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Pericarditis: Pathophysiology, Diagnosis, and Management

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Abstract Pericarditis, the most common disease of the pericardium, may be isolated or a manifestation of a systemic disease. The etiology of pericarditis is varied and includes infectious (especially viral and tuberculosis) and noninfectious causes (autoimmune and autoinflammatory diseases, pericardial injury syndromes, and cancer [especially lung cancer, breast cancer, and lymphomas]). Most cases remain idiopathic with a conventional diagnostic evaluation. A targeted etiologic search should be directed to the most common cause on the basis of the patient's clinical background, epidemiologic issues, specific presentations, and high-risk features associated with specific etiologies or complications (fever higher than 38°C, subacute onset, large pericardial effusion, cardiac tamponade, lack of response to NSAIDs). The management of pericardial diseases is largely empiric because of the relative lack of randomized trials. NSAIDs are the mainstay of empiric anti-inflammatory therapy, with the possible addition of colchicine to prevent recurrences.

Keywords Pericarditis · Pathophysiology · Diagnosis · Therapy · Management

Introduction

Pericarditis is the more common form of pericardial disease in the clinical setting, as it is responsible for about 5% of presentations to emergency departments for nonischemic chest pain. Few epidemiologic data are available; in a recent prospective study, the incidence of acute pericarditis was 27.7 cases per 100,000 population/year in an urban area [1•]. Pericarditis may be diagnosed as an isolated form or a manifestation of a systemic disease. Although the clinical diagnosis of pericarditis is relatively simple, establishing the etiology may be more difficult [2•, 3••, 4•]. Knowledge of the pathophysiology of the disease is still in its infancy and notably, the mechanisms of recurrence, the most common and troublesome complication, are not well-understood.

The management of pericardial diseases is largely empiric because of the relative lack of randomized trials. Management of most cases is handled by general practitioners or different health care specialists and does not require specific expertise; nevertheless, incessant and recurrent cases and specific forms (eg, tuberculous pericarditis, neoplastic pericardial disease, autoimmune conditions) require cooperation among different specialties (eg, cardiology, infectious diseases, rheumatology, oncology) [3••].

This review highlights recent research on the pathophysiology, diagnosis, and management of pericarditis based on articles published during the past 3 years.

Etiology and Pathophysiology

The pericardium consists of an outer sac (the fibrous pericardium) and an inner double-layered sac (the serous pericardium). The proximal portions of the great vessels (aorta and pulmonary artery) reside in the pericardial sac. The pericardium provides mechanical protection of the heart, reduces the friction between the heart and surrounding structures, and limits the distention of the heart

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contributing to diastolic coupling of the ventricles. Normally, this function is achieved via the presence of a small amount of pericardial fluid (25–50 mL) produced by the visceral pericardium, and intrapericardial pressure is equal to intrapleural pressure. Infectious and noninfectious noxa are usually responsible for inflammation of pericardial layers leading to increased production of pericardial fluid as exudate.

Acute Pericarditis

Several possible causes of pericarditis are listed in Table 1, as the pericardium may be involved in many systemic disorders. Alternatively, it may be involved as an isolated process [2•, 5]. Most cases of acute pericarditis are thought to be infectious (two thirds), especially of viral etiology (coxsackievirus, influenza, Epstein-Barr virus, cytomegalovirus, adenovirus, varicella, rubella, mumps, hepatitis B virus, hepatitis C virus, HIV, parvovirus B19 [6], and human herpesvirus 6), although serology data are often lacking or inconclusive [4•]. The definitive diagnosis of viral pericarditis requires the direct demonstration of the etiologic agent in the pericardial fluid or tissue, and this is not possible or recommended in most cases with mild or absent pericardial effusion. Thus, most cases of acute pericarditis are labeled as "idiopathic" at the end of the initial diagnostic evaluation [3••, 7].

A special consideration is for HIV infection. The pericardium, myocardium, coronary arteries, and pulmonary arteries are the main targets of cardiac disease in people who are infected with HIV. Geography and access to highly active antiretroviral therapy (HAART) have a major influence on which of these targets is affected. In sub-Saharan Africa, where tuberculosis is endemic and access to HAART is limited, the dominant forms of HIV-associated heart disease are pericardial tuberculosis and cardiomyopathy. In contrast, in industrialized countries in which tuberculosis is rare and HAART is widely available,

Table 1 Etiology and estimated incidence of pericarditis in developed countries with a low prevalence of tuberculosis

Etiology	Estimated incidence,%
Idiopathic	80–85
Infectious:	60–70
Viral (most common: echovirus and coxsackievirus, influenza, Epstein-Barr virus, cytomegalovirus, adenovirus, varicella, rubella, mumps, hepatitis B virus, hepatitis C virus, HIV, parvovirus B19, and human herpesvirus 6)	
Bacterial (most common: tuberculous [4%–5%], other bacterial rare)	
Fungal (rare: Histoplasma more likely in immunocompetent patients; aspergillosis, blastomycosis, Candida more likely in immunosuppressed host)	
Parasitic (very rare: Echinococcus, Toxoplasma)	
Non-infectious:	30–40
Autoimmune pericarditis (<10%):	
➢ *Pericardial injury syndromes* (post–myocardial infarction syndrome, postpericardiotomy syndrome, post-traumatic pericarditis including iatrogenic pericarditis)	
➢ *Pericarditis in systemic autoimmune and inflammatory diseases* (more common in systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis, systemic sclerosis, systemic vasculitides, Behçet's syndrome, sarcoidosis familial Mediterranean fever, TRAPS)	
➢ *Autoreactive pericarditis*	
Neoplastic pericarditis (5%–7%):	
➢ Primary tumors (rare, above all pericardial mesothelioma)	
➢ Secondary metastatic tumors (common, above all lung and breast cancer, lymphoma)	
Metabolic pericarditis (common: uremia, myxedema; other rare)	
Traumatic pericarditis (rare):	
➢ *Direct injury* (penetrating thoracic injury, esophageal perforation, iatrogenic)	
➢ *Indirect injury* (nonpenetrating thoracic injury, radiation injury)	
Drug-related pericarditis **(rare)**:	
➢ *Procainamide, hydralazine, isoniazid, and phenytoin* (lupus-like syndrome)	
➢ *Penicillins* (hypersensitivity pericarditis with eosinophilia)	
➢ *Doxorubicin and daunorubicin* (often associated with a cardiomyopathy)	

TRAPS tumor necrosis factor receptor–associated periodic syndrome

coronary artery disease is the main cause of death and disability in these patients, whereas myopericardial disease and pulmonary hypertension are less common [8].

Bacterial pericarditis beyond tuberculosis has become relatively rare in developed countries. Purulent pericarditis is especially rare (<1%) [3••]. The most common causes include *Propionibacterium acnes*, staphylococci, and streptococci. A common predisposing factor is an immune-compromised state [9]. Other rare infectious forms cited in contemporary literature include pneumococcal pericarditis [10] and pericarditis caused by *Coxiella burnetii* [11].

An autoimmune pathogenesis is responsible for cases related to connective tissue diseases. The pericardium may be involved in different systemic autoimmune diseases (ie, systemic lupus erythematosus, rheumatoid arthritis, progressive systemic sclerosis, mixed connective tissue disease, Sjögren's syndrome, polyarteritis, giant cell arteritis, and other systemic vasculitides) in a symptomatic form (usually during the active phase of the disease) or as an asymptomatic pericardial effusion. Inflammatory bowel disease (IBD) may involve the pleural space and pericardium, causing inflammatory exudative pleural and/or pericardial effusions. Pleuropericardial inflammatory disease and effusion can be directly related to IBD, its complications, associated infections, or the medications used to treat it. Although the specific pathophysiology of pleuropericardial disease in patients with IBD remains unclear, the response to systemic steroids is usually adequate, supporting an autoimmune pathogenesis [12].

An emerging cause of pericarditis, especially when recurrent, is represented by autoinflammatory diseases that are characterized by a primary dysfunction of the innate immune system. This is mostly caused by mutations of genes involved in the regulation or activation of the inflammatory response, without any apparent involvement of antigen-specific T cells or significant production of autoantibodies. These disorders usually manifest in the pediatric population, with onset ranging from the first hours to the first decade of life; however, a limited number of patients experience disease onset during adulthood. Autoinflammatory syndromes include familial Mediterranean fever (FMF), caused by mutations in the *MEFV* gene, and tumor necrosis factor (TNF) receptor–associated periodic syndrome (TRAPS), caused by mutations in the *TNFRSF1A* gene. Recurrent pericarditis is a common feature of both conditions, but it rarely occurs alone [13, 14].

FMF is an autosomal recessive disease largely restricted to certain ethnic groups and presenting with recurrent febrile serositis attacks. Peritonitis, pleuritis, and synovitis are common manifestations; however, the pericardium is rarely affected. FMF should be considered in patients with idiopathic recurrent pericarditis unresponsive to NSAIDs and corticosteroids [14].

TRAPS, the most common autosomal dominant autoinflammatory disorder, is caused by mutations in the *TNFRSF1A* gene encoding the 55-kD receptor for TNF-α. Serosal membrane inflammation is a common feature of TRAPS, usually in the form of polyserositis. In addition, patients affected with recurrent pericarditis as the only clinical manifestation of TRAPS have been described recently. Familial clustering has been reported in up to 10% of patients with recurrent pericarditis recently, suggesting a possible genetic predisposition in some cases. Familial clustering may represent a clue for investigating mutations in the *TNFRSF1A* gene in these patients and may eventually disclose TRAPS [15].

Postpericardial injury syndrome is defined as pericarditis or pericardial effusion that results from recent or earlier injury of the pericardium (postinfarction, postsurgery, post-traumatic). The clinical features of this syndrome include fever, leukocytosis, and elevated erythrocyte sedimentation rate. Recent studies have established a connection between this clinical presentation and an underlying autoimmune process. [16].

Postinfarction pericarditis has become rare in the primary percutaneous coronary intervention era. In the largest report (n=743), early post–acute myocardial infarction (AMI) pericarditis was diagnosed in 4.2% of cases, with an increasing prevalence according to presentation delay (P<0.001): 1.7% for less than 3 h, 5.4% for 3 to 6 h, and 13.6% for more than 6 h. Late post-AMI pericarditis (Dressler's syndrome) was recorded in only 0.1% of cases. Patients with presentation times greater than 6 h (OR, 4.4) and percutaneous coronary intervention failure (OR, 2.8) were at increased risk of developing early post-AMI pericarditis. Although pericarditis is associated with a larger infarct size, rates of in-hospital and 1-year mortality and major adverse cardiac events were similar in patients with and without pericarditis [17].

The postpericardiotomy syndrome (PPS) was reported in 10% to 40% of cases after cardiac surgery [18•]. However, in developed countries, emerging causes of pericarditis include iatrogenic, post-traumatic pericarditis following percutaneous coronary interventions, pacemaker insertion, and catheter ablation [16]. These cases are new contemporary examples of postcardiac injury syndromes in which the pathogenesis is determined by a combination of direct pericardial trauma, pericardial bleeding, and individual predisposition.

Radiation therapy may affect all layers of the heart (epicardial arteries, pericardium, valves, and myocardium). This is especially important after mediastinal or breast irradiation. Coronary artery disease with resultant myocardial infarction is the most common cause of death, but

radiation therapy is an important cause of constrictive pericarditis [19].

Recurrent Pericarditis

The etiology and pathogenesis of idiopathic recurrent acute pericarditis (IRAP) remain controversial, standing like a bridge that crosses infectious, autoimmune, and autoinflammatory pathways. Recurrences occur in up to 20% to 50% of patients. An immuno-mediated pathogenesis is suggested by the presence of proinflammatory cytokines in pericardial fluid, the presence of antinuclear autoantibodies in sera of the patients, the occurrence of new autoimmune diagnoses, and good response to anti-inflammatory or immunosuppressive therapy [20••]. Low-positive antinuclear autoantibody titers have been reported in more than 40% of IRAP cases [21]. In a recently published study, serum anti-heart, anti-intercalated disk (AIDA) were found in 68% of patients with IRAP. AIDA in IRAP were associated with a higher number of recurrences and hospitalizations. The detection of anti-heart and of AIDA supports the involvement of autoimmunity in the majority of patients with IRAP [22•]. Moreover, IRAP may be a feature of some autoinflammatory disorders [23•]. Despite an often troublesome course with worsening of quality of life, the long-term outcome of IRAP seems good, without evidence of constriction, even after a very long follow-up [20••].

Diagnosis

In clinical practice, the diagnosis of pericarditis is based on clinical criteria: typical chest pain, pericardial friction rub, widespread ST-segment elevation, and pericardial effusion. At least two of four should be present for the diagnosis of acute pericarditis to be made [3••, 5, 24••]. Evidence of elevated inflammatory markers (eg, C-reactive protein) is confirmatory of the diagnosis of pericarditis [3••, 25•].

Diagnostic evaluation, including physical auscultation, electrocardiogram [26], transthoracic echocardiography, markers of inflammation (eg, C-reactive protein) and myocardial lesion (creatine kinase, troponin), and chest x-ray, is mandatory in all cases of suspected pericarditis [3••, 24••].

The reported diagnostic yield of extensive laboratory evaluation and pericardiocentesis is low in the absence of cardiac tamponade or suspected neoplastic, tuberculous, and purulent pericarditis. A targeted etiologic search should be directed to the most common cause on the basis of the clinical background, epidemiologic issues, or specific presentations. In developed countries, clinicians should rule out neoplastic, tuberculous, and purulent pericarditis, as well as pericarditis related to a systemic disease [4•].

The role of different types of infections in heart diseases is more important than commonly thought with new and re-emerging infections (ie, *Mycobacterium tuberculosis*). Molecular investigations are important ancillary diagnostic tools and, combined with other conventional approaches, provide a more precise final diagnosis. A close collaboration and communication among cardiologists, cardiac surgeons, pathologists, and microbiologists is essential to ensure optimal diagnosis [27].

For instrumental techniques, echocardiography is the basic investigation and allows an easy semiquantitative analysis of the pericardial effusion. Echogenic materials in pericardial effusion predict pericardial complications such as recurrence and constrictive pericarditis irrespective of underlying diseases [28].

Three-dimensional transthoracic echocardiography may be superior to two-dimensional transthorathic echocardiography in uncovering mass lesions involving the pericardium, such as tuberculous granulomas, metastatic disease, hematomas, and pericardial cysts. It is also valuable in determining the extent of pericardial calcification in pericardial constriction and in measuring the size of pericardial masses [29].

The physiologic and structural information obtained from transthoracic echocardiography and the anatomic detail provided by cardiac CT and cardiac magnetic resonance (CMR) have led to growing interest in the complementary use of these techniques. Because of its high spatial and temporal resolution, multiplanar reconstruction capability, and large field of view, CT is a very useful tool in the comprehensive anatomic and functional evaluation of the pericardium [30]. CMR combines excellent anatomic detail and tissue characterization with accurate evaluation of cardiac function and assessment of the hemodynamic consequences of pericardial constraint on cardiac filling [31].

One of the most challenging diagnostic tasks is to diagnose the evolution toward constriction. In patients with clinical suspicion of underlying constrictive pericarditis, the traditionally most important radiologic diagnostic feature is abnormal pericardial thickening, which can be shown readily by CT and CMR. Nevertheless, constrictive pericarditis can occur without pericardial thickening [32].

Understanding the pathophysiology and integrating the results of invasive and noninvasive techniques is important in the differential diagnosis of constrictive pericarditis and, for example, restrictive cardiomyopathy. New echocardiographic techniques such as tissue Doppler imaging and two-dimensional speckle tracking, dual-source CT (CT imaging), and especially tagged cine-MRI with the analysis of phase contrast angiography sequences are promising novel approaches [33].

Nowadays, optimal management of the patient with suspected pericardial disease requires familiarity with the key imaging modalities and the ability to choose the appropriate imaging tests for each patient [34•, 35•].

Management

The treatment of pericardial diseases is largely empiric because of the relative lack of randomized trials compared with other cardiovascular diseases [3••, 24••, [36]. Medical treatment should be targeted to the cause of the disease as much as possible. However, the cause of pericardial diseases may be varied and depends on the prevalence of specific diseases (especially tuberculosis). As reported in the section on etiology and pathophysiology, the search for an etiology is often inconclusive, and most cases are classified as idiopathic in developed countries in which tuberculosis is relatively rare, whereas a tuberculous etiology is often presumed in developing countries in which tuberculosis is endemic [37•, 38].

Triage

Patients with pericarditis can be managed safely on an outpatient basis without a thorough diagnostic evaluation, unless a specific cause is suspected, the patient has high-risk features, or both [5]. Most cases are idiopathic, and the course is often benign following anti-inflammatory treatment and is not affected by a more precise diagnostic evaluation. On this basis, a triage of pericarditis can be safely performed according to the clinical and echocardiographic presentation (Fig. 1). High-risk features associated with specific etiologies or complications include fever higher than 38°C, subacute onset, large pericardial effusion, cardiac tamponade, and lack of response to aspirin or NSAIDs [7, 37•]. Cardiac tamponade represents a life-threatening condition that may complicate almost any cause of pericarditis. In contemporary series from developed countries, the leading cause is currently malignant disease, which carries a very poor prognosis [39].

Medical Therapy

Resolution of symptoms and normalization of markers of inflammation and other signs of the disease should guide the length and intensity of therapy [25•]. A detailed discussion of specific therapies is beyond the scope of the present review. Data on empiric anti-inflammatory therapies for viral and idiopathic acute and recurrent pericarditis (Table 2) are reviewed following papers published during the past 3 years.

NSAIDs

For viral and idiopathic forms, aspirin or NSAIDs at medium to high dosages are the mainstay of treatment (eg, aspirin, 2–4 g/d; ibuprofen, 1,200–1,800 mg/d; indomethacin, 75–150 mg/d). Treatment can be tailored to the specific patient, although the optimal length of treatment is not clearly established [25•].

Corticosteroids

Although high-dose steroid treatment is often effective, it may have serious side effects. Corticosteroid use is widespread in recurrent pericarditis, even if rarely indicated, and high doses (eg, prednisone, 1.0–1.5 mg/kg per day) are generally recommended, although only weak evidence

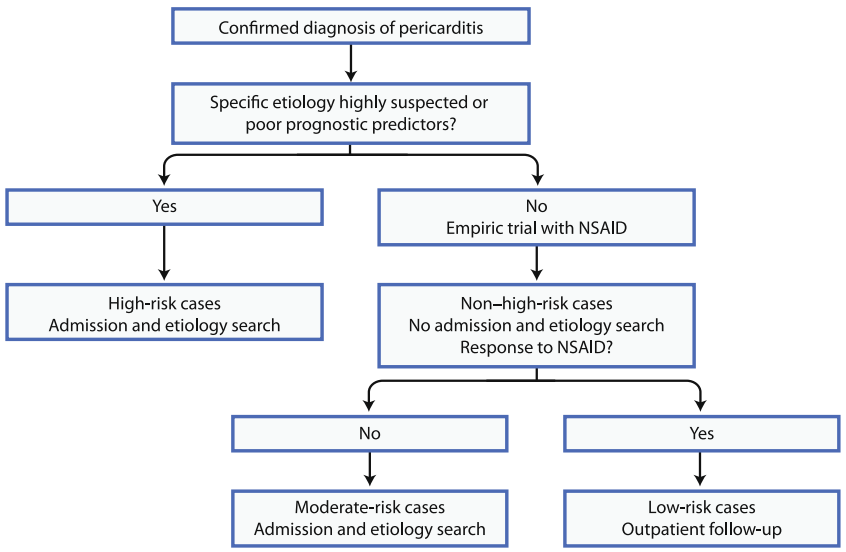

Fig. 1 Triage of pericarditis according to the Torino experience

Table 2 Empiric anti-inflammatory therapy for pericarditis

Drug	Usual attack dose	Usual dosing	Treatment length[a]	Monitoring
Acetylsalicylic acid (aspirin)	2–4 g/d	1.5–4 g/d	2–4 wk	Blood cell count, CRP
Ibuprofen	600 mg 3 times/d	1,200–1,800 mg/d	2–4 wk	Blood cell count, CRP
Indomethacin	50 mg 3 times/d	75–150 mg/d	2–4 wk	Blood cell count, CRP
Prednisone	0.2–0.5 mg/kg per day	0.2–0.5 mg/kg per day	2–4 wk for attack dose, several months for slow tapering	–
Colchicine	0.5 mg 2 times/d (0.5 mg/d for patients weighing <70 kg)	0.5 mg 2 times/d (0.5 mg/d for patients weighing <70 kg)	3 mo for acute pericarditis; 6–12 mo for recurrent pericarditis	Blood cell count, CRP, transaminases, CK, creatinine

[a] Optimal treatment length should be individualized. Anti-inflammatory therapies should be maintained until resolution of symptoms and normalization of CRP [25•]. Weekly assessment of CRP is warranted. Tapering of anti-inflammatory therapies is recommended according to some authors to reduce the risk of recurrence. A very low tapering is especially recommended for corticosteroids (ie, for prednisone, 5–10 mg/d every 1–2 wk [prednisone daily dose >25 mg]; 2.5 mg/d every 2–4 wk [prednisone daily dose, 15–25 mg]; and 1.0–2.5 mg/d every 2–6 wk [prednisone daily dose <15 mg]). Use of NSAIDs and colchicine may be necessary during tapering of corticosteroids

CK creatine kinase; *CRP* C-reactive protein

supports their use, and one must be aware of the possibly severe side effects. In one study, after adjustment for potential confounders (age, female gender, nonidiopathic origin), only high doses of prednisone were associated with severe side effects, recurrences, and hospitalizations (hazard ratio, 3.61; 95% CI, 1.96–6.63; $P<0.001$) [40•]. In other studies [41] and in a recently published meta-analysis [42•], steroids were associated with a trend toward increased risk of recurrent pericarditis (OR, 7.50). Conversely, low-dose steroids proved superior to high-dose steroids in cases involving treatment failure or recurrent pericarditis (OR, 0.29), rehospitalization (OR, 0.19), and adverse effects (OR, 0.07) [42•]. The explanation is not completely clear but seems related to impaired clearance of the infectious agent, possible chronicization of the infection, fast tapering, and corticosteroid side effects. Corticosteroid use should be restricted, but when used in low to medium doses (eg, prednisone, 0.2–0.5 mg/kg per day), they are preferred [25•].

To avoid systemic side effects of corticosteroids, the intrapericardial route has been proposed. One case series and three open-label trials evaluating intrapericardial triamcinolone for the management of autoreactive pericarditis have been reviewed [43]. The included studies were limited by small sample sizes (n=2–84), lack of control groups, short durations of follow-up (24 h–12 months), use of adjuvant agents, omission of patient demographic data, subjective reports of symptom relief, and lack of a consistent dose of intrapericardial triamcinolone. Available data suggest symptom resolution and reduced pericarditis recurrence with administration of intrapericardial triamcinolone to patients with autoreactive pericarditis. The appropriate regimen (dose and duration of treatment), adverse effect profile, and specific therapeutic role require further investigation [43].

Colchicine

Colchicine has been used effectively in the treatment of several inflammatory conditions (eg, gouty attacks, serositis related to FMF and Behçet's syndrome). Growing evidence has shown that the drug may be useful to treat an acute attack and may be a way to cope with the prevention of pericarditis. Nevertheless, clinicians are often skeptical about the efficacy of the drug, and concerns have arisen regarding possible side effects and tolerability [44•]. Colchicine concentrates in white blood cells, particularly neutrophils, inhibiting tubulin polymerization and thus interfering with migration and phagocytosis and reducing the inflammatory cycle. Although the exact number of responders is unknown, the drug has been used successfully in the treatment and prevention of recurrences and to taper corticosteroids in patients with recurrent pericarditis in several retrospective studies and an open-label, randomized trial in which the recurrence rate was halved in the treatment arm. Less evidence supports use of the drug in the treatment of acute pericarditis, for which colchicine remains optional and requires further multicenter confirmatory studies. Colchicine, 0.5 to 1.2 mg/d, is effective for reducing recurrences [25•].

However, careful monitoring of possible contraindications, drug interactions, and side effects is necessary [45]. Colchicine shows a large interindividual bioavailability. Furthermore, interactions with drugs interfering with CYP3A4-dependent enzymes and P-glycoprotein occur and are clinically important. The drug has a narrow therapeutic–toxicity window, and potentially serious drug–drug interactions (eg, with clarithromycin and cyclosporine) are recognized and therefore preventable [46]. The dosage of colchicine must be reduced in patients with hepatic and/

or renal dysfunction. However, when appropriately used and if there are no contraindications, oral colchicine is a safe treatment [47].

In the cited meta-analysis, colchicine was associated with a reduced risk of treatment failure (OR, 0.23) and recurrent pericarditis (OR, 0.39), but with a trend toward more adverse effects [42•]. More recently, colchicine has been shown to be safe and efficacious in the primary prevention of the PPS. In the Colchicine for the Prevention of the Post-pericardiotomy Syndrome (COPPS) trial, colchicine significantly reduced the incidence of the PPS at 12 months compared with placebo (21.1% vs 8.9%; P=0.002; number needed to treat=8). The rate of side effects (mainly related to gastrointestinal intolerance) was similar in the colchicine and placebo groups (8.9% vs 5.0%; P=0.212) [18•].

Other Intrapericardial Therapies

Local (intrapericardial) chemotherapy has been reported to be useful in the treatment of neoplastic pericardial disease, but it has never been compared to systemic chemotherapy, a combination of the two and simple pericardial drainage, or sclerosis. In a retrospective study of 119 patients with neoplastic pericarditis due to lung cancer, the outcomes of four different treatment strategies (extended catheter drainage/sclerosis, systemic chemotherapy, local chemotherapy, and combined local plus systemic chemotherapy) were analyzed at the last available follow-up or at the change in therapy after a treatment failure. Local chemotherapy,alone or with systemic chemotherapy, was effective in treating pericardial metastases from lung carcinoma, leading to a good control of pericardial effusion in 92% of cases and to complete disappearance of effusion and masses in 65%. Combined therapy was significantly better than any other treatment. On this basis, pericardiocentesis and intrapericardial chemotherapy should be used whenever possible in lung cancer neoplastic pericardial disease, and not only in case of tamponade [48•].

Pericardiectomy

Pericardiectomy is almost never indicated for recurrent pericarditis, except in cases with repeated recurrences with cardiac tamponade and evidence of serious steroid toxicity, although other approaches may be equally effective and less invasive (eg, pericardial window by conventional heart surgery or video-assisted thoracoscopy). On the contrary, pericardiectomy is recommended for persistent constrictive pericarditis. Pericardiectomy in experienced centers with complete decortication (if technically feasible) is the treatment of choice for constrictive pericarditis and results in symptomatic relief in most patients. However, some patients may not benefit from pericardiectomy, possibly due to myocardial compliance abnormalities, myocardial atrophy after prolonged constriction, residual constriction, or other myocardial processes. An important predictor of long-term outcome after pericardiectomy is the etiology of the pericardial disease. The overall mortality as detailed in the current literature is nearly 5% to 6%. Survival rates in cases of postsurgical constrictive pericarditis are worse than with idiopathic constrictive pericarditis but significantly better than with postradiation constrictive pericarditis [33].

Patients with newly diagnosed constrictive pericarditis who are hemodynamically stable may be given a trial of conservative management (anti-inflammatory therapy with NSAIDs and/or corticosteroids) for 2 to 3 months before pericardiectomy is recommended because transient cases of constriction have been described, especially in the presence of pericarditis [2•, 3••].

Myopericarditis

Myopericarditis is common in clinical practice. Up to 15% of acute pericarditis patients have significant myocardial involvement as assessed by markers of myocardial lesion. In clinical practice, pericarditis and myocarditis coexist because they share common etiologic agents, mainly cardiotropic viruses. The term *myopericarditis* indicates a primarily "pericarditic syndrome," and it is responsible for most cases [49•]. Patients with myopericarditis are younger and have more ST-segment elevation and lower systemic inflammation [50]. Echocardiography is essential for the diagnosis of left ventricular dysfunction and follow-up. CMR holds promise as an effective noninvasive diagnostic tool. For acute pericarditis or myopericarditis, there is a lack of adequate controlled clinical trials and follow-up studies. In myopericarditis, NSAIDs should be used with caution because in animal models of myocarditis, NSAIDs are not effective and may actually enhance the myocarditic process and increase mortality. Lower anti-inflammatory doses are mainly considered to control symptoms. On follow-up, most of these cases had objective normalization of echocardiography, electrocardiography, laboratory testing, and functional status, although up to 15% may report atypical, nonlimiting chest discomfort. The prognosis for myopericarditis is generally good [1•, 49•], although a possibly higher cardiac mortality rate for myopericarditis was reported in a single study [50].

Conclusions

Pericarditis, the most common disease affecting the pericardium, has several possible causes (infectious and noninfectious). In developed countries with a low prevalence of tuberculosis, most cases remain idiopathic. Viruses

are the most commonly recognized etiologic agents. The pathophysiology of pericarditis is still under investigation. A targeted etiologic search should be directed to the most common cause according to the epidemiology and presentation. Management is largely empiric because of the relative lack of randomized trials. NSAIDs are the mainstay of empiric anti-inflammatory therapy, with the possible addition of colchicine to prevent recurrences.

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- • Of importance
- •• Of major importance

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