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Pericardial Disease: Etiology, Pathophysiology, Clinical Recognition, and Treatment

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General Considerations

Pericardial heart disease is relatively uncommon; therefore, evidence-based data derive only from guidelines published by the European Society of Cardiology (ESC)[1] and reports of large series from centers to which many patients with pericardial disease are referred.

Pericardial heart disease is much less common than heart disease, originating with primary disorders of the coronary arteries, the myocardium, or the cardiac valves, or hypertensive heart disease. On the other hand, the pericardium can become involved in a far greater number of systemic diseases than affect the myocardium, and furthermore, diseases that may affect both myocardium and pericardium almost always affect the latter more often than the former. In many disorders, for example, AIDS and myocardial infarction, pericardial involvement is often occult and therefore not detected unless specifically sought, usually by echocardiography. In other instances, the pericardium, because it may be the source of pain resembling myocardial ischemia, or dyspnea and edema resembling heart failure, may come to dominate the clinical picture of a widespread systemic disorder. Examples include the wrong diagnosis of hepatic cirrhosis when the true diagnosis is constrictive pericarditis, heart failure when the correct diagnosis is constrictive pericarditis, cardiomegaly when the patient really has a pericardial effusion, and pulmonary embolism or acute myocardial infarction when the patient really has acute pericarditis. Confusion between restrictive cardiomyopathy and constrictive pericarditis occurs in many patients who have one of these two disorders. To make matters worse, some patients, for example, those who have had prior therapeutic radiation, have both. Clinicians often miss or arrive at the diagnosis of pericardial disease too late.

We have not advanced to the point at which Sir William Osler's[2] statement no longer applies:

> Even with copious effusions, the onset and course may be so insidious that no suspicion of the true nature of the disease is aroused. . . . Probably no serious disease is so frequently overlooked by the practitioner. And postmortem experience shows how often pericarditis is not recognized, or goes on to resolution and adhesion without attracting notice.

Pericardial heart disease and pericardial disease present a number of highly distinctive clinical syndromes. Pericardial heart disease is impaired cardiac function secondary to pericardial pathology, whereas pericardial disease is disease limited to the pericardium and does not affect cardiac function. The major entities include pericardial effusion, cardiac tamponade, constrictive pericarditis, and acute fibrinous pericarditis including recurrent pericarditis. These clinical entities do not bear a strong relationship to etiology, since many forms of pericarditis or other pericardiopathy may be associated with effusion, and effusion of any cause may go on to cardiac tamponade. Furthermore, while progression to constrictive pericarditis is uncommon in some pericardial disorders, examples of constrictive pericarditis have been reported following pericardial disease of almost every known etiology.

Etiology

Idiopathic Pericardial Disease

In spite of complete clinical and laboratory investigation, many cases of pericardial disease remain idiopathic. It is generally believed that some 90% of cases of idiopathic acute pericarditis are in reality secondary to an undetected viral infection. The same consideration applies to a lesser percentage of cases with large pericardial effusion. In the instance of constrictive pericarditis, in which many of the cases unfortunately must still be labeled as idiopathic, a number are probably related to unrecognized prior tuberculosis or other infection, or to remote trauma. The syndrome of effusive-constrictive pericarditis is often associated with tuberculous pericarditis, neoplastic pericardial disease following mediastinal radiation, and in idiopathic and viral pericarditis.

Viral Infections

Infections constitute an important cause of acute pericarditis. Viral infection, for the most part, causes an illness indistinguishable from acute idiopathic pericarditis. The major offenders include Coxsackie A, Coxsackie B, and echovirus. Less common offenders are adenovirus, mumps virus, infectious mononucleosis, hepatitis B, and varicella. Influenza A is an important pathogen in the acute pericarditis of infants and children. Lymphogranuloma venereum and *Mycoplasma pneumoniae* have been reported as causes of acute pericarditis.

Of particular importance in the present era is pericarditis associated with AIDS.[3] These pericarditides are usually caused by commensal infection with such organisms as avian tubercle bacillus and *Mycobacterium tuberculosis*, but hybridization studies have now proven that the AIDS virus itself can infect the pericardium.

Bacterial Infections

Bacterial infections are an important cause of purulent pericarditis.[4] As with so many other bacterial infections, the clinical spectrum has changed as a consequence of the widespread use of potent antibiotics and to a lesser extent of immunosuppressive agents. Thus, *Pneumococcus* and *Streptococcus*, which in the past were frequent causes of acute pericarditis often ending fatally, are now less common, having been replaced to some extent by such organisms as coagulase-positive *Staphylococcus*,[5] which increasingly are resistant to antibiotics. Pneumococcal pericarditis secondary to empyema is still however an important cause of purulent pericarditis, and, due, at least in part, to late recognition, it continues to have a high mortality rate. Other bacterial infections include meningococcus, *Haemophilus influenzae*, and *Legionella*. Pericarditis can occur in the course of psittacosis. Even salmonella infection can involve the pericardium. Tuberculosis is on the rise, especially in developing countries,[6] and is an important cause of pericardial disease.[7]

Other Infections

Pericarditis may occur as a result of fungal infection, notably histoplasmosis, blastomycosis, coccidioidomycosis, and *Candida albicans*. Aspergillosis and rickettsial pericarditis have now been well described. The pericardium may be infected in toxoplasmosis, amebiasis, mycoplasma, nocardia, actinomycosis, echinococcosis, and Lyme disease.

Trauma

A very important cause of pericardial disease is trauma. Examples include blunt[8] and sharp chest trauma as well as a number of iatrogenic causes, including surgical pericardiotomy,[9] transseptal cardiac catheterization, intramyocardial contrast injection, perforation from a pacing[10] or central venous catheter,[11,12] and implantation of epicardial and defibrillating devices, and after electrical cardioversion.[13]

Radiation

An important example of noninfectious acute and chronic inflammation is radiation.[14,15]

Neoplasia

The pericardium is frequently involved in neoplastic disease.[16–19] Primary tumors are uncommon, but the most common primary tumor is mesothelioma. Even less common are teratoma, fibroma, lipoma, angioma, and leiomyofibroma. Metastatic neoplasm involving the pericardium is an important and quite frequent problem encountered in the practice of internal medicine. The major primary sources are carcinoma of the lung and carcinoma of the breast. Also of extreme importance are lymphoma and leukemia.

Metabolic Disorders

Of the metabolic causes of pericardial disease, pericarditis associated with chronic renal disease[20,21] is the most common. In the current era, this means the pericarditis associated with chronic dialysis, but a few cases associated with severe uremia are still encountered. Effusive pericarditis in patients with myxedema is a less frequent metabolic cause of pericarditis.

Collagen Vascular and Immune Disorders

The autoimmune disorders quite frequently involve the pericardium.[22,23] Acute pericarditis is a feature of acute rheumatic pancarditis. Pericarditis with or without effusion, and sometimes going on to constrictive pericarditis, may be found in lupus erythematosus, rheumatoid arthritis, scleroderma, mixed connective tissue disease, Wegener's granulomatosis, polyarteritis nodosa, dermatomyositis, and vasculitis.

Myocardial Infarction

Pericarditis, with or without effusion, may occur in the course of acute myocardial infarction,[24–26] either in the form of acute contiguous pericarditis or delayed pericardial effusion, that is, Dressler's syndrome, which, along with the postpericardiotomy syndrome and traumatic pericardial disease, is an example of the postpericardial injury syndrome.[27,28]

Pericardial effusion associated with myocardial infarction is discussed in the section on pericardial effusion.

Drug-Induced Pericardial Disease

Anticoagulant drugs may cause or facilitate the appearance of pericarditis, usually hemorrhagic. Other drug-induced pericarditides can occur with the use of such agents as procainamide, hydralazine, methysergide, mesalamine, minoxidil, cromolyn, isoniazid, doxorubicin, and diphenylhydantoin. Pericarditis following penicillin administration is an allergic reaction. The wide availability of pharmacy services has greatly facilitated inquiry as to whether a particular drug is known to cause pericarditis.

Chylopericardium

Chylopericardium may be idiopathic[29] but more commonly is traumatic or arises as a complication of thoracic surgery[30] in which the thoracic duct or one of its tributaries is injured. Chylopericardium may complicate cardiac transplantation.[31] Chylopericardium should not be confused with cholesterol pericarditis, a complication of chronic pericarditis with or without effusion, in which cholesterol crystals are deposited in the pericardial tissue and fluid. In this condition, the fluid is not milky, but has exceedingly high cholesterol content.

Pericardial Effusion

Pericardial effusion may be small or large, hemodynamically benign or life threatening, transudative, exudative, sanguineous, or chylous. Pericardial effusion may develop from what in the classic literature, written before the era of echocardiography, was described as dry or fibrinous pericarditis. The clinician's approach to pericardial effusion should be a logical progression from recognition of its presence, to diagnosing the etiology and determining its hemodynamic significance, to appropriate treatment.

Recognition of Pericardial Effusion

In a number of clinical circumstances pericardial effusion must first be suspected, after which its presence or absence must be definitely established. Pericardial effusion is suspected when a patient has one of the diseases that may be associated with pericardial involvement or when a finding, such as the appearance of a pericardial friction rub or unexpected radiographic cardiomegaly, alerts the physician to the possibility of a pericardial effusion. In some instances, the patient is known or found to have a disease that can affect the pericardium, and a search for pericardial involvement is instituted. AIDS is a classic example.[32] In other cases, the patient is found to have evidence of pericarditis, and the attending systemic disease is discovered during the course of a search for the etiology of pericarditis. Usually, once pericardial effusion is suspected, its presence is definitively documented by echocardiography, which unquestionably is the most common means of establishing the presence of a pericardial effusion.[33]

Physical Examination

Older textbooks emphasized physical findings, such as the ability to percuss cardiac dullness beyond the cardiac apex and dullness in Ewing's triangle, but these signs are so unreliable and so seldom sought by today's clinicians as to be virtually worthless.

Laboratory Examination

Chest Radiography

The unexpected development of cardiomegaly on the chest radiogram of a patient in whom prior chest radiograms showed a normal sized heart can be strong evidence pointing to the probability of a pericardial effusion, especially if the heart is somewhat flask-shaped and if the lung fields are clearer than one would have anticipated with cardiomegaly owing to heart failure. The radiographic findings in severe heart failure complicated by tricuspid regurgitation may be similar, because blood that would have congested the lungs regurgitates into the systemic circulation.

In a minority of cases the lucency created by subepicardial fat separates the cardiac from the pericardial density, thereby betraying the true nature of apparent cardiomegaly.[34]

Scintigraphy

When the heart is imaged, for instance, for a radionuclide ventriculogram, the scintigram shows a clear zone of pericardial effusion, separating the radioactivity in the heart from that in the liver.

Echocardiography

Echocardiography is, without doubt, the best tool for establishing the presence of pericardial effusion. Not only can the presence or absence of pericardial effusion be established with remarkable certainty[33] (Fig. 68.1), but, in addition, one can make a reliable estimate as to whether the effusion is trivial, small, medium, large, or massive. For clinical purposes, more precise quantification is not needed. Clinicians use the width of the echo-free space in diastole as a critical measure of its accessibility for pericardiocentesis, as follows: small, up to 1 cm; moderate, 1.1 to 1.9 cm; large, 2 cm or larger. Most pericardial effusions surround the heart, but echocardiography may show that the pericardial effusion is localized. Localized pericardial effusion is particularly common following cardiac surgical operations. When pericardial effusion begins to organize with the deposition of fibrin, this change is often recognizable by the appearance of opacities within the pericardial fluid.[35] Smaller pericardial effusions may not be visible behind the left atrium; the large effusions are well seen here as they are around the rest of the heart.

Pericardial effusion is imaged as an echo-lucent region surrounding the heart separating the echo dense epicardium from the echo dense mediastinal structures. With a particularly large pericardial effusion, the heart demonstrates a rocking or pendular motion within the motionless pericardial space.[36] This finding appears to be more common with malignant pericardial effusion and has also been associated with cardiac tamponade. On the electrocardiogram, this pendular motion may be reflected electrocardiographically as electrical alternans.

The extent of the echocardiographic or echo Doppler examination is sometimes tailored to the clinical need. In some patients, a brief examination to document whether or not pericardial effusion is present and roughly in what amount may be all that is required. In others, as for example,

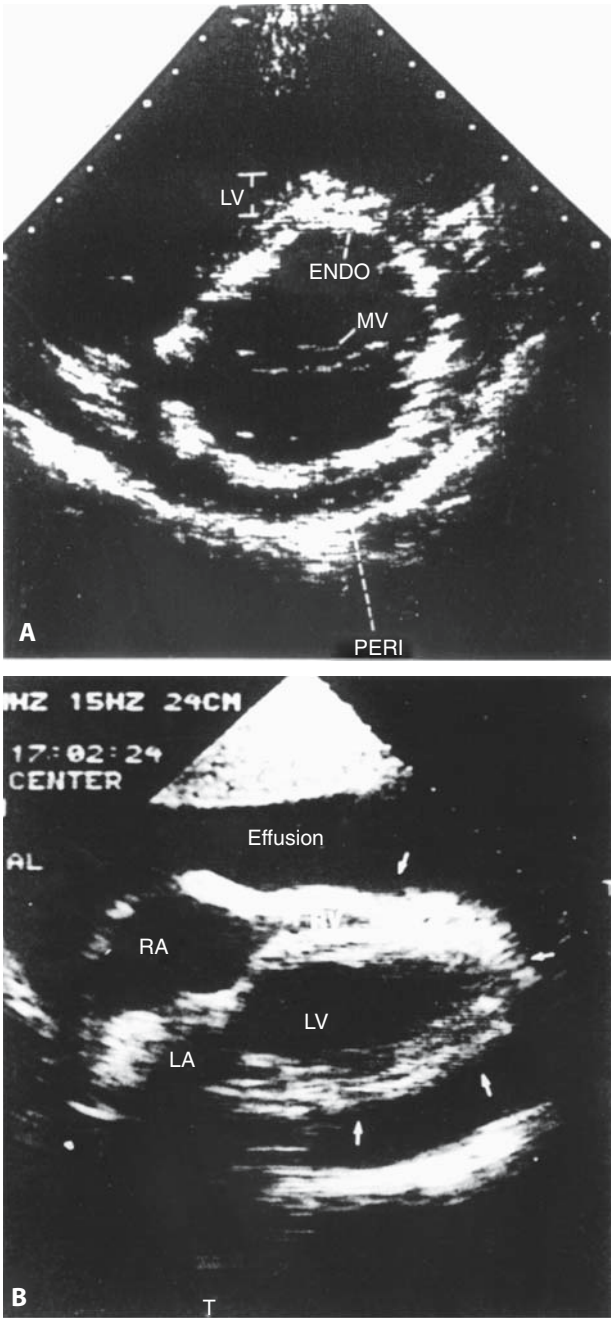

FIGURE 68.1. Echocardiogram of a moderate to large pericardial effusion. (A) Short axis. ENDO, endocardium; MV, mitral valve; PERI, pericardium. (B) Large pericardial effusion, subcostal view. Effusion is present behind the compressed right ventricle (RV) and the left atrium (LA). LV, left ventricle. (C) Massive pericardial effusion, four chamber view.

when the diagnosis of cardiac tamponade is suspected, a comprehensive echo Doppler examination should be done and should include imaging of the inferior vena cava and hepatic veins, which are distended and, when the venous pressure is greatly elevated, fail to show the decrease in dimension during inspiration or with a sniff.

In uncomplicated pericardial effusion, the examination documents the presence and extent of pericardial effusion, and quickly determines that all cardiac chambers are of normal size and exhibit normal systolic and, in the absence of tamponade, diastolic function. However, if unrelated heart disease coexists, it is readily identified.

Echocardiography may demonstrate clinically unsuspected pericardial effusion. Serial echocardiography in pregnant women has shown that a benign pericardial effusion is not uncommon in normal pregnancy.[37] Likewise, serial echocardiography after acute myocardial infarction will reveal pericardial effusion in a number of patients without pericardial friction rub or other evidence of pericarditis. In patients with AIDS, pericardial effusion can be found even in patients with no cardiovascular complaints and also as a further complication in those who develop dilated heart failure. At autopsy, congestive heart failure is considered the leading cause of pericardial effusion, but clinically this finding is distinctly uncommon. Echocardiography is thus an essential tool for detecting, describing, sizing, and evaluating the pathophysiology of pericardial effusion and therefore the guidelines issued jointly by the American Heart Association

(AHA), American College of Cardiology (ACC), and American Society of Echocardiography (ASE) include echocardiography for pericardial effusion.[38]

Pericardioscopy

Pericardioscopy with epicardial biopsy is limited to a few centers where there is a special interest in the technique. Both rigid instruments and fiberoptic instruments have been employed, the former in the operating room.

Etiology

All the causes of pericarditis listed earlier under the etiology of pericarditis may cause pericardial effusion. In the practice of internal medicine, the commoner causes are bronchogenic carcinoma, mammary carcinoma, lymphoma, idiopathic pericarditis, dialysis-related pericarditis, and the pericarditis of collagen vascular disease. The number of cases attributable to AIDS continues to grow.[39] In the setting of the emergency room, common causes include sharp trauma, such as by bullets and sharp instruments,[40] and blunt trauma, which is often inflicted by a car's steering wheel in the course of a motor vehicle accident. Rupture of an aortic aneurysm or dissecting hematoma of the aorta into the pericardial space is often first encountered in the emergency room. Rupture of the myocardial infarction is more likely to be encountered in the coronary care unit since this event usually occurs around the third day after acute infarction. These massive hemorrhages into the pericardium are potent causes of cardiac tamponade.

In surgical practice, cardiac tamponade is an ever-present danger following cardiac operation. This complication, reviewed in detail elsewhere,[41] usually occurs when the patient is still in the surgical intensive care unit or even in the recovery room, but can be delayed and not develop until after the patient has been discharged to a regular surgical ward or even has been discharged home.[42] A high index of suspicion that cardiac tamponade may be present is mandatory in any postoperative cardiac patient showing unexplained hemodynamic compromise.

When the commoner causes of pericardial effusion have been ruled out, a detailed history and extensive physical examination, the latter often repeated as the patient is observed over days or weeks, should be carried out in an endeavor to identify one of the systemic disorders that can be associated with pericardial disease. In most patients, routine blood chemistry, the erythrocyte sedimentation rate or C-reactive protein, viral titers, and a tuberculin skin test should be carried out. A screen of the plasma proteins, including rheumatoid factor and antinuclear antibodies, is done in many patients, but particularly in those with arthralgia or other evidence suggesting collagen vascular disease or vasculitis. Suggestive abnormality of the blood count should be investigated for the possibility of leukemia or lymphoma. In older patients, neoplasm, especially of the breast or lung, must be carefully considered, and it must be recalled that many other neoplasms can metastasize to the mediastinum, including the pericardium. Pericardial effusion is common in severe myxedema, but is much less common in mild hypothyroidism as commonly diagnosed in the present era.[43] No simple rule of thumb regarding the extent of investigation for neoplasm that is indicated can be provided.

Although, at first blush, the task of making a correct etiological diagnosis appears daunting, in many instances it is straightforward. Examples include a previously healthy young individual with a short history of malaise followed by chest pain and the discovery of a pericardial effusion; that individual probably has idiopathic or viral pericarditis. An elderly patient with an abnormal opacity in the lung field probably has malignant pericardial effusion, secondary to carcinoma of the lung. A young adult with splenomegaly, fever, and enlarged lymph nodes, especially mediastinal nodes and a pericardial effusion, is liable to have lymphoma. Dermatologic, muscular, and joint abnormalities may quickly lead to the diagnosis of rheumatoid or lupus pericardial disease.

Examination of Pericardial Fluid and Tissue

When exhaustive and appropriate laboratory evaluations have failed to disclose the etiology of pericardial effusion, the question often arises as to whether a diagnostic pericardial tap or pericardial biopsy should then be undertaken. It should be remembered that the so-called diagnostic pericardial tap or pericardiocentesis has a remarkably low diagnostic yield, whereas, paradoxically, the so-called therapeutic tap, usually done for the relief of cardiac tamponade, or because the clinician strongly suspects the presence of pus in the pericardium, has a high diagnostic yield.[44,45] These results were derived from large clinical series studied prospectively, not from formal clinical trials; nevertheless, they are evidence based. Thus, pericardiocentesis performed for the relief of tamponade often leads to the diagnosis of neoplastic pericardial effusion. Also, in the absence of a therapeutic need to drain the pericardium and when the clinician does not suspect pus in the pericardium, pericardiocentesis or surgical pericardial drainage can often be delayed or not performed. It is usually futile to seek the etiology of a pericardial effusion in a patient with normal venous pressure and no symptoms or signs of bacterial or purulent infection. However, some authorities recommend that a pericardial effusion persisting unchanged or increasing after 3 weeks warrants a diagnostic tap, and if this tap does not prove to be of diagnostic value, then a pericardial biopsy should be done.[44] The decision about whether or not to perform these low-yield and slightly hazardous procedures rests to some extent on whether the circumstances permit close long-term follow-up. If the patient can be observed at appropriate intervals with careful determination of the jugular pressure, chest x-ray, echocardiogram, and renewed efforts to uncover an underlying disorder, then invasive procedures can be delayed or put off altogether.

Chronic Effusive Pericarditis

Periodically, patients present with an idiopathic moderate or large pericardial effusion, normal jugular venous and systemic arterial blood pressures, and absence of pulsus paradoxus or echocardiographic signs of cardiac tamponade. Such patients are often asymptomatic. When an extensive

investigation fails to uncover the etiology for pericardial effusion, and effusion persists in varying amounts for months or years, the patient may be considered to have chronic idiopathic effusive pericarditis.[46] A number of authorities recommend pericardiectomy,[47] which certainly abolishes the chronic pericardial effusion, but whether the patient is rewarded by relief of previously unnoticed symptoms or by increased exercise tolerance is a moot point.

In a study of 28 patients with chronic idiopathic large pericardial effusion, identified in a cohort of 461 patients with pericardial effusion,[48] the pericardial pressure was slightly elevated. Right atrial pressure, however, remained higher than pericardial pressure, and the transmural right atrial pressure was slightly reduced, thus meeting the criteria for subclinical or latent tamponade.[49] The median duration of pericardial effusion was 3 years (range 6 months to 15 years). During follow-up, eight of these patients unexpectedly developed overt cardiac tamponade. All patients therefore underwent pericardiocentesis with prolonged catheter drainage, which restored hemodynamics to normal. If effusion recurs, pericardiocentesis should be repeated. Further recurrence is best treated by pericardiectomy, which is a safe operation under these circumstances. An alternative strategy for truly asymptomatic patients with documented good exercise tolerance is to defer intervention until symptoms or evidence of early tamponade appears. This approach is suitable only for patients whose circumstances and compliance permit regular follow-up and who can be educated regarding changes that should prompt unscheduled return visits.

Purulent pericarditis is discussed in more detail later (see Acute Pericarditis).

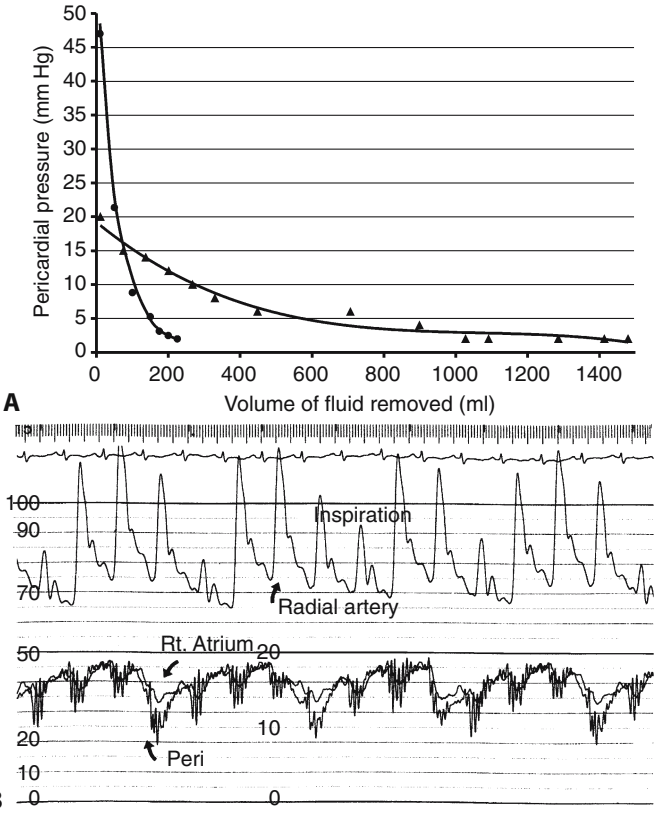

FIGURE 68.2. (A) Pericardial pressure-volume curves obtained during pericardiocentesis. The steep narrow curve on the left is from a patient with acute iatrogenic tamponade, the gentle curve on the right is from a patient with tamponade complicating acute pericarditis. (B) Pressures recorded in the acute case before pericardiocentesis. Pericardial pressure (Peri) was over 40 mm Hg, but the effusion was small. The radial artery tracing shows extreme pulsus paradoxus. Note *x* descent of right atrial pressure.

Cardiac Tamponade

Clinically, cardiac tamponade entails central venous, atrial, and ventricular diastolic pressures being governed not by their normal determinants but by the intrapericardial pressure. When intrapericardial pressure is measured in a patient following pericardiocentesis, or in an animal in which the physiologic pericardial effusion has not been aspirated, the pressure is a few millimeters of mercury less than the central venous and atrial pressures, being slightly subatmospheric. Even pericardial effusion considered to be lax increases pericardial pressure, but to a level that remains below right atrial pressure, defining latent tamponade.[49] When effusion or blood (or air) accumulates in sufficient quantity and at sufficient speed in the pericardial space, intrapericardial pressure rises, soon coming to equal the right atrial and central systemic venous pressures. At this stage, cardiac tamponade can be considered to have begun, but there may well be no symptoms or abnormal physical findings (preclinical tamponade). In such a case, the right atrial and intrapericardial pressures may have equilibrated at 4 or 5 mm Hg. If additional fluid accumulation occurs, intrapericardial pressure rises further, the degree of increase being highly dependent on the rate of further effusion or bleeding[50] (Fig. 68.2A). At this point, right atrial and pericardial pressures may have risen to some 8 to 10 mm Hg. The patient may continue to be asymptomatic, and the blood pressure and pulse remain normal. However, abnormal elevation of the jugular venous pressure is apparent by bedside examination. By this time, cardiomegaly is usually apparent on the chest radiogram unless the fluid collection was rapid.

When the intrapericardial pressure rises to exceed the preexisting left atrial and pulmonary wedge pressures, pericardial and right and left atrial pressures become equal to each other and to diastolic pressures in the ventricles and the pulmonary artery. Moderately severe classic cardiac tamponade is now present with the pressures equilibrated around 10 mm Hg. Before the full spectrum of cardiac tamponade came to be appreciated by clinicians, the diagnosis of cardiac tamponade was seldom if ever made before this stage had appeared.

In severe tamponade, the intrapericardial pressure rises to or exceeds approximately 15 mm Hg with a corresponding increase in the venous pressures on both sides of the circulation. Now, pulsus paradoxus is likely to appear and there may be a significant but not profound fall in systemic arterial pressure. Dyspnea and fatigue may appear, indicating some decrease in cardiac output. For the most severe cardiac tamponade, pericardial and cardiac diastolic pressures may increase to 20 mm Hg or even higher. When this degree of tamponade has developed, severe decompensation occurs

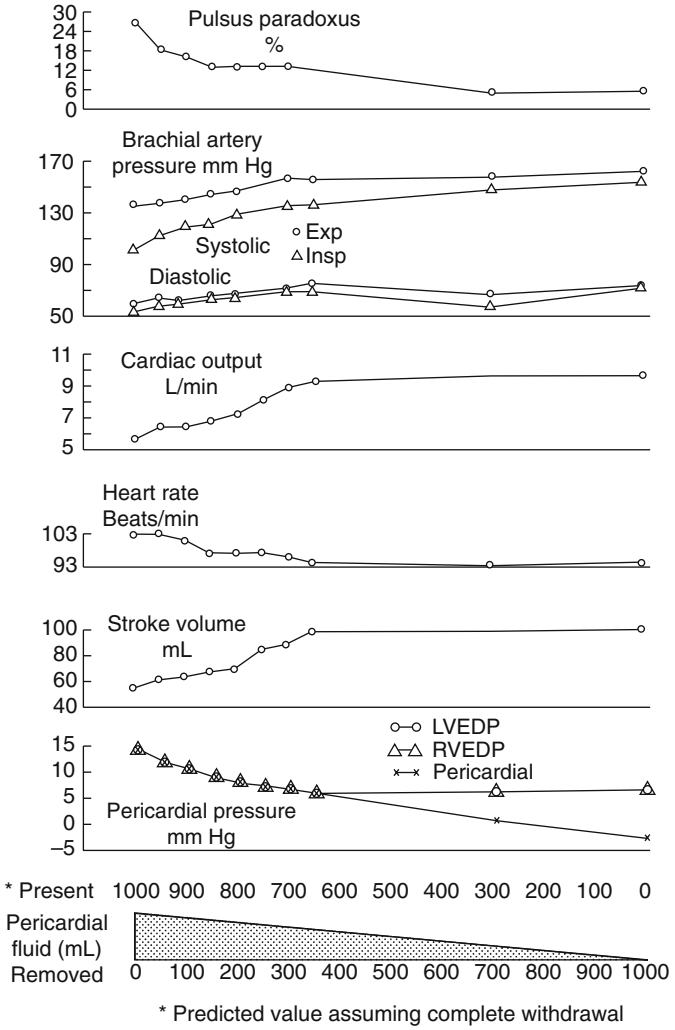

FIGURE 68.3. The severity spectrum of cardiac tamponade. Data from serial fluid aspirations from a patient with uremic tamponade. For details, see text. LVEDP, left ventricular end-diastolic pressure; RVEDP, right ventricular end-diastolic pressure.

with a profound drop in arterial pressure, a major fall in cardiac output with dyspnea, chest discomfort, and decreased renal function. The severity spectrum can be seen from data acquired during pericardiocentesis for a large effusion with severe tamponade[50] (Fig. 68.3).

Etiology

Cardiac tamponade may complicate pericardiopathy of diverse etiology, but the principal causes of cardiac tamponade are listed in Table 68.1.

TABLE 68.1. Etiology of cardiac tamponade

Acute viral or idiopathic pericarditis
Postpericardial injury: trauma, cardiac surgery, or intervention
Neoplastic pericardial disease
Uremia and dialysis or ultrafiltration
Prior thoracic radiation, therapeutic or accidental exposure
Nonviral infectious pericarditis

Clinical Recognition

Physical Examination

The key physical finding is the jugular pressure. When this pressure remains normal and there is no reason for profound hypovolemia, such as major hemorrhage, cardiac tamponade is either absent or of such a mild degree that no treatment for the condition per se is warranted. With more severe cardiac tamponade, bedside examination shows an increase in the jugular pressure. At the stage of moderate cardiac tamponade, the venous pressure may approximate 10 to 12 mm Hg but falls slightly in the normal manner during inspiration.

A skilled observer can also detect abnormality of the waveform of the jugular pulsations. In normal subjects, jugular pressure falls, first during ventricular ejection (*x* descent) and again during early rapid ventricular filling (*y* descent). During early rapid filling, the ventricles are actively dilating and sucking blood from the pulmonary veins and atria. The *x* and *y* descents correspond with two peaks in venous return. In cardiac tamponade, the *y* descent is attenuated in mild cases and absent in moderate or severe cases. Absence of the *y* descent is owing to reduced diastolic compliance caused by the abnormally high external constraint. Heart size decreases during ventricular ejection, which is more rapid than cardiac filling; therefore, ventricular ejection lowers intrapericardial pressure causing venous return to peak, as denoted by the *x* descent of venous pressure. Venous return in diastole does not peak, but continues evenly from early to late diastole. The *y* descent is therefore replaced by a continuous upward sloping segment. This pattern of venous return is reflected in the jugular pulse by a single nadir, the *x* descent, instead of the normal two nadirs, the *x* and *y* descents.

In mild cases, systemic arterial pressure, the peripheral pulses, and the heart rate remain normal. Once pericardial and right and left atrial pressures are elevated and have equalized, the phenomenon of pulsus paradoxus usually appears. Pulsus paradoxus can be defined as an abnormally large decrease in systemic arterial pressure during inspiration. In normal physiology, systemic blood pressure declines slightly, but this decline, while easily measured via a catheter in a systemic artery, is too small to be perceptible to clinical examination, especially during normal breathing. Arbitrarily, the maximum fall in arterial pressure with inspiration has been set at 10 mm Hg, although it is frequently considerably less than that. On clinical examination, pulsus paradoxus can be appreciated as a decreased force of the pulse synchronous with inspiration. In the most severe cases, the pulse disappears altogether during inspiration, hence the term *pulsus paradoxus*, the paradox being a regular heartbeat but an apparently irregular peripheral pulse. In the most severe cases, when hypotension has developed, pulsus paradoxus may be hard to detect in the radial pulse, but often is still apparent in the carotid and femoral pulses.

Pulsus paradoxus can be semiquantified by sphygmomanometry. It is observed that the first blood pressure sound can be heard when the patient is breathing out only to disappear when the patient breathes in. As the cuff is slowly deflated and the phase of respiration is monitored by the eye or with a hand on the chest, there comes a point when the

first blood pressure sound is audible throughout the respiratory cycle. The difference in systolic blood pressure between the level at which the first blood pressure sound can be heard only during expiration to the pressure when it can be heard all the time provides a clinical estimate of the degree of pulsus paradoxus.

Laboratory Examination

Echo-Doppler Cardiography and Pathophysiology

As we have seen, cardiac tamponade is a clinical syndrome that can be recognized and classified as to severity at the bedside. However, the echo-Doppler cardiographic features of cardiac tamponade are highly characteristic and therefore are also of great help in establishing the diagnosis and assessing its severity. In most cases, the diagnosis is first established on clinical grounds, but in others is first suspected after echocardiography. In complex cases, such as those with additional atrial septal defect, aortic regurgitation, heart failure, shock, or pulmonary hypertension, tamponade may be difficult to diagnose with confidence at the bedside. On the other hand, the echocardiographic signs of cardiac tamponade may be absent in specific cases, particularly when complicated by some other cardiac condition. Clinicians must consider both the clinical and echo-Doppler findings and weigh the relative importance of each in individual cases.

Over the years, a number of echocardiographic abnormalities have been described as evidence for cardiac tamponade[51]; of these, the three most important are right atrial compression,[52,53] right ventricular diastolic collapse[54] (Fig. 68.4), and increased respiratory variation in atrioventricular inflow velocity[55,56] (Fig. 68.5).

Whenever cardiac tamponade is a reasonable diagnostic possibility, the important information that must be determined is whether or not the patient has a pericardial effusion. If pericardial effusion (or, in very rare instances, tension pneumopericardium) is absent, the diagnosis of tamponade cannot be entertained. Unless tamponade is acute, the volume of effusion varies from several hundred milliliters to well over a liter, because the pericardium stretches and becomes more compliant. In the case of acute tamponade, the pericardial effusion amounts to only 200 or 300 mL, because the pericardium cannot be stretched far (Fig. 68.2A).

Under normal physiologic conditions, pericardial pressure is slightly below atmospheric, whereas right atrial pressure is a few millimeters of mercury above atmospheric, providing a significantly positive transmural atrial pressure. The free wall of the normally distended right atrium in the four-chamber and the subcostal views is convex. With cardiac tamponade, transmural pressure is reversed, becoming zero or even slightly negative so that the right atrial free wall becomes concave[57] (Fig. 68.6). When there is pulmonary hypertension, heart failure, or tricuspid valve disease, right atrial pressure may be substantially higher than pericardial pressure in spite of tamponade. Right atrial compression is therefore absent.

In early diastole, right ventricular diastolic pressure is at its lowest point. In cardiac tamponade, therefore, right ventricular diastolic pressure falls a little below intrapericardial pressure during early diastole. This transient negative right

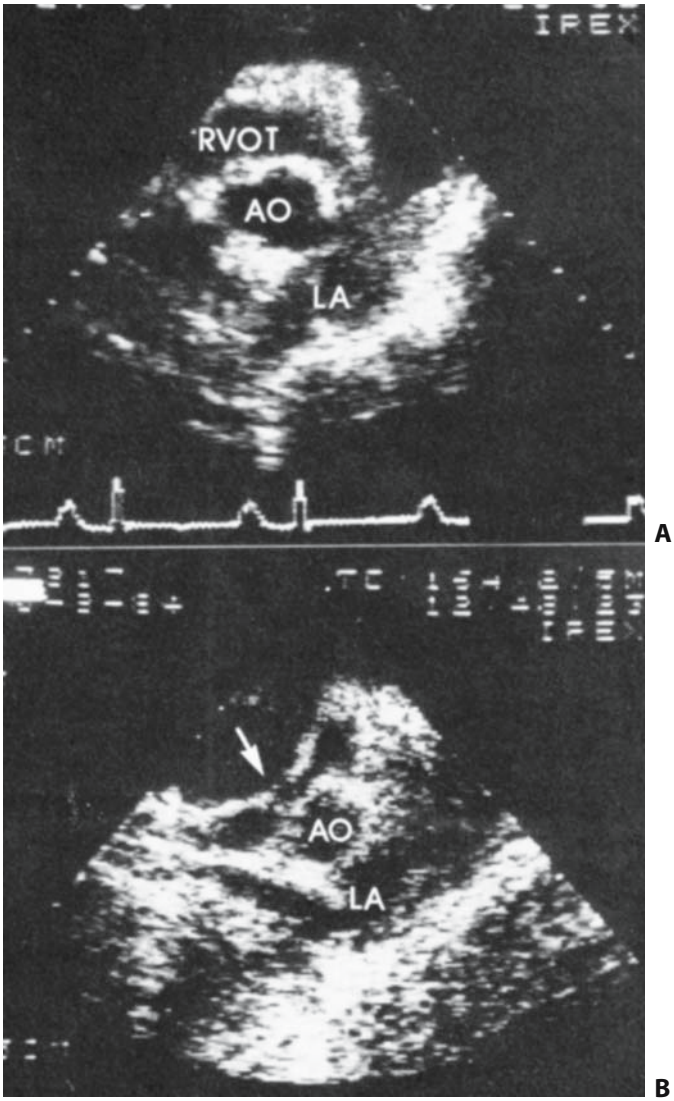

FIGURE 68.4. Subcostal view echocardiogram. (A) Normal appearance of the right ventricle. (B) Right ventricular early diastolic collapse.

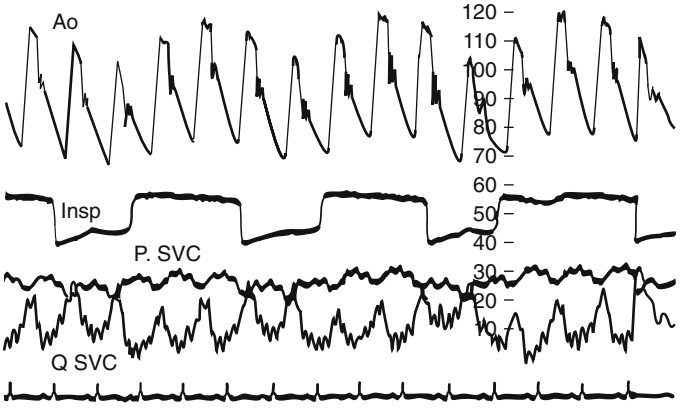

FIGURE 68.5. Cardiovascular pressures recorded from a patient with moderately severe cardiac tamponade. From above down, aorta (Ao) showing pulsus paradoxus without hypotension, respirometry, superior caval pressure (P SVC) and velocity (Q SVC), and electrocardiogram. Insp, inspiration.

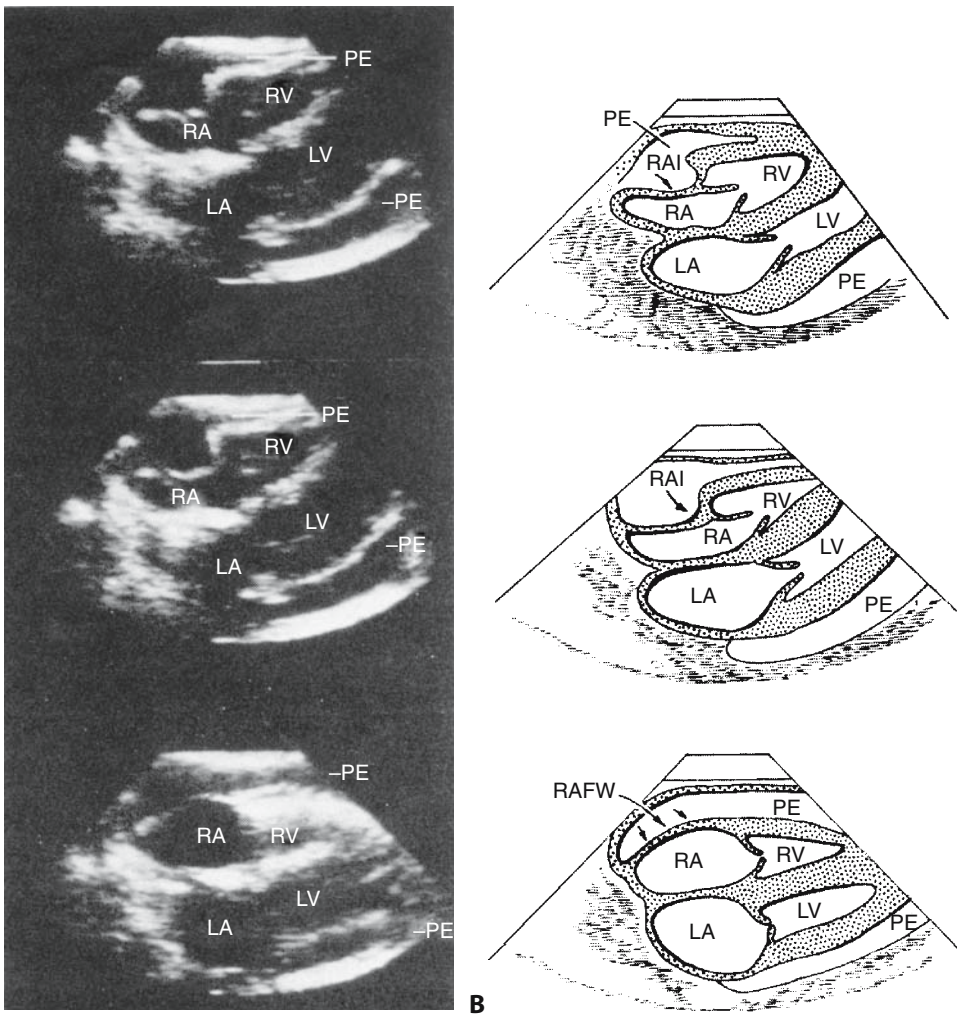

FIGURE 68.6. Right atrial compression, subcostal cross section. (A) Imaging. (B) Line drawing. Inversion of the right atrial free wall (RAI) begins at end-diastole (top) and continues through early systole (middle). By end-systole (bottom) the configuration of the free wall (RAFW) has normalized. PE, pericardial effusion.

ventricular transmural diastolic pressure causes the cavity of the right ventricle to collapses during early diastole[58] (Fig. 68.4). When cardiac tamponade is severe, heart rate is rapid and the reversed transmural right ventricular diastolic pressure persists longer into diastole.

The ability to assess right ventricular collapse requires skill and experience in echocardiography. When using real-time images it is optimal to employ a stop frame technique to be certain that the collapse indeed occurs during diastole. M-mode images are easier to interpret in this regard because diminishing right ventricular dimension is easily seen to occur when the mitral valve is open, the aortic valve is closed, or after the T wave of the electrocardiogram.

Right ventricular diastolic collapse has been observed in some patients without cardiac tamponade and has been correlated with hemodynamic alterations of tamponade.[58] Likewise, right ventricular diastolic collapse fails to appear when there is right ventricular failure or hypertrophy of any cause. Collapse of the right ventricular outflow tract during early diastole can be recognized by M-mode echocardiography and was indeed first described before the advent of the two-dimensional technique. Atrial compression occurs earlier than right ventricular diastolic collapse in the course of cardiac tamponade.[57] Right ventricular diastolic collapse occurs earlier when blood volume is decreased[59] and is associated with a significant decline in cardiac output, although it precedes marked hypotension and pulsus paradoxus.[60] Much less commonly, left atrial compression and even left ventricular diastolic collapse may be seen.[61,62]

That compression of the thin-walled right ventricle and atria and great veins is a frequent finding when tamponade is at least moderately severe implied that compression of these susceptible chambers, not direct compression of the left ventricle, is the major cause of hemodynamic impairment by tamponade. Left ventricular performance would then be limited by inadequate venous return, not directly by increased external restraint. This concept was verified in canine models of tamponade.[63–65]

A crucial feature of the pathophysiology of tamponade is that, because the pericardium is stretched to its limit, it becomes inextensible; therefore, increased volume of the cardiac chambers of one side of the heart can only take place by reducing the volume of the contralateral chambers by an equal amount. This phenomenon is known as ventricular interaction. In healthy subjects ventricular interaction is weak because the pericardium is sufficiently distensible to allow total cardiac volume to vary. On the other hand, in both cardiac tamponade and constrictive pericarditis it becomes

extremely strong. Inspiration increases right ventricular volume and reduces left, but total cardiac volume remains constant throughout the cardiac cycle. The reciprocal changes in ventricular volumes induce respiratory variation in the compliance of the two ventricles that in turn change their capacity to fill. The Doppler evidence for the last phenomenon is greatly exaggerated respiratory variation in transatrioventricular inflow velocities.[55] For the same reasons that account for exaggerated respiratory variation in ventricular filling, a highly exaggerated respiratory variation in the relative size of the two ventricles is a characteristic of cardiac tamponade, readily visualized on the echocardiogram.[66] Cardiac tamponade does not prevent the normal augmentation of systemic venous return during inspiration,[67] but now the increase in right ventricular volume is accommodated, not by distending the thin free wall of the right ventricle, but by leftward bulging of the interventricular septum, with the result that the dimension of the right ventricle increases while that of the left ventricle decreases. The clinical manifestation of increased ventricular interaction is pulsus paradoxus, a manifestation of reduced left ventricular stroke volume with inspiration[67] (Fig. 68.5). A second phenomenon that contributes to diminished left ventricular volume and therefore increased right ventricular volume is high pericardial pressure partly blocking transmission of decreased thoracic pressure to the left ventricle, thus decreasing its venous return.[55]

In normal subjects during quiet respiration, tricuspid peak inflow velocity increases by approximately 15% and mitral inflow velocity decreases by a maximum of 10%. With cardiac tamponade, however, the degree of respiratory variation is greatly exaggerated and becomes obvious on the Doppler tracings of ventricular inflow velocities.[55] Inspiration is characterized by a dramatic increase in tricuspid blood flow velocity and decrease in mitral blood flow velocity of 25% to 40%. These exaggerated respiratory variations of blood flow velocity appear early, certainly before the advent of pulsus paradoxus. It can be detected even in what is usually considered to be a hemodynamically insignificant pericardial effusion, the so-called lax pericardial effusion.[68,69]

The systemic congestion enlarges the inferior vena cava. When central venous pressure is in the range of 20 cm, the inferior vena cava does not diminish in diameter during inspiration.[70]

In some patients with tamponade and a very large, usually malignant, pericardial effusion, the whole heart swings dramatically in the large echo-free space. The rate of the swinging motion is often exactly half the heart rate. The occurrence of this phenomenon has been explained on hemodynamic grounds, but also has been modeled using nonlinear dynamics. While this phenomenon is most dramatically observed on two-dimensional echocardiograms, the changing position of the heart is also readily apparent on the M-mode echocardiogram. The large shift in the mechanical position of the heart influences its electrical axis, explaining the frequent association of electrical alternans with abnormal pendular motion of the heart in cardiac tamponade.[71,72]

Successful management is based on understanding, first, that cardiac compression can sometimes occur when tamponade is relatively mild and possibly can sometimes be managed conservatively. Second, false positive compression can occur as, for example, from a massive pleural effusion. Third, severe cardiac tamponade can exist in the absence of echocardiographic right heart compression or pulsus paradoxus, especially, but not exclusively, when there is preexisting heart disease and after cardiac surgery. Pericardiocentesis or open drainage should almost never be performed on a patient who is not in cardiorespiratory distress and lacks clinical findings of cardiac tamponade simply because an echocardiographic report, especially one issued by a physician who has not examined the patient, states that the study shows cardiac tamponade.

Electrocardiogram

Low voltage and sinus tachycardia are usual; the higher the pericardial pressure, the lower the voltage. If the case is acute, the changes of acute pericarditis may be present. Alternans of the P, QRS, and T is virtually pathognomonic of a large pericardial effusion.[72] However, this form of alternans, while highly specific, is not at all sensitive.[71]

Chest Radiogram

Some degree of enlargement of the cardiopericardial silhouette is to be expected in cardiac tamponade. Acute effusion or hemorrhage induces severe cardiac tamponade after a relatively small accumulation (Fig. 68.2). In such cases, cardiac enlargement is modest or not apparent. Cardiac tamponade, secondary to many disorders such as neoplasm and viral or tuberculous pericarditis, in which fluid accumulation is slower, allowing the pericardium time to stretch, is associated with the considerably larger cardiopericardial silhouette. Because the left and right sides of the heart are equally constrained, pulmonary congestion is less pronounced when an enlarged cardiopericardial silhouette is caused by tamponade rather than heart failure.

Cardiac Catheterization

The diagnosis of cardiac tamponade can usually be established without resort to cardiac catheterization. However, except in extraordinary emergencies, monitoring of at least the right atrial and systemic arterial pressures should be part of pericardiocentesis. In some cases, the procedure is limited to right heart catheterization performed in an intensive care unit, emergency department, or operating room. In others, standard cardiac catheterization is appropriate.

Right Heart Catheterization

When a diagnosis of cardiac tamponade is made or strongly suspected and drainage of the fluid is considered necessary, a minimum of three pressures should be recorded: right atrial, systemic arterial, and intrapericardial. Measurement of cardiac output is desirable but less important in most of the cases.

Commonly, a Swan-Ganz catheter is employed. Because equalization of filling pressure on the two sides of the heart is so crucial to the hemodynamic diagnosis of cardiac tamponade, one should not rely on sequential pressure measurements recorded as the catheter is pulled back from the pulmonary wedged position to the right atrium. Rather, advantage can be taken of the two lumina of the catheter to record right atrial and pulmonary wedge pressures simulta-

neously. Superior quality tracings are obtained when two multipurpose catheters are used. If the right atrial and pulmonary wedge pressures are separated by more than 5 mm Hg, provided the transducers have been properly calibrated and leveled to the same height, the diagnosis of uncomplicated cardiac tamponade comes into serious question. In cardiac tamponade, the right atrial pressure is elevated (Fig. 68.5), the magnitude of the elevation depending on the severity of cardiac tamponade except in the presence of severe hypovolemia, a situation that may arise in patients with dialysis-related cardiac tamponade. Close inspection of the tracing reveals that the pressure drops slightly during inspiration. The *y* descent is attenuated in mild cases and absent in moderate or severe cases. The only negative deflection is single descent—the *x* wave. When elevated, right atrial pressure is of other etiology, the pressure pulse is characterized by a dominant *y* descent. The pulmonary wedge pressure may vary more with respiration than does the right atrial pressure, for which reason equilibration between the two pressures may not be exact throughout the respiratory cycle.

In mild cardiac tamponade, the cardiac output is normal but falls progressively with increasing severity of cardiac tamponade (Fig. 68.3). Likewise, there may be little discernible abnormality in the tracing of systemic arterial pressure, but, with increasing severity of cardiac tamponade, the pressure begins to fall and pulsus paradoxus begins to make its appearance. When pulsus paradoxus is evaluated from a direct tracing of arterial pressure, it is observed that inspiration is accompanied not only by a decline in peak systolic pressure but also by a decline in pulse pressure (Figs. 68.2B and 68.5). The latter reflects diminished stroke volume during inspiration.

In the most severe cases, atrial pressures are elevated to the range of 20 mm Hg or higher. Blood gas analysis shows a progressive drop in mixed venous oxygen saturation from its normal value of around 75% to values in extreme cases, which may be as low as the teens. More commonly, mixed venous oxygen saturation around 50% to 60% is observed.

In many cases, pericardiocentesis is done in the cardiac catheterization laboratory, less often in the operating room. Increasingly, however, the procedure is carried out in an intensive care unit or echocardiography laboratory with echocardiographic rather than fluoroscopic monitoring.[73]

Formal Cardiac Catheterization

The cardiac catheterization laboratory is the ideal place in which to record hemodynamics in patients who have, or are suspected of having, cardiac tamponade, especially when coronary arteriography is also required. In most institutions, the best monitoring and recording systems and the personnel most adept at using them are in the cardiac catheterization laboratory.

There, procedure can be monitored either by echocardiography or fluoroscopy. Correct positioning of the needle or catheter within the pericardium is ascertained by visualizing bubble contrast on the echocardiogram (Fig. 68.7) or opaque contrast fluoroscopically. Recording of the appropriate pressures are shown in Figure 68.5.

Fluoroscopically, the lack of normal convexity of the right atrial border is easily observed in the anterior posterior projection and better so in a shallow right anterior oblique projection. If a multipurpose catheter is advanced into the right atrium and its tip is made to engage the endocardium, the tip is separated from the edge of the cardiac silhouette by the width of the pericardial effusion.

The pericardial pressure-volume relation is extremely steep at greatly elevated intrapericardial pressure[74] (Fig. 68.2A). Thus, after removal of approximately the first 100 mL of pericardial fluid, pericardial, right atrial, and pulmonary wedge pressures drop dramatically, systemic arterial pressure and pulse pressure rise, pulsus paradoxus and heart rate diminish, and cardiac output and stroke volume increase. Withdrawal of intrapericardial fluid progressively lessens the severity of cardiac tamponade. For as long as tamponade persists, the drop in right atrial and pulmonary wedge

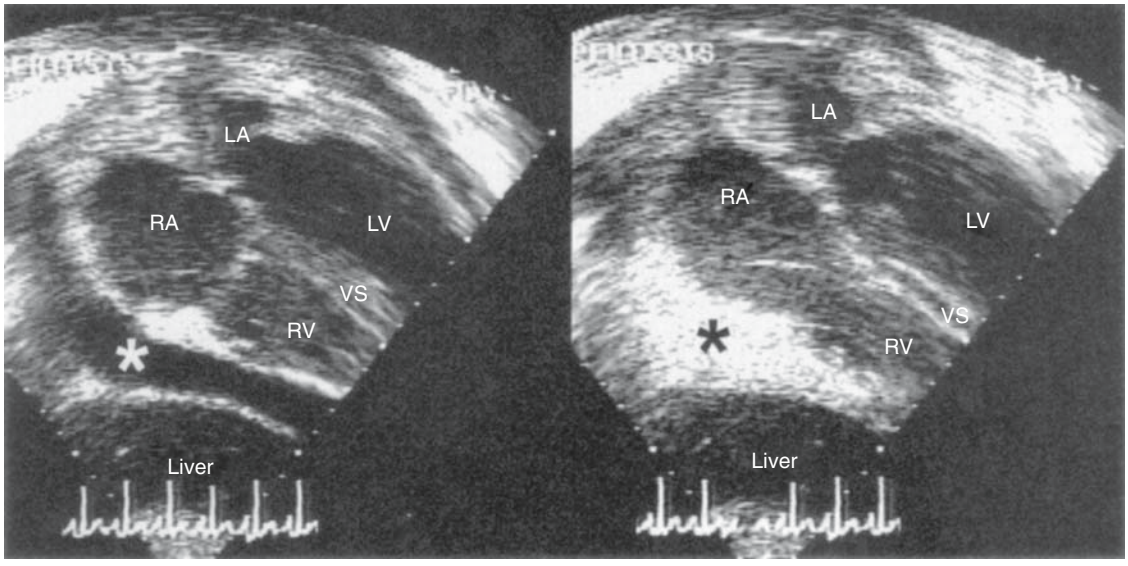

FIGURE 68.7. Echocardiographically monitored pericardiocentesis. (A) Before injection. (B) After injection. Bubble contrast opacifies the effusion (*).

pressures is identical to that in pericardial pressure with the result that all three pressures remain in equilibration.[75]

After pericardial pressure has been reduced to a level lower than the preexisting pulmonary wedge pressure, for example, 10 mm Hg, further pericardiocentesis has no further effect on pulmonary wedge pressure, but right atrial and pericardial pressures remain identical until the normal right atrial pressure is reached, at which point pericardial pressure declines below right atrial pressure (Fig. 68.3). The former becomes subatmospheric and the latter levels off around 5 mm Hg.[76]

The sequence of hemodynamic events described in the preceding paragraphs applies to uncomplicated cardiac tamponade in a patient without preexisting heart disease or constrictive pericarditis. When there is a preexisting increase in left ventricular end-diastolic and pulmonary wedge pressures, these pressures may be higher than intrapericardial and right atrial pressures measured before removal of a significant quantity of pericardial fluid has been accomplished. Pericardiocentesis would normalize pericardial and right atrial pressures, but pulmonary wedge pressure would remain elevated. In patients with right heart failure, pericardiocentesis may normalize the pericardial pressure, but right atrial pressure would remain elevated. Likewise, if there is effusive-constrictive pericarditis, a condition characterized by pericardial fluid under pressure combined with cardiac constriction by the visceral layer of the pericardium, right atrial and pulmonary wedge pressures would both remain elevated and equal to one another, even after pericardial pressure had been restored to normal[76] (see Effusive Constrictive Pericarditis in the section on Constrictive Pericarditis, below). If a patient has severe tricuspid regurgitation, large systolic waves may be present in the right atrial pressure but not in the pericardial pressure. Thus, following pericardiocentesis, if right atrial pressure remains abnormal, one needs to consider effusive constrictive pericarditis, right heart failure, and tricuspid valve disease. If the problem is effusive constrictive pericarditis, the characteristic hemodynamic findings are unmasked by pericardiocentesis. Suspected tricuspid valve disease and right ventricular dysfunction are best documented echocardiographically.

The dip-and-plateau phenomenon of ventricular diastolic pressure is a feature of constrictive pericarditis but does not occur in cardiac tamponade,[77] unless there is an element of constriction. In the majority of cases of cardiac tamponade, in the absence of preexisting heart disease, ventricular systolic function is normal or supranormal.[78] Increased ejection fraction and heart rate partially compensate for reduced end-diastolic ventricular volume.

Treatment

Pericardial pressure may be only 7 to 10 mm Hg, or may be 30 mm Hg or higher. Treatment, therefore, is not the same for all patients. While the usual treatment of cardiac tamponade is pericardiocentesis with the object of lowering pericardial pressure, there are exceptions. For instance, when a patient arrives at the emergency room in extremis after an automobile accident, and the physician suspects cardiac tamponade, pericardiocentesis may be necessary without waiting for diagnostic tests, including echocardiography, a prerequisite in all other cases. At the other end of the spectrum, a patient without clinical evidence of cardiovascular compromise, excepting a modest increase of jugular pressure, may not require evacuation of pericardial fluid, especially if the likely etiology is idiopathic or viral pericarditis that would be expected to respond to antiinflammatory treatment. Such patients, however, should be observed in case the hemodynamic situation deteriorates, indicating the need for pericardiocentesis. Between these extremes lie the majority of patients who have moderate or severe but not end-stage or decompensated cardiac tamponade. These patients require elective, planned removal of pericardial fluid via pericardiocentesis followed by catheter drainage or surgical pericardiotomy. Which of the techniques to select is largely a matter of local preference, the facilities available, and the training and expertise of the medical and surgical staff. Pericardiocentesis has the advantages of being less expensive and less invasive and allowing for optimal measurement of hemodynamic parameters. Surgical pericardiotomy has the advantages of being performed under direct vision and facilitating the procurement of adequate pericardial biopsy material. Pericardiotomy can also be accomplished by inflating a balloon in the pericardial cavity, and then pulling back until it tears the pericardium.[79] This method for pericardiectomy was most often used for malignant pericardial effusion, but now is no longer much favored.

Pericardiocentesis

Ideally, before pericardiocentesis is begun, right heart catheterization, including simultaneous measurement of pulmonary wedge and right atrial pressures, is carried out and right atrial pressure is monitored throughout the procedure. A reliable arterial pressure cannula should be placed before commencing pericardiocentesis. Before the decision to carry out pericardiocentesis, an echocardiogram will have been performed, but it is advantageous to have an echocardiograph available in the laboratory to make a final determination of the distribution of pericardial fluid when the patient is in the laboratory.[80] Often, it is desirable to have the thorax propped up, particularly if the subxiphoid approach is to be used. Although the subxiphoid approach is preferred by many, the final selection of where to place the needle when the effusion is not large can be based on where the echocardiogram shows the effusion to be closest to the skin. The procedure is best performed using a needle with a short bevel; long, large-bore needles with a long bevel increase the risk of a failed, traumatic procedure. As soon as it is apparent that the pericardial space has been entered, pericardial pressure along with pulmonary wedge and right atrial pressures should be measured before the removal of a substantial volume of pericardial fluid. If the fluid is deeply sanguineous, pressure should immediately be measured to ascertain that the needle does not lie within the cavity of the right ventricle. If a venous type of pressure is recorded, it may still be necessary to distinguish between right atrial and pericardial location since the two pressures will be identical. The hematocrit of blood in the right atrium and fluid from the pericardium can quickly be compared, but the quickest and easiest way to

distinguish between these two sites is to inject opaque or bubble contrast (Fig. 68.7) through the needle, provided that fluid or blood can be aspirated freely throughout the cardiac and respiratory cycles.

Constrictive Pericarditis

Constrictive pericarditis is another of the major compressive diseases of the heart. It can be subacute or chronic, or be only a transient phenomenon. When first described,[81] it was considered rare, but it is now known to be quite frequent.[82]

Pathophysiology

Constrictive pericarditis is a condition in which the pericardium, responding to prior insult, becomes scarred and stiff. Venous return to the heart and diastolic filling of the ventricles are therefore impeded by the increased external constraint. In the most severe cases, the heart is compressed so tightly that ventricular end-diastolic volume is reduced. Stroke volume then falls. In this example of heart failure with preserved ejection fraction, the myocardium is usually normal. In the majority of cases, systemic congestion is more profound than pulmonary congestion.

In most cases of both constrictive pericarditis and cardiac tamponade, the abnormal external constraint is global. In both disorders, therefore, one finds elevation and equalization of the left and right ventricular diastolic pressures and equilibration of pulmonary wedge, right atrial, and pulmonary arterial diastolic pressures. Elevated jugular pressure is a feature of both disorders and in both, pulmonary hypertension is commensurate with the elevated left ventricular diastolic pressure, and thus seldom exceeds 35 to 45 mm Hg. Both constrictive pericarditis and cardiac tamponade can be localized, creating atypical syndromes.

Greatly enhanced diastolic ventricular interaction is a critical component of the pathophysiology of cardiac tamponade and constrictive pericarditis. In the absence of the pericardium, ventricular interaction is present but weak. It is somewhat strengthened by a normal pericardium and greatly so by increased external constraint such as tamponade or constriction. When one side of the heart enlarges, the other must shrink. This interaction underlies the mechanism of pulsus paradoxus and the echo-Doppler and hemodynamic signs of tamponade and constriction. It has not been adequately explained why pulsus paradoxus is less frequent in constriction.

Pathophysiologic Characteristics Distinguishing Constrictive Pericarditis from Cardiac Tamponade

The most important feature distinguishing the pathophysiology of constrictive pericarditis from that of tamponade is how the atria and ventricles fill. In constrictive pericarditis, the velocity of early rapid filling is considerably faster than normal, but once early rapid filling has been completed, the ventricles attain their largest possible volume, having engaged the resisting pericardium, and therefore cannot increase in volume after the end of the early rapid filling period. The most likely explanation for this phenomenon is the combination of impeded venous return with a small rapidly recoiling ventricle. This pattern of ventricular filling confined to early diastole is reflected in the configuration of ventricular pressure in the two ventricles. The early rapid phase of filling is represented by a sharp dip in early diastolic pressure. The period of diastasis that constitutes the remainder of diastole is represented by an elevated plateau of pressure. In the normal ventricle, the *y* descent is smaller and is followed, after diastasis, by late ventricular filling, during which pressure rises steadily until the origin of the A wave. The contour of ventricular diastolic pressure in constrictive pericarditis is known as the dip and plateau, or the square root sign[83] (Fig. 68.8).

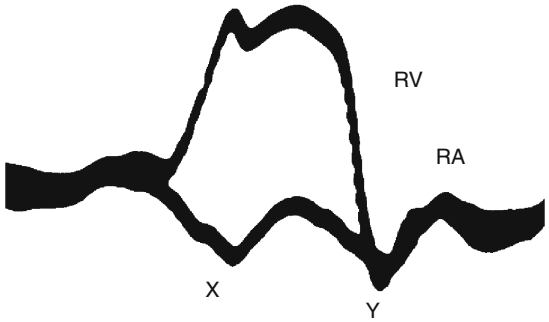

FIGURE 68.8. Right atrial and ventricular pressures from a case of traumatic constrictive pericarditis. Note prominent *y* descent.

The pattern of ventricular filling and therefore diastolic pressure in cardiac tamponade is altogether different. Increased external restraint is present throughout the cardiac cycle and is not limited to the later two thirds of diastole. Ventricular filling, consequently, is pandiastolic, as reflected by diastolic pressure rising progressively and steeply from the beginning to the end of diastole (Fig. 68.9).

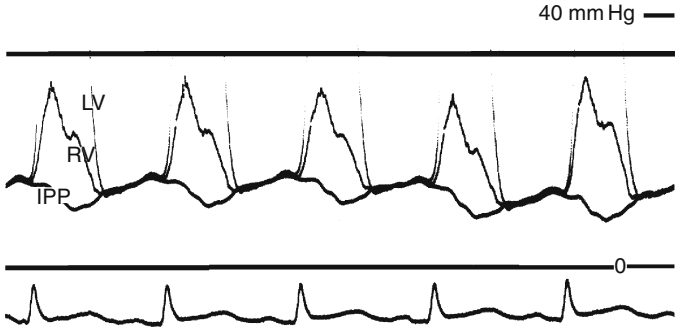

FIGURE 68.9. Cardiac tamponade. Pressure recordings from the left and right ventricles and the pericardium. Diastolic pressures equilibrate at 17 mm Hg.

The patterns of atrial filling and pressure consequently differ in important ways when constrictive pericarditis is compared with cardiac tamponade.[77] In constrictive pericarditis, a prominent *y* descent in atrial pressure corresponds with the early diastolic dip of ventricular diastolic pressure. In cardiac tamponade, although early rapid filling is more rapid than normal, increased external restraint is present and therefore venous return does not increase and the *y* descent is absent (Fig. 68.2B).

Although difficult to see clinically, the normal inspiratory decline in systemic venous pressure in cardiac tamponade is easily documented by intravascular and right atrial or superior vena caval pressure recordings. In constrictive pericarditis, however, this inspiratory decrease in systemic venous pressure is greatly attenuated or absent. The entire curve (mean pressure) varies little, if at all, during respiration, although the *y* descent becomes sharper and deeper with inspiration. The *x* descent is preserved in both constriction and tamponade. The older literature stressed paradoxical increase in jugular venous pressure, as observed at the bedside, as important in the diagnosis of constrictive pericarditis. First described by Kussmaul,[84] this sign still bears his name. However, Kussmaul's sign is rarely overt in constrictive pericarditis when the patient is breathing normally, but instead the pressure does not change (forme fruste). When the patient is asked to take slow deep breaths, the true Kussmaul sign can sometimes be elicited, but it is not diagnostic of constrictive pericarditis[85]; the respiratory behavior of the systemic venous pressure tracing is similar, if not identical, in restrictive cardiomyopathy or right heart failure of any cause, and tricuspid regurgitation.

Two mechanisms contribute to diminished left and increased right ventricular volume in tamponade. The first and most important is that right heart and pericardial pressures drop during inspiration, and therefore systemic venous return increases and the volume of the right heart enlarges by bowing the atrial and ventricular septa to the left. Consequently, right heart enlargement takes place much as in normal subjects, but does so at greater expense to the left heart, which becomes smaller. The second mechanism is that, because the pulmonary veins are wholly intrathoracic, the drop in pulmonary venous pressure equals that of intrathoracic pressure. The fall in intrathoracic pressure, however, is incompletely transmitted to the pericardium; hence, the drop in left ventricular pressure is less than that in the pulmonary veins of the left ventricle. Thus the pressure head for left ventricular filling is diminished and its volume decreases.[75] In constrictive pericarditis, although the inspiratory decline in intrathoracic pressure is freely transmitted to the great veins, it is not transmitted through the pericardial scar to either side of the heart. The results are that systemic venous return fails to increase with inspiration and that inspiration, by lowering the pressure head, becomes the only mechanism responsible for diminished left ventricular volume. The increase in right volume with inspiration occurs because the smaller left heart provides room in the pericardial space that remains constant throughout respiration.

A number of clinical observations fit the pathophysiology described above. Postextrasystolic beats fail to show an increased end-diastolic pressure.[86] The large *a* wave of right atrial pressure may exceed pulmonary arterial diastolic pressure, causing the pulmonary valve to open prematurely in presystole.[87] In the last trimester of pregnancy, cardiac output increases when the patient is turned into the left lateral decubitus position.[88] The proposed mechanism is a fall in arteriolar vascular resistance since, in constrictive pericarditis, cardiac output is not influenced by increases in central venous pressure.

Right atrial pressure is characteristically greatly elevated in severe cases, but atrial distention is characteristically limited compared with heart failure and restrictive cardiomyopathy. The stimulus to atrial natriuretic peptide secretion is therefore less, which contributes to severe salt and water retention.[89]

Etiology

Any cause of pericarditis, with the probable exception of rheumatic heart disease, may eventually result in constrictive pericarditis, but the commoner causes should always be considered first.[90] These are neoplastic pericardial disease, usually secondary to carcinoma of the breast or lung, and postradiation pericardiopathy, which must always be considered in patients who have received thoracic therapeutic radiation. Trauma is a significant etiologic factor requiring that any patient with constrictive pericarditis should be questioned carefully about prior thoracic trauma, which, in many cases, may have occurred some years earlier. Regrettably, infections may still be the cause of constrictive pericarditis, although in many instances this undesirable sequel to purulent pericarditis can be avoided by prompt and adequate medical or surgical treatment. Nevertheless, tuberculosis can still cause constrictive pericarditis.[91] Although tuberculous pericarditis is relatively uncommon in the United States and Western Europe, regrettably it is still rampant in many parts of the world[92] where it remains an important cause of effusive-constrictive pericarditis, which, if not adequately managed, results in chronic constrictive pericarditis. *H. influenzae* can cause constrictive pericarditis, especially in children, and is often subacute. The collagen vascular diseases often involve the pericardium, which may eventually develop constrictive pericarditis.[93] Rheumatoid arthritis is the commonest offender among this group and, again, this is a form of constrictive pericarditis that may be subacute rather than chronic.[94] Less frequently, constrictive pericarditis is drug-induced, the most notorious example being methysergide.[95] Constrictive pericarditis may be iatrogenic, most commonly following cardiac surgery.[96] Fortunately, this complication is far less common than one might have anticipated, considering the trauma to which the pericardium is exposed. It is thought to occur after 0.1% to 0.3% of cardiac operations. Nevertheless, in spite of its low prevalence, constrictive pericarditis must be included in the differential diagnosis of any patient who, after cardiac surgery, demonstrates signs suggestive of right heart failure without apparent cause, such as left heart failure, malfunction of a prosthesis, or severe ischemia. Evaluation may require imaging of the pericardium, as well as noninvasive or invasive hemodynamic studies. Cases have been reported after placing patch electrodes for implantable defibrillators[97] and after asbestos exposure.[98]

Clinical Features

History

A history of any condition known to be associated with pericarditis, particularly those mentioned in the preceding paragraph, is of great importance in establishing the diagnosis. The symptoms are edema, increased abdominal girth, increased weight, breathlessness, and fatigue. Right-sided congestion usually predominates over left. When the condition is chronic, these symptoms are progressive. Unfortunately, by the time many of the patients consult a physician, these complaints are long-standing and debilitating.

Clinical Examination

The findings on clinical examination clearly depend on the severity and chronicity. The most important physical finding, the critical nature of which cannot be overemphasized, is the abnormal jugular pressure. In severe cases, the jugular venous pressure is often elevated to as much as 20 cm H_2O or more. To appreciate elevated jugular pressure of this severity, the patient must be examined sitting upright or standing up, as the characteristic jugular pulsations are damped when the patient is examined in a semirecumbent posture. Frequently, the external jugular vein is distended and prominent, but it is still desirable to evaluate the pulsation of the internal jugular vein whenever possible. As described earlier (see Pathophysiology), the dominant abnormality is the rapid deep *y* descent. The correct timing of this event is ascertained by palpating the contralateral carotid artery, enabling the clinician to confirm that the inward movement of the jugular pulse is out of phase with the carotid pulse and is in fact the *y* descent. In less extreme cases, the jugular pressure may best be determined with the patient's thorax elevated to 30, 45, or 70 degrees from the horizontal, depending on the severity of increase in central venous pressure. Atrial fibrillation is an almost invariable sequel in chronic cases. In mild, moderate, and early cases, sinus rhythm is the rule.

In the more severe and chronic cases, edema is impressive and may extend to the thighs and, in males, may involve the scrotum, which may become huge. Also, in far advanced cases, ascites, often tense, can be diagnosed at the bedside by the usual maneuvers. In the most severe cases, dullness and decreased volume of breath sounds may indicate pleural effusion, which is common in long-standing constrictive pericarditis. Its origin is hemodynamic and does not imply, in most cases, associated pleural disease. In milder cases, signs of ascites and pleural effusion are usually absent and edema is less impressive and, in the mildest cases, even absent. In these mild cases, the jugular pressure is usually only about 7 or 8 cm H_2O, although the characteristic *y* descent is readily elicited.

One might anticipate that constrictive pericarditis may render the cardiac impulse impalpable. However, while this is sometimes true, often it is not. Likewise, the heart sounds are not necessarily diminished in amplitude. In some cases, there is retraction of the chest wall such that an inward motion accompanies the apex beat.

Examination of the abdomen is particularly important in constrictive pericarditis, for not only must the possibility of ascites be assessed, but also the liver must be carefully examined. In severe cases, it is enlarged and usually pulsates synchronously with the jugular pulse. In far advanced cases, cutaneous markers of hepatic insufficiency, such as spider angiomata and even jaundice, may be present.

There may be a loud third heart sound occurring about 100 ms after the second heart sound (pericardial knock), and thus at a time close to that of the third heart sound of heart failure and the opening snap of mitral stenosis.

Laboratory Findings

The plasma concentration of sodium, chloride, and potassium may be decreased, especially in patients receiving large doses of diuretic. The blood urea nitrogen (BUN) and serum creatinine concentrations are elevated and creatinine clearance is markedly diminished. Liver function tests are abnormal, showing increased levels of bilirubin and enzymes, secondary to hepatic congestion. Hepatic congestion is also largely responsible for decreased levels of serum albumin, although in severe cases protein-losing enteropathy may contribute to this phenomenon.[99] Additional laboratory abnormalities may be those associated with the underlying cause of constrictive pericarditis, such as collagen vascular disease or infection.

Electrocardiogram

The electrocardiogram characteristically shows no abnormality of ventricular depolarization, but nonspecific ST segment and T-wave changes are common.[100] Rarely, depolarization changes, such as bundle branch block, may occur and have been attributed to involvement of the epicardial coronary arteries in the scar process.[101] Atrial fibrillation is common in long-standing cases. Other arrhythmias are uncommon.

Chest Radiogram

One might anticipate that the heart would appear small on the chest radiogram. While this is often true, it is by no means a universal finding. In some cases, cardiac enlargement is preexisting from valvular or other disease of the heart. Sometimes cardiac size is difficult to evaluate because of pleural effusion and high diaphragm. In some cases, especially the more chronic and those due to tuberculosis, calcification of the pericardium is easily seen. Its presence is best evaluated in a lateral or oblique projection (Fig. 68.10). Calcification is also easily recognized on chest computed tomography (CT). Small areas of calcification may be seen in the pericardium of patients who have no evidence of pericarditis, constrictive or otherwise. The appearance of calcification in constrictive pericarditis is that of a complete or nearly complete ring. Calcification of the pericardium can be appreciated at cardiac fluoroscopy. Both ventricles are constricted; therefore, the lungs are not severely congested. Severe pulmonary hypertension does not develop.

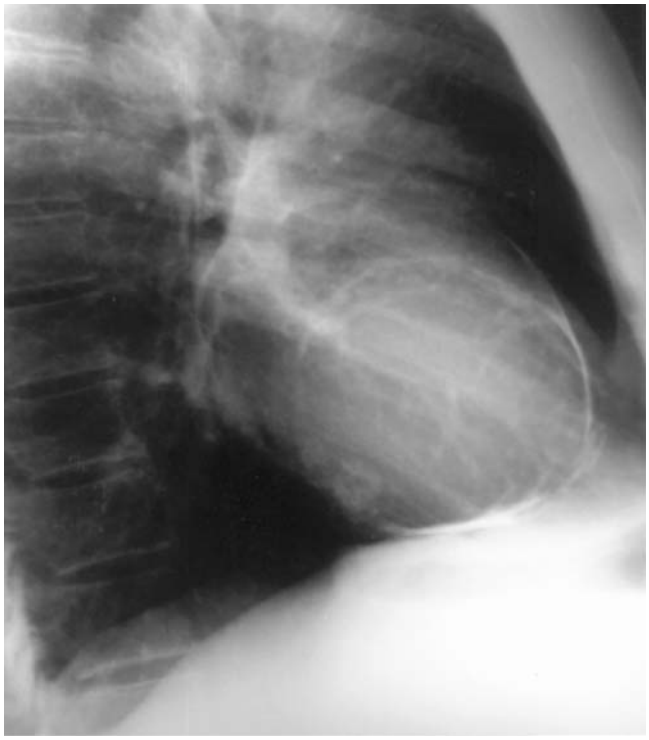

FIGURE 68.10. Constrictive pericarditis, right anterior oblique chest x ray. Note ring of calcium around the cardiac silhouette.

Echo-Doppler Cardiography

While the transthoracic echocardiogram is the best laboratory test for pericardial effusion, it has not proven to be particularly helpful in providing a diagnostic image of the pericardium. Images of the pericardium obtained by transesophageal echocardiography, however, are superb and allow accurate measurement of its thickness.[102] Some features, such as atrial notching, are easily visible on M-mode transthoracic images.[103] In very severe cases, the increased thickness and calcification of the pericardium are reasonably apparent on the M-mode and two-dimensional echocardiogram. Inspection of diastole shows that ventricular volume increases rapidly in early diastole but remains static during the rest of diastole. This abnormality does not differentiate between restrictive cardiomyopathy and constrictive pericarditis. Abnormal notching of the interventricular septum related to atrial systole has been described[104,105] but the finding, although fairly specific, is highly insensitive.

Other Imaging Modalities

The pericardium is imaged well by CT.[106,107] In normal subjects, it is either invisible or does not exceed 2 to 3 mm in thickness. Using newer machines, it is almost always visible. In many cases of constrictive pericarditis, the pericardial thickness is greatly increased, sometimes to as much as 1 cm or more (Fig. 68.11). Calcification can be identified when

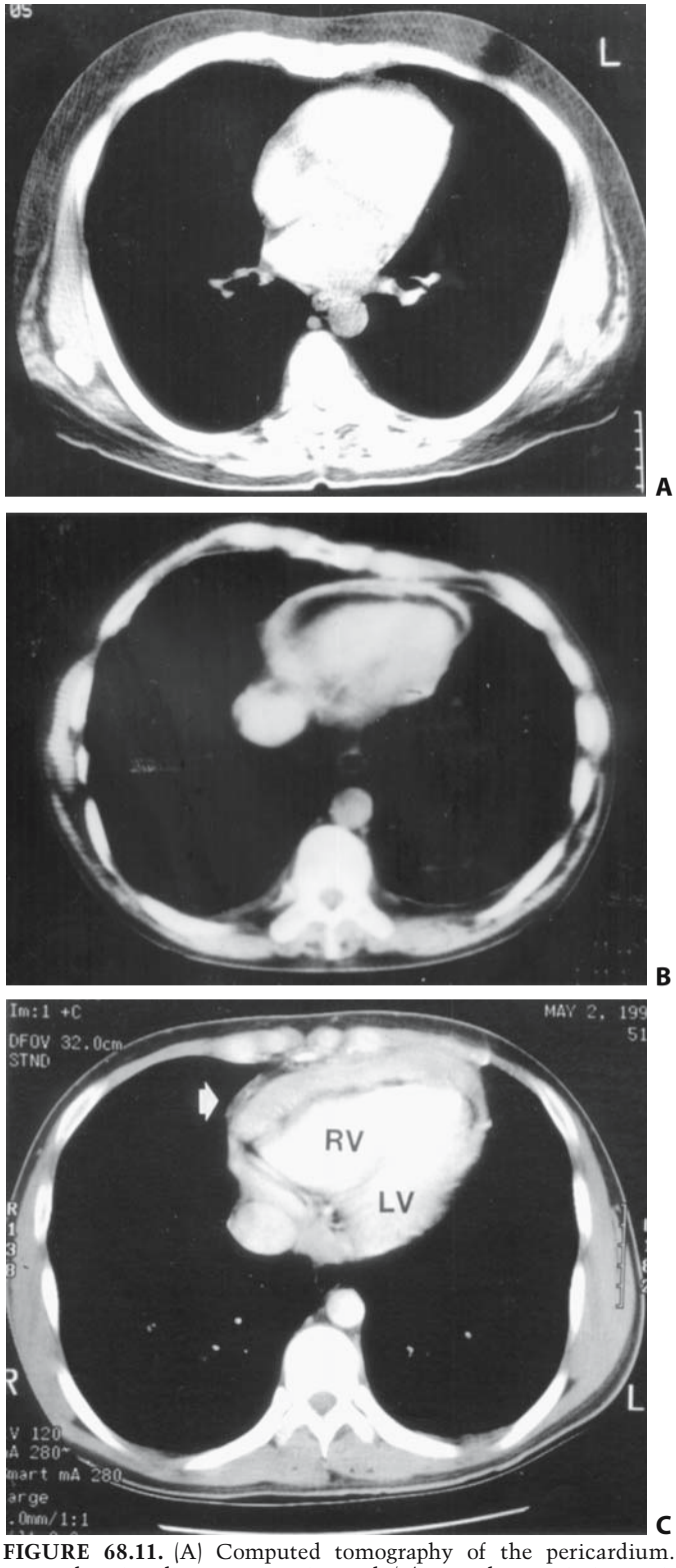

FIGURE 68.11. (A) Computed tomography of the pericardium. Normal pericardium was not imaged. (B) Fungal constrictive pericarditis. (C) Mesothelioma.

present. In some cases, the scarred visceral pericardium forms a very tight skin around the heart but is not increased in thickness. Thus, while detection of increased pericardial thickness is of great value in the diagnosis and in the differential diagnosis from restrictive cardiomyopathy, false negatives do occur.

Magnetic resonance imaging (MRI) is another technique that provides highly satisfactory images of the pericardium. An abnormally thickened pericardium is also defined by this technique as exceeding 3 mm.[108] Some authors consider MRI superior to CT because it better documents such anatomic features of constrictive pericarditis as tethering of the ventricular walls and their consequences, including the function of both ventricles and abnormal ventricular septal motion. Either one of these techniques is indicated for any case in which the diagnosis of constrictive pericarditis is reasonable.

Cardiac Catheterization

In many cases, the diagnosis of constrictive pericarditis can be reached on the basis of clinical and noninvasive laboratory studies. Nevertheless, two major uses for cardiac catheterization are to verify the diagnosis in doubtful cases and to evaluate for pericardiectomy. In the former case, endomyocardial biopsy performed during cardiac catheterization may be of critical value in the differential diagnosis,[109] and in the latter, assessment of the coronary arteries is important. The hemodynamic findings have been described in detail under pathophysiology. Additionally, the coronary arteries show lack of the normal accordion effect[110] and an abnormal profile of blood flow.[111] Furthermore, the vessels do not appear to lie on the surface of the cardiopericardial silhouette in any fluoroscopic projection. Constrictive pericarditis, like cardiac tamponade, increases external constraint globally. Equalization of pressures is therefore a feature of both. The technical details described for cardiac tamponade are equally important for constrictive pericarditis.

It is important to recall that pulmonary wedge pressure varies normally, indeed often in an exaggerated way during the respiratory cycle, whereas right atrial pressure varies little, if at all, with respiration. Therefore, equilibration between pulmonary wedge and right atrial pressures may not be present throughout the respiratory cycle, but is instead confined to inspiration.

Tight ventricular interaction and insulation of the cardiac chambers from variation of intrathoracic pressure during the respiratory cycle are two key mechanisms underlying the hemodynamics of constrictive pericarditis. These mechanisms explain why respiratory variation of peak systolic pressures in the two ventricles is out of phase[112] (maximal left ventricular pressure occurring when right ventricular pressure is minimal) and its importance. Systolic pressure increases in the right ventricle during inspiration because its filling has increased. Any tricuspid regurgitation that may be present increases in magnitude and velocity in the first beat after the onset of inspiration.[113] In restrictive cardiomyopathy, ventricular interaction is not increased above normal and the left ventricle is not insulated from respiratory fluctuations of thoracic pressure. The diastolic pressure gradient from pulmonary vein to left ventricle does not decline significantly during inspiration, the left and right ventricular peak systolic pressures are in phase, right ventricular systolic pressure declines during inspiration, and tricuspid regurgitation does not increase in velocity and magnitude in the first beat following inspiration.

Diagnosis

In clinical practice, confusion of constrictive pericarditis with cirrhosis of the liver is a considerably more common problem than confusion with heart disease. Common to both constrictive pericarditis and heart failure is massive edema and ascites, sometimes with a pleural effusion, and an enlarged liver with abnormal liver function tests. Not surprisingly, a significant number of such patients are referred to a gastroenterology department for further evaluation that often is extensive. When a patient is first seen with anasarca, the most important step is to evaluate the central venous pressure. Usually, this can be done by simple bedside examination. In the few cases where it cannot, the size and compressibility of the inferior vena cava by echocardiography can be substituted, or a catheter can be placed into the superior vena cava or right atrium, to establish the pressure. Both procedures are simple and cheap and the results are rewarding.

Differentiation from Restrictive Cardiomyopathy

Differentiation is vitally important in view of the different treatment needed for the two problems.[114,115] In some cases, this distinction is straightforward and easily made; in a minority, it is difficult to make the distinction without extensive laboratory investigation. It should also be recalled that some patients have a combination of myocardial disease and constrictive pericarditis. In these cases, the clinician's function is to assess the relative contributions of myocardial and pericardial pathology in order to predict the outcome of pericardiectomy. Radiation injury is an important cause of combined cardiomyopathy and constrictive pericarditis. Patients who have constrictive pericarditis as a complication of prior cardiac surgery may also have sustained intraoperative myocardial injury. Neoplasm more commonly affects the pericardium than the myocardium, but cases occur in which both tissues are involved in the neoplastic process.

Diastolic Dysfunction and Restrictive Cardiomyopathy

In recent years, considerable attention has been focused on diastolic dysfunction and diastolic heart failure, otherwise known as heart failure with preserved ejection fraction. Restrictive cardiomyopathy is numerically a small subset of diastolic dysfunction or heart failure, but is highly relevant to constrictive pericarditis. This condition has been defined in many different ways, but in connection with the differential diagnosis from constrictive pericarditis, restrictive cardiomyopathy can be defined as cardiomyopathy with diastolic

dysfunction in which the clinical picture and hemodynamic alterations simulate constrictive pericarditis. Thus, significant ventricular hypertrophy or dilatation and systolic dysfunction are absent or mild.

History

The history may be of great value. Prior acute pericarditis, tuberculosis, rheumatoid arthritis, radiation therapy malignancy, trauma, or other disease that frequently involves the pericardium strongly favors constrictive pericarditis. A history of a disease such as amyloidosis, hemochromatosis, or cardiac transplantation[116] that may involve the myocardium would point strongly to restrictive cardiomyopathy, although it is important to bear in mind that restrictive cardiomyopathy may be idiopathic.[114,115] Restrictive cardiomyopathy may occur following orthotropic cardiac transplantation in which it may be a transient phenomenon in the early weeks after the procedure, but uncommonly, may persist indefinitely.[116]

Physical Examination

The foregoing definition of restrictive cardiomyopathy requires that the physical findings closely simulate those of constrictive pericarditis. It stands to reason, therefore, that clinical examination is not helpful in the differential diagnosis. Both conditions are characterized by an elevated jugular pressure, the pulse displaying a prominent *y* descent. Edema, hepatomegaly, and other manifestations of systemic congestion may be present in both disorders. It is not possible to distinguish reliably between a pericardial knock and a third heart sound that may be present in restrictive cardiomyopathy. In both conditions, if the cardiac impulse is palpable, evidence of cardiac enlargement may be lacking but, as mentioned previously, the heart size is not necessarily normal in constrictive pericarditis, and, in restrictive cardiomyopathy, massive atrial enlargement may cause radiologic, if not clinical, cardiomegaly. Prominent systolic murmurs are unusual in either condition, and diastolic murmurs should not occur at all unless caused by an unrelated valvular lesion or localized constriction simulating stenotic valve disease.

Electrocardiogram

The electrocardiogram shows nonspecific ST-segment and T-wave changes. In more advanced cases, the P wave is wide in lead 2 and biphasic in lead V_1 and thus indistinguishable from the P mitrale of mitral stenosis. In the later stages, atrial fibrillation supervenes. As may be anticipated, depolarization changes are present in restrictive cardiomyopathy in addition to the repolarization changes that characterize constrictive pericarditis. The most common is left bundle branch block, although in some cases right bundle branch block or a nonspecific interventricular conduction defect is found. Other cases may show left ventricular hypertrophy with attendant repolarization abnormalities. Delayed atrial ventricular conduction may also be present. In addition to atrial fibrillation, other arrhythmias are common. They include ventricular extrasystoles from numerous sites, ventricular tachycardia, and an assortment of supraventricular tachycardias. In some cases, sinus rhythm or sinus tachycardia is dominant. Abnormal Q waves simulating myocardial infarction are found in the minority of cases, in spite of a normal coronary arteriogram. In a minority of cases of constrictive pericarditis, conduction and depolarization changes similar to those of myocardial disease may be encountered.[101] Abnormalities of depolarization or conduction very strongly favor myocardial over pericardial disease, but abnormalities confined to repolarization are equally likely in myocardial or pericardial disease and therefore are entirely unhelpful in their differential diagnosis.

Chest Radiogram

The chest radiographic finding most likely to be helpful in the differential diagnosis is calcification of the pericardium as may occur in the more chronic cases (Fig. 68.10). However, in many cases of severe constrictive pericarditis, calcification is absent. Minor degrees of calcification can be detected in the pericardium by fluoroscopy or, with greater sensitivity, by CT. These minor degrees of calcification are, for the most part, unrelated to constrictive pericarditis. Significant calcification of the pericardium is absent in restrictive cardiomyopathy. Thus, the finding of a dense ring of calcium on the chest radiogram virtually assures the diagnosis of constrictive pericarditis, but its absence is equally compatible with constrictive pericarditis or restrictive cardiomyopathy. Atrial enlargement is a feature of both constrictive pericarditis and restrictive cardiomyopathy, but is considerably more prominent in the latter. Obvious atriomegaly by plain chest radiography favors restrictive cardiomyopathy.

Imaging Modalities

A thick pericardium demonstrated by imaging is strong evidence for constrictive pericarditis. In some cases, the abnormal thickness of the pericardium can be appreciated by transthoracic echocardiography, which, in addition, may show increased echogenicity. The transthoracic echocardiogram does not detect increased thickness of the pericardium unless it is gross. The normal sliding of the heart on the pericardium, best seen in the subcostal views, is absent in constrictive pericarditis. Transesophageal,[102] tomographic,[103] and magnetic resonance[104] images are far superior. In some cases, those primarily involving the visceral pericardium, the appearance of the pericardium may be normal. Nonetheless, imaging the pericardium remains a useful tool because false-negative results are uncommon.[105]

Echo-Doppler Cardiography

Echo-Doppler cardiography is a noninvasive and reliable method to help distinguish constrictive pericarditis from restrictive cardiomyopathy.[106] The enhanced rate of ventricular relaxation shortens the deceleration time of the early rapid filling wave from its normal lower limit of 150 ms. In

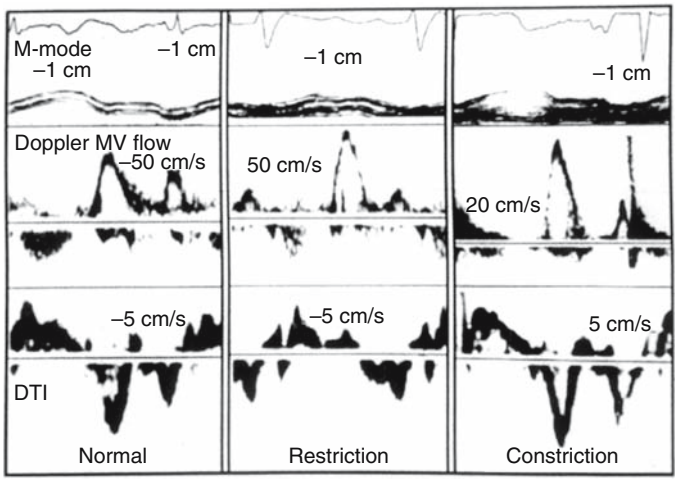

FIGURE 68.12. M-mode echocardiogram (top), transmitral velocity (middle) and tissue Doppler (bottom). Compared with normal, in constrictive pericarditis, transmitral and tissue velocities show more rapid filling and short deceleration time. In restriction, transmitral velocity is rapid, but tissue velocity is slow.

restrictive cardiomyopathy, but not in constrictive pericarditis, inspiration further abbreviates the shortened deceleration time of early rapid ventricular filling.[117,118] Tissue Doppler and M-mode color Doppler make it easy to determine whether a severely restrictive transmitral blood flow velocity profile represents constrictive pericarditis or restrictive cardiomyopathy.[119] Tissue Doppler measures the motion of myocardium. In constrictive pericarditis, the transmitral early rapid filling wave, E, is tall and narrow and, likewise, the early diastolic motion of the mitral annulus, E′, is also deep and narrow. In restrictive cardiomyopathy, the transmitral E wave is again tall and narrow but, because the mitral annular motion is severely restricted, E′ is diminutive[120,121] (Fig. 68.12). Color M-mode Doppler shows rapid transfer of blood from the mitral orifice to the apex, whereas this transfer is sluggish in restrictive cardiomyopathy (Fig. 68.13).

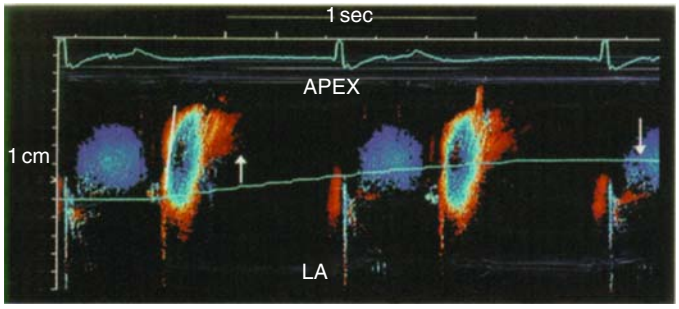

FIGURE 68.13. Color M-mode Doppler from left atrium toward the ventricular apex, comparing constrictive pericarditis (top) in which flow is rapid, and restrictive cardiomyopathy (bottom) in which it is slow. Isovolumic flow in restriction is rapid (yellow line).

In normal subjects breathing quietly, the E wave may decline up to 10% during inspiration, and the transtricuspid E wave may increase up to about 15% during inspiration. In patients with constrictive pericarditis, reciprocal variations in the rate of left and right ventricular filling related to the respiratory cycle are greatly exaggerated, and can be as much as 40%.[51,121] When constrictive pericarditis is strongly suspected, but exaggerated respiratory variation in transmitral and transtricuspid blood flow velocity is not detected, the patient can be reexamined in the head-up tilt position to bring out this Doppler sign. Ejection through the semilunar valves shows similar reciprocal variation. However, many investigators have found that pulsus paradoxus is unusual in constrictive pericarditis. In restrictive cardiomyopathy, respiratory variation in the rate of ventricular filling during early diastole does not exceed normal. It is not always possible to obtain a good record of pulmonary venous flow, but respiratory variation of pulmonary venous flow is a more sensitive sign than that of transmitral flow, and may even be present when the latter is absent.[121,122]

In both constrictive pericarditis and restrictive cardiomyopathy, diastolic inflow velocity exceeds systolic and shows increased respiratory variation. Retrograde flow during atrial systole may be found in restrictive cardiomyopathy and to a lesser extent in constrictive pericarditis. Satisfactory evaluation of pulmonary venous blood flow velocity may require transesophageal echocardiography. In both constrictive pericarditis and restrictive cardiomyopathy, the velocity profile of systemic venous return resembles that of pulmonary venous return.

Transient Constrictive Pericarditis

A subset of patients with constrictive pericarditis, amounting to 17% in the largest published series,[123] may experience spontaneous resolution of constriction or respond to medical therapy.

The most common cause of transient constrictive pericarditis is postpericardiotomy constriction in nine cases. Infection (viral, bacterial, or tuberculous), idiopathic, collagen vascular disease, trauma, and malignancy account for the remaining cases. Treatment with nonsteroidal antiinflammatory agents usually resolves the constriction, and some cases remit spontaneously.

The clinical course implies that the patients had acute inflammatory pericarditis and that constriction is a reversible sequel of inflammation. Patients with newly diagnosed constrictive pericarditis who are hemodynamically stable should be given a trial of conservative management before pericardiectomy is recommended.

Effusive Constrictive Pericarditis

Patients with this syndrome[76] have cardiac compression by tamponade enhanced by coexisting constrictive pericarditis. The clinical features, hemodynamics, and treatment have been discussed earlier (see Pericardiocentesis in the Cardiac Tamponade section). Figure 68.14 illustrates cardiac and pericardial pressures before and after pericardiocentesis.[124]

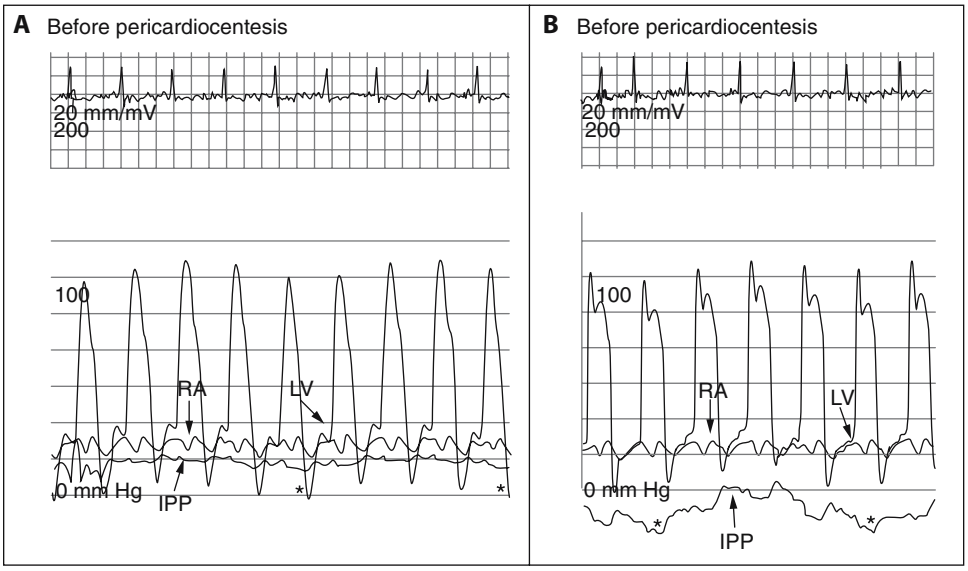

FIGURE 68.14. Hemodynamics of effusive constrictive pericarditis. For discussion, see text. IPP, intermittent positive pressure.

Acute Pericarditis

Etiology

Acute pericarditis is often idiopathic or secondary to viral infection. These are low-risk cases that respond promptly to antiinflammatory treatment.[125] Approximately 90% of the idiopathic cases, in reality, are secondary to viral infection, but this etiology can only be presumed unless acute and chronic viral titers establish that there has been recent infection by a virus, especially one that tends to infect the heart and pericardium. The discussion that follows focuses first on low-risk acute pericarditis. High-risk patients and their management are discussed thereafter. Whether a patient should be considered low or high risk can be rapidly established by history, electrocardiogram, chest x-ray, echocardiogram, and chemistry results in a same-day hospital setting. An outpatient clinic is appropriate for subsequent follow-up.[125]

Pathology

The pathology is acute inflammation. The pericardium is slightly thickened owing to edema. Acute fibrinous pericarditis owes its name to the widespread shaggy coat of fibrin noted at autopsy or surgical exploration. This feature is particularly noticeable in patients with hemodialysis-related acute pericarditis, which also tends to have a hemorrhagic appearance.

Symptoms

In the case of viral pericarditis, the specific findings of pericarditis are often preceded by a nonspecific influenza-like prodromal syndrome. The commonest major presenting complaint is chest pain that frequently has features resembling both myocardial ischemic pain and pleuritic pain. It is commonly retrosternal and somewhat crushing in nature, but is often aggravated by inspiration and coughing, and may be relieved by sitting up. It tends not to radiate in a manner characteristic of myocardial ischemic pain, but its crushing nature can lead to an initial misdiagnosis of acute myocardial infarction. A characteristic site of radiation is the left trapezius ridge. The chest pain is sometimes accompanied by dysphagia. As in pleurisy, respiration may be shallow and rapid, causing the patient to complain of shortness of breath. Additionally, symptoms of viremia and toxemia may also be present, as may symptoms of the underlying cause.

Clinical Examination

Clinical examination frequently shows a patient in varying degrees of acute distress with fever, tachycardia, sweating, and flushing. The pathognomonic physical finding is the pericardial friction rub. This abnormal auscultatory feature is commonly best heard along the middle to lower left sternal edge, or between the sternal edge and apex, or at the apex itself. However, it may be widespread and audible over the entire precordium. It has a superficial scratching character and seems to originate closer to the skin than do heart sounds and murmurs. It is usually fairly fine and high pitched, but in some cases, especially those associated with uremia, may be lower pitched and coarser, and may even be palpable. The friction rub may vary in distribution and intensity from time to time. In acute pericarditis following myocardial infarction, the rub is often inconstant and is not detected unless the patient is carefully auscultated on frequent occasions. The intensity and character of the pericardial friction rub are apt to change with patient posture and in many cases become louder during inspiration. When the murmur is heard only during inspiration, it is frequently referred to as a pleuropericardial rub. The rub is usually heard better using the diaphragm chest piece of the stethoscope. Firm pressure with the diaphragm over the chest facilitates recognition of the pericardial friction rub. The friction may obscure cardiac murmurs that may be present.

The classic pericardial friction rub has three components: atrial systolic, ventricular systolic, and diastole.[126] Sometimes only the systolic and diastolic components are present, in which case the clinician must be careful to differentiate it from a to-and-fro murmur, such as that of aortic regurgitation. Less commonly, the pericardial friction rub is confined to systole and must then be differentiated from various causes of systolic murmurs. Mediastinal air may simulate the pericardial friction rub, and in some thin patients with a hyperactive precordium an artifactual sound caused by the skin rubbing on the stethoscope's chest piece may be confused with a pericardial friction rub. A pericardial friction rub is almost routinely audible for the first several days following a cardiac operation. A large pericardial effusion does not prevent the development of a pericardial friction rub and is a common observation that suggests that the mechanism causing pericardial friction rubs is more complex than the rubbing of the epicardium against the parietal pericardium.

It is not difficult to distinguish between tachypnea as a sign or guarding against pain and dyspnea due to pulmonary congestion and low cardiac output.

Electrocardiogram

Electrocardiogram of acute pericarditis is characterized by diffuse elevation of the ST segment[127] (Fig. 68.15). Myocardial ischemia, unlike acute pericarditis, is not likely to cause elevation of the ST segment in leads 1, 2, 3, and aVF. The ST segment is usually depressed; however, it is elevated in aVR and V_1. In contrast to the pattern of evolving myocardial infarction, the T wave remains upright at the time that the ST segment is elevated. Depression of the PR segment is a specific but not sensitive sign of acute pericarditis. As the ST segment moves toward the baseline, the electrocardiogram may become normal before showing the T inversions of chronic pericarditis.[100]

Clinical Laboratory Findings

Elevation of the erythrocyte sedimentation rate, C-reactive protein, and leukocytosis, as expected in any acute viral infection, is usual. If acute pericarditis is a manifestation of a systemic disease, such as uremia, rheumatoid arthritis, or myocardial infarction, the laboratory data help determine the underlying cause of pericarditis. Mild elevation of the creatine kinase MB and troponins may be present when there is no other evidence of myocarditis. Elevation below the myocardial infarction threshold has no influence on prognosis or outcome, but persisting elevation suggests clinical myocarditis.[128] Some cases of acute pericarditis are indeed a manifestation of acute myopericarditis.

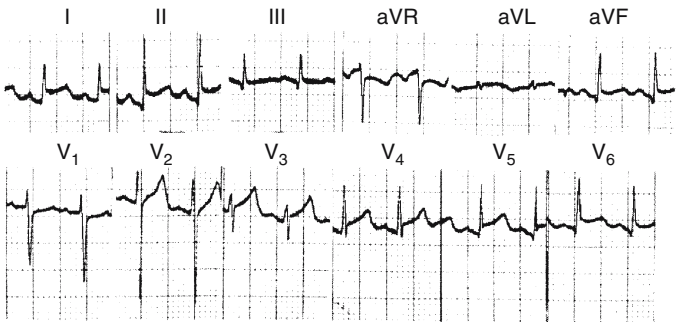

FIGURE 68.15. Electrocardiogram, acute pericarditis. For description, see text.

Echocardiogram

Echocardiography is performed to confirm or establish the clinical diagnosis. In some of these cases, the study will show a small, unsuspected pericardial effusion. This finding is a useful confirmation of pericarditis. Patients with a small pericardial effusion are still considered to have "dry" pericarditis. Unless the effusion is growing large or causing cardiac tamponade, it should be managed in the same way as patients without a pericardial effusion. The absence of pericardial effusion by no means excludes the diagnosis of pericarditis. In uncomplicated cases, the echocardiogram confirms the absence of myocardial or valvular disease.

Chest Radiogram

Radiographically, the chest appears normal unless there is a large pericardial effusion, but in some cases an associated parenchymal capacity or pleural effusion may be detected.

Clinical Course

Low-Risk Patients

The majority of patients pursue a benign course. The initial treatment consists of an antiinflammatory agent. Aspirin may be used for this purpose, but more commonly a nonsteroidal antiinflammatory agent such as indomethacin or ibuprofen is employed. With this treatment, most cases are free from pain and fever within 24 to 48 hours. Treatment is usually continued for 1 or 2 weeks. In a few patients, this treatment is unsuccessful. Colchicine, 0.6 to 2 mg daily, may then be effective with or without continuing the other antiinflammatory agent, the dose of which can be escalated if need be. Only when these therapies fail should the use of prednisone be contemplated. Initial evaluation and follow-up can safely be accomplished in a same-day hospital service and outpatient clinic,[124] making hospital admission unnecessary.

High-Risk Patients

High-risk acute pericarditis is less common and is much more challenging. Imazio et al.[125] categorized acute pericarditis into low risk and high risk. When a patient first presents, it may be immediately obvious that it is a high-risk case; examples include symptoms and signs of right heart failure, shock, and patients receiving hemodialysis or ultrafiltration. Table 68.2 lists the common causes of high-risk acute pericarditis.[125]

The risk category is assigned either at presentation or during evaluation in the same-day hospital service. Failure to respond quickly to standard treatment demands thorough investigation of etiology and treatment of the underlying cause, necessitating hospital admission. Tuberculous, malignant, and pyogenic pericarditis ranks high on the list.

TABLE 68.2. Common causes of high-risk acute pericarditis

Cause	*Comment*
Failure to respond quickly to antiinflammatory treatment	Indicates etiology other than the usual viruses; treatment differs
Evidence or suspicion of cardiac tamponade	Increased jugular pressure, pulsus paradoxus, hypotension, excess tachycardia
Evidence of suspected purulent pericarditis	High mortality; often recognized too late
Suspected or proven tuberculous pericarditis	
Large pericardial effusion that does not rapidly diminish during antiinflammatory treatment	Indicates nonviral etiology
Recurrent pericardial effusion	Investigate the cause
Immunosuppression	Likely to be infected with an unusual organism
Recurrent pericarditis	An autoimmune pericardial reaction causing multiple relapses of pericarditis or pericardial pain
Renal failure or dialysis with pericardial effusion	Possible hypovolemia, low-pressure tamponade Hypervolemia may be due to renal insufficiency, not tamponade

Treatment of cardiac tamponade has already been discussed. It is important to be aware that some patients receiving hemodialysis and who have low pressure tamponade[128] do not tolerate treating the pericardial effusion with intensified hemodialysis, which often is appropriate when these patients are hypervolemic.

Recurrent Pericarditis

Recurrence may follow an episode of idiopathic or viral pericarditis in 15% to 20% of cases. Although more common in women and younger patients, it cannot be predicted. It may also follow Dressler's syndrome, traumatic pericarditis, and other postpericardial injury syndromes.

Recurrent pericarditis often is an extremely troublesome and difficult syndrome to manage,[129] but some patients experience only a single recurrence that yields to simple treatment. Recurrences, however, may occur for a few weeks or months, but in many cases for years, sometimes many years. The principles of treatment are similar to those applying to an initial episode of acute pericarditis, but unfortunately patients may be more resistant to nonsteroidal antiinflammatory agents. Once more, colchicine has been proposed as a means to prevent or lessen the need for prednisone treatment.[130] Colchicine is more effective in populations among whom familial Mediterranean fever is endemic.[131] Because of the complications associated with frequent administration of high-dose prednisone, every effort should be made to avoid treatment with it. This is particularly important because it is thought that withdrawal from prednisone can precipitate a further recurrence. Nevertheless, some patients simply do not respond to any combination of nonsteroidal agents, and so the recourse must be to prednisone or other immunosuppressive drugs.[129]

When prednisone must be used, it should be initiated in high dose, for example, 1 to 1.5 mg/k per day.[132] This high dose should be maintained until all symptoms and signs of pericarditis, including the erythrocyte sedimentation rate, have returned to normal. After 2 to 4 weeks of total suppression, the dose should be progressively but slowly reduced. In the most successful cases, the use of the drug can be discontinued at the end of the dose reduction schedule. In other cases, symptoms or signs may reoccur, for example, when the patient has achieved a drop from 60 to 10 mg a day. In such cases, the lowest suppressing dose should be reinstituted, for instance, 15 mg a day, and maintained for 3 or 4 weeks, after which another attempt can be made to reduce the dose or to stop treatment. The same protocol is continued until all evidence of pericarditis disappears. After an interval of weeks, months, or occasionally years, the syndrome may recur, in which case treatment must begin all over again. Patients who do require prednisone must be followed carefully for symptoms of osteoporosis or other evidence of major prednisone toxicity. When these symptoms occur, or when it is clear that prednisone is not having the desired effect, consideration should be given to pericardiectomy.[133] While this operation sometimes cures the patient, relapses may still occur, even after pericardiectomy. However, in many such cases, recurrences are fewer and milder and the syndrome probably burns out faster than it would have without the operation.

Summary

The prevalence of pericardial disease and pericardial heart disease is considerably less than that of most other heart diseases seen in practice. Consequently, the diagnosis may be missed or made late, sometimes too late. A second consequence is that placebo-controlled randomized trials are infrequent and guidelines are few. It is incumbent on health care providers to consider a pericardial origin as the cause for unexplained hemodynamic deterioration, especially after cardiac surgery or intervention.

Purulent pericarditis carries a high mortality rate and often is only one component of multisystem disease. Catheter drainage and lavage with a fibrinolytic agent may be helpful, but usually only as a preliminary to surgical drainage.

Trauma, recent or remote, sharp or blunt, is an important cause of pericardial effusion, including hemopericardium and constrictive pericarditis. Whenever pericardial disease is a possibility and not otherwise explained, the patient must

be questioned about chest trauma of any kind. Any injury to the pericardium may be followed by the postpericardial injury syndrome, often manifest by effusion.

Echocardiography is indicated for the diagnosis of possible pericardial effusion quantification and its hemodynamic impact. In many cases, transthoracic echocardiography is not particularly helpful for evaluating the structure and pathology of the pericardium itself.

In the absence of tamponade and evidence of, or suggesting, purulent pericarditis or neoplastic pericardial disease, pericardiocentesis seldom reveals the cause of the effusion. Chronic effusive pericarditis usually has little hemodynamic impact, although the effusion is often huge. Cardiac tamponade may supervene years after the initial diagnosis; therefore, pericardiocentesis is advised for most cases and pericardiectomy for subsequent recurrence.

Cardiac tamponade is the most frequent and dangerous major complication of pericardial effusion. The chief clinical findings are raised jugular pressure and pulsus paradoxus. Echocardiography, in addition to showing the presence and size of the effusion, usually shows right atrial or right ventricular diastolic compression, or both. Respiratory variation of the rate and amount of ventricular filling greatly exceeds normal. Moderate or severe tamponade requires drainage of the effusion. Hemodynamic variables should be measured during pericardiocentesis to rule out effusive constrictive pericarditis.

The major features shared by tamponade and constriction are a global increase in external restraint that limits chamber volumes and impairs ventricular filling, an invariable total pericardial volume with strong ventricular interaction, preserved ventricular systolic function, mild pulmonary hypertension, and diastolic pressure of both ventricles equally elevated. Features that differ between the two diseases include etiology and the pattern of ventricular diastolic and atrial pressure pulses. In constrictive pericarditis, ventricular diastolic pressure shows an early diastolic dip followed by a plateau, and the venous pressure contour features prominent *x* and *y* descents. In tamponade, the dip and plateau is not seen and the *y* descent is absent.

Constrictive pericarditis must be distinguished from restrictive cardiomyopathy. In many instances, the history, echocardiogram, electrocardiogram and CT suffice. In others, the absence of strong ventricular interaction, a larger drop in pulmonary wedge pressure than left ventricular diastolic pressure, and tissue and M-mode color Doppler elucidate the correct diagnosis.

Acute pericarditis is usually of viral or uncertain etiology and responds quickly to simple antiinflammatory treatment. Steroidal therapy must be avoided as much as possible. Workup for myocardial ischemia is necessary only in cases with evidence supporting this possibility. A variety of systemic conditions cause the rest of the cases and, in many of these, treatment is directed to the cause, and complications are common. Cardiac tamponade may complicate acute pericarditis of any etiology. High-risk patients can be identified quite rapidly and need to be hospitalized. Low-risk patients do not usually require admission.

Recurrent pericarditis is an autoimmune disorder, highly distressing to the patients and troublesome for physicians, but the ultimate outcome is satisfactory to both. As for a first attack of acute pericarditis, avoiding treatment with a steroid is important.

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