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

Clinical Approach to Recurrent Pericarditis: Challenges and Practical Insights

Allan L Klein[1]

[1]*Center for the Diagnosis and Treatment of Pericardial Diseases, Section of Cardiovascular Imaging, Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Instituite, Cleveland Clinic, Cleveland, Ohio, USA*
Email: kleina@ccf.org

Abstract

Recurrent pericarditis is a difficult clinical entity whereby patients experience recurrent attacks of pericardial inflammation after an initial acute event. It is associated with the high morbidity rate, high relapses rates, and poor quality of life. This is a narrative review that involves a clinical discussion of recurrent pericarditis, its pathophysiology, diagnostic evaluation and management strategies. The disease is now considered an immune-mediated pathology that combines autoimmune and autoinflammatory pathways and is mainly mediated by the interleukin-1 (IL-1) pathway. Diagnosis is predominantly clinical and laboratory features are C-reactive protein or high-quality imaging, such as cardiac magnetic resonance imaging. Nonsteroidal anti-inflammatory drugs and colchicine are used as the first-line therapy, whereas corticosteroids are used in a few cases. The refractory disease may require immunosuppressive medications or special biologic treatment such as IL-1 inhibitors. Despite any enhancement of therapy regimens, such problems as steroid addiction, treatment resistance, and frequent relapses persist. The long-term management is aimed at preventing recurrence, patient adherence, and periodic follow-up. There are new directions that have the potential to achieve better results, such as individualized medicine and biomarker-driven therapy. This review identifies practical clinical implications to aid in the effective diagnosis and management of recurrent pericarditis.

Keywords: Recurrent pericarditis; Pericardial inflammation; Colchicine; Interleukin-1 inhibitors; Cardiac MRI; Immunotherapy; Pericardiectomy

1. Introduction

Pericarditis is inflammation of the pericardium, the fibroelastic sac that encloses the heart, and one of the most frequent types of pericardial disease that is observed in clinical practice (Adler et al., 2016). It can be acute, incessant, chronic or recurrent, based on the duration of the symptoms and breakdown of relapse. Recurrent pericarditis refers to the appearance of symptoms after a symptom-free period of at least four to six weeks of occurrence of an initial case of acute pericarditis (Imazio et al., 2013). The condition is clinically challenging because it has a relapsing nature, affects the quality of life of the patient and challenging to manage.

Acute pericarditis epidemiologically takes about 5% of emergency department visits of non-ischemic chest pain, and a significant number of these patients ultimately end up with a recurrent illness (Imazio & Gaita, 2015). It has a recurrence of almost 15- 30% of the patients in a first episode and can increase to 50 percent when corticosteroids are taken early and inappropriately (Imazio et al., 2005). Though idiopathic and presumed viral etiologies prevail in developed nations, secondary etiologies like autoimmune disorders, infections, and malignancies bring about a global burden, especially in low- and middle-income areas (Adler et al., 2016; Klein et al., 2021). Recurrent pericarditis is chronic and relapsing, which not only escalates healthcare consumption but also has serious impacts on the functional ability and mental health of patients.

Timely diagnosis and treatment of recurrent pericarditis are very important in helping to avoid complications and decrease the rates of recurrence. The patients are usually characterized by chest pain, which is often pleuritic and positional in nature, as well as pericardial friction rub, electrocardiographic changes, and systemic inflammation (Imazio et al., 2013). Nevertheless, clinical manifestations may be diverse, and not all classical manifestations are always present, which can make it difficult to diagnose in a timely manner. Moreover, recurrent episodes might be less characteristic and might have some subtle or atypical findings, which require a high index of clinical suspicion and use multimodal diagnostic methods, such as biomarkers and sophisticated imaging techniques, such as cardiac magnetic resonance imaging (Klein et al., 2013).

Although progress has been made in understanding the disease, there are still various clinical issues that are linked to recurrent pericarditis. Diagnostic uncertainty, especially in differentiating recurrent pericarditis and other causes of chest pain like myocardial ischemia or myocarditis, is among the biggest challenges (Adler et al., 2016). Also, the pathophysiological mechanisms underlying the disease are not completely understood, usually being autoimmune or autoinflammatory, which does not allow the creation of specific therapies (Brucato et al., 2018). Recurrent pericarditis is also associated with frequent recurrence, steroid addiction, and non-responsiveness to standard treatment, including nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine (Imazio et al., 2011).

Another critical issue of concern is treatment resistance, especially in patients who have had several recurrences. Although colchicine has proven to be effective in decreasing recurrence rates and is a key part of treatment regimens, some patients are still refractory or unable to tolerate conventional treatment regimens (Imazio et al., 2013). Corticosteroids, despite their effectiveness in controlling symptoms, are linked with a higher risk of recurrence and long-term negative consequences, which is why their use is a controversial issue (Imazio et al., 2005). Recently, the development of specific biologic therapies, especially interleukin-1 (IL-1) inhibitors, has shown new treatment options, but only their cost, accessibility, and long-term safety profiles are subject to study (Brucato et al., 2016).

Considering these complexities, recurrent pericarditis is a more complex clinical phenomenon that needs a holistic and personalized approach to both diagnosing and treating. To enhance patient outcomes, better insight into its mechanisms, better diagnosis, and better treatment regimens are required.

The aim of this review is to provide a clinically oriented overview of recurrent pericarditis, focusing on its pathophysiology, diagnostic evaluation, and management strategies. In addition, this review highlights key challenges encountered in clinical practice and discusses practical insights for optimizing patient care. By integrating current evidence with clinical experience, this article seeks to support healthcare professionals in effectively managing this challenging condition.

2. Pathophysiology and Etiology of Recurrent Pericarditis

Recurrent pericarditis is a complicated clinical disorder that is defined by repeated attacks of pericardial inflammation after an initial acute attack. Mechanisms of recurrence are multifaceted and entail a combination of long-standing inflammation, immune dysregulation, and personal susceptibility. Recurrent forms become more and more often recognized as immune-mediated disorders, but not necessarily as a process of pure infection, as opposed to acute pericarditis, which is often self-limiting (Chiabrando et al., 2020).

One key characteristic of the pathophysiology of recurrent pericarditis is the continuation or re-initiation of inflammatory pathways following resolution of the initial insult. The innate immune system is activated in most instances by the initial trigger, which in most instances is viral or idiopathic. Although this response is usually self-regulated, there are patients who have hyperirritable or dysregulated immune responses, which cause repeated inflammation of the pericardium. This is a combination of both autoimmune and autoinflammatory pathways, which can be co-occurring and/or dominant, depending on the underlying etiology (Imazio et al., 2016).

The autoimmune pathways are defined by the development of the adaptive immunity, i.e., the appearance of the autoreactive T cells and the generation of the autoantibodies formed against the

pericardial or cardiac antigens. The latter mechanisms have frequently been implicated in systemic autoimmune diseases, like systemic lupus erythematosus or rheumatoid arthritis, in which patients have been known to show pericardial involvement (Caforio et al., 2013). Autoinflammatory processes, in contrast, entail dysregulation of the innate immune system but without much contribution of antigen-specific immune responses. This type is becoming more accepted in idiopathic recurrent pericarditis, in which there is no apparent external precipitant. These two pathways differ enough to have a clinical impact, as they determine treatment approaches, especially the application of more specific biologic therapies (Imazio et al., 2017).

Cytokines are some of the inflammatory mediators, and especially interleukin-1 (IL-1). The IL-1 is one of the most important regulators of inflammatory response and is secreted by activated macrophages and other immune cells in response to tissue damage or infection. Excessive IL-1 pathway activation in recurrent pericarditis helps to promote chronic inflammation and relapse of symptoms. High concentrations of IL-1 enhance the inflammatory cell recruitment to the pericardium, elevate vascular permeability, and trigger an inflammatory-tissue damage cycle (Klein et al., 2013). The clinical significance of this pathway is supported by the effectiveness of IL-1 inhibitors, including anakinra and rilonacept, in decreasing the number of recurrences and the outcomes of patients with refractory cases (Imazio, Andreis, et al., 2020).

The general pathophysiological mechanism can be thought of as a cascade that starts with a trigger and then progresses to the inflammatory pathway activation, malfunctioning of the immune response, and subsequent recurrence of the symptoms. Figure 1 shows this progression, pointing out the shift of acute inflammation to chronic or recurrent disease with maladaptive immune responses. The figure underlines how inadequate remedies of inflammation or improper control of immune mechanisms may result in recurrent incidences of pericardial inflammation.

Etiologically, recurrent pericarditis is caused by a broad range of etiologies, with idiopathic or presumed viral etiologies being the largest in developed countries. The inflammatory process is thought to be initiated by viral infections such as the enteroviruses, adenoviruses, and other cardiotropic viruses. In spite of the fact that the direct viral persistence is hardly proven, the primary infection can cause an immune reaction that persists despite the viral clearance (Asteggiano et al., 2015).

Another significant type of etiology is autoimmune diseases. The pericardium can be affected by such conditions as systemic lupus erythematosus, rheumatoid arthritis, and Sjogren syndrome, as a component of systemic inflammation. Recurrent pericarditis in such instances can be an indication of persistent systemic immune activation, as opposed to pericardial disease alone (Caforio et al., 2013). Likewise, post-cardiac injury syndromes such as post-myocardial infarction (Dressler syndrome) and post-pericardiotomy syndromes are related to immune-mediated reactions to cardiac tissue damage,

which results in delayed and persistent inflammation.

Infectious etiologies, especially tuberculosis (TB), are also very important in the endemic areas and are an important cause of recurrent pericarditis in the world. Tuberculous pericarditis is linked to the increased risk of complications, such as constrictive pericarditis, and needs particular antimicrobial treatment, as well as anti-inflammatory treatment (Ntsekhe & Mayosi, 2013). There might be other infectious agents, such as bacterial and fungal pathogens, which also might have a role to play, especially in immunocompromised patients.

Pericardial disease as a result of malignancy is also another factor that should be taken into consideration, particularly in patients with known cancer or recurrent effusions whose cause is not very clear. Persistent or repeated inflammation of the pericardium may result in neoplastic infiltration of the pericardium, which, in most cases, is accompanied by large pericardial effusions and hemodynamic impairment (Maisch, 2025). These secondary causes must be identified because the management of these causes varies greatly when compared to the idiopathic or immune-mediated causes.

Recurrence risk factors are well-researched and comprise clinical and treatment-related factors. The number of recurrences is highly linked to inadequate initial treatment, especially the lack of or premature cessation of colchicine (Imazio et al., 2015). Corticosteroid use, particularly in high amounts or at the beginning of the disease course, has also been associated with an increased risk of relapse because of the possible inhibition of viral clearance and encouragement of immune dysregulation. Other risk factors are a severe initial presentation, increased levels of inflammatory markers, and the underlying systemic disease (Chiabrando et al., 2020).

Table 1 gives a synopsis of the etiological factors, underlying mechanisms, and clinical features related to recurrent pericarditis and summarizes the various causes of recurrent pericarditis and their associated risk of recurrence. Such a tabulated representation will help clinicians determine possible underlying etiologies and customize diagnostic and treatment strategies to these etiologies.

To the point, repeated pericarditis is a disease that is facilitated by the inflammatory and immune-mediated mechanisms, and the IL-1 pathway is the one that plays the leading role in the disease perpetuation. It is heterogeneous and has a broad range of etiologies such as idiopathic etiologies, viral etiologies, autoimmune etiologies, infectious etiologies and malignant etiologies. The importance of these mechanisms and risk factors is to be able to come up with specific management strategies to curtail the burden of recurrence in affected patients.

Table 1: Etiology and Risk Factors of Recurrent Pericarditis

Cause	Mechanism	Clinical Features	Recurrence Risk
Idiopathic/Viral	Post-viral immune activation	Chest pain, mild effusion	Moderate
Autoimmune disorders	Adaptive immune response, autoantibodies	Systemic symptoms, chronic inflammation	High
Post-cardiac injury	Immune response to cardiac tissue damage	Fever, chest pain after surgery/MI	Moderate-High
Tuberculosis	Granulomatous inflammation	Fever, weight loss, large effusion	High
Malignancy	Direct infiltration or inflammation	Recurrent effusion, tamponade	High
Corticosteroid use	Immune suppression and rebound inflammation	Frequent relapses	High
Inadequate colchicine therapy	Poor inflammation control	Early recurrence	Moderate-High

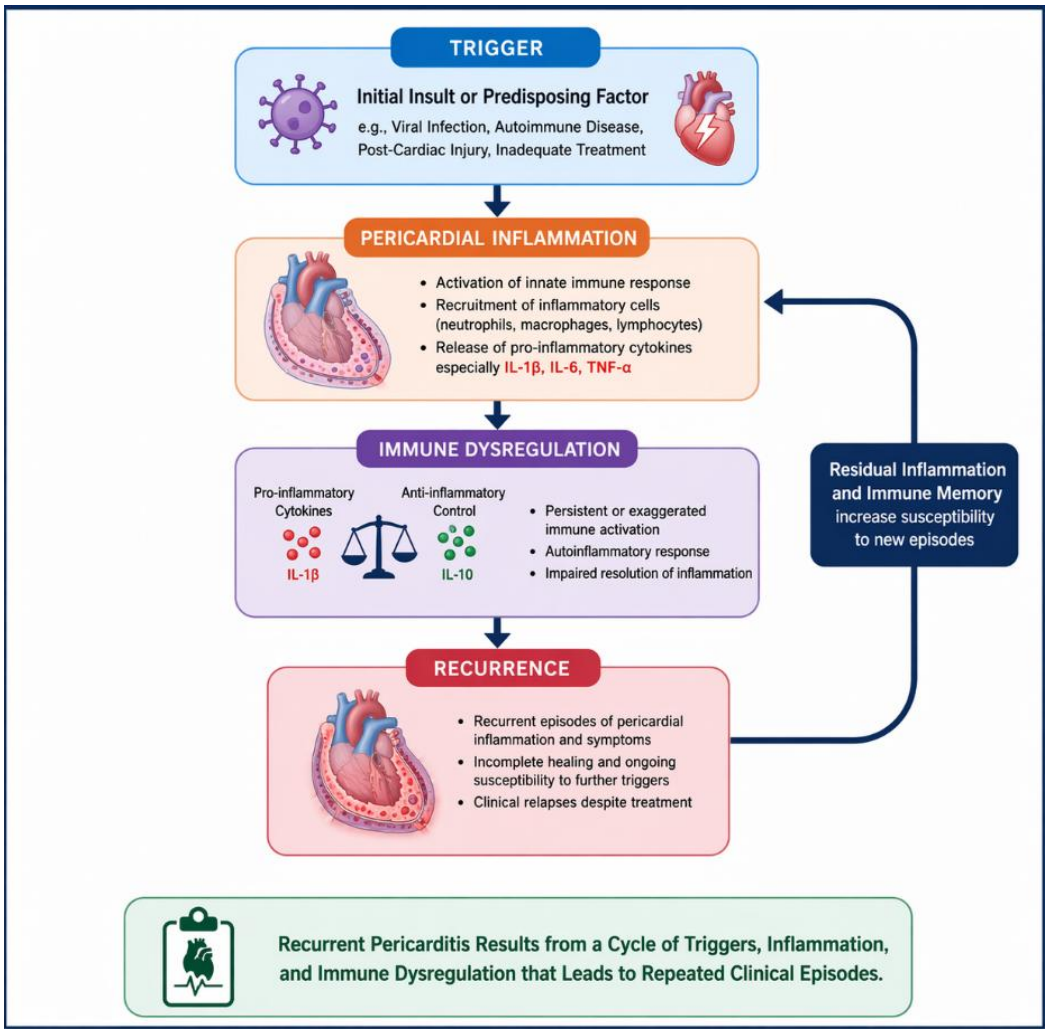

Figure 1: Pathophysiological Mechanisms of Recurrent Pericarditis

3. Clinical Presentation and Diagnostic Evaluation

Recurring pericarditis has a range of clinical manifestations that can be similar to those of acute pericarditis but can be more or less intense and common in different episodes. The characteristic symptom is chest pains, which are usually sharp and pleuritic and are worsened with breathing in and improved with sitting up (Asteggiano et al., 2015). But, in recurrent episodes, the pain can be milder or non-characteristic, which adds to the ambiguity of diagnosis. Other symptoms can be low-grade fever, fatigue, and dyspnea, especially where there is pericardial effusion. A pericardial friction rub, which is highly specific but not always present, can be intermittent, particularly in recurrent cases (Chiabrando et al., 2020).

Recurrent pericarditis diagnosis is mainly clinical and is based on the criteria that the modern European Society of Cardiology (ESC) recommends. The conditions that must be diagnosed include: typical chest pain, typical pericardial friction rub, typical electrocardiographic (ECG) alterations, and new or progressive pericardial effusion (Asteggiano et al., 2015). In recurrent cases, the symptoms must recur following at least four to six weeks of a symptom-free period (Andreis et al., 2021). Positive results, such as increased inflammatory markers and imaging data of pericardial inflammation, support accuracy in the diagnosis.

Laboratory tests are used to ensure inflammation and keep track of the disease activity. Active disease is usually associated with increased levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (Imazio, Andreis, et al., 2020). CRP is more useful in determining the duration of treatment and assessing response to treatment. In a few patients, cardiac troponins might be slightly increased (as an indication of concomitant myocardial involvement (myopericarditis) (Wang & Klein, 2022). Nevertheless, a significant troponin increase is a condition to consider other conditions, including acute coronary syndrome.

Imaging modalities cannot be ignored when it comes to the assessment of recurrent pericarditis because it gives both a diagnostic and prognostic understanding. Transthoracic echocardiography is the imaging tool of first choice because of its accessibility and capabilities to identify pericardial effusion, evaluate hemodynamic implications, and cardiac performance (Adler et al., 2016). Nevertheless, its effusion-free sensitivity to detect active inflammation is less than ideal.

Modern imaging modalities, such as computed tomography (CT) and cardiac magnetic resonance imaging (CMR), have better diagnostic potential. CMR is especially useful to detect pericardial inflammation with late gadolinium enhancement and T2-weighted image, which allows detecting edema and inflammation persistence (Wang & Klein, 2022). These modalities are of special use when there is diagnostic uncertainty or abnormal presentation, or suspected subclinical disease.

Table 2 elaborates the diagnosis tools, results, strengths and weaknesses of these diagnostic tools. This highlights the complementary aspect of laboratory and imaging modalities in regard to clinical

assessment.

The differential diagnosis should also be added to the diagnosis since there are a variety of cardiovascular diseases that may be similar to recurrent pericarditis. Myocarditis should be considered, particularly in those patients who have elevated cardiac biomarkers or dysfunctional ventricular function. Compared to isolated pericarditis, myocarditis can be accompanied by inflammation of the myocardium and present itself through the symptoms of arrhythmias or heart failure (Wang & Klein, 2022). There must also be a rule out of acute coronary syndrome (ACS), particularly in high-risk patients. Prices of pericarditis, like diffuse ST-segment elevation and PR-depression, are ECG results that can be used to differentiate between pericarditis and ACS, where regional alterations are usually observed (Asteggiano et al., 2015).

Although there has been improvement in diagnostic tools, there are still issues. Atypical presentation is typical, especially in patients who experience recurrence on many occasions, as symptoms could be subtle or non-specific. The other diagnostic challenge is the existence of subclinical inflammation, where patients can be found to have continued inflammatory activity without any symptomatic manifestations. The condition can be diagnosed with the help of high biomarkers or high-level imaging, especially CMR (Imazio, Andreis, et al., 2020).

Another issue to consider is differentiating between true recurrence and persistent or chronic pericarditis. The initial episode may not be completely resolved, resulting in persistent inflammation that simulates a recurrence, hence the importance of proper treatment and follow-up. The lack of a single diagnostic test that is definitive has led to the need to use a combination of clinical approaches.

Flexibility: A systematic diagnostic route is required to aid clinical decision-making. Figure 2 shows a gradual process, starting with the clinical assessment and moving to the laboratory tests and X-rays. This algorithm enumerates the value of combining both clinical and objective evidence to make correct diagnoses.

Overall, recurrent pericarditis has unpredictable clinical manifestations and can be confused with other heart diseases. Diagnosis is based on a set of clinical, lab, and imaging features. Although echocardiography is still the gold standard of the primary evaluation, the use of advanced imaging, especially CMR, has been much more effective in detecting pericardial inflammation, especially in non-characteristic or subclinical scenarios. It is essential to comprehend these diagnostic complexities in order to manage them effectively and promptly.

Table 2: Diagnostic Tools and Their Clinical Utility in Recurrent Pericarditis

Tool	Findings	Advantages	Limitations
CRP / ESR	Elevated inflammatory markers	Widely available, useful for monitoring	Non-specific
Troponin	Mild elevation in myopericarditis	Detects myocardial involvement	Limited specificity
ECG	ST elevation, PR depression	Rapid, inexpensive	May be absent in recurrence
Echocardiography	Effusion, hemodynamic effects	First-line, bedside tool	Limited in detecting inflammation
CT-Scan	Pericardial thickening, calcification	Good anatomical detail	Radiation exposure
Cardiac MRI	Edema, inflammation (LGE)	High sensitivity for inflammation	Limited availability, cost

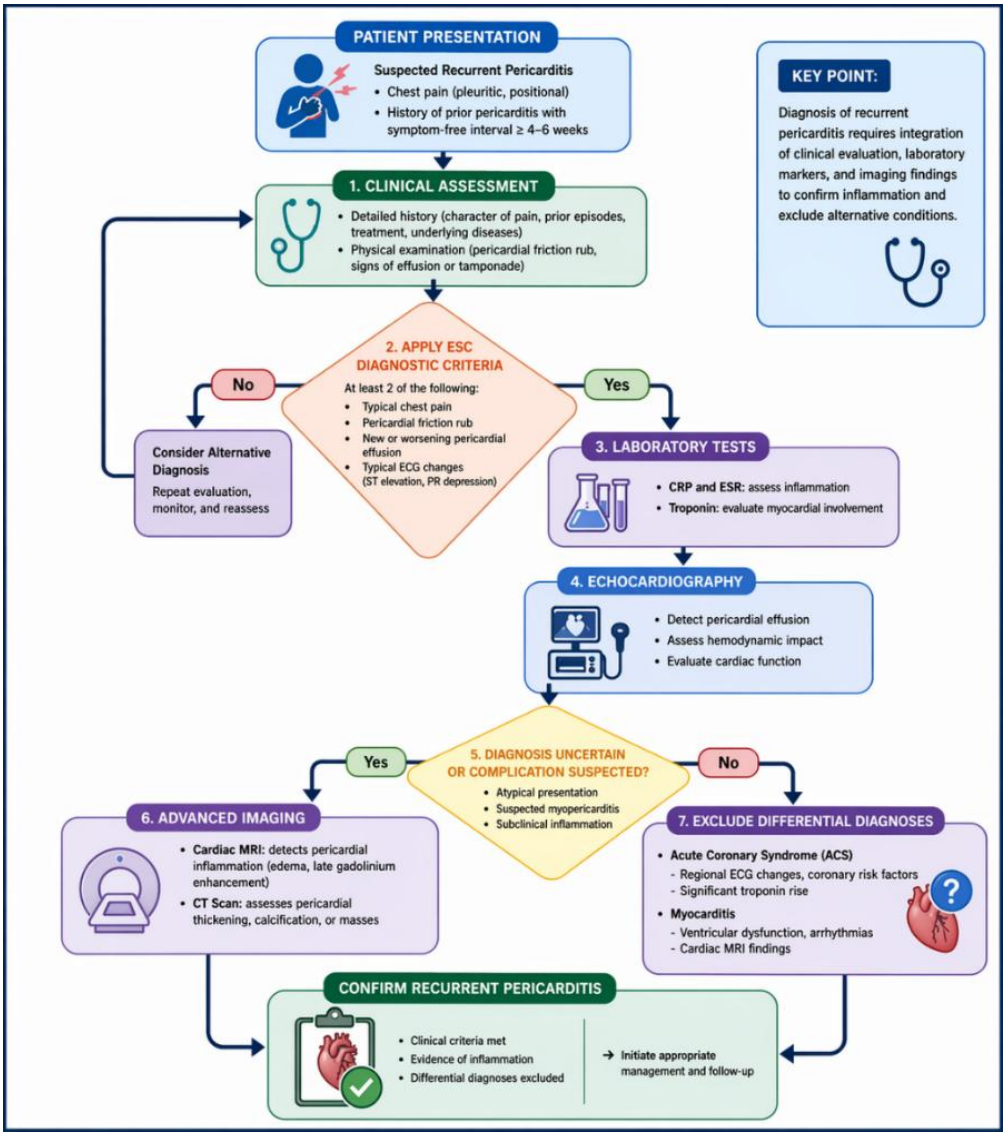

Figure 2: Diagnostic Algorithm for Recurrent Pericarditis

4. Medical Management Strategies

The management of recurrent pericarditis is done to reduce inflammation, symptom relief, prevent relapses, and minimize treatment complications. The use of conventional anti-inflammatory therapy and then followed by targeted immunomodulatory and biologic therapies in the case of refractory patients is advisable. Decisions on treatment are informed by the severity of the disease, the recurrence pattern, and etiology (Lazarou et al., 2022).

The initial treatment involves nonsteroidal anti-inflammatory drugs (NSAIDs) plus colchicine. NSAIDs like ibuprofen, aspirin, and indomethacin decrease inflammation by inhibiting cyclooxygenase and are slowly tapered depending on the symptom resolution and restoration of normal levels of inflammatory markers (Burkett & Younoszai, 2021). Ibuprofen is more often preferred since it has a good safety profile, but aspirin is advised in patients with ischemic heart disease.

Colchicine is in the middle of preventing recurrence and achieving better results. It works by preventing the formation of microtubules and inhibiting the activation of inflammasomes, thus decreasing interleukin-1 (IL-1)-induced inflammation (Nidorf & Thompson, 2019)Thompson, 2019). Clinical trials have continually shown that colchicine is an important adjunctive therapy in terms of reducing the rate of recurrence. Recurrent cases usually require long-term administration (≥6 months). The gastrointestinal intolerance is the most prevalent side effect that is usually dose-dependent.

Corticosteroids are used as second-line treatment in case of intolerant or unresponsive patients to NSAIDs and colchicine, or in particular clinical situations like autoimmune diseases. Despite the rapid effect of corticosteroids on the reduction of the symptoms, there is a risk of a higher recurrence rate as a result of possible immune regulation (Cremer et al., 2016). The modern approaches focus on low-dose treatment, including gradual tapering, in order to reduce dependency and relapse.

In case of patients with steroid-dependent or refractory disease, immunosuppressive agents could be considered, including azathioprine and methotrexate. Azathioprine is also effective in suppressing lymphocyte growth, disrupting purine production, and is especially effective in pericarditis related to autoimmune conditions (Ammirati et al., 2022). The use of folate antagonist methotrexate has also proven to be beneficial in some cases in regulating immune reactions, but its application is less common. Close observation is necessary as there are risks of hepatotoxicity and bone marrow suppression.

Intravenous immunoglobulin (IVIG) therapy may be considered in selected refractory cases, particularly when an autoimmune mechanism is suspected. IVIG has immunomodulatory effects and neutralizes pathogenic antibodies and controls the production of cytokines (Bizzi et al., 2021). Its application, though, is restricted by expensive costs, a lack of availability, and a comparatively low level of evidence as a result of small studies.

More recent therapeutic improvements have been made in biologic agents that block the IL-1 pathway, which is central in the pathophysiology of recurrent pericarditis. An IL-1 receptor antagonist, anakinra, has demonstrated prompt and lasting clinical response among patients with colchicine-resistant and steroid-dependent illness (Lazaros et al., 2016). Moreover, IL-1 cytokine trap rilonacept has proven to be effective in preventing recurrence as well as improving patient-reported outcomes in clinical trials (Brucato et al., 2022). These therapies would be a major paradigm shift to precision medicine, as the underlying inflammatory pathways are directly addressed.

Randomized controlled trials and observational studies are sources of evidence to support present management strategies. Colchicine continues to be first-line therapy based on strong evidence of its effectiveness, whereas biologic therapies provide promising treatments for refractory disease. Nevertheless, the long-term safety, availability, and affordability are also significant factors in clinical practice (Shahid et al., 2023).

Table 3 presents a summary of the pharmacological treatments, their mechanisms, indications, advantages, and limitations to aid clinical decision-making.

In general, recurrent pericarditis needs a personalized and evidence-based management. Though traditional therapies are effective in the majority of patients, there is a need to diagnose early refractory disease and to escalate to the advanced therapies in time. The invention of IL-1-targeted biologics has provided a great chance in improving the outcomes and increasing the range of therapy available to patients with a disease that is hard to treat.

Table 3: Pharmacological Treatments for Recurrent Pericarditis

Drug	Mechanism	Indications	Advantages	Limitations
NSAIDs (Ibuprofen, Aspirin)	Inhibit cyclooxygenase → ↓ inflammation	First-line therapy	Effective, widely available	GI, renal side effects
Colchicine	Inhibits microtubules, ↓ IL-1 activation	First-line + recurrence prevention	Reduces relapse rates	GI intolerance
Corticosteroids	Broad anti-inflammatory effect	Second-line, autoimmune cases	Rapid symptom control	↑ recurrence risk, side effects
Azathioprine	Inhibits lymphocyte proliferation	Steroid-dependent cases	Steroid-sparing	Myelosuppression, hepatotoxicity
Methotrexate	Immunosuppressive (folate antagonist)	Refractory cases	Effective in select patients	Toxicity monitoring required
IVIG	Immunomodulation, ↓ autoantibodies	Autoimmune/refractory cases	Useful in select patients	Expensive, limited evidence

Anakinra	IL-1 receptor antagonist	Refractory, steroid-dependent cases	Rapid symptom relief	Cost, injection site reactions
Rilonacept	IL-1 trap (binds IL-1α/β)	Refractory recurrent pericarditis	Reduces recurrence	High cost

5. Challenges in Management and Special Clinical Situations

Although significant progress has been made in treatment, recurrent pericarditis is challenging to treat due to its relapsing nature, variable response to treatment, and balancing control against treatment toxicity. One of the most significant issues is the development of corticosteroid dependence that is typical of patients with persistent or recurrent disease. Despite the rapid suppressive effect of corticosteroids on the inflammatory process, repeated intake and the fast taper are linked to relapse, extended treatment regimens, and cumulative side effects. In modern practice, this has led to a change of focus onto steroid-saving measures and a more timely consideration of specific therapy in the chosen patients (Kumar et al., 2022).

The relapses are frequent and put a significant clinical burden. Patients can have recurrent symptomatic flares, which may last months or years and require hospitalization and long-term therapy. This does not confine itself to physical symptoms and can be seen to extend to impaired quality of life, anxiety, and reduced functional capacity. There is a strong association between persistent inflammation and incomplete remission and recurring patterns of disease (Agrawal et al., 2024).

Long-term care is further complicated by adverse effects that come as a result of treatment. NSAIDs can cause gastrointestinal, renal, and cardiovascular toxicity, whereas colchicine intolerance can reduce compliance. The most common effects of corticosteroids include metabolic imbalances, osteoporosis, and immunosuppression. Immunomodulators and biologics can decrease recurrence in refractory disease, although close attention should be paid to the prevention of infection and systemic toxicity (Imazio, Andreis, et al., 2020; Imazio, Brucato, et al., 2020).

It is more complicated with special clinical populations. Recurrent pericarditis in pediatric patients is frequently autoinflammatory in nature and can have a systemic inflammatory appearance. Research indicates that interleukin-1 blockade may be very effective in cases of refractoriness in children, yet long-term outcomes have yet to be assessed (Caorsi et al., 2023).

Pregnancy poses special therapeutic issues because of the issue of maternal and fetal safety. Management approaches focus on control of the disease before conception, and this is through the selection of drugs during pregnancy. NSAIDs are usually not used in later pregnancy, and colchicine is gradually becoming a relatively safe drug, according to the emerging data. It is advised to use multidisciplinary management to maximize the results (Pryor et al., 2023).

The second issue is to treat immunocompromised patients or those at higher risk of infection. Infectious etiologies should always be ruled out in such people before immunosuppressive or biologic therapy is commenced. In such situations, individual treatment approaches regarding risk profile and disease characteristics play a crucial role (Kumar et al., 2022).

Pericardiectomy can be a last resort intervention in patients with refractory recurrent pericarditis who fail to respond to medical treatment. The results of surgeries are unpredictable, and the operation is extremely risky; thus, the selection of patients and their referral to specialized facilities are crucial (Khandaker et al., 2012).

In addition to pharmacological issues, patient compliance and quality of life are important issues. The recurrent pericarditis is chronic and unpredictable and may result in psychological distress and diminished quality of life. Patient education, frequent follow-up, and shared decision-making are critical to enhance adherence and outcomes in the long run (Agrawal et al., 2024).

Refractory disease needs a step-by-step approach to management. This includes reevaluation of diagnosis, assessment of inflammatory activity, and gradual replacement of conventional therapy by immunomodulatory agents and biologic therapy. This would allow a more personalized approach and the best treatment results (Kumar et al., 2022).

Overall, recurrent pericarditis is a difficult disorder because of steroid addiction, recurrent relapses, adverse effects of treatment, and intricacies of special populations. Individualized and patient-centered care with the help of newly developed specific therapies is necessary to enhance the quality of life and outcomes.

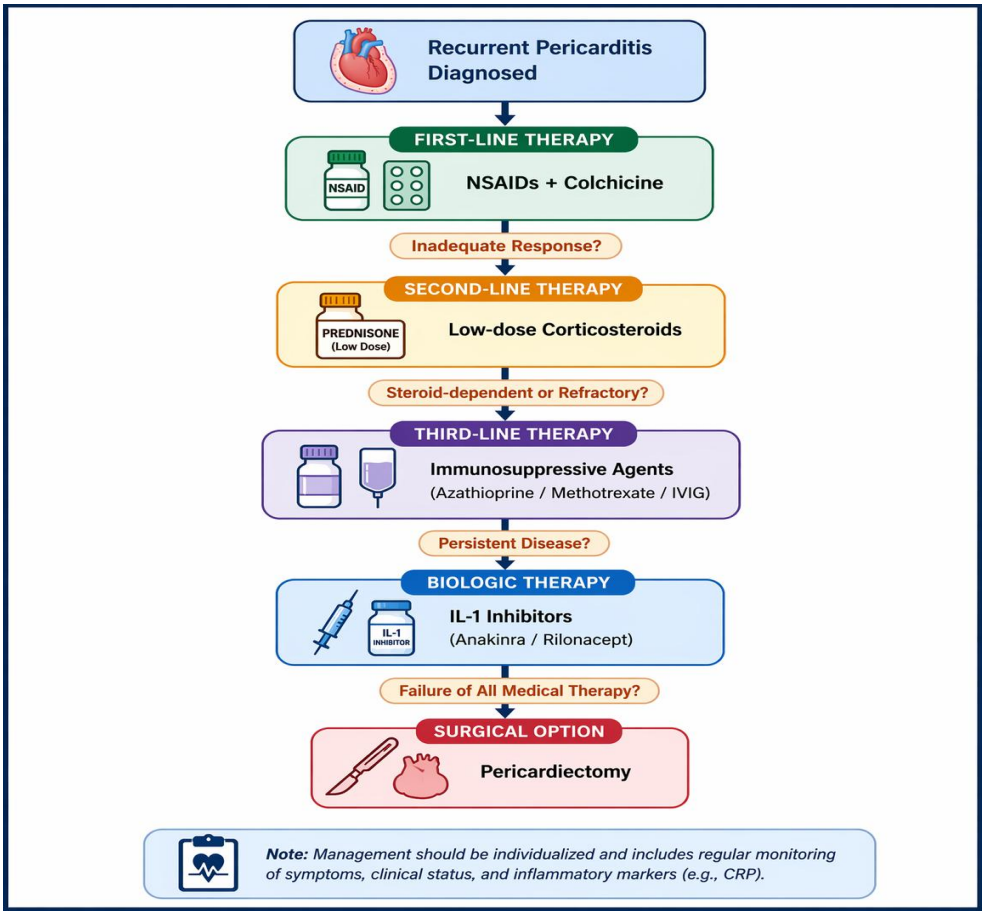

Figure 3: Management Pathway for Refractory Recurrent Pericarditis

6. Long-Term Management and Prognosis

The management of recurrent pericarditis over the long term is aimed at preventing recurrence, reducing complications, and ensuring a better patient outcome. Since the disease is chronic and relapsing, a progressive and long-term management plan is crucial. This method combines drug treatment, nutrition change, and regular check-ups in order to guarantee the full elimination of inflammation and decrease the likelihood of recurrence (Furqan et al., 2021).

The prevention of recurrence has been the cornerstone of long-term care. The use of the anti-inflammatory therapy, especially colchicine-based therapy, has been linked to long-term remission and a low rate of recurrence. Close tapering of treatment in accordance with clinical signs and inflammatory indicators is critical to prevent early termination and flare-up. Moreover, the reduction of the corticosteroid exposure is highly encouraged since the long-term steroid use is linked with the increased rates of recurrence and long-term negative outcomes (Yesilyaprak et al., 2024).

Long-term management includes lifestyle changes and patient education as key elements. It is recommended that during active inflammation, patients limit their physical activity and resume

normal activities gradually after clinical and biochemical remission. Intense physical activity can be a cause of inflammation and risk of relapse when resumed early. Moreover, the compliance of patients to therapy and the detection of the signs of recurrence early on play a vital role in the long-term outcomes (Imazio, 2022).

Follow-up is a focal point in the overall management of the disease and makes therapeutic choices. Laboratory findings that help to understand the presence of ongoing inflammatory processes include the C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR). Sustained higher-level inflammatory markers, even in patients without symptoms, can be a sign of subclinical inflammation and a higher risk of relapse. Selectively, imaging techniques (echocardiography or cardiac magnetic resonance (CMR) imaging) can be used to evaluate pericardial inflammation and identify complications (Markousis-Mavrogenis et al., 2022).

The prognosis of recurrent pericarditis is usually good, especially when treated properly. Nonetheless, some patients might acquire chronic or complicated diseases. Constrictive pericarditis can be considered one of the most severe long-term complications, with the development of pericardial fibrosis and the inability to fill the ventricle. Even though it is not very frequent, the risk is increased in patients with ongoing inflammation or certain etiologies like infectious pericarditis (Welch, 2018). It is important to detect high-risk patients early to avoid the disease.

Along with physical complications, recurrent pericarditis is a serious problem that affects psychological well-being and quality of life. Repeated episodes of chest pain, long course of treatment, and inability to know how the disease has progressed can lead to anxiety, depression, and low functional capacity. Long-term management should include addressing these psychosocial factors with the help of patient counseling and supportive care (Henein et al., 2022).

The recent developments in the study of the mechanisms of diseases have given rise to the personalized approach to treatment. With the help of personalized therapy according to the phenotype of the disease, its recurrence rate, and underlying inflammation mechanisms, more effective and targeted therapy can be provided. This method is specifically applicable to patients with refractory disease, whose usual treatments might not be effective (Cacciatore et al., 2025).

The other developing field of treatment of recurrent pericarditis is through biomarker-guided therapy. To determine the duration of treatment and tapering, inflammatory markers like CRP are being used more to monitor disease activity in addition to guiding treatment. New biomarkers and novel imaging methods can also improve the predictive capabilities of recurrence and tailoring of treatment in the future (Markousis-Mavrogenis et al., 2022).

In conclusion, multidisciplinary approach to recurrent pericarditis treatment should be considered in the long run, with the emphasis on individualized and holistic treatment. Although the prognosis is

usually favorable, attention should be paid to the prevention of recurrence, treatment adherence, and the early detection of complications. The development of personalized medicine and biomarker-directed therapy has promising prospects to enhance the long-term outcomes and cut the disease burden.

7. Conclusion

Recurrent pericarditis is a complex and typically disabling condition, which requires an individualized and comprehensive clinical intervention. Despite the generally positive prognosis of the disease, its recurrence and diagnostic issues combined with complications of treatment make it incredibly challenging in the context of every day clinical practice. This disease is sensitive to early detection and administration of anti-inflammatory medications and close follow-ups to prevent relapse. Colchicine is one of the mainstays in therapy, and corticosteroids are necessary with cautious use because they are linked to higher chances of a recurrence. The introduction of specific biologic treatment, especially IL-1 inhibitors, has greatly enhanced disease management and patient outcome in refractory cases. Special clinical populations and the possible effects on quality of life should also be taken into account when managing recurrent pericarditis. Plans that emphasize recurrence prevention, patient compliance, and follow-up on a regular basis should be implemented in the long term to maximize the results. Moreover, the development of knowledge about the immunopathogenesis of the disease has also facilitated more personalized and biomarker-based therapeutic strategies. Further studies are needed to perfect treatment algorithms, make new therapies more available, and determine good predictors of recurrence. All in all, a multidisciplinary and patient-centered strategy continues to be pivotal to enhance the long-term management and prognosis of recurrent pericarditis.

8. References

1. Adler, Y., Charron, P., Imazio, M., Badano, L., Barón-Esquivias, G., Bogaert, J., Brucato, A., Gueret, P., Klingel, K., & Lioni, C. (2016). 2015 esc guidelines for the diagnosis and management of pericardial diseases: The task force for the management of infective endocarditis of the european society of cardiology (ESC): Endorsed by: European association for cardio-thoracic surgery (EACTS). Rossijskij Kardiologiceskij Zurnal, 133(5), 117–162.
2. Agrawal, A., Kumar, A., Yesilyaprak, A., Zumpano, J., Pozuelo, L., & Klein, A. (2024). Quality of Life in Patients With Recurrent Pericarditis. Canadian Journal of Cardiology, 40(11), 2275–2278. https://doi.org/10.1016/j.cjca.2024.05.018
3. Ammirati, E., Bizzi, E., Veronese, G., Groh, M., Van de Heyning, C. M., Lehtonen, J., Pineton de Chambrun, M., Cereda, A., Picchi, C., Trotta, L., Moslehi, J. J., & Brucato, A. (2022). Immunomodulating Therapies in Acute Myocarditis and Recurrent/Acute Pericarditis. Frontiers in Medicine, 9. https://doi.org/10.3389/fmed.2022.838564
4. Andreis, A., Imazio, M., Casula, M., Avondo, S., & Brucato, A. (2021). Recurrent pericarditis: An update on diagnosis and management. Internal and Emergency Medicine, 16(3), 551–558. https://doi.org/10.1007/s11739-021-02639-6
5. Asteggiano, R., Bueno, H., Caforio, A. L., Carerj, S., & Ceconi, C. (2015). 2015 ESC

Guidelines for the diagnosis and management of pericardial diseases–Web Addenda. Eur Heart J, 36, 2921–2964.

6. Bizzi, E., Trotta, L., Pancrazi, M., Nivuori, M., Giosia, V., Matteucci, L., Montori, D., & Brucato, A. (2021). Autoimmune and Autoinflammatory Pericarditis: Definitions and New Treatments. Current Cardiology Reports, 23(9), 128. https://doi.org/10.1007/s11886-021-01549-5
7. Brucato, A., Imazio, M., Gattorno, M., Lazaros, G., Maestroni, S., Carraro, M., Finetti, M., Cumetti, D., Carobbio, A., Ruperto, N., Marcolongo, R., Lorini, M., Rimini, A., Valenti, A., Erre, G. L., Sormani, M. P., Belli, R., Gaita, F., & Martini, A. (2016). Effect of Anakinra on Recurrent Pericarditis Among Patients With Colchicine Resistance and Corticosteroid Dependence: The AIRTRIP Randomized Clinical Trial. JAMA, 316(18), 1906–1912. https://doi.org/10.1001/jama.2016.15826
8. Brucato, A., Lim-Watson, M. Z., Klein, A., Imazio, M., Cella, D., Cremer, P., LeWinter, M. M., Luis, S. A., Lin, D., Lotan, D., Pancrazi, M., Trotta, L., Klooster, B., Litcher-Kelly, L., Zou, L., Magestro, M., Wheeler, A., Paolini, J. F., & for the RHAPSODY Investigators. (2022). Interleukin-1 Trap Rilonacept Improved Health-Related Quality of Life and Sleep in Patients With Recurrent Pericarditis: Results From the Phase 3 Clinical Trial RHAPSODY. Journal of the American Heart Association, 11(20), e023252. https://doi.org/10.1161/JAHA.121.023252
9. Burkett, D. A., & Younoszai, A. K. (2021). Restrictive Cardiomyopathy and Pericardial Diseases. In Echocardiography in Pediatric and Congenital Heart Disease (pp. 794–821). John Wiley & Sons, Ltd. https://doi.org/10.1002/9781119612858.ch37
10. Cacciatore, S., Andaloro, S., Bernardi, M., Oterino Manzanas, A., Spadafora, L., Figliozzi, S., Asher, E., Rana, J. S., Ecarnot, F., Gragnano, F., Calabrò, P., Gallo, A., Andò, G., Manzo-Silberman, S., Roeters van Lennep, J., Tosato, M., Landi, F., Biondi-Zoccai, G., Marzetti, E., & Sabouret, P. (2025). Chronic Inflammatory Diseases and Cardiovascular Risk: Current Insights and Future Strategies for Optimal Management. International Journal of Molecular Sciences, 26(7), 3071. https://doi.org/10.3390/ijms26073071
11. Caforio, A. L. P., Pankuweit, S., Arbustini, E., Basso, C., Gimeno-Blanes, J., Felix, S. B., Fu, M., Heliö, T., Heymans, S., Jahns, R., Klingel, K., Linhart, A., Maisch, B., McKenna, W., Mogensen, J., Pinto, Y. M., Ristic, A., Schultheiss, H.-P., Seggewiss, H., … Elliott, P. M. (2013). Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. European Heart Journal, 34(33), 2636–2648. https://doi.org/10.1093/eurheartj/eht210
12. Caorsi, R., Insalaco, A., Bovis, F., Martini, G., Cattalini, M., Chinali, M., Rimini, A., Longo, C., Federici, S., Celani, C., Filocamo, G., Consolini, R., Maggio, M. C., Fadanelli, G., Licciardi, F., Romano, M., Teruzzi, B. L., Taddio, A., Miniaci, A., … Gattorno, M. (2023). Pediatric Recurrent Pericarditis: Appropriateness of the Standard of Care and Response to IL-1 Blockade. The Journal of Pediatrics, 256, 18-26.e8. https://doi.org/10.1016/j.jpeds.2022.11.034
13. Chiabrando, J. G., Bonaventura, A., Vecchié, A., Wohlford, G. F., Mauro, A. G., Jordan, J. H., Grizzard, J. D., Montecucco, F., Berrocal, D. H., Brucato, A., Imazio, M., & Abbate, A. (2020). Management of Acute and Recurrent Pericarditis. JACC, 75(1), 76–92. https://doi.org/10.1016/j.jacc.2019.11.021
14. Cremer, P. C., Kumar, A., Kontzias, A., Tan, C. D., Rodriguez, E. R., Imazio, M., & Klein, A. L. (2016). Complicated Pericarditis: Understanding Risk Factors and Pathophysiology to Inform Imaging and Treatment. Journal of the American College of Cardiology, 68(21), 2311–2328. https://doi.org/10.1016/j.jacc.2016.07.785
15. Furqan, M. M., Verma, B. R., Cremer, P. C., Imazio, M., & Klein, A. L. (2021). Pericardial Diseases in COVID19: A Contemporary Review. Current Cardiology Reports, 23(7), 90.

https://doi.org/10.1007/s11886-021-01519-x
16. Henein, M. Y., Vancheri, S., Longo, G., & Vancheri, F. (2022). The Role of Inflammation in Cardiovascular Disease. International Journal of Molecular Sciences, 23(21), 12906. https://doi.org/10.3390/ijms232112906
17. Imazio, M. (2022). Current treatment of recurrent pericarditis: Safety considerations and future directions. Expert Opinion on Drug Safety, 21(2), 183–190. https://doi.org/10.1080/14740338.2021.1960980
18. Imazio, M., Andreis, A., De Ferrari, G. M., Cremer, P. C., Mardigyan, V., Maestroni, S., Luis, S. A., Lopalco, G., Emmi, G., Lotan, D., Marcolongo, R., Lazaros, G., De Biasio, M., Cantarini, L., Dagna, L., Cercek, A. C., Pivetta, E., Varma, B., Berkson, L., … Adler, Y. (2020). Anakinra for corticosteroid-dependent and colchicine-resistant pericarditis: The IRAP (International Registry of Anakinra for Pericarditis) study. European Journal of Preventive Cardiology, 27(9), 956–964. https://doi.org/10.1177/2047487319879534
19. Imazio, M., Bobbio, M., Cecchi, E., Demarie, D., Demichelis, B., Pomari, F., Moratti, M., Gaschino, G., Giammaria, M., Ghisio, A., Belli, R., & Trinchero, R. (2005). Colchicine in Addition to Conventional Therapy for Acute Pericarditis: Results of the COlchicine for acute PEricarditis (COPE) Trial. Circulation, 112(13), 2012–2016. https://doi.org/10.1161/CIRCULATIONAHA.105.542738
20. Imazio, M., Brucato, A., Cemin, R., Ferrua, S., Maggiolini, S., Beqaraj, F., Demarie, D., Forno, D., Ferro, S., Maestroni, S., Belli, R., Trinchero, R., Spodick, D. H., & Adler, Y. (2013). A Randomized Trial of Colchicine for Acute Pericarditis. New England Journal of Medicine, 369(16), 1522–1528. https://doi.org/10.1056/NEJMoa1208536
21. Imazio, M., Brucato, A., Lazaros, G., Andreis, A., Scarsi, M., Klein, A., De Ferrari, G. M., & Adler, Y. (2020). Anti-inflammatory therapies for pericardial diseases in the COVID-19 pandemic: Safety and potentiality. Journal of Cardiovascular Medicine, 21(9), 625. https://doi.org/10.2459/JCM.0000000000001059
22. Imazio, M., Brucato, A., Maestroni, S., Cumetti, D., Belli, R., Trinchero, R., & Adler, Y. (2011). Risk of Constrictive Pericarditis After Acute Pericarditis. Circulation, 124(11), 1270–1275. https://doi.org/10.1161/CIRCULATIONAHA.111.018580
23. Imazio, M., & Gaita, F. (2015). Diagnosis and treatment of pericarditis. https://doi.org/10.1136/heartjnl-2014-306362
24. Imazio, M., Gaita, F., & LeWinter, M. (2015). Evaluation and Treatment of Pericarditis: A Systematic Review. JAMA, 314(14), 1498–1506. https://doi.org/10.1001/jama.2015.12763
25. Imazio, M., Gribaudo, E., & Gaita, F. (2017). Recurrent Pericarditis. Progress in Cardiovascular Diseases, A New Renaissance in Pericardial Diseases, 59(4), 360–368. https://doi.org/10.1016/j.pcad.2016.10.001
26. Imazio, M., Lazaros, G., Brucato, A., & Gaita, F. (2016). Recurrent pericarditis: New and emerging therapeutic options. Nature Reviews Cardiology, 13(2), 99–105. https://doi.org/10.1038/nrcardio.2015.115
27. Khandaker, M. H., Schaff, H. V., Greason, K. L., Anavekar, N. S., Espinosa, R. E., Hayes, S. N., Nishimura, R. A., & Oh, J. K. (2012). Pericardiectomy vs Medical Management in Patients With Relapsing Pericarditis. Mayo Clinic Proceedings, 87(11), 1062–1070. https://doi.org/10.1016/j.mayocp.2012.05.024
28. Klein, A. L., Abbara, S., Agler, D. A., Appleton, C. P., Asher, C. R., Hoit, B., Hung, J., Garcia, M. J., Kronzon, I., & Oh, J. K. (2013). American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: Endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. Journal of the American Society of Echocardiography, 26(9), 965–1012.
29. Klein, A. L., Imazio, M., Cremer, P., Brucato, A., Abbate, A., Fang, F., Insalaco, A., LeWinter, M., Lewis, B. S., Lin, D., Luis, S. A., Nicholls, S. J., Pano, A., Wheeler, A., &

Paolini, J. F. (2021). Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis. New England Journal of Medicine, 384(1), 31–41. https://doi.org/10.1056/NEJMoa2027892

30. Kumar, S., Khubber, S., Reyaldeen, R., Agrawal, A., Cremer, P. C., Imazio, M., Kwon, D. H., & Klein, A. L. (2022). Advances in Imaging and Targeted Therapies for Recurrent Pericarditis: A Review. JAMA Cardiology, 7(9), 975–985. https://doi.org/10.1001/jamacardio.2022.2584
31. Lazaros, G., Imazio, M., Brucato, A., Vassilopoulos, D., Vasileiou, P., Gattorno, M., Tousoulis, D., & Martini, A. (2016). Anakinra: An emerging option for refractory idiopathic recurrent pericarditis: a systematic review of published evidence. Journal of Cardiovascular Medicine, 17(4), 256. https://doi.org/10.2459/JCM.0000000000000266
32. Lazarou, E., Tsioufis, P., Vlachopoulos, C., Tsioufis, C., & Lazaros, G. (2022). Acute Pericarditis: Update. Current Cardiology Reports, 24(8), 905–913. https://doi.org/10.1007/s11886-022-01710-8
33. Maisch, B. (2025). Pericardial Diseases. In Clinical Cardiology (pp. 379–390). Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-662-69938-6_26
34. Markousis-Mavrogenis, G., Giannakopoulou, A., Belegrinos, A., Pons, M. R., Bonou, M., Vartela, V., Papavasiliou, A., Christidi, A., Kourtidou, S., Kolovou, G., Bacopoulou, F., Chrousos, G. P., & Mavrogeni, S. I. (2022). Cardiovascular Magnetic Resonance Imaging Patterns in Rare Cardiovascular Diseases. Journal of Clinical Medicine, 11(21), 6403. https://doi.org/10.3390/jcm11216403
35. Nidorf, S. M., & Thompson, P. L. (2019). Why Colchicine Should Be Considered for Secondary Prevention of Atherosclerosis: An Overview. Clinical Therapeutics, 41(1), 41–48. https://doi.org/10.1016/j.clinthera.2018.11.016
36. Ntsekhe, M., & Mayosi, B. M. (2013). Tuberculous pericarditis with and without HIV. Heart Failure Reviews, 18(3), 367–373. https://doi.org/10.1007/s10741-012-9310-6
37. Pryor, K., Tarter, L., Economy, K., Honigberg, M. C., Valente, A. M., Garshick, M., & Weber, B. (2023). Pericarditis Management in Individuals Contemplating Pregnancy, Currently Pregnant, or Breastfeeding. Current Cardiology Reports, 25(10), 1103–1111. https://doi.org/10.1007/s11886-023-01930-6
38. Shahid, R., Jin, J., Hope, K., Tunuguntla, H., & Amdani, S. (2023). Pediatric Pericarditis: Update. Current Cardiology Reports, 25(3), 157–170. https://doi.org/10.1007/s11886-023-01839-0
39. Wang, T. K. M., & Klein, A. L. (2022). Multi-Modality Cardiac Imaging for Pericardial Diseases: A Contemporary Review. Reviews in Cardiovascular Medicine, 23(10), 336. https://doi.org/10.31083/j.rcm2310336
40. Welch, T. D. (2018). Constrictive pericarditis: Diagnosis, management and clinical outcomes. Heart, 104(9), 725–731. https://doi.org/10.1136/heartjnl-2017-311683
41. Yesilyaprak, A., Kumar, A. K., Agrawal, A., Furqan, M. M., Verma, B. R., Syed, A. B., Majid, M., Akyuz, K., Rayes, D. L., Chen, D., Kai Ming Wang, T., Cremer, P. C., & Klein, A. L. (2024). Predicting Long-Term Clinical Outcomes of Patients With Recurrent Pericarditis. JACC, 84(13), 1193–1204. https://doi.org/10.1016/j.jacc.2024.05.072