Contemporary Reviews in Cardiovascular Medicine

Controversial Issues in the Management of Pericardial Diseases

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The management of pericardial diseases is largely empirical because of the relative lack of randomized trials. The first published guidelines[1,2] are a first attempt to organize current knowledge. At present, no specific guidelines have been issued by the American Heart Association and American College of Cardiology. After a literature review including a Medline search with the MeSH terms "pericarditis" and "pericardium," we identified the following controversial issues related mainly to the management of pericarditis and pericardial effusion: (1) etiological search and hospitalization; (2) role of pericardiocentesis, pericardial biopsy, and pericardioscopy; (3) myopericarditis; (4) use of corticosteroids, nonsteroidal antiinflammatory drugs (NSAIDs), and colchicine; (5) management of refractory cases and long-term outcome; (6) role of pericardiectomy, pericardial window, and other interventional techniques; and (7) management of chronic idiopathic pericardial effusion.

At the end of each issue, key points are summarized. Management of most cases is done by general practitioners or different healthcare 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 specialties (eg, cardiology, infectious diseases, rheumatology, oncology). Specific interventional techniques (eg, pericardioscopy) and pericardiectomy should be performed in referral centers.

Etiological Search and Hospitalization

Pericarditis

Although the clinical diagnosis of pericarditis is relatively simple (Tables 1 and 2),[1–13] establishing the cause may be more difficult. A major controversy in "pericardiology" is the role of an extensive etiologic search and hospital admission for all patients with pericarditis or pericardial effusion.[1–8] The causes of pericarditis are varied (Table 3),[9] and the clinician should identify causes that require targeted therapies. The epidemiological background is essential to develop a rational cost-effective management program[3,4,15,16]; the approach may be different for research, when we attempt to reduce the number of "idiopathic" cases. In developed countries, idiopathic or viral pericarditis is the commonest final diagnosis in the immunocompetent patient,[5–7] and a more precise diagnosis is often irrelevant for the management of most patients.[10–13]

Basic diagnostic evaluation should include auscultation; ECG; transthoracic echocardiography; routine blood tests, including markers of inflammation (ie, C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) and myocardial lesion (creatine-kinase, troponins); and chest x-ray in all cases of suspected pericarditis.[2] Additional tests should be related to suspected origin.

The major specific causes to be ruled out are tuberculous pericarditis, neoplastic pericarditis, and pericarditis associated with a systemic disease (generally an autoimmune disease). Each of these specific causes has a frequency of ≈5% of all unselected cases of pericarditis from developed countries (Table 4).[5–7] Emerging additional causes include iatrogenic origins (percutaneous coronary interventions, pacemaker insertion, catheter ablation).[14] These are contemporary examples of postcardiac injury syndromes in which the etiology is determined by a combination of direct pericardial trauma, pericardial bleeding, and individual predisposition. Tuberculous pericarditis may be found in North America and Western Europe, especially among immigrants from areas with a high prevalence of tuberculosis and HIV-infected patients. The etiologic spectrum is different in developing countries, with a high prevalence of tuberculosis (eg, 70% to 80% of pericarditis in sub-Saharan Africa, and ≥90% when associated with HIV infection).[15,16]

Certain clinical features indicating high risk are proposed for triage of pericarditis and the need for a full etiologic search and admission (Table 5).[4,8,17,18] Some of these features were validated by multivariable analysis[7]; fever >38°C (hazard ratio [HR], 3.56), subacute course (symptoms developing over several days or weeks; HR, 3.97), large pericardial

Table 1.   Diagnostic Criteria for Pericarditis

Criteria

Typical chest pain

Pericardial friction rub

Suggestive ECG changes (typically widespread ST-segment elevation, PR depression)

New or worsening pericardial effusion*

*The inclusion of pericardial effusion, not universally accepted,[1,5] is justified considering that this feature, although not necessary, is a confirmatory finding when present. Elevation of CRP is a confirmatory finding and is required for the diagnosis of acute and recurrent pericarditis by some authors.[4,11–13]

effusion (diastolic echo-free space >20 mm in width) or cardiac tamponade (HR, 2.15), and failure of aspirin or NSAIDs (HR, 2.50) were independent predictors of a specific cause (nonviral or nonidiopathic) in a prospective study of >450 consecutive cases of acute pericarditis. Large effusion

Table 2.   Recommended Basic Routine Diagnostic Evaluation for Pericarditis

Diagnostic Tool*	Data to Evaluate for the Diagnosis
Mandatory (class I)	
Cardiac auscultation	Pericardial rub
ECG	PR ST-T changes
Transthoracic echocardiography	Pericardial effusion
Blood tests†	Markers of inflammation (ESR, CRP), blood cell count, creatinine, markers of myocardial lesion (troponin, CK-MB)
Chest x-ray	Pleural effusion, cardiac size, concomitant pleuropulmonary disease
According to presentation features	Etiology search on pericardial fluid
Pericardiocentesis for cardiac tamponade (class I)	
Pericardiocentesis for persistent significant pericardial effusion without clear diagnosis (class IIa)	
Pericardiocentesis for persistent mild pericardial effusion (class IIb)	
Optional if persistent disease and initial diagnostic test are inconclusive (class IIa) and with suspicion of nonidiopathic cause	Search for specific disease (eg, tuberculosis, neoplasia)
CT	
CMR	
Pericardioscopy and pericardial biopsy	
	Targeted pericardial biopsy

CK-MB indicates creatine kinase-MB; CMR, cardiac magnetic resonance. At least 2 of the 4 criteria should be present.

*Classes of recommendations are based on 2004 European Society of Cardiology guidelines.[2]

†Additional blood testing should be performed if a specific cause is suspected; routine viral serology and viral etiology search are not routinely recommended and have no impact on subsequent therapy in the clinical setting.

Table 3.   Causes of Pericarditis: A Simple Basic Classification in Infectious and Noninfectious Forms

Infectious pericarditis (2/3 of cases)

Viral (most common: echovirus and coxsackievirus (usual), influenza, EBV, CMV, adenovirus, varicella, rubella, mumps, HBV, HCV, HIV, parvovirus B19, and human herpes virus 6 (increasing reports)

Bacterial (most common: tuberculous [4%–5%], *Coxiella burnetii*; other bacterial [rare] may include pneumococcosis, meningococcosis, gonococcosis, haemophilus, staphylococci, chlamydia, mycoplasma, legionella, leptospira, listeria)

Fungal (rare; histoplasma more likely in immunocompetent patients; aspergillosis, blastomycosis, candida more likely in immunosuppressed host)

Parasitic (very rare; echinococcus, toxoplasma)

Noninfectious pericarditis (1/3 of cases)

Autoimmune pericarditis (<10%)

Pericardial injury syndromes (post–myocardial infarction syndrome, postpericardiotomy syndrome, posttraumatic pericarditis including iatrogenic pericarditis, eg, post–percutaneous coronary interventions, post–pacemaker insertion, postablation)

Pericarditis in systemic autoimmune and autoinflammatory diseases (more common in systemic lupus erythematosus, Sjögren syndrome, rheumatoid arthritis, systemic sclerosis, systemic vasculitides, Behçet syndrome, sarcoidosis, familial Mediterranean fever)

Autoreactive pericarditis

Neoplastic pericarditis (5% to 7%)

Primary tumors (rare; above all pericardial mesothelioma)

Secondary metastatic tumors (common; above all lung and breast cancer, lymphoma)

Metabolic pericarditis (common; uremia, myxedema; others 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; may cause a pericardiopathy)

EBV indicates Epstein-Barr virus; CMV, cytomegalovirus; HBV, hepatitis B virus; and HCV, hepatitis C virus. Percentages refer to unselected cases. The diagnosis of autoreactive pericarditis is established in the European guidelines using the following criteria: (1) increased number of lymphocytes and mononuclear cells >5000/mm^3 (autoreactive lymphocytic) or the presence of antibodies against heart muscle tissue (antisarcolemmal) in the pericardial fluid (autoreactive antibody mediated), (2) signs of myocarditis on epicardial/endo-myocardial biopsies by ≥14 cells/mm^2, and (3) exclusion of infections, neoplasia, systemic, and metabolic disorders.[2]

and tamponade (HR, 2.51) and aspirin or NSAID failure (HR, 5.50) identified increased risk of complications during follow-up.[7] Women were at increased risk of specific causes and complications because of a higher prevalence of systemic autoimmune diseases. For patients with poor prognostic predictors (Table 5), hospitalization and a full etiologic search are warranted (Figure 1).[4,8,17,18] On the contrary, when these negative predictors are absent, patients are at low risk of specific causes and complications, and outpatient management has been proposed. In a prospective study of 300 consecutive patients with acute pericarditis, 254 patients (85%) were at low risk and not admitted to hospital but were

Table 4.   Final Etiologic Diagnosis in Major Published Series of Acute Pericarditis (Unselected Patients)

	Permanyer-Miralda et al[5] (n=231)	Zayas et al[6] (n=100)	Imazio et al[7] (n=453)	Reuter et al[16] (n=233)*
Years	1977–1983	1991–1993	1996–2004	1995–2001
Setting	Western Europe	Western Europe	Western Europe	Africa
Idiopathic, n (%)	199 (86.0)	78 (78.0)	377 (83.2)	32 (13.7)
Specific cause, n (%)	32 (14.0)	22 (22.0)	76 (16.8)	201 (86.3)
Neoplastic	13 (5.6)	7 (7.0)	23 (5.1)	22 (9.4)
Tuberculosis	9 (3.9)	4 (4.0)	17 (3.8)	161 (69.5)
Autoimmune	4 (1.7)	3 (3.0)	33 (7.3)	12 (5.2)
Purulent	2 (0.9)	1 (1.0)	3 (0.7)	5 (2.1)

*Based on pericardial effusions.

treated empirically with aspirin 800 mg every 6 or 8 hours for 7 to 10 days without an etiologic search. The protocol was safe (no cases of cardiac tamponade) and cost-effective; 230 of 254 low-risk cases (90.6%) had a final diagnosis of viral or idiopathic pericarditis after a mean follow-up of 38 months.[10]

The same approach is also useful for patients with recurrences that may generally be treated as outpatient unless poor prognostic predictors are present or a specific cause can be ruled out. With a clear diagnosis of idiopathic origin, it is also unnecessary to repeat a new etiologic search at each recurrence unless new clinical features become evident. The commonest causes of recurrences are idiopathic, viral, autoimmune (usually related to a connective tissue disease or a pericardial injury syndrome), inadequate medical treatment of either the index attack or the recurrence, and less commonly, a neoplastic origin.[11,19] Recurrent pericarditis often has the features of a systemic inflammatory disease, particularly at the onset. Pleuropulmonary involvement occurs in one third of adults[13] and in two thirds of pediatric patients,[20] and liver involvement is seen in 8%,[13] so idiopathic recurrent pericarditis shares several features with autoinflammatory diseases[21] such as familial Mediterranean fever.

Pericardial Effusion

Clinical series with pericardial effusion have reported a lower rate of idiopathic causes compared with acute pericarditis (Table 6). Moderate to large pericardial effusions had specific diagnoses (nonidiopathic origins) in up to 90%, and neoplasms, tuberculosis, and myxedema should be considered.[22–24] Although reported frequencies vary according to geographic distribution, selection criteria (ie, definition of effusion severity), and medical setting (ie, general versus tertiary referral centers), the origin of pericardial effusion can be suspected by the clinical presentation. A selective approach may consider the presence/absence of cardiac tamponade; any inflammatory signs, including CRP and/or ESR (ie, pericarditis); known medical conditions (up to 60% of cases); and effusion size. Cardiac tamponade requires drainage and etiology search and, when the presentation is without inflammatory signs, is associated with a higher risk of

Table 5.   Clinical Poor Prognostic Predictors* for Pericarditis

Major
Fever >38°C
Subacute onset
Large pericardial effusion
Cardiac tamponade
Lack of response to aspirin or NSAIDs after at least 1 wk of therapy

Minor
Myopericarditis
Immunodepression
Trauma
Oral anticoagulant therapy

See text for details.
*Major predictors have been validated in multivariable analysis.[7]

neoplasia (likelihood ratio, 2.9).[23] If inflammatory signs are present, the clinical approach should be that of pericarditis. Known medical conditions are reported in up to 60% of cases with a moderate to large effusion.[23] A large effusion without cardiac tamponade, inflammatory signs, and a known medical condition is usually associated with a chronic idiopathic origin (likelihood ratio, 20).[23] In this condition, a normal chest computed tomography scan may be helpful in ruling out neoplasms and tuberculosis. A practical approach is depicted in Figure 2. A detailed discussion of laboratory tests and integrated cardiovascular imaging for the etiology search for pericarditis and pericardial effusion is beyond the scope of this article (see the online-only Data Supplemental). Table 7 summarizes the relative contributions of diagnostic tools for specific etiologic search.

Key points: (1) Basic diagnostic tests for all cases with suspected pericarditis include ECG, transthoracic echocardiography, markers of inflammation (CRP and/or ESR) and myocardial lesion (eg, troponin), and chest x-ray; (2) additional tests, hospitalization, and etiology search should be restricted to high-risk patients; (3) major high-risk features (predictive of possible nonviral, nonidiopathic origins, and complications during follow-up) include fever >38°C, subacute course, large pericardial effusion or cardiac tamponade, and failure of aspirin or NSAIDs.

Role of Pericardiocentesis and Pericardial Biopsy

The first studies of pericarditis[5,6] reported a low diagnostic yield for diagnostic pericardiocentesis and pericardial biopsy. Other authors have advocated a more extensive use of the techniques for diagnostic purposes.[2]

When a significant pericardial effusion is present, diagnostic pericardiocentesis is mandatory if a specific origin is suspected and diagnosis cannot be reached by other means.[2] Pericardiocentesis may also be considered for large or symptomatic effusions refractory to medical treatment. Pericardiocentesis may be guided by fluoroscopy or echocardiography. If hemorrhagic fluid is aspirated, it is practical to remember that fibrinolytic activity in the pericardium prevents blood clotting in subacute and chronic effusion. However, acute hemorrhage into the pericardium overwhelms fibrinolysis,
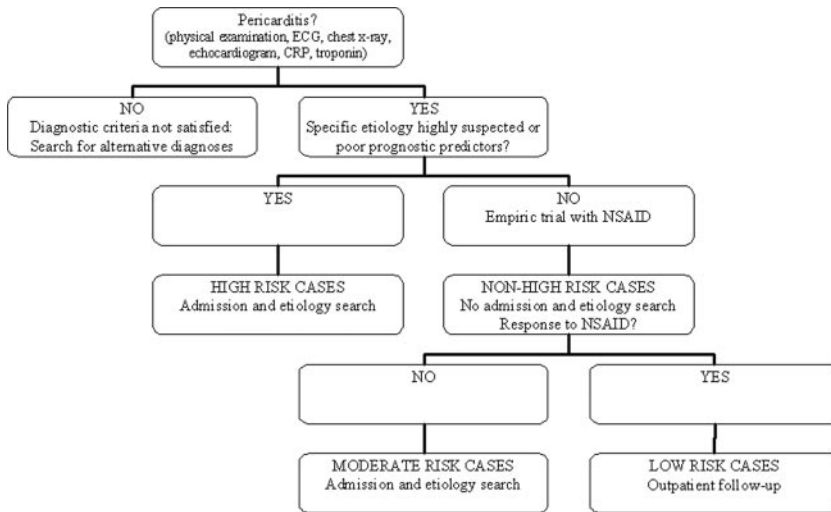
Figure 1. In developed countries, a probabilistic approach is advisable in the immunocompetent patient. Etiologic search should rule out commonest causes: tuberculous, purulent, and neoplastic pericarditis and pericarditis related to a systemic disease. Triage of pericarditis according to the Torino experience.

and blood clotting can occur in fluid aspirated in such cases. If the answer is not clear, contrast medium may be injected under fluoroscopic observation and agitated saline under echocardiographic observation to exclude cardiac puncture.[25] Echocardiography-guided pericardiocentesis is safe and allows different approaches to the effusion beyond the standard "subxiphoid" route. The clinician may choose the best puncture site closest to the large amount of pericardial fluid identified by the echocardiogram also without a catheterization laboratory.[26] However, hemodynamic evaluation may detect effusive-constrictive pericarditis.[27] Elective pericardiocentesis should be performed in a catheterization laboratory when available. In this setting, the use of the echocardiography-guided technique of pericardiocentesis will provide the best integration of available diagnostic techniques to guide pericardiocentesis. Echocardiography-guided pericardiocentesis remains sufficient when a catheterization laboratory is not available or in urgency/emergency settings.

In the first published studies, pericardial biopsy was generally performed as part of a therapeutic procedure (surgical drainage) in patients with cardiac tamponade relapsing after pericardiocentesis (therapeutic biopsy). It was also used

as a diagnostic procedure in patients with illness lasting >3 weeks without definite diagnosis.[5]

Technical advances in instrumentation with the introduction of pericardioscopy, in contemporary virology, and in molecular biology improved the diagnostic value of epicardial/pericardial biopsy.[2,28,29] Targeted biopsy during pericardioscopy was particularly useful for diagnosing neoplastic pericardial disease.[29] Yet pericardioscopy is not generally available outside tertiary referral centers, but advanced diagnostic methods seem warranted in cases refractory to full conventional therapy, suspected tuberculous, or purulent or neoplastic pericarditis when the diagnosis cannot be reached by other means (Table 8). The diagnostic yield of pericardial biopsy is higher in patients with pericardial effusion with or without pericarditis than in those with apparent acute pericarditis without effusion and increases with large effusions.[22–24,30] Polymerase chain reaction represents a useful adjunct to conventional laboratory studies of pericardial samples, allowing rapid identification of microorganisms not easily found otherwise.[31] However, some authors underlined the need for careful selection of patients because molecular methods led to an absolute increase in specific useful diagnoses in <5% of cases in an already selected population.[32] Although potentially useful, if indicated without clinical judgment, molecular diagnostic techniques could lead to irrelevant findings such as viral infections for which specific drugs are not available or necessary in most cases.[32] Table 7 summarizes the relative value of different diagnostic tests.

Key points: (1) Pericardiocentesis is indicated for cardiac tamponade, high suspicion of tuberculous, purulent, or neoplastic pericarditis, and large or symptomatic effusions refractory to medical treatment; (2) pericardial biopsy may be indicated for diagnosis in patients with persistent worsening illness without a definite diagnosis despite medical therapy and as part of a therapeutic procedure for relapsing cardiac tamponade or moderate to large effusions with severe symptoms; and (3) pericardioscopy for targeted diagnostic imaging and biopsy may be indicated in refractory, difficult cases at experienced tertiary referral centers.

Table 6. Etiologic Diagnosis in Major Published Series With Pericardial Effusions

	Corey et al[22] (n=57)	Sagrista et al[23] (n=322)	Levy et al[24] (n=204)
Year	1993	2000	2003
Size of effusion, mm	>10	>10	NR
Tamponade, %	NR	37	NR
Idiopathic, %	7	29	48
Neoplasia, %	23	13	15
Infection, %	27	2	16
Connective tissue diseases, %	12	5	9
Metabolic, %	12	6	11
Iatrogenic, %	0	16	0
Other, %	19	29	1

NR indicates not reported. Data include main clinical diagnoses.
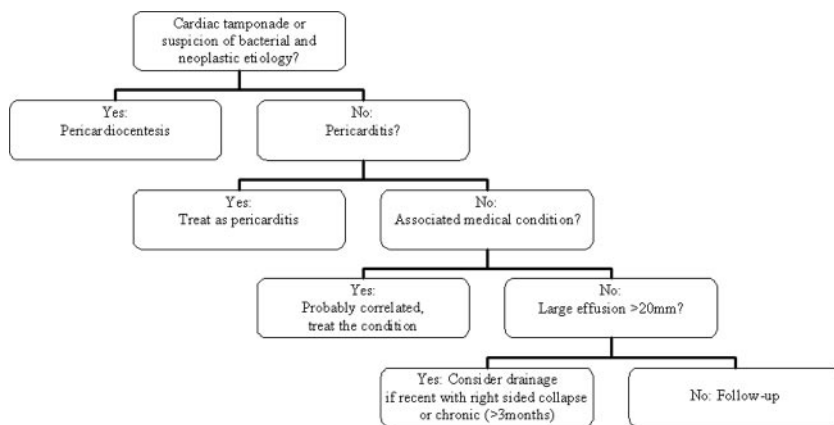
Figure 2. Management of pericardial effusion (see text for details).

Myopericarditis

Cases of pericarditis may present with troponin elevation,[33–35] an expression of concomitant myocardial involvement. Concomitantly, widespread ST-segment elevation, usually considered a hallmark of acute pericarditis,[1,2,17,18] shows subepicardial myocardial involvement rather than simple "pericarditis" (Figure 3). Thus, mixed myocardial and pericardial involvement is probably present in most cases with pericarditis. Myocarditis and pericarditis share common etiologic agents, mainly viruses; thus, a spectrum of

myopericardial inflammatory syndromes, ranging from pure pericarditis to forms with increasing myocardial involvement such as myopericarditis (predominant pericarditis), perimyocarditis (predominant myocarditis), and pure myocarditis, can be encountered.[36–38] Myopericardi-

Table 7. Utility of Diagnostic Tests for the Etiologic Diagnosis of Pericarditis According to Targeted Causes

Test	General	Tuberculous	Systemic Disease	Neoplastic	Purulent
Auscultation	+++	+/−	+/−	+/−	+/−
ECG	+++	+/−	+/−	+/−	+/−
Echocardiography	+++	+++	++	+++	+++
Markers of inflammation	+++	+++	+++	+++	+++
Markers of myocardial lesion	+++	+/−	+	+/−	+/−
Tumor markers	−	−	+/−	+	−
Tuberculin skin test	−	+/−	+/−	−	−
QuantiFERON-TB	−	+	+/−	−	−
ANA, ENA (anti-SSA)	−	−	+	−	−
HIV testing	−	+	+	−	+
Viral serology	−	−	−	−	−
Blood culture	−	−	−	−	+
Chest x-ray	++	+++	+++	+++	++
CT	−	+++	+++	+++	+++
CMR	−	++	++	+++	+++
Mammography	−	−	−	+++	−
Pericardiocentesis	−	+++	+/−	+++	+++
Pericardial biopsy	−	+++	+/−	+++	+

ANA indicates antinuclear antibody; CT, computed tomography; CMR, cardiac magnetic resonance; ENA, antibodies anti-extractable nuclear antigen; SSA, Sjogren Syndrome type A; +++, very high; ++, high/good; +, discrete; +/−, low/insufficient; and −, not useful. QuantiFERON-TB is an interferon-γ release assay used in tuberculosis diagnosis.

Table 8. Management of Pericarditis: Indications for Pericardiocentesis, Pericardial Biopsy, Pericardioscopy, Pericardial Window, and Pericardiectomy

Pericardiocentesis

  Cardiac tamponade

  Moderate to large effusions refractory to medical therapy and with severe symptoms

  Suspected bacterial or neoplastic pericarditis

  Advantages: allows drainage and analysis of pericardial fluid

  Limits: invasive technique, requires monitoring and hospitalization

Pericardial biopsy and pericardioscopy (targeted biopsy in specialized center)

  Relapsing cardiac tamponade

  Suspected bacterial or neoplastic pericarditis

  Worsening pericarditis (despite medical therapy) without a specific diagnosis

  Advantages: allows analysis of pericardial tissue

  Limits: invasive technique, requires monitoring and hospitalization, possible trigger for pericardial bleeding and recurrences

Pericardial window

  Recurrent cardiac tamponade

  Recurrent moderate to large effusion refractory to medical therapy and with severe symptoms

  Advantages: allows pericardial drainage or obliteration of pericardial space preventing or reducing pericardial effusion size

  Limits: invasive therapy, requires monitoring and hospitalization, possible trigger for pericardial bleeding and recurrences

Pericardiectomy

  Permanent constrictive pericarditis

  Recurrent cardiac tamponade

  Advantages: allows partial or almost total removal of diseased pericardial tissue

  Limits: invasive therapy; operatory risk may be not negligible according to disease stage, comorbidities, and surgeon skill; requires experienced heart surgery team, monitoring, and hospitalization; possible failure for incomplete removal; trigger for pericardial bleeding and recurrences
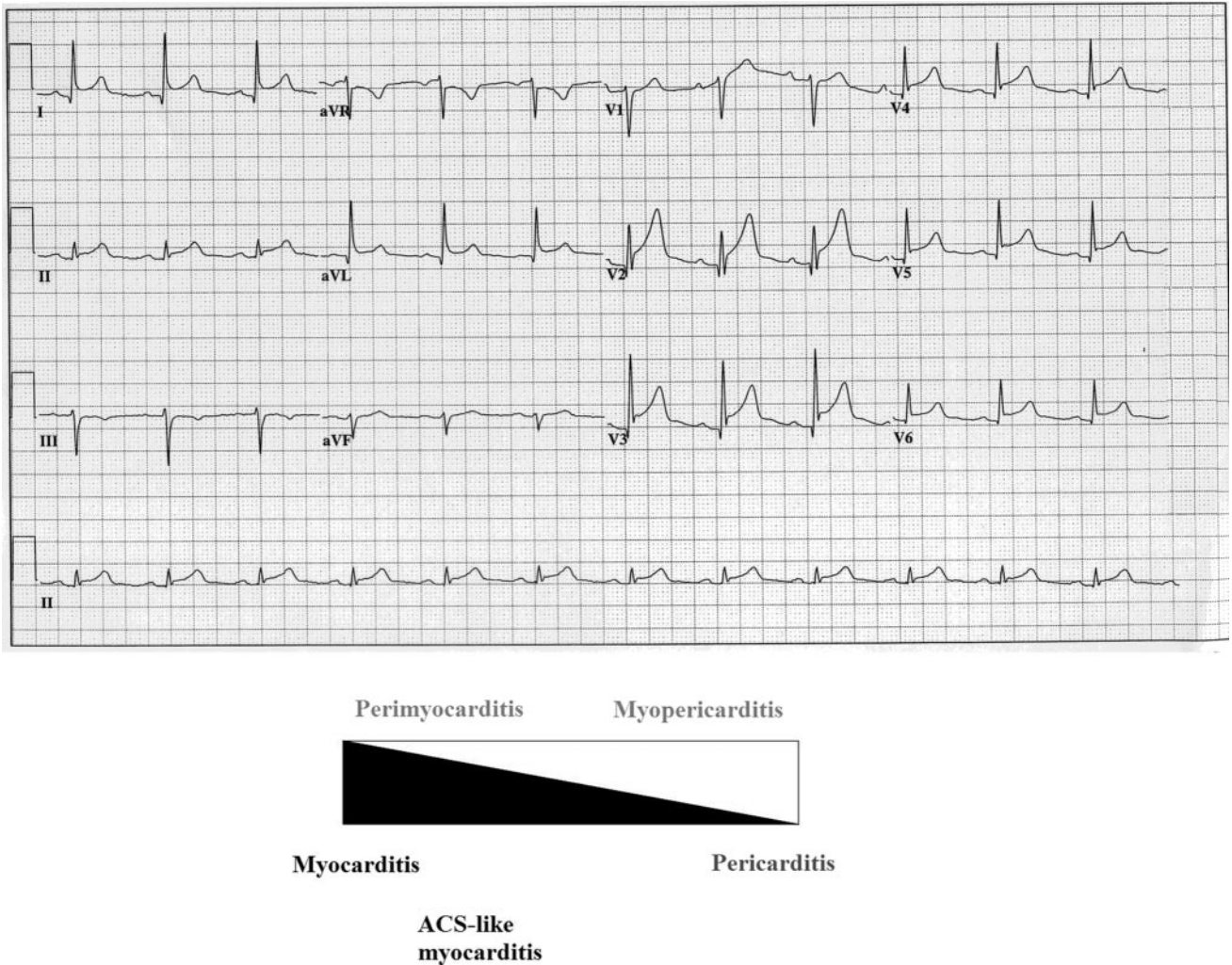
Figure 3. A 53-year-old man with apparently idiopathic acute pericarditis: nearly ubiquitous J (ST) elevations with corresponding J (ST) depression in aVR. As is common in III and aVF when the QRS axis is horizontal (or these leads are of small voltage), the J (ST) is not elevated. The height of J (ST) is >25% of the height of the T-wave peak in V_5 and V_6. Most PR segments are slightly depressed with respect to the T-P baseline (corresponding PR elevation in aVR). In the clinical setting, a spectrum of myopericardial inflammatory syndromes can be encountered, ranging from pure pericarditis to forms with increasing myocardial involvement (sometimes mimicking an acute coronary syndrome).

tis, generally with a preserved or mildly reduced left ventricular ejection fraction (ie, 45% to 50%), has a good prognosis without evolution to heart failure, constrictive pericarditis, or increasing recurrence rates.[36,37] In these cases, normalization of the ECG, left ventricular function, and exercise capacity is reported within 12 months.[36] Subtle myocardial involvement beyond ECG changes, eg, troponin elevation and wall motion abnormalities on echocardiography (usually discordant with ECG changes, unlike acute coronary syndromes), can also be detected noninvasively by cardiac magnetic resonance.[37] Myopericarditis requires admission for monitoring and therapy. In myopericarditis, antiinflammatory drugs should be evaluated against the degree of myocardial involvement because, in animal models of myocarditis, they may enhance the myocarditic process and increase mortality.[36,37] Lower doses of antiinflammatory drugs (ie, aspirin 500 mg TID) are usually prescribed mainly to control symptoms for 1 to 2 weeks rather than reaching full high antiinflammatory

effects such as in simple pericarditis.[36,37] Exercise restriction is recommended for 4 to 6 weeks, as well as echocardiographic monitoring of ventricular function (at 1, 6, and 12 months), especially in patients with left ventricular dysfunction in whom angiotensin-converting enzyme inhibitors and β-blockers may be beneficial such as in heart failure settings.[37] For athletes, a return to competitive sports is considered after 6 months but only if the patient is asymptomatic with normalization of ECG, markers of inflammation, left ventricular function, wall motion, and cardiac dimensions. Moreover, clinically relevant arrhythmias should be absent on Holter monitoring and exercise test.[39,40]

Key points: (1) Myocarditis and pericarditis share common etiologic agents, mainly viruses, with a spectrum ranging from pure pericarditis to forms with increasing myocardial involvement (myopericarditis and perimyocarditis); (2) myocardial involvement requires admission for monitoring, and antiinflammatory therapy is reduced to control symptoms and

to minimize possible deleterious effects on the myocarditic process; and (3) prevalent pericarditis (ie, myopericarditis) generally has a good overall prognosis.

Antiinflammatory Therapy

Corticosteroids

Although reviews and guidelines[1,2,17–19] suggest limiting the use of corticosteroids in inflammatory pericardial syndromes to patients with intolerance, contraindications, or real failure of aspirin and other NSAIDs, these drugs are widespread in general practice, especially for recurrent cases, and the majority of patients with recurrent pericarditis are treated with corticosteroids.[12,13,20,41,42] The main reason for their success is that corticosteroids are able to induce a quick response with symptom control and initial remission. Nevertheless, the treatment often is quickly tapered because of the fear of possible side effects, and relapses and severe side effects related to the need of prolonged treatment are common. Moreover, they are recognized as a risk factor for recurrences, probably because of impaired virus clearance.[19,43–46] Thus, a troublesome issue is how to manage a patient with recurrent pericarditis and corticosteroid dependence.

The evidence to support the use of corticosteroids for pericarditis is rather weak. Specific data come from only 1 retrospective study on recurrent pericarditis.[47] In this study, 12 patients with recurrent pericarditis unrelated to any systemic disease were treated for 3 months with high-dose prednisone (1.0 to 1.5 mg·kg^{-1}·d^{-1}) for 1 month with subsequent gradual tapering. When prednisone tapering was started, all patients received a 5-month course of aspirin (1.6 g/d until steroid withdrawal and then 0.8 g/d). During follow-up (mean, 42 months), high-dose prednisone resulted in stable remission in all but 1 patient. Prolonged treatment with aspirin cannot be excluded to explain the overall good remission rate. Moreover, 3 patients (25%) had severe steroid-related adverse effects; 2 were treated with other immunosuppressive treatments (1 with azathioprine and 1 with cyclophosphamide).

Lower doses of steroids are commonly used to treat serositis in patients with autoimmune diseases such as systemic lupus erythematosus and Sjögren syndrome.[48,49] These therapeutic schemes might be reasonably applied to recurrent pericarditis.

A recent retrospective, nonrandomized study challenges the common practice of using these high doses of corticosteroids.[50] One hundred patients with recurrent pericarditis were assigned to 2 alternative therapeutic regimens of prednisone; one half received "low" doses of prednisone (0.2 to 0.5 mg·kg^{-1}·d^{-1}), and the other half received prednisone 1.0 mg·kg^{-1}·d^{-1}. Baseline characteristics were well balanced across the groups. Each initial dose was maintained for 4 weeks and then slowly tapered. During 5580 patient-months of follow-up, patients treated with high doses of prednisone had a higher rate of severe side effects (23.5% versus 2.0%, respectively; $P=0.004$) but also of recurrences (64.7% versus 32.6%, respectively; $P=0.003$) and disease-related hospitalizations (31.4% versus 8.2%, respectively; $P=0.008$). On this

basis, a premise for a possible future randomized study, low doses of corticosteroids may be considered before resorting to higher doses. Most of the observed severe side effects were vertebral fractures. Guidelines recommend osteoporosis prevention when corticosteroids are used, an issue often forgotten in practice. Supplementation with calcium and vitamin D (1500 mg/d and 800 IU/d, respectively) or an activated form of vitamin D (eg, alfacalcidiol 1 μg/d or calcitriol 0.5 μg/d) should be offered to all patients receiving glucocorticoids to restore normal calcium balance. Moreover, bisphosphonates are recommended to prevent bone loss in all men and postmenopausal women in whom long-term treatment with glucocorticoids is initiated at a dose $\geq$5 mg/d of prednisone or equivalent.[51,52] On the contrary, proton pump inhibitors are not routinely indicated when corticosteroids are used without NSAIDs.[53]

A very low tapering only after stable remission with symptom resolution and normalization of CRP is the key to successful management of the disease, similar to what is often done in polymyalgia rheumatica. A critical threshold for recurrences is a 10- to 15-mg/d dose of prednisone; at this threshold, very slow decrements as small as 1.0 to 2.5 mg at intervals of 2 to 6 weeks are useful (Table 9). If symptoms recur during tapering, every effort should be made not to increase the dose of or to reinstitute corticosteroids and to control symptoms by beginning or increasing the doses of aspirin or NSAIDs.[19,48,50] During tapering, colchicine should always be considered, starting with low doses, eg, 0.5 to 0.6 mg, to improve gastrointestinal tolerability. An alternative proposed approach to minimize systemic side effects related to corticosteroids may be the intrapericardial administration of nonabsorbable corticosteroids,[54] but the technique remains investigational for the most part.[44]

NSAIDs and Aspirin

Aspirin or NSAIDs remain the mainstay of treatment for pericarditis (Table 9). Unsatisfactory results are often reported when NSAIDs are used.[20,21,55] Some of these failures are due to low dosages or courses that are too short, with interruption of the therapy while the disease is still active, as manifested by persistently elevated CRP. Articles often give no details on the specific drug. NSAIDs should be used at appropriate antiinflammatory dosages (eg, aspirin at 2 to 4 g daily, indomethacin at 75 to 150 mg daily, and ibuprofen at 1600 to 3200 mg daily), considering long courses until complete normalization of CRP (Table 9). This is particularly important during corticosteroid tapering.[48] The selection of the specific NSAID should be based on physician experience and the patient's previous history (eg, an NSAID that was effective in previous attacks should be the favorite choice) and comorbidities; eg, aspirin is the favored choice in patients with ischemic heart disease or when the patient is already on aspirin or needs antiplatelet treatment, whereas indomethacin and other NSAIDs should be avoided in patients with coronary artery diseases.[56–58]

The optimal length of treatment is debatable, and CRP should probably be considered not only for initial diagnosis but also as a marker of disease activity to guide management and treatment length. In addition, the need for gradual

Table 9.   Medical Therapy for Pericarditis and Tapering Regimen of Prednisone in Pericarditis

Drug	Usual Attack Dose* (Dose Range)	Time for Attack Dose†	Tapering (Every 1–2 wk)†
Acetylsalicylic acid	750–1000 mg TID (2–4 g/d)	First attack: 1–2 wk Recurrence: 2–4 wk	750–1000 mg BID and then 750–1000 mg/d
Ibuprofen	600 mg TID (1600–3200 mg)	First attack: 1–2 wk Recurrence: 2–4 wk	600 mg BID or 400 mg TID and then 600 mg/d
Indomethacin	50 mg TID (75–150 mg)	First attack: 1–2 wk Recurrence: 2–4 wk	75–150 mg/d (ie, TID but reduce the daily dose of 25 mg every 1–2 wk)
Nimesulide	200 mg/d	First attack: 1–2 wk Recurrence: 2–4 wk	100–200 mg/d
Prednisone	0.2–0.5 mg · /kg^{-1} · d^{-1}	First attack: 2 wk Recurrence: 2–4 wk	>50 mg: 10 mg/d every 1–2 wk 50–25 mg: 5–10 mg/d every 1–2 wk 25–15 mg: 2.5 mg/day every 2–4 wk <15 mg: 1.0–2.5 mg/day every 2–6 wk
Colchicine	0.5 mg BID 0.5 mg/d (<70 kg)‡	First attack: 3 mo Recurrence: 6–12 mo	Optional for worse recurrent cases; consider tapering over 2–4 wk

Very slow tapering is recommended especially in recurrent cases. Osteoporosis prevention should follow guidelines.[2,53] Higher doses of corticosteroids are not proven to improve the outcome in unselected recurrences but may increase the risk of side effects, further recurrences, and hospitalization.[50–52]

*Proton-pump inhibitors are recommended for aspirin and NSAIDs.

†Every decrease in drug dose should be only done if the patient is asymptomatic and CRP and/or ESR are normal, usually after 1 to 2 weeks or longer for corticosteroids with prednisone <25 mg/d or equivalent. Minimal monitoring for antiinflammatory drugs includes blood cell count and CRP at baseline and weekly until CRP normalizes; for colchicine, consider blood cell count, CRP, transaminases, creatine kinase, and creatinine at baseline and at least after 1 month.

‡For colchicine, an attack dose is not necessary (risk of increased rate of side effects; use the maintenance dose); 0.5 to 0.6 mg/d is the maximum dose for children <5 years of age and elderly >70 years of age. For renal impairment, use 0.5 to 0.6 mg/d if creatinine clearance is 35 to 50 mL/min and 0.5 to 0.6 mg/d every 2 to 3 days if creatinine clearance is 10 to 34 mL/min; it should be avoided if creatinine clearance is <10 mL/min.

tapering is not well established although often proposed in recent publications on pericarditis management.[10,13,45,46,48]

Colchicine

Besides the indication for gout, colchicine is effective for treating serositis in familial Mediterranean fever.[59] Following this successful use, Rodriguez de la Serna[60] first proposed colchicine for recurrent pericarditis in 1987.

A number of small retrospective studies support the use of colchicine for recurrent cases (Table 10)[43,55,61–63]; in addition, in a retrospective multicenter analysis of 119 patients, corticosteroids attenuated the efficacy of colchicine in preventing recurrent pericarditis.[41] On this basis, more for expert consensus than randomized clinical trials, colchicine has been recommended to treat recurrent pericarditis (class I recommendation) and is considered optional but probably useful in acute pericarditis (class IIa recommendation) in the 2004 European guidelines.[2] The guidelines recommend 2 mg/d for 1 to 2 days, followed by a maintenance dose of 1 mg/d.

The stronger evidence base to support the use of the drug, above all for primary or secondary prevention of recurrences, comes from the subsequent first 2 open-label randomized trials in which colchicine at least halved the recurrence rate.[45,46] In the COlchicine for PEricarditis (COPE) trial, colchicine (0.5 to 1 mg daily for 3 months) as an adjunct to conventional treatment significantly decreased the recurrence rate (actuarial rates at 18 months were 10.7% and 32.3%, respectively; $P=0.004$; number needed to treat, 5.0) and symptom persistence at 72 hours (11.7% and 36.7%; $P=0.003$) in 120 patients with a first episode of acute pericarditis. In this study, colchicine was discontinued in 5 patients (8.3%) because of diarrhea.[45]

In the COlchicine for Recurrent Pericarditis (CORE) trial, colchicine (0.5 to 1 mg daily for 6 months) as an adjunct to conventional treatment for recurrent pericarditis significantly decreased the recurrence rate (actuarial rates at 18 months, 24.0% versus 50.6%, respectively; $P=0.022$; number needed to treat, 4.0) and symptom persistence at 72 hours (9.5% versus 31.0%, respectively; $P=0.029$) in 84 patients with recurrent pericarditis.[46] In both CORE and COPE, a maintenance dose of 0.5 mg BID was adopted and reduced to 0.5 mg daily in patients <70 kg; thus, lower doses may be equally efficacious but with a possible lower rate of side effects. Treatment was for 3 months in the first episode (COPE) and 6 months in recurrent pericarditis (CORE).[45,46] In recurrent more severe cases, some authors advocate a longer use of the drug: up to 12 to 24 months after the last recurrence, tailored to the individual patient and with gradual tapering, considering that recurrences have been described after colchicine discontinuation.[12,41,48,61] In the United States, colchicine is usually prescribed as 0.6 mg once or twice a day rather than 0.5 mg once or twice a day.

A sustained antiinflammatory effect may be beneficial in autoimmune (autoreactive) pericarditis, but whether it may delay the clearance of an infectious agent is still unclear in some cases, especially for acute pericarditis. This does not seem to be the case in the COPE trial, but further evidence is needed before routine use can be recommended in the first attack of pericarditis.

Clinicians are often skeptical about the possible utility of colchicine for pericarditis. Common reasons include further recurrences on treatment (colchicine halves, but does not erase all recurrences); failure as monotherapy (efficacy has been demonstrated almost exclusively for combination therapy with an NSAID or corticosteroid); incorrect use in chronic pericardial effusions with normal CRP,[64,65] a condition in which colchicine is generally not efficacious; and drug withdrawal because of gastrointestinal intolerance. Practical tips to improve drug compliance may be using appropriate

Table 10. Main Published Studies on the Use of Colchicine to Treat Recurrent Pericarditis

Study	Year	Design	Patients, n	Maintenance Dose, mg/d	Adjunct to Standard Therapy	Follow-Up, mo	Recurrence, n (%)
Guindo et al[55]	1990	NR	9	1.0	Yes	10–54	0/9 (0.0)
Adler et al[62]	1994	NR	8	1.0	Yes	18–34	0/8 (0.0)
Millaire et al[63]	1994	NR	19	1.0	No	32–44	4/19 (21.0)
Adler et al[61]	1998	NR	51	1.0	Yes	6–128	7/51 (13.7)
Imazio et al[43]	2005	NR	35	1.0	Yes	48–108	3/35 (8.6)
CORE[46]	2005	R	84	0.5–1.0	Yes	8–44	9/42 (21.0)

NR indicates nonrandomized; R, randomized.

weight-adjusted doses and starting with lower doses without a loading dose and then increasing the dose if tolerated. Compared with other drug treatments, colchicine appears to be one of the cheapest (daily cost of $0.23 in the United States and €0.13 in Western Europe).

Follow-Up

Uncomplicated cases require relatively few follow-up visits: at 7 to 10 days to assess response to treatment, at 1 month to check blood tests and CRP, and thereafter only if symptoms recur. However, patients with high-risk features or recurrences require close monitoring according to symptoms and laboratory findings (CRP, echocardiography data).

Key points: (1) Corticosteroid therapy is a risk factor for recurrences and should be restricted to cases with intolerance, contraindication, or true failure of aspirin or NSAIDs, favoring low to moderate doses (ie, prednisone 0.2 to 0.5 $mg \cdot kg^{-1} \cdot d^{-1}$) with very slow tapering; (2) aspirin and NSAIDs are mainstays of treatment and should be used at full antiinflammatory doses (eg, aspirin 2 to 4 g daily, indomethacin 75 to 150 mg daily, and ibuprofen 1600 to 3200 mg daily) until symptoms disappear and CRP completely normalizes; and (3) colchicine (usually 0.5 to 0.6 mg BID for several months or 0.5 to 0.6 mg daily for patients <70 kg) is useful for halving the recurrence rate when used as adjunct to other inflammatory drugs.

Management of "Refractory" Cases and Long-Term Outcome of Idiopathic Recurrent Pericarditis

Cases that recur after steroid tapering (very common) should not be considered refractory; this definition should apply to those cases that require unacceptably high long-term doses of corticosteroids to be controlled (eg, prednisone >25 mg daily). They probably represent <5% of recurrent cases. In this situation, several drugs (azathioprine, cyclophosphamide, cyclosporine, methotrexate, hydroxychloroquine, intravenous immunoglobulin, anakinra) have been used[21,65,66]; azathioprine is the preferred choice if tolerated[2] (at the common dosage of 2 to 3 $mg \cdot kg^{-1} \cdot d^{-1}$), but it should be acknowledged that strong evidence-based data are lacking. Less toxic and less expensive drugs (eg, azathioprine or methotrexate) should be preferred, with the therapy tailored to the individual patient and physician experience and, importantly, with informed consent.[66] In many cases, combined triple therapy with a corticosteroid, aspirin or an NSAID, plus colchicine

may be considered in more difficult cases. This approach is comparable to that adopted in ischemic heart diseases in which a combination of drugs (ie, nitrates, β-blockers, calcium channel blockers) is prescribed to control symptoms in more difficult cases.

Long-term outcome of idiopathic recurrent pericarditis has been considered controversial with a fear of possible evolution to constrictive pericarditis. Nevertheless, a systematic review of all publications from 1966 to 2006 including a total of 230 patients with idiopathic recurrent pericarditis followed up for 61 months has shown that the overall prognosis is excellent and complications are uncommon.[12] Constrictive pericarditis was never reported in these patients despite numerous recurrences, and the overall risk is lower than in idiopathic acute pericarditis (≈1%). Thus, it is important to reassure patients on their prognosis, explaining the nature of the disease and its likely course. Drug treatment should take into account this good outcome to avoid more toxic agents.[12]

Key points: (1) Refractory cases include patients who require unacceptably high long-term doses of corticosteroids for control (eg, prednisone >25 mg daily); (2) the first step is considering the combination of aspirin or an NSAID plus a corticosteroid and colchicine; (3) other therapies are based on less solid evidence: (4) less toxic and less expensive drugs (eg, azathioprine or methotrexate) should be preferred, with the therapy tailored to the individual patient and physician experience; and (5) the overall long-term prognosis of idiopathic recurrent cases is very good without risk of constriction.

Role of Pericardiectomy, Pericardial Window, and Other Interventional Techniques

The 2004 European Society of Cardiology guidelines[2] gave a class IIa recommendation to pericardiectomy for frequent and highly symptomatic recurrences resistant to medical treatment. Other reported indications include repeated recurrences with cardiac tamponade, as well as evidence of serious steroid toxicity. Although surgical experiences are not always concordant,[42,67,68] pericardiectomy is generally considered a therapeutic option of doubtful efficacy in recurrent idiopathic pericarditis and should be considered only in exceptional cases (Table 8). We agree with these conclusions; moreover, the largest retrospective survey with favorable results for pericardiectomy[68] has several limitations. In this retrospective analysis of the records of 60 patients who underwent pericardiectomy over a 10-year period (1980 to 1990), both

patients with and without constriction were included (60% with constriction, 40% with effusive disease). Only 10% of patients had pain as the primary symptom necessitating intervention, and a specific analysis of recurrent symptoms in patients with effusion and patients with constriction is not available.

There have been cases in which, for unknown reasons, pericardial removal has ended the syndrome, but there are also many cases in which the syndrome either is unchanged or returns postoperatively after a period of improvement or even disappearance. In our experience, this frequent "lucent period" may last from as little as 9 days to 6 months and is probably responsible for early reports of successful surgery (ie, the follow-up was inadequate).

At present, indications for pericardiectomy in recurrent pericarditis are based on expert opinion more than proven beneficial effects. On the other hand, the benefits of pericardiectomy are well established for permanent constrictive pericarditis.

All the material is still anecdotal or observational. For patients with recurrent, particularly incessant, pericarditis resistant to all medical options, there should be an appropriately designed randomized controlled study, which will probably be rather difficult to undertake. Nevertheless, such an investigation might establish the actual frequency of success with pericardiectomy and may delineate the characteristics of patients who would benefit from it.

Another important and controversial issue is the timing of pericardiectomy when pericardial constriction is diagnosed. Transient constriction has been reported in 9% of cases with effusive acute idiopathic pericarditis in which features of constriction were recorded in the subacute phase of pericarditis resolution when pericardial effusion had disappeared or was minimal.[69]

A subsequent review by the Mayo Clinic of 212 patients with echocardiographic findings of constrictive pericarditis recorded 36 patients (17%) with follow-up studies showing resolution after medical therapy at an interval ranging from 2 months to 2 years. Treatment included NSAIDs, a steroid, antibiotics, chemotherapy, and angiotensin-converting enzyme inhibitors plus diuretics. Five patients had resolution of constriction without any specific therapy.[70]

Some patients may go through a transient phase of cardiac constriction at the end of the effusive period of pericarditis. Thus, in the absence of evidence that the condition is permanent and chronic, patients with newly diagnosed constrictive pericarditis who are hemodynamically stable may be given a trial of conservative management (antiinflammatory therapy with NSAIDs and/or corticosteroids) for 2 to 3 months before pericardiectomy is recommended.[70]

Less invasive options for recurrent symptomatic effusions are derived mainly from experience in the management of neoplastic pericardial effusions and include prolonged catheter drainage and the creation of the so-called "pericardial window."[71–76] In patients with cardiac tamponade or significant effusion, initial relief can easily be obtained with percutaneous pericardiocentesis followed sometimes by drainage with an indwelling catheter. Prolonged catheter drainage is an effective means of preventing fluid reaccumu-

lation, although the mechanism by which this occurs is probably related more to the obliteration of the pericardial space after inflammation provoked by the catheter than to fluid drainage itself. This approach was successful in >70% of cases, although the duration of effusion control is often not reported. Catheter drainage may be required for several days, and the catheter should not be removed until drainage is <20 to 30 mL/24 h.[77]Alternative strategies include surgical decompression of the pericardium (also known as pericardiotomy, pericardiostomy, and "window" pericardiectomy) by either conventional heart surgery or video-assisted thoracoscopy (Figure 4) with a possible lower incidence of effusion recurrence compared with pericardiocentesis and prolonged catheter drainage.[72,74]

Balloon pericardiotomy is an alternative to surgical creation of a pericardial window. The technique has been especially adopted for patients with malignancies and reduced life expectancy to improve the quality of life. It involves inserting a deflated single catheter or double balloon catheters into the pericardial space using a subxiphoid approach under fluoroscopic guidance. Although successful in preventing recurrence in >80% of cases, stretching of the pericardium is often painful, so appropriate analgesia is recommended. Reported complications include fever (up to 28%), pneumothorax or need for a chest tube (up to 20%), and rarely bleeding from a pericardial blood vessel.[75,76]

Key points: (1) Pericardiectomy is recommended for persistent constrictive pericarditis; (2) patients with newly diagnosed constrictive pericarditis who are hemodynamically stable may be given a trial of conservative management (antiinflammatory therapy with NSAIDs and/or corticosteroids) for 2 to 3 months before pericardiectomy is recommended; and (3) pericardiectomy is almost never indicated for recurrent pericarditis except for patients with repeated recurrences with cardiac tamponade and those with evidence of serious steroid toxicity, although other approaches may be equally effective and less invasive (eg, pericardial window by either conventional heart surgery or video-assisted thoracoscopy).

Management of Chronic Idiopathic Pericardial Effusion

A chronic idiopathic pericardial effusion can be defined as a collection of pericardial fluid that persists for >3 months and has no apparent cause; large effusions have a theoretical risk of progression to cardiac tamponade (up to one third).[78] Thus, some authors have advocated the need for pericardiectomy for such cases whenever a large effusion recurs after pericardiocentesis. Because drainage is relatively safe and easy in some cases with guided pericardiocentesis, some authors have advocated drainage for large effusions that are stable after several weeks (eg, 6 to 8 weeks), especially when there are signs of right-sided collapse to prevent the possible decompensation of the effusion after additional events (eg, pericarditis, bleeding after chest trauma).[18] Careful monitoring may be sufficient in many cases, but the course may be unpredictable with either partial regression of the effusion or evolution to cardiac tamponade. Unfortunately, there are no proven effective medical therapies to reduce an isolated
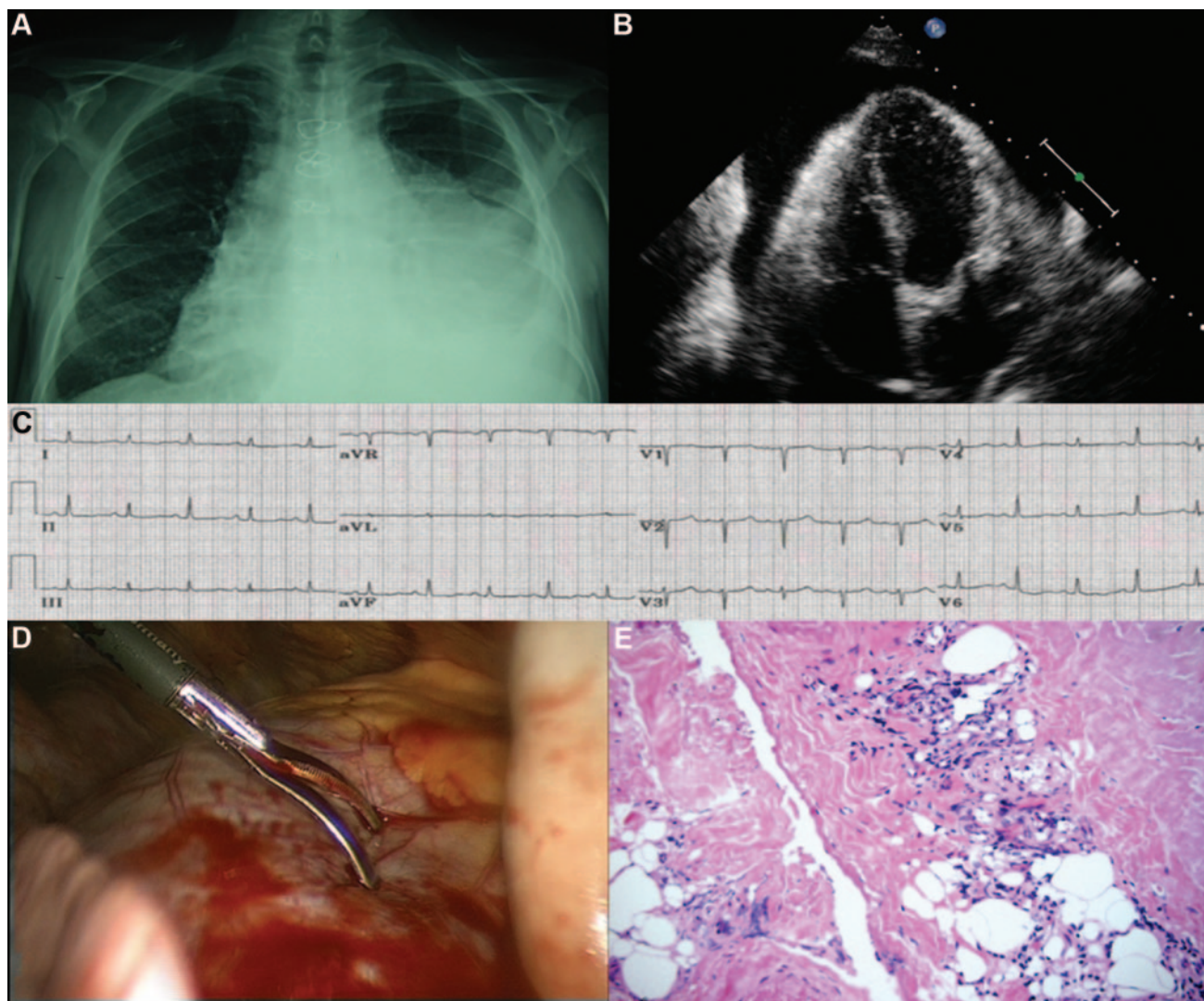
Figure 4. A case of recurrent pleuropericardial effusion after postpericardiotomy syndrome. A, Enlarged cardiac silhouette on chest x-ray caused by pleuropericardial effusion. B, Large pericardial effusion on echocardiography. C, Sinus tachycardia, low voltage, and electric alternans are evident on the ECG strip. D, View of the inflamed parietal pericardium on video-assisted thoracoscopy after pericardiocentesis. E, Nonspecific findings of chronic inflammation and fibrosis on histology.

effusion; in the absence of inflammation, NSAIDs, colchicine, and corticosteroids are generally not efficacious.[64,65] Pericardiocentesis alone may frequently resolve large effusions, but recurrences are also common,[78] and pericardiectomy or less invasive options (ie, pericardial window) should be considered whenever fluid reaccumulates, the effusion is loculated, or biopsy material is required. The need for intervention in all cases remains controversial and requires the understanding of the possible benefits but also risks (ie, possible trigger of recurrences and a new iatrogenic pericardial disease),[17,79] as well as informed consent. A simplified approach for pericardial effusion management is reported in Figure 2.

Key points: (1) Management is guided by the size and hemodynamic importance of the effusion, the presence of inflammation (ie, pericarditis), and associated medical conditions; (2) an inflammatory effusion is managed like pericarditis, whereas a moderate to severe effusion without inflammatory signs requires the exclusion of a malignancy or

other medical condition as a possible cause to treat; and (3) a true isolated effusion may not require a specific treatment if the patient is asymptomatic, but large ones have a theoretical risk of progression to cardiac tamponade (up to one third).

Future Perspectives

Further research is needed to evaluate the etiology of recurrent pericarditis, especially its relationship with autoimmune or autoinflammatory diseases, and a possible therapeutical role of interleukin-1 antagonists.[21] Additional investigations should evaluate the impact and clinical application of pericardioscopy to improve standard diagnostic capabilities and to develop tailored treatments. Ongoing and future randomized clinical trials, registries, and updated guidelines (ie, first American Heart Association/American College of Cardiology guidelines and new European guidelines) are needed to improve the clinical management of pericardial diseases.

Conclusions

Limited evidence-based data are available to guide the management of pericardial diseases. Diagnostic efforts are worthy if they affect subsequent treatments and prognosis, and a targeted etiologic search should be directed to the commonest causes on the basis of clinical background, epidemiological issues, or specific presentations. Treatment should be targeted to the cause when available, favoring aspirin or NSAIDs for idiopathic and viral forms. Corticosteroid use should be restricted, and therapeutic schemes starting with lower doses may be equally or more effective than high doses, reducing side effects. Colchicine may be a useful drug to prevent recurrences in inflammatory pericardial syndromes. Pericardiocentesis is indicated for cardiac tamponade; high suspicion of tuberculous, purulent, or neoplastic pericarditis; and large or symptomatic effusions refractory to medical treatment. Pericardiectomy should be considered mainly for persistent chronic constrictive pericarditis.

Disclosures

None.

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