Journal of Pericardiology
Vol.01, No.02
www.jopjournal.com

Clinical Predictors and Long-Term Outcomes in Patients with Acute Pericarditis: A Prospective Observational Study

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Received: 14/06/2026 **Revised:** 15/07/2026 **Accepted:** 21/07/2026 **Published:** 29/07/2026

Abstract

Acute pericarditis may follow a self-limiting course, yet recurrence, persistent inflammation, rehospitalization, tamponade, and constrictive complications remain clinically important. This prospective observational cohort study evaluated clinical predictors and long-term outcomes in adults with acute pericarditis. Consecutive patients were enrolled between January 2023 and December 2024 and followed for up to 24 months. Baseline demographic, clinical, laboratory, electrocardiographic, echocardiographic, etiological, and treatment variables were recorded. Cox proportional hazards regression and Kaplan–Meier analysis were used to identify predictors of composite adverse outcomes and estimate recurrence-free survival. Among 240 patients, the mean age was 42.7±15.6 years, 61.7% were male, and 65.4% had idiopathic or presumed viral disease. Clinical improvement within seven days occurred in 82.1%, while C-reactive protein normalized within four weeks in 80.9% of tested patients. Recurrent pericarditis occurred in 20.0%, while 27.1% experienced a composite adverse outcome. Initial treatment failure was the strongest independent predictor of adverse outcomes (adjusted hazard ratio [aHR], 3.84; 95% confidence interval [CI], 2.18–6.77), followed by moderate or large pericardial effusion (aHR, 2.11), previous pericarditis (aHR, 1.96), and subacute presentation (aHR, 1.89). Colchicine therapy was independently protective (aHR, 0.52). These findings support early risk stratification using treatment response, effusion size, recurrence history, and presentation pattern, with intensified follow-up for high-risk patients and reduced preventable long-term clinical complications.

Keywords: Acute pericarditis, Clinical predictors, Colchicine, Long-term outcomes, Recurrent pericarditis

1. Introduction

Acute pericarditis is an inflammatory disease of the sac and often has sharp pleuritic chest pain, a pericardial friction rub, diffuse findings on the ECG, and acute onset or worsening of pericardial effusion. The clinical course of many cases is self-limited, while some cases may be recurrent, chronic, with cardiac tamponade, or constrictive pericarditis. Idiopathic and presumed viral causes are predominant in developed health care systems, of which autoimmune, tuberculous, bacterial, malignant, or post-cardiac injury etiology is still clinically significant in selected groups. Early detection and diagnosis of high-risk features are key to managing triage, treatment selection, and planning for follow-up (Chiabrando et al., 2020).

Acute pericarditis is typically diagnosed if at least two of the typical clinical or diagnostic features are present, although imaging is important to diagnose effusion, hemodynamic compromise, myocardial involvement and structural complications. In general, transthoracic echocardiography is the first investigation performed and is readily available to be used to quickly assess the size of effusion, the function of the ventricles and the physiology of tamponade. Computed tomography and cardiac magnetic resonance imaging can also help provide information on the thickness, edema and enhancement of the pericardium, calcification and other thoracic abnormalities, when the diagnosis is unclear, or the clinical history is atypical (Fadl et al., 2020). New multimodality imaging approaches have also enhanced the capacity to define the nature of ongoing inflammation, differentiate reversible inflammatory constriction from fixed constrictive disease, and determine the length of treatment and surveillance (Klein et al, 2024).

Although the short-term prognosis is generally good, acute pericarditis can result in significant lengths of hospital stays, repeated imaging, rehospitalization, and frequent ED visits, which can result in high levels of health care resource utilization. Early readmission can occur due to ongoing pain, inadequate inflammatory control, reoccurring effusion, intolerance to medication, and a problem with an underlying systemic disease. A clinically significant proportion of patients are readmitted soon after discharge from hospital-based analyses, thus making discharge assessment and structured follow-up (Sreenivasan et al., 2020) important. There is also evidence from long-term observation of variability in prognosis depending on the cause of pericarditis, on the severity of the underlying disease, on the occurrence or history of recurrent attacks and on the response to the therapy; in particular, the prognosis of secondary forms of pericarditis may be worse than that of idiopathic disease (Giordani et al., 2024).

One of the most difficult complications after an attack of pericarditis is recurrent pericarditis. A symptom-free period followed by the return of symptoms and/or objective signs of inflammation is generally considered to be a recurrence; continual symptoms without complete remission are considered to be an incessant disease. A more complicated course has been associated with previous recurrence, delayed response to treatment, exposure to corticosteroids, continued inflammatory activity, and inadequate treatment duration. There is more to recurrent chest pain than just the chest pain itself; repeated chest pain can also affect physical activity, occupational function, mental health,

and quality of life (Andreis et al., 2021). Combined with aspirin or nonsteroidal anti-inflammatory drugs, colchicine has proven to be a central treatment, although the dosage, duration, contraindications, and gastrointestinal tolerability of this treatment need to be addressed on a case-by-case basis (Andreis et al., 2021).

The clinical use of targeted inhibition of IL-1 has been stimulated by patients who are corticosteroid-dependent and/or refractory to colchicine. Anakinra is clinically useful in reducing the inflammatory activity and in corticosteroid withdrawal in selected patients with recurrent pericarditis, but the issues of long-term use and injection side effects remain pertinent, and relapse after cessation of anakinra treatment (de Oliveira Correia et al., 2020). Rilonacept, a long-acting interleukin-1 trap, has also proven to be a good alternative in patients with recurrent inflammatory disease who have failed conventional therapy or in whom conventional therapy has not been successfully tapered (Presti et al., 2021). Further clinical studies have supported its use for the rapid control of symptoms, normalization of inflammatory markers, and decrease in the risk of recurrence (Fava et al., 2022). There is some comparative evidence that both colchicine and anti-interleukin-1 treatments are effective, though the optimal sequence for treatment is dependent on disease severity, the pattern of recurrence, extent of treatment dependence and individual patient risk (Ehsan et al., 2025).

The importance of clinical prediction cannot be overstated because it is important not to monitor all patients at the same level. A high-risk phenotype may be suggested by fever, subacute presentation, large pericardial effusion, cardiac tamponade, myocardial involvement, elevated inflammatory markers, and lack of response to initial anti-inflammatory treatment. About the first episode, post-cardiac MRI might be useful to better identify persistent inflammation and patients with a higher risk of an unfavorable course; however, more validation is still needed (Conte et al., 2022). Individuals who were deemed to be at high risk for the development of VTE may therefore benefit from a prospective evaluation that combines demographic, clinical, laboratory, electrocardiographic, imaging, and treatment-related data to help better early risk stratify patients. The primary objective of this study was to determine independent predictors of recurrence and composite long-term outcomes in patients with acute pericarditis, and assess response to treatment, rehospitalization, major complications, and survival rates at 24 months.

Objectives of the study:

1.To identify clinical, laboratory, electrocardiographic, and imaging predictors of adverse outcomes in acute pericarditis.

2.To determine the incidence and timing of recurrent pericarditis during 24 months of follow-up.

3.To evaluate treatment response, rehospitalization, major complications, and long-term survival.

2. Materials and Methods

2.1 Study Design and Setting

A prospective observational cohort study was performed from January 2023 to December 2024 in

adult patients presenting with a suspected diagnosis of acute pericarditis. The subjects were consecutively recruited from the cardiology outpatient department, emergency room, and inpatient service of the participating institution. The study involved the assessment of baseline clinical characteristics, diagnosis, treatment patterns, early treatment response, recurrence, and long-term adverse outcomes. All participants were followed up until 24 months after enrolment.

2.2 Study Population and Eligibility Criteria

Eligible patients were 18 years or older, with a diagnosis of acute pericarditis based on the presence of at least 2 of the following criteria: new or worsening pericardial effusion; new or persistent widespread ST-segment elevation or PR-segment depression; and pleuritic chest pain. Patients with a first or previously diagnosed episode of acute pericarditis were included. Patients with isolated myocarditis without confirmed involvement of the pericardium at presentation, chronic constrictive pericarditis at presentation, alternative diagnosis other than constrictive pericarditis that could explain the symptoms, baseline investigations that were incomplete, failure to complete follow-up, or failure to provide informed consent were excluded. Twenty-seven patients were assessed, and 240 patients were enrolled who met the inclusion criteria.

2.3 Baseline Clinical and Diagnostic Assessment

Demographic data, smoking, BMI, comorbidities, previous pericarditis, duration of symptoms, presence of fever, chest pain nature, dyspnea, hemodynamic status, and pericardial friction rub were determined at enrolment. A subacute presentation was considered to be a presentation where the symptoms were present for more than 7 days before diagnosis. A 12-lead electrocardiography and transthoracic echocardiography were performed in all patients. The electrocardiographic findings were diffuse ST-segment elevation, PR-segment depression, low voltage complexes, and arrhythmias. Echocardiography included evidence of pericardial effusion, effusion size, left ventricular ejection fraction, and cardiac tamponade. Pericardial effusion was defined as small, moderate, or large, based on the maximal echo-free space. Laboratory tests conducted were complete blood count, creatinine, blood urea nitrogen, cardiac troponin, C-reactive protein, liver function tests, and erythrocyte sedimentation rate. Other autoimmune, infective, tuberculous or malignant investigations were carried out if clinically appropriate. The etiology was classified as idiopathic, presumed viral, autoimmune, post-cardiac injury syndrome, tuberculous, malignant, bacterial, or other identified causes.

2.4 Treatment and Follow-Up Protocol

The attending cardiologist performed treatment as per the clinical condition and etiology of the patient. First-line treatment was aspirin or another nonsteroidal anti-inflammatory drug (NSAID), colchicine, corticosteroid, or, if the cause of the attack was known, specific treatment. The dose and duration of colchicine treatment were documented. In patients with cardiac tamponade and/or large symptomatic effusion, pericardiocentesis was performed, and a window was created in the pericardium when

clinically indicated. Clinical improvement was defined as a significant decrease in symptoms within 7 days of treatment. Failure to achieve initial treatment was considered a failure if symptoms did not resolve or got worse after 7 days of appropriate treatment. The participants were assessed at approximately 2, 1, 3, 6, 12, 18 and 24 months. At follow-up, assessment of symptom status, treatment adherence, adverse effects, repeat CRP measurement, electrocardiography and echocardiography (if indicated) were performed.

2.5 Outcome Definitions

The main outcome was a composite adverse outcome (CAO), defined as recurrent pericarditis, incessant pericarditis, rehospitalization for pericarditis, recurrent cardiac tamponade, constrictive pericarditis, further pericardiocentesis or surgery, or death related to pericarditis. Recurrent pericarditis: a new episode following complete resolution of symptoms and symptom-free period. When symptoms were present without any symptom-free interval, the disease was considered to be incessant pericarditis; when the disease was present for more than three months, it was considered chronic pericarditis. Secondary endpoints were time to resolution of chest pain, normalization of C-reactive protein within 4 weeks, time to first recurrence, recurrence within 6 and 12 months, requirement for immunomodulatory therapy, all-cause mortality and recurrence-free survival. Recurrence-free survival was calculated from the time of enrolment to the first composite adverse event or last completed follow-up.

2.6 Statistical Analysis and Ethical Considerations

The continuous variables were summarised as mean ± SD for normally distributed variables and median (IQR) for non-normally distributed variables. Categorical data were displayed in frequencies and percentages. Independent-samples t-test or Mann–Whitney U test were used for continuous variables, and chi-square or Fisher's exact test was used for categorical variables to compare patients with and without composite adverse outcomes. A Cox proportional hazards regression was used to determine the factors associated with the composite adverse outcome. The multivariable model included variables that demonstrated clinical importance or an association with the outcome in the univariable model. Confidence intervals for HRs were reported. The final model was checked for multicollinearity and proportional hazards assumptions before model interpretation. Harrell's concordance index (c-index) was used to assess model discrimination. Recurrence-free and outcome-free survival were estimated using the Kaplan–Meier method and compared with the log-rank test. Of the 15 cases of malignant pericarditis and 10 cases of bacterial pericarditis, sensitivity analysis was conducted after excluding these conditions. The two-tailed p-value < 0.05 was regarded as statistically significant. Ethical approval was given by the institutional ethics committee, and informed written consent was obtained from all the participants before they were included in the study.

3. Results

3.1 Participant Recruitment and Follow-Up

Between January 2023 and December 2024, a total of 278 patients with suspected acute pericarditis were assessed, of which 14 patients had inadequate baseline investigations, 9 had isolated myocarditis, 6 had chronic constrictive pericarditis, 5 declined to participate, and 4 had incomplete baseline investigations. 240 patients were included in the final analysis. In total, 232, 225 and 218 patients had follow-up data after 6, 12 and 24 months, which is equivalent to a retention rate of 90.8%. This was achieved with a median follow-up of 23.1 months (IQR 20.4 - 24.0 months); there was no significant difference between patients with follow-up and those lost to follow-up at baseline.

3.2 Baseline Clinical and Diagnostic Characteristics

The mean age of the cohort was 42.7 ± 15.6 years, and 148 patients (61.7%) were male. The most common etiology included idiopathic or presumed viral (157 patients, 65.4%), autoimmune (35, 16.5%), post-cardiac injury (13, 6%), tuberculosis (7, 3%), malignancy (4, 1.9%), bacterial infection (4, 1.9%), and other identified causes (4, 1.9%). Pericardial friction rub, fever over 38°C, subacute presentation, and typical pericarditic chest pain were present in 46 (19.2%), 49 (20.4%), and 57 (23.8%) patients, respectively. In 172 patients (71.7%), diffuse ST-segment elevation or PR-segment depression had been documented, and 142 patients (59.2%) had pericardial effusion, of whom 47 (19.6%) had moderate or large effusion. In 12 patients (5.0%), cardiac tamponade was noted; elevated troponin was seen in 39 (16.3%), and the median baseline C-reactive protein concentration was 41.8 mg/L (IQR, 18.6–86.3 mg/L). The distribution of acute pericarditis etiology is shown in Figure 1. Baseline demographic, clinical, laboratory, and imaging characteristics are illustrated in Table 1.

Table 1. Baseline demographic, clinical, laboratory, and imaging characteristics

Characteristic	Overall cohort (n=240)
Age, years, mean ± SD	42.7 ± 15.6
Male sex, n (%)	148 (61.7)
Body mass index, kg/m², mean ± SD	25.8 ± 4.3
Current smoker, n (%)	51 (21.3)
Hypertension, n (%)	54 (22.5)
Diabetes mellitus, n (%)	27 (11.3)
Previous pericarditis, n (%)	34 (14.2)
Symptom duration, days, median (IQR)	4.0 (2.0–9.0)
Subacute presentation >7 days, n (%)	57 (23.8)
Typical pericarditic chest pain, n (%)	226 (94.2)
Fever >38°C, n (%)	49 (20.4)
Pericardial friction rub, n (%)	46 (19.2)
Diffuse ST elevation or PR depression, n (%)	172 (71.7)
C-reactive protein, mg/L, median (IQR)	41.8 (18.6–86.3)
Elevated cardiac troponin, n (%)	39 (16.3)
Pericardial effusion, n (%)	142 (59.2)
Moderate or large effusion, n (%)	47 (19.6)
Cardiac tamponade, n (%)	12 (5.0)
Left ventricular ejection fraction, %, mean ± SD	58.9 ± 6.7
Idiopathic or presumed viral etiology, n (%)	157 (65.4)

Autoimmune etiology, n (%)	25 (10.4)
Post-cardiac injury syndrome, n (%)	21 (8.8)
Tuberculous etiology, n (%)	14 (5.8)
Malignant etiology, n (%)	9 (3.8)
Other identified etiology, n (%)	14 (5.8)

SD: standard deviation; IQR: interquartile range.

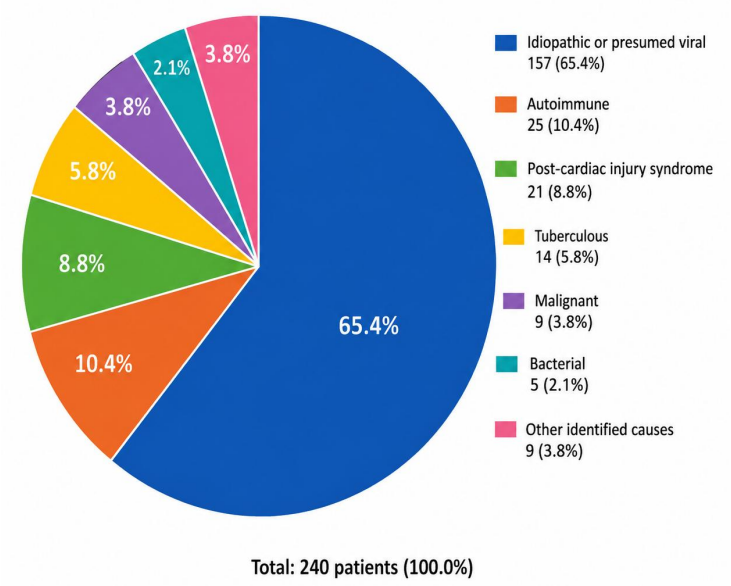

Figure 1: Etiological Distribution of Acute Pericarditis

3.3 Initial Treatment and Early Clinical Response

A total of 223 patients (92.9%) received aspirin (or another nonsteroidal anti-inflammatory drug), and 205 patients (85.4%) received colchicine for a median of 12 weeks (IQR, 10-16 weeks). Thirty-one patients received corticosteroid treatment (12.9%), and 19 (7.9%) received treatment for the specific disease. Pericardiocentesis was performed in 15 patients (6.3%), including all patients with cardiac tamponade, and two patients had a surgical pericardial window. 197 patients (82.1%) had clinical improvement within 7 days; the median time to resolution of chest pain was 6.0 days (IQR, 4.0–11.0 days). In a total of 220 patients who had repeated testing, 178 (80.9%) achieved normalization of CRP after four weeks, while 32 (13.3%) failed to normalize CRP after the first treatment. Initial treatment patterns and early clinical response are shown in Table 2.

Table 2. Initial treatment patterns and early clinical response

Treatment or early outcome	Overall cohort (n=240)
Aspirin or nonsteroidal anti-inflammatory drug, n (%)	223 (92.9)
Colchicine therapy, n (%)	205 (85.4)
Colchicine duration, weeks, median (IQR)	12 (10–16)
Corticosteroid therapy, n (%)	31 (12.9)
Etiology-specific treatment, n (%)	19 (7.9)

Pericardiocentesis, n (%)	15 (6.3)
Surgical pericardial window, n (%)	2 (0.8)
Clinical improvement within seven days, n (%)	197 (82.1)
Time to chest-pain resolution, days, median (IQR)	6.0 (4.0–11.0)
CRP normalization within four weeks, n/N (%)	178/220 (80.9)
Initial treatment failure, n (%)	32 (13.3)
Treatment-related adverse event, n (%)	18 (7.5)
Initial hospital stay, days, median (IQR)	4.0 (2.0–7.0)

IQR: interquartile range; CRP: C-reactive protein.

3.4 Long-Term Clinical Outcomes

In follow-up, 48 patients (20.0%) developed recurrent pericarditis, with the median time to the first recurrence being 4.8 months (IQR, 2.6–9.7 months) and 35 cases happening within 6 months and 43 within 12 months. Fifteen (6.3%) patients had a diagnosis of incessant pericarditis, six (2.5%) had a diagnosis of chronic pericarditis, and 27 (11.3%) had rehospitalization for pericarditis. Recurrent cardiac tamponade was seen in 4 patients (1.7%), constrictive pericarditis was seen in 5 patients (2.1%), and 8 patients (3.3%) required additional pericardiocentesis or surgery. Sixty-five patients (27.1%) had a composite adverse outcome. Follow-up resulted in three deaths – one from pericarditis and two from advanced malignancy. Recurrence-free survival at 24-month follow-up is displayed in Figure 2. The long-term clinical results after follow-up are summarized in Table 3.

Table 3. Long-term clinical outcomes during follow-up

Outcome	Overall cohort (n=240)
Recurrent pericarditis, n (%)	48 (20.0)
Time to first recurrence, months, median (IQR)	4.8 (2.6–9.7)
Recurrence within six months, n (%)	35 (14.6)
Recurrence within 12 months, n (%)	43 (17.9)
Incessant pericarditis, n (%)	15 (6.3)
Chronic pericarditis, n (%)	6 (2.5)
Pericarditis-related rehospitalization, n (%)	27 (11.3)
Recurrent cardiac tamponade, n (%)	4 (1.7)
Constrictive pericarditis, n (%)	5 (2.1)
Additional pericardiocentesis or surgery, n (%)	8 (3.3)
Immunomodulatory therapy, n (%)	13 (5.4)
Composite adverse outcome, n (%)	65 (27.1)
All-cause mortality, n (%)	3 (1.3)
Pericarditis-related mortality, n (%)	1 (0.4)

IQR: interquartile range.

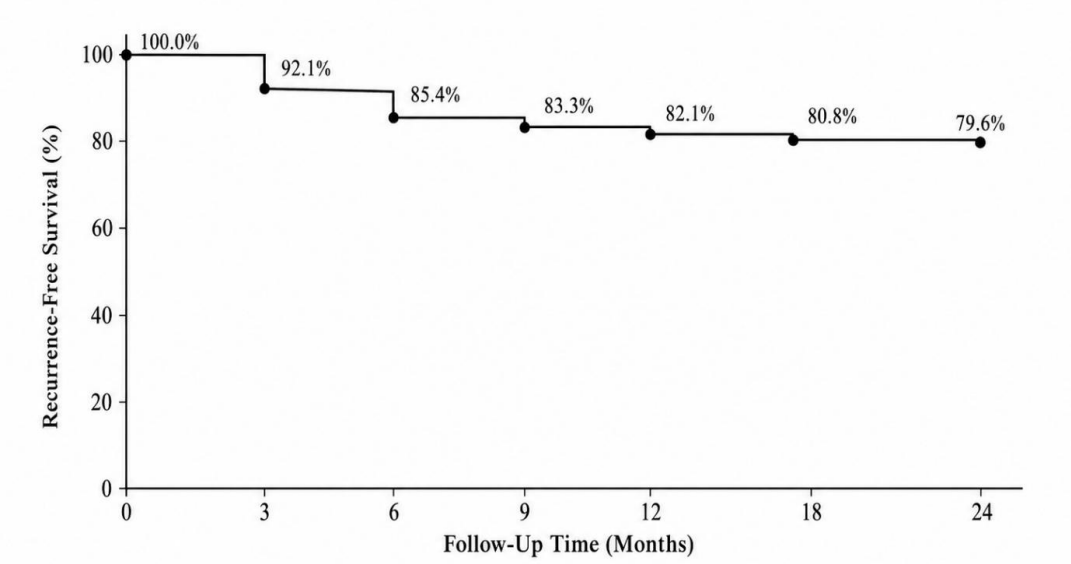

Figure 2: Kaplan–Meier Estimate of Recurrence-Free Survival During 24-Month Follow-Up

3.5 Comparison Between Patients With and Without Adverse Outcomes

Patients with a composite adverse outcome were more likely to have a history of pericarditis, subacute presentation, fever, moderate or large PE, cardiac tamponade, persistently elevated inflammatory markers, and initial treatment failure. Patients who had an adverse outcome had higher median baseline C-reactive protein levels (72.6 mg/L [IQR, 36.8–128.4] versus 33.5 mg/L [IQR, 14.2–64.7] for those without an adverse outcome; p<0.001). Larger effusion was seen in 36.9% of patients compared to 13.1%, and initial treatment failure was seen in 33.8% versus 5.7% of patients. Adverse outcome patients were less likely to be using colchicine (75.4% versus 89.1%; p=0.007), but more likely to be using corticosteroids (29.2% versus 6.9%; p<0.001). The patients who had composite adverse outcomes are compared with those who didn't in Table 4.

Table 4. Comparison of patients with and without composite adverse outcomes

Variable	Adverse outcome (n=65)	No adverse outcome (n=175)	p-value
Age, years, mean ± SD	45.8 ± 16.2	41.5 ± 15.2	0.056
Male sex, n (%)	38 (58.5)	110 (62.9)	0.532
Previous pericarditis, n (%)	17 (26.2)	17 (9.7)	0.001
Subacute presentation, n (%)	27 (41.5)	30 (17.1)	<0.001
Fever >38°C, n (%)	22 (33.8)	27 (15.4)	0.002
CRP, mg/L, median (IQR)	72.6 (36.8–128.4)	33.5 (14.2–64.7)	<0.001
Elevated troponin, n (%)	15 (23.1)	24 (13.7)	0.079
Moderate or large effusion, n (%)	24 (36.9)	23 (13.1)	<0.001
Cardiac tamponade, n (%)	8 (12.3)	4 (2.3)	0.003
Secondary identified etiology, n (%)	31 (47.7)	52 (29.7)	0.009
Colchicine therapy, n (%)	49 (75.4)	156 (89.1)	0.007
Corticosteroid therapy, n (%)	19 (29.2)	12 (6.9)	<0.001
Initial treatment failure, n (%)	22 (33.8)	10 (5.7)	<0.001
CRP normalization within four weeks, n/N (%)	38/60 (63.3)	140/160 (87.5)	<0.001

SD: standard deviation; IQR: interquartile range; CRP: C-reactive protein.

3.6 Predictors of Recurrence and Composite Adverse Outcomes

Previously known pericarditis, subacute presentation, fever, C-reactive protein > 50 mg/L, moderate or large PE, cardiac tamponade, failure to treat initially with corticosteroid, and normalization of CRP early were predictors of adverse outcomes, whereas colchicine therapy was protective, in univariable Cox regression analyses. In the adjusted analysis, initial treatment failure was the strongest independent predictor of the composite adverse outcome (adjusted hazard ratio [aHR], 3.84; 95% confidence interval [CI], 2.18–6.77; p<0.001), followed by moderate or large pericardial effusion (aHR, 2.11; 95% CI, 1.24–3.59; p=0.006), previous pericarditis (aHR, 1.96; 95% CI, 1.12–3.42; p=0.018), and subacute presentation (aHR, 1.89; 95% CI, 1.12–3.18; p=0.017). Colchicine treatment remained independently protective (aHR, 0.52; 95% CI, 0.30–0.89; p=0.017). The final model had good discrimination (concordance index of 0.78) and sensitivity analyses excluding the cases of malignant or bacterial origin yielded comparable results. Figure 3 shows the difference in outcome-free survival based on the response to initial treatment. The predictors of composite adverse outcomes identified by Cox regression are presented in Table 5.

Table 5. Cox regression analysis of predictors of composite adverse outcomes

Predictor	Univariable HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age, per 10-year increase	1.13 (0.98–1.30)	0.091	1.08 (0.92–1.27)	0.348
Previous pericarditis	2.48 (1.42–4.34)	0.001	1.96 (1.12–3.42)	0.018
Subacute presentation	2.37 (1.45–3.87)	<0.001	1.89 (1.12–3.18)	0.017
Fever >38°C	1.91 (1.15–3.18)	0.013	1.43 (0.83–2.47)	0.198
CRP >50 mg/L	2.16 (1.31–3.55)	0.003	1.48 (0.87–2.52)	0.145
Elevated cardiac troponin	1.52 (0.86–2.69)	0.148	1.21 (0.65–2.25)	0.552
Moderate or large effusion	2.83 (1.72–4.65)	<0.001	2.11 (1.24–3.59)	0.006
Cardiac tamponade	2.76 (1.31–5.84)	0.008	1.67 (0.74–3.77)	0.216
Secondary identified etiology	1.78 (1.10–2.87)	0.019	1.39 (0.82–2.35)	0.218
Colchicine therapy	0.43 (0.26–0.73)	0.002	0.52 (0.30–0.89)	0.017
Corticosteroid therapy	2.68 (1.59–4.51)	<0.001	1.54 (0.86–2.76)	0.145
Initial treatment failure	4.62 (2.72–7.85)	<0.001	3.84 (2.18–6.77)	<0.001
CRP normalization within four weeks	0.39 (0.23–0.65)	<0.001	0.61 (0.34–1.08)	0.091

HR: hazard ratio; CI: confidence interval; CRP: C-reactive protein.

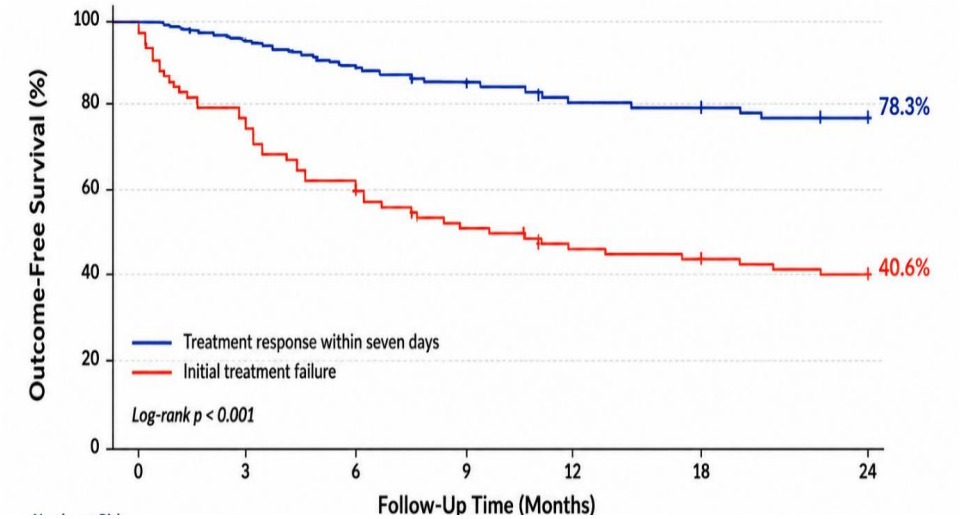

Figure 3: Kaplan–Meier Outcome-Free Survival According to Initial Treatment Response

4. Discussion

This prospective observational study showed that the incidence of a clinically significant recurrence event and long-term adverse outcomes was present in patients with acute pericarditis. The incidence of recurrent pericarditis was 20.0% for the study population, and the composite adverse outcome was 27.1% after 24 months of follow-up. Moderate or large effusion, prior pericarditis, and subacute presentation were the other factors that were independent predictors of an unfavorable course, with initial treatment failure being the most significant. A lower risk for adverse outcomes was independently associated with colchicine therapy. These results suggest that the response to early treatment, inflammatory severity when assessed at the initial visit, and structural involvement of the pericardial space may be useful clinically as a source of information at the very first clinical evaluation.

The rate of recurrence was similar to that expected in the known tendency towards relapse of pericarditis following an apparently cured first attack. The majority of the recurrences occurred in the first year, and the majority of those in the first six months of the year. This pattern allows for careful monitoring through the immediate post-discharge stage, especially for individuals who continue to experience symptoms, have not normalized their biomarkers, or have a history of pericarditis. In children, too, evidence has demonstrated that inflammatory burden and treatment aspects have been proven to influence recurrence risk, but there are restrictions in comparing the children with the adults due to the different characteristics of the disease in the children population (Krasic et al., 2021). In the present study, we extend this concept by showing that previous pericarditis, as well as delayed clinical resolution, remained relevant also in the mostly adult population.

The strongest association with the composite adverse outcome was found for initial treatment failure. Those who did not improve within 7 days had significantly poorer 24-month outcome-free survival when compared to those who improved early. If symptoms continue despite the correct anti-inflammatory use, it could be a sign of unmanaged inflammation of the pericardium, an undiagnosed

secondary cause of the inflammation, insufficient intensity of the treatment, not taking the treatment as prescribed, or the onset of the disease is early enough that it already has progressed to the stage of incessant inflammation. The duration of the disease and the number of times the pericarditis recurs have been the focus of long-term studies on recurrent pericarditis, which has been shown to lead to a chronic phenotype requiring treatment and having significant clinical and quality-of-life implications (Ceriani et al., 2025). Early identification of nonresponders, therefore, may allow for a timely reevaluation of therapy, intensification of drug therapy, and an etiological investigation of the nonresponder.

Large (or moderate) pericardial effusion was also an independent predictor of poor outcome. Effusions are larger in volume when the inflammatory activity, malignancy, or infectious process is greater or when drainage of the fluid from the pericardial space is compromised. In the univariable analysis, cardiac tamponade was linked to worse outcomes, but in multivariable analysis, this effect was no longer independent, and it may be that the impact of cardiac tamponade is partly shared with the amount of effusion and disease severity. Another serious complication, especially in the case of persistent or recurrent disease, is inflammatory constriction, which has been demonstrated to be reversible by interleukin-1 inhibition in some patients (Andreis et al., 2020). These observations suggest serial echocardiographic evaluation for patients with large amounts of effusion or chronic symptoms.

No association was seen between the composite outcome and use of colchicine therapy. This is a finding that is consistent with its previously demonstrated efficacy in decreasing recurrence when used in combination with aspirin or nonsteroidal anti-inflammatory drugs. This protective association was still present after adjustment for clinical severity and treatment-related variables. Combined therapy with anakinra has also been found to be beneficial for disease control in refractory recurrent pericarditis, and this may justify the use of colchicine in these patients (Collini et al., 2024). Treatment adherence and tolerability, as well as weight dosing and adequate treatment duration, are also factors to consider, as early discontinuation could be a factor in relapse.

In univariable analysis, corticosteroid exposure was associated with adverse outcomes, but in the adjusted model, exposure to corticosteroids was not associated with adverse outcomes. This finding could be due to confounding by indication, as patients with autoimmune disease were more likely to be given the corticosteroid, patients who had contraindications to nonsteroidal anti-inflammatory drugs (NSAIDs) were more likely to be given the corticosteroid, and patients who had inflammation severe enough to require treatment with a corticosteroid were more likely to be prescribed the corticosteroid. Those who develop corticosteroid dependence and are not colchicine responsive may benefit from specific anti-IL1 therapy. Taubman (2009) found that in this high-risk population anakinra significantly decreases the number of recurrences, emergency visits, and corticosteroid use when used in a registry setting (Imazio et al., 2020). Findings from the present study are not conclusive proof of a harmful effect of corticosteroids but confirm the need to use them at the minimal effective dose and to slowly taper their dosage.

Rilonacept has also revolutionised the treatment of recurrent inflammatory pericarditis by offering a prolonged-action IL-1 inhibitor. In patients with active recurrent disease, Phase II showed a quick reduction in pain, normalization of inflammatory markers, and decreased recurrent episodes (Klein et al., 2021). The more recent evidence has made rilonacept a potential treatment option for patients who have a history of recurrent, corticosteroid-dependent or treatment-refractory pericarditis, but there are factors to consider, including cost, accessibility and duration of treatment and relapse after stopping (Vlachakis et al., 2024). Treatment response combined with clinical history, imaging and inflammatory biomarkers may aid in the identification of patients that are most likely to benefit from early escalation to these treatments (Yesilyaprak et al., 2024).

Multiple strengths of the study included prospective enrollment, a standardized diagnostic assessment, pre-established follow-up time periods, and multiple follow-up domains of prognosis. There was no random allocation of treatment and few events of uncommon complications; neither did the observational design allow causal inferences. Generalizability may also be limited due to single-center recruitment. These predictors need to be confirmed in larger multicenter studies and need to be combined with other imaging data, effusion size, and inflammatory markers and a previous history of recurrence, to create practical risk scores for the determination of urgent drainage.

5. Conclusion

Acute pericarditis showed a clinically significant risk for recurrence and long-term outcome, but overall early treatment was favorable. Recurrence was more likely to be within the first year, suggesting the importance of more careful monitoring in the early follow-up period. Treatment failure was the largest independent risk factor for an unfavorable course, whereas moderate and large pericardial effusion, a history of previous pericarditis, and acute presentation were also associated with an unfavorable course. Colchicine was associated with improved outcome-free survival, irrespective of the use of aspirin or nonsteroidal anti-inflammatory drugs, and use of colchicine is therefore recommended in conjunction with these drugs, if not contraindicated. Long-term symptoms, lack of inflammatory resolution and significant effusion should lead to re-evaluation of treatment compliance, underlying cause and increased monitoring and/or advanced treatment. After the data was adjusted, however, there was no evidence of a separate bad effect of corticosteroid exposure but rather an indication that it was a marker of the severity of the disease. The results suggest a risk-graded management strategy that incorporates clinical presentation, echocardiogram, inflammatory markers, and early response to therapy. These predictors need to be confirmed via larger, multicenter prospective studies, and to assess whether more rapid treatment escalation would improve outcomes of reduced recurrence, less rehospitalization, and long-term pericardial complications.

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