

# Day-Hospital Treatment of Acute Pericarditis

## A Management Program for Outpatient Therapy

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<b>OBJECTIVES</b>	We sought to investigate the safety and efficacy of a protocol for acute pericarditis triage and outpatient management of low-risk cases.
<b>BACKGROUND</b>	Acute pericarditis has generally a brief and benign course after empiric treatment by non-steroidal anti-inflammatory drugs, and routine hospitalization of most patients may be unnecessary.
<b>METHODS</b>	From January 1996 to December 2001, all consecutive cases of acute pericarditis were evaluated on a day-hospital basis. Patients without clinical poor prognostic predictors (fever >38°C, subacute onset, immunodepression, trauma, oral anticoagulant therapy, myopericarditis, severe pericardial effusion, cardiac tamponade) were considered low-risk cases and assigned to outpatient treatment with high-dose oral aspirin. Patients with poor prognostic predictors or aspirin failure were hospitalized for etiology search and treatment. A clinical and echocardiographic follow-up was performed at 48 to 72 h, 7 to 10 days, 1 month, 6 months, and 1 year.
<b>RESULTS</b>	Two hundred fifty-four out of 300 (84.7%) patients were selected as low-risk cases. Outpatient treatment was efficacious in 221 out of 254 (87%) cases. Thirty-three out of 254 patients were hospitalized because of aspirin failure. Patients treated on an out-of-hospital basis had no serious complications after a mean follow-up of 38 months (no cases of cardiac tamponade). A higher frequency of recurrences and constriction was recorded in aspirin-resistant cases than in aspirin responders (60.6% vs. 10.4% for recurrences and 9.1% vs. 0.5% for constriction, respectively; all $p < 0.01$ ).
<b>CONCLUSIONS</b>	A protocol for acute pericarditis triage and outpatient therapy of low-risk cases is safe and efficacious and may reduce management costs. (J Am Coll Cardiol 2004;43:1042-6) © 2004 by the American College of Cardiology Foundation

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Acute pericarditis is a common and frequent disease to be considered in the differential diagnosis of chest pain. Most patients with acute pericarditis have either viral or idiopathic pericarditis. In many cases, acute pericarditis has a brief and benign course after empiric treatment by non-steroidal anti-inflammatory drugs (NSAIDs). A viral etiology is often presumed, but evidence for this is often not sought, because of the expense involved and the time required before the results of laboratory tests are available. Treatment aims to relieve symptoms, and most patients are hospitalized for complete diagnosis and observation of complications, particularly pericardial effusion and cardiac tamponade (1,2).

In many cases, neither the performance of tests to establish a specific etiologic diagnosis nor hospitalization of the patient may be necessary. However, it is important to determine in every patient whether significant effusion or tamponade is present and to be able to select patients at high risk of complications who really need hospitalization.

After a review of the literature reporting previous series

(3,4), we developed a protocol for acute pericarditis triage on a day-hospital basis and for outpatient management of low-risk cases. The aim of this work is to investigate the safety and efficacy of this protocol.

## METHODS

**Study protocol.** From January 1996 to December 2001, we prospectively studied all consecutive cases of acute pericarditis on a day-hospital basis. Acute pericarditis was diagnosed when at least two of the following criteria were present: pericarditic chest pain, pericardial friction rub, and widespread ST-segment elevation on the electrocardiogram (ECG) (1-3). All patients had M-mode, two-dimensional, and Doppler echocardiographic studies performed using a Hewlett-Packard Sonos 2500 or 5500 machine (Palo Alto, California).

Considering that most cases probably had a viral or idiopathic etiology, with a possible brief and benign course after NSAIDs, we intentionally avoided performing an initial full diagnostic evaluation in all cases. We selected patients on the basis of a clinical examination, results of routine laboratory tests (blood cell count, sedimentation rate, acute-phase reactants, creatine kinase [CK], CK-MB,

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**Abbreviations and Acronyms**

CK	= creatine kinase
ECG	= electrocardiogram/electrocardiograph/ electrocardiographic
NSAIDs	= non-steroidal anti-inflammatory drugs
RR	= relative risk

troponin I [5], serum urea, and creatinine), and transthoracic echocardiography to determine the amount of pericardial effusion. Following the criteria of Weitzman et al. (6), we considered a small effusion as an echo-free space (anterior plus posterior) of <10 mm during diastole, a moderate effusion as an echo-free pericardial space of 10 to 20 mm, and a severe effusion as an echo-free space of >20 mm.

Patients without clinical or echocardiographic poor prognostic predictors were considered at low risk (Fig. 1) and assigned to outpatient treatment with high-dose oral aspirin. A clinical and echocardiographic follow-up was performed at 48 to 72 h, 7 to 10 days, 1 month, 6 months, and 1 year in non-complicated cases. Patients with clinical and echocardiographic poor prognostic predictors or patients without a response to aspirin were considered high-risk patients to be studied and treated after hospitalization. In these cases, a complete search for specific causes was performed. We considered aspirin failure in case of an unfavorable clinical reaction with persistence of fever, pericardial effusion appearance, or worsening and general illness lasting more than seven days despite treatment with a full dose of aspirin.

**Day-hospital care.** Day-hospital care consists of a programmed patient admission during the daytime, without traditional hospitalization with a night stay. Patients can have laboratory tests, diagnostic examinations, and therapies in the daytime and are discharged on the same day. Day-hospital care commonly reduces the need for a full hospitalization and management charges.

For acute pericarditis, day-hospital care included a tradi-

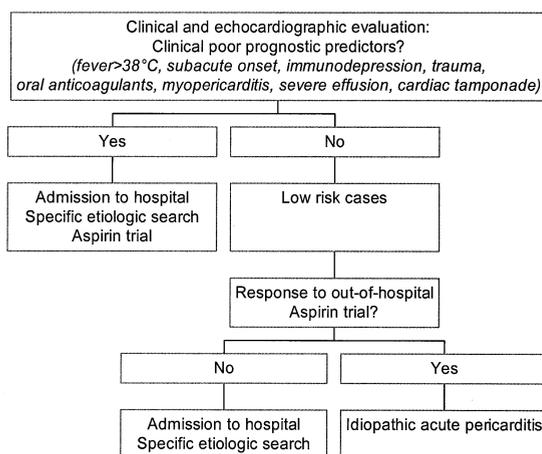
tional patient evaluation with physical examination, ECG, laboratory tests (if necessary), and echocardiography, offering a more complete approach to the patient with acute pericarditis than a simple outpatient visit. Low-risk cases were observed for a period of several hours, generally the time required to perform protocol examinations; then, patients were discharged on the same day without a night stay and returned for scheduled follow-up visits. Follow-up visits were performed on a day-hospital basis and included at least a focused history, physical examination, and echocardiogram; ECG and laboratory tests were included if necessary, according to clinical judgment.

**Poor prognostic predictors.** After a literature review, we identified as "poor prognostic predictors" those clinical features that were more frequently associated with an increased risk of short-term complications or a high likelihood of a specific disease. These clinical features included fever >38°C (7-9), subacute onset (3,10,11), immunodepression (11,12), trauma (1,11), oral anticoagulant therapy (1,13), myopericarditis (1,14), severe pericardial effusion, and cardiac tamponade (3,4,10).

**Drug treatment.** Aspirin was given at the dose of 800 mg orally every 6 or 8 h for 7 to 10 days, with gradual tapering over two to three weeks; commonly, the aspirin dose was reduced by 800 mg/day every week. Aspirin dose-tapering was prescribed in an attempt to reduce the recurrence rate, as suggested by our previously unpublished experience and recommended by Spanish guidelines on the management of acute pericarditis (15). Aspirin side effects were recorded. We considered serious or major adverse effects, events such as allergic reactions, peptic ulcer, and gastrointestinal bleeding which resulted in drug withdrawal.

We recommended a gastroprotection with misoprostol (600 to 800 µg/day) or omeprazole (20 mg/day). The rationale for this recommendation is based on published data (1,16,17). Several studies have evaluated factors that place patients at increased risk of gastroduodenal toxicity from NSAIDs. A committee appointed by the American College of Gastroenterology (16) identified the five most important risk factors: age >60 years (relative risk [RR] 5.52), a history of an adverse gastroduodenal event (RR 4.76), high-dosage NSAIDs (more than twice normal; RR 10.1), concurrent use of glucocorticoids (RR 4.4), and concurrent use of anticoagulants (RR 12.7). Patients with several risk factors are at highest risk of NSAID-induced gastroduodenal toxicity. Our protocol includes a high dosage of aspirin for more than one week, on an outpatient basis. Thus, our patients have at least one major risk factor for gastroduodenal toxicity. Moreover, another possible risk factor (17) is also the duration of NSAID therapy (more than 1 week but less than 3 months).

**Statistical analysis.** Continuous data are reported as the mean value ± SD and compared using the unpaired *t* test. Categorical variables are expressed as proportions or percentages and compared using chi-square analysis. A value of *p* < 0.05 was considered to show statistical significance.



**Figure 1.** Initial clinical and echocardiographic evaluation of patients with suspected acute pericarditis, according to the study protocol.

**Table 1.** Clinical Features and Follow-Up Results of Patients With or Without an Initial Response to Aspirin

	Response to Aspirin Treatment for 7-10 Days		p Value
	Yes (n = 221/254 [87.0%])	No (n = 33/254 [13.0%])	
Age (yrs)	50.6 ± 17.4	55.6 ± 13.6	NS
Male gender	131 (59.3%)	11 (33.3%)	0.009
Acute onset	210 (95.0%)	30 (90.9%)	NS
ST-segment elevation	201 (91.0%)	30 (90.9%)	NS
Pericardial effusion	130 (58.8%)	19 (57.6%)	NS
Etiology*			
Presumed idiopathic/viral	217 (98.2%)	13 (39.4%)	<0.001
Autoimmune disorders†	4 (1.8%)	14 (42.4%)	<0.001
Tuberculosis	0	6 (18.2%)	<0.001
Follow-up (months)	37.5 ± 28.9	39.5 ± 27.5	NS
Cardiac tamponade	0	0	NS
Recurrent pericarditis	23 (10.4%)	20 (60.6%)	<0.001
Constrictive pericarditis	1 (0.5%)	3 (9.1%)	0.004

\*A full diagnostic evaluation was performed only in aspirin-resistant cases and in patients with poor prognostic predictors according to the study protocol. †Including connective tissue disease and post-pericardiectomy syndromes. Data are presented as the mean value ± SD or number (%) of cases.

NS = not significant.

## RESULTS

During the study period, we observed 300 new cases of acute pericarditis (mean age 51.3 ± 17.1 years [range 16 to 90 years]; 194 men and 106 women [male/female ratio of 1.83]).

At presentation, pericardial chest pain was present in 295 (98.3%) patients, pericardial friction rub in 105 (35.0%) cases, and ECG ST-segment elevation in 268 (89.3%) cases with a typical ECG evolution in 161 (60.1%) of 268 cases.

Pericardial effusion was present in 180 patients (60.0%): mild effusion in 143 (79.4%), moderate in 18 (10.0%), and severe in 19 (10.6%). Cardiac tamponade was present in 15 (5.0%) of 300 cases. An acute onset was present in 267 (89.0%) of 300 cases.

After a clinical and echocardiographic evaluation, 254 (84.7%) of 300 patients were selected as low-risk cases and treated on an outpatient basis, as stated in the protocol. Among low-risk cases, outpatient treatment was effective in 221 (87.0%) of 254 cases (group I). In 33 (13.0%) of 254 cases (group II), initial treatment with aspirin was ineffective, and the patients were hospitalized. A clinical response was observed after administration of corticosteroids in 27 cases and after antituberculosis therapy in six cases.

In group I, we did not routinely obtain viral studies, as the yield is low and management is not altered by laboratory

tests results. In these cases with a response to aspirin treatment, our final diagnosis was idiopathic pericarditis. In group II, after a complete search for specific causes, we observed 13 cases of idiopathic pericarditis, 10 cases of pericarditis secondary to connective tissue diseases, 6 cases of tuberculous pericarditis, and 4 post-pericardiectomy syndromes. A comparison of clinical and echocardiographic features between group I and group II is reported in Table 1. Idiopathic and specific etiology frequencies in low-risk versus moderate- to high-risk cases are reported in Table 2.

The gastroprotection protocol with misoprostol or omeprazole was efficacious. Aspirin treatment was well tolerated without serious drug side effects. We recorded only minor side effects, including dyspepsia, abdominal pain, and gastritis, in 8 (3.2%) of 254 cases.

After a mean follow-up of 38 months in the overall group with low-risk acute pericarditis (n = 254), we observed 43 cases of relapses (16.9%), four cases of constrictive pericarditis (1.6%), and no cases of cardiac tamponade. After subgroup analysis, we observed a greater number of complications in patients who did not respond to the initial therapy with aspirin (Table 1; all p < 0.01).

## DISCUSSION

**Major findings.** Acute pericarditis diagnosis was performed according to commonly accepted diagnostic criteria (1-3). As an incidental finding of repeated examinations, we confirmed the poor sensitivity of pericardial friction rub which is one of the diagnostic criteria and is considered the pathognomonic specific physical finding of acute pericarditis (18). Pericardial friction rub is frequently evanescent and may vary in intensity and characteristics, even during a single day. Furthermore, it may disappear at times; thus, adequate evaluation sometimes may require careful and

**Table 2.** Etiology of Acute Pericarditis According to Clinical Risk Groups

Etiology*	Low Risk (n = 254)	Moderate to High Risk (n = 46)	p Value
Presumed idiopathic/viral	230 (90.6%)	10 (21.7%)	<0.001
Specific etiology	24 (9.4%)	36 (78.3%)	<0.001

\*A full diagnostic evaluation was performed in aspirin-resistant cases (n = 33) for low-risk patients and in all moderate to high-risk patients.

repeated examination. The presence of pericardial rub guarantees the diagnosis, but its absence does not exclude it.

To the present, this is the largest reported group of unselected patients with acute pericarditis and the first study to test formally the safety and efficacy of a diagnostic and therapeutic approach for acute pericarditis triage and outpatient treatment of low-risk cases.

Our diagnostic and therapeutic protocol is based on patient triage by clinical and echocardiographic evaluation. Echocardiography can be very helpful in confirming the diagnosis of pericarditis, disclosing even a small effusion, and it is very useful to rule out important complications such as cardiac tamponade and myopericarditis. Patients without clinical or echocardiographic poor prognostic predictors (fever  $>38^{\circ}\text{C}$ , subacute onset, immunodepression, trauma, oral anticoagulant therapy, myopericarditis, severe pericardial effusion, cardiac tamponade) were considered at low risk. In many of such patients, even an extensive diagnostic evaluation is likely to result in negative etiologic conclusions (2-4). Therefore, we did not routinely obtain viral studies, as the yield is low and management is not altered. This approach may change with the introduction of new treatments for specific viral infections into clinical practice. Low-risk cases of acute pericarditis were assigned to day-hospital treatment with high-dose oral aspirin (800 mg orally every 6 or 8 h for 7 to 10 days, with gradual tapering over 2 to 3 weeks) and gastroprotection with misoprostol or omeprazole.

Overinvestigation leading to inappropriate intervention is a common problem in managing acute pericarditis. Application of a conservative management protocol and gradual tapering of aspirin might be particularly important to reduce the risk of recurrences that were present in 43 (16.9%) of 254 patients of low-risk cases in our group, whereas the reported recurrence rate after an initial attack of idiopathic pericarditis may be as high as 32% (19,20). As previously reported (3,4), the initial response to aspirin identified a group of patients with a good outcome and a low risk of complications. Application of this protocol led to a specific diagnosis in 60 (20.0%) of 300 cases in the unselected group (14% to 22% of cases in previously published data) (3,4) but up to 36 (78.3%) of 46 moderate- to high-risk patients who were hospitalized (Table 2), showing the possible importance and utility of patient selection to initiate a search for a specific etiologic diagnosis.

Outpatient treatment was efficacious in 221 (87%) of 254 cases. Patients treated on a day-hospital basis had no serious complications during follow-up (no cases of cardiac tamponade). Aspirin was at least as safe and efficacious as more recent and expensive NSAIDs commonly recommended in recent reports.

A program for outpatient treatment of acute pericarditis in low-risk cases is probably not only safe and efficacious but also cost-effective in reducing hospitalization rates and management costs.

**Study limitations.** No studies have formally tested the safety and efficacy of out-of-hospital treatment of acute pericarditis. Some limitations of our study must be acknowledged. To study the validity of a protocol for day-hospital treatment of low-risk cases, we performed a prospective cohort study. A possible study limitation is the lack of a control group; all patients were stratified by clinical risk, and all low-risk cases were treated on an outpatient basis. However, the comparison with published data shows that this protocol is at least as safe and efficacious as previous series of hospitalized patients (3,4). Moreover, out-of-hospital treatment with aspirin was efficacious in the majority of low-risk cases (87%), and no serious complications were detected during a mean follow-up of 38 months. Even without a control group, this prospective cohort study provides evidence that a management program delivered by day-hospital care could be safe and efficacious in the treatment of acute pericarditis in low-risk cases and may reduce management costs. The main novelty of the present study is to propose acute pericarditis risk stratification in order to select low-risk cases to be treated on an out-of-hospital basis.

To date, even though this was a single-center, observational study, this report represents the largest survey of patients with acute pericarditis who were stratified by clinical risk and evaluated for out-of-hospital treatment of low-risk cases.

**Conclusions.** Day-hospital care of low-risk cases of acute pericarditis is safe and efficacious and may reduce management costs. A lack of an initial response to aspirin can identify a group of patients at greater risk of relapses and complications. Acute pericarditis risk stratification based on clinical and echocardiographic evaluation could be useful to select the appropriate care setting (day-hospital vs. hospitalization) as well as high-risk cases (Fig. 1). High-risk patients need to be hospitalized for a specific etiology search and more intensive follow-up.

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