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Pericardial Disease

William C. Little, MD; Gregory L. Freeman, MD

In contrast to coronary artery disease, heart failure, valvular disease, and other topics in the field of cardiology, there are few data from randomized trials to guide physicians in the management of pericardial diseases. Although there are no American Heart Association/American College of Cardiology guidelines on this topic, the European Society of Cardiology has recently published useful guidelines for the diagnosis and management of pericardial diseases.¹ Our review focuses on the current state of knowledge and the management of the most important pericardial diseases: acute pericarditis, pericardial tamponade, pericardial constriction, and effusive constrictive pericarditis.

The Normal Pericardium

The pericardium is a relatively avascular fibrous sac that surrounds the heart. It consists of 2 layers: the visceral and parietal pericardium. The visceral pericardium is composed of a single layer of mesothelial cells that are adherent to the cardiac epicardium.^{2,3} The parietal pericardium is a fibrous structure that is <2 mm thick and is composed primarily of collagen and a lesser amount of elastin. The 2 layers of the pericardium are separated by a potential space that can normally contain 15 to 35 mL of serous fluid distributed mostly over the atrial-ventricular and interventricular grooves.

The pericardium surrounds the heart and attaches to the sternum, the diaphragm, and the anterior mediastinum and is invested around the great vessels and the venae cavae, serving to anchor the heart in the central thorax. Because of its location, the pericardium may also function as a barrier to infection.

The pericardium is well innervated such that pericardial inflammation may produce severe pain and trigger vagally mediated reflexes. The pericardium also secretes prostaglandins that modulate cardiac reflexes and coronary tone.⁴

As a result of its relatively inelastic physical properties, the pericardium limits acute cardiac dilatation and enhances mechanical interactions of the cardiac chambers.⁵ In response to long-standing stress, the pericardium dilates, shifting the pericardial pressure-volume relation substantially to the right (Figure 1).^{6–8} This allows a slowly accumulating pericardial effusion to become quite large without compressing the cardiac chambers and for left ventricular remodeling to occur without pericardial constriction.

Despite the known important functions of the normal pericardium, congenital absence or surgical resection of the pericardium does not appear to have any major untoward effects.⁹

Acute Pericarditis

Etiology

Acute inflammation of the pericardium with or without an associated pericardial effusion can occur as an isolated clinical problem or as a manifestation of systemic diseases.^{1,10–13} Although as many as 90% of isolated cases of acute pericarditis are idiopathic or viral, the list of other potential causes is extensive (Table 1). Although formerly common, tuberculous and bacterial infections have become rare causes of pericarditis.¹⁴ Other causes of acute pericarditis include uremia,¹⁵ collagen vascular diseases,¹⁶ neoplasms, and pericardial inflammation after an acute myocardial infarction or pericardial injury.¹⁷

Pericarditis after an acute myocardial infarction most commonly occurs 1 to 3 days after transmural myocardial infarction presumably because of the interaction of the healing necrotic epicardium with the overlying pericardium. A second form of pericarditis associated with myocardial infarction (Dressler's syndrome) typically occurs weeks to months after a myocardial infarction. It is similar to the pericarditis that may occur days to months after traumatic pericardial injury, after surgical manipulation of the pericardium, or after a pulmonary infarction.¹⁸ This syndrome is presumed to be mediated by an autoimmune mechanism and is associated with signs of systemic inflammation, including fever, and polyserositis. The frequency of pericarditis after myocardial infarction has been reduced by the use of reperfusion therapy.¹⁹

Clinical Manifestations

Most patients with acute pericarditis experience sharp retrosternal chest pain that can be quite severe and debilitating. In some cases, however, pericarditis may be asymptomatic, as is often the case with the pericarditis accompanying rheumatoid arthritis. Pericardial pain is usually worse with inspiration and when supine and is relieved by sitting forward. Typically, pericardial pain is referred to the scapular ridge, presumably due to irritation of the phrenic nerves, which pass adjacent to

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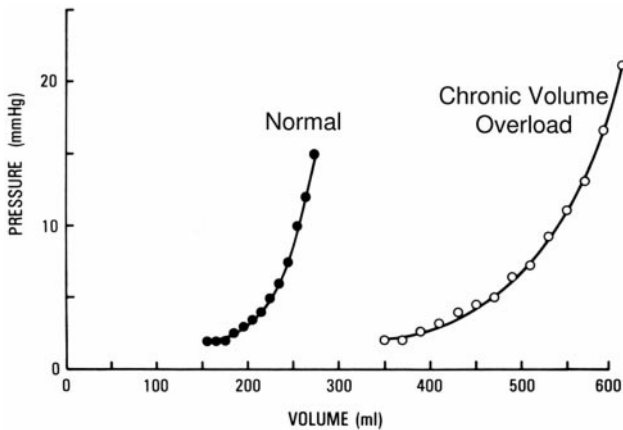


Figure 1. Pericardial pressure-volume relations determined in pericardium obtained from a normal experimental animal and from an animal with chronic cardiac dilation produced by volume loading. The pericardial pressure-volume relation is shifted to the right in the volume-loaded animal, demonstrating that the pericardium can dilate to accommodate slowly increasing volume. Reproduced with permission from Freeman and LeWinter.⁶ Copyright 1984, American Heart Association.

the pericardium.¹² The chest pain of acute pericarditis must be differentiated from that of pulmonary embolism and myocardial ischemia/infarction (Table 2).¹⁰

The pericardial friction rub is the classic finding in patients with acute pericarditis. It is a high-pitched, scratchy sound that can have 1, 2, or 3 components. These components occur when the cardiac volumes are most rapidly changing: during ventricular ejection, during rapid ventricular filling in early diastole, and during atrial systole. Thus, patients with atrial fibrillation have only 1 or 2 component rubs. The pericardial friction rub can be differentiated from a pleural rub, which is absent during suspended respiration, whereas the pericardial rub is unaffected. Although it is easy to imagine that the pericardial rub arises from the inflamed visceral and parietal layers of the pericardium rubbing together, most patients with acute pericarditis (including those with audible rubs) have at least a small pericardial effusion, which should lubricate the interaction of the 2 layers of the pericardium.¹²

Early in the course of acute pericarditis, the ECG typically displays diffuse ST elevation in association with PR depression (Figure 2).¹² The ST elevation is usually present in all leads except for aVR, but in post-myocardial infarction pericarditis, the changes may be more localized. Classically,

TABLE 1. Causes of Acute Pericarditis

Idiopathic
Infections (viral, tuberculosis, fungal)
Uremia
Acute myocardial infarction (acute, delayed)
Neoplasm
Post-cardiac injury syndrome (trauma, cardiothoracic surgery)
Systemic autoimmune disease (systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, systemic sclerosing periarteritis nodosa, Reiter's syndrome)
After mediastinal radiation

the ECG changes of acute pericarditis evolve through 4 progressive stages: stage I, diffuse ST-segment elevation and PR-segment depression; stage II, normalization of the ST and PR segments; stage III, widespread T-wave inversions; and stage IV, normalization of the T waves.¹² Patients with uremic pericarditis frequently do not have the typical ECG abnormalities.¹⁹

Patients with acute pericarditis usually have evidence of systemic inflammation, including leukocytosis, elevated erythrocyte sedimentation rate, and increased C-reactive protein. A low-grade fever is common, but a temperature >38°C is unusual and suggests the possibility of purulent bacterial pericarditis.^{10,20}

Troponin is frequently minimally elevated in acute pericarditis, usually in the absence of an elevated total creatine kinase.^{21,22} Presumably, this is due to some involvement of the epicardium by the inflammatory process. Although the elevated troponin may lead to the misdiagnosis of acute pericarditis as a myocardial infarction, most patients with an elevated troponin and acute pericarditis have normal coronary angiograms.²² An elevated troponin in acute pericarditis typically returns to normal within 1 to 2 weeks and is not associated with a worse prognosis.¹⁰

Echocardiography usually demonstrates at least a small pericardial effusion in the presence of acute pericarditis. It is also helpful in excluding cardiac tamponade (see below). Pericardiocentesis is indicated if the patient has cardiac tamponade (see below) or in suspected purulent or malignant pericarditis.^{1,10,23} In the absence of these situations, when the cause of the acute pericarditis is not apparent on the basis of routine evaluation, pericardiocentesis and pericardial biopsy rarely provide a diagnosis and thus are not indicated.^{23,24}

Treatment

If acute pericarditis is a manifestation of an underlying disease, it often responds to the treatment of the primary condition. For example, uremic pericarditis usually resolves with adequate renal dialysis.¹⁵ Most acute idiopathic or viral pericarditis is a self-limited disease that responds to treatment with aspirin (650 mg every 6 hours) or another nonsteroidal antiinflammatory agent (NSAID). The intravenous administration of ketorolac, a parenteral NSAID, was effective in relieving the pain of acute pericarditis in 22 consecutive patients.²⁵ Aspirin may be the preferred nonsteroidal agent to treat pericarditis after myocardial infarction because other NSAIDs may interfere with myocardial healing.¹⁰ Indomethacin should be avoided in patients who may have coronary artery disease.

If the pericardial pain and inflammation do not respond to NSAIDs or if the acute pericarditis recurs, colchicine has been observed to be effective in relieving pain and preventing recurrent pericarditis.²⁶ The routine use of colchicine is supported by recently reported results of the Colchicine for Acute Pericarditis (COPE) Trial.²⁷ One hundred twenty patients with a first episode of acute pericarditis (idiopathic, acute, postpericardiotomy syndrome, and connective tissue disease) entered a randomized, open-label trial comparing aspirin plus colchicine (1.0 to 2.0 mg for the first day followed by 0.5 to 1.0 mg/d for 3 months) with treatment with

TABLE 2. Differentiation of Pericarditis From Myocardial Ischemia/Infarction and Pulmonary Embolism

	Myocardial Ischemia or Infarction	Pericarditis	Pulmonary Embolism
Chest pain			
Character	Pressure-like, heavy, squeezing	Sharp, stabbing, occasionally dull	Sharp, stabbing
Change with respiration	No	Worsened with inspiration	In phase with respiration (absent when the patient is apneic)
Change with position	No	Worse when supine; improved when sitting up or leaning forward	No
Duration	Minutes (ischemia); hours (infarction)	Hours to days	Hours to days
Response to nitroglycerin	Improved	No change	No change
Physical examination			
Friction rub	Absent (unless pericarditis is present)	Present in 85% of patients	Rare; a pleural friction rub is present in 3% of patients
ECG			
ST-segment elevation	Localized convex	Widespread concave	Limited to lead III, aVF, and V ₁
PR-segment depression	Rare	Frequent	None
Q waves	May be present	Absent	May be present in lead III or aVF or both
T waves	Inverted when ST segments are still elevated	Inverted after ST segments have normalized	Inverted in lead II, aVF, or V ₁ to V ₄ while ST segments are elevated

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aspirin alone. Colchicine reduced symptoms at 72 hours (11.7% versus 36.7%; $P \leq 0.03$) and recurrence at 18 months (10.7% versus 36.7%; $P = 0.004$; number needed to treat=5). Colchicine was discontinued in 5 patients because of diarrhea. No other adverse events were noted. Importantly, none of 120 patients developed cardiac tamponade or progressed to pericardial constriction.²⁸

Although acute pericarditis usually responds dramatically to systemic corticosteroids, their use early in the course of acute pericarditis appears to be associated with increased incidence of relapse after tapering the steroids.^{28,29} An observational study strongly suggests that use of steroids increases the probability of relapse in patients treated with colchicine.³⁰ Furthermore, in the COPE Trial, steroid use was an independent risk factor for recurrence (odds ratio=4.3).²⁷ Accord-

ingly, systemic steroids should be considered only in patients with recurrent pericarditis unresponsive to NSAIDs and colchicine or as needed for treatment of an underlying inflammatory disease. If steroids are to be used, an effective dose (1.0 to 1.5 mg/kg of prednisone) should be given, and it should be continued for at least 1 month before slow tapering.³¹ Experts have suggested that a detailed search for the cause of recurrent pericarditis should be undertaken before steroid therapy is initiated in resistant or relapsing cases of pericarditis.^{1,28}

The intrapericardial administration of steroids has been reported to be effective in acute pericarditis without producing the frequent reoccurrence of pericarditis that complicates the use of systemic steroids, but the invasive nature of this procedure limits its utility.^{29,32} A very few patients with

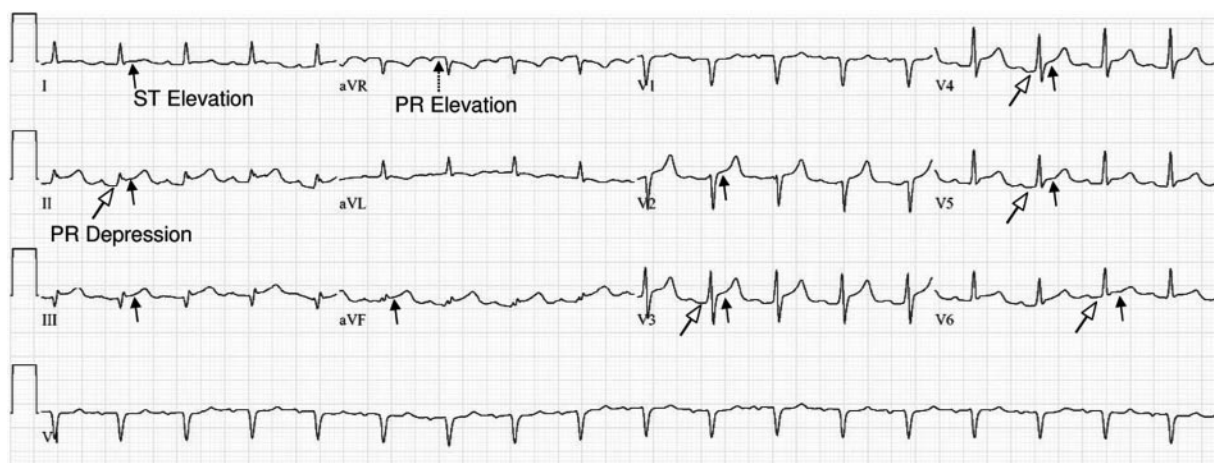


Figure 2. ECG demonstrating typical features seen on presentation of acute pericarditis. There is diffuse ST elevation and PR depression except in aVR, where there is ST depression and PR elevation.

frequent, highly symptomatic recurrences of pericarditis despite intensive medical therapy may require surgical pericardiectomy.³² However, painful relapses can occur even after pericardiectomy, especially if the pericardium is not completely removed.²⁸

Most patients with acute pericarditis recover without sequelae. Predictors of a worse outcome include the following: fever $>38^{\circ}\text{C}$, symptoms developing over several weeks in association with immunosuppressed state, traumatic pericarditis, pericarditis in a patient receiving oral anticoagulants, a large pericardial effusion (>20 mm echo-free space or evidence of tamponade), or failure to respond to NSAIDs.²⁰ In a recent series of 300 patients with acute pericarditis, 254 (85%) did not have any of the high-risk characteristics and had no serious complications.²⁰ Of these low-risk patients, 221 (87%) were managed as outpatients, and the other 13% were hospitalized when they did not respond to aspirin.²⁰

On the basis of these considerations, we manage patients presenting with acute pericarditis in the following manner. Patients are hospitalized but are discharged in 24 to 48 hours if they have no high-risk factors and their pain has improved. Initial therapy includes aspirin (650 to 975 mg every 6 to 8 hours) and colchicine (2 g initially followed by 1 g/d). In addition, we use a proton pump inhibitor in most patients to improve the gastric tolerability of the aspirin. We advise against exercise until after the chest pain completely resolves. Even if the pain responds promptly, we continue aspirin for 4 weeks and colchicine for 3 months to minimize the risk of recurrent pericarditis. If pericarditis reoccurs, we reload with colchicine and use intravenous ketorolac (30 mg every 6 hours) and then continue an oral NSAID and colchicine for at least 3 more months. We make every effort to avoid the use of steroids, reserving steroids for patients who cannot tolerate aspirin and other NSAIDs or who have a recurrence not responsive to colchicine and intravenous NSAIDs.

It is important to recognize that there are no clear data to guide this set of recommendations. In general, if a recurrence of pericarditis is mild it can be treated with intensification of NSAID therapy; various combinations of aspirin, NSAIDs, and colchicine have been successfully applied in such cases.

Cardiac Tamponade

Pathophysiology

Cardiac tamponade occurs when fluid accumulation in the intrapericardial space is sufficient to raise the pressure surrounding the heart to the point where cardiac filling is altered. Ultimately, compression of the heart by a pressurized pericardial effusion results in markedly elevated venous pressures and impaired cardiac output producing shock; if untreated, it can be rapidly fatal.³³

Under normal conditions, the space between the parietal and visceral pericardium can accommodate only a small amount of fluid before the development of tamponade physiology. It is not surprising, therefore, that cardiac perforation quickly results in tamponade. With a gradually accumulating effusion, however, as is often the case in malignancy, very large effusions can be accommodated without tamponade (Figure 1). The key concept is that once the total intraperi-

cardial volume has caused the pericardium to reach the noncompliant region of its pressure-volume relation, tamponade rapidly develops.

Because of its lower pressures, the right heart is most vulnerable to compression by a pericardial effusion, and abnormal right heart filling is the earliest sign of a hemodynamically significant pericardial effusion. Under these conditions, adequate filling of the right heart requires a compensatory increase in systemic venous pressure, which results from venoconstriction and fluid retention. Of note, when cardiac tamponade results from hemorrhage into the pericardium, there can be rapid circulatory collapse because not only does pericardial pressure rapidly rise but intravascular volume falls, preventing a compensatory increase in venous pressure.

The increased pericardial pressure in cardiac tamponade accentuates the interdependence of the cardiac chambers as the total cardiac volume is limited by the pericardial effusion.^{33–36} The volume in any cardiac chamber can only increase when there is an equal decrease in the volume in other chambers. Thus, venous return and atrial filling predominantly occur during ventricular systole as the ejection of blood out of the right and left ventricles lowers cardiac volume and allows blood to enter the atria. Moreover, the normal effects of respiration are accentuated such that venous return and right-sided filling occur during inspiration as intrathoracic pressures fall, providing a pressure gradient from the systemic veins to the right atrium. Because the total intrapericardial volume is fixed by the pressurized effusion, this increased inspiratory right ventricular filling crowds the left ventricle and impairs its filling. Thus, in tamponade, left heart filling occurs preferentially during expiration when there is less filling of the right heart. The small normal respiratory variation in left ventricular stroke volume and systolic arterial pressure is markedly accentuated in cardiac tamponade, resulting in the clinical finding of “paradoxical pulse” (see below).

Clinical Presentation

Cardiac tamponade is a treatable cause of cardiogenic shock that can be rapidly fatal if unrecognized. As such, cardiac tamponade should be considered in the differential diagnosis of any patients with shock or pulseless electric activity.¹

Patients with impending or early tamponade are usually anxious and may complain of dyspnea and chest pain.³³ The increased venous pressure is usually apparent as jugular venous distension. The X descent (during ventricular systole) is typically the dominant jugular venous wave with little or no Y descent. In rapidly developing cardiac tamponade, especially hemorrhagic cardiac tamponade, there may not have been time for compensatory increase in venous pressure, and the jugular veins may not be distended. Such “low-pressure” tamponade may also occur in patients with uremic pericarditis who have been volume depleted.³⁷ The heart sounds are classically soft or muffled, especially if there is a large pericardial effusion.

The hallmark of cardiac tamponade is a paradoxical pulse. This is defined as a >10 -mm Hg drop in systolic arterial pressure during inspiration.¹ When severe, the paradoxical

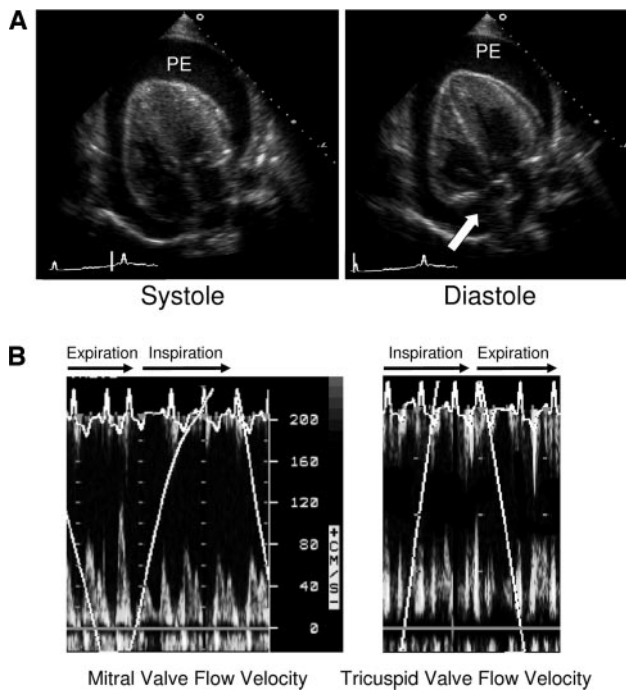


Figure 3. A, Two-dimensional echocardiogram in 4-chamber view from a patient with cardiac tamponade. There is a large pericardial effusion apparent as an echo-free space around the heart. In diastole, there is collapse of the right atrium (arrow). B, Doppler measurement of mitral valve and tricuspid flow velocities in a patient with cardiac tamponade. There is marked reciprocal respiratory variation: during inspiration, mitral valve flow velocity decreases, and tricuspid valve flow velocity increases.

pulse can be apparent as an absence of a palpable brachial or radial pulse during inspiration. A paradoxical pulse can also occur when there are wide swings in intrathoracic pressure and in other conditions such as pulmonary embolism and hypovolemic shock. It is important to recognize that the paradoxical pulse may be difficult to recognize in the presence of severe shock and may be absent in cardiac tamponade if there is coexisting aortic insufficiency, atrial septal defect, or preexisting elevated left ventricular end-diastolic pressure due to left ventricular hypertrophy or dilatation.^{33,38}

Echocardiography

Echocardiography is an important part of the evaluation in patients with cardiac tamponade and should be performed without delay in any patient who is suspected of having this condition.³⁹ Echocardiography visualizes pericardial effusions as an echo-free space around the heart (Figure 3). Patients with acute hemorrhagic effusions may have pericardial thrombus apparent as an echo-dense mass.⁴⁰ Small pericardial effusions are only seen posteriorly. Pericardial effusions large enough to produce cardiac tamponade are almost always circumferential (both anteriorly and posteriorly).²

Echocardiography can also provide information on the significance of the pericardial effusion.⁴¹ In the presence of cardiac tamponade, there is diastolic collapse of the free walls of the right atrium and/or right ventricle.^{42,43} This is due to compression of these relatively low-pressure structures by the

higher-pressure pericardial effusion. The collapse is exaggerated during expiration when right heart filling is reduced. Right atrial collapse is more sensitive for tamponade, but right ventricular collapse lasting more than one third of diastole is a more specific finding for cardiac tamponade. Of note, right ventricular collapse may also be present with large pleural effusions in the absence of pericardial effusion or cardiac tamponade.⁴⁴

There are other echo-Doppler findings that are indicative of the hemodynamic consequence of cardiac tamponade.^{41,45} Distention of the inferior vena cavae that does not diminish with inspiration is a manifestation of the elevated venous pressure in tamponade,⁴⁶ whereas venous flow predominantly occurs in systole, not diastole, because of the limited cardiac volume.⁴⁷ In addition, there can be marked reciprocal respiratory variation in mitral and tricuspid flow velocities reflecting the enhanced ventricular interdependence that is the mechanism of the paradoxical pulse (Figure 3).⁴⁸ Collapse of right-sided chambers is a sensitive indicator of tamponade, but abnormalities of cardiac filling are a more specific finding.⁴⁷

Thus, echocardiography demonstrates the presence and size of the pericardial effusion and reflects its hemodynamic consequences. Right atrial and ventricular collapse indicates cardiac compression, whereas enhanced respiratory variation of ventricular filling is a manifestation of increased ventricular interdependence. Although echocardiography provides important information, it must be emphasized that cardiac tamponade is ultimately a clinical diagnosis (see below).⁴⁷

Treatment

The treatment of cardiac tamponade is drainage of the pericardial effusion. Medical management is usually ineffective and should be used only while arrangements are made for pericardial drainage. Fluid resuscitation may be of transient benefit if the patient is volume depleted (hypovolemic cardiac tamponade). The use of inotropic agents is usually ineffective because there is already intense endogenous adrenergic stimulation. The initiation of mechanical ventilation in a patient with tamponade may produce a sudden drop in blood pressure because the positive intrathoracic pressure will contribute to a further impairment of cardiac filling.³⁹

In the absence of clinical evidence of tamponade, echocardiographic findings of right-sided diastolic collapse do not mandate emergency pericardiocentesis. For example, we do not recommend emergency pericardial drainage in a patient who has a nontraumatic pericardial effusion with right-sided collapse if there is an adequate stable blood pressure (>110 mm Hg systolic) without a paradoxical pulse (ie, <10 mm respiratory variation in systolic pressure). However, the patient must be observed carefully because the development of only a small additional amount of pericardial fluid can result in tamponade. In some patients, the echocardiographic signs of cardiac compression will resolve within a few days, and pericardiocentesis can be avoided if there is no other indication.

Traditionally, nonemergent pericardiocentesis has been performed in the cardiac catheterization laboratory under fluoroscopic guidance with invasive hemodynamic monitor-

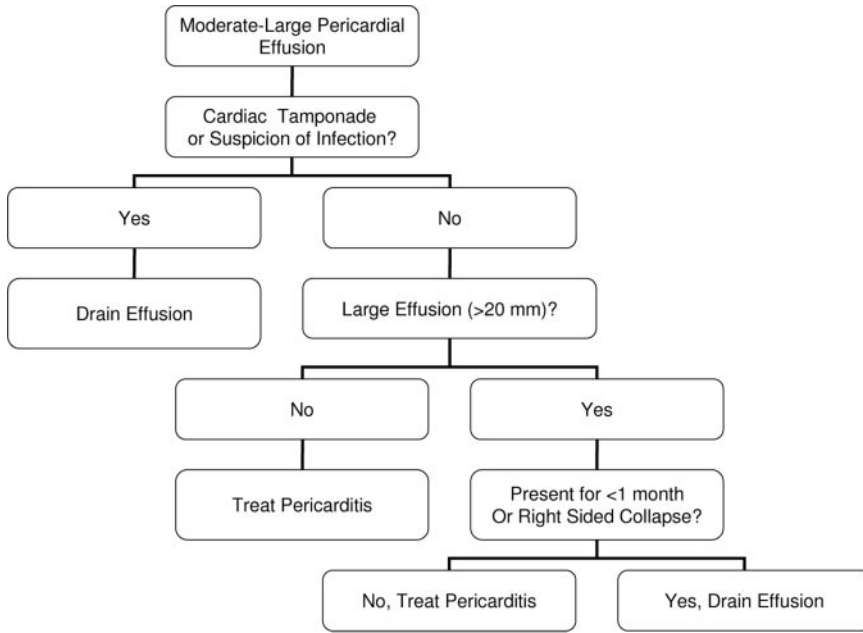


Figure 4. Potential algorithm for managing patients with a moderate to large pericardial effusion. See the text for a discussion of methods to drain the pericardial effusion. Adapted and redrawn with permission from Hoit.⁵⁴ Copyright 2002, American Heart Association.

ing.¹ Performing pericardiocentesis in this setting provides the option of utilizing right heart catheterization before and after the procedure to confirm the diagnosis, if necessary, and to detect effusive-constrictive pericardial disease (see below). More recently, echocardiographic-guided pericardiocentesis has been demonstrated to be a safe and effective procedure that can be performed at the bedside.⁴⁹ During this procedure the ideal entry site (minimal distance from skin to pericardial fluid without intervening structures) can be defined. Continued drainage of the pericardial fluid through an indwelling catheter minimizes the risk of reoccurrence of the effusion. If pericardial tissue is required for diagnosis or in the case of purulent pericarditis or recurrent effusions, surgical drainage may be the preferred treatment. Surgery is also the treatment for traumatic hemopericardium.¹

Surgical drainage of a pericardial effusion is usually performed through a limited subxiphoid incision. This allows direct visualization and biopsy of the pericardium. The diagnosis accuracy can be improved by inserting a pericardioscope.⁵⁰ This provides direct visualization of a much larger area of the pericardium and the ability to obtain multiple biopsies. Recently, a flexible pericardioscope has been developed that can be inserted percutaneously.⁵¹

Malignant pericardial effusions frequently reoccur. Such recurrent pericardial effusions may necessitate the surgical creation of a pericardial window that allows the effusion to drain into the pleural space, preventing reoccurrence of cardiac tamponade. An attractive alternative in these patients, especially if their overall prognosis is poor from the malignancy, is the percutaneous creation of a pericardial window by balloon dilation.^{52,53}

Pericardial Effusion Without Tamponade

Acute pericarditis is often accompanied by a small pericardial effusion that does not produce tamponade.²⁰ If there is no hemodynamic compromise and the diagnosis can be established by other means, pericardiocentesis may not be neces-

sary.^{1,23,54} If it accumulates slowly, a large pericardial effusion of a liter or more can be present without cardiac tamponade. However, nearly 30% of a series of 28 patients with large idiopathic pericardial effusions developed cardiac tamponade unexpectedly.⁵⁵ In this series, pericardiocentesis with catheter drainage alone resulted in resolution of the effusion without reoccurrence in about half of the patients. Thus, pericardiocentesis may be advisable in patients with very large pericardial effusions (>20 mm on echocardiography), even in the absence of tamponade. In contrast, Merce et al⁴⁷ demonstrated that none of 45 patients with large pericardial effusions managed without pericardial drainage subsequently developed tamponade. It must be recognized that pericardiocentesis will not yield a diagnosis in most patients, and therefore the reason for draining large effusions is to avoid potential progression to tamponade.⁴⁷ We believe that the risk of progression to tamponade is greatest in patients with the recent development of large effusions or who have evidence of diastolic right-sided collapse. Some experts have recommended routine drainage of pericardial effusions that persist for >3 months.⁵⁴ We do not believe that this is necessary. A potential algorithm for the management of pericardial effusions is shown in Figure 4.

Pericardial Constriction

Pathophysiology

Pericardial constriction occurs when a scarred, thickened, and frequently calcified pericardium impairs cardiac filling, limiting the total cardiac volume.^{1,36,56} The pathophysiological hallmark of pericardial constriction is equalization of the end-diastolic pressures in all 4 cardiac chambers. This occurs because the filling is determined by the limited pericardial volume, not the compliance of the chambers themselves.

Initial ventricular filling occurs rapidly in early diastole as blood moves from the atria to the ventricles without much change in the total cardiac volume. However, once the

pericardial constraining volume is reached, diastolic filling stops abruptly. This results in the characteristic dip and plateau of ventricular diastolic pressures. The stiff pericardium also isolates the cardiac chambers from respiratory changes in intrathoracic pressures, resulting in Kussmaul's sign (see below).

Etiology

Pericardial constriction is usually the result of long-standing pericardial inflammation leading to pericardial scarring with thickening, fibrosis, and calcification.⁵⁶ The most frequent causes are mediastinal radiation, chronic idiopathic pericarditis, after cardiac surgery, and tuberculous pericarditis.^{1,57–59}

Clinical Manifestations

Patients with pericardial constriction typically present with manifestations of elevated systemic venous pressures and low cardiac output.⁵⁸ Because there is equalization of all cardiac pressures (including right and left atrial pressures), systemic congestion is much more marked than pulmonary congestion. Typically, there will be marked jugular venous distension, hepatic congestion, ascites, and peripheral edema, while the lungs remain clear. The limited cardiac output typically presents as exercise intolerance and may progress to cardiac cachexia with muscle wasting. In long-standing pericardial constriction, pleural effusions, ascites, and hepatic dysfunction may be prominent clinical features.¹ Patients with pericardial constriction are much more likely to have left-sided or bilateral pleural effusions than solely right-sided effusions.⁶⁰

The jugular veins are distended with prominent X and Y descents. The normal inspiratory drop in jugular venous distention may be replaced by a rise in venous pressure (Kussmaul's sign). This sign may also be present with severe right heart failure, especially in association with tricuspid regurgitation. The classic auscultatory finding of pericardial constriction is a pericardial knock. This occurs as a high-pitched sound early in diastole when there is the sudden cessation of rapid ventricular diastolic filling.⁶¹ When accurately recognized, a pericardial knock is a specific but insensitive indicator of pericardial constriction.

Pericardial calcification seen on the lateral plane chest x-ray is suggestive of pericardial constriction.⁶² Similarly, most patients with pericardial constriction have a thickened pericardium (>2 mm) that can be imaged by echocardiography, CT, and MRI (Figure 5).^{1,56,63} It is important to recognize, however, that pericardial constriction can be present without pericardial calcium and, in some cases, even without pericardial thickening. For example, in a series of 143 patients from the Mayo Clinic with surgically proven pericardial constriction, 26 (18%) had a normal pericardial thickness (<2 mm).⁶⁴ Finally, the pericardial constriction may be predominantly localized to one region of the heart.

Tagged cine MRI has been reported to be able to demonstrate adhesion of the pericardium to the myocardium in pericardial constriction.⁶⁵ This is recognized by persistent concordance of tagged signals between the pericardium and myocardium throughout the cardiac cycle.

Doppler echocardiography is important in the evaluation of patients with suspected pericardial constriction. The echocar-

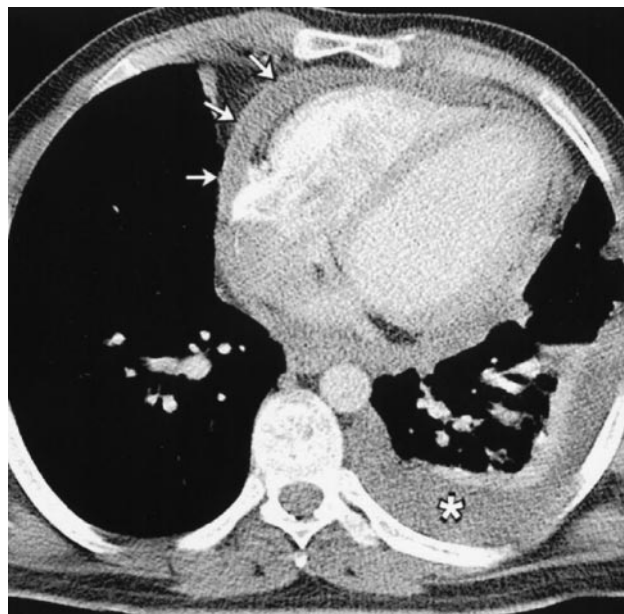


Figure 5. Chest CT from a patient with pericardial constriction showing thickened pericardium (arrows) and a left pleural effusion. Reproduced with permission from *Circulation*. 2005;111:e364. Copyright 2005, American Heart Association.

diogram may demonstrate pericardial thickening and calcification. However, increased pericardial thickness can be missed on a transthoracic echocardiogram. Transesophageal echocardiography is more sensitive and accurate in determining pericardial thickness.⁶⁶ Transesophageal echocardiography can also assess pulmonary venous flow.

Doppler echocardiography frequently demonstrates restricted filling of both ventricles with a rapid deceleration of the early diastolic mitral inflow velocity (E wave) and small or absent A wave. In addition, there is substantial (>25%) respiratory variation of the mitral inflow velocity (Figure 6).⁶⁷ Wide swings in the E wave velocity may also occur in patients with respiratory disease, but these are associated with marked respiratory variation in the superior vena caval flow velocity (typically >20 cm/s), whereas the variation with pericardial constriction is less.^{46,68} Other findings in constrictive pericarditis include preserved diastolic mitral annular velocity, rapid diastolic flow propagation to the apex, and diastolic mitral regurgitation.⁶⁹

Differential Diagnosis

Pericardial constriction should be considered in any patient with unexplained systemic venous congestion. Echocardiography is useful in differentiating pericardial constriction from right heart failure due to tricuspid valve disease and/or associated pulmonary hypertension.

The most difficult differentiation is between pericardial constriction and restrictive cardiomyopathy (Table 3). Clinical manifestations of restrictive cardiomyopathy most typically due to cardiac amyloid may be very similar to those due to pericardial constriction.^{70,71} Doppler echocardiography is the most useful method to distinguish constriction from restriction. Patients with pericardial constriction have marked respiratory variation (>25%) of mitral inflow, whereas this is

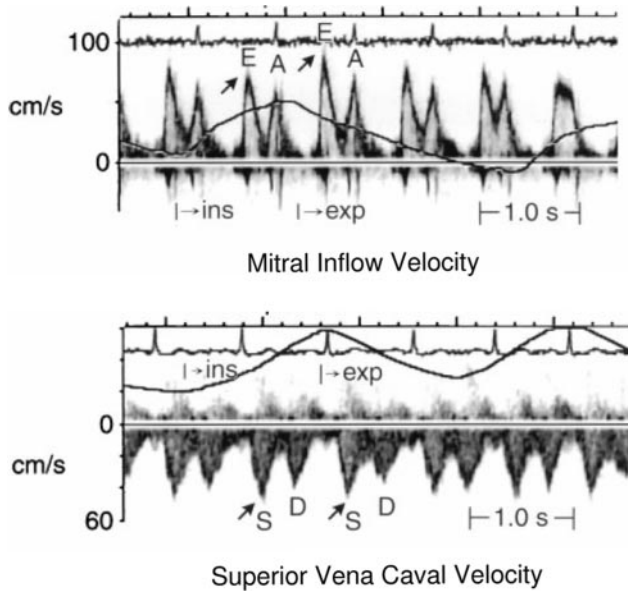


Figure 6. Doppler mitral flow and superior vena caval velocity in a patient with pericardial constriction. There is marked (>25%) respiratory variation in the peak early diastolic initial flow velocity E (decreased during inspiration [ins] and increased during expiration [exp]). In contrast, there is less respiratory variation of the flow velocity in the vena cava. S indicates systole; D, diastole. Reproduced with permission from Boonyaratavej et al.⁶⁸ Copyright 1998, American College of Cardiology Foundation.

not present in restrictive cardiomyopathies.⁶⁷ In some cases of pericardial constriction with markedly elevated venous pressures, the respiratory variation may only be present after head-up tilt.⁷² The tissue Doppler measurement of mitral annular velocities is useful in distinguishing constriction from

restriction. The early diastolic mitral annular velocity (Ea) is almost always reduced in patients with myocardial restriction, whereas it remains normal in patients with pericardial constriction.^{69,73,74} The optimal discrimination occurs with an Ea velocity of 8 cm/s. Similarly, rapid propagation of early diastolic flow to the apex is preserved in constriction and reduced in restriction. A slope ≥ 100 cm/s of the first aliasing contour in the color M-mode best distinguishes the 2.⁶⁹

It has recently been reported that patients with pericardial constriction have only minimally elevated B-type natriuretic peptide (<200 pg/mL), whereas the B-type natriuretic peptide levels are typically markedly increased in patients with restrictive cardiomyopathy (>600 pg/mL).⁷⁵

Traditionally, constriction and restriction were differentiated at cardiac catheterization by hemodynamic criteria. In constriction, there is usually almost exact equalization of late diastolic pressures in both the right and left heart. With restriction, typically left ventricular end-diastolic pressure exceeds right ventricular pressure by at least a few mm Hg. Pulmonary hypertension is frequently seen with restriction but is not typically present with constriction. Thus, right ventricular diastolic pressure should be more than one third of the right ventricular systolic pressure in pericardial constriction.

It should be recognized that the aforementioned classic hemodynamic criteria have limited specificity (24% to 57%) in distinguishing pericardial constriction from cardiomyopathies.⁷⁶ In contrast, dynamic respiratory variations indicating increased ventricular interdependence are superior. In constriction during inspiration, right ventricular systolic pressures increase, while left ventricular systolic pressure decreases. The inverse occurs during expiration. This finding

TABLE 3. Differentiation of Pericardial Constriction From Restrictive Cardiomyopathy

	Pericardial Constriction	Restrictive Cardiomyopathy
Physical examination		
Pulmonary congestion	Usually absent	Usually present
Jugular venous pulse	Prominent Y descent	
Early diastolic sound	Pericardial knock	S3 (low pitched)
Pericardial thickness	>2 mm (but <2 mm in 15%)	<2 mm
Echo/Doppler findings		
LV myocardium	Normal	"Sparkling" myocardium in amyloid
Atrial size	+/- Atrial enlargement	Atrial enlargement
Mitral valve flow pattern	Restricted	Restricted
Respiratory variation in E wave	>25%	<20%
Mitral annular diastolic velocity	>8 cm/s	<8 cm/s
Biomarker		
B-type natriuretic peptide	<200 pg/mL	>600 pg/mL
Hemodynamics		
Y descent	Prominent	Variable
PA systolic pressure	<50 mm Hg	>60 mm Hg
PCW-RA pressure	0	5 mm Hg
Reciprocal respiratory variation in right ventricular/left ventricular peak systolic pressure	Present	Absent

PA indicates pulmonary arterial; PCW, pulmonary capillary wedge; and RA, right atrial.

had >90% sensitivity and specificity in recognizing constrictive pericarditis versus restriction in a series of 36 patients from the Mayo Clinic.⁷⁶

Endomyocardial biopsy performed during catheterization can also be utilized in selected cases to distinguish myocardial disease from pericardial constriction.⁷⁷

Bush et al⁷⁸ first observed that, in some patients, the hemodynamic findings of constriction may only be present after rapid volume loading and labeled this syndrome occult constrictive pericarditis. Some patients with this syndrome may improve after removal of the pericardium. The sensitivity and specificity of the response to volume loading and the role of pericardiectomy in treating this condition are not well established.⁷⁹ Thus, we do not recommend volume loading as part of the routine hemodynamic evaluation of patients with suspected pericardial constriction.

Treatment

In some patients with relatively acute onset pericardial constriction, the symptoms and constrictive features may resolve with medical therapy alone.⁸⁰ For example, Haley et al⁸¹ reported a series of 36 patients with pericardial constriction that resolved with treatment with the use of antiinflammatory agents, colchicine, and/or steroids.

In more chronic pericardial constriction, definitive treatment is surgical pericardial decortication, widely resecting both the visceral and parietal pericardium.¹ This operation is a major undertaking with substantial risk (>6% mortality even in the most experienced centers).^{57,58} In some patients, it does not immediately restore normal cardiac function, which may require some time after removal of the constricting pericardium to return to normal. The largest surgical series from the Mayo Clinic and the Cleveland Clinic indicate that patients with constriction due to idiopathic or viral pericarditis do best and patients with radiation-induced constriction fare most poorly after surgery.^{57,58}

Effusive Constrictive Pericarditis

Hancock⁸² first recognized that some patients presenting with cardiac tamponade did not have resolution of their elevated right atrial pressure after removal of the pericardial fluid. In these patients, pericardiocentesis converted the hemodynamics from those typical of tamponade to those of constriction (Figure 7). Thus, the restriction of cardiac filling was not only due to the pericardial effusion but also resulted from pericardial constriction (predominantly the visceral pericardium).

Sagristá-Sauleda et al⁷⁹ recently reported a consecutive series of >1000 patients with pericarditis, 218 of whom had cardiac tamponade and underwent pericardiocentesis. In 15 of these patients, the right atrial and right ventricular diastolic pressures remained elevated with a dip and plateau morphology after the pericardiocentesis, and thus they were considered to have effusive constrictive pericarditis. The most common cause was idiopathic pericarditis as well as malignancies and after radiation. One patient had tuberculous pericarditis. Three of the patients with idiopathic effusive constrictive pericarditis had subsequent resolution of their symptoms. Others required pericardiectomy, including removal of the visceral pericardium. Effusive constrictive

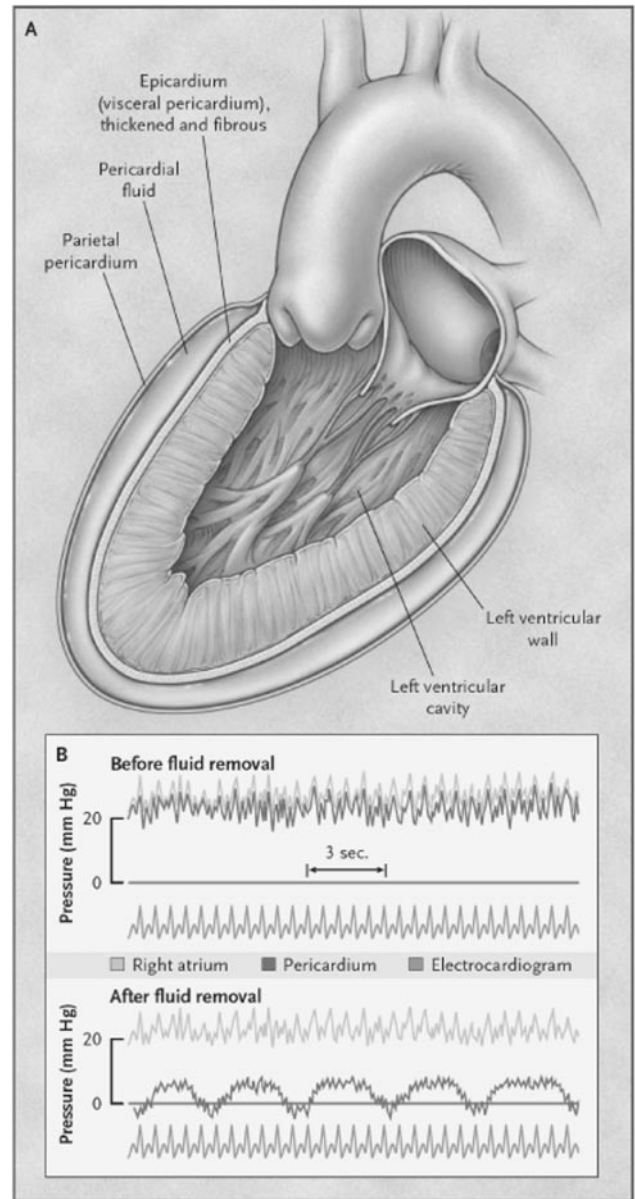


Figure 7. Effusive pericardial constriction. A, The presence of pericardial fluid causes tamponade, and a thickened visceral pericardium (epicardium) causes constriction. Pressure tracings (B) show marked and equal elevations of the pericardial and right atrial pressures typical of cardiac tamponade before the removal of fluid. After fluid removal, the pericardial pressure is normal (increasing and decreasing with respiration), but the right atrial pressure remains elevated, indicating the presence of pericardial constriction. Reproduced with permission from Hancock.⁸³ Copyright 2004, Massachusetts Medical Society.

pericarditis most likely represents an intermediate transition from acute pericarditis with pericardial effusion to pericardial constriction.⁸³

Summary

Acute pericarditis typically is a self-limited disease, usually idiopathic or of viral origin, that responds to treatment with NSAIDs. The recent COPE Trial indicates a better outcome if all patients receive a 3-month course of colchicine. The use of steroids to treat acute pericarditis should be avoided because

they increase the risk of recurrence. Cardiac tamponade is a life-threatening condition caused by a pressurized pericardial effusion. Doppler echocardiography plays a key role in its recognition, and echocardiogram-guided pericardiocentesis has become the treatment of choice in most instances. Pericardial constriction is a potentially treatable cause of chronic heart failure that must be distinguished from restrictive cardiomyopathy. This can be accomplished with a combination of Doppler echocardiography, Doppler tissue imaging, MRI, and cardiac catheterization. In effusive constrictive pericarditis, the cardiac compression is due to both a pressurized pericardial effusion and pericardial restriction. Pericardiocentesis converts the hemodynamics from tamponade to constriction.

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Disclosures

None.

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KEY WORDS: cardiac tamponade ■ pericarditis ■ pericardium