

Good Prognosis for Pericarditis With and Without Myocardial Involvement

Results From a Multicenter, Prospective Cohort Study

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Background—The natural history of myopericarditis/perimyocarditis is poorly known, and recently published studies have presented contrasting data on their outcomes. The aim of the present article is to assess the prognosis of myopericarditis/perimyocarditis in a multicenter, prospective cohort study.

Methods and Results—A total of 486 patients (median age, 39 years; range, 18–83 years; 300 men) with acute pericarditis or a myopericardial inflammatory syndrome (myopericarditis/perimyocarditis; 85% idiopathic, 11% connective tissue disease or inflammatory bowel disease, 5% infective) were prospectively evaluated from January 2007 to December 2011. The diagnosis of acute pericarditis was based on the presence of 2 of 4 clinical criteria (chest pain, pericardial rubs, widespread ST-segment elevation or PR depression, and new or worsening pericardial effusion). Myopericardial inflammatory involvement was suspected with atypical ECG changes for pericarditis, arrhythmias, and cardiac troponin elevation or new or worsening ventricular dysfunction on echocardiography and confirmed by cardiac magnetic resonance. After a median follow-up of 36 months, normalization of left ventricular function was achieved in >90% of patients with myopericarditis/perimyocarditis. No deaths were recorded, as well as evolution to heart failure or symptomatic left ventricular dysfunction. Recurrences (mainly as recurrent pericarditis) were the most common complication during follow-up and were recorded more frequently in patients with acute pericarditis (32%) than in those with myopericarditis (11%) or perimyocarditis (12%; $P<0.001$). Troponin elevation was not associated with an increase in complications.

Conclusions—The outcome of myopericardial inflammatory syndromes is good. Unlike acute coronary syndromes, troponin elevation is not a negative prognostic marker in this setting. (*Circulation*. 2013;128:42-49.)

Key Words: myopericarditis ■ pericarditis ■ perimyocarditis ■ prognosis

Myocarditis and pericarditis may share common etiologic agents, either infectious (mainly cardiotropic viruses) or noninfectious (ie, immune mediated such as systemic inflammatory diseases, vaccine-related).^{1,2} Thus, in clinical practice, a spectrum of myopericardial syndromes can be encountered, ranging from pure pericarditis to increasing degrees of inflammatory myocardial involvement (myopericarditis and perimyocarditis) to pure myocarditis.¹⁻⁴ The term myopericarditis has been designated to indicate a primarily pericarditic syndrome, whereas perimyocarditis refers to a primarily myocarditic syndrome.^{1,2} However, in the literature, these terms are often confused and used interchangeably.

Clinical Perspective on p 49

Despite a large amount of data published on myopericarditis related to smallpox vaccination as a consequence of the recent US federal government vaccination program for military forces,⁵⁻⁷ few data are available on the prognosis of sporadic cases not related to vaccination.⁸⁻¹¹ Moreover, published outcome results presented contrasting data, and diagnostic evaluation has been heterogeneous (eg, based on simple clinical criteria and troponin elevation) and did not rely on the confirmatory findings of cardiac magnetic resonance (CMR).⁸⁻¹¹

The aims of this work are to evaluate the clinical presentation and outcome of acute myopericarditis/perimyocarditis

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confirmed by CMR and to compare these features with those of simple acute pericarditis in a prospective, multicenter study including all consecutive cases of acute inflammatory pericardial syndromes (acute pericarditis, myopericarditis, and perimyocarditis).

Methods

Participants

Between January 2007 and December 2011, all consecutive patients with pericardial inflammatory syndromes (acute pericarditis, myopericarditis, and perimyocarditis) were prospectively enrolled in 3 Italian referral centers for pericardial diseases (Torino, Bergamo, and Modena). The protocol was designed prospectively before data collection. Patients with pure acute myocarditis were excluded.

All patients provided informed consent. The investigation conforms to the principles outlined in the Declaration of Helsinki and local legal requirements.

Diagnostic Criteria

A diagnosis of acute pericarditis was based on the presence of at least 2 of the following clinical criteria: pericarditis chest pain, pericardial friction rub, widespread ST-segment elevation or PR depression on the ECG, and new or worsening pericardial effusion.¹² A clinical diagnosis of myopericarditis was made in patients with a definite diagnosis of acute pericarditis and elevation of cardiac markers of injury (troponin I or T, creatine kinase-MB fraction) without new onset of focal or diffuse depressed left ventricular (LV) function by echocardiography or CMR.^{4,12} Perimyocarditis was diagnosed in patients with clinical criteria for acute pericarditis, elevation of cardiac markers of injury, and evidence of new onset of focal or diffuse depressed LV function by echocardiography or CMR. The rationale for these diagnostic criteria is that pure pericardial or predominant pericardial inflammatory involvement is not characterized by significant impairment of myocardial function and that, on the contrary, focal or diffuse abnormalities of ventricular wall motion or function imply a substantial myocardial inflammatory involvement.¹³

Myocardial inflammatory involvement was clinically suspected in cases of atypical ECG changes for pericarditis (ie, localized ECG changes, abnormal ST-segment or T-wave changes or evolution, new Q waves), arrhythmias, cardiac troponin elevation, or new or worsening ventricular dysfunction on echocardiography and was confirmed by CMR.^{14,15} CMR imaging included T2-weighted imaging for the assessment of edema, T1-weighted imaging before and after contrast administration for the evaluation of hyperemia, and the assessment of late gadolinium enhancement. CMR results were considered to be consistent with the diagnosis of myocardial inflammatory involvement if 2 of 3 CMR techniques were positive.^{14,15}

Diagnostic Workup

Each patient was assessed by clinical evaluation, routine blood chemistry (including blood count, markers of inflammation and myocardial lesion, creatinine, transaminases), and additional tests aimed at the identification of the origin of disease based on the presentation features. All patients were submitted to echocardiography at presentation. CMR was performed within 2 weeks from symptom onset when myocardial inflammatory involvement was suspected. Pericardial effusion was assessed in a semiquantitative way by 2-dimensional echocardiography as mild (echo-free space of <10 mm during diastole), moderate (10–20 mm), and large (>20 mm). To facilitate the correct definition of the effusion size and to allow follow-up studies, the largest size, the site, and the view were recorded.¹²

Cardiac tamponade was diagnosed by the combination of clinical features (pulsus paradoxus, elevated jugular venous pressure, and tachycardia) and echocardiographic data (pericardial effusion with echocardiographic signs of tamponade).

Coronary artery disease was excluded in patients with coronary risk factors or dubious presentation with a need for differential

diagnosis with acute coronary syndromes by means of coronary angiography at initial presentation. Subsequent CMR was also used to rule out possible cases of acute myocardial infarction necrosis but without significant coronary artery disease.¹⁶

Histopathological confirmation of the presence of concomitant inflammatory myocardial involvement requires an endomyocardial biopsy (EMB), but this is usually not performed in patients with no or mild LV systolic dysfunction and no symptoms of heart failure according to the indications for EMB issued by the American Heart Association/American College of Cardiology/European Society of Cardiology in a scientific statement.¹⁷ In this study, the following indications were considered for EMB: subacute or acute symptoms of heart failure refractory to standard management, substantial worsening of the ejection fraction despite optimized pharmacological treatment, development of hemodynamically significant arrhythmias, heart failure with concurrent rash, fever or peripheral eosinophilia, history of collagen vascular disease, or suspicion of possible giant-cell myocarditis (young age, new subacute heart failure, or progressive arrhythmias without an apparent cause).

Treatment

Aspirin or a nonsteroidal anti-inflammatory drug, generally ibuprofen, was considered the mainstay of treatment in patients with an established diagnosis of acute pericarditis or myopericarditis/perimyocarditis. Aspirin was the first-choice drug and was given at a dose of 750 to 1000 mg orally every 6 or 8 hours for 7 to 10 days with gradual tapering over 2 to 3 weeks. Ibuprofen was prescribed at the attack dose of 600 mg 3 times a day and then tapered in 2 to 3 weeks. In animal models of myocarditis, nonsteroidal anti-inflammatory drugs are not effective and may actually enhance the myocarditic process and increase mortality.^{18,19} Thus, reducing the dose of aspirin to 500 mg every 8 to 12 hours was considered for patients with myopericarditis/perimyocarditis.⁴ Corticosteroids were considered the second choice for patients with contraindications to or intolerance of aspirin and nonsteroidal anti-inflammatory drugs. In every case, gastroprotection with a proton pump inhibitor was prescribed. Colchicine use (0.5 mg twice daily for 3 months or 0.5 mg once daily in patients <70 kg) was optional for patients with pure acute pericarditis and was limited in patients with myopericarditis and perimyocarditis because of the lack of clinical trials or studies to support this indication.²⁰

Clinical Measures and Follow-Up

The relative frequency of myopericarditis/perimyocarditis was assessed among patients with acute pericardial inflammatory syndromes. Main clinical characteristics and treatments were recorded for all cases. During follow-up, clinical evaluation, ECG, and routine blood chemistry were performed at 1, 6, and 12 months and then every year if the course was uncomplicated. Treadmill testing was performed at 6 months for patients with myopericarditis/perimyocarditis. All adverse events were recorded, including recurrent pain, relapses (either of pericarditis or other inflammatory myocardial syndrome), cardiac tamponade, constrictive pericarditis, residual LV dysfunction, heart failure, and overall and cardiovascular mortality.

Statistical Analysis

Continuous data are reported as mean±SD. Patients groups were compared by use of the *t* test for continuous variables and χ^2 analysis for categorical variables. Time to event distributions were estimated with the Kaplan-Meier method and compared by use of the log-rank test. A value of *P*<0.05 was considered to show statistical significance. Analyses were performed with SPSS version 13.0 (SPSS, Chicago, IL).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

During the study period, 486 cases of inflammatory myopericardial syndromes were recorded (346 cases of acute pericarditis, 114 cases of myopericarditis, and 26 cases of perimyocarditis; Figure 1).

Clinical Presentation and Baseline Features

Detailed baseline features are reported in Table 1. Patients with inflammatory myocardial involvement were younger and more frequently were male compared with those with acute pericarditis ($P<0.001$). Moreover, the following features were more commonly associated with acute pericarditis: pericardial rubs on physical examination and pericardial effusion on echocardiography ($P<0.01$ for both). On the contrary, heart failure signs and symptoms and cardiac arrhythmias were recorded with increasing frequency in patients with myocardial inflammatory involvement (myopericarditis/perimyocarditis). Left ventricular ejection fraction was only mildly reduced in patients with perimyocarditis ($44\pm 9\%$). White blood cells and C-reactive protein elevations were more common in patients with acute pericarditis than in patients with myopericarditis and perimyocarditis ($P<0.001$), whereas markers of myocardial lesions (cardiac troponin I and creatine kinase-MB) were overlapping in patients with myopericarditis and perimyocarditis. CMR was performed in 255 cases: all patients with troponin elevation ($n=140$) and patients with a clinical suspicion of inflammatory myocardial involvement on the basis of clinical presentation (atypical ECG changes for pericarditis, arrhythmias, and cardiac troponin elevation or new or worsening ventricular dysfunction on echocardiography). CMR data on myocardial involvement included edema (T2-weighted imaging)/hyperemia in 93.0% of patients with myopericarditis and 92.3% of patients with perimyocarditis; late gadolinium enhancement was detected in all cases. In patients with a final diagnosis of pericarditis who had CMR performed for a clinical suspicion of myocardial involvement ($n=115$), pericardial abnormal T2-weighted imaging

(edema and hyperemia) and late gadolinium enhancement were recorded in 104 of 115 patients (90.4%).

The initial presentation mimicked a ST-segment-elevation myocardial infarction in 87 of 114 patients (76.3%) with myopericarditis, in 20 of 26 patients (76.9%) with perimyocarditis, and in only 8 of 346 patients (2.3%; $P<0.001$) with simple acute pericarditis. All these patients underwent coronary angiography that excluded the presence of significant coronary artery disease. Acute myocardial infarction in the absence of significant coronary artery disease was also excluded by CMR.

The origin of disease (Table 2) was similar in different myopericardial subgroups (idiopathic in 84%–85%, infectious in 4%–5%, and connective tissue disease or inflammatory bowel disease in 10%–12%).

Patient Management

Aspirin or ibuprofen was prescribed as anti-inflammatory therapy in 95% of patients with acute pericarditis, 89% of those with myopericarditis, and 18% of patients with perimyocarditis. Corticosteroids were prescribed in 6% of patients with acute pericarditis and 4 to 6% of patients with myopericarditis/perimyocarditis. Colchicine was added to anti-inflammatory therapies in 55% of patients with acute pericarditis, 18% of patients with myopericarditis, and 15% of those with perimyocarditis. In patients with myocardial inflammatory involvement, a β -blocker (bisoprolol 1.25 mg and then increased to reach a heart rate of 55–60 bpm at rest) was prescribed in 49% to 77% of patients, and an angiotensin-converting enzyme inhibitor (ramipril 1.25 mg as the starting dose and then uptitrated as tolerated) was prescribed in 25% to 58% of patients with myopericarditis/perimyocarditis with evidence of LV dysfunction (Table 2). Patients with a clinical diagnosis of myopericardial inflammatory syndromes were temporarily excluded from competitive, amateur, or leisure-time sport activity. This recommendation was independent of age, sex, degree of symptom, and concurrent medical therapy. After

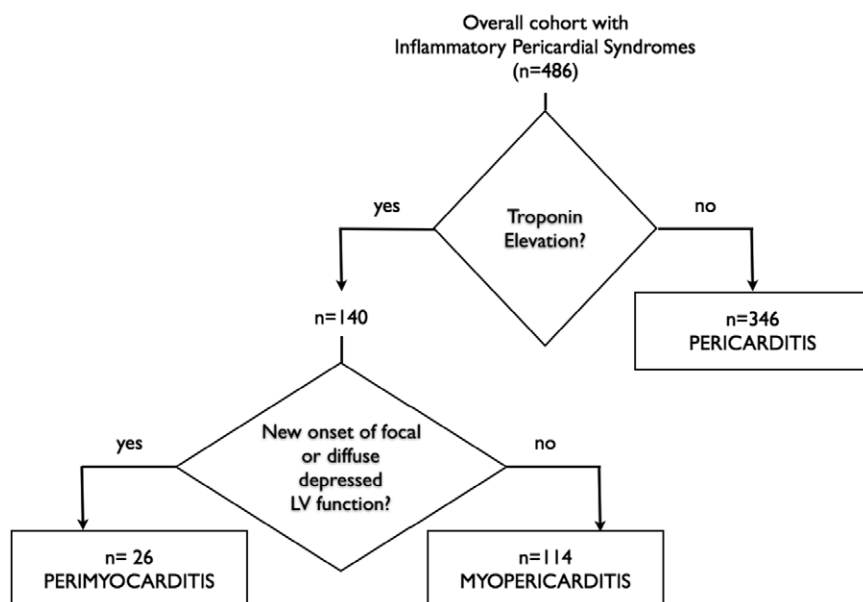


Figure 1. Study population of pericardial inflammatory syndromes. LV indicates left ventricular.

Table 1. Demographics and Clinical Presentation of Patients With Inflammatory Myopericardial Syndromes

Feature	Pericarditis (n=346)	Myopericarditis (n=114)	Perimyocarditis (n=26)	P Value*
Age, median (IQR), y	41.0 (22.0)	29.0 (14.5)	24.0 (17.3)	<0.001
Male sex, n (%)	189 (54.6)	89 (78.1)	22 (84.6)	<0.001
Recent febrile syndrome, n (%)	237 (68.5)	69 (60.5)	18 (69.2)	0.212
Chest pain, n (%)	336 (97.1)	112 (98.2)	23 (88.5)	0.909
Pericardial rub, n (%)	83 (24.0)	15 (13.2)	2 (7.7)	0.005
ECG changes, n (%)	190 (55.0)	100 (88.2)	20 (76.9)	<0.001
Supraventricular arrhythmias, n (%)	20 (5.8)	10 (8.8)	5 (19.2)	0.09
Ventricular arrhythmias, n (%)	1 (0.3)	5 (4.4)	2 (7.7)	<0.001
Pericardial effusion, n (%)	254 (73.4)	30 (26.3)	10 (38.5)	<0.001
AV block, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NS
HF symptoms/signs, n (%)	0 (0.0)	4 (3.5)	3 (11.5)	<0.001
EF, mean (SD), %	58.9±3.6	58.1±4.2	44.0±9.0	By definition
WBC elevation, n (%)	249 (72.0)	31 (27.1)	6 (23.1)	<0.001
CRP, mg/dL	7.7±4.7	5.3±4.6	3.2±2.1	<0.001
cTnI, ng/mL†	0.0 (0.0–0.0)	7.2 (0.5–34.7)	9.4 (0.5–44.0)	By definition
CK-MB, ng/mL†	0.0 (0.0–0.0)	24.0 (12–52)	34.2 (17–83)	By definition

AV indicates atrioventricular; CK-MB, creatine kinase-MB; CRP, C-reactive protein; cTnI, cardiac troponin I; ECG changes, ST-segment elevation or PR depression; EF, ejection fraction; HF, heart failure; IQR, interquartile range; and WBC, white blood cell.

*Comparison of acute pericarditis with myopericarditis and perimyocarditis.

†Median (range).

resolution of the clinical picture (at least 3 months after the onset of the disease for simple acute pericarditis and 6 months for those with myopericarditis/perimyocarditis), clinical reassessment was performed before the patients resumed physical activity beyond sedentary life and competitive sports.^{21–23}

Outcome and Follow-Up Data

After a median follow-up of 36 months (range, 6–66 months), no cases of deaths or heart failure were recorded (Table 3). A residual mild LV dysfunction was recorded in 8% of the patients with myopericarditis and 15% of the patients with

perimyocarditis (*P*<0.001). An increase in mean LV ejection fraction was recorded in all subgroups at 12 months (Figure 2).

Recurrences were more common in acute pericarditis (31.8%) than in myopericarditis (10.5%) or perimyocarditis (11.5%; *P*<0.001). In >95%, recurrences of pericarditis and myopericarditis/perimyocarditis were manifested as relapses of pericarditis and only rarely as myopericarditis or perimyocarditis in patients with either previous simple pericarditis or myopericarditis/perimyocarditis. Recurrence-free survival was similar in patients with myopericarditis and perimyocarditis (Figure 3). No cases of cardiac tamponade

Table 2. Causes and Treatments of Different Inflammatory Myopericardial Syndromes

Feature	Pericarditis (n=346), n (%)	Myopericarditis (n=114), n (%)	Perimyocarditis (n=26), n (%)	All (n=486), n (%)
Idiopathic*	294 (85.0)	96 (84.2)	22 (84.6)	412 (84.8)
Infectious†	16 (4.6)	5 (4.4)	1 (3.9)	22 (4.5)
Connective tissue disease/ inflammatory bowel disease	36 (10.4)	13 (11.4)	3 (11.5)	52 (10.7)
Aspirin/NSAID	327 (94.5)	101 (88.6)	5 (17.6)	433 (89.1)
Corticosteroids	19 (5.5)	7 (6.1)	1 (3.8)	27 (5.6)
Colchicine	191 (55.2)	21 (18.4)	4 (15.4)	216 (44.4)
β-Blockers	2 (0.6)	56 (49.1)	20 (76.9)	78 (16.1)
ACE inhibitor	2 (0.6)	28 (24.6)	15 (57.7)	45 (9.3)

ACE indicates angiotensin-converting enzyme; and NSAID, nonsteroidal anti-inflammatory drug.

*Without a known specific origin after diagnostic workup.

†Including known viral and bacterial (tuberculosis) causes. Detailed infectious causes included the following: pericarditis: coxsackievirus in 4 cases (25.0%), Epstein-Barr virus in 3 cases (18.75%), parvovirus in 3 cases (18.75%), adenovirus in 3 cases (18.75%), cytomegalovirus in 2 cases (12.5%), and influenza in 1 case (6.25%); myopericarditis: coxsackievirus in 3 cases (60.0%) and parvovirus in 2 cases (40.0%); and perimyocarditis: parvovirus in 1 case (100%). Percentages are reported according to diagnosed infectious cases in each group: acute pericarditis, myopericarditis, and perimyocarditis.

Table 3. Follow-Up Data

Feature	Pericarditis (n=346), n (%)	Myopericarditis (n=114), n (%)	Perimyocarditis (n=26), n (%)	PValue*
Recurrence	110 (31.8)	12 (10.5)	3 (11.5)	<0.001
Cardiac tamponade	8 (2.3)	0 (0.0)	0 (0.0)	NS
Constrictive pericarditis	2 (0.6)	1 (0.9)	0 (0.0)	NS
Heart failure	0 (0.0)	0 (0.0)	0 (0.0)	NS
LV dysfunction (EF <55%) at 12 mo	4 (1.1)	9 (7.9)	4 (15.4)	<0.001
All-cause death	0 (0.0)	0 (0.0)	0 (0.0)	NS

EF indicates ejection fraction; and LV, left ventricular. Median follow-up was 36 months (range, 6 to 88 months). Recurrences were manifested as recurrent pericarditis in >90% of cases.

*Comparison of acute pericarditis with myopericarditis and perimyocarditis.

were recorded in patients with myopericarditis and perimyocarditis, and 1 case of constrictive pericarditis was recorded in patients with myopericarditis. Troponin elevation was not associated with an increase in complications during follow-up.

Discussion

Relative Frequency of Myopericarditis/Perimyocarditis

This prospective cohort study provides evidence for the first time of the relative frequency of myopericardial inflammatory syndromes in adults. Myocardial involvement is relatively frequent and was recorded in one third of patients with acute pericardial inflammatory syndromes. Myopericarditis is more frequent than perimyocarditis (23.5% versus 5.4%, respectively, of all patients with acute pericardial inflammatory syndromes; $P<0.001$).

Peculiar Features of Myopericarditis/Perimyocarditis

Patients with myocardial involvement are younger than those with simple acute pericarditis; moreover, more patients with

myopericarditis/perimyocarditis are male, as already reported in previous reports,^{4,9-11} which suggests the possibility that hormonal factors may play a role in the etiopathogenesis of myopericardial inflammatory syndromes.

This study also underlines specific peculiarities of the clinical presentation. The presence of pericardial rubs and pericardial effusion is usually associated with less myocardial involvement, whereas the presence of ST and PR abnormalities suggests an increased likelihood of myocardial involvement.

ST-segment elevation or PR depression, usually considered hallmarks of acute pericarditis, can be recorded in only 50% to 60% of patients with simple acute pericarditis. These ECG changes reflect the extent of subepicardial involvement because the pericardium is electrically silent, and they are especially suggestive of concomitant myocardial inflammatory involvement rather than simple acute pericarditis. Myocardial involvement is often associated with ST-segment elevation (>75% of cases), with an initial presentation that may simulate an acute coronary syndrome in a substantial number of patients ($\approx 75\%$). In addition, arrhythmias are peculiar of myocardial inflammatory involvement and should alert

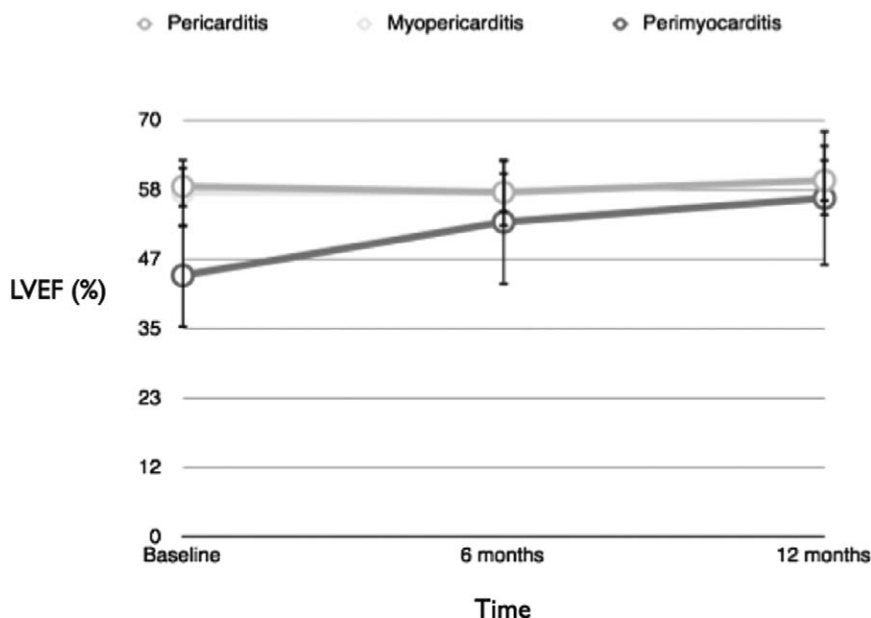


Figure 2. Evolution of mean values of left ventricular ejection fraction (LVEF) in study subgroups from baseline to 12 months. Values are mean \pm SD.

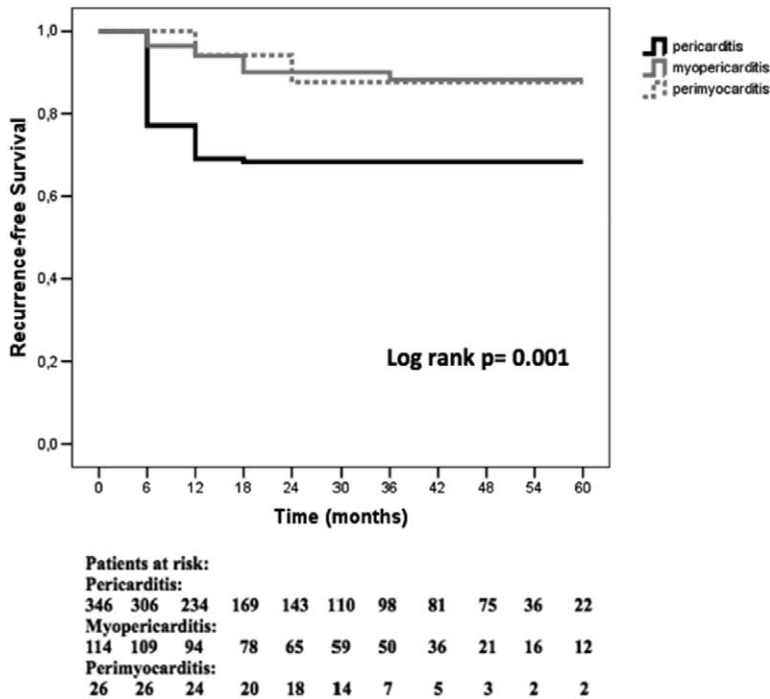


Figure 3. Recurrence-free survival in different subgroups of inflammatory myopericardial syndromes.

the clinician when recorded in a patient with presumed acute pericarditis.

Another significant issue is related to biomarker expression in different types of inflammatory myopericardial syndromes. Elevation of C-reactive protein is recorded in all subgroups, but higher levels are found in patients with simple pericarditis compared with those with myopericarditis/perimyocarditis. Cardiac troponin elevation is roughly related to the extent of myocardial involvement (median, 9.4 ng/mL; range, 1.0–44.0 ng/mL in perimyocarditis; median, 7.2 ng/mL; range, 1.0–34.7 ng/mL in myopericarditis) and was largely overlapping in the 2 syndromes.

Origin and Therapeutic Issues

The origin is similar in different subgroups, regardless of the entity of myocardial inflammatory involvement. Most cases remain idiopathic with a conventional diagnostic approach; these results are consistent with previously published data.^{4,10,11}

Empirical anti-inflammatory therapies with aspirin or a nonsteroidal anti-inflammatory drug were adopted mainly for patients with prevalent pericardial involvement (>85% of cases), whereas reduced doses were considered in patients with perimyocarditis because of the fear of possible negative effects of these therapies in myocarditis. Additionally, corticosteroids should probably not be used in this setting as first-line therapy; we have limited data on the use of colchicine because patients with myocardial involvement were excluded in previous clinical trials of the treatment and prevention of pericarditis.²⁰

Prognostic Issues

Unlike acute coronary syndromes, cardiac troponin elevation was not a negative prognostic marker in myopericarditis/

perimyocarditis, and the degree of troponin elevation did not correlate with the likelihood of subsequent recovery. Most of these patients had a normal or nearly normal LV function at presentation and generally improved during a 12-month follow-up, with normalization of LV function in >90% of patients with myopericarditis and >80% of patients with perimyocarditis. No deaths correlated to pericardial or myocardial involvement were recorded during follow-up. These data are reassuring and confirm preliminary findings in pediatric populations and adults (Table 4).^{4,10,11} Recurrences were more common with prevalent pericardial involvement and generally were recurrent pericarditis.

Clinical Implications

Some involvement of the myocardium should be suspected in any young patient with chest pain, ST-segment elevation at presentation, and cardiac arrhythmia (sustained or not, either supraventricular or ventricular; Table 1), whereas rubs and pericardial effusion are more suggestive of isolated pericardial involvement. In the setting of myopericarditis/perimyocarditis, the differential diagnosis should especially include acute coronary syndromes, and up to 3 of 4 of these patients may have a presentation that may simulate an acute coronary syndrome. Coronary angiography is necessary to rule out and promptly treat acute myocardial infarction with ST-segment elevation. For patients without evidence of coronary artery disease or a pseudoinfarct presentation, CMR is a useful noninvasive diagnostic tool for the clinical diagnosis of myopericardial inflammatory syndromes and to rule out acute myocardial infarction with normal coronary arteries.^{16,24–28} In these cases, the diagnostic utility of EMB is clearly reduced for clinicians. Although EMB may establish a definite diagnosis, it is difficult to justify its clinical utility in patients with myopericarditis/perimyocarditis

Table 4. Major Clinical Studies on the Outcome of Myopericarditis and Perimyocarditis

Study	Year	Setting	Peak Troponin I (Range), ng/ml	Follow-Up	Mortality
Imazio et al ⁸	2008	Myopericarditis/adult (40 patients)	7.7±6.7 (1.5–22.5)	12 mo	0% Normalization of parameters in 97.5%
Machado et al ⁹	2010	Myopericarditis/adult (14 patients)	7.3 (4.4–10.2)	20 mo	21.4%
Kobayashi et al ¹⁰	2012	Myopericarditis/pediatric (12 patients)	4.75 (1.35–9.72)	2 mo (2 wk–3 y)	0% Normal LVEF and function
Buiatti et al ¹¹	2012	Perimyocarditis/adult (62 patients)	10.5±17.0	4.5±0.8 y	0% Normalization of echo features in 100%

LVEF indicates left ventricular ejection fraction.

in the absence of major cardiac arrhythmias, heart failure, or failure of conventional therapies because treatment and management are not affected by the results of EMB and the prognosis seems benign. Moreover, recently published data have compared the diagnostic performance of CMR imaging with EMB.²⁹ In 132 patients with suspected acute myocarditis (symptoms lasting ≤14 days) or chronic myocarditis (defined as symptoms lasting >14 days), the overall diagnostic sensitivity, specificity, and accuracy of CMR were 76%, 54%, and 68%, respectively, and were better in the setting of acute disease (81%, 71%, and 79%, respectively). Thus, in clinical practice, CMR is useful for the noninvasive diagnosis of myocardial inflammatory involvement, especially in patients with recent symptom onset (<2 weeks) like the patients included in the present study.

This cohort study is reassuring in terms of the prognosis of myopericardial inflammatory syndromes. Patients with acute pericarditis and myopericarditis have a very good prognosis with no worsening of LV function and no recorded deaths. During follow-up, recurrences were the only significant complications and generally manifested as recurrent pericarditis after either acute pericarditis or myopericarditis and perimyocarditis.

Study Limitations

This is the first study to date to include patients with myopericarditis and perimyocarditis and to emphasize the clinical spectrum of myopericardial inflammatory syndromes.³ The first limitation of the study is that the diagnosis was based on clinical criteria and was not confirmed by EMB because no patients fulfilled the indications for EMB according to American Heart Association/American College of Cardiology/European Society of Cardiology guidelines.¹⁷ However, there is now good and growing evidence to support the use of CMR as a noninvasive diagnostic tool for clinicians,²⁹ especially when additional invasive tools do not affect the subsequent therapy and management of patients. The second and third limitations are related to the length of our follow-up and the subgroup sample size. Longer follow-up and larger populations are needed to confirm the benign outcome, although this study includes the largest published group of patients with inflammatory myopericardial syndromes to date.

Conclusions

Myopericardial inflammatory syndromes (myopericarditis/perimyocarditis) are benign clinical syndromes that can frequently be encountered in patients with an initial suspicion of pericarditis. The main differential diagnosis is with ST-segment–elevation myocardial infarction, and coronary angiography may be required. CMR is a useful diagnostic tool for the noninvasive diagnosis of concomitant myopericardial inflammatory involvement and may help to distinguish these syndromes from myocardial infarction.

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Disclosures

None.

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CLINICAL PERSPECTIVE

A group of 486 patients with inflammatory myopericardial syndromes (pericarditis, myopericarditis, and perimyocarditis) were followed up for a median follow-up of 36 months. Myocardial involvement was relatively frequent and recorded in one third of patients. Myopericarditis was defined as pericarditis and elevation of cardiac markers of injury without new onset of focal or diffuse depressed left ventricular function by echocardiography or cardiac magnetic resonance; perimyocarditis was diagnosed as pericarditis plus elevation of cardiac markers of injury and evidence of new onset of focal or diffuse depressed left ventricular function by echocardiography or cardiac magnetic resonance. Myocardial inflammatory involvement was confirmed by cardiac magnetic resonance. Clinical clues of myocardial involvement included ST-segment elevation (>75% of cases), arrhythmias, and troponin elevation, which was roughly related to the extent of myocardial involvement but largely overlapping in myopericarditis/perimyocarditis. Unlike acute coronary syndromes, cardiac troponin elevation was not a negative prognostic marker in myopericarditis/perimyocarditis, and the degree of troponin elevation did not correlate with the likelihood of subsequent recovery. In the setting of myopericarditis/perimyocarditis, the differential diagnosis should especially include acute coronary syndromes, and the presentation in up to 3 of 4 of these patients may simulate an acute coronary syndrome. Left ventricular function was normalized in 90% of the patients. No deaths correlated to pericardial or myocardial involvement were recorded during follow-up. Recurrences generally manifested as recurrent pericarditis and were more common with simple pericarditis. Cardiac magnetic resonance is a useful diagnostic tool for the noninvasive diagnosis of concomitant myocardial inflammatory involvement.