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Pericardial Diseases:

International Position Statement on New Concepts and Advances in Multimodality Cardiac Imaging

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Abstract

Pericardial diseases have gained renewed clinical interest, leading to a renaissance in the field. There have been many recent advances in pericardial diseases in both multimodality cardiac imaging of diagnoses, such as recurrent, transient constrictive and effusive-constrictive pericarditis, and targeted therapeutics, especially anti-interleukin (IL)-1 agents that affect the inflammasome as part of autoinflammatory pathophysiology. There remains a large educational gap for clinicians, leading to variability in evaluation and management of these patients. The latest pericardial imaging (American Society of Echocardiography, European Association of Cardiovascular Imaging) and clinical guidelines (European Society of Cardiology) are >8-10 years of age and may not reflect current practice. Recent clinical trials involving anti-IL-1 agents in recurrent pericarditis, including anakinra (AIRTRIP), rilonacept (RHAPSODY), and goflikicept have demonstrated their efficacy. The present document represents an international position statement from world leaders in the pericardial field, focusing on novel concepts and emphasizing the role of multimodality cardiac imaging as well as new therapeutics in pericardial diseases.

Keywords

cardiac magnetic resonance; constrictive pericarditis; echocardiography; pericardial effusion; pericarditis; pericardium

INTRODUCTION

OBJECTIVES AND WRITING COMMITTEE.

This document aims to inform health professionals regarding new concepts and recent advances in the clinical applications of multimodality cardiac imaging in the management of pericardial diseases, with emphasis on diagnosis, risk stratification, and surveillance. Sections II-VI provide an overview of the clinical, anatomic, and pathophysiologic

perspectives of the pericardium. Sections VII–XIII delve into the major pericardial clinical syndromes in turn to discuss the critical and combined roles of multimodality cardiac imaging, with recommendations and key points for each section, and concluding remarks at the end. Disease-specific algorithms for diagnosis and management are proposed. This document follows an expert consensus format, in part because of few randomized trials, as well as to provide a timely update to prior pericardial disease guidelines.^{1,2} The Writing Committee consists of an international panel of cardiovascular clinicians and imagers experienced in the imaging and management of pericardial diseases. This document was reviewed and endorsed by the American College of Cardiology Imaging Council and Society of Cardiovascular Magnetic Resonance.

CONTEMPORARY CLINICAL AND THERAPEUTIC PERSPECTIVES AND ADVANCES.

Pericardial diseases encompass a broad category of diseases, but this document focuses on pericarditis pericardial effusion (PEff), constrictive pericarditis (CP), pericardial masses, and congenital anomalies.² Pericardial diseases are frequently encountered in the emergency department, outpatient clinic, and primary care settings, and etiologies are classified broadly as idiopathic, infectious, traumatic and iatrogenic, autoimmune, neoplastic, drug-related and metabolic, and other miscellaneous causes. Given the rapid rise in cardiac procedures and the COVID-19 pandemic, there is vast recent interest in post-cardiac injury syndrome and COVID-19—or post-vaccine associated etiologies. Clinical presentations of pericardial diseases include a constellation of chest pain, shortness of breath, peripheral and/or abdominal swelling, and other symptoms associated with underlying etiologies, but often it remains mis-diagnosed.^{2,3} Traditional management includes nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and exercise restriction as first-line and low-dose corticosteroids as second-line for acute/recurrent pericarditis (RP), pericardiocentesis, or window for PEff with cardiac tamponade (CTP), and diuretic therapy and/or radical pericardiectomy surgery for CP and intractable RP.^{2,4} Anti-interleukin (IL)-1 agents, such as anakinra, rilonacept, and goflikicept, have recently demonstrated in randomized trials superior efficacy for colchicine-resistant or steroid-dependent RP.^{5–7} Advances in multimodality imaging (MMI) are an important cornerstone in the accurate diagnosis, prognostication, and monitoring of pericardial diseases, to enable imaging-guided therapy (IGT) to facilitate appropriate therapies and improve clinical outcomes (Central Illustration).^{1,8}

OVERVIEW OF MMI.

MMI plays complementary roles in the evaluation of all pericardial diseases. Table 1 lists the strengths and limitations of the 3 main noninvasive modalities utilized: echocardiography, cardiac computed tomography (CT), and cardiac magnetic resonance (CMR); and Table 2 describes their main techniques and protocols for evaluation of the pericardium. It is important to take a stepwise approach when ordering these tests, as downstream imaging may not be needed if the diagnosis is confirmed after initial imaging.

ECHOCARDIOGRAPHY.

Following a detailed clinical assessment, transthoracic echocardiography (TTE) remains the first-line imaging modality for pericardial evaluation.^{1,9} This is because of its ability

to assess pericardial disease, cardiac chamber, and function as well as valvular pathology, along with availability, portability, and low cost. Two-dimensional M-mode and Doppler techniques are mandatory, and 3-dimensional and speckle tracking may add further information. Transesophageal echocardiography is required only when TTE has poor windows or is not feasible, such as during or immediately after cardiac surgery, and stress echocardiography also is seldom indicated, except for quantifying exercise and functional capacity, including VO_2 (maximum rate of oxygen consumption) and assessing pulmonary hypertension, diastolic dysfunction, and left ventricular filling pressures associated with stress in CP.

CARDIAC CT.

CT is a second-line imaging modality, with the main indications of assessing pericardial calcifications in CP and fluid or tissue characterization of PEff or masses.^{1,9,10} These are sometimes incidental findings seen on CT performed for nonpericardial indications. Advanced CT scanners and dedicated protocols currently allow for a greater number of and thinner slices, electrocardiography (ECG) gating, and 4-dimensional whole-heart cycle cine acquisition, with or without iodinated contrast administration.

CARDIAC MAGNETIC RESONANCE.

CMR is another second line imaging modality with comprehensive evaluation of most pericardial conditions.^{1,8,9} The contemporary CMR pericardial protocol includes steady-state free precession to evaluate chamber size and function, including real-time free breathing imaging for physiology such as ventricular interdependence, black-blood spin echo sequence with and without contrast (T1- and T2-weighted inversion-recovery turbo spin echo sequences) to depict pericardial anatomy and provide tissue characteristics of masses, T2 short tau inversion recovery (STIR) to identify pericardial edema, and late gadolinium enhancement (LGE) sequences to identify pericardial inflammation and fibrosis.^{11,12} Other optional techniques include phase contrast flow, tagging, and T1 and/or T2 mapping sequences. The most important value of CMR is its tissue characterization capabilities, including diagnosing and monitoring pericardial inflammation with the use of IGT, and characterizing PEff and masses.¹¹ This modality is increasingly considered to be an essential part of diagnosing complex pericardial clinical syndromes.

EPIDEMIOLOGY, ETIOLOGY, AND CLASSIFICATION

EPIDEMIOLOGY.

Despite the relative high frequency of pericardial diseases, there is little epidemiologic data, especially from primary care. Pericarditis is the most common disease of the pericardium encountered in clinical practice. The incidence of acute pericarditis has been recently reported as 32.4 ± 3.5 cases per 100,000 population per year in an Italian region.¹³ Pericarditis is responsible for 0.1% of all hospital admissions and 5% of emergency department admissions for chest pain.¹⁴⁻¹⁶ Data collected from a Finnish national registry (2000-2009) showed a standardized incidence rate of hospitalizations for acute pericarditis of 3.32 per 100,000 person-years.¹⁷ These data were limited to hospitalized patients and therefore may account for only a minority of cases, because many patients with pericarditis

are not admitted to hospital.¹⁷⁻²⁰ Men aged 16-65 years were at higher risk for pericarditis (RR: 2.02) than women in the general admitted population, with the highest risk difference among young adults compared with the overall population. Acute pericarditis caused 0.20% of all cardiovascular admissions. The proportion of caused admissions declined by an estimated 51% per 10-year increase in age. The in-hospital mortality rate for acute pericarditis was 1.1% and increased with age and severe co-infections (pneumonia or septicemia).¹⁷ However, that was in a study based on hospital admissions only. A recent study with 20 year follow-up showed an significant upward trend in the incidence rate of pericarditis from 7.2 cases per 100,000 patients in 2000 to 29.2 cases per 100,000 patients in 2019.²¹ Recurrences affect about 30% of patients within months after a first episode of acute pericarditis, and up to 50% after the first recurrence,^{22,23} with overall 40,000 RP patients estimated in the United States.³

ETIOLOGY.

Etiologies for pericardial diseases are listed in Table 3.^{14,20,24,25} The etiology is varied and depends on the epidemiologic background, patient population, and clinical setting. In developed countries, idiopathic and viral are usually the most common etiologic agents of pericarditis,²⁰ whereas tuberculosis (TB) is the most frequent cause of pericardial diseases in developing countries where TB is endemic. In that setting, TB is often associated with HIV infection, especially in sub-Saharan Africa.

CLASSIFICATION.

Classification of pericardial diseases is presented in Table 4 and will be further discussed in the remainder of this document. The clinical diseases arise by several pathophysiologic processes, including inflammation (ie, pericarditis), excess fluid accumulation (PEff), pericardial stiffening restricting cardiac expansion (CP), along with masses (including benign and malignant lesions) and congenital anomalies (absence of pericardium).² Pericarditis is typically subdivided by time course and etiology. PEff can be categorized based on size, hemodynamic impact (presence or absence of CTP), and fluid characteristics. CP has 2 important subcategories: transient constrictive pericarditis (TCP), whereby CP resolves after a period of time with anti-inflammatory therapy or spontaneously; and effusive-constrictive pericarditis (ECP), whereby CP appears after initial presentation and removal of PEff. The clinical presentation of pericardial diseases varies between chest pain, symptoms and signs of systemic inflammation to hemodynamic compromise or chronic heart failure. Symptoms attributable to pericardial disease may be very dramatic (as in an episode of acute pericarditis) or rather minor, particularly in the context of a systemic disease. PEff may be asymptomatic and detected incidentally.²⁶ Pericardial disease may also trigger atrial arrhythmia, sinus tachycardia, and, importantly, atrial fibrillation.²⁷

ANATOMY OF THE PERICARDIUM IN HEALTH AND DISEASE

PERICARDIAL HISTOLOGY AND ANATOMY.

The pericardium has a parietal component and a visceral component (Figure 1). The parietal pericardium is an outer fibrous sac (the fibrosa) lined by a single layer of mesothelial cells (the serosa). The serosa invests the proximal great arteries in one sheath and pulmonary

veins and venae cavae in another sheath. The impressions of the serosa around the arteries and veins form the pericardial sinuses and recesses (Figure 2).²⁸ The serosa covers the entire surface of the heart, and it is referred to as the visceral pericardium or epicardium. Importantly, the pericardium together with the elastic properties of the epicardium restrain the heart chambers from expansion and play a role in determining the passive pressure-volume relationship.^{14,15}

VASCULAR SUPPLY, LYMPHATIC DRAINAGE, AND INNERVATION.

The pericardial cavity contains an average of 25 mL of fluid (up to 50 mL). The pericardial fluid is considered to be a serum ultrafiltrate, and this ingenious design allows for smooth motion during cardiac contraction and at the same time fixes the heart in the mediastinum and protects it from contact with the surrounding structures, infections, and tumors. This fluid is drained by the lymphatic system on the epicardial surface of the heart and in the parietal pericardium. The lymphatic vessels of the pericardium drain to the anterior and posterior mediastinal, peribronchial, and tracheobronchial lymph nodes.^{29,30} The pericardium is supplied by arterial branches from the internal thoracic artery and the descending thoracic aorta. The pericardiophrenic veins drain directly or via the superior intercostal veins and internal thoracic veins into the brachiocephalic veins.³¹ The phrenic nerve supplies sensory fibers to the pericardium. The parasympathetic nerve supply is from the vagus, left recurrent laryngeal nerves, and esophageal plexus. Sympathetic innervation is derived from the first dorsal ganglion, stellate ganglion, and the aortic, cardiac, and diaphragmatic plexuses.³²

EFFECTS OF DISEASE ON THE PERICARDIUM AND PERICARDIAL RESPONSE TO INJURY.

The pericardial response to injury consists of mesothelial cell desquamation, increased vascular permeability, neovascularization, and exudation of fluid, fibrin and/or inflammatory cells (Figure 3).³³ The repair phase shows granulation tissue with proliferation of fibroblasts and thin-walled blood vessels that in turn may result in focal or diffuse adhesions between the parietal and visceral pericardium and in pericardial thickening that may lead to CP.

PATHOPHYSIOLOGY OF THE PERICARDIUM IN HEALTH AND DISEASE **PERICARDIAL FUNCTION.**

The normal pericardium functions to maintain a relatively constant position of the heart in the thorax and provides a barrier to infection (Table 5).³⁴ It is innervated with mechano- and chemoreceptors and phrenic afferent receptors that participate in cardiac reflex responses and transmission of pericardial pain. The pericardium also secretes prostaglandins, which may modulate coronary tone.³⁵

MECHANICAL EFFECTS, RESERVE VOLUME, AND PRESSURE-VOLUME RELATIONS.

Normal parietal pericardial tissue has a flat stress-strain relationship at low stresses that abruptly steepens at higher stresses. The transition is likely dictated by collagen fibers, which are wavy at low strains but straighten as the tissue is stretched. The pressure-volume relationship of the normal pericardial sac mimics isolated tissue (Figure 4).³⁵ The transition

to a steep pressure-volume relationship occurs at a volume roughly corresponding to that of the upper range of the normally filled heart. Thus, the pericardial sac has a relatively small reserve volume, above which it markedly restrains further increases in cardiac volume. As cardiac volume increases, the normal pericardium exerts an increasing positive pressure on the epicardial surface, which is transmitted to the cardiac chambers, elevating intracavitary filling pressure. This effect is most prominent in the thin-walled right ventricle where a substantial portion of intracavitary filling pressure is accounted for by the pericardium. Restraint of cardiac volume by the pericardium dictates that changes in the filling of a cardiac chamber occurs reciprocally with the volume of other chambers, amplifying ventricular interdependence. With PEff, small increases in volume result in large increases in intrapericardial pressure and clinical worsening when the steep portion of the pressure-volume relationship is encountered. With chronic cardiac dilation or large, slowly accumulating PEffs, the pressure-volume relationship flattens and shifts to the right (Figure 4).

PATHOPHYSIOLOGY OF CTP, CP, AND ECP.

When pericardial fluid volume exceeds the pericardial reserve volume or when the pericardium becomes scarred, inelastic, or severely inflamed, one of 3 pericardial compressive syndromes may ensue:^{34,35} CTP, characterized by pericardial fluid under pressure, CP caused by loss of pericardial elasticity, or ECP caused by coexistent PEff and CP, the latter often caused by pericardial inflammation. Some patients with CP or ECP have spontaneous resolution or resolve with anti-inflammatory therapy and are considered to have TCP, a diagnosis that can be considered with the use of imaging and inflammatory biomarkers as well as clinical history, but definitively made only in retrospect.

CTP and CP share several features, but they differ in the pattern of impaired diastolic filling of the ventricles (Table 6).³⁴⁻³⁶ In CTP, filling is impaired throughout diastole, whereas in CP, early diastolic filling is more rapid than normal until mid-late diastole. In CP, the obliterated pericardial space markedly diminishes pleural pressure transmission to the heart, resulting in dissociation of pleural and intracardiac pressures.^{34,35} Consequently, the pressure gradient from pulmonary circulation to the left heart decreases with inspiration. Owing to interventricular dependence, the ventricular septum bows to the left, increasing blood flow to the right heart. With expiration, left-side filling increases and the septum moves to the right, limiting right heart filling. In CTP, the pressure transmission is less affected and systemic venous return increases with inspiration, and the right heart expands at the expense of the left (ventricular interdependence).³⁶ Owing to these pathophysiologic mechanisms of CTP and CP, there is a substantial diastolic flow reversal in the hepatic vein with expiration when right heart filling is thwarted. In both conditions, right atrial pressure is elevated and there is a competition between the superior (SVC) and inferior (IVC) venae cavae filling. With inspiration, IVC pressure overcomes SVC pressure because of increased abdominal pressure, resulting in less filling from the SVC, which presents as the Kussmaul sign.

Although the pericardial sac is typically obliterated in patients with CP, in some instances, a PEff co-exists.³⁵ When this occurs, the scarred, inelastic pericardium may not only limit

cardiac filling, but may also pressurize the pericardial fluid, leading to signs of CTP. Thus, the clinical and TTE findings and hemodynamics of ECP fall on a continuum between pure CTP and chronic CP. Cases of TCP commonly present as ECP or acute pericarditis with significant pericardial inflammation. Patients may be erroneously assumed to have only CTP, but the underlying CP is revealed by the persistent elevation of right atrial pressure (failure to drop by 10 mm Hg or by >50% after pericardiocentesis) or persistent Doppler pattern of constriction in mitral inflow, tissue Doppler, and hepatic vein.³⁷ Before pericardiocentesis, ECP is suggested by the unexpected persistence of a “V” wave in the right atrial pressure recording. In TTE, pure CTP shows grade 1 diastolic mitral inflow velocity pattern with E velocity lower than A velocity. However, in patients with ECP, mitral inflow velocity pattern is more like that of CP before pericardiocentesis.

ROLE OF INNATE AND ADAPTIVE IMMUNITY IN PERICARDIAL DISEASE

PERICARDIAL INFLAMMATION AND THE IMMUNE SYSTEM.

Pericarditis is an intense inflammatory syndrome in response to injury of the mesothelial cells of the pericardium.² The triggers include viral infections, cardiac surgery or ablation, and autoimmunity. Typically, autoinflammatory and autoimmune syndromes are characterized by innate and adaptive immunity dysregulation.

Unrelated stimuli activate the formation of the inflammasome, a macromolecular cellular structure central to the sensing of the infectious pathogen or injury, leading to the institution and amplification of the inflammatory response. A typical autoinflammatory response is central to the pathophysiology of RP, as indicated in Figure 5. Infectious agents (eg, viruses) release pathogen-associated molecular patterns, and the damage to the pericardial layer from infection or external factors, such as during radiofrequency ablation procedures, leads to the release of danger-associated molecular patterns, such as the IL-1 α and extracellular adenosine triphosphate. These events promote the transcription and translation of proinflammatory genes, such as the precursors of IL-1 β , as well as components of the inflammasome.³⁸ The inflammasome forms a macromolecular aggregate that leads to the autocatalytic cleavage of pro-caspase-1 to active caspase-1 and activation of pro-IL-1 β and other proinflammatory cytokines into their mature and active forms.

ANIMAL MODELS.

In an experimental mouse model, zymosan, an activator of the inflammasome, injected in the pericardial space, induced inflammation and thickening of the pericardial layer and PEff formation of the inflammasome, as well as expression of IL-1 α and IL-1 β , thus recapitulating a phenotype of pericarditis, which was improved by colchicine, a specific inflammasome inhibitor, and anti-IL-1 agents (Figure 6).³⁹ A similar pattern of an intense pattern of inflammasome activation is seen in the pericardial layers in patients with chronic pericarditis.

ROLE OF ANTI-INFLAMMATORY THERAPIES.

Colchicine has been central to treatment of pericarditis, promoting the resolution of acute attacks and preventing recurrences.⁴⁰ In some patients with RP, the inflammation

becomes unresolved and not responsive to colchicine, which appears to be mediated by excessive IL-1 α and IL-1 β . The recombinant human anti-IL-1 agent anakinra, 100 mg/day administered to 21 patients with RP who were resistant to colchicine and dependent on corticosteroid therapy, provided control of pericarditis symptoms in all cases and allowed for suspension of corticosteroid therapy.⁵ After remission of symptoms, patients were assigned continuation of anakinra or switch to placebo. Those randomized to anakinra experienced a 90% survival free of recurrence, compared with 18% in those randomized to placebo.⁵ A similar benefit was seen with rilonacept, a soluble decoy receptor, or IL-1 α and IL-1 β cytokine trap, binding to IL-1 α and IL-1 β and preventing engagement with the cell surface receptor, administered to patients with RP refractory to standard treatment for 12 weeks; when symptoms were controlled, concomitant therapy was discontinued and 61 patients who were symptom free on rilonacept monotherapy entered the randomized withdrawal period in which they were randomly assigned in a 1:1 ratio to receive either continued rilonacept or matching placebo each week. During this period, 7% of patients in the rilonacept group had a pericarditis recurrence, compared with 74% patients in the placebo group. More recently, the novel anti-IL-1 agent goflkicept was evaluated in a phase II/III randomized control trial in 20 patients, with pericarditis recurrence in 0 of 10 patients on goflkicept and in 9 of 10 patients receiving placebo.⁷ Figure 7 illustrates the Kaplan-Meier curves of time-to-RP efficacy endpoints from randomized trials of these 3 anti-IL-1 agents compared with placebo.⁴¹ A clinical trial entitled the MAvERIC-Pilot ([NCT05494788](https://clinicaltrials.gov/ct2/show/study/NCT05494788)) with cannabidiol is currently ongoing to assess its effect on patient-reported pericarditis pain score following 8 weeks of treatment.

Pericarditis is a common cardiac manifestations of systemic lupus erythematosus and other autoimmune diseases.⁴² Treatment is often guided by the underlying disorder, although frequently used options include corticosteroids, azathioprine, and mycophenolate mofetil.⁴³ Intravenous immunoglobulin has been used with some success in systemic lupus erythematosus.⁴⁴

GENETICS.

Monogenic systemic autoinflammatory diseases such as familial Mediterranean fever, an autosomal recessive disorder caused by sequence variants in *MEFV* gene, result in the overactivation of the inflammasome and periodic febrile inflammatory episodes characterized by pericarditis and other serositis.⁴⁵ In a retrospective study of 128 patients with RP, analysis of 4 common systemic autoinflammatory disease pathogenic genes revealed that 7.8% of the patients harbored variants in *MEFV* that were either predicted or known to be pathogenic. In a study that specifically examined sequence variants in the tumor necrosis factor receptor-associated periodic syndrome gene (*TNFRSF1A*), 6.1% were found to harbor a sequence variant. A meta-analysis of genome-wide association studies in 4,894 pericarditis patients found 2 independent sequence variants at the IL-1 gene locus to be associated with pericarditis.⁴⁶ These findings may suggest a genetic basis for autoinflammation seen in RP, with potential to guide targeted therapies.

IMAGING INFLAMMATION IN ACUTE AND CHRONIC PERICARDITIS AND RESPONSE TO THERAPY

CMR imaging has emerged as an important imaging modality for both diagnosis and management of pericarditis.¹¹ CMR allows for anatomic and functional/physiologic assessment of the heart and pericardium. Black-blood spin-echo sequences provide high-resolution assessment of pericardial anatomy and thickness.⁴⁷ Acute pericardial edema/inflammation can be identified by pericardial enhancement on fat-suppressed T2-weighted imaging in the acute setting (T2-STIR images). Pericardial enhancement on LGE imaging also identifies pericardial inflammation because of neovascularization of the pericardium.⁴⁸ Furthermore, LGE imaging provides important evaluation of the myocardium to determine the presence of concomitant myocarditis, myopericarditis, or perimyocarditis. Chronic changes in after pericardial inflammation may result in the development of fibrinous tissue and calcification.

CMR's ability to identify, stage, and quantify the degree of pericardial inflammation with the integration of LGE evaluation and edema-weighted T2-STIR imaging has been shown to significantly improve diagnostic accuracy compared with conventional clinical evaluation.^{11,48-51} Furthermore, severity of pericardial enhancement on T2 STIR and LGE imaging provides the ability to stage and grade the severity of pericardial enhancement, as well as prognosticate likelihood of RP (Figure 8).^{52,53} Standardized methodology for pericardial enhancement for clinical reporting has not yet been determined. We propose a pericardial LGE grading criteria based on the extent of circumferential enhancement and thickness of enhancement (Figure 9). This can be particularly helpful for patients with RP and frequent flares in the context of tapering anti-inflammatory medications (Figure 10).

It is important to note that T2 STIR is the first to resolve and that pericardial LGE is likely the last imaging biomarker to resolve, so resolution or nearresolution of pericardial LGE can provide more definitive confidence in resolution of pericardial inflammation. Therefore, CMR can be used to guide therapy, and this approach has been shown to decrease the likelihood of recurrence, exposure to steroids, and pericardiocentesis.⁵⁴ Consequently, the integration of pericardial enhancement in conjunction with inflammatory markers and patient symptoms can be used to devise individualized treatment plans in terms of intensity and duration of anti-inflammatory therapy to prevent potential complications such as recurrence, CP, and CTP.^{49,55} In addition, CMR may be useful to help rule out pericarditis in patients with atypical chest pain referred for possible RP. Although CMR-directed therapy can provide important guidance, caution is warranted with long-term repeated contrast-enhanced CMR, because studies have demonstrated gadolinium deposition in multiple organs after repeated contrast MR studies, although the clinical significance of gadolinium deposition remains unclear.^{56,57} Finally, it is unclear how long pericardial LGE persists in the setting of neovascularization of the pericardium in patients with previous severe pericarditis or even years after cardiac surgery suggesting subclinical postpericardiotomy inflammation.^{58,59} Therefore, serial CMR is considered mainly in the setting of severe cases, refractory symptoms, or unclear therapeutic management based on clinical assessment alone.

Parametric T1/T2 mapping techniques have demonstrated important improvement in diagnostic accuracy in myocarditis, with potential application in pericarditis (Figure 11).⁶⁰ However, limitations related to spatial resolution and current lack of histologic validation prevent widespread clinical adoption in pericarditis. Further technical developments and innovation to enable contrast-free CMR evaluation would significantly shorten CMR scan time and minimize risk of repeated gadolinium exposure in patients with RP.

In patients with contraindications for CMR, ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT may be a potential alternative. High uptake with this modality has been shown to identify active inflammation of the pericardium (Figure 12). Therefore, response to anti-inflammatory medications could potentially be predicted with ¹⁸F-FDG PET/CT imaging.⁶¹ However, limitations in spatial resolution may limit the sensitivity for identifying milder presentations of pericarditis. In addition, the PET-CT scan requires a diet low in carbohydrates to prevent physiologic uptake of the glucose.

CLINICAL SYNDROMES

ACUTE PERICARDITIS.

Clinical perspectives and novel concepts. Acute pericarditis is an inflammatory condition with or without PEff. It may be diagnosed in the presence of 2 of the following clinical criteria: chest pain (85%-90% of cases), typically sharp and pleuritic, improved by sitting up and leaning forward; pericardial friction rub (<33% of cases); ECG changes (up to 60% of cases), with new widespread ST-segment elevation or PR-segment depression; and PEff (up to 60% of cases, generally small).² Confirmatory findings may be C-reactive protein (CRP) or erythrocyte sedimentation rate elevation, neutrophil leukocytosis, and CT or CMR.

Pericarditis probably encompasses several conditions, ranging from a noninflammatory phenotype with normal or near normal CRP (~17%) to an inflammatory phenotype with high fever, raised CRP, pleural involvement, neutrophil leukocytosis with low lymphocytic count, and high neutrophil/lymphocyte ratio (51% in referral centers).^{62,63} Different pathogenic pathways are probably involved, with IL-1 playing a pivotal role in this inflammatory subset. In these cases anti-IL-1 agents may be considered in the first attack, when other therapies are contraindicated, ineffective, or not tolerated. In this situation clinicians are probably ahead of basic scientists, and the pathogenesis of this inflammatory condition is still not completely elucidated.

Role of integrated MMI. MMI is essential when myocardial involvement is suspected and when the diagnosis is not clear, to exclude other thoracic pathologies (mainly with CT¹⁰) and/or to confirm pericardial involvement (mainly with CMR: pericardial thickness, PEff, edema in T2-STIR, LGE) (Table 7).^{4,11} TTE remains the first-line imaging modality, and may demonstrate pericardial thickening, PEffs (Figure 13), evidence of CP, and myocardial involvement (depressed left ventricular systolic function and regional wall motion abnormalities), but is often normal, though tachycardia may be noted. In complicated cases, CMR may be considered to help rule out pericardial inflammation for atypical chest pain to guide therapy and to assess prognosis and risk of recurrence (Figure 14).^{8,55} It is

not mandatory to search for the etiology in all patients, because most cases are viral or idiopathic and benign. Only a minority of cases should be hospitalized. The major risk factors associated with poor prognosis include high fever ($>38^{\circ}\text{C}$ [$>100.4^{\circ}\text{F}$]), subacute course, large PEffs (diastolic echo-free space >20 mm), CTP, and failure to respond within 7 days to NSAIDs. One can also consider assessing severe pericardial inflammation on CMR including T2-STIR and severe LGE as having a poor prognosis in acute pericarditis, but further data are necessary.

When to consider additional imaging. CMR is recommended in patients when there is uncertainty about the acute pericarditis diagnosis, in complicated cases of acute pericarditis, such as those not responding to first-line therapy, and for patients with clinical concerns for myocarditis (such as elevated cardiac troponins, depressed left ventricular ejection fraction, or regional wall motion abnormalities on TTE). A recent study showed that CMR was prognostic for pericardial complications in high-risk acute pericarditis patients.⁵⁵ CMR may be used when patients with acute pericarditis with noninflammatory phenotype (normal laboratory biomarkers for inflammation), although sometimes CMR findings for LGE and edema may be unremarkable, and therefore reliance would be on an empirical course of therapy and evaluating clinical symptoms for treating and monitoring these patients.

Contemporary management. Treatment is based on low-dose colchicine (0.6-1.2 mg/day) plus high-dose NSAIDs: 1.5-3 g/day aspirin (preferred in case of concomitant ischemic heart disease or older patients), 1,200-2,400 mg/day ibuprofen, 75-150 mg/day indomethacin, in divided doses every 8 hours during the attack.² The choice of drug and the dose should be based on tolerability, contraindications, previous efficacy, and clinical conditions. In elderly patients the dose must be reduced, as well as in subjects at risk for renal failure. Corticosteroid use should be restricted to cases that are refractory or intolerant to other therapies. Apart from cases in which NSAIDs are contraindicated, corticosteroids should be added to colchicine and NSAIDs, and low to medium doses of corticosteroids (eg, 0.2-0.5 mg/kg/day prednisone) are usually effective. When a prednisone course is planned, other preventive measures are recommended, including for osteoporosis, such as vitamin D and bisphosphonates in all men aged 50 years and older and postmenopausal women, infection prophylaxis with antibiotics such as trimethoprim/sulfamethoxazole, and gastric protection with proton-pump inhibitors (also applicable for NSAIDs).

After the first episode of acute pericarditis, NSAIDs are recommended for at least 2 weeks and colchicine for 3 months. If chest pain persists (incessant) or there is recurrent or chronic pericarditis, necessitating the use of corticosteroids, then all 3 medications should be used at their top doses for 2-4 weeks before starting to wean. Prednisone would be weaned first, by 2.5-5.0 mg every 2-4 weeks for doses above 15 mg, and by 1-2.5 mg every 2-4 weeks thereafter. Following this, NSAIDs would be weaned after 2-4 weeks, eg, ibuprofen starting at 2,400 mg is then weaned to 1,800 mg to 1,200 mg to 800 mg then 200 mg and off every 2-4 weeks, and finally colchicine can be weaned from 0.6 mg twice daily to once daily, with at least 6 months on colchicine. Often the tapering is based on symptoms and inflammatory markers (CRP).

Recommendations and key points.

- Acute pericarditis is mainly a clinical entity. Different pathogenetic pathways are probably involved, with IL-1 playing a pivotal role in the inflammatory subset.
- MMI is essential when myocardial involvement is suspected or when the diagnosis is not clear, to exclude other thoracic pathologies (mainly with CT), and/or to confirm pericardial involvement (mainly with CMR: pericardial thickness, PEff, edema in T2-STIR, LGE) (Table 8, Video 1).
- In some cases, CMR may also be considered to guide therapy and to assess prognosis and risk of recurrence.

RECURRENT, INCESSANT, AND CHRONIC PERICARDITIS.

Clinical perspectives and novel concepts. RP is one of the most common and troublesome complications, affecting 20%-30% of patients with a first episode of acute pericarditis and up to 50% of patients with recurrences.^{23,64} To have a recurrence, the patient should have a remission with a symptom-free interval of 4-6 weeks after the acute episode. This time interval, established by current European guidelines, allows completion of the medical therapy for the acute episode.² Those who are experiencing persistent symptoms without remission are labeled as patients with incessant pericarditis. Similarly to acute pericarditis, the pathogenesis of recurrent and incessant pericarditis may have a noninflammatory (less common) or inflammatory (more common) phenotype with fever and/or elevation of CRP at each episode or for the majority of them.⁶⁵ Cardiac troponin I and T elevation is not infrequent in pericarditis in ~30%, and often suggest myopericarditis (predominantly pericarditis) or perimyocarditis (predominantly myocarditis), the latter especially if there is impaired left ventricular involvement and myocardial LGE on CMR. Of note, some studies have not found worse prognosis in the setting of RP with troponin leaks.^{4,66}

Current medical therapy is based on empiric first-line anti-inflammatory therapy with colchicine and NSAIDs (Table 9). If clinical response is insufficient, then treatment can be personalized according to the presentation phenotype (Figure 15): for those with an inflammatory phenotype, anti-IL-1 agents are preferred,⁶⁷ whereas for those without inflammatory phenotype, corticosteroids may be a better option as second-line agents. Azathioprine and intravenous immunoglobulins could be considered for such patients after failure of corticosteroids.⁶⁸ The treatment of COVID- or mRNA therapy-related pericarditis is mainly targeted at the control of inflammation and is not different from the recommended therapy for incessant or RP.

Role of integrated MMI. TTE remains the first modality of imaging for the evaluation of a patient with a suspicion of pericardial disease. However, although TTE remains essential to assess the presence and size of a PEff and to assess the presence or absence of a constrictive physiology,⁶⁹ because of its limitations in tissue characterization it is not able to assess the presence of active inflammation or fibrosis. The inflamed pericardium is neovascularized and contrast enhanced in CT and CMR (Figure 16). During active inflammation, pericardial edema can be depicted by T2-STIR and can be responsible for pericardial thickening

that can be measured in CT or CMR. In the chronic phase, chronic inflammation with neovascularization and possible pericardial fibrosis can be assessed by the presence of LGE in CMR.^{1,11} On this basis, integrated MMI (TTE, CT, and CMR) can be clinically useful to assess all stages of pericarditis: acute inflammation, chronic inflammation, fibrosis, and remission (Table 10). The extent of pericardial thickening and LGE predicts the severity of the disease and the outcome.^{3,8,74} IGT assessing pericardial inflammation could be useful for the diagnosis and monitoring of therapy, providing objective assessment of the achievement of remission in more difficult cases.

When to consider additional imaging. TTE remains the first-level imaging technique for the diagnosis and monitoring of pericarditis.^{1,2,73} However, in complicated and atypical cases, the clinical suspicion of pericarditis can be confirmed by means of CMR (pericardial edema and LGE). CMR can also be used to follow the patient and assess the response to treatment and remission in a more objective way.^{11,74} CT is the criterion standard for the identification of pericardial calcifications, also allowing the evaluation of their extension by reconstruction.^{1,2,73} On this basis, second-level imaging is recommended for patients with complicated pericarditis to achieve the diagnosis and monitor the disease activity and response to treatments.^{3,8,74} There are no specific rules on the timing of second-level imaging, especially CMR, which can be used at baseline and then at 6-month intervals to assess the response to treatment.

Contemporary management. Contemporary management of recurrent and incessant pericarditis includes the evaluation of the presentation phenotype (inflammatory vs noninflammatory). Basic treatment includes NSAIDs plus colchicine (Table 9). Therapies targeted at specific pathogenesis include anti-IL-1 agents (such as anakinra, rilonacept, and goflikicept⁵⁻⁷), colchicine, and corticosteroids (Figure 7). For those with an inflammatory phenotype, anti-IL-1 agents and possibly colchicine are first options to consider,⁶⁷ whereas for those without inflammatory phenotype, corticosteroids are a better option. As alternative to corticosteroids or in patients who are steroid dependent, anti-IL-1 agents have high efficacy as second-line agents for RP not responding to first-line agents. The duration of anti-IL-1 therapy remains uncertain, because recurrence rates are very low while on therapy, but a significant proportion of patients (75%) experience recurrence on their discontinuation.⁷¹ Azathioprine and intravenous immunoglobulins also could be considered for such patients after failure of corticosteroids.⁷² Radical pericardiectomy may be considered as an alternative option at high-volume experienced surgical centers for patients who fail to respond to medical therapy.

Recommendations and key points.

- RP is characterized by the relapse of symptoms and signs of pericarditis after clinical remission.
- Incessant pericarditis is characterized by persistent symptoms and signs without remission.
- Presentation phenotype can be inflammatory (fever and/or elevation of inflammatory markers) or noninflammatory without CRP elevation.

- MMI (TTE, CT, and CMR) can be useful to assess the diagnosis in complicated/atypical cases and monitoring the response to treatment and the achievement of remission (Table 11, Video 1).
- Personalized therapy for recurrent/incessant pericarditis is guided by the presentation phenotype: Anti-IL-1 agents and colchicine are recommended for those with elevation of CRP, whereas corticosteroids and additional options should be considered for those without CRP elevation.

PERICARDIAL EFFUSION AND CARDIAC TAMPONADE.

Clinical perspective and novel concepts. PEff refers to the accumulation (>50 mL) of pericardial fluid in response to a range of pathologic processes (Table 12).^{1,2} Acute, presumably postviral pericarditis is the primary cause in the United States and Western Europe, whereas TB is the leading cause in the developing world; however, the cause remains unknown in approximately 50% of cases.⁷²⁻⁷⁴ A recent study found that 37% of patients with pectus excavatum undergoing chest CT had PEffs.⁷⁵ Malignancies are an important cause of “unexplained” PEffs, which may be detected before the diagnosis of cancer and are often inflammatory with negative cytology for malignant cells.⁷⁶⁻⁷⁸

PEffs have been traditionally classified as transudative, exudative, purulent, chylous, and hemorrhagic, though the distinction of transudative vs exudative is based on extrapolation of Light’s criteria.⁷⁹ Recent data have shown that normal pericardial fluid, in contrast to pleural fluid, is rich in nucleated cells (lymphomonocytic predominance), protein/albumin, and lactate dehydrogenase. Therefore, normal fluid is misclassified as exudative, and Light’s criteria should not be applied to the pericardium.^{80,81}

PEffs can be categorized according to volume (trivial meaning PEff is only seen in some phases of the cardiac cycle, small 50-100 mL, moderate 100-500 mL, or large >500 mL), onset (acute, subacute, or chronic), distribution (dependent, circumferential, or loculated), and hemodynamic impact. The hemodynamic consequences of a PEff are more closely related to the rapidity of effusion accumulation rather than absolute size.⁸²⁻⁸⁴ Once pericardial compliance and reserve volume are exhausted, further pericardial fluid accumulation results in a marked increase in intrapericardial pressure (>15 mm Hg) with equalization of pericardial and intracardiac end-diastolic pressures.^{85,86} Early in CTP, the cardiac output is maintained by a compensatory increase in heart rate, but ultimately, frank chamber compression occurs and compensatory mechanisms are exhausted, leading to hemodynamic collapse.^{1,2}

Role of integrated MMI. TTE is recommended in all patients with suspected or known PEff. Complementary advanced cardiac imaging might be justified in highly selected cases.¹ The goals of MMI in the evaluation of PEff are presented in Figure 17.

Transthoracic echocardiography. TTE is the initial test of choice because of high accuracy and widespread availability (Tables 12 and 13).⁸⁷ The size of the PEff is determined by the largest dimension of the echo-free space at end-diastole (trivial seen only in systole, small <1 cm, moderate 1-2 cm, large >2 cm, and very large >2.5 cm). Exudative/complex

effusions usually exhibit heterogeneous echogenicity, whereas transudative effusions have a typical anechoic appearance (Table 13, Figure 18).¹ Typical mimickers of PEffs include epicardial fat (heterogeneous echodensity that moves with the myocardium, and usually anterior to the right ventricle), left pleural effusion (traditionally located posterior to the descending thoracic aorta), and pericardial cyst (most commonly adjacent to the right atrium) (Figure 19).⁸⁸

In CTP, the key TTE findings include a plethoric IVC, diastolic cardiac chamber collapse, and exaggerated ventricular interdependence (Figure 20). A dilated IVC (>2.1 cm) with minimal or no respiratory collapse (<50%) is the most sensitive marker of CTP,⁸⁹ whereas end-diastolic right ventricular collapse in 2D imaging or M-mode (near the T wave) is the most specific echocardiographic finding^{90,91} (Video 2). Right atrial inversion can be seen in CTP during early systole (near peak R wave). Specificity is improved when the inversion/collapse duration is > one-third of the cardiac cycle.^{92,93} Enhanced interventricular dependence is supportive of CTP, and these findings include an augmented respirophasic variation (transmitral >30% and transtricuspid >60%) in atrioventricular inflow velocities), respirophasic septal shift, and expiratory end-diastolic hepatic venous flow reversals.^{85,94,95} When concern for CTP remains high despite TTE, transesophageal echocardiography or MMI is recommended. This is particularly relevant after cardiac surgery when focal intrapericardial hematoma might cause local compression (Figure 21). TTE is also a valuable tool for assessing the feasibility of percutaneous drainage and directly guiding pericardiocentesis.

Cardiac CT. Cardiac CT, typically with diastolic-phase ECG gating, provides high spatial resolution and the ability to perform multiplanar reconstructions (Table 13), which aids in localizing and sizing PEffs.⁹⁶⁻⁹⁸ Fluid density in CT is helpful in characterizing PEff (Table 12).⁹⁷ Cardiac CT can also identify the presence of pericardial enhancement, which may be seen with acute pericarditis, after administration of intravenous contrast. In addition, CT can identify secondary causes, such as contained myocardial rupture or iatrogenic perforation, and in the setting of malignancy can detect pericardial masses, cardiac tumors, and extracardiac neoplasms (Figure 21). Mimickers of PEff are well delineated on CT (Figure 20). Finally, this modality may be useful in directly guiding pericardiocentesis (CT-guided pericardiocentesis) in challenging cases (eg, small effusion, multiloculated effusion).⁹⁷

Cardiac magnetic resonance. CMR is used less often to assess PEffs and is not recommended for patients at risk of acute decompensation (Tables 12 and 13). Although it can precisely assess pericardial volume, PEff size is typically assessed visually and with 2D measurements. Transudative PEffs, given their high water content, have low intensity on T1-weighted imaging, and high signal on T2-weighted imaging and steady-state free precession cine imaging. In contrast, complex PEffs typically have heterogeneous T1 and T2 signals. The main added value of CMR in PEffs derive from its capacity to assess for pericardial inflammation.^{97,98} Emerging evidence suggests that T1 mapping may play a role in differentiating transudative (<3,013 msec) and exudative (>3,013 msec) PEff.^{99,100}

Although echocardiography is often enough for the evaluation of PEffs, complementary multimodality imaging (TEE, Cardiac CT or CMR) may be warranted when a diagnosis of PEff (vs mimickers) remains equivocal (Figure 19), secondary causes are suspected, clinical concern exist for CTP despite negative transthoracic echocardiography (Figure 21), or guide the drainage of challenging/complex effusions. (Table 13).

Contemporary management. Patients with PEff may complain of symptoms of pericarditis and may present with dyspnea, orthopnea, tachycardia, or hemodynamic compromise with CTP. However, many patients are asymptomatic.¹⁰¹ Diagnostic pericardiocentesis is required when a purulent or malignant PEff is suspected. Therapeutic drainage is indicated for large PEffs with concern for progression to CTP, significant associated symptoms, and in the setting of frank CTP.^{1,2} Imaging-guided pericardiocentesis is the favored drainage approach, and surgical pericardial windows are recommended when there is no safe percutaneous windows or path, or recurrences are expected with risk for CTP (eg, malignant PEff) or autoimmune disease. Conversely, the management of PEff associated with heart failure, uremia, and cancer should be tailored to treat the underlying condition. Exercise restriction is not necessary for PEffs in the absence of pericardial inflammation, and typically regular TTE surveillance is all that is needed for small to moderate PEffs until the criteria for pericardial drainage are reached.

Recommendations and key points.

- Acute pericarditis is the primary cause of PEff in the United States and Western Europe; however, postprocedural and malignancy-related PEffs are increasingly recognized in current practice.
- Light's criteria should not be used to classify PEffs, because normal pericardial fluid would be labeled as exudative.
- The goals of imaging in PEff include the following: 1) detect, size, and characterize the PEff; 2) evaluate for CTP; 3) guide pericardiocentesis when needed; 4) identify potential causes; and 5) evaluate for coexisting constrictive pathophysiology. Echocardiography is the first-line choice, but cardiac CT and CMR can provide valuable supplementary information (Table 14, Video 1).
- The key TTE findings in CPT include the presence of plethoric IVC, diastolic cardiac chambers collapse, and exaggerated ventricular interdependence.

CONSTRICTIVE PERICARDITIS.

Clinical perspectives and novel concepts. CP is characterized by loss of elasticity of the pericardium, which is usually thickened, resulting in compromised diastolic filling. Chronic CP is typically irreversible, because of scarring and fibrosis of the pericardium, but can be managed by pericardiectomy and represents a curable form of heart failure with preserved ejection fraction. In the developed world, idiopathic and post-cardiac surgery etiologies are most common, followed by radiation pericarditis.¹⁰² Tuberculosis remains the most common cause of CP in the developing world.¹⁰³

ECP is characterized by the coexistent presence of a hemodynamically significant PEff with CP hemodynamics after pericardiocentesis. The diagnosis has traditionally been made by identifying persistent right atrial pressure elevation after pericardiocentesis, as assessed with cardiac catheterization. Currently, ECP can be diagnosed by echocardiographic demonstration of CP hemodynamics after pericardiocentesis. TB is the most common etiology in the developing world, with one-half of patients with tuberculous PEff having evidence of ECP.¹⁰⁴ Idiopathic and radiation-related etiologies are most common in the developed world, where they are reported to occur in 8%-24% of patients with PEff.^{87,105,106} Long-term prognosis is favorable, with one series demonstrating spontaneous resolution in 92% of patients (24/26) who underwent repeat TTE and only 6% (2/33) needing pericardiectomy.¹⁰⁶

Some CP without coexistent PEff may have significant and reversible pericardial inflammation resulting in CP physiology, which resolves spontaneously or after medical therapy, termed TCP. However, some TCP may cross over to needing surgical therapy.

Role of integrated MMI. The role of imaging in CP serves 2 principal roles: 1) to confirm hemodynamics of CP physiology (Table 15); and 2) to define the presence or absence of pericardial inflammation to determine optimal initial treatment strategy.

Transthoracic echocardiography. TTE is the first-line imaging modality of choice in the assessment of CP and ECP, because of its ability to assess hemodynamics. CP has 2 unique hemodynamic features: 1) dissociation between intrathoracic and intracardiac pressure with respiration; and 2) interventricular dependence along with increased diastolic filling pressure in both right and left sides of the heart. These features translated into E-predominant mitral inflow with respiratory variation, respirophasic ventricular septal shift caused by ventricular interdependence, and expiratory end-diastolic hepatic venous flow reversals (Figure 22). In addition, medial mitral early diastolic velocities (e0) are elevated. These 4 parameters were proposed as the Mayo Clinic Echocardiographic Diagnostic Criteria for CP and were validated by another major pericardial center (Figure 23). Doppler features of ECP typically lie between those seen in CTP and CP. The presence of ECP before pericardiocentesis is suggested by elevated mitral annular e' velocities, high expiratory mitral inflow E velocities, and higher E/A ratios compared with patients with CTP.^{37,106} Compared with CP, E/A ratios were lower without other significant differences.³⁷ Post-pericardiocentesis findings mimic those of CP, with higher right atrial pressure, unchanged mitral E velocities, and persistent expiratory diastolic hepatic venous flow reversals compared with patients with CTP.³⁷

Cardiac magnetic resonance. CMR is a useful adjunctive imaging modality in this disease, providing excellent anatomic definition and assessment of pericardial inflammation (Figure 24). Although increased pericardial thickness supports the diagnosis, the absence of pericardial thickening does not exclude CP; one series reported normal pericardial thickness in 18% of patients with surgically proven CP.¹⁰⁷ Pericardial edema as assessed with the use of T2-STIR also has been shown to correlate with surgical pathology.¹⁰⁸ LGE is common, correlating with increased fibroblast proliferation, neovascularization, and chronic inflammation.^{48,108} Qualitative and quantitative assessment of LGE has been shown

to predict response to anti-inflammatory therapy in CP patients, incrementally to clinical assessment and inflammatory markers.^{109,110}

Cardiac CT. Cardiac CT may be useful as a complimentary modality to assess pericardial thickness, pericardial calcification, and, before pericardiectomy, relationships to adjacent structures (Figure 24).¹ Pericardial calcification can be localized to a circumferential band-like pattern sparing the basal anterior left ventricle and apical regions of the left and right ventricles, with extension into the mitral and tricuspid annuli.¹¹¹ However, pericardial calcification was not associated with adverse outcomes in a recent study.¹¹²

When to consider additional imaging. TTE and CMR are complementary in the assessment of patients with CP or ECP. Although cardiac catheterization is the traditional criterion standard for hemodynamics, there is a significant overlap between CP and restrictive cardiomyopathy in the traditional criteria. The characteristic hemodynamic changes of CP result in discordant respiratory changes between left and right ventricular systolic pressures.¹¹³ TTE provides reliable CP hemodynamic assessment with a high positive predictive value for this diagnosis. Concordant echocardiographic findings can be used to make a confident diagnosis of CP without the need for invasive cardiac catheterization. Discrepant echocardiographic parameters or high clinical suspicion should prompt assessment with invasive cardiac catheterization to confirm the diagnosis before pericardiectomy. CMR offers superior anatomic pericardial assessment and assessment of pericardial inflammation, and in addition can evaluate for myocardial fibrosis and scar by means of LGE and mapping sequences to assess for concomitant myocardial disease, such as when there is diagnostic uncertainty or for preoperative evaluation. Both TTE and CMR should be considered as key investigations in the assessment of this patient population, with cardiac CT as a supplementary test for pericardial calcifications assessment and preoperative evaluation.

Contemporary management. Initial therapy should target the underlying etiology where applicable. Where pericardial inflammation is identified, potent anti-inflammatory therapy should be initiated before consideration of surgical intervention. Pericardiectomy should be considered in symptomatic patients without evidence of pericardial inflammation or who fail anti-inflammatory therapy, and for whom surgical risk is not prohibitive.

Medical management. Volume overload in the setting of CP physiology may be treated with diuretic therapy for the restoration of euvolemia. This does not alter the natural history of CP, and pericardiectomy should be recommended in those patients without reversible inflammatory features, and for whom surgical risk is not prohibitive.

Identification of pericardial inflammation, by means of clinical and imaging evaluation, in conjunction with CP or ECP indicates severe pericardial inflammation. Initial response to therapy is typically poor and recovery slow. Nonetheless, antiinflammatory therapy should be the initial treatment of choice, because in some cases there may be reversal of CP (which may be considered transient) or ECP. No data exist comparing NSAIDs, colchicine, corticosteroids, and immunomodulatory agents in this patient population, and rapid escalation of therapies is frequently required. Corticosteroids (0.25-0.5 mg/kg per day)

or anti-IL-1 agents, in combination with colchicine, may be instituted for a period of at least 8-12 weeks before clinical and imaging reevaluation. Anti-inflammatory therapy may be needed for 3-6 months to assess adequate resolution of the pericardial inflammation and constrictive physiology.

Antituberculous therapy may result in resolution of CP physiology in 75% of patients with tuberculous pericarditis within 6 months of treatment commencement.¹⁰³ Early pericardiectomy is not warranted in this population, except in cases of hemodynamically instability or deterioration after 4-8 weeks of therapy.¹⁰³ Concomitant prednisone use was associated with a trend toward more rapid clinical improvement, reduced need for pericardiectomy, and reduced 24-month mortality, though without reaching statistical significance.^{103,114}

Surgical management. Symptomatic CP should be treated with radical surgical pericardiectomy including excision of the diaphragmatic and posterior pericardium, ideally performed by an expert pericardial surgeon. Cardiopulmonary bypass may be necessary to decompress the heart and allow access to these portions of the pericardium.¹⁰² Conventional partial pericardiectomy removing the anterior and/or diaphragmatic pericardium is insufficient, carrying a poorer long-term survival and less improvement in echocardiographic features.^{115,116} Repeated pericardiectomy for recurrent CP after incomplete pericardiectomy carries a significant (7.3%) 30-day mortality, highlighting the importance of a radical surgical pericardiectomy at the initial operation.¹¹⁷ Pooled data suggest significant 30-day all-cause mortality (6.9%), with post-cardiac surgery and radiation CP carrying 2-3 times higher risks of long-term mortality compared with idiopathic etiologies.¹¹⁸ Multivariate predictors of increased 30-day mortality include worse NYHA functional class, nonidiopathic etiologies, moderate or greater tricuspid valve regurgitation, renal function, urgent operative status, previous sternotomy, need for cardiopulmonary bypass, lower body surface area, female sex, and reduced left ventricular ejection fraction.¹¹⁹ Need for concomitant procedures, including tricuspid valve surgery, was not associated with worse outcomes.^{119,120} Recent reports from high volume pericardial specialty centers suggest operative risk is largely dependent on etiology and comorbidities, with operative mortality for idiopathic cases <1.5%.^{121,122} Echocardiographic features of CP may persist in up to 20% in the early postoperative period, particularly among those with longstanding preoperative symptoms.¹²³ These may resolve at long-term follow-up and should not be interpreted as treatment failure in the absence of symptoms.¹¹³ The waffle procedure, involving a small grid-like incision of the epicardium, can be performed for CP patients with epicardial thickening.¹²⁴

Recommendations and key points.

- TTE and CMR are complementary in the assessment of CP and ECP, offering reliable assessment of hemodynamics and of anatomy and inflammation, respectively, whereas CT has a limited role assessing pericardial calcifications and thickening (Table 16, Video 3).
- Distinguishing inflammatory and noninflammatory etiologies is essential to identify those patients who may benefit from anti-inflammatory therapy.

- Symptomatic noninflammatory CP should be treated with radical pericardiectomy performed by experienced pericardial surgeons.

PERICARDIAL MASSES (CYSTS, DIVERTICULA, AND TUMORS).

Overview. Etiology of pericardial masses traverse from benign incidental findings to advanced-stage malignancies. Frequently, pericardial lesions are identified incidentally on chest CT studies for other clinical indications. Pericardial involvement may also be detected on chest CT or PET-CT studies performed for cancer staging. Evaluation often begins with TTE because of prompt availability and immediate determination of hemodynamic importance. Limited field of view and inability of tissue characterization leads to additional assessment. MMI is an integral part of modern management of all patients with suspected pericardial masses. After TTE, data are integrated with clinical evaluation and CMR or CT to allow detailed anatomic assessment of the entire pericardium and adjacent structures.

Pericardial cysts and diverticula.

Clinical perspective, novel concepts, and contemporary management. A pericardial or mesothelial cyst is lined with a single layer of mesothelium. It is mostly congenital, caused by a defect in embryogenesis. It is usually filled with clear fluid, and the majority are located at the right cardiophrenic angle.¹²⁵ Pericardial cysts are uncommon, mostly asymptomatic, and primarily found incidentally. Large cysts can cause chest pain, shortness of breath, or persistent cough. At times, they are confused with localized PEff, tumor, ventricular aneurysm, or cardiomegaly without further work-up. Rarely, pericardial cysts can rupture, leading to CTP. Treatment of symptomatic patients may include percutaneous drainage or surgical excision; otherwise, the majority are managed conservatively.

Pericardial diverticulum is extremely rare and consist of out-pouching of the pericardium. Similarly to pericardial cyst, it occurs mostly at the costophrenic angle. Distinction from a cyst is based on presence of a communication with the pericardial space, which can be identified by changes in size and shape depending on body position and respiration. Pericardial diverticulum is managed conservatively.

Role of integrated MMI and when to consider additional imaging. TTE is the first baseline imaging modality to assess pericardial cysts and diverticulum, but depending on location, pericardial cysts may not be clearly visualized. They may also be seen incidentally on CT or CMR, both of which can confirm the diagnosis (Figure 25).¹ Characteristics imaging features are presented in Table 17.

Transthoracic echocardiography. Pericardial cyst is composed of fluid and appears as an echo-free structure, differentiating it from solid masses. Lack of flow on color Doppler also supports the diagnosis of a cyst. Depending on location, it is not always clearly seen in TTE and can be mistaken for drop-out.

Cardiac magnetic resonance. CMR provides excellent tissue characterization to exclude a malignant process. Pericardial cyst has a low to intermediate signal intensity on T1-weighted images and near-uniform high signal intensity on T2-weighted images. There is an absence

of LGE. Pericardial cyst is encapsulated with a well-defined border. CMR is also helpful to differentiate from other mediastinal cysts, such as bronchogenic, duplication, and thymic. When a complete circumferential lining cannot be identified on a cyst, diverticulum should be suspected. In symptomatic patients, serial imaging with CMR can determine interval growth without exposure to radiation. In asymptomatic patients, observation or serial imaging to follow pericardial cyst or diverticulum interval growth is warranted.

Cardiac CT. CT provides excellent delineation of pericardial cysts. They are encapsulated, nonenhancing with IV contrast, and sharply demarcated with homogeneous appearance at near water attenuation. Although pericardial cysts and diverticula can be identified in TTE, their size, location, involvement of surrounding structures, and confirmatory diagnosis are determined by CT or CMR. When a highproteinaceous cyst appears as a solid lesion on CT, CMR can establish the cystic nature of the lesion. Pericardial diverticulum appears similar to a cyst except that open communication to the pericardium is visualized.

Pericardial tumors.

Role of integrated MMI and when to consider additional imaging. Evaluation of pericardial tumors follows the same stepwise approach as any cardiac mass. TTE can identify pericardial tumors as echodense masses with or without associated PEff. It is especially important in identifying the hemodynamic significance of the lesion. CMR or CT can provide tissue characterization and differentiate a solid mass from a simple cystic lesion. It can also detect features that suggest a malignant nature of the pericardial mass. CMR provides detailed characterization with T1-weighted, T2-weighted, first-pass perfusion, and LGE imaging that can often allow distinction between benign vs malignant processes.¹²⁶ CT offers an alternative to CMR, with fast acquisition time and high spatial resolution delineating lesion margins and tissue planes. It is also useful for staging metastatic malignancies. PET/CT can assess lesion metabolic activity with the use of ¹⁸F-FDG. The degree of ¹⁸F-FDG uptake (standard uptake value) by tumor also can differentiate between benign vs malignant masses, and is commonly used for tumor staging and response to therapy. More recently, hybrid CMR/PET scanners may combine the strengths of both techniques. Table 18 lists the characteristic features of various pericardial tumors on CMR and CT.

Pericardial metastasis and direct tumor invasion. More than 10% of oncology patients have pericardial or cardiac metastasis at autopsy, although most are clinically silent.¹²⁷ Primary lung, breast, and esophageal cancers are the most frequent cause of pericardial neoplastic disease, although melanoma has the greatest propensity for cardiac involvement. Hematologic malignancies can also invade the pericardium. Pericardial involvement can occur with direct spread or hematologic or lymphatic dissemination. Symptoms of pericardial metastasis, if present, are related to associated PEff or inflammation. Rarely, there is encasement of the pericardium, leading to CP instead of CTP.¹²⁸ Four major routes of tumor spread to the pericardium include direct, hematogenous, lymphatic, and transvenous. Lymphatic spread can often seed in the pericardium or epicardium.¹²⁹

The primary role of TTE is identification of an abnormality and its hemodynamic consequence of pericardial tumor infiltration. Pericardial echodense masses or diffuse thickening may be visualized. Some benign lesions may appear cystic. CMR or CT is necessary for tissue characterization, tumor location, and determining extent of surrounding structure involvement. With pericardial metastasis, there is a lack of structural boundary and absence of low-intensity pericardial line. The majority of malignancies show low to isointense T1 and high T2 signal with heterogeneous contrast enhancement on LGE imaging (Figure 26). Melanoma, uniquely, has high signal intensity on T1 images because of the paramagnetic effect of melanin. Fatty tumors (lipoma, liposarcoma) and recent hemorrhage also can have high T1 signal. Beyond tissue characterization, real-time imaging with CMR can identify hemodynamic significance of PEff and presence of ventricular interdependence. CT offers excellent spatial resolution and may aid in determining the source of metastasis. Disruption of the pericardial layers and presence of PEff are typical. Pericardium may appear thickened and nodular with pericardial enhancement after contrast. CT has the advantage of fast image acquisition and a large field of view.

Pericardial invasion signals increased oncologic staging. MMI plays a critical role in delineating the extent of pericardial invasion to define if and how surgical resection can be performed. The most common tumors that invade the pericardium are lung cancer and esophageal cancer. Non-small cell lung cancer invading the pericardium is classified as a T3 lesion even when small and can be deemed as resectable or unresectable depending on the extent of invasion.^{130,131} Esophageal cancer involving the pericardium is classified as T4a and is still considered as resectable, but there must be clear demonstration that the heart itself is not involved, which would deem the tumor as unresectable (T4b).¹³²

Primary malignant pericardial tumors: mesothelioma, lymphoma, and sarcoma. Primary neoplasm of the pericardium is extremely rare. Mesothelioma is the most common where a causal relationship to asbestos has not been definitively established. It originates from the mesothelial cells of the parietal pericardium and is often associated with hemorrhagic effusion. It is very aggressive with extremely poor prognosis. Echocardiography may show PEff. CMR and CT would demonstrate an enhancing mass that encases the pericardial space (Figure 27). Obliteration of the pericardial space can lead to CP. Diagnosis is primarily obtained with pericardial biopsy. There is no established standard treatment, and surgery with and without chemotherapy are often used.¹²⁸

Pericardial lymphoma is also extraordinarily rare and usually non-Hodgkin B-cell type.¹³³ It accounts for <1% of all extranodal lymphomas and can occur with large PEff.

The majority of pericardial sarcomas are angiosarcomas. Owing to necrosis and hemorrhages associated with the tumor, T1- and T2-weighted images show variable intensities (Figure 28). Classically, angiosarcoma has a “sunray” appearance on CMR with enhancing lines radiating from epicardium to pericardium.¹³⁴

Primary benign pericardial tumors: hemangioma, lipoma, fibroma, teratoma, and paraganglioma. Hemangiomas are usually asymptomatic and found at autopsy. Owing to

high vascularity, hemangiomas have rapid gadolinium uptake on first-pass perfusion imaging in CMR and prominent subsequent LGE.

Lipomas also are usually found incidentally and exist as a single lesion. They have high T1 and T2 intensities on CMR, similarly to fat. Diagnosis can be confirmed by applying a fat saturation sequence. Owing to low vascularity, they enhance with gadolinium.

Pericardial fibromas primarily affect children. They have the unique CMR profile of low signal intensity on both T1- and T2-weighted images because of their fibrous content (Figure 29). They can have minimal to near uniform intense LGE from the presence of collagen.

Teratomas are most often detected in utero. They are often associated with PEff and can lead to fetal from germ cells located within the pericardium and frequently attached to the aortic or pulmonary trunk. Calcification and fat are usually seen within the tumor.

Paragangliomas are exceptionally rare and arise from chromaffin cells of an extra-adrenal location. Most are clinically silent until the tumor causes compression or encasement of coronary arteries leading to dyspnea or angina. They are highly vascular with feeding arteries from the coronaries. Immediate gadolinium enhancement is seen in CMR first-pass perfusion imaging. ¹²³I-metaiodobenzylguanidine scan can help confirm the diagnosis. Treatment is surgical resection. Rarely, paragangliomas can be malignant.

Recommendations and key points.

- Pericardial masses are most often asymptomatic and discovered incidentally. If symptoms occur, they are related to development of PEff or inflammation.
- TTE is usually the first imaging modality, followed by CMR because of its tissue characterization capability and ability to assess physiologic importance (Table 19, Video 4).
- Cardiac CT is useful because of superior spatial resolution, evaluation of surrounding structure, and potentially determining the source of the primary tumor.
- ¹⁸F-FDG PET/CT is useful in assessing primary and metastatic pericardial tumors. More recently, hybrid CMR/PET scanners combine the advantages of both techniques in one setting.
- Benign lesions respect the tissue plane and malignancies do not. In CMR, most tumors have isointense to hypointense signal on T1-weighted images and hyperintense signal on T2-weighted images. Fibroma is unique among benign tumors as it has low T1 as well as T2 signal. Melanoma and liposarcoma have high T1 signal intensity because of the paramagnetic effect of melanin and the presence of adipose tissue, respectively.
- TTE remains the most convenient and widely available technique to evaluate patients with pericardial process with suspected pericardial masses.

- In the modern era, MMI with CMR, CT, ¹⁸F-FDG PET/CT, and hybrid CMR/PET is essential. Combination of these techniques facilitates patient treatment by determining the pericardial pathology.

CONGENITAL ABSENCE OF THE PERICARDIUM.

Clinical perspectives and novel concepts. Congenital absence of the pericardium (CAP) is a rare embryologic anomaly where there is: 1) complete absence of the entire pericardium; 2) complete absence of the right or left pericardium; 3) partial absence (foramen-type) of the right or left pericardium; or 4) diaphragmatic absence of the pericardium. Although most patients with CAP are detected incidentally, presentation with a spectrum of acute dangerous to benign chronic cardiac symptoms may occur (Figure 30, Table 20).¹³⁵⁻¹³⁷ Left-side complete absence is the most common type (~70%). Left-side partial absence is the most ominous form, associated with serious complications. Case series of CAP describe a higher prevalence in young and male patients, as an isolated condition or with other cardiac or noncardiac congenital abnormalities.¹³⁶⁻¹³⁸

Role of integrated MMI. Because most patients with CAP are asymptomatic, initial detection usually occurs when there are suggestive features on chest x-ray, chest or cardiac CT, or CMR done for other indications (Tables 20 and 21).

Transthoracic echocardiography. Although there are classic findings on TTE, these can be underappreciated even by experienced readers (Figure 31).^{138,139}

Cardiac CT/CMR. Signature findings on chest imaging include (Figure 32): 1) levorotation of the heart; 2) absence of the pericardial layer; 3) interposition of lung tissue between the aorta and pulmonary artery or between the diaphragm and the base of the heart; and 4) a subepicardial myocardial crease. A more definitive diagnosis is usually made with ECG-gated cardiac CT or CMR, which enables comprehensive structural evaluation at high resolution, such that the pericardium can be visualized. Cine imaging by means of CMR provides additional assessment of cardiac function, which can be most useful in cases of partial absence, where there can be regional CP and strangulation of the ventricles caused by herniation through the band-like foramen created by the partial pericardial absence.

When to consider additional imaging. For any patient with suspected cardiac or pulmonary-related symptoms, baseline testing typically includes ECG, chest x-ray, and TTE (Figures 31 and 32). If findings are suggestive of CAP, a definitive diagnosis based on cardiac CT or CMR should be driven by degree of symptoms and whether management decisions will be modified. For asymptomatic patients where CAP is suspected or diagnosed incidentally on chest imaging (usually chest x-ray or chest CT), further testing should be reserved for patients for whom there may be therapeutic implications.^{140,141}

Contemporary management. Surgical interventions for CAP are described in small numbers and limited to patients with disabling symptoms and those with high-risk for complications, when operative risk is considered acceptable.¹⁻³ High risk features for complications include 1) a myocardial crease or hinge point indicating external cardiac

compression; 2) coronary compression or ischemia; 3) chamber herniation (most often the left atrial appendage); and 4) left-side partial absence where compression, herniation, or strangulation of cardiac structures is a potential occurrence. In patients with CAP without symptoms, with nonrefractory symptoms, and without risk features, reassurance should be given and downstream testing minimized.

Recommendations and key points.

- CAP is a rare embryologic anomaly, with potential for associated morbidity and mortality.
- Testing should be weighted to symptomatic CAP patients and asymptomatic patients who are at risk for complications (such as left-side partial absence) (Table 22).

DISEASE-SPECIFIC ALGORITHMS FOR DIAGNOSIS AND MANAGEMENT

INFLAMMATORY ACUTE AND CHRONIC PERICARDITIS.

The diagnosis of acute pericarditis primarily depends on clinical evaluation supported by biochemical markers, such as CRP, and imaging techniques, including TTE and CMR (Figure 33). Both CMR and TTE play important roles in identifying the presence of PEff, constrictive physiology, or a combination of both, known as ECP. Once the diagnosis is established, initial therapy typically involves NSAIDs, colchicine, and exercise restriction. However, the presence of CP physiology should prompt early follow-up with imaging and a lower threshold for considering a second-line agent, such as corticosteroids. The clinical status and biomarkers of the patient should be periodically reassessed, typically 2-4 weeks after initiating therapy. Medications should be tapered only when there is clinical resolution of the symptoms and normalization of CRP. If symptoms recur after a 6-week period of tapering all therapies, a diagnosis of recurrence is established, and a similar approach to the initial management should be pursued. In cases of pericarditis resistant to NSAIDs, corticosteroids, and colchicine, the use of an anti-IL-1 agent (anakinra, rilonacept, and goflikicept) may be warranted as a third-line treatment, and increasingly anti-IL-1 agents are used as a second-line option because of the multiple adverse effects of corticosteroids. Importantly, if CMR (including LGE) and elevated CRP indicate an inflammatory phenotype, there may be a rationale for initiating anti-IL-1 agents at an earlier stage. In certain instances where tapering biologic therapies proves unsuccessful, the option of radical pericardiectomy may be considered, alongside a referral to a specialized high-volume pericardial center. It is advisable to conduct follow-up CMR and CRP assessment to ensure that inflammation levels are effectively minimized before surgery. Furthermore, a CT scan can be performed to aid in perioperative planning.

PERICARDIAL EFFUSION.

PEffs are typically first detected with the use of TTE or CT imaging (Figure 34). The size of the PEff and its impact on cardiac hemodynamics should be assessed both clinically and with imaging. Clinical assessment involves evaluating signs such as hypotension, tachycardia, and pulsus paradoxus. Imaging findings such as chamber collapse, IVC

plethora, and respiratory flow variation also indicate the presence of a hemodynamically significant PEff causing CTP physiology. In such cases, prompt measures should be taken to perform either a pericardiocentesis or a pericardial window to relieve the CTP physiology. After the drainage procedure, it is important to assess the hemodynamics for potential CP physiology, particularly ECP. This condition is often associated with ongoing pericardial inflammation, as indicated by elevated levels of CRP and confirmed with CMR imaging. Therefore, the administration of anti-inflammatory agents is crucial in addressing the inflammatory component and ensuring comprehensive management of the condition. However, for chronic PEffs without increased intrapericardial pressure and no evidence of inflammation, conservative management and regular imaging are typically recommended.¹⁴²

CONSTRUCTIVE PERICARDITIS.

TTE remains the primary imaging modality for evaluating CP physiology, relying on the identification of IVC plethora and respirophasic septal shift as key indicators (Figure 35). In the absence of these features, the likelihood of CP is low. However, if clinical suspicion persists, a dynamic CMR study with free breathing sequences can provide additional diagnostic information. In cases where impaired ventricular filling and abnormal annular motion are observed, careful assessment is performed to exclude concomitant myocardial disease. Normal or supranormal annular motion (annulus reversus), supported by increased expiratory flow reversal compared with forward diastolic flow in the hepatic veins, suggests a diagnosis of CP when the e' value is >8 cm/s. Conversely, significantly abnormal annular motion (<6 cm/s), particularly in the absence of respirophasic septal shift, is more indicative of restrictive cardiomyopathy as the cause of impaired ventricular filling. The presence of abnormal tissue motion (6-8 cm/s) in conjunction with respirophasic septal motion may indicate mixed CP and restrictive physiology. This can be further supported by the presence of abnormal global longitudinal strain, indicating subclinical myocardial dysfunction. In cases of either mixed or pure CP, CMR is recommended for detailed characterization of the pericardium, identification of active pericardial inflammation (T2-STIR, LGE) as well as assessment of concurrent myocardial disease and its extent. These findings obtained in CMR can subsequently guide the selection of appropriate therapeutic strategies.

CONCLUSIONS

This document represents an international position statement on novel concepts and advances in the diagnosis of pericardial diseases using MMI. There is a 2013 MMI pericardial (American Society of Echocardiography) and 2014 (European Association of Cardiovascular Imaging) and 2015 European Society of Cardiology pericardial guidelines,⁷⁴ but there is no recent American College of Cardiology/American Heart Association guideline on the topic, and thus this paper provides a position statement from experts in the field highlighting important MMI recommendations for pericardial diseases for the clinician.

What are the novel concepts regarding pericardial diseases? It is important to recognize that when evaluating these patients, there is a spectrum of disease activity, from acute pericarditis with active inflammation and CP physiology to burned-out calcific CP with right-side heart failure.²⁴ Within this framework, MMI plays a major role in assessing inflammation and

edema (CMR) and PEff and CP physiology (TTE) in acute pericarditis, as well as assessing the hemodynamic consequences of CP, eg, in interventricular dependence (TTE and CMR), and location and degree of calcification (CT). These MMI data allow the clinician to plan the proper management of these complex patients with the use of IGT.⁸

Because MMI is not universally available to assess pericardial diseases, it is important to understand the strengths and limitations of each of these techniques.^{1,2} TTE is usually first-line therapy because of its noninvasive nature, mobility, and low cost. CMR is becoming first-line in certain pericardial syndromes, such as acute and RP, because of excellent imaging of inflammation, which can provide important information about prognosis and long-term outcome.¹¹ CT excels with its ability to assess pericardial calcification and allows for preoperative planning in patients with previous open heart surgery.

There is a huge interest in the dysregulated innate immune system.⁴ Nonspecific pathogen- and damage-associated molecular patterns damage the pericardial cells, and the NLPR3 inflammasome is activated with release of IL-1 α and IL-1 β and subsequent activation of an autoinflammatory cycle. Targeted therapies with anti-IL-1 agents in IGT using CMR have now allowed us to visualize inflammation and edema and provide a roadmap to severity of therapy and prognosis.^{70,143} With the use of these imaging capabilities, there is a paradigm shift in the management of the inflammatory phenotype in RP and possible acute pericarditis as well as TCP. For those with this phenotype, there may be earlier use of anti-IL-1 agents, including anakinra, rilonacept, and goflikicept, in these conditions, thus avoiding the complications of steroids.⁷⁴ In the noninflammatory phenotype, biologics are less likely to work and low-dose prednisone may empirically be started, although this strategy requires further research. A novel machine-learning risk score was recently developed to predict clinical remission in RP patients for clinical utility though warranting external validation.¹⁴⁴ Further studies are necessary to study the role of exercise in pericarditis and the ability to exercise while on biologics.^{145,146}

Finally, tertiary pericardial centers of excellence have been established to provide expertise in diagnosis and management of these complex patients and to allow for the proper IGT with the newer anti-IL-1 agents.¹⁴⁷

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS AND ACRONYMS

CAP	congenital absence of the pericardium
CMR	cardiac magnetic resonance
CRP	C-reactive protein
CP	constrictive pericarditis
CTP	cardiac tamponade
ECP	effusive-constrictive pericarditis
FDG	fluorodeoxyglucose
IGT	imaging-guided therapy
IVC	inferior vena cava
LGE	late gadolinium enhancement
MMI	multimodality imaging
NSAID	nonsteroidal anti-inflammatory drug
PEff	pericardial effusion
PET	positron emission tomography
RP	recurrent pericarditis
STIR	short-tau inversion recovery
TCP	transient constrictive pericarditis
TTE	transthoracic echocardiography

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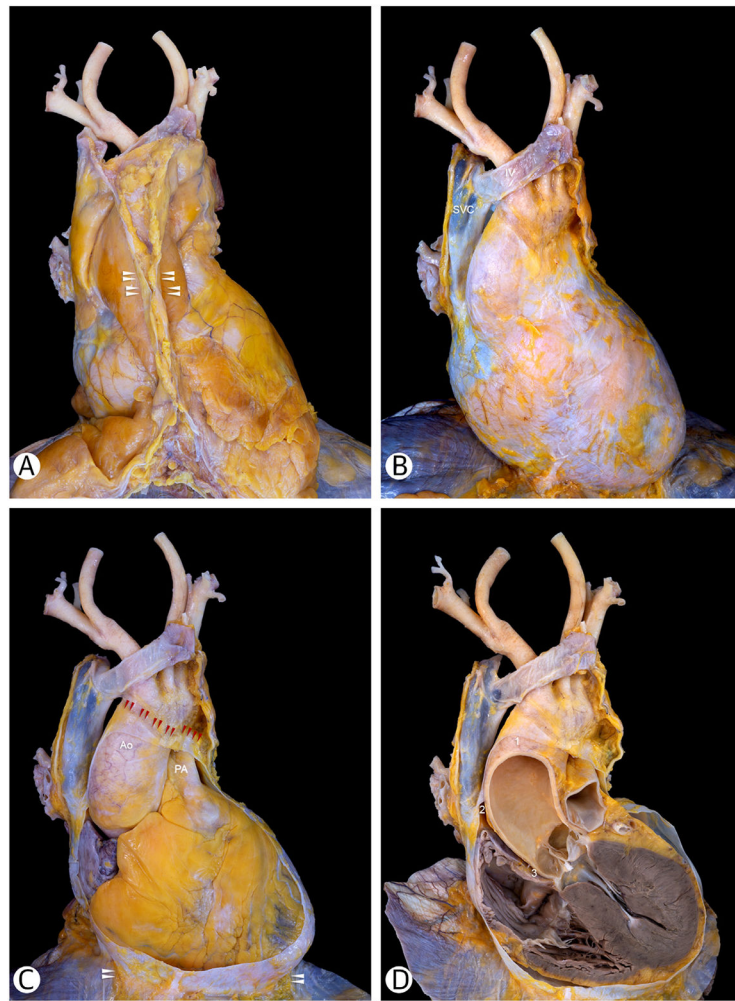
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HIGHLIGHTS

- The spectrum of pericardial disorders encompasses pericardial inflammation, effusion, constriction, masses, and congenital anomalies.
- MMI plays important an role in the diagnosis, prognostication, and surveillance of pericardial diseases.
- Recent advances in biologic therapies, including rilonacept, necessitate IGT strategies to manage pericardial diseases.

**FIGURE 1. Pericardial Anatomy**

(A) Pericardium with mediastinal pleura and epipericardial adipose tissue. Arrowheads indicate the sternopericardial ligaments. (B) Fibrous pericardium after removal of adipose tissue. (C) The fibrous pericardium is continuous with the adventitia of the aorta (Ao) and pulmonary artery (PA) superiorly (red arrowheads) and is anchored to the central tendon of the diaphragm inferiorly (white arrowheads). (D) Anterior (1), superior (2), and inferior (3) aortic recesses of the transverse sinus. IV = innominate vein; SVC = superior vena cava.

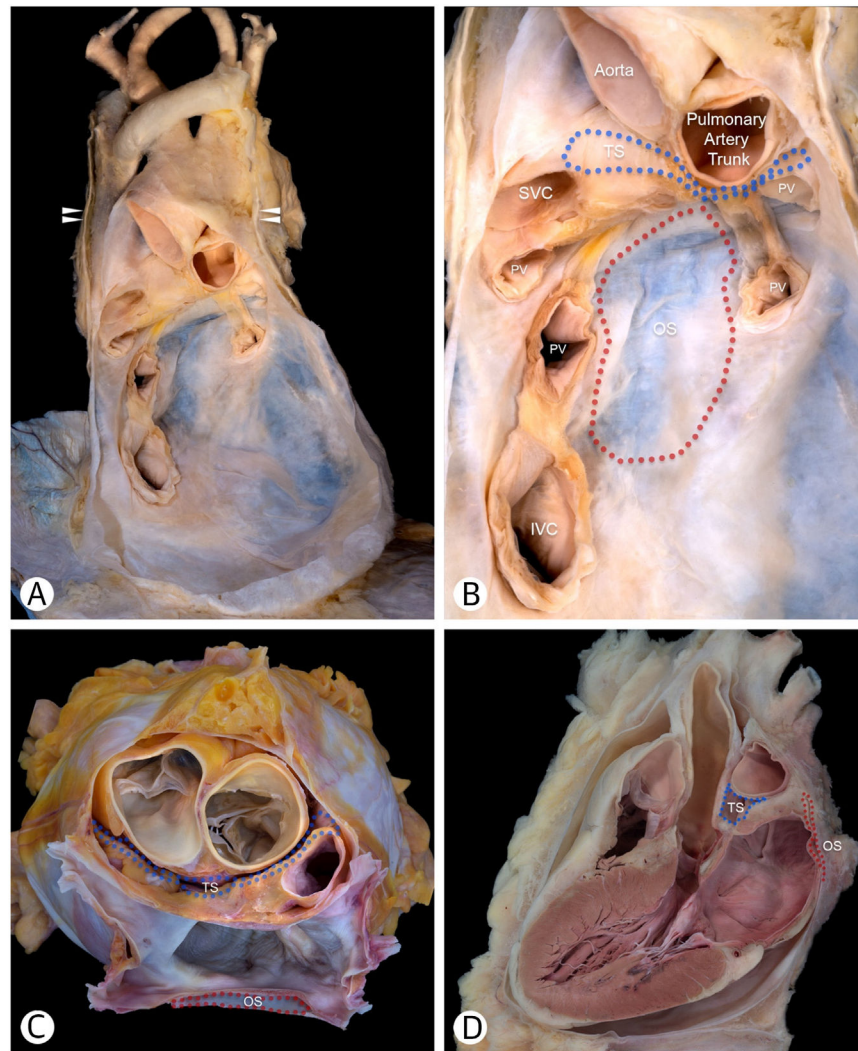


FIGURE 2. Pericardial Sinuses Anatomy

(A) Dorsal portion of the fibrous pericardium after removal of the heart. The phrenic nerves are indicated by arrowheads. (B) The transverse sinus (TS) is the space between the anterior great arteries and posterior veins (PVs) (blue dots). The oblique sinus (OS) is delineated by the pulmonary veins and inferior vena cava (IVC) (red dots). (C) Axial view of TSs and OSs. (D) Sagittal image of TS and OS, which do not communicate with each other. Abbreviation as in Figure 1.

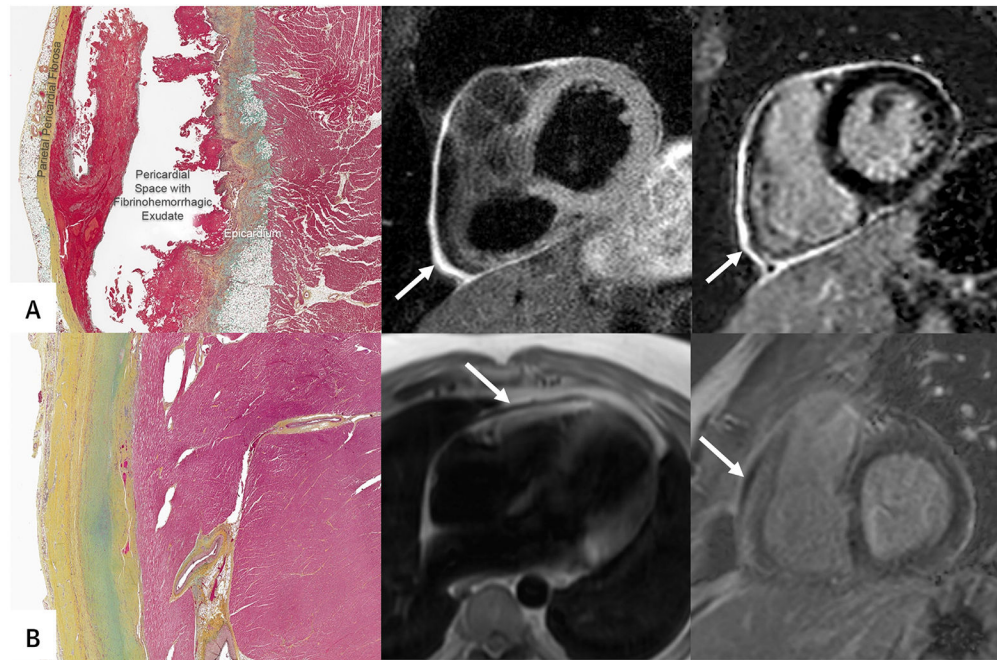


FIGURE 3. Histopathologic Correlations With CMR of Inflammatory and CP

(A) Fibrinous inflammatory pericarditis involving the serosa of both parietal and visceral pericardium: (left) histology, (middle) T2-STIR imaging indicating pericardial edema (arrow), and (right) late gadolinium enhancement (LGE) imaging indicating pericardial inflammation (arrow). (B) CP with obliteration of the pericardial cavity and fibrous thickening of both pericardial layers: (left) histology, (middle) black-blood spin-echo imaging indicating pericardial thickening (arrow), and (right) LGE imaging indicating pericardial calcific thickening (arrow) without LGE. CMR = cardiac magnetic resonance; CP = constrictive pericarditis; STIR = short-tau inversion recovery.

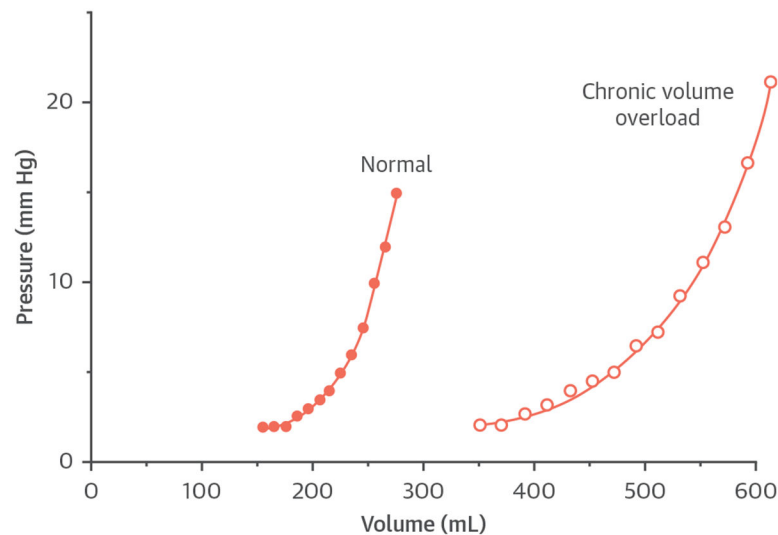


FIGURE 4. Pericardial Pressure-Volume Relationship Determined Postmortem in a Normal Canine Heart and During Chronic Volume Overload Due to an Experimental Systemic Arteriovenous Fistula

The smallest volume is that of the empty heart with no fluid in the pericardial sac. Fluid was added to the pericardial sac to determine the pressure-volume relationship. Note the abrupt transition to a very steep pressure-volume relationship in the normal heart. Above the transition point, small increases in volume result in large increases in pressure. In the chronically dilated heart or with chronic pericardial effusions (PEffs), the pressure-volume relationship shifts to the right and flattens. This change reduces pericardial restraint to filling during chronic cardiac dilation, allowing accommodation for the markedly enlarged heart, and accounts for the observation that large chronic PEffs are better tolerated than smaller, rapidly developing PEffs. Adapted with permission from Freeman and LeWinter.¹⁴⁸

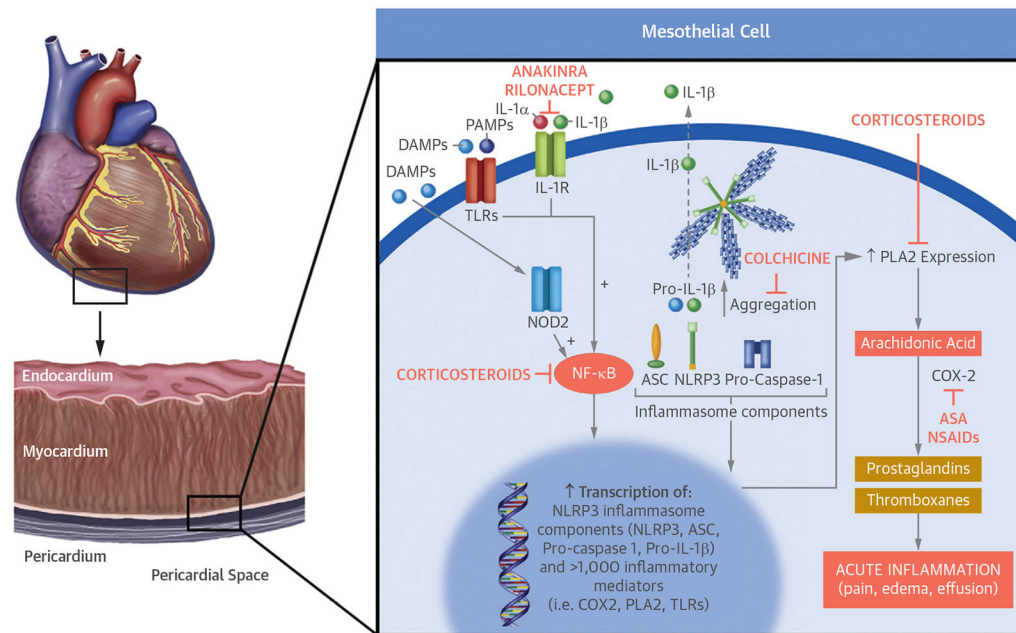


FIGURE 5. Pathophysiology of Pericardial Inflammation

Injury to the pericardium leads to the release of DAMPs and PAMPs and induces NF- κ B synthesis, which increases the transcription of precursors of inflammatory molecules and associated cytokines (NLRP3, ASC, pro-caspase-1) required for the polymerization of the NLRP3 inflammasome, ultimately releasing IL-1 β and IL-18. NF- κ B stimulates the synthesis of phospholipase-A2 required for promoting the arachidonic acid pathway and the subsequent synthesis of prostaglandins and thromboxanes. The IL-1 receptor (IL-1R) occupies a central role as IL-1 α functions as an alarmin or DAMP being released during tissue injury, and IL-1 β is processed and released by the inflammasome leading to amplification of the process. ASA = acetylsalicylic acid; ASC = apoptosis-associated Speck-like protein containing a carboxy-terminal caspase-recruiting domain; DAMP = damage-associated molecular pattern; IL = interleukin; NF- κ B = nuclear factor kappa-light-chain enhancer of activated B cells; NLRP3 = NACHT, leucine-rich repeat, and pyrin domain-containing protein 3; NOD = nucleotide-binding oligomerization domain; NSAID = nonsteroidal anti-inflammatory drug; PAMP = pathogen-associated molecular pattern; PLA2 = phospholipase A2; TLR = Toll-like receptor. Reproduced with permission from Chiabrando et al.⁴

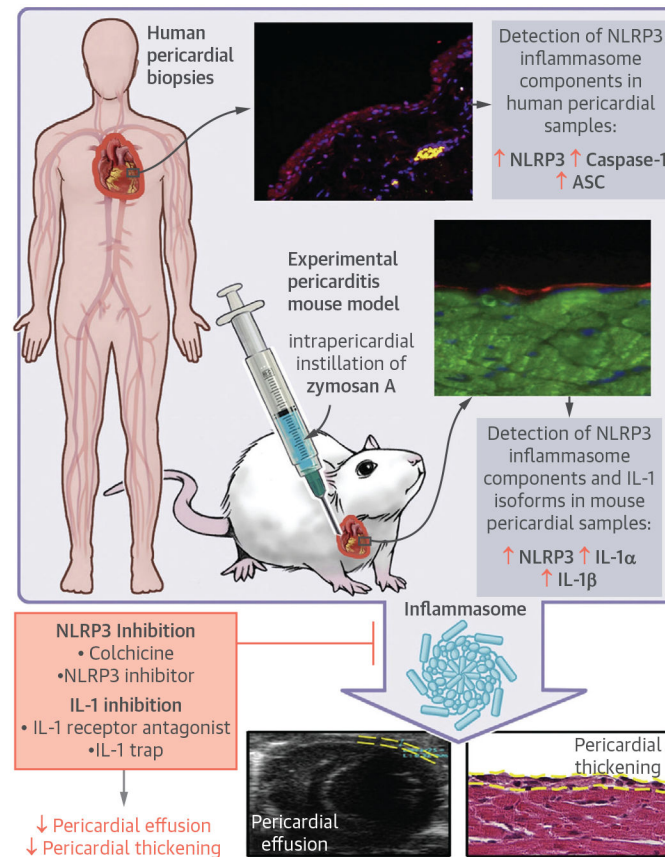


FIGURE 6. Mouse Model of Pericardial Inflammation Pathophysiology and Therapeutics
 A mouse model of acute pericarditis was developed through the intrapericardial injection of zymosan A, leading to the classic features of the inflamed pericardium: PEff, pericardial thickening, and increased expression of the NLRP3 inflammasome. By inhibiting the NLRP3 inflammasome or IL-1 β , the PEff and pericardial thickening and the NLRP3 inflammasome expression were greatly reduced compared with vehicle. Treatment with IL-1 trap, neutralizing both IL-1 β and IL-1 α , produced a powerful effect on pericardial inflammation in the experimental pericarditis model. Reproduced with permission from Mauro et al.¹⁴⁹ Abbreviations as in Figures 4 and 5.

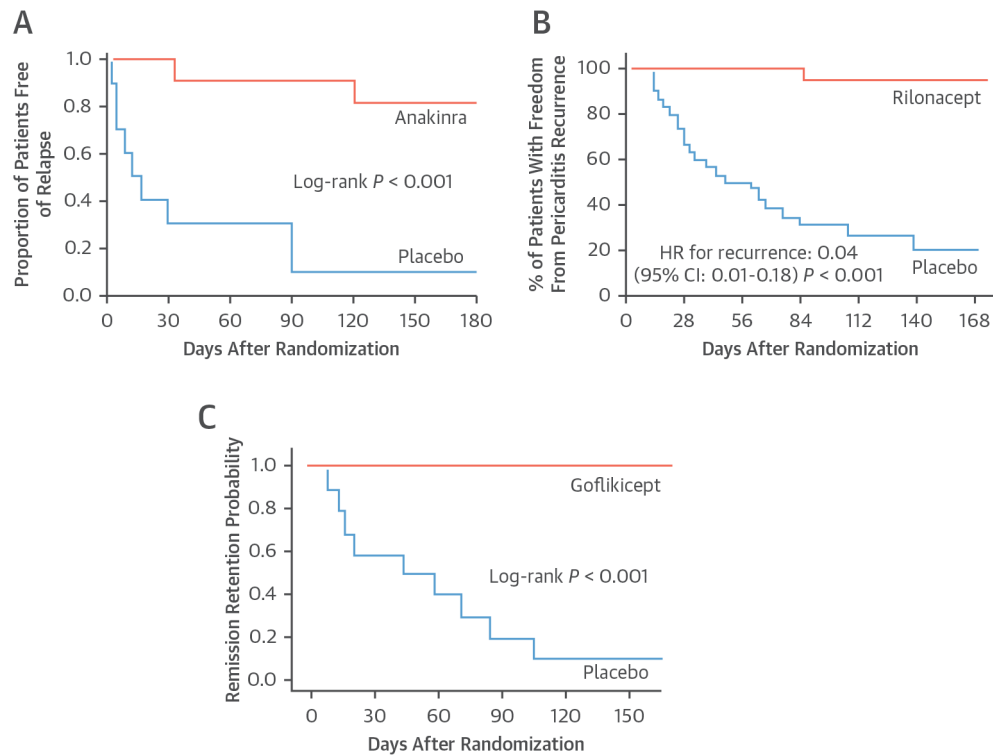


FIGURE 7. Time to Pericarditis Recurrence in Anti-IL-1 Agents Randomized Withdrawal Trials

Survival curves for time to pericarditis recurrence in the (A) AIRTRIP (anakinra), (B) RHAPSODY (rilonacept), (C) and Myachikova et al⁷ (goflikicept) randomized withdrawal trials, reproduced with permission from Klein et al.⁴¹ All 3 studies showed a significant reduction in pericarditis recurrence compared with placebo after randomized withdrawal of the treatment drug. AIRTRIP = Anakinra—Treatment of Recurrent Idiopathic Pericarditis; RHAPSODY = Rilonacept Inhibition of Interleukin-1 Alpha and Beta for Recurrent Pericarditis: A Pivotal Symptomatology and Outcomes Study.

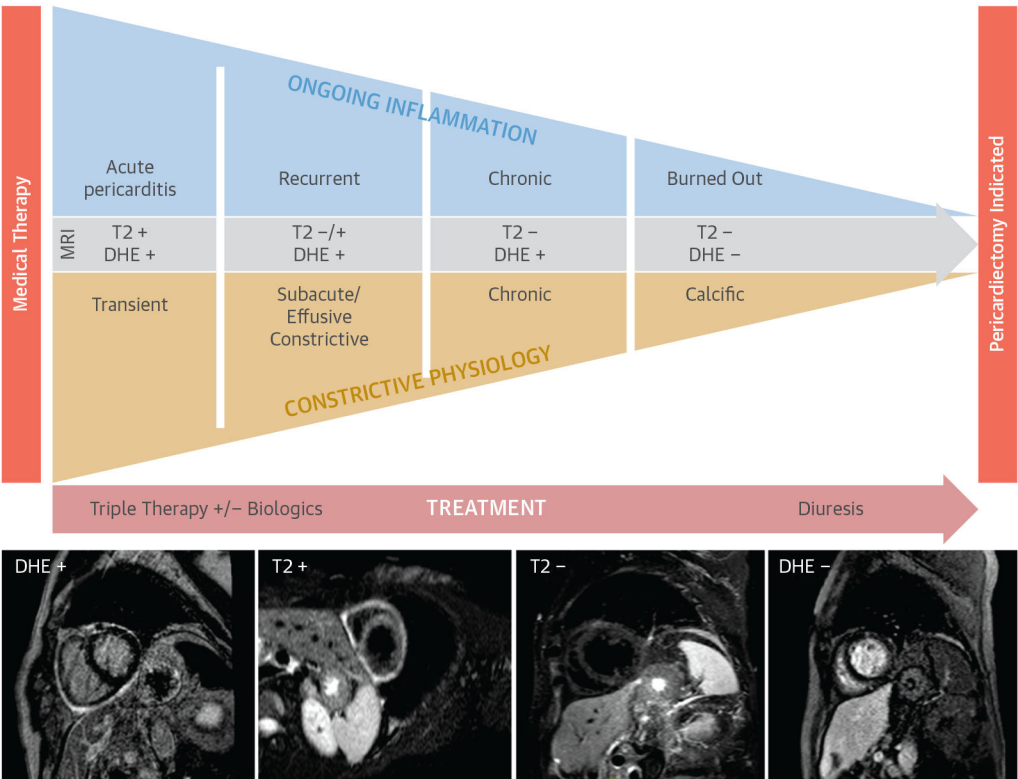


FIGURE 8. Spectrum of Pericardial Diseases, CMR Findings, and Imaging-Guided Therapies
The use of CMR-based pericardial characterization, demonstrating the continuum of inflammatory pericardial diseases starting from acute inflammation (with or without CP physiology) and ending in either burned-out pericarditis or calcific CP. Reproduced with permission from Chetrit et al.⁸ DHE = delayed hyperenhancement (LGE); other abbreviations as in Figure 3.

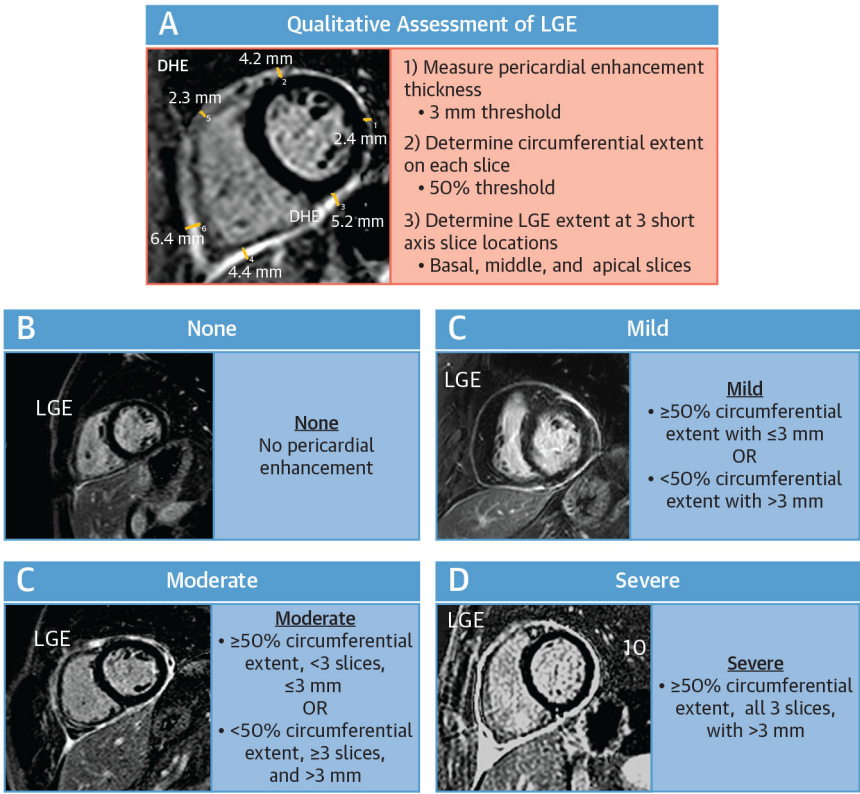


FIGURE 9. Proposed Pericardial LGE Severity Grading Criteria in CMR
Pericardial LGE severity grading criteria on CMR PSIR-LGE sequence (fat-suppressed sequence suggested), based on pericardial enhancement thickness and circumferential extent on short-axis imaging at basal, mid, and apical slices. PSIR = phase-sensitive inversion-recovery; other abbreviations as in Figure 3.

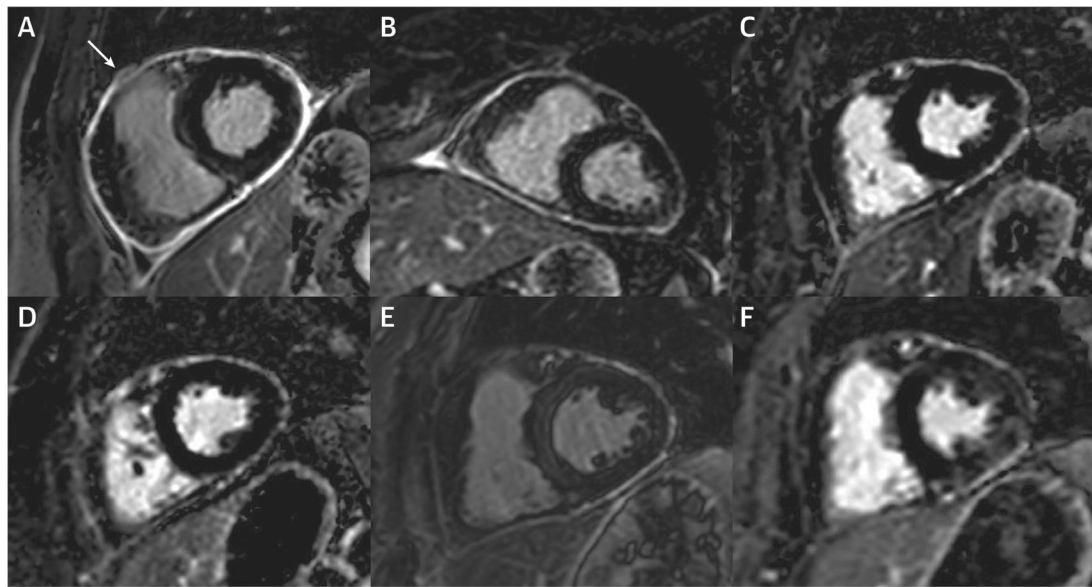


FIGURE 10. Serial Pericardial LGE Evaluation With CMR for a Complex Case of RP to Show Time Course and to Assess Pericarditis Severity, Surveillance, and Response to Therapy

(A) Initial encounter with incessant pericarditis with chest pain symptoms despite ibuprofen and colchicine, C-reactive protein (CRP) 30.5 mg/dL, sedimentation rate 30 mm/h, severe pericardial LGE (arrow). Added prednisone. (B) 6-month follow-up, persistent symptoms on ibuprofen + colchicine + prednisone, CRP 6.8 mg/dL, sedimentation rate 33 mm/h still elevated, moderate pericardial LGE. Switched prednisone to anakinra. (C) 1-year follow-up, symptoms resolution on anakinra and colchicine, CRP 0.1 mg/dL, sedimentation rate 2 mm/h, mild pericardial LGE. (D) 2-years later, anakinra and colchicine had been stopped after course completed, recurrence of symptoms, CRP 7.4 mg/dL, sedimentation rate 41 mm/h, mild pericardial LGE. Started rilonacept after this examination. (E) 1-year follow-up on rilonacept, symptoms resolution, CRP <0.3 mg/dL, sedimentation rate 2 mm/h, trivial pericardial LGE. Consider stopping rilonacept. (F) 18-month followup on rilonacept, symptom free, CRP <0.3 mg/dL, sedimentation rate 2 mm/h, trivial pericardial LGE. Other abbreviation as in Figure 3.

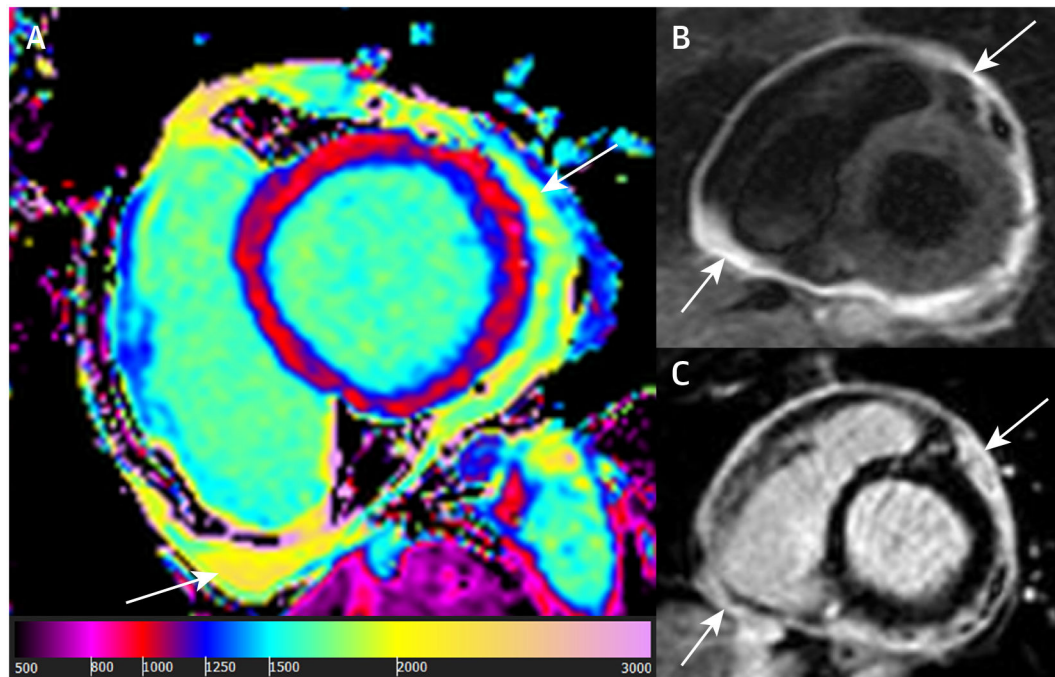


FIGURE 11. Pericardial Native T1-Mapping Sequence Correlation With Other Tissue Characterization Sequences in CMR

(A) Pericardial native T1-mapping sequence (modified look-locker inversion recovery) indicated elevated T1 times in the pericardium (white arrows). (B) Correlations with elevated signal on T2-STIR sequence indicating pericardial edema. (C) Correlations with LGE on PSIR-LGE sequence indicating pericardial inflammation/fibrosis (white arrows). Abbreviations as in Figures 3 and 9.

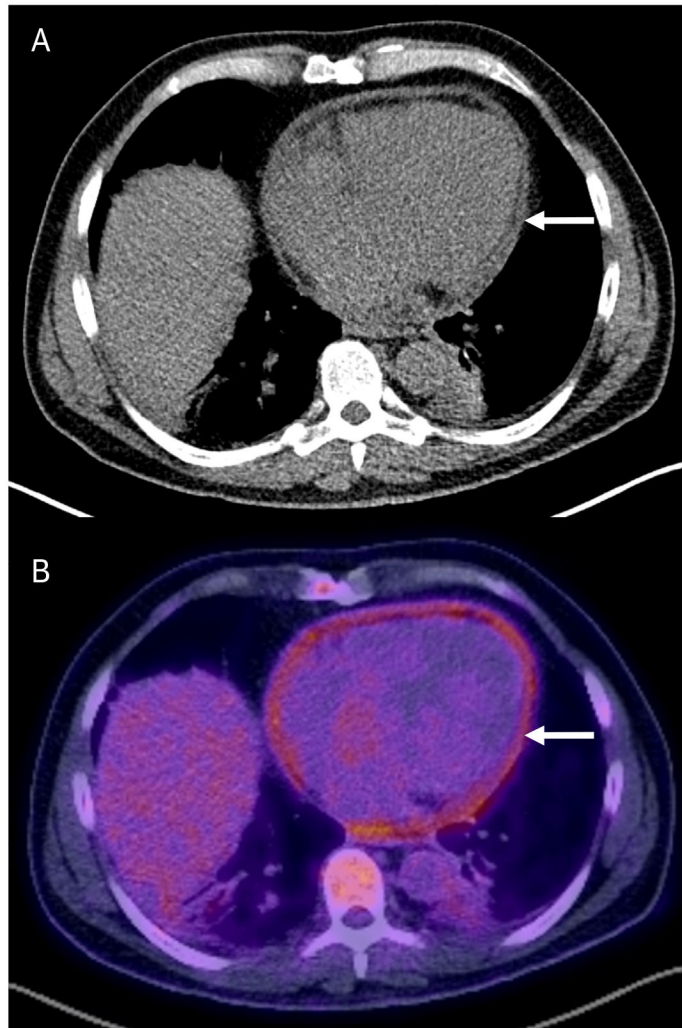


FIGURE 12. Pericarditis Case in FDG-PET

(A) Noncontrast computed tomography demonstrates pericardial thickening (arrow). (B) ^{18}F -FDG-PET indicating increasing pericardial signal consistent with acute pericarditis (arrow). FDG = fluorodeoxyglucose; PET = positron emission tomography.

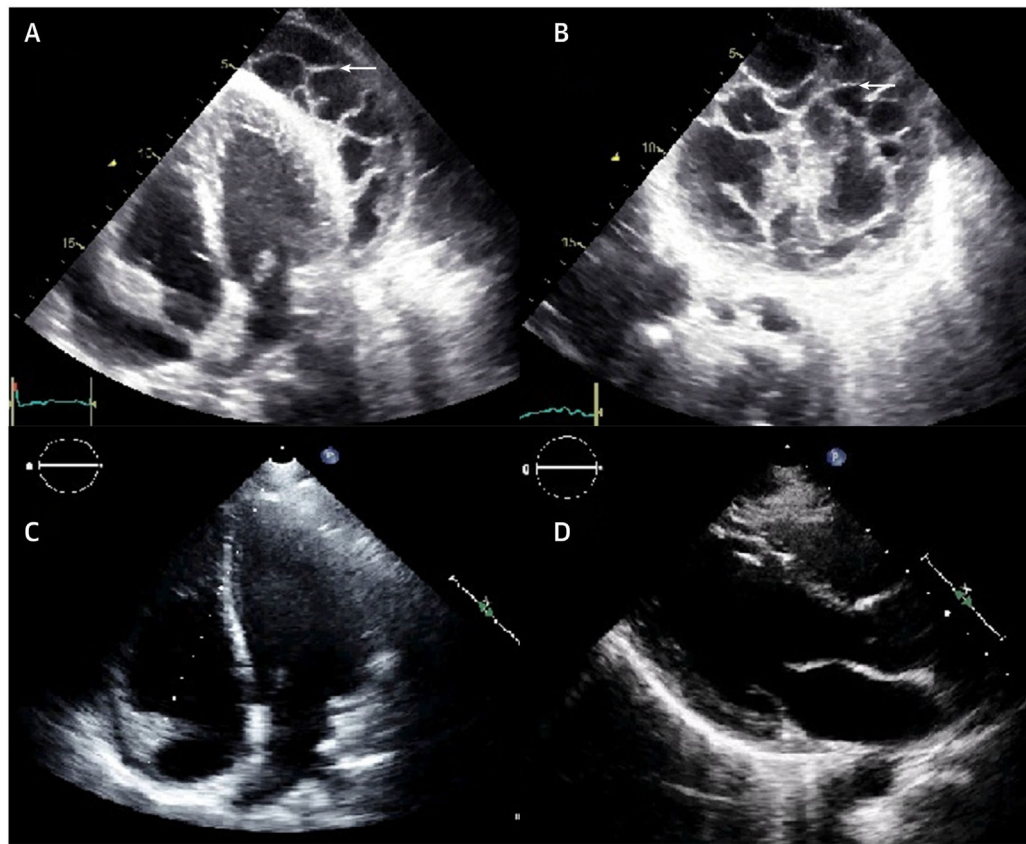


FIGURE 13. TTE Case of Intensely Inflammatory Acute Pericarditis With Fever, Raised CRP, and Neutrophil Leukocytosis

Two-dimensional TTE revealed a large circumferential PEff with remarkable intrapericardial fibrin strands indicated by white arrows ([A] apical view and [B] short axis). (C and D) Complete resolution after several days of indomethacin. TTE = transthoracic echocardiography; other abbreviation as in Figure 4.

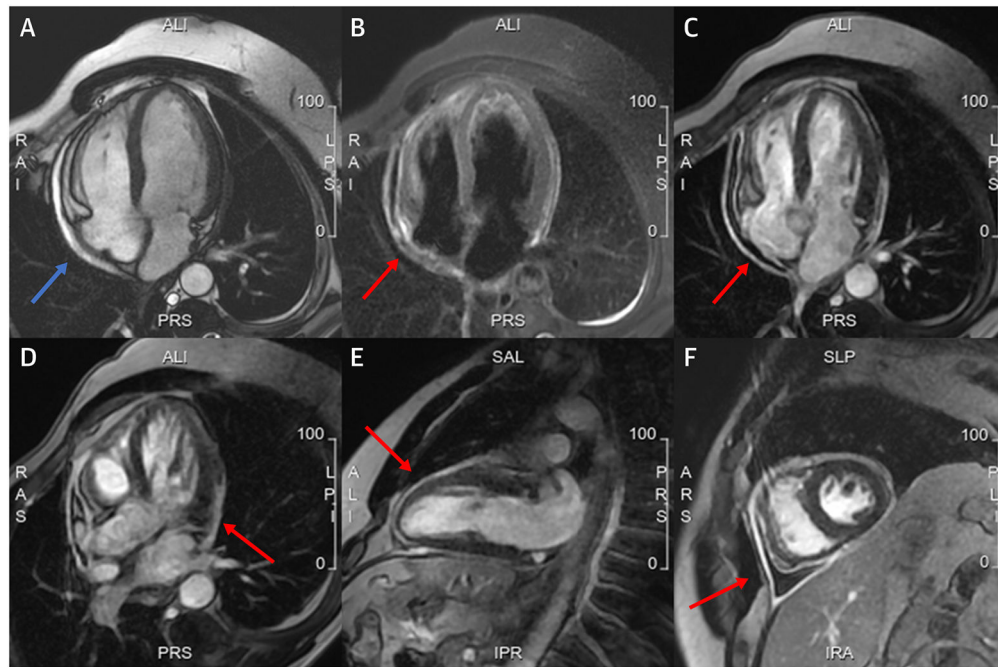


FIGURE 14. CMR Case of Acute Pericarditis

(A) A mild PEff is well evident (blue arrow). Of interest, at the same location, a hyperintense pericardium, in both (B) T2-weighted and (C) LGE images, is suggestive for acute pericardial inflammation (red arrows). (D-F) Similarly, different views of pericardial hyperintensity in LGE images supporting pericardial inflammation (red arrows) are presented. Abbreviations as in Figures 3 and 4.

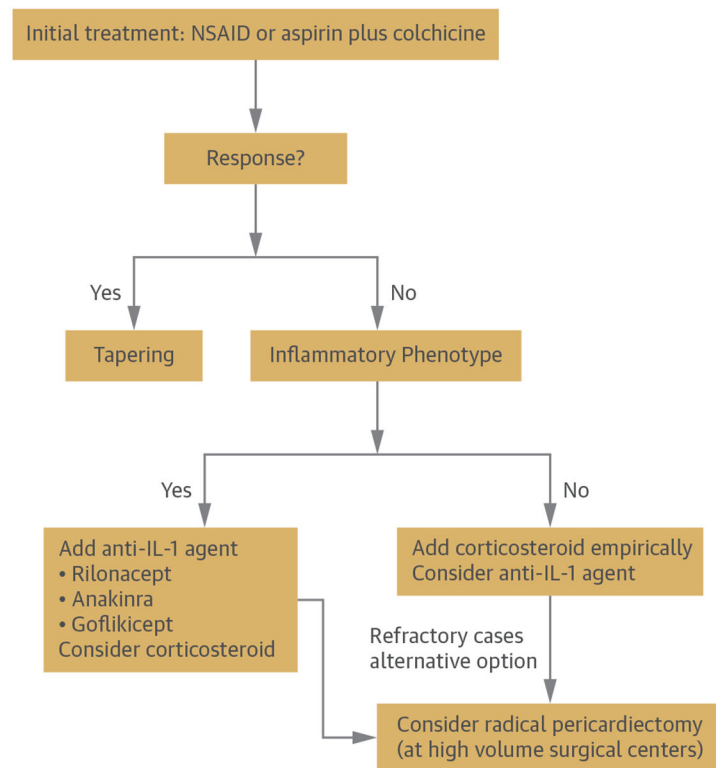


FIGURE 15. New Therapeutic Algorithm for RP According to the Presentation Phenotype
RP = recurrent pericarditis; other abbreviations as in Figure 5.

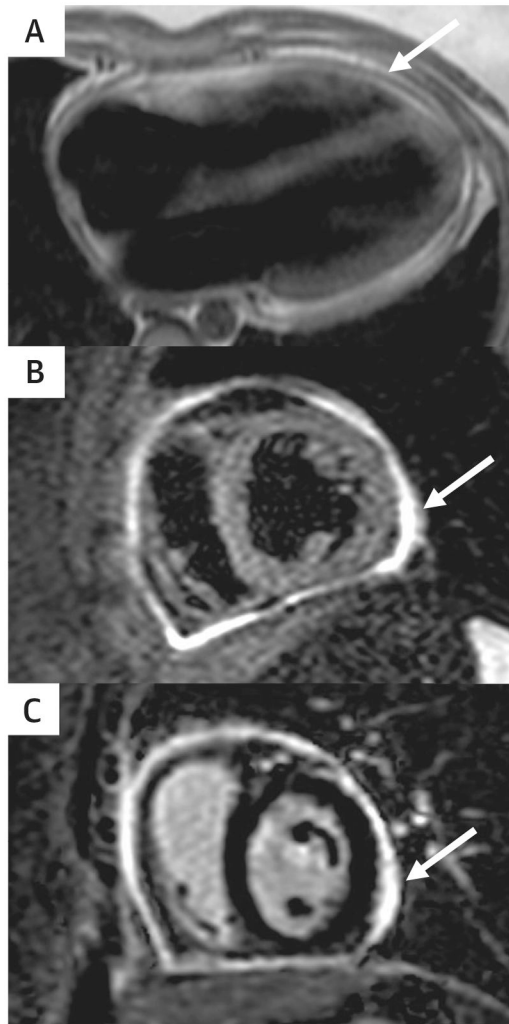


FIGURE 16. Hallmarks of Pericarditis in CMR: Evidence of Pericardial Thickening, Edema, and LGE

(A) Black-blood spin-echo sequence axial image showing pericardial thickening (arrow). (B) T2-STIR sequence short-axis imaging showing pericardial edema (arrow). (C) PSIR-LGE sequence short-axis images with fat suppression showing pericardial LGE indicating inflammation (arrow). Abbreviations as in Figures 3 and 9.

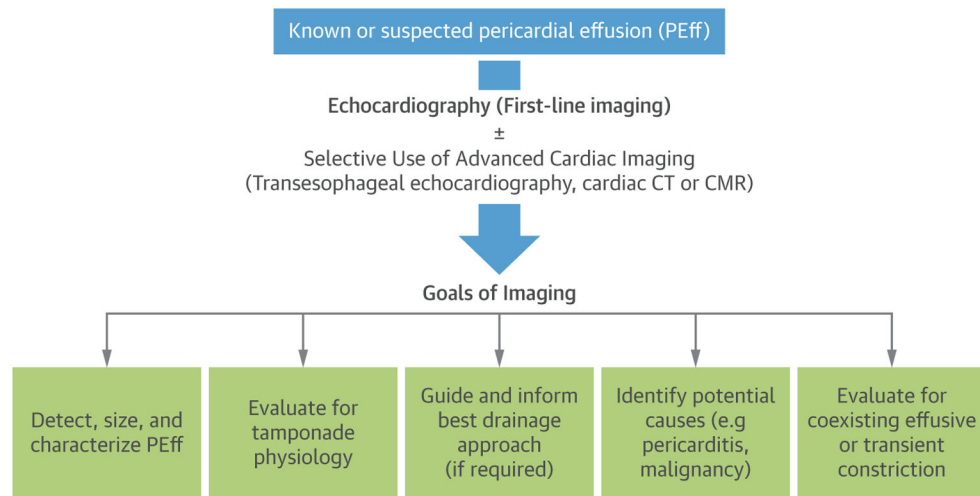


FIGURE 17. Goals of MMI in PEff and CTP

CT = computed tomography; CTP = cardiac tamponade; MMI = multimodality imaging; other abbreviations as in Figures 3 and 4.

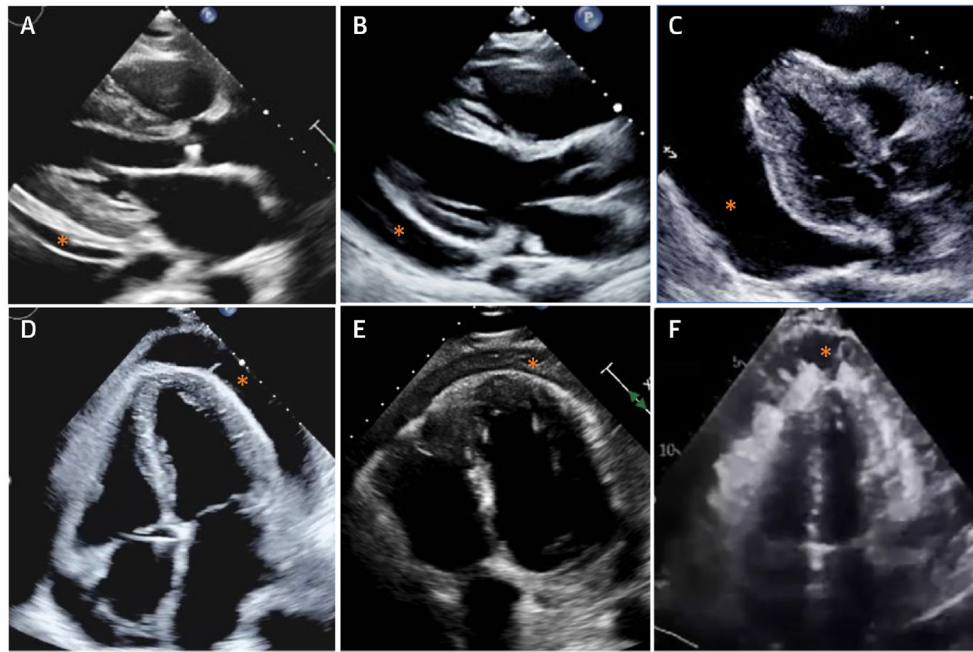


FIGURE 18. Sizing and Characterization of PEffs With TTE

Representative (A) small, (B) moderate, and (C) large PEffs (stars). Representative (D) simple PEff with fibrin strands, (E) exudative PEff, and (F) malignant PEff (stars) caused by pericardial mesothelioma. TTE = transthoracic echocardiography; other abbreviation as in Figure 4.

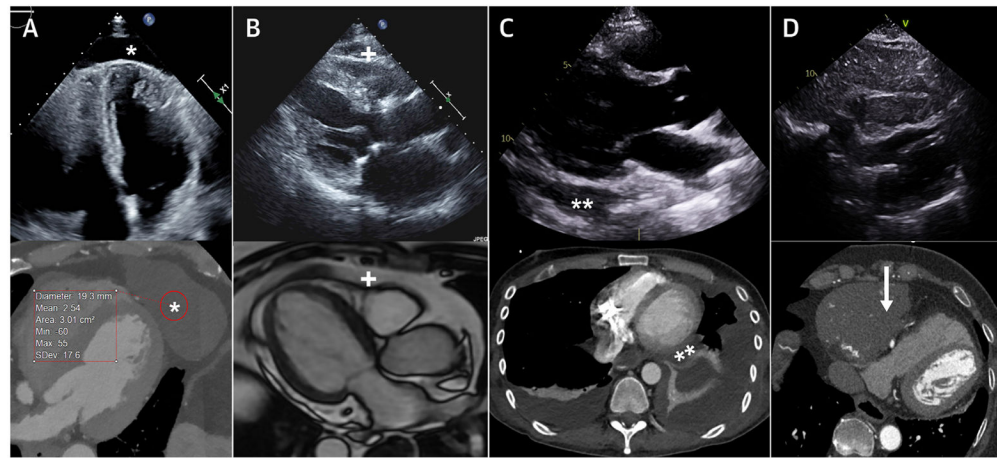


FIGURE 19. PEff Mimickers on MMI

(A) Pericardial cyst (star) masquerading as PEff in TTE (top), which is better characterized on cardiac CT (bottom). (B) Prominent pericardial fat (plus sign) mimicking complex PEff on TTE (top), which is better characterized in CMR (bottom). (C) Pleural effusion (double star) with lung atelectasis giving the appearance of a PEff. (D) Subcostal view of a TTE (top) demonstrates a large heterogenous echodensity anterior to the right atrium and ventricle (arrow) with associated chamber compression. In computed tomographic angiography (bottom), the soft tissue attenuation and vascularity of the large mass is appreciated. On resection, pathology demonstrated a benign hemangioma. Abbreviations as in Figures 3, 4, 17, and 18.

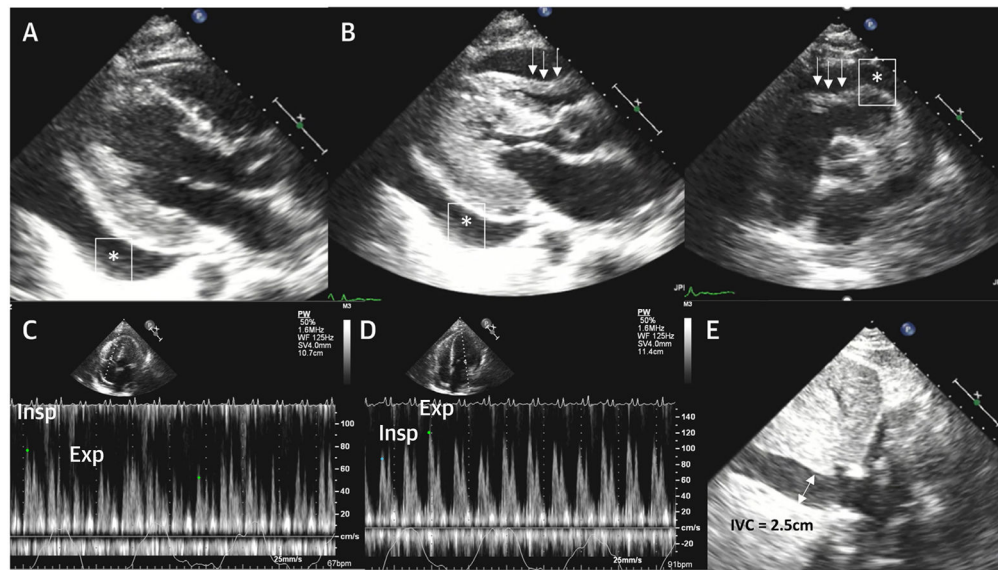


FIGURE 20. TTE Signs of CTP

(A) TTE in parasternal long-axis view featuring moderate PEff (asterisk). (B) Parasternal long-axis and short-axis views demonstrate end-diastolic right ventricular free wall collapse. Significant respirophasic tricuspid (C) and mitral (D) inflow velocity variation is noted, and there is a plethoric IVC (E). Exp = expiration; Insp = inspiration; other abbreviations as in Figures 2, 4, and 18.

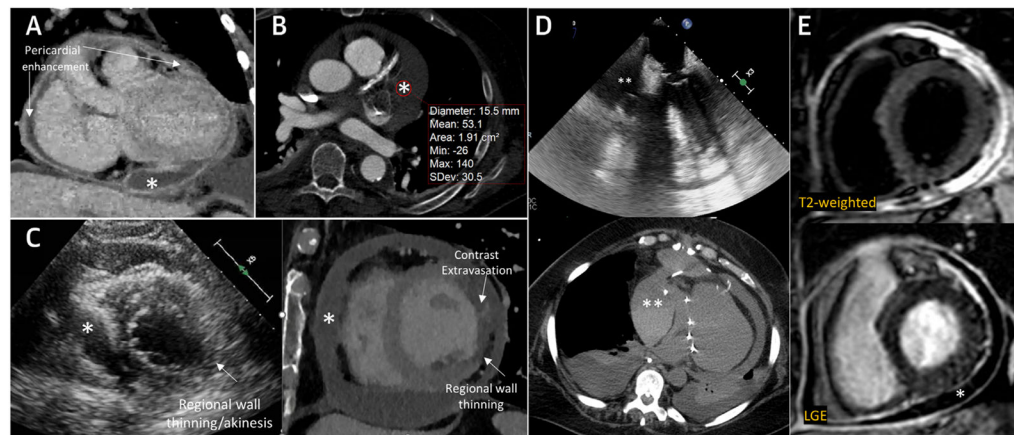


FIGURE 21. Characterization of PEff With CT and CMR

(A) Cardiac CT with delayed acquisition featuring pericardial enhancement (pericardial inflammation) with associated (asterisk) small exudative PEff. (B) Cardiac CT demonstrating (asterisk) hemorrhagic PEff (53 HU) caused by left atrial appendage perforation from Watchman device migration. (C) TTE (left) in short-axis view demonstrates abnormal lateral wall thinning in continuity with intrapericardial hematoma and moderate-sized (asterisk) hemorrhagic PEff (49 HU). (D) Transesophageal echocardiogram (top) and CT (bottom) demonstrates a hematoma causing focal CTP because of collapse of the right atrium. (E) CMR demonstrates underlying pericardial edema on T2 weighted imaging and pericardial inflammation on LGE sequence. Findings are consistent with acute pericarditis with associated small PEff. Abbreviations as in Figures 3, 4, 17, and 18.

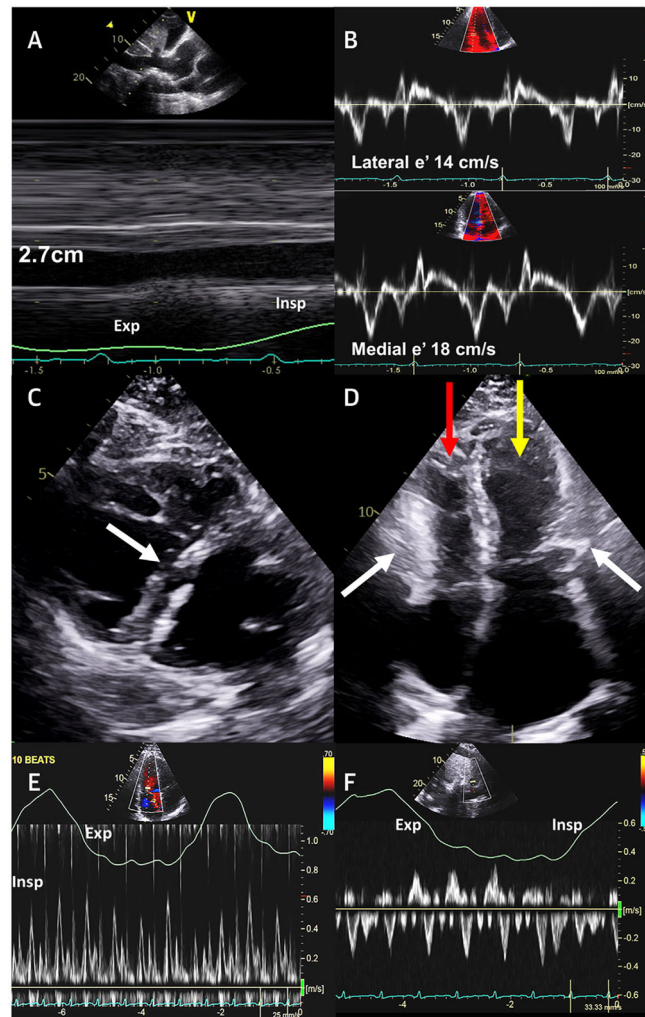


FIGURE 22. TTE Features of CP

(A) M-mode subcostal view showing dilated IVC measuring 2.7 cm with <50% collapse. (B) Tissue Doppler of mitral annulus lateral e' lower than medial e' , indicating annulus reversus. (C) Parasternal ventricular short axis view with respiratory interventricular septal shift (arrow). (D) Apical 4-chamber view with pericardial calcifications and tethering at the lateral to mitral and tricuspid annulus (white arrows); and left ventricle cylindrical (yellow arrow) and right ventricle conical (red arrow) deformities. (E) Mitral valve inflow pulsed-wave Doppler indicating significant >25% respirophasic variation. (F) Hepatic vein pulsed-wave Doppler indicating expiratory end-diastolic reversal velocity/forward flow velocity >0.8. Abbreviation as in Figure 2.

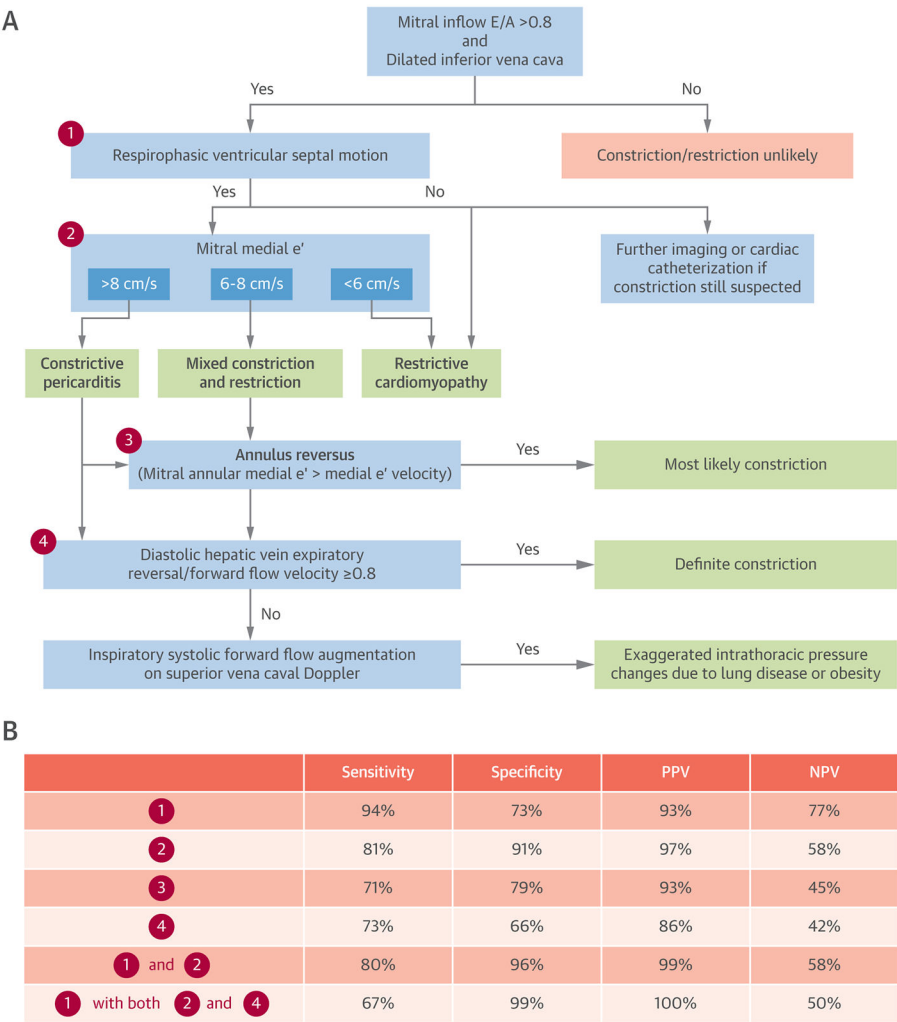


FIGURE 23. Diagnostic Algorithm and Validation of TTE Parameters for CP
NPV = negative predictive value; PPV = positive predictive value; other abbreviations as in Figures 3 and 18.

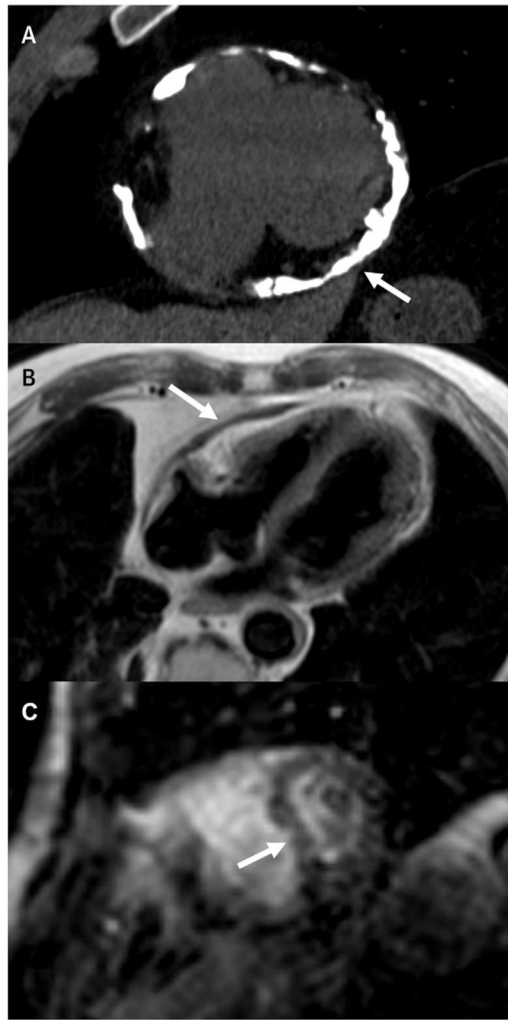


FIGURE 24. Cardiac CT and CMR Features of CP

(A) Noncontrast cardiac CT ventricular short-axis view showing severe pericardial calcifications (arrow). (B) CMR black-blood spin-echo axial view showing significant pericardial thickening. (C) Free breathing cine sequence ventricular short-axis view showing respirophasic interventricular septal shift (typically flattening of septum with inspiration; white arrow). Abbreviations as in Figures 3 and 17.

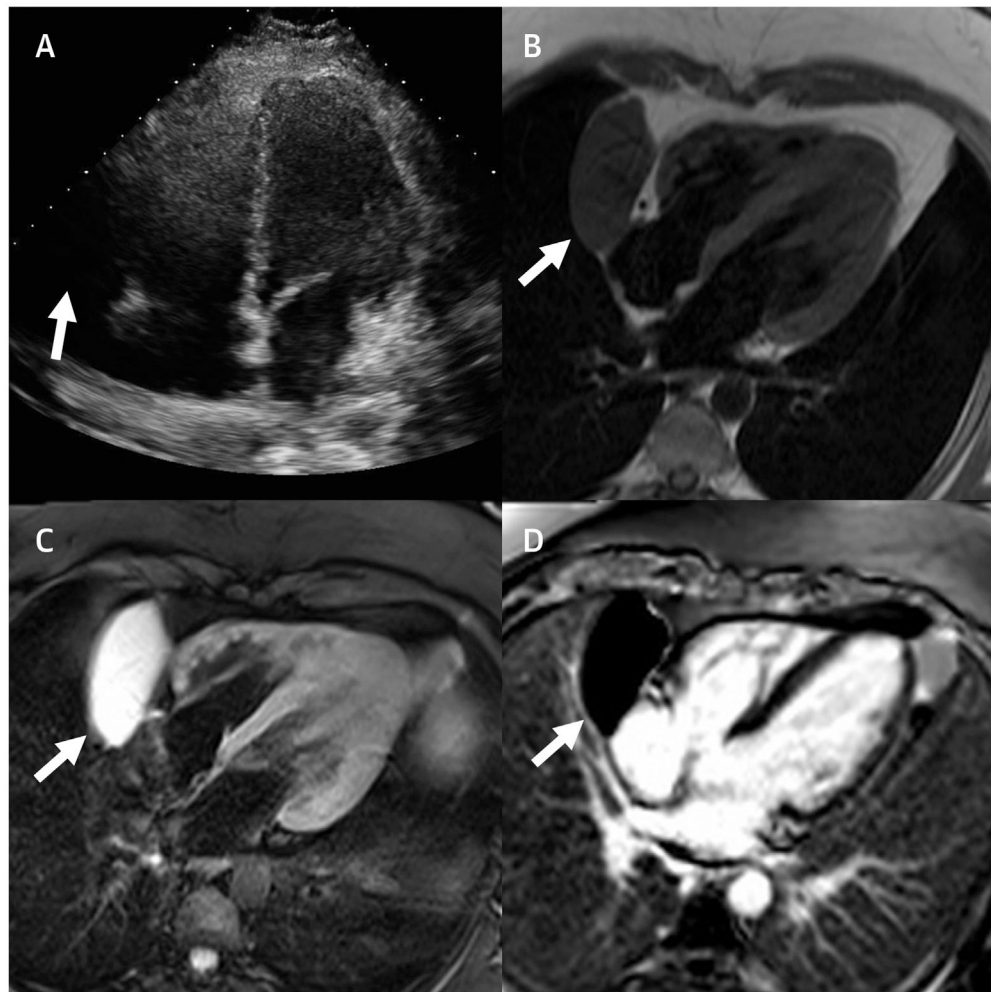


FIGURE 25. Pericardial Cyst Multimodality Cardiac Imaging Evaluation

Pericardial cyst at the right cardiophrenic angle, indicated by arrows. (A) TTE with possible echo lucency vs drop-out adjacent to the right atrium and ventricle. (B) CMR showing T1 (isointense). (C) T2 fat saturation (hyperintense). (D) Post-contrast delayed enhancement imaging (no gadolinium uptake) consistent with a pericardial cyst. Abbreviations as in Figures 3 and 18.

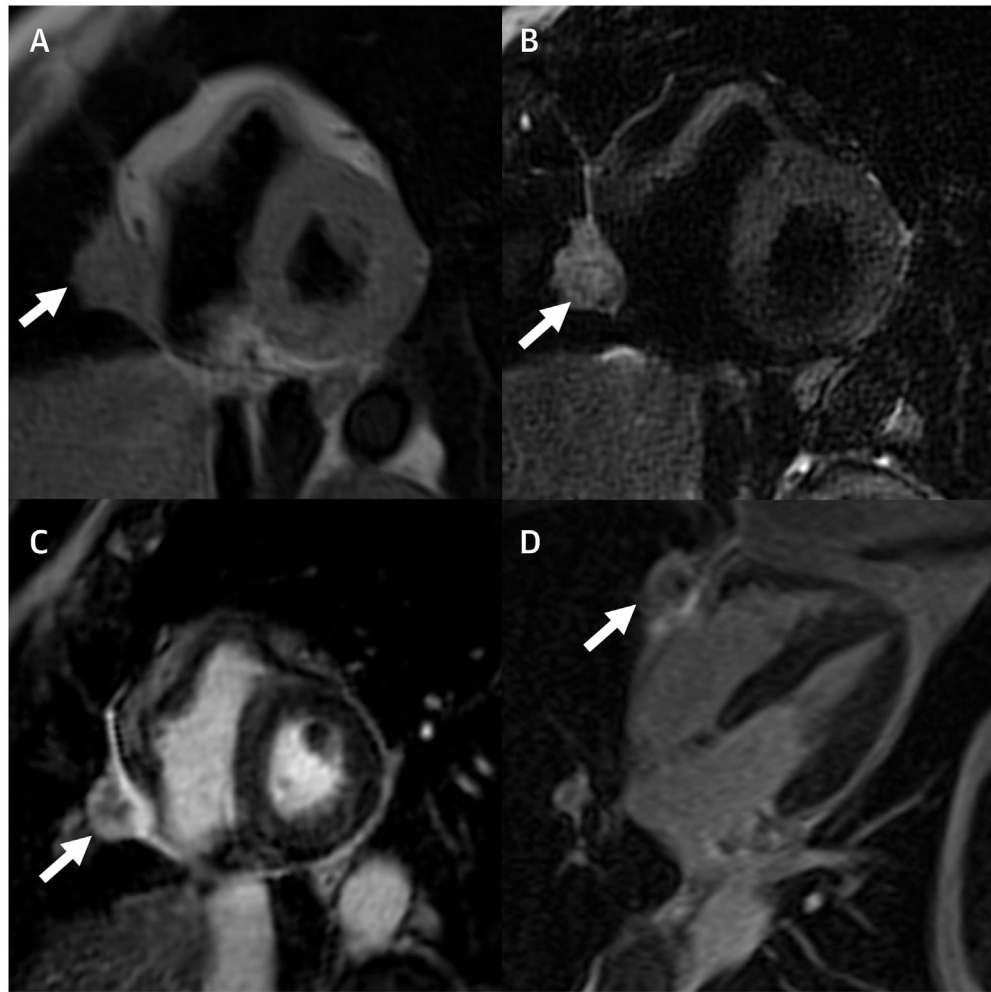


FIGURE 26. Pericardial Invasion From Lung Cancer Evaluation in CMR

Patient with known non–small cell lung cancer, indicated by arrows. (A) CMR T1-weighted image showing mass with isointense signal and invasion into the epicardium near the right atrioventricular groove. (B) In T2-weighted image, mass is hyperintense. (C and D) In LGE images, mass has heterogeneous gadolinium uptake. Findings are consistent with a malignant lesion. Abbreviations as in Figure 3.

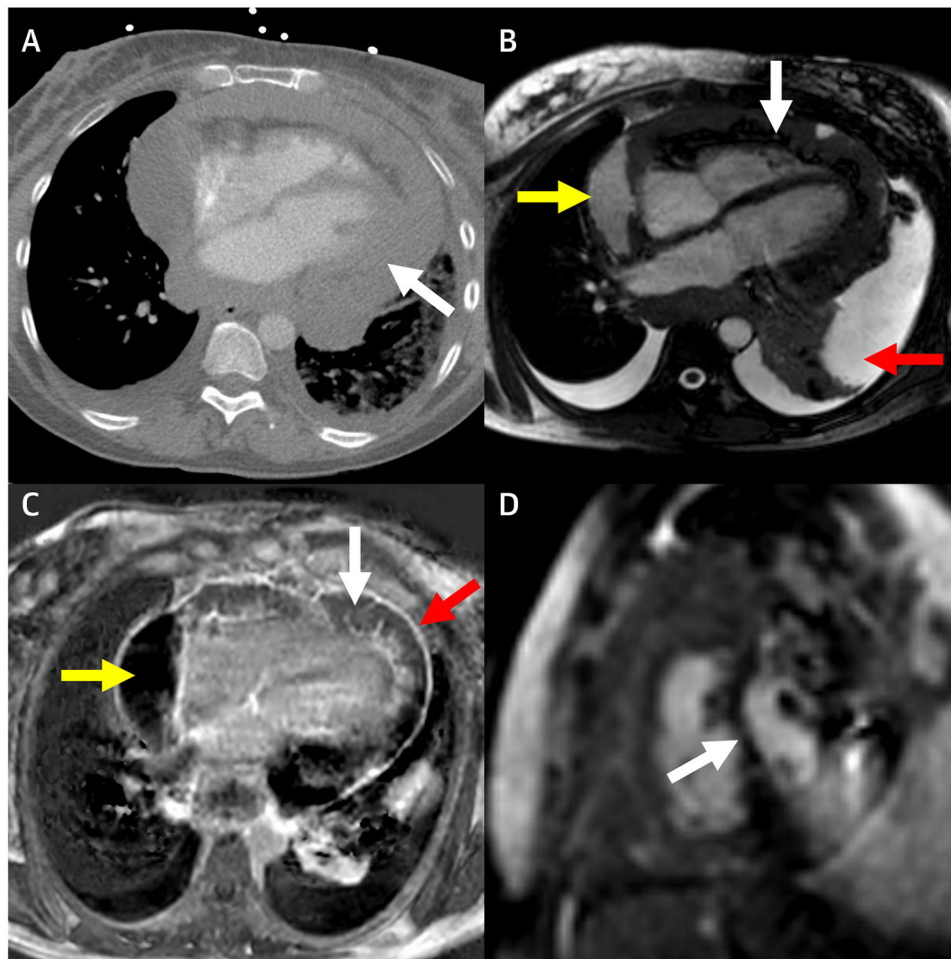
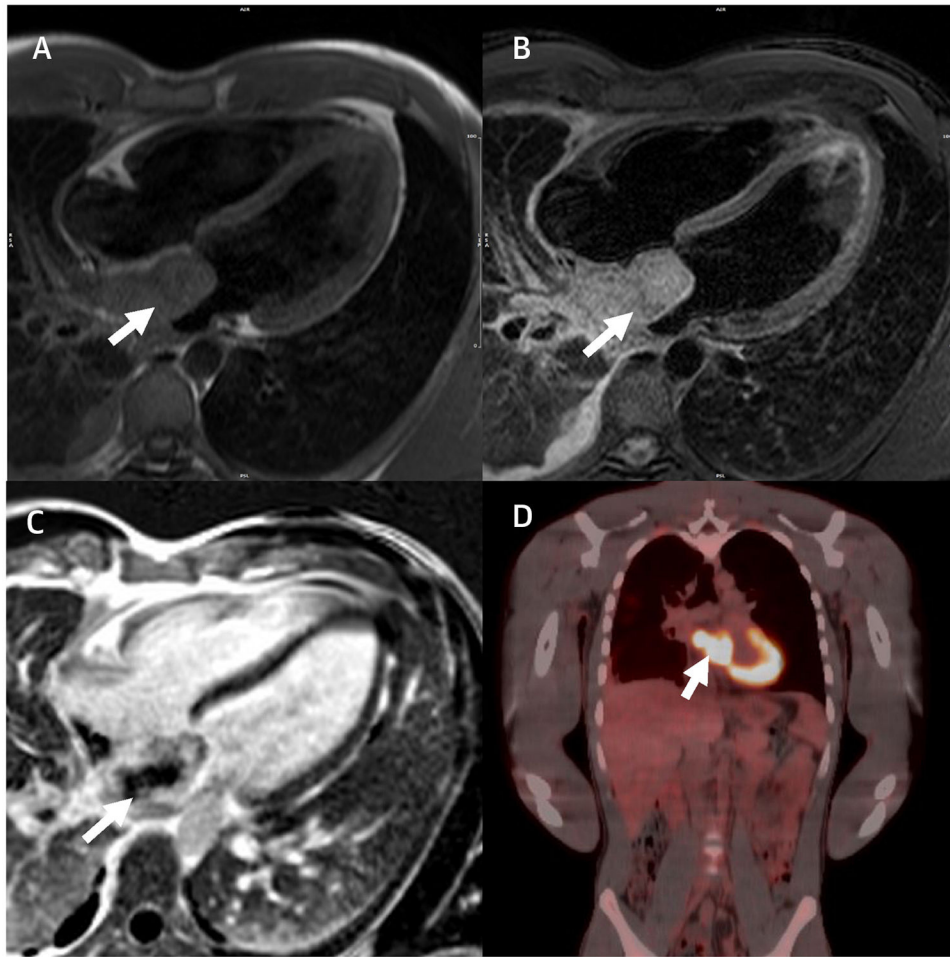
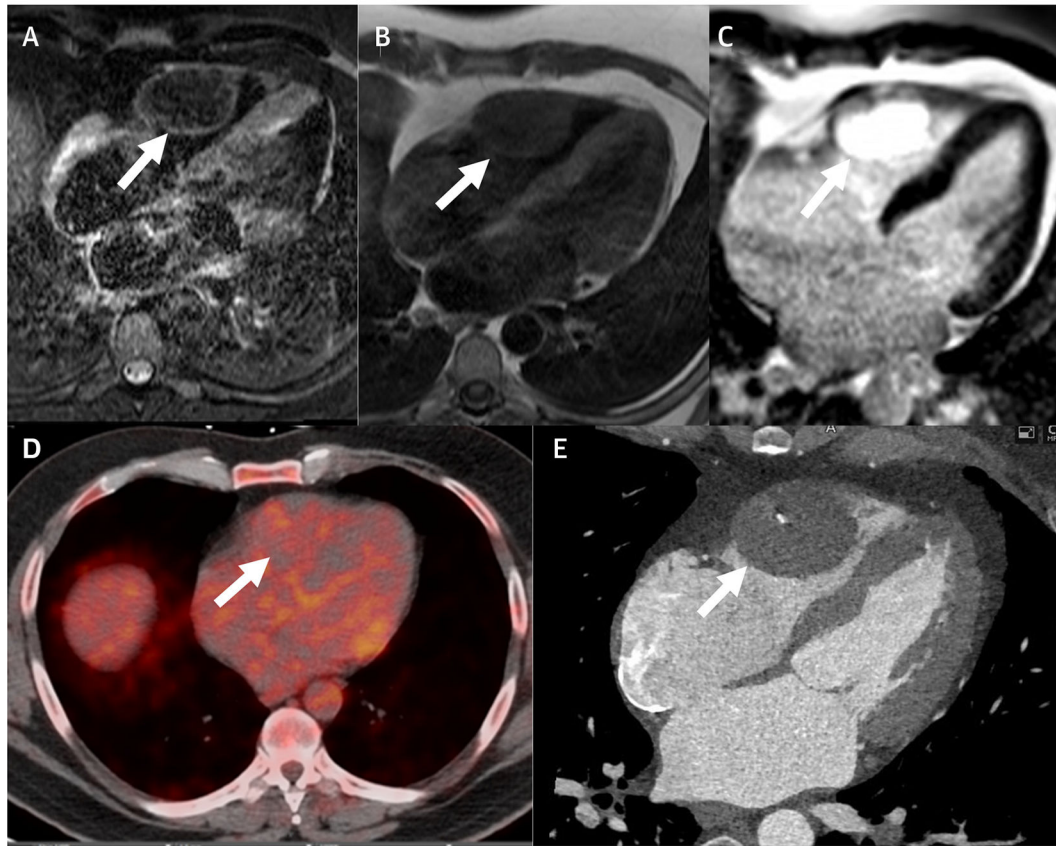


FIGURE 27. Pericardial Mesothelioma Case in CT and CMR

(A) Axial slice in cardiac CT with contrast: homogeneous mass vs PEff surrounding the heart (white arrow). (B) Axial slice on CMR steady-state free-precession sequence before contrast, showing the mesothelioma mass (white arrow) with associated loculated PEff adjacent to right atrium (yellow arrow), along with pleural effusions (red arrow). (C) Phase-sensitive inversion-recovery LGE sequence after contrast, showing mild contrast uptake but relatively low heterogeneous signal within the pericardial mesothelioma mass (white arrow), expected no uptake within the PEff (yellow arrow), and circumferential pericardial LGE, indicating degree of inflammation (red arrow). (D) Free breathing cine sequence showing respirophasic septal shift (white arrow) representing degree of CP physiology. Abbreviations as in Figures 3, 4, and 17.

**FIGURE 28. Cardiac Sarcoma Evaluation in CMR and PET**

Primary cardiac sarcoma involving the left atrium invading into the right pulmonary vein and pericardium, indicated by arrows. (A) Isointense signal on T1-weighted sequence. (B) Hyperintense signal on T2-weighted sequence. (C) Heterogeneous gadolinium uptake with central core of necrosis. (D) FDG-PET–computed tomography showing hypermetabolic activity of the left atrial mass consistent with a malignancy. Abbreviations as in Figures 3 and 12.

**FIGURE 29. Cardiac Fibroma Evaluation in CMR**

Patient presented with heart block with MMI evaluation of fibroma (arrows). CMR: (A) Hypointense signal on T2-weighted imaging with well-defined border, (B) also hypointense signal on T1-weighted image, and (C) LGE sequence, often homogeneous gadolinium uptake from collagen. (D) FDG PET: low metabolic activity. (E) Cardiac CT showing mass with focal calcifications. Abbreviations as in Figures 3, 12, and 17.

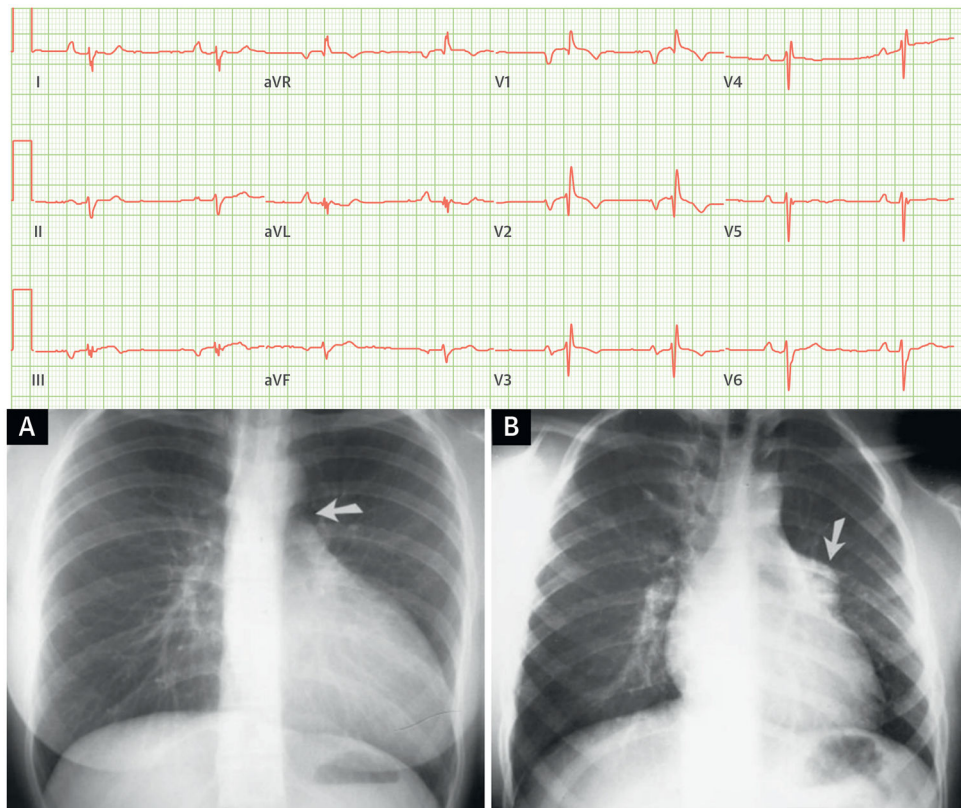


FIGURE 30. ECG and Chest X-Ray Findings in CAP

(Top) Typical electrocardiogram of patient with absent pericardium showing right axis deviation, incomplete right bundle branch block, and right ventricular hypertrophy. (Bottom) Chest x-ray findings in complete (A) and partial (B) absence of the pericardium. Note the interposition of lung tissue causing a prominent aortopulmonary window (arrow in A). Arrow in B indicates herniated left atrial appendage through a partial pericardial defect. Adapted with permission from Gatzoulis et al.¹³⁵ CAP = congenital absence of the pericardium; ECG = electrocardiography.

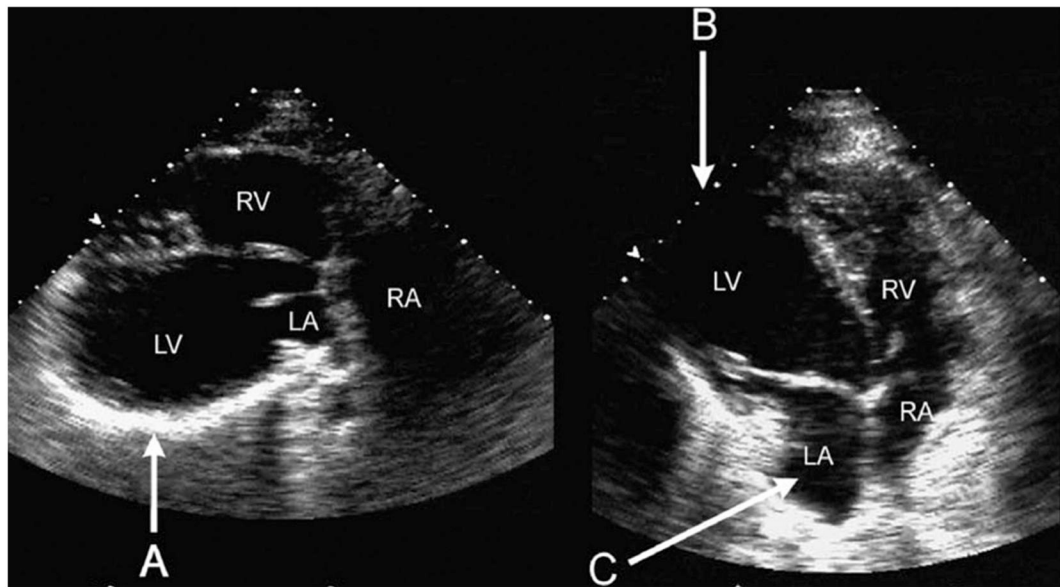


FIGURE 31. TTE Evaluation of CAP

Parasternal long-axis (left) and apical 4-chamber (right) views. TTE images show, (A) unusual echo window with posterior orientation of the LV apex, (B) “tear-drop” appearance due to bulbous ventricles and abnormal atrial-ventricular angle and (C) elongated atrium. Reproduced with permission from Abbas et al.¹³⁹ LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; other abbreviation as in Figure 18.

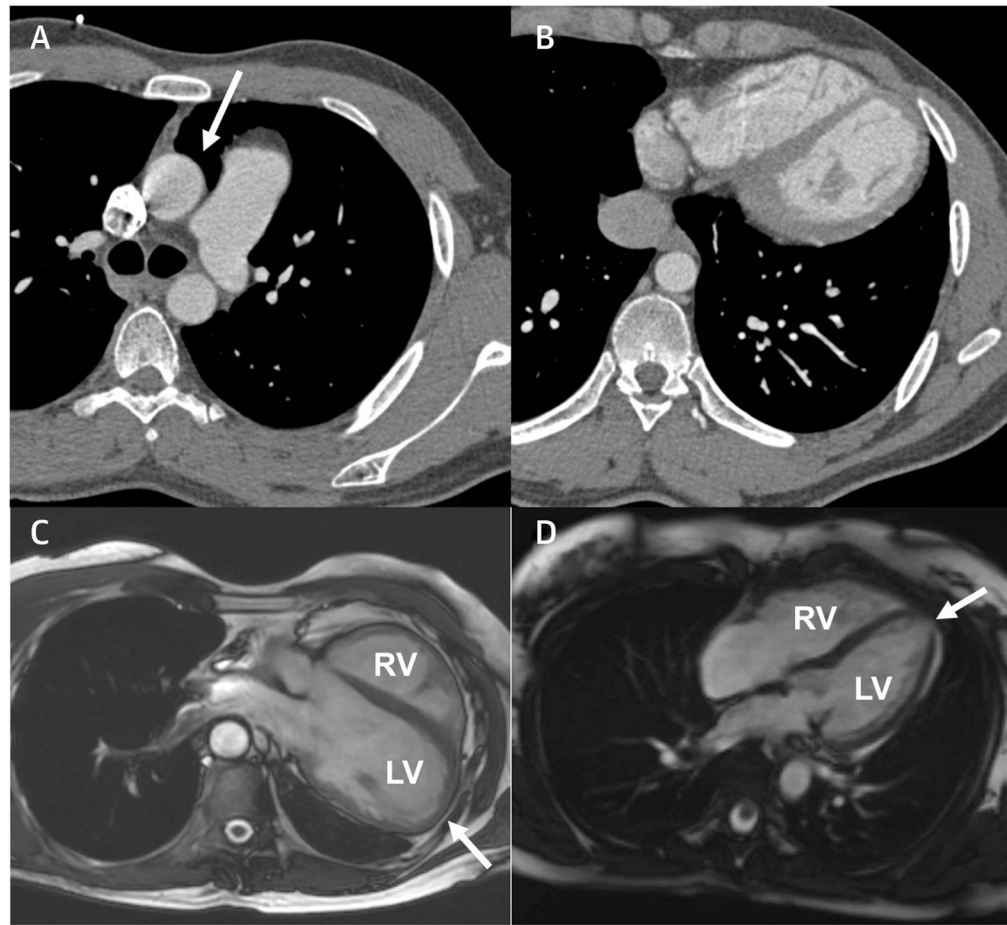


FIGURE 32. CT and CMR Evaluation of CAP

(Top) Cardiac CT evaluation. (A) Note the interposed lung between the aorta and main pulmonary artery (arrow). (B) Mediastinal shift to the left is noticeable with clockwise rotation of the heart. (Bottom) Cardiac CMR steady-state free precision sequence showing (C) significant displacement of the heart into the left hemithorax with complete absence of the pericardium (arrow pointing to apex), compared with (D) normal pericardial position (arrow pointing to apex). Reproduced with permission from Asher et al.¹⁵⁰ Abbreviations as in Figures 3, 17, and 31.

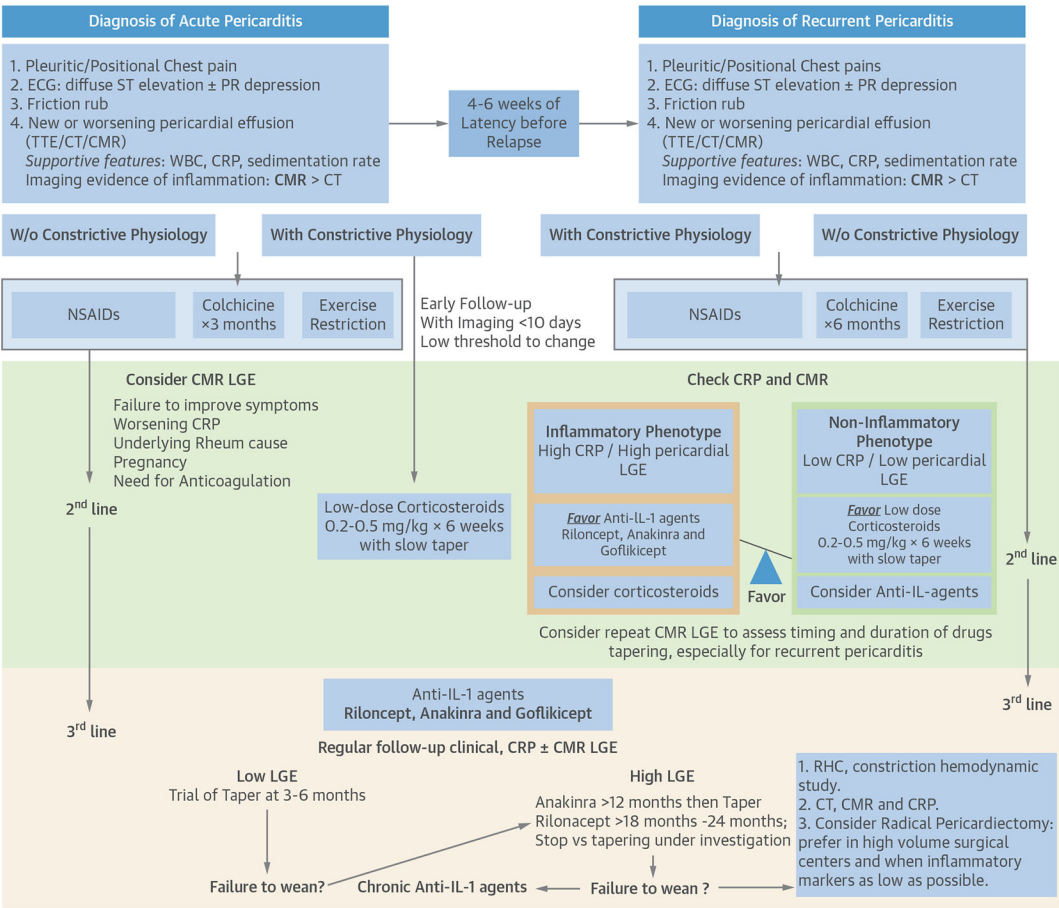


FIGURE 33. Novel Algorithm for the Diagnostic and Therapeutic Approach to Acute and RP
Of note, radical pericardiectomy surgery should be performed at high-volume experienced surgical centers. DHE = delayed hyperenhancement (LGE); LGE = late gadolinium enhancement; NSAID = nonsteroidal antiinflammatory drug; RHC = right heart catheterization; RP = recurrent pericarditis; other abbreviations as in Figures 3, 5, 10, 17, 18, and 30.

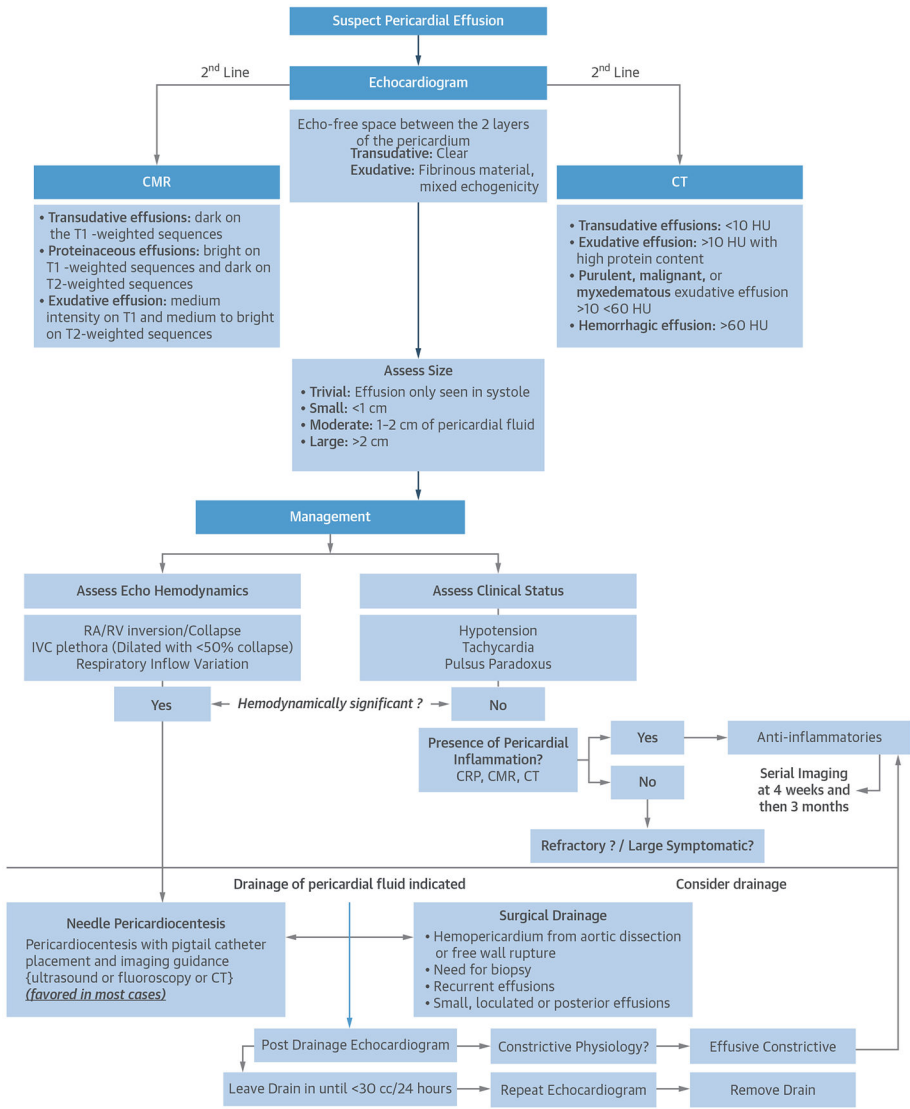


FIGURE 34. Novel Algorithm for the Diagnostic and Therapeutic Approaches to a PEff
Abbreviations as in Figures 2, 3, 4, 10, 17, and 30.

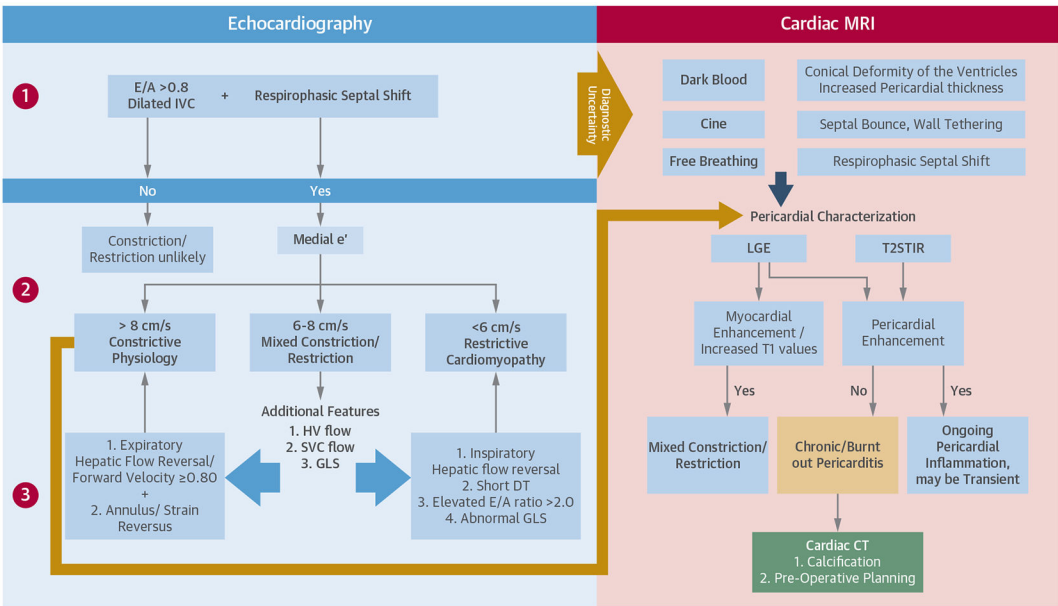
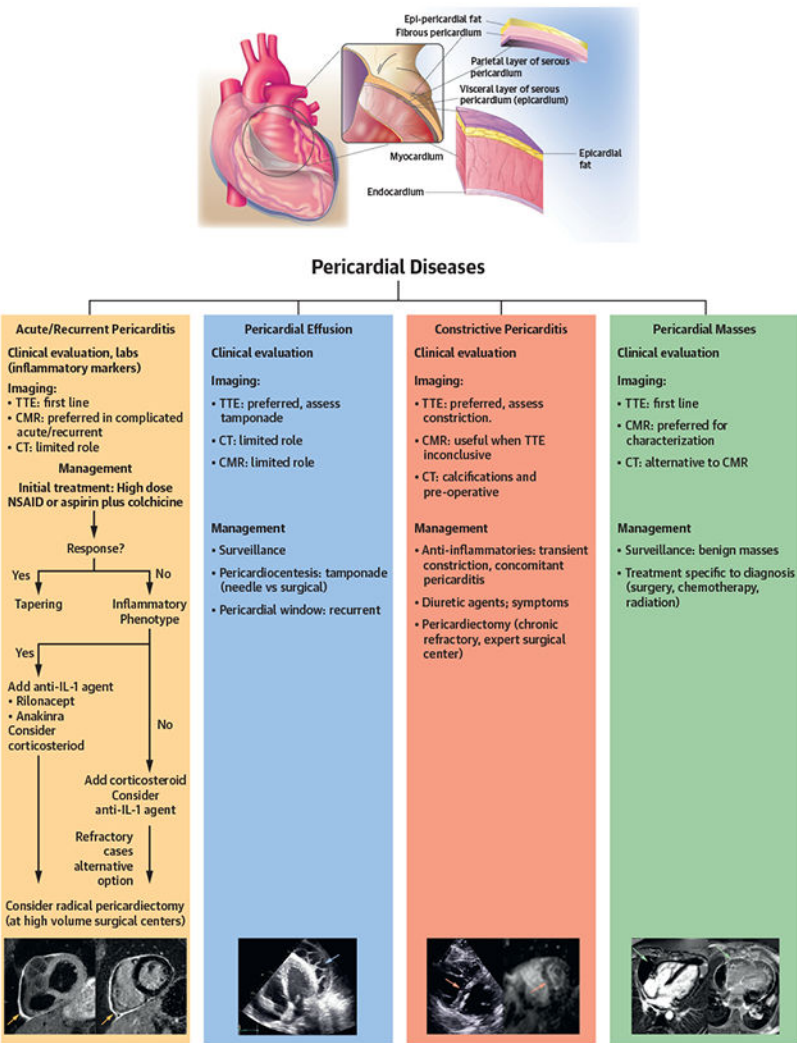


FIGURE 35. A Multimodal Approach to the Noninvasive Diagnosis of CP
LVGLS = left ventricular global longitudinal strain; MRI = magnetic resonance imaging; T2 STIR = T2-weighted short-tau inversion recovery; other abbreviations as in Figures 1, 2, and 17.



CENTRAL ILLUSTRATION. Multimodality Cardiac Imaging and Therapies for Pericardial Diseases
CMR = cardiac magnetic resonance; CT = computed tomography; IL = interleukin; NSAID = nonsteroidal anti-inflammatory drug; TTE = transthoracic echocardiography.

TABLE 1 Strengths and Limitations of Cardiac Imaging Modalities in Pericardial Evaluation

	TTE	CT	CMR
Advantages	• Portability • High availability • Lower cost • High temporal resolution • Assess PEff, CTP, and CP • Intraprocedural guidance	• High availability • Short study • High spatial resolution • Assess pericardial calcifications, PEff, and masses • Preprocedural planning • Extracardiac and vascular assessment	• High spatial resolution • Tissue characterization • Assess inflammation (and monitor), PEff, CP, and masses • Chamber quantification (criterion standard) • Extracardiac and vascular assessment
Disadvantages	• Operator and body habitus dependent, may have limited views • Lower spatial resolution • Limited tissue characterization	• Nonportable • Lower temporal resolution • Ionizing radiation • Iodinated contrast (avoid in renal failure) • Breath holding • Motion artifacts, especially if nongated or arrhythmia	• Nonportable • Lower availability • Lower temporal resolution • Higher cost • Longer study • Gadolinium contrast • Breath holding • Claustrophobia, cardiac devices

CMR = cardiac magnetic resonance; CP = constrictive pericarditis; CT = computed tomography; CTP = cardiac tamponade; PEff = pericardial effusion; TTE = transthoracic echocardiography.

TABLE 2 Standard Multimodality Cardiac Imaging Techniques and Protocols for Evaluating Pericardial Diseases

Technique	TTE		CT		CMR	
	a.	b.	a.	b.	a.	b.
	2-dimensional echocardiography		Axial imaging, multiplanar reconstruction volume-rendered imaging ± contrast and delayed phase		Cine bright-blood imaging (steady-state free precession)	Black-blood imaging (T1/T2 turbo spin echo, fat suppression may be considered)
	Doppler echocardiography					T2 STIR
	M-mode echocardiography					LGE imaging (fat suppression recommended)
	Speckle-tracking echocardiography					Free breathing imaging (gradient echo)
Evaluation						Myocardial tagging
						Other T1, T2, fat saturation sequences
	a.	Pericardial thickness	a.	Pericardial thickening, calcifications	a.	Chamber quantification, septal bounce, conical deformity, wall tethering PEff: location, size
		PEff: location, size, fluid characteristics, pericardiocentesis approach		PEff: location, size, fluid characteristics, pericardiocentesis approach Pericardial mass characterization	b.	Pericardial thickness, IVC plethora Pericardial mass: location, size CAP
		CTP: IVC plethora, cardiac chamber collapse, swinging heart			c.	Pericardial edema, myocardial edema
		CP: IVC plethora, interventricular septal shift, wall tethering, ventricle conical deformity, pericardial thickening	b.	Chamber quantification Chamber tethering Septal bounce	d.	Pericardial inflammation/fibrosis, myocardial inflammation/fibrosis
		Pericardial mass: location, size			e.	Respirophasic septal shift
		CTP: respirophasic variation E-wave mitral inflow >30%/tricuspid inflow >60%			f.	Wall tethering
		CP: Mitral E/A ratio >0.8, mitral medial e' >8 cm/s, annulus reversus, hepatic vein expiratory end-diastolic reversal/forward velocity >0.8, respirophasic variation E-wave mitral inflow >25%/tricuspid inflow >40%			g.	PEff and pericardial mass characterization
	b.					

ECG = electrocardiography; IVC = inferior vena cava; STIR = short-tau inversion recovery; other abbreviations as in Table 1.

TABLE 3 Etiologies of Pericardial Diseases

Category	Examples
Idiopathic	• Idiopathic
Infective	• Viral: coxsackieviruses, echoviruses, adenoviruses, parvovirus B-19, herpesviruses, HIV, COVID-19 • Bacterial: <i>Mycobacterium</i> species including tuberculosis, <i>Staphylococcus</i>, <i>Streptococcus</i>, <i>Pneumococcus</i>, <i>Mycoplasma</i>, <i>Hemophilus</i>, <i>Neisseria</i>, <i>Mycoplasma</i>, <i>Chlamydia</i>, <i>Legionella</i>, <i>Listeria</i>, <i>Coxiella</i>, <i>Borrelia burgdorferi</i>, • Fungal (<i>Candida</i>, histoplasmosis, coccidioidomycosis) • Protozoal (<i>Toxoplasma</i>)
Autoimmune	• Systemic conditions: systemic lupus erythematosus, rheumatoid arthritis, scleroderma/systemic sclerosis, dermatomyositis/polymyositis, mixed connective tissue disease, polyarteritis nodosa, temporal arteritis, Takayasu disease, Churg-Strauss disease, inflammatory bowel disease • Autoinflammatory conditions: familial Mediterranean fever, tumor necrosis factor receptor 1—associated periodic syndrome • Drug-induced: procainamide, isoniazid, hydralazine, cyclosporine • Miscellaneous: sarcoidosis, Behçet disease, Still disease, immunoglobulin G4-related diseases, Erdheim-Chester disease
Neoplastic	• Primary: mesothelioma, fibrosarcoma, lipoma • Secondary/metastatic: lung cancer, breast cancer, lymphoma, Kaposi sarcoma
Radiation	• Radiotherapy
Hemopericardium (including iatrogenic)	• Post-cardiotomy/thoracotomy (any cardiac and thoracic surgery) • Percutaneous/transcatheter procedures (catheter ablation, including epicardial access), cardiac implantable electronic devices, percutaneous coronary intervention, transcatheter valve or congenital heart interventions, endomyocardial biopsy • Trauma • Myocardial infarction free wall rupture • Aortic dissection • Anticoagulation
Primary cardiac	• Myocardial infarction (Dressler syndrome) • Myocarditis (perimyocarditis and myopericarditis) • Stress cardiomyopathy
Congenital	• Pericardial cysts/diverticuli • CAP
Metabolic	• Uremia, dialysis-associated

Category	Examples
Other	• Endocrine: hyperthyroidism, hypothyroidism, cholesterol, anorexia • Amyloidosis • Polycystic kidney disease • Chylopericardium • Pulmonary arterial hypertension • Pectus excavatum • Other drugs including chemotherapy

TABLE 4 Classification of Pericardial Diseases

Pericarditis
By time-course
• Acute (<4-6 wk) • Incessant (>4-6 wk to 3 mo without remission) • Chronic (>3 mo) • Recurrent (new pericarditis flare after symptom-free interval of >4-6 wk)
By etiology
• See Table 3
By predominant disease
• Myopericarditis (pericarditis dominates) • Perimyocarditis (myocarditis dominates)
PEff
Fluid characteristics
• Transudate • Exudate • Hemorrhagic • Suppurative • Malignant • Chylous • Hydropericardium
Size and hemodynamic impact
• Trivial/physiologic (<1.0 cm, not visible in chamber diastole) • Small (<1.0 cm, visible in chamber diastole) • Medium (1.0-1.9 cm) • Large (2.0+ cm) • CTP (Figure 4)
Chronic CP
• TCP • ECP
Pericardial masses/tumors
• Primary • Secondary

ECP = effusive-constrictive pericarditis; TCP = transient constrictive pericarditis; other abbreviations as in Table 1.

TABLE 5 Functions of the Pericardium

Category	Specific Functions
Mechanical	• Limits short-term cardiac distention • Facilitates cardiac chamber coupling and interaction • Maintains pressure-volume relations of cardiac chambers and their output
Membranous/serosal	• Lubricates, reduces friction • Equalizes gravitational, hydrostatic, and inertial forces • Mechanical barrier to infection
Metabolic	• Immunologic • Vasomotor • Fibrinolytic • Modulates sympathetic neurotransmission and contractility
Ligamentous	• Limits displacement of the heart • Neutralizes the effects of respiration and change of body position • Contributes to apparent compliance of the pericardium

TABLE 6 Pathophysiology Similarities and Differences Between CTP and CP

	CTP	CP
Similarities	• Diastolic dysfunction • Elevated central venous, pulmonary venous, and ventricular diastolic pressures • Heightened ventricular interdependence • Respiratory variation of transvalvular inflow velocities	
Differences	• ↓ Early diastolic filling (↓Y descent) • Pericardial space transmits respiratory swings in thoracic pressure • Inspiratory ↑ in venous return • Septal shift caused by ↑ relative size of RV • Uniform inspiratory ↓ in diastolic pressures	• ↑ Early diastolic filling (↑Y descent) • Pericardial space does not transmit swings in thoracic pressure • No inspiratory ↑ in venous return • Septal shift caused by ↓ relative size of LV • With inspiration, either no change or ↑ of RA pressure and ↓PA wedge pressure

These differences account for the physical, echocardiographic, and hemodynamic findings of the pericardial compressive disorders. Adapted with permission from Hoit.³⁵ LV = left ventricular; PA = pulmonary artery; RA = right atrium; RV = right ventricle; other abbreviations as in Table 1.

TABLE 7 Main Imaging Features of Acute Pericarditis

TTE	CT	CMR
• Normal findings in some patients • Segmental wall motion abnormalities or pathologic myocardial strain values (in case of myocarditis) • PEff with or without CTP (present in 40%-50% of cases) • Sign of CP (often transient) • Tachycardia	• Noncalcified pericardial thickening (>3 mm) • Enhancement of the thickened visceral and parietal surfaces of the pericardial sac in late post-contrast CT scan • CT attenuation values of the PEff may help identify hemorrhagic pericardial effusion	• Thickening of pericardium in T1-weighted images (>3 mm) • Enhancement of pericardium in LGE images and edema on T2-STIR is consistent with active inflammation and neovascularization (of prognostic importance) • Loss of the normal sliding between pericardial layers during the cardiac cycle could be interpreted as a sign of visceral and parietal pericardium inflammation and constrictive physiology

STIR = short-tau inversion recovery; other abbreviations as in Table 1.

TABLE 8 Recommendations for Multimodality Cardiac Imaging and Treatment in Acute Pericarditis

Assessment of the presence of systemic inflammation by means of CRP, fever, neutrophil leukocytosis, and presence of pericardial and pleural effusion to target specific treatments	Recommended
TTE for evaluating and surveillance of PEff, signs of constriction and myocardial involvement of acute pericarditis	Recommended
CMR for evaluation of pericardial LGE, edema, thickening, effusion, signs of constriction, and myocardial involvement for diagnosis and risk stratification of acute pericarditis	Reasonable
CMR for routine assessment of treatment response and surveillance of acute pericarditis, especially with clinical resolution to treatment	Not recommended
CT for evaluation of other chest pain causes other than acute pericarditis	Reasonable
High-dose NSAID in combination with colchicine as first-level therapies for acute pericarditis (aspirin is preferred in case of concomitant ischemic heart disease)	Recommended
Anti-IL-1 agents may be considered in the inflammatory phenotype when other therapies are contraindicated, ineffective, or not tolerated	Reasonable
Corticosteroid use should be restricted to cases that are refractory or intolerant to other therapies (usually low-medium doses).	Reasonable

IL = interleukin; LGE = late gadolinium enhancement; NSAID = nonsteroidal antiinflammatory drug; other abbreviations as in Table 1.

TABLE 9 Common Therapeutic Options for Acute Pericarditis and RP

Therapy	Dosing	Duration ^d	Tapering	Monitoring ^b	LOE ^c
Aspirin ^d	500-1,000 mg 3 times daily	1-2 weeks to months (recurrent)	Weekly in 3-4 wk	Needed	A
Ibuprofen ^d	600-800 mg 3 times daily	1-2 weeks to months (recurrent)	Weekly in 3-4 wk	Needed	A
Indomethacin	25-50 mg 3 times daily	1-2 weeks to months (recurrent)	Weekly in 3-4 wk	Needed	B
Colchicine ^d	0.6 mg once (<70 kg or severe renal impairment) or 0.6 mg twice daily	3 mo (acute), 6-12 mo (recurrent) for colchicine duration	May be considered	Needed	A
Prednisone	0.2-0.5 mg/kg per day	2-4 wk	Several months	Needed	B
Azathioprine	Starting with 1 mg/kg per day then gradually increased to 2-3 mg/kg/day	Several months	Several months	Needed	C
IVIg	400 to 500 mg/kg IV daily for 5 d	5 d	Not required	Needed	C
Anti-IL-1 agents					
Anakinra	1 to 2 mg/kg/day up to 100 mg/day in adults	6-12 mo	Needed	Needed	A
Rilonacept	320 mg once followed by 160 mg weekly	>12 mo	Under investigation	Needed	A
Goflikicept (not yet available in the USA)	80 mg every 2 wk	>6 mo (under investigation)	Unknown	Needed	B
Pericardiectomy	High-volume surgical centers	Not applicable	Not applicable	Needed	C

^aTherapy duration at initial dosing; duration of therapy is until clinical remission (usually longer times for recurrent cases).

^bMonitoring is essentially based on the assessment of blood count, creatinine, creatine kinase (CK), transaminases, CRP, and TTE.

^cA = data derived from multiple randomized clinical trials or meta-analyses; B = data derived from a single randomized clinical trial or large nonrandomized studies (in this review, a study with at least 100 patients is considered to be "large"); and C = consensus of opinion of experts and/or small studies, retrospective studies, and registries.

^dIbuprofen and aspirin are common first-level treatments for the first episode of pericarditis (acute pericarditis) associated with colchicine for 3 months (usually longer times for recurrent cases).
IVIg = intravenous immunoglobulin; IL = interleukin; LOE = level of evidence.

TABLE 10 Assessment of Pericarditis Stages With MMI

Stage	TTE	CT	CMR
Acute inflammation	Possible presence of PEff	Assessment of pericardial contrast enhancement	Pericardial edema and LGE
Chronic inflammation	Assessment of PEff	Pericardial thickening	Pericardial LGE
CP	CP evaluation (Table 2)	CP evaluation (Table 2)	CP evaluation (Table 2)
Remission	Normalization	Normalization	Normalization

LGE = late gadolinium enhancement; other abbreviations as in Table 1.

TABLE 11 Recommendations for Multimodality Cardiac Imaging and Treatment for Recurrent, Incessant, and Chronic Pericarditis

Assessment of the presence of systemic inflammation by means of CRP, fever, leukocytosis, and presence of PEff when suspecting recurrent/incessant pericarditis	Recommended
TTE for evaluating and surveillance of PEff, signs of constriction and myocardial involvement of acute pericarditis	Recommended
CMR for evaluation of pericardial LGE, edema, thickening, effusion and signs of constriction for diagnosis and risk stratification of recurrent/incessant pericarditis	Recommended
CMR for assessing treatment response and surveillance of recurrent/incessant pericarditis, especially with persistent symptoms	Reasonable
CT for routine assessment of recurrent/incessant pericarditis	Not recommended
Aspirin or NSAID in combination with colchicine as first-level therapies for recurrent/incessant pericarditis	Recommended
Anti-IL-1 agents in recurrent/incessant pericarditis after failure of first level therapies (and failure of corticosteroids), especially with evidence of inflammatory phenotype	Recommended
Corticosteroids after failure of first-line therapies for pericarditis, especially without evidence of CRP elevation or specific conditions (eg, autoimmune diseases).	Reasonable
In high-volume experienced surgical centers, radical pericardiectomy is an alternative option for patients who do not respond to medical therapy	Reasonable

Abbreviations as in Tables 1 and 8.

TABLE 12 Indications, PEff Characterization, and Added Value of Cardiac Imaging Modalities in the Evaluation of PEff

Echocardiography		Cardiac CT	CMR
Indications			
First-line imaging		Second-line if echocardiography inconclusive, or suspects secondary causes	Rarely used if other imaging inconclusive, or suspects pericarditis/pericardial malignancy
PEff characterization	Transudate: Anechoic, homogenous, free flowing Exudate/complex: Echogenic, heterogeneous ± loculations, stranding or adhesions	Transudate: 0-20 HU Exudate: 20-50 HU Hemorrhagic: >50-60 HU If very high HU: pericardial leakage of contrast (eg, ruptured aortic dissection) Chylous: -60 to -80 HU	Transudate (homogenous): Low SI on T1W/T2W imaging T1 time <3,013 ms Jet-black on LGE PSIR imaging Exudate/complex: (nonhomogenous) Medium/mixed SI on T1W/T2W imaging T1 time >3,013 ms Hemorrhagic: High SI in T1W/T2W imaging
Added value	Evaluate for coexisting CTP or ECP/TCP Guide pericardiocentesis TEE useful in detecting focal CTP (eg, post cardiac surgery)	Identify secondary causes and mimickers Assess for loculated PEff/focal CTP (stable patients) May identify pericardial inflammation with late iodine enhancement CT-guided pericardiocentesis in challenging cases	Evaluate for coexisting pericarditis Evaluate for constriction if echocardiography equivocal Useful when suspecting pericardial malignancy

CMR = cardiac magnetic resonance; CT = computed tomography; CTP = cardiac tamponade; ECP = effusive constrictive pericarditis; LGE PSIR = late gadolinium enhancement with phase sensitive inversion recovery; PEff = pericardial effusion; SI = signal intensity; T1W = T1 weighted; T2W = T2 weighted; TCP = transient constrictive pericarditis; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

TABLE 13 Suggested Protocols for MMI of PEff

Echocardiography	Cardiac CT	CMR
2D with respirometer		Cine imaging ± tagging
Size and characterize PEff in multiple projection ± off-axis views	Non-contrast ECG-gated (single phase)	Detect and size PEff
Diastolic chamber collapse with CTP	Distinguish mimickers	Distinguish mimickers
Respirophasic septal shift and IVC dilatation with CTP, ECP and TCP	Detect pericardial calcification	Evaluate for ECP and TCP
Identify pocket with clear path off vital structures for pericardiocentesis		Assess pericardial thickness and identify adhesions (tagging)
M-mode with respirometer		T1W (± T1 mapping)
Higher sensitivity for diastolic chamber collapse with CTP	Arterial ECG-gated (single or multiphase)	Detect and characterize PEff
Higher sensitivity for respirophasic septal shift with CTP, ECP and TCP	Detect, size, and characterize PEff	Distinguish mimickers
Doppler with respirometer	Identify secondary causes and mimickers	
Respiraphasic changes in atrio-ventricular and hepatic vein velocities with CTP, ECP and TCP	Evaluate pericardial thickness	
	± Delayed ECG-gated (single phase)	T2W/fat-suppressed
± 3D echocardiography	Detect pericardial inflammation	Detect and characterize PEff
	Evaluate for contrast extravasation into pericardium	Evaluate for pericardial edema
		LGE
		Ascertain for pericardial thickening and inflammation
		Evaluate for pericardial malignancies

Abbreviations as in Table 12.

TABLE 14 Recommendations for Multimodality Cardiac Imaging for PEff and CTP

TTE to confirm clinical diagnosis of PEff and CTP	Recommended
Cardiac CT/CMR or TEE to confirm clinical diagnosis of PEff when clinically indicated if TTE inconclusive.	Recommended
Cardiac CT/CMR to assess for secondary causes of PEff when clinically indicated	Reasonable
Cardiac CT/CMR to confirm clinical diagnosis of CTP	Not recommended
TEE/cardiac CT to confirm clinical diagnosis of focal CTP in stable cases of high suspicion with unrevealing/equivocal TTE	Recommended
TTE for surveillance of PEff (at least moderate in size)	Reasonable

Abbreviations as in Tables 1 and 12.

TABLE 15 MMI Features of CP

TTE	CT	CMR
• Respiriophasic ventricular dependence/septal shift • E-wave predominant LV filling with respirophasic variation • Hepatic vein end-diastolic expiratory reversal velocity/forward flow >0.8 • Normal or increased medial mitral annular e' velocity (>8 cm/s) • Annulus reversus (medial > lateral e' mitral annular velocity) • Loss of superior vena cava systolic flow variation	• Increased pericardial thickness • Pericardial calcification	• Increased pericardial thickness • Respirophasic ventricular dependence on free breathing cine sequences • Wall tethering and conical deformity of the ventricle • Late gadolinium pericardial enhancement and pericardial edema (in inflammatory TCP)

No single isolated imaging finding is diagnostic of CP; a constellation of findings in conjunction with clinical features of CP is required to make the diagnosis.
Abbreviations as in Tables 1, 4, and 6.

TABLE 16 Recommendations for Multimodality Cardiac Imaging and Treatment for CP

Noninvasive hemodynamic assessment by TTE for the diagnosis of CP and ECP	Recommended
CMR to provide supportive evidence of CP and ECP, especially when TTE inconclusive	Recommended
CMR to identify pericardial inflammation as an etiology of for CP and ECP	Recommended
CT for evaluation pericardial calcifications as supplementary evidence for constriction, and preoperative evaluation for pericardiectomy surgery	Reasonable
Invasive cardiac catheterization for the diagnosis of CP and ECP, where noninvasive methods are nondiagnostic or equivocal	Recommended
First-line treatment of inflammatory CP and ECP with anti-inflammatory therapy	Recommended
Conventional or partial (anterior and/or diaphragmatic) pericardiectomy for CP and ECP	Not recommended
Radical surgical pericardiectomy for noninflammatory CP and inflammatory CP failing anti-inflammatory therapy	Recommended

Abbreviations as in Tables 1 and 4.

TABLE 17 MMI Features of Pericardial Cyst and Diverticulum

TTE		CT		CMR
Pericardial cyst	• Echolucency adjacent to cardiac border	• Attenuation signal of water	• Well circumscribed	• Encapsulated, smooth border, abutting the pericardium • Hypointense on T1- and hyperintense on T2-weighted imaging
Pericardial diverticulum	• Indistinguishable from pericardial cyst	• Communication with the pericardial sac		• Similar to pericardial cyst except communication with the pericardial sac (may be difficult to visualize)

Abbreviations as in Table 1.

TABLE 18 MMI Features of Pericardial Tumors

	CMR (LGE)	CMR (T1-Weighted)	CMR (T2-Weighted)	CT (With or Without Contrast)
Primary malignant tumor				
Mesothelioma	++	↔	↓ ↔ ↑	Ring-enhancing mass
Lymphoma	++	↓	↓ ↔ ↑	Polypoid, large PEffs
Sarcoma	++/+++	↓ ↔ ↑	↓ ↔ ↑	Determine extension beyond pericardium
Metastasis	++/+++	↓ (except melanoma)	↑	Lesions beyond the pericardium
Primary benign tumor				
Hemangioma	++++	↔	↑	Highly vascular
Lipoma	-	↑	↑ (with fat saturation)	Low attenuation mass
Fibroma	+ /++++	↓ ↔	↓	Homogeneous, sharp margin, occasional calcification
Teratoma	++	↓	↑	Heterogeneous with calcification and fat
Paraganglioma	++	↔	↑	Identify tumor location and vascularity

All tumors can have atypical appearance because of altered tissue composition.

+ = minimal LGE; ++ = heterogeneous LGE; +++ = homogeneous LGE; ++++ = intense LGE; ↓ = hypointense signal relative to the myocardium; ↔ = isointense; ↑ = hyperintense; ↓ ↔ ↑ = variable signal intensity; other abbreviations as in Tables 1 and 8.

TABLE 19 Recommendations for Multimodality Cardiac Imaging for Pericardial Masses

CMR/CT to confirm and identify presence of pericardial mass	Recommended
CT to determine source and extent of pericardial metastasis	Recommended
TTE to establish hemodynamic consequence of pericardial mass	Recommended
CMR/CT to confirm presence of pericardial cyst if TTE is inconclusive	Recommended
CMR/CT to follow size of pericardial cyst	Reasonable
CMR/CT to distinguish pericardial cyst vs diverticulum	Reasonable
TTE to identify type of pericardial tumor	Not recommended

Abbreviations as in Table 1.

TABLE 20 Clinical, ECG, and Chest X-Ray Findings Suggestive of CAP

Category	Findings
Symptoms	• Atypical, nonexertional left-side chest pain (sharp, stabbing) • Positional symptoms, chest pain, or dyspnea lying on left side (trepopnea) • Uncomfortable sensation of pounding, “shifting heart” sensation
Physical examination	• Apical displacement of the point of maximal impulse • Pectus excavatum • Systolic ejection murmur at left sternal border (related to mobility of heart)
ECG	• Peaked P waves • Right axis deviation • Incomplete right bundle branch block • Poor R-wave progression (late transition) • Postural changes in QRS vector • Sinus bradycardia and marked sinus arrhythmia
Chest X-ray	• Levorotation of the heart (posteroanterior projection) • Posterior shift of the heart (lateral view) • Elongated left heart border (“Snoopy” sign) • Cardiomegaly appearance (caused by leftward rotation) • Loss of the right heart border with overlying spine • Sharp aortopulmonary window with prominent PA • Radiolucency (lung tissue) between the aortic arch and PA and inferior heart border and diaphragm

Note that most findings are associated with left-side complete or partial absence. Adapted with permission from Klein et al.¹

Abbreviations as in Tables 2 and 6.

TABLE 21 Multimodality Cardiac Imaging Findings With Congenital Pericardial Absence

	TTE	CT or CMR	Fluoroscopy and Angiography
M-mode:			
•	Paradoxical septal motion	• Absence of the pericardial layer	• Normal-caliber coronary vessels
•	Accentuated movement of the posterior LV wall	• Levocardia	• Abrupt focal kink or angulation (external coronary obstruction by pericardial rim)
•	Absent separation of the epicardium-pericardium	• Interposition of lung tissue in the anterior space between aorta and PA, or between diaphragm and base of the heart	• Migratory obstruction
2-dimensional echocardiography:			
•	Unusual, off-axis windows, and lateral probe position	• Subepicardial myocardial crease caused by external pressure from a partial pericardial defect	
•	Exaggerated mobility of the heart (cardioptosis), “pendulum heart,” or “rocking motion”	• Tethering of right pericardium to anterior chest wall	
•	Paradoxical septal motion in systole, vigorous posterior wall motion, or anterior motion of the LV during systole	• Clockwise rotation of the heart >60° (normal ~40°)	
•	Appearance of RV dilation (caused by shift of RV to the left)	• Whole heart volume changes	
•	Posterior orientation of the LV apex (PLAX)	• Cine: similar to 2D echocardiographic findings, including exaggerated mobility of the heart, posterior orientation of the LV apex, “tear-drop appearance” with abnormal atrial-ventricular angle	
•	Elongated atria and widened ventricles “tear-drop appearance” (A4C)		
•	Abnormal sharp atrial-ventricular angle (A4C)		
•	Bulging outward diastolic motion inferior-posterior wall (A4C)		
•	Y LV torsion with preserved longitudinal, radial, and circumferential strain		
•	Image appearance may shift in right lateral decubitus view		
Doppler:			
•	↓ Pulmonary venous and SVC systolic flow (↑ diastolic waves)		
•	Tricuspid regurgitation (annular dilation, chordal rupture)		

Note that most findings are associated with left-sided complete or partial absence. Adapted with permission from Klein et al.¹
Abbreviations as in Tables 1 and 6.

TABLE 22 Recommendations for Multimodality Cardiac Imaging for CAP

CMR/CT to confirm or identify presence of CAP if clinical history, CXR, ECG, TTE are suggestive, patient is symptomatic or high-risk features are suspected and management interventions may be considered	Recommended
CMR/CT for follow-up of established CAP if progression to high risk features/complications are suspected and management interventions may be considered	Reasonable
CMR/CT for initial follow-up of CAP after surgical intervention	Reasonable
CMR/CT to confirm or identify presence of CAP if clinical history, CXR, ECG, and TTE are suggestive, patient is asymptomatic, and management interventions will not likely be altered	Not recommended

CXR = chest x-ray; other abbreviations as in Table 1.

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