases of recurrent effusion, percutaneous balloon pericardial window creation is an option for temporary drainage into the pleural space. In this technique, a balloon dilator threaded over the guidewire is straddled across the pericardium and dilated to create a window in the pericardium. This allows the pericardial fluid to drain into the pleural space where it is absorbed.

Complication rates of pericardiocentesis range from 4 to 10% depending on the method used, operator skills, and clinical settings [7]. Complications can be serious and potentially fatal, including ventricular arrhythmias and laceration of the heart, coronary arteries, internal thoracic arteries, lung, and liver.

Pericardiotomy and Pericardial Biopsy

When the pericardial effusion is large, pericardiocentesis under image guidance is relatively safe. When the effusions are small or loculated or when the character of the fluid is not suitable for pericardiocentesis (such as purulent effusion, fibrin, or clot), open surgical drainage is a safer and more effective approach. With the open approach, pericardial tissue biopsy can also be obtained.

Subxiphoid pericardiotomy can be performed under general anesthesia or local anesthesia with monitored sedation. A vertical incision is made over the xiphoid process toward the upper abdomen, and the rectus abdominis muscle is divided at the linea alba. Once the xiphoid process is exposed, it can be excised or retracted. Dissection is carried cephalad in the substernal space until the inferior surface of the pericardium is encountered. The pericardium is grasped, pulled down, and incised, and drainage of pericardial fluid should be observed. The pericardial fluid should be collected and sent for culture, cytology, cell count, and biochemical analysis. A small portion of the pericardium should also be excised and sent for histological analysis. The pericardial space should now be inspected with direct visualization and digital examination. Adhesions and loculations can be broken up by the operator's finger. Two drainage catheters are placed into the pericardial space (one anterior and one posterior to the heart) through two separate counter incisions. The incision is then closed in layers.

If the pericardial effusion is persistent or recurrent, a transpleural pericardiotomy can be done to allow drainage into the pleural space. This so-called pericardial window can be achieved through a left anterior thoracotomy at the fourth intercostal space. With this exposure, an incision into the pericardium is made and the pericardial fluid is sampled for diagnostic studies. To allow reliable drainage of the effusion into the pleural space, a large portion of the pericardium should be removed when creating the window. Pericardial tissue should also be sent for histological analysis. This procedure can also be accomplished by the video-assisted thoracoscopic approach, using single lung ventilation. Once the pericardial window has been created, temporary drainage catheters are left in both pericardial and pleural spaces. For drainage of purulent pericarditis, the subxiphoid approach is usually preferred to avoid contamination of the pleural space.

In patients' recurrent pericardial effusions associated with metastatic malignancy, pericardial-peritoneal drainage can be achieved by creating a transdiaphragmatic pericardial window or by inserting a large drainage catheter connecting the pericardial sac with the abdomen. The latter is performed with a 15 cm drain inserted half in the pericardial sac and half in the peritoneal cavity, and the drain is secured with a suture at the diaphragm level. This will enable continued drainage of the pericardium into the peritoneum, avoiding repeated interventions.

Pericardioscopy

Pericardioscopy has been suggested by some authors as a diagnostic tool when evaluating pericardial effusions. It can be done at the time of subxiphoid pericardiotomy as an adjunctive technique to allow exploration of the pericardial space. This

is accomplished by inserting a rigid or flexible pericardioscope through the pericardiotomy for visual inspection of the pericardium and epicardium and for targeted tissue sampling. The use of pericardioscopy with targeted biopsy in addition to pericardial fluid analysis and open pericardial biopsy may increase diagnostic yield [25]. Percutaneous pericardioscopy under image guidance has also been described by some. This procedure is technically demanding and is only available in a limited number of experienced referral centers [26].

Pericardiectomy

Pericardiectomy is typically indicated for the treatment of recurrent pericarditis refractory to medical treatment or for constrictive pericarditis. Several surgical approaches have been described, including left anterolateral thoracotomy, bilateral thoracotomies, and median sternotomy. The advantage of the left anterolateral thoracotomy is avoidance of a redo median sternotomy. The disadvantage is limited exposure of the right phrenic nerve which could potentially compromise the completeness of pericardial resection. Bilateral thoracotomy approach is associated with higher morbidity and is usually employed for redo surgery or when extension of left anterolateral thoracotomy is needed. Median sternotomy provides the best exposure and is the most common approach used for this operation.

The extent of pericardiectomy is still a matter of controversy. Complete pericardiectomy involves removal of the entire pericardium overlying the heart and great vessels except for the pericardium posterior to the left atrium. Radical pericardiectomy is defined by removal of the anterior portion of the pericardium anterior to the left to right phrenic nerves, the diaphragm portion of the pericardium, and the pericardium posterior to the left phrenic nerve. Anterior pericardiectomy refers to removal of the anterior portion of the pericardium only (phrenic nerve to phrenic nerve). In all cases, care is taken to preserve the phrenic nerves. For patients who undergo pericardiectomy for recurrent pericarditis, the pericardium is inflamed and generally non-calcified and non-adherent to the underlying pericardium. Extensive resection may be more feasible in this group of patients. Since the goal for this indication is to remove as much of inflamed pericardium as possible to prevent recurrent symptoms, effort should be made to be more complete. In patients who undergo pericardiectomy for constrictive pericarditis, heavily calcified and thicken pericardium, sometimes with extension into myocardium, may be encountered. The pericardial space is obliterated, and separation is tedious and technically challenging. More complete resection may be wrought with potential complications. For this reason, some surgeons recommend only anterior pericardiectomy based on the rationale that anterior resection alone can improve constrictive hemodynamics in most patients [27]. On the other hand, others have shown that for constrictive pericarditis, complete resection is associated with superior survival and functional outcome when compared to partial resection [28]. In most large series of pericardiectomy for constrictive pericarditis, the standard technique described is radical pericardiectomy [14, 28, 29].

The depth of resection is also important. In some cases, after removal of the outer layer, a constricting peel overlying the epicardium may still limit ventricular function. Effort should be made to remove this peel to relieve the constriction. If removal is not possible, the epicardial peel may be scored in a checkerboard manner, leaving behind non-contiguous islands of the epicardium. This may be sufficient to allow expansion of the ventricles.

Pericardiectomy can be performed with or without cardiopulmonary bypass. In a large series of 513 pericardiectomies performed over 20 years at the Mayo Clinic, cardiopulmonary bypass was used in 40% of the cases [14]. Hemodynamic support with cardiopulmonary bypass is used in many instances to allow greater manipulation of the heart and to decompress the chambers to facilitate epicardial dissection. Furthermore, in cases when the myocardium is injured during the dissection, repair is easier with cardiopulmonary bypass.

In-hospital mortality for pericardiectomy ranges from 2.5 to 10% [14, 29]. The reported mortality rate is generally lower for pericardiectomy done for recurrent/effusive pericarditis compared to constrictive pericarditis [14]. The most common reason for in-hospital mortality is low cardiac output and post-operative renal failure. Patients who present at time of surgery with advanced hepatic congestion tend to have worse outcomes. The overall 5-, 10-, and 15-year survival of patients undergoing pericardiectomy is reported to be 80%, 60%, and 40%, respectively [14, 30]. The most important variable for long-term outcomes of pericardiectomy is the etiology of constriction. Patients with idiopathic constrictive pericarditis have the best 5- and 10-year survival. Patients with post-radiation pericarditis have the worst long-term outcomes because these patients also have concomitant myocardiopathy and coronary arterial disease [31]. Other conditions associated with worse long-term outcomes include advanced heart failure, poor renal function, abnormal left ventricular function, advanced liver disease, and older age [23].

References

1. Imazio M, Cecchi E, Demichelis B, et al. Myopericarditis versus viral or idiopathic acute pericarditis. Heart. 2008;94:498–501.
2. Kyto V, Sipila J, Rautava P. Clinical profile and influences on outcomes in patients hospitalized for acute pericarditis. Circulation. 2014;130(18):1601–6.
3. Kumar N, Pandey A, Jain P, et al. Acute pericarditis-associated hospitalization in the USA: a nation-wide analysis, 2003–2012. Cardiology. 2016;135(1):27–35.
4. LeWinter MM. Clinical practice. Acute pericarditis. N Engl J Med. 2014;371(25):2410–6.
5. Imazio M, Gaita F. Acute and recurrent pericarditis. Cardiol Clin. 2017;35(4):505–3.
6. Maisch B, Seferovic PM, Ristic AD, et al. Guidelines on the diagnosis and management of pericardial diseases executive summary; Task Force on the diagnosis and management of pericardial diseases of the European Society of Cardiology. Eur Heart J. 2004;25(7):587–610.
7. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: The task force for the diagnosis and management of pericardial diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2015;36(42):2921–64.

8. Imazio M, Brucato A, Maestroni S, et al. Prevalence of C-reactive protein elevation and time course of normalization in acute pericarditis: implication for the diagnosis, therapy, and prognosis of pericarditis. Circulation. 2011;123(10):1092–7.
9. Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systemic review. JAMA. 2015;314(14):1498–506.
10. Imazio M, Brucato A, Cemin R, et al. A randomized trial of colchicine for acute pericarditis. N Engl J Med. 2013;369(16):1522–8.
11. Lotrionte M, Biondi-Zoccai G, Imazio M, et al. International collaborative systematic review of controlled clinical trials on pharmacologic treatments for acute pericarditis and its recurrences. Am Heart J. 2010;160(4):662–70.
12. Hatcher CR, Logue RB, Logan WD, et al. Pericardiectomy for recurrent pericarditis. J Thorac Cardiovasc Surg. 1971;62(3):371–8.
13. Khandaker MH, Schaff HV, Greason KL, et al. Pericardiectomy vs medical management in patients with relapsing pericarditis. Mayo Clin Proc. 2012;87(11):1062–70.
14. Gillaspie EA, Stulak JM, Daly RC, et al. A 20-year experience with isolated pericardiectomy: analysis of indications and outcomes. J Thorac Cardiovasc Surg. 2016;152(2):448–58.
15. Bentata Y, Hamdi F, Chemlal A, et al. Uremica pericarditis in patients with end stage renal disease: prevalence, symptoms and outcome in 2017. Am J Emerg Med. 2018;36(3):464–6.
16. Spector D, Alfred H, Siedlecki M, et al. A controlled study of the effect of indomethacin in uremic pericarditis. Kidney Int. 1983;24(5):663–9.
17. Busselmeier TJ, Davin TD, Simmons RL, et al. Treatment of intractable uremic pericardial effusion. Avoidance of pericardiectomy with local steroid instillation. JAMA. 1978;240(13):1358–9.
18. Augustin P, Desmard M, Mordant P, et al. Clinical review: intrapericardial fibrinolysis in management of purulent pericarditis. Crit Care. 2011;15(2):220.
19. Strang JI, Kakaza HH, Gibson DG, et al. Controlled trial of prednisolone as adjuvant in treatment of tuberculous constrictive pericarditis in Transkei. Lancet. 1987;2(8573):1418–22.
20. Mayosi BM, Ntsekhe M, Bosch J, et al. Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis. N Engl J Med. 2014;371(12):1121–30.
21. Imazio M, Brucato A, Maestroni S, et al. Risk of constrictive pericarditis after acute pericarditis. Circulation. 2011;124(11):1270–5.
22. Troughton RW, Asher CR, Klein AL. Pericarditis. Lancet. 2004;363(9410):717–27.
23. Welch TD. Constrictive pericarditis: diagnosis, management and clinical outcomes. Heart. 2018;104(9):725–31.
24. Guberman BA, Fowler NO, Engel PJ, et al. Cardiac tamponade in medical patients. Circulation. 1981;64(3):633–40.
25. Nugue O, Millaire A, Porte H, et al. Pericardioscopy in the etiologic diagnosis of pericardial effusion in 141 consecutive patients. Circulation. 1996;94(7):1635–41.
26. Seferović PM, Ristić AD, Maksimović R, et al. Diagnostic value of pericardial biopsy: improvement with extensive sampling enabled by pericardioscopy. Circulation. 2003;107(7):978–83.
27. Nataf P, Cacoub P, Dorent R, et al. Result of subtotal pericardiectomy for constrictive pericarditis. Eur J Cardiothorac Surg. 1993;7(5):252–5.
28. Chowdhury UK, Subramaniam GK, Kumar AS, et al. Pericardiectomy for constrictive pericarditis: a clinical, echocardiographic, and hemodynamic evaluation of two surgical techniques. Ann Thorac Surg. 2006;81(2):522–9.
29. Cho YH, Schaff HV. Surgery for pericardial disease. Heart Fail Res. 2013;18(3):375–87.
30. George TJ, Arnaoutakis GJ, Beaty CA, et al. Contemporary etiologies, risk factors, and outcomes after pericardiectomy. Ann Thorac Surg. 2012;94(2):445–51.
31. Vistarini N, Chen C, Mazine A, et al. Pericardiectomy for constrictive pericarditis: 20 years of experience at the Montreal Heart Institute. Ann Thorac Surg. 2015;100(1):107–13.