Infective Pericarditis

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33.1 Overview

Pericarditis can be divided into infective pericarditis and noninfective pericarditis (Table 33.1). Infective pericarditis can be caused by a variety of pathogens such as viruses and bacteria (such as *Mycobacterium tuberculosis*) invading the pericardium. In developed countries such as the United States and Western Europe, viruses are the most common cause of infectious pericarditis, while in developing countries, tuberculous pericarditis is the most common and tuberculous pericarditis is often complicated by HIV infection [1]. A study on the etiology of massive pericardial effusion in 140 Chinese Han people has shown that *Mycobacterium tuberculosis* infection accounts for about 28% [2] and other infections are caused by uncommon bacteria including pneumococcus, meningococcus, gonococcus, streptococcus, and staphylococcus. Fungal and parasitic infections are rare.

Pericarditis is divided into acute pericarditis, persistent pericarditis, chronic pericarditis, and recurrent pericarditis (RP) according to the duration of symptoms (Table 33.2). Acute pericarditis is an inflammatory pericardial syndrome with or without pericardial effusion. The typical manifestation of acute pericarditis is chest pain, usually pleurisy sharp pain, which can be alleviated by sitting and leaning forward. Pericardial fricative sounds and abnormal electrocardiogram may be found, manifested as new extensive ST segment elevation or PR segment depression and pericardial effusion. Infectious pericarditis may show symptoms and signs of systemic infection, such as fever and increased leukocyte count. Viral pericarditis may show flu-like respiratory or digestive tract prodromal symptoms.

Table 33.1 Etiology of pericarditis

Classification	Etiology
Infective	
Viruses (common)	Enterovirus (Coxsackie, Echo), herpesvirus (EBV, CMV, HHV6), adenovirus, parvovirus B19, etc.
Bacteria	*Mycobacterium tuberculosis* (common), rickettsia, pneumococcus, streptococcus, etc.
Fungi (rare)	Histoplasmosis (common in immunodeficient patients), aspergillus
Parasites (rare)	Echinococcus, toxoplasma gondii
Noninfective	
Immunity (common)	SLE, rheumatoid arthritis, vasculitis
Tumor	Metastatic tumor (common, lung cancer/breast cancer/lymphoma); primary tumor (rare, mesothelioma)
Metabolism	Uremia, myxedema, anorexia nervosa
Traumatic and iatrogenic	Early onset (direct or indirect, rare) Later onset (pericardial injury is common, after events such as myocardial infarction, trauma, thoracotomy, or interventional therapy)
Drug-related	Lupus-like syndrome (procainamide, etc.); antitumor drugs (often complicated with cardiomyopathy): adriamycin, daunorubicin, cytarabine, etc.
Others (common)	Amyloidosis, aortic dissection, pulmonary hypertension, heart failure
Others (uncommon)	Congenital partial or complete pericardial defects

Recurrent pericarditis: After the first attack of acute pericarditis, the probability of recurrent pericarditis is usually 15–30% [3]. The etiology of recurrent pericarditis is not completely clear, and it is generally believed that immune-mediated mechanism may play a major role in the pathogenesis. Clear etiological basis cannot be found in most patients, and nonspecific myocardial antibodies can be found in serum. Such cases are called idiopathic recurrent pericarditis, as the major type of recurrent pericarditis, accounting for 60–70%. In addition, 20–30% of patients with recurrent

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Table 33.2 Classification and diagnostic criteria of pericarditis

Classification	Diagnostic criteria
Acute	If at least 2 of the following 4 items are met, the disease can be diagnosed as inflammatory pericardial syndrome: 1. Chest pain consistent with pericarditis (sharp pain can be alleviated by sitting and leaning forward) 2. Pericardial fricative sound 3. Extensive ST-segment elevation or PR-segment depression on electrocardiogram 4. Pericardial effusion (new or deteriorating) Additional evidence: Elevated inflammatory markers [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell count (WBC)] Imaging evidence of pericardial inflammation (CT, CMR)
Persistent	Persistent for more than 4–6 weeks but less than 3 months, without remission
Recurrent	Recurrent acute pericarditis recorded for the first time, with the asymptomatic interval of 4–6 weeks or longer
Chronic	Persistent for more than 3 months

pericarditis show infection, especially viral infection, with common ones such as enterovirus (Coxsackie virus, echovirus), herpes virus, and parvovirus B19.

Constrictive pericarditis: It refers to a series of circulatory disorders caused by compliance-decreased pericardium (fibrosis or calcification) compressing the heart and resulting in increased diastolic pressure and limited diastolic function. Constriction refers to the pathophysiological compression of the heart, and pericarditis is a common cause of pericardial constriction. Among acute pericarditis, bacterial pericarditis, especially suppurative pericarditis (20–30%) are most likely to develop into constrictive pericarditis, followed by immune-mediated pericarditis and tumor-related pericarditis (2–5%), and viral and idiopathic pericarditis (<1%) are the least common [4]. Most of the physiological processes of constrictive pericarditis have no history of active pericarditis or definite pericarditis, but constrictive pericarditis is still very common because constriction often occurs during or immediately after pericarditis (especially tuberculous pericarditis). Constrictive pericarditis is often manifested as low cardiac output syndrome, including fatigue, dyspnea, oliguria, jugular vein filling, liver enlargement, edema of both lower limbs, ascites, and so on.

33.2 Pathological Manifestations

Pericardium is a fibrous sac that wraps the heart and the roots of great vessels, which is divided into visceral (serosal) layer and parietal (fibrous) layer. The visceral layer is a single layer of ciliated mesenchymal cells covering the inner surface of the whole pericardial cavity. The normal visceral layer is very thin and cannot be displayed by ultrasound, CT, and MRI. The parietal layer is the lateral layer of pericardium, which constitutes the outer side of pericardial cavity. The parietal layer is mainly composed of collagen fibers, which is very tough and forms a physiological barrier. The normal parietal layer is about 1 mm thick, which constitutes the thickness of "normal pericardium" described in general images. Due to the limitation of imaging conditions, the pericardium thickness defined by CT and MRI ($\leq$3 mm) is higher than the thickness of normal pericardium. Normal pericardial cavity contains 10–50 mL of fluid, which acts as a lubricant in pericardium. Inflammation caused by any pathological process can increase the production of pericardial effusion (exudate).

Acute pericarditis often has fibrinous exudation, and the course of disease is generally short; self-healing may occur in some cases, but some develop into chronic pericarditis. Chronic pericarditis is mainly characterized as hyperplasia of pericardial fibrous tissue, and fibrosis causes diastolic dysfunction, resulting in constriction, which is called constrictive pericarditis. Foci of calcification and infiltration of plasma cells and lymphocytes can be found between fibrous thickened pericardium. Common causes of chronic pericarditis include viruses and tuberculosis.

Viral pericarditis usually shows straw yellow or even bloody pericardial effusion, and the acute stage is mostly short (1–2 weeks). At the beginning, polymorphonuclear leukocyte infiltration occurs in the pericardium, followed by leukocyte infiltration around small blood vessels. Serous exudation may occur in the pericardial cavity.

In the first 2 weeks, tuberculous pericarditis is manifested as fibrin exudation in pericardial cavity, moderate amount of bloody pericardial effusion, mainly containing neutrophils, and 2 weeks later, pericardial effusion mainly contains monocytes, especially lymphocytes. Subsequently, pericardial effusion is absorbed with typical tuberculous granuloma formation. In the later stage, pericardial thickening and fibrosis occur, pericardial cavity fusion and contraction occur, and pericardium might calcify, thus forming constrictive pericarditis which hinders diastolic filling.

33.3 Imaging Manifestations

1. Acute Pericarditis
   (a) Echocardiography: It is the most commonly used imaging examination method for acute pericarditis, which can sensitively detect pericardial effusion and evaluate the resulting cardiac tamponade or cardiac activity restriction. However, sometimes pericarditis is not accompanied by pericardial effusion, so the sensitivity and specificity of echocardiography for acute pericarditis are insufficient. Compared with CT and MRI, echocardiography has limited visual field and limited diagnosis of pericardial thickening and inflammation, so the diagnosis of some acute pericarditis depends on further imaging examination, mainly MRI examination.
   (b) X-ray: It is of little diagnostic value for acute pericarditis. X-ray is insensitive to a small amount of pericardial effusion. If a large amount of pericardial effusion is manifested as heart enlargement and the cardiac shadow enlargement can be found on both sides, showing flask shape or even spherical shape.
   (c) CT: As a supplement to echocardiography, it can show pericardial thickening and pericardial effusion. The observation of pericardial thickening on CT is not as reliable as that of cardiac magnetic resonance imaging (CMR). Normal pericardial thickness is only 1–2 mm on CT (Fig. 33.1). If the diagnostic criterion for normal pericardial thickness is less than 3 mm, the cases with mild pericardial thickening may be misdiagnosed. CT is very sensitive to pericardial calcification, which is common in tuberculous pericarditis. CT can evaluate the amount of pericardial effusion and determine the character of pericardial effusion by measuring the CT value of pericardial effusion: leakage (0–20 HU), protein/hemorrhagic effusion (>20 HU), and chylous pericardial effusion (<0 HU).
   (d) Cardiac magnetic resonance (CMR): Compared with echocardiography and CT, CMR is the best imaging method for evaluating pericardial diseases. Normal pericardium is very thin. Anatomically, the thickness of pericardium is less than 1 mm. There are epicardial fat and extrapericardial fat on both sides of pericardium. Fat is significantly different from pericardial wall on CT and MRI, so the sandwich-like changes can be clearly found on pericardial wall and adjacent fat. Most epicardial fat and extrapericardial fat exist in right ventricular free wall, interalrial groove, and interventricular sulcus, so pericardial thickness is often observed and measured in these sites (Fig. 33.1). Due to the influence of motion and chemical shift artifacts, CMR may overestimate pericardial thickness, so the normal pericardial thickness on CMR is ≤3 mm, and the criterion to diagnose pericardial thickening is generally ≥4 mm. Some acute pericarditis is manifested as pericardial thickening, but it is not characteristic for diagnosis of acute pericarditis. Pericardial edema is manifested as hyperintensities of fat suppression sequence T_2WI (STIR), which is a characteristic change of acute pericarditis but needs to be differentiated from pericardial effusion. Pericardial delayed enhancement after intravenous injection of gadolinium contrast agent indicates pericardial inflammation (Fig. 33.2). In addition, CMR can clearly show pericardial effusion.

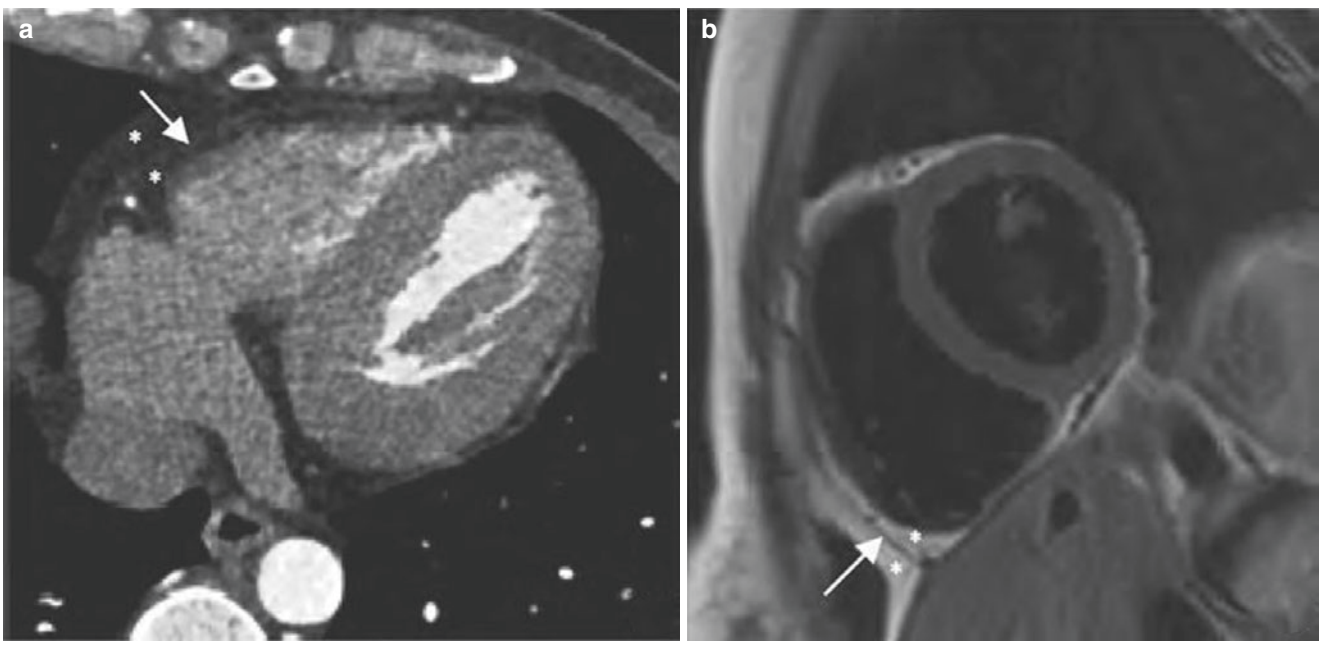

Fig. 33.1 Normal pericardium. (**a**, **b**) CT and MRI showed that the normal pericardium (arrow) and adjacent fat (*) in the free wall of right ventricle were manifested as sandwich-like changes, and the thickness of normal pericardium was less than 3 mm

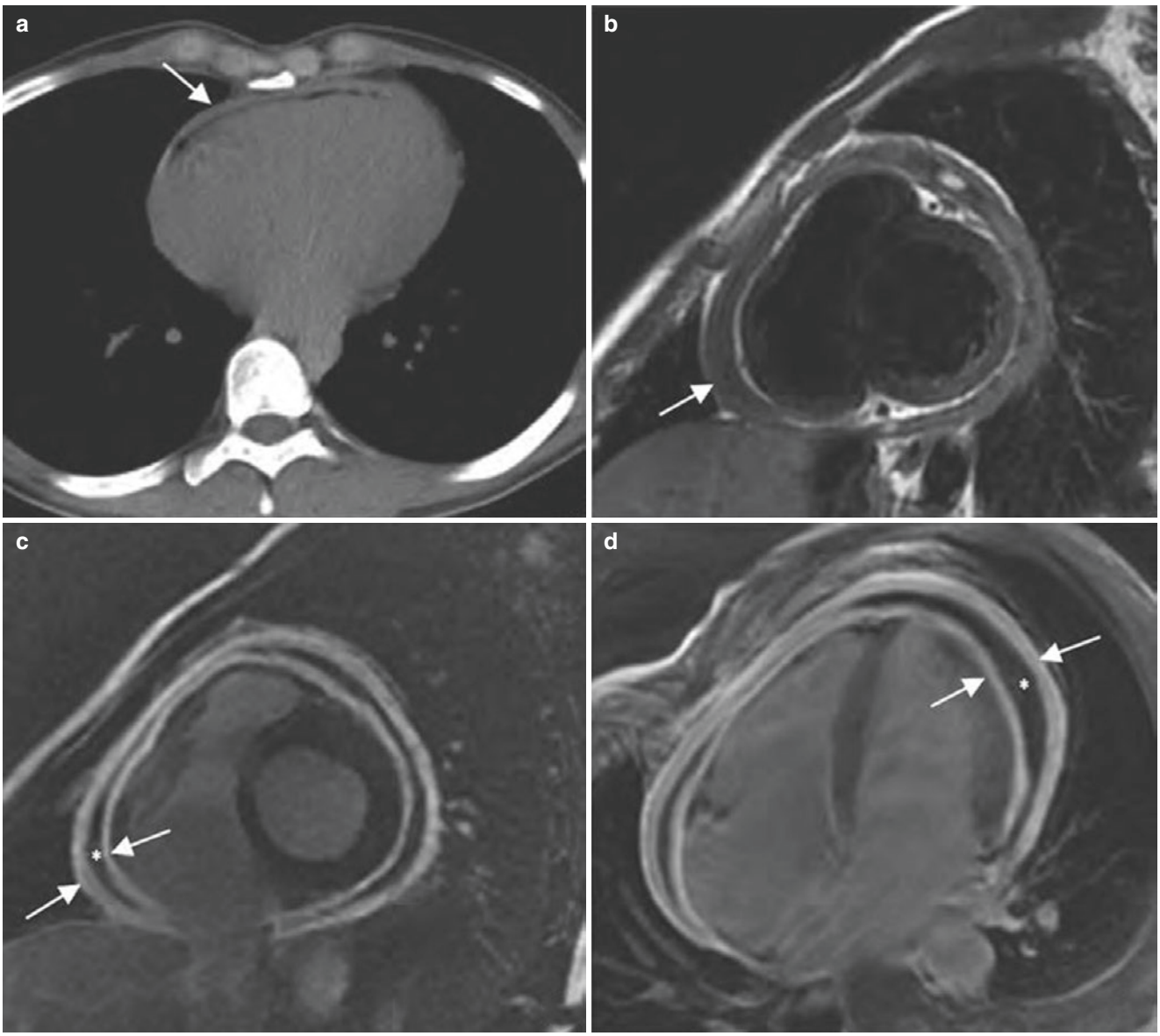

Fig. 33.2 Acute pericarditis. (**a**) CT plain scan showed diffuse pericardial thickening (arrow), which was limited by imaging conditions, and a small amount of pericardial effusion was not clearly displayed on CT; (**b**) cardiac MRI plain scan (black-blood technique) clearly showed diffuse pericardial thickening (arrow), and stripe-like hyperintensities on both sides of thickened pericardium were adjacent fat; and (**c**, **d**) MRI enhanced scan clearly showed thickened and significantly enhanced visceral and parietal pericardium (arrow), and no enhanced pericardial effusion (*)

2. Constrictive Pericarditis
   (a) Echocardiography: Typical echocardiographic manifestations of constrictive pericarditis include pericardial thickening, especially atrioventricular ring, sometimes showing calcification. Abnormal ventricular septal motion can be found. Both atria are enlarged, and ventricles are relatively shrunk. Superior vena cava and inferior vena cava are dilated.
   (b) X-ray: Constrictive pericarditis is manifested as enlarged cardiac shadow, especially enlarged left atrium (due to the existence of pericardial bare area in left atrium). Pericardial calcification can range from none to extensive, and the predilection sites are the anterior edge of right ventricle and diaphragm. Extensive pericardial calcification is the characteristic change of constrictive pericarditis (Fig. 33.3). Pericardial calcification can also be manifested as rigidity of heart edge, dilatation of superior vena cava, and bulging of pulmonary artery.

CT: The direct sign of constrictive pericarditis is pericardial thickening, sometimes accompanied by calcification. The indirect signs include normal or shrunk ventricles, limited ventricular diastole, and mild atrial enlargement (Fig. 33.3).

(c) MRI: It can accurately show pericardial thickening, but insensitive to pericardial calcification. Gadolinium contrast-enhanced MR showed delayed enhancement of the pericardium of constrictive pericarditis, indicating fibroblast proliferation, chronic inflammation, and neovascularization, identifying local active inflammatory reaction. If not showing delayed enhancement, it indicates more fibrosis and calcification locally, which may be helpful for the choice of drug treatment (Fig. 33.4). MRI is of high value in evaluating atrioventricular morphology, systolic, and diastolic function of the heart. MRI can also show the hemodynamic characteristics of constrictive pericarditis.

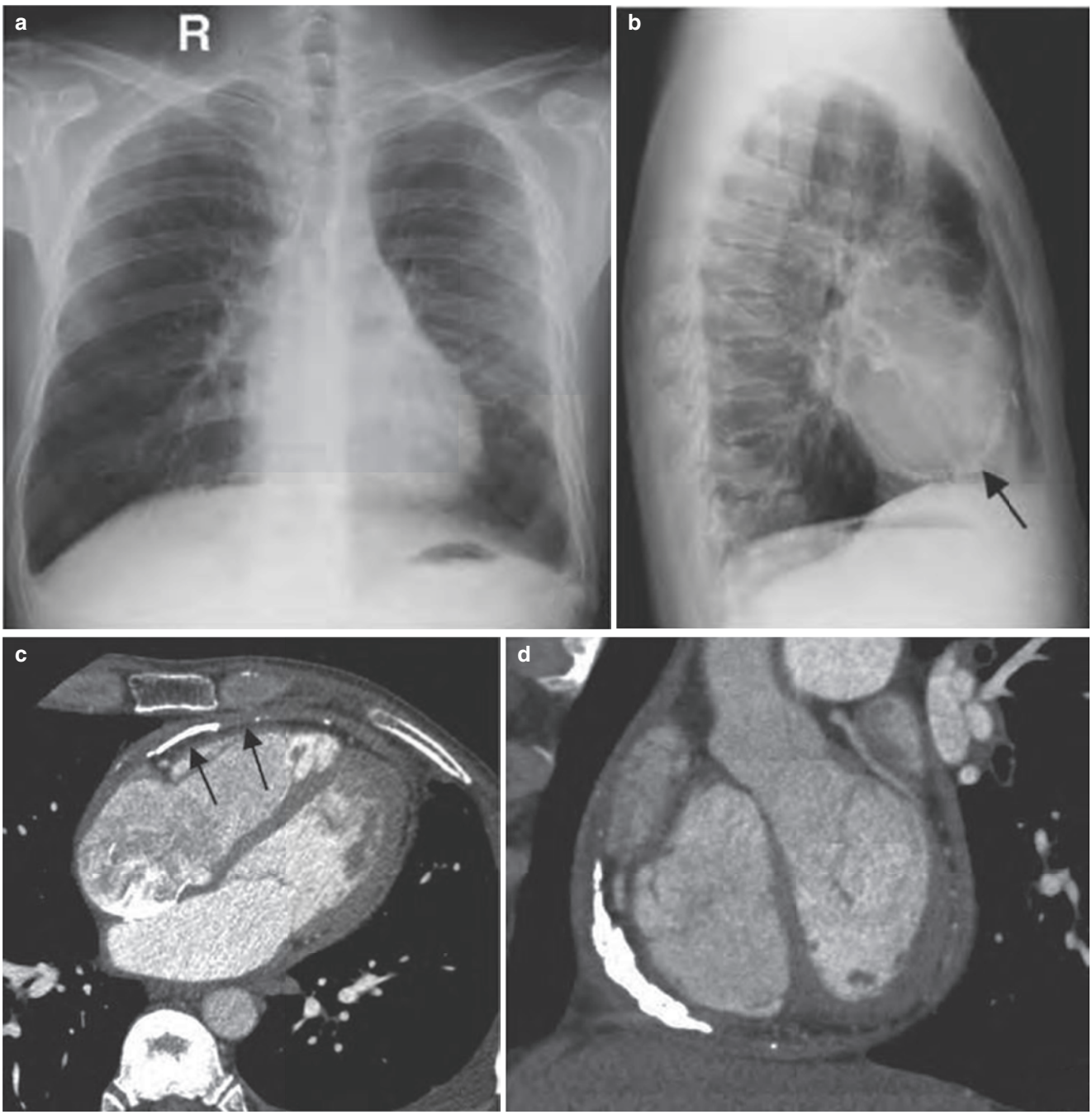

Fig. 33.3 Constrictive pericarditis (I). (**a**, **b**) Chest radiograph showed diffuse pericardial thickening (arrow) and (**c**, **d**) CT enhanced scan of the heart showed thickened pericardium with stripe-like calcification (arrow) and slightly enlarged right atrium

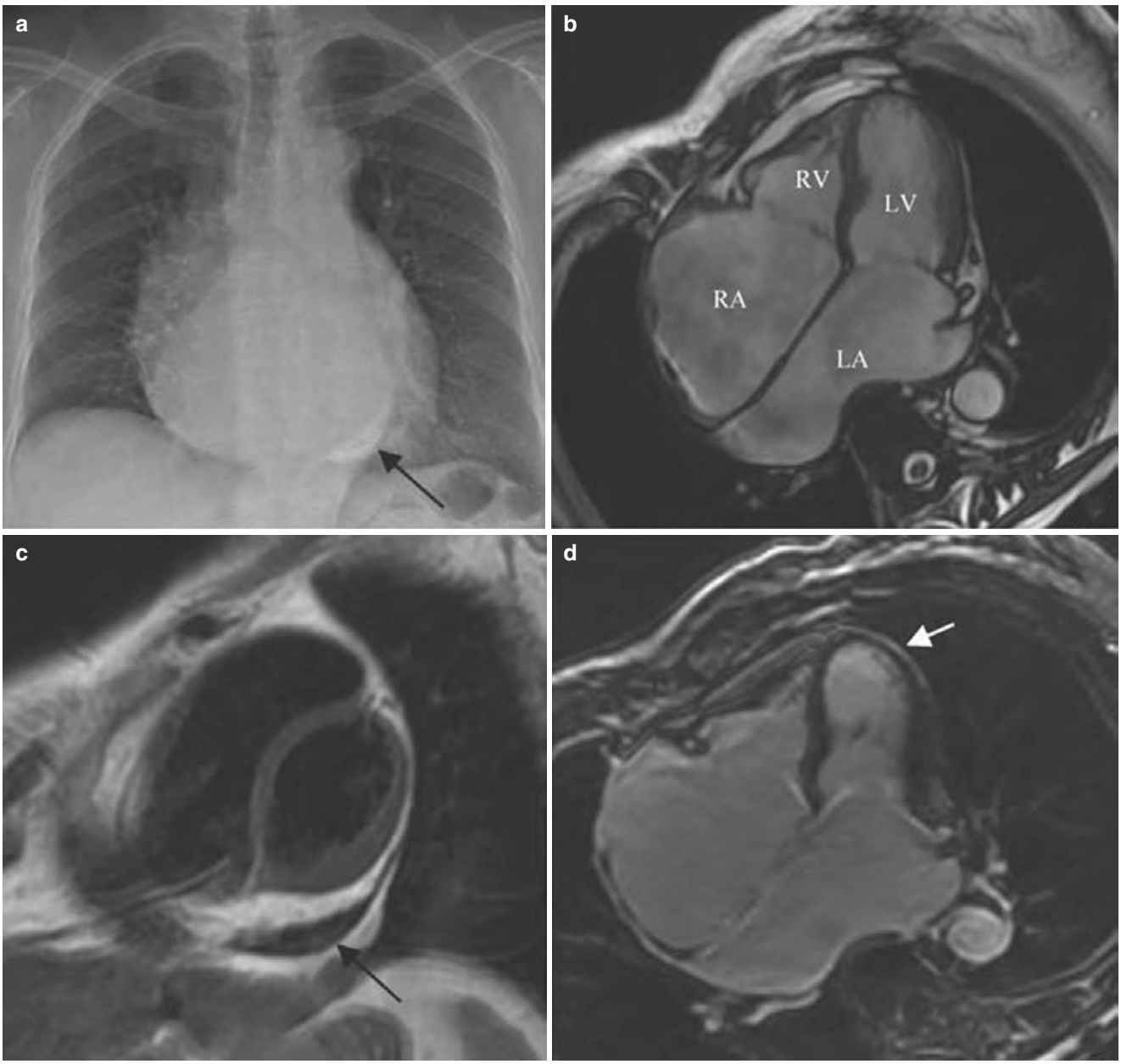

Fig. 33.4 Constrictive pericarditis (II). (**a**) Chest X-ray showed arcuate calcification of the lower edge of pericardium (arrow); (**b**) cardiac MRI cine sequence showed that left and right ventricles (LV, RV) were limited in diastole and reduced in volume, and left and right atria (LA, RA) were significantly dilated; (**c**) black-blood sequence showed uneven thickening of pericardium and arcuate hypointensity calcification of lower edge (arrow); and (**d**) gadolinium contrast agent T_1WI delayed enhancement showed the delayed enhancement locally in pericardium (arrow)

33.4 Diagnostic Key Points

1. Acute pericarditis
   (a) Echocardiography: It is the most commonly used imaging examination method for acute pericarditis.
   (b) CT examination: For pericardial thickening and pericardial effusion, pericardial thickness >3 mm is the diagnostic criterion for pericardial thickening.
   (c) MRI examination: Pericardial thickening (≥4 mm) and pericardial edema. After intravenous injection of gadolinium contrast agent, pericardial-delayed enhancement can be found. Pericardial effusion.
2. Constrictive pericarditis
   (a) Echocardiographic examination: Pericardial thickening, often with calcification and abnormal ventricular septal motion. Both atria are enlarged, and ventricles

are relatively shrunk. Superior vena cava and inferior vena cava are dilated.

(b) X-ray examination: Cardiac shadow is enlarged, especially the left atrium. Calcification of pericardium, stiffness of heart edge, dilatation of superior vena cava, and bulging of pulmonary artery.

(c) CT examination: Pericardial thickening, sometimes accompanied by calcification. Ventricles are normal or shrunk, ventricular diastole is limited, and atrium is slightly enlarged.

(d) MRI examination: Pericardial thickening, but MRI is not sensitive to pericardial calcification. Gadolinium contrast agent-enhanced MRI shows pericardium-delayed enhancement, indicating local active inflammatory reaction.

33.5 Differential Diagnosis

1. Noninfectious pericarditis: The differential diagnosis of tuberculous pericarditis includes pericarditis caused by other infectious causes (such as viruses, bacteria, and fungal pathogens) and noninfectious causes (including sarcoidosis, malignant tumor, radiation injury, trauma, and pericardial hematocele).
2. Restrictive cardiomyopathy is a kind of nonischemic cardiomyopathy characterized by the filling of bilateral ventricles or unilateral ventricle and diastolic restriction, while the ventricular wall thickness and systolic function are normal or slightly damaged. It needs to be distinguished from constrictive pericarditis, and the distinguishing point is mainly whether pericardium is thickened because constrictive pericarditis is often accompanied by obvious pericardial thickening.

33.6 Research Status and Progress

Multimodal imaging diagnosis mode is very important for the diagnosis, follow-up visit, and treatment of pericarditis. At present, multimodal imaging mainly includes echocardiography, cardiac magnetic resonance, and CT. Echocardiography is the preferred imaging method for acute pericarditis, which is helpful for the diagnosis and differential diagnosis of acute pericarditis. More importantly, it can find adverse consequences such as cardiac tamponade, myocarditis, and pericardial constriction. Clinically, most patients with acute pericarditis have a good prognosis, while a few may develop into chronic or recurrent pericarditis. Such patients may benefit from further imaging examination. Cardiac magnetic resonance imaging can better evaluate the stage and severity of pericarditis, which is helpful for better guiding the treatment of patients with complex pericarditis. If pericardial gadolinium contrast agent can show delayed enhancement of recurrent pericarditis, it suggests that anti-inflammatory treatment needs to be strengthened or anti-inflammatory treatment needs to be prolonged in clinical practice. If without delayed enhancement by gadolinium contrast agent, it suggests that anti-inflammatory treatment can be reduced or stopped [5]. Cardiac magnetic resonance is also helpful for the management of patients of constrictive pericarditis. If gadolinium contrast agent enhancement shows delayed enhancement in pericardium, it indicates that there is active inflammation in pericardium. After anti-inflammatory treatment, inflammation subsides and pericardial constriction may be reversible. On the contrary, if without delayed pericardial enhancement in patients of constrictive pericarditis, it suggests that anti-inflammatory treatment may not be effective and may require surgical treatment [6, 7]. Before surgical treatment of patients of constrictive pericarditis in the end stage, CT examination is helpful for evaluating the degree of pericardial thickening and calcification, and making surgical plans before pericardiectomy.

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