Infection: Pericarditis

6

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6.1 Pericardial Anatomy

The normal pericardium consists of two principal layers: an outer fibrous layer made up of collagen and to a lesser extent elastin and an inner serous layer of ciliated mesothelium that covers the myocardium and great vessels (visceral pericardium) and reflects back to form the serous inner surface of the fibrous layer (parietal pericardium) [1, 2]. The tough outer sac functions as a barrier to infection, prevents excessive cardiac motion, and helps to maintain interventricular dependence by

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F. Caobelli (ed.), *Imaging of Inflammation and Infection in Cardiovascular Diseases*, https://doi.org/10.1007/978-3-030-81131-0_6

limiting cardiac distension (Fig. 6.1). Histologically, the pericardium is typically 1 mm thick and therefore approaches the limits of the spatial resolution of cardiac imaging techniques. The parietal pericardium is often apposed with a variable amount of epicardial fat which serendipitously provides intrinsic contrast on cardiovascular magnetic resonance imaging (CMR, Fig. 6.2). However, the relative absence of epicardial fat over the lateral wall of the left ventricle in some individuals can make it challenging to differentiate the pericardium from surrounding lung tissue. The fibrous pericardium itself is attached to the sternum anteriorly, the diaphragm inferiorly, and to the thoracic vertebrae posteriorly by the pericardial ligaments. Superiorly, it extends to the proximal aortic arch just prior to the origin of the innominate, and to the level of the pulmonary artery bifurcation [1]. The

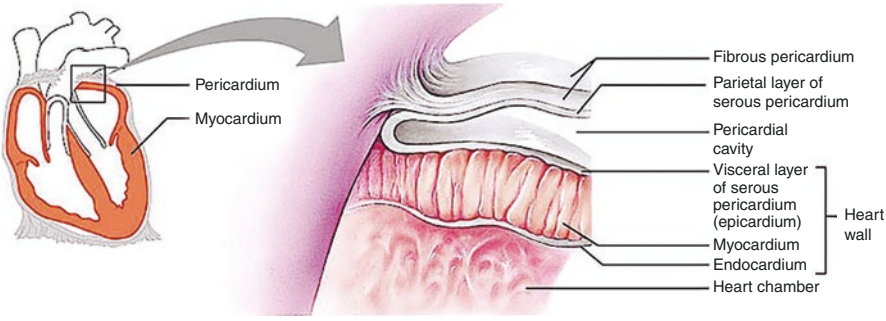


Fig. 6.1 The pericardial layers and layers of the heart wall. Note that the visceral layer of the pericardium and the epicardium of the heart are the same structure. From: Pearson Education 2013, Chapter 18, The cardiovascular system: The heart: Part A

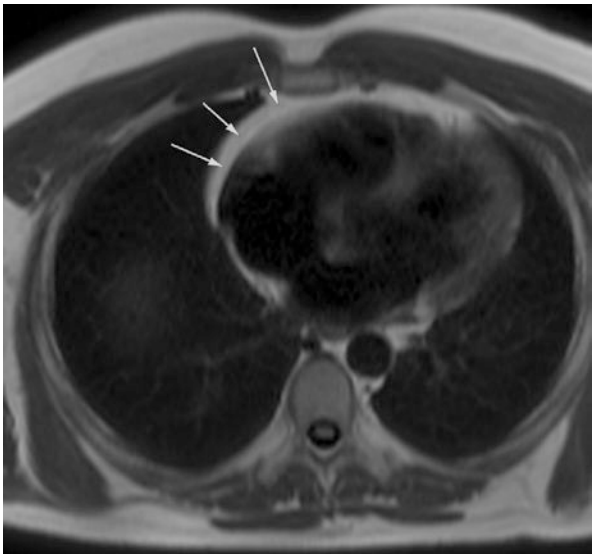


Fig. 6.2 Axial Half-Fourier Acquisition Single-Shot Turbo Spin Echo (HASTE) commonly used as a pilot scout. The pericardium is a thin often barely perceptible structure (white arrows) best seen anteriorly where the contrast with RV epicardial fat can help render it visible. Over the lateral wall where there is a relative paucity of fat, and the pericardium is related to lung tissue, it can be challenging to discern

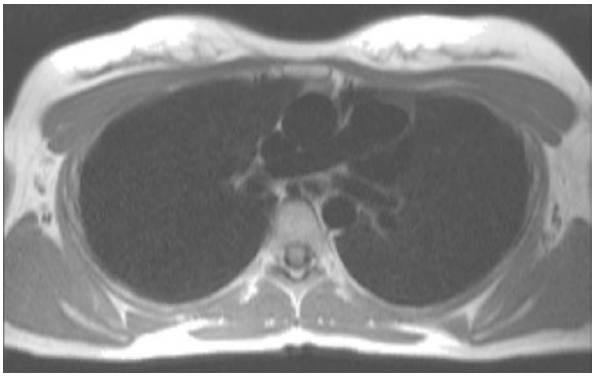


Fig. 6.3 Lung parenchyma interposed between the aorta and pulmonary trunk in a patient with congenital absence of the pericardium

presence of congenital absence of the pericardium can therefore be inferred by interposition of a tongue of lung parenchyma between the ascending aorta and the main pulmonary artery (which would normally be excluded by intact pericardium) or lung tissue between the inferior surface of the heart and the diaphragm [3] (Fig. 6.3). The inner serous layer is too thin to directly image in health. Its ciliated surface facilitates the synthesis and resorption of pericardial fluid which is a dynamic process and physiologically can reach up to 50 ml in volume. The fluid serves to reduce friction between the myocardium and surrounding structures. It tends to congregate around the atrioventricular grooves hinting at its role in lubricating the motion of the coronary arteries. In most patients who are imaged supine, it is not usually possible to see a complete layer of fluid surrounding the whole myocardium unless an effusion is present.

6.2 Pericardial Pathologies

Pericardial abnormalities include several pathological conditions (pericardial effusion, pericardial constriction, tamponade, pneumopericardium, fistulas, pericardial rupture, congenital abnormalities, pericardial tumours) but inflammation of pericardial layers is the most frequent disease of the pericardium worldwide. It often occurs in young and middle-aged subjects. Exact epidemiological data for acute pericarditis are lacking. In Italy, an incidence of about 28 cases/100,000/year has been reported [4]. In a Finnish national registry, the rate of hospitalisation for acute pericarditis was 3.32 per 100,000 person/years, with men more affected than women [5]. Non-specific symptoms, which may overlap with other diseases such as myocarditis, acute coronary syndrome or Takotsubo syndrome, may complicate the diagnosis of pericarditis. In the emergency department, pericarditis is diagnosed in about 5% of patients with non-ischaemic chest pain and the in-hospital mortality is relatively low (about 1.1%) [6, 7]. This could produce the misconception that pericarditis is a benign disease with low morbidity and mortality. However, the exact incidence of pericarditis is probably underestimated and if not diagnosed and properly treated, the disease tends to recur, it can become chronic and it can entail

serious complications. A recent database analysis in the USA (years 2016 and 2017), including 21,335 patients hospitalised for acute pericarditis, found a rate of 30-day readmission of 12.9% [8]. In-hospital mortality was significantly higher following readmission than for the index hospitalisation (3.4% vs 1.0%, $p < 0.001$). Therefore, a high level of clinical suspicion and multimodal imaging is crucial for the prompt identification of the disease and the correct management of the patient to minimise possible complications and to ameliorate the patient's outcome.

6.3 Aetiology and Pathophysiology

Inflammation of pericardial layers can have both an infectious and non-infectious aetiology. In developed countries, most cases (80–90%) are labelled as "idiopathic" and probably have a viral origin [6, 7]. Other relatively frequent infectious aetiologies are tuberculous pericarditis (about 4%) and purulent pericarditis (<1%). Non-infectious pericarditis can occur in primary or secondary metastatic tumours (5–10%), in systemic inflammatory diseases, and pericardial injury syndromes (2–7%) [9–11]. In a recent prospective cohort of 1162 patients, Gouriet et al. found a lower incidence of idiopathic cases (55%) and a higher number of autoimmune or post-cardiac injury syndromes (24%) [12]. It is likely that, in developed countries, ageing of the population increases cardiovascular invasive procedures and the risk of pericardial complications. Conversely, in developing countries the most frequent cause of pericarditis is tuberculosis (70%), often associated with human immunodeficiency virus and poor outcome (40% mortality) [13]. Common causes of acute pericarditis are summarised in Table 6.1.

Inflammation of pericardium may be an acute, subacute, or chronic fibrinous, "non-effusive" or exudative process that reflects the aetiology of the disease [14]. With infectious aetiologies, the response to injury is the exudation of fluid, fibrin, and inflammatory cells. Healing can lead to an obliteration of the pericardial space by adhesions between the pericardial layers and, sometimes, late focal or extensive calcification. Following acute coronary syndrome, trauma or pericardiotomy, a post-cardiac injury syndrome can occur. The damage of the pericardial layers is thought to release cardiac antigens that stimulate an immune response and sustain the inflammatory process.

When the amount of fluid in the pericardial space exceeds the normal 15–50 ml, a pericardial effusion is present. The amount and the rate of accumulation of pericardial effusion, the thickness and compliance of pericardium, and the coexistence of heart diseases influence the clinical presentation of the disease. Cardiac tamponade is a serious complication in which the pericardial effusion increases pericardial pressure and determines a compression of the cardiac chambers. Haemodynamic consequences are reduced cardiac filling, an exaggerated expiratory decrease in aortic systolic pressure (*pulsus paradoxus*) and arterial hypotension. Acute tamponade is sudden and life-threatening, and it requires a prompt diagnosis because pericardiocentesis may be life-saving. Persistence of pericarditis or recurrence of the disease, cardiac surgery or radiation therapy can result in a constrictive pericarditis.

Table 6.1 Aetiology of pericarditis

Infectious pericarditis	Prevalence	Non-infectious pericarditis	Prevalence
Viral (coxsackievirus; echovirus; influenza; Epstein-Barr virus; cytomegalovirus; parvovirus B19; human herpes virus 6; varicella; rubella; adenovirus; human immunodeficiency virus; hepatitis B, C viruses, COVID19)	Common in developed countries (80–90% labelled as "idiopathic" and probably of viral origin	*Autoimmune* (post-myocardial infarction; post-pericardiotomy; posttraumatic; in systemic autoimmune diseases: Systemic sclerosis; lupus; vasculitis)	Relatively frequent (range 10–24%)
Bacterial (tuberculous; pneumococci; meningococci; *Coxiella burnetii*; *Haemophilus*; *chlamydia*; *mycoplasma*; staphylococci)	Frequent in developing countries (tuberculosis 70%), uncommon or rare in developed regions	*Neoplastic* (primary tumour: mesothelioma; metastatic tumours: lung cancer, breast cancer; lymphoma)	Relatively rare (5–10%)
Fungal and parasitic (histoplasmosis; candida; aspergillosis; echinococcus; toxoplasma)	Rare, more likely in immunosuppressed patients	*Metabolic* (myxoedema; uraemia)	Rare

Table 6.2 Aetiology of constrictive pericarditis and associated clinical features

Aetiology	Clinical features/diagnostic clues
Idiopathic	Absence of other positive features/findings, i.e., a diagnosis of exclusion
Tuberculosis	Cavitating lung lesions, pulmonary consolidation
Purulent bacterial pericarditis	Associated pulmonary consolidation, history of instrumentation/surgery/trauma
Surgery	Sternotomy wires or other features of cardiothoracic or other surgical intervention
Trauma	Bony injury, haemopericardium
Radiation	Features of radiation-associated RV disease or coronary disease
Neoplastic	Signs of underlying neoplasm, e.g., metastases, tumour deposits, pleural effusions
Autoimmune rheumatic disease	Multi-organ involvement, signs of associated myocarditis
Sarcoid	Mediastinal lymphadenopathy, pulmonary fibrosis, myocardial involvement (see Chap. 5)
Asbestosis	Pleural thickening, round atelectasis, mesothelioma, bronchogenic carcinoma, interstitial fibrosis

This is a condition in which a thickened-inelastic, inflamed, fibrotic and/or calcified pericardium limits cardiac diastolic filling, reduces ventricular volumes and stroke volumes. Table 6.2 summarises common causes of constrictive pericarditis and associated clinical features.

6.4 Clinical Manifestations and Diagnosis

Some red flags leading to clinical suspicion of inflammation of the pericardial layers include chest pain, pericardial friction rubs, electrocardiographic changes, and new or worsening of pericardial effusion.

The chest pain of acute pericarditis is sudden in onset, retrosternal, it changes with the position of the patient (improved by sitting up and leaning forward) and can be exacerbated by inspiration (pleuritic). Sometimes dull and oppressive, radiating to the neck, arms and shoulders, it mimics an acute coronary syndrome and patients may even be submitted to urgent coronary angiography [15]. An audible friction rub, reported in about one-third of cases and linked to increased friction of inflamed pericardial layers, is considered highly suggestive for pericarditis. Typical ECG changes in acute pericarditis include widespread upward concave ST-segment elevation and PR-segment depression and can evolve in four stages of abnormalities [16, 17]. Low QRS voltage and isolated ST-T abnormalities are common in constrictive pericarditis. In this case, peripheral oedema and exertional fatigue or dyspnoea are frequent and associated with an elevated jugular venous pressure.

Serological markers of inflammation confirm the presence of an active process but they provide little information on the aetiology. Considering the prevalence of "idiopathic" forms, viral cultures and antibody titres are often investigated but rarely useful [18]. For the same reason, routine serological tests for autoimmune disease are not recommended. Tuberculin skin test or QuantiFERON-TB assay needs to be assessed in the suspicion of tuberculous pericarditis, particularly in developing countries. Elevation of serum troponins raises the clinical suspicion of myopericarditis, and can be observed in about 20–30% of patients and is associated with a higher rate of complications [19].

Chest radiography has been used in the past but is often of limited value unless in the case of a massive pericardial effusion or if pericardial calcifications are present (25% of cases of constrictive pericarditis). However, a chest radiograph can detect concomitant lung, mediastinal, and pleural diseases of which pericarditis is a clinical manifestation (e.g., pulmonary tuberculosis, lung cancer). Transthoracic Doppler echocardiography is the first-line imaging modality because it is widely available and safe. Echocardiography allows the assessment of the presence and the amount of pericardial effusion, permits the identification of cardiac tamponade, can be used to guide pericardiocentesis and remains the method of choice for the follow-up of pericardial diseases [20]. An abnormal ventricular septal motion to the left in early diastole, in inspiration, due to the enhanced ventricular interdependence (septal bounce) should alert the cardiologist to consider the diagnosis of constriction. Other echocardiographic findings include normal ventricular systolic function and thickened pericardium, and vena cava dilatation with little respiratory variation (suggestive of elevated right atrial pressures).

Fever at presentation, leucocytosis, a subacute course, important pericardial effusion and lack of response to initial therapy are considered markers of adverse prognosis and identify patients that may need hospitalisation [21].

Table 6.3 Diagnostic criteria for pericarditis (modified from reference 22)

Pericarditis	Diagnostic criteria
Acute	Pericardial inflammation with at least 2 of the following criteria: 1. Chest pain (sudden in onset, changes with the position, exacerbated by inspiration). 2. Audible friction rub. 3. ECG changes (widespread upward concave ST-segment elevation, PR-segment depression) 4. New onset or worsening of pericardial effusion Additional criteria: a. Elevation of serological markers of inflammation b. Pericardial inflammation on CT and/or CMR
Incessant	Persistent pericarditis for 2–4 weeks without remission (<3 months)
Recurrent	Recurrence of the disease following an acute episode with a symptoms-free period >4–6 weeks
Chronic	Pericarditis lasting >3 months

The European Society of Cardiology (ESC) has established diagnostic criteria for the diagnosis of acute and recurrent pericarditis (level of evidence C) [22] (Table 6.3). Diagnosis of acute pericarditis requires the presence of at least two clinical criteria among chest pain, pericardial friction rubs, electrocardiographic changes and pericardial effusion. Diagnosis of recurrent pericarditis needs the presence of a documented first attack of acute pericarditis, a symptom-free interval of 4–6 weeks or longer, recurrent pain combined with other symptoms and serological findings. Evidence of inflammation of the pericardial layers by an imaging technique is considered as an additional supportive criterion. However, contemporary diagnosis and patient management cannot ignore a multimodal imaging approach, including second-level imaging techniques such as computed tomography, cardiovascular magnetic resonance and molecular imaging.

6.5 Computed Tomography

Cardiac CT is increasingly used in clinical practice, mainly to study coronary arteries but it is able to provide morphological information about all cardiac structures. Baseline non-contrast and contrast-enhanced CT images permit the identification of thickened pericardium by an inflammatory process or tumours [23, 24], and the presence of calcification of pericardial layers. Although thickened pericardium can be observed in constrictive pericarditis, it does not prove the presence of constriction [25]. Conversely, a “normal” pericardium on CT images does not exclude the presence of constriction [26]. Moreover, inflamed pericardium may show contrast enhancement. CT is superior to echocardiography for the characterisation of pericardial effusion [27]. Generally, pericardial effusion has a low density (0–20 HU) but a high protein concentration, such as in infective aetiology or when the effusion is haemorrhagic, can increase density up to 50HU. These data can be used to speculate about the aetiology of the disease as serous fluid is more common in viral

pericarditis while tuberculous, neoplastic, and purulent pericarditis tend to produce more haemorrhagic exudates. CT can also reveal valuable ancillary findings, such as the presence of mediastinal lymphadenopathy, enlargement of the atria and venae cavae in cases of pericardial constriction, and can be used for disease staging where neoplasia is the culprit.

ESC guidelines do not recommend CT in acute pericarditis with small or no effusion, while in presence of moderate to severe effusion, the use of CT could be reasonable. In cardiac tamponade, CT imaging is considered reasonable to confirm the clinical suspicion of aortic dissection or to confirm diagnosis in case of thoracic trauma. In constrictive pericarditis, a CT scan is reasonable if echocardiography is inconclusive or to plan a pericardiotomy. CT imaging of the pericardium is not recommended in patients with severely decreased renal insufficiency (eGFR<30 ml/min/1.73 m^2) and during pregnancy [22].

6.6 Cardiovascular Magnetic Resonance (CMR)

6.6.1 Typical CMR Protocol for the Evaluation of Pericardial Disease

The full gamut of sequences available for modern CMR needs to be used to comprehensively evaluate pericardial disease and refine differential diagnosis [28]. These are summarised in Table 6.4. Pericardial thickness should be evaluated on breath-held T1-weighted turbo spin echo sequences as these afford excellent tissue contrast and are less liable to motion and susceptibility effects that can result in overestimation of pericardial thickness. These are best done in an axial configuration to maximally leverage the intrinsic contrast afforded by pericardial fat which usually overlies the bulk of the right ventricle (RV) even in slim individuals. Comprehensive bright and black blood scouts in axial, sagittal, and coronal orientations can be invaluable for detecting extracardiac pathology that may give clues to the aetiology of the underlying pericardial disease. T2-weighted spin echo sequences with fat saturation (achieved either through inversion recovery or spectral pre-saturation techniques) performed in long axis (2 chamber, 4 chamber, 3 chamber) and short-axis orientations can be helpful for delineating acute myocardial and pericardial inflammation which results in increased extracellular water and increased mobility of intracellular water in injured cells. Balanced steady-state-free-precession (SSFP) cine sequences are being used to evaluate cardiac function (Fig. 6.4) and may also be used to visualise the pericardium. Tagging sequences in 4 chamber and representative short-axis orientations can be helpful to identify pericardial adhesions or confirm appropriate slippage between the myocardium and the surrounding pericardium or other structures [29] (Fig. 6.5). Late gadolinium enhancement (LGE) imaging is then conducted in the normal way and can reveal the concomitant presence of myocarditis or contrast uptake by the inflamed pericardium. The normal pericardium does not avidly take up contrast, however, LGE sequences (which are inversion recovery prepared heavily T1-weighted sequences) can be complementary to

Table 6.4 Summary of CMR protocol for the Evaluation of pericardial disease

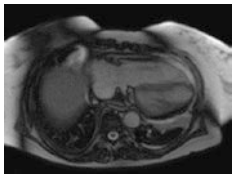
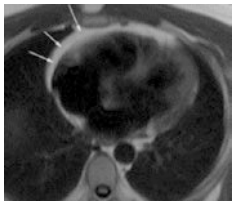
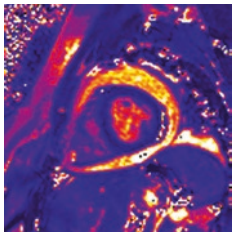
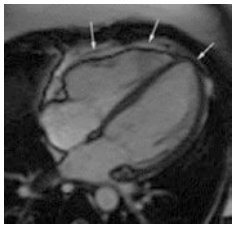
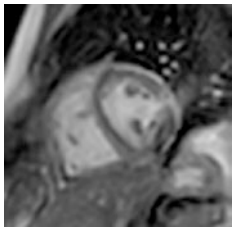
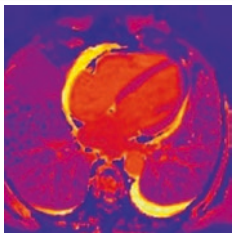
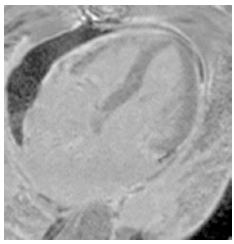
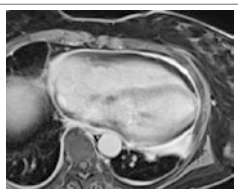
Sequence		Main findings
Scouts/localisers (*bright and black blood*)		Extracardiac findings • Pleural effusions, • Parenchymal lung abnormalities, • Lymphadenopathy
Axial T1-Turbo spin Echo (without fat saturation)		Morphological assessment • Pericardial thickness and effusion, • Pericardial lesions and tumours
T2w-imaging/T2 mapping		Oedema • Myocardial inflammation/oedema, • Pericardial inflammation/oedema
Balanced SSFP cine sequences		Haemodynamic assessment • Global and regional contractile dysfunction (concomitant myocarditis?) • Haemodynamic relevance of pericardial effusion (RV/RA collapse), loculation, fibrous stands in pericardial effusion, • Septal bounce (increased interventricular dependence)
Tagging		Constrictive pericarditis • Pericardial adhesions
Real-time cine imaging		Dynamic effects • Increased ventricular interdependence during deep inspiration

Table 6.4 (continued)

Sequence		Main findings
Native T1 mapping		Characterisation of pericardial effusion • Pericardial effusion vs. epi−/paracardial fat, • Transudative vs. exudative pericardial effusion vs. haemopericardium
LGE with PSIR reconstruction		Active pericardial inflammation • Pericardial inflammation and concomitant myocardial injury (myocarditis or infarction). • Confirm presence of pericardial effusions (black/signal poor on PSIR reconstructions)
ECG-gated Dixon fat-water separation sequences		Characterisation of pericardium • Pericardial thickness, • Pathological pericardial contrast uptake/ active inflammation

SSFP steady-state-free-precession, *LGE* late gadolinium enhancement, *PSIR* phase-sensitive inversion recovery

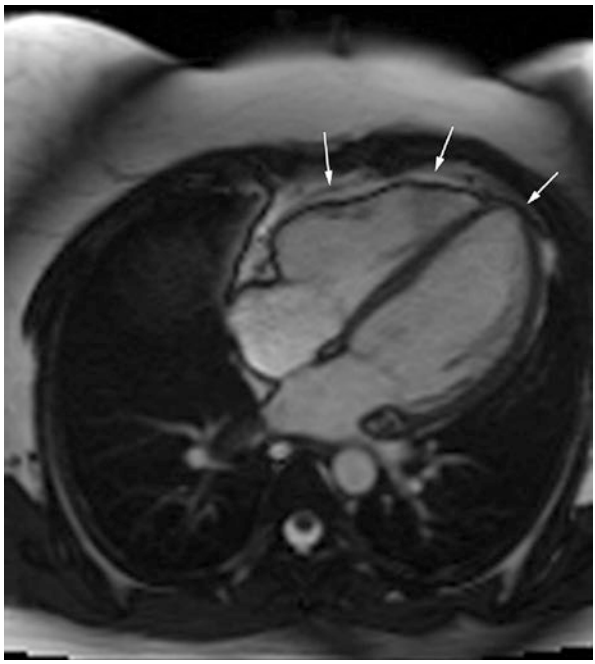


Fig. 6.4 Balanced steady-state free precession cine sequence in the horizontal long-axis orientation. This sequence has high intrinsic T1 and T2 contrast and is best used to evaluate cardiac function. The pericardium can be seen as a thin black line (arrows)

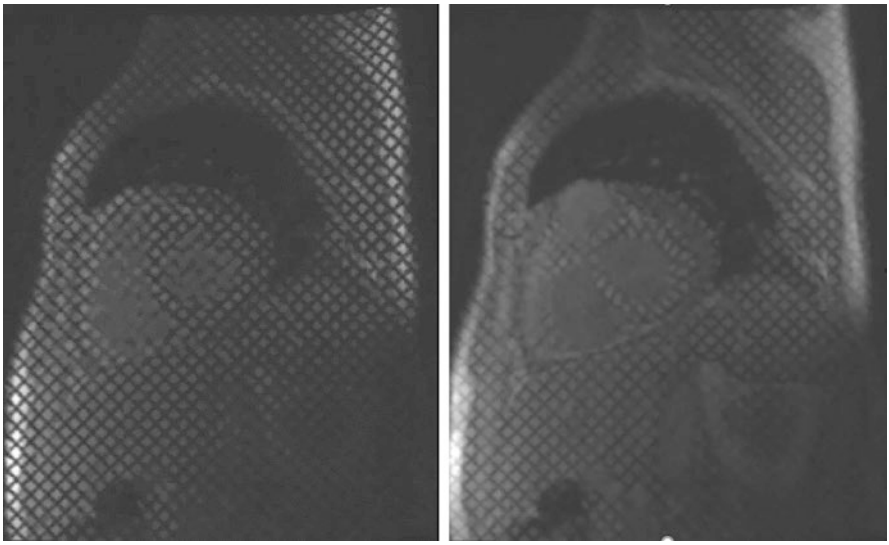


Fig. 6.5 Tagging sequence at mid-ventricular short-axis level demonstrating appropriate slippage between myocardium and surrounding pericardium

T1-TSE for evaluating pericardial anatomy (Fig. 6.6). ECG-gated Dixon fat-water separation sequences may be helpful for the assessment of pericardial thickness and confirm pericardial late enhancement of LGE sequences. Finally, real-time free breathing sequences (Fig. 6.7) are undertaken for assessment of pericardial constriction/constrictive pericarditis. Images are acquired over 10–20 s in a mid-ventricular short-axis orientation and/or 4-chamber orientation with the patient asked to take gentle breaths in and out [5, 6]. A breath hold should be avoided for this acquisition so as not to engender an inadvertent Valsalva manoeuvre that might confound the interpretation of septal motion.

6.6.2 CMR and Acute Pericarditis

Most cases of pericarditis are idiopathic and presumed viral in aetiology (see Table 6.1). Pericarditis can be categorised as acute (<4–6 weeks), incessant (>4–6 weeks), recurrent (with symptom-free interval of 4–6 weeks), or chronic (>3 months) [22, 30] (see Table 6.2). If required for diagnostic purposes, an effusion can usually be readily visualised by echocardiography. CMR or other advanced imaging is seldom required. However, CMR may play a role in the assessment of patients with "red flags" including a history of fever, trauma, a large effusion (>20 mm), history of systemic autoimmune disease, immunodeficiency or failure to respond to conventional anti-inflammatory therapy which usually consists of non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine. CMR should also be considered in any patient with signs of accompanying myocardial contractile

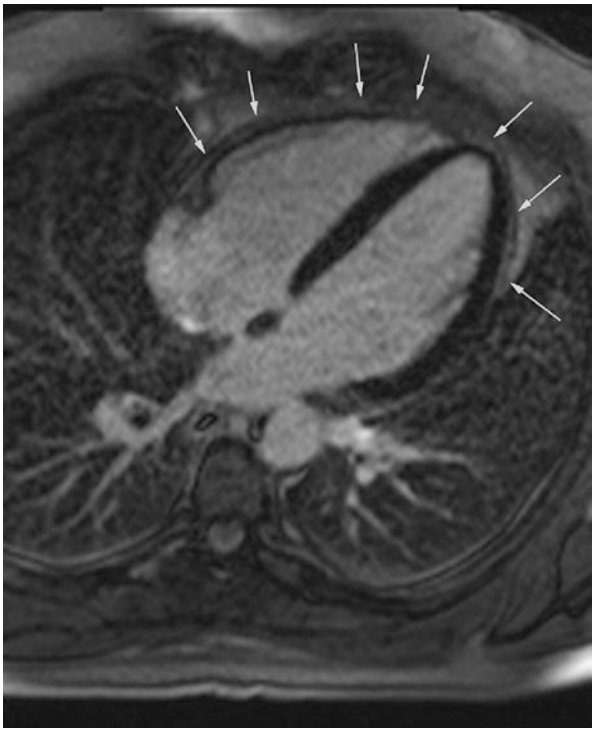


Fig. 6.6 Late gadolinium enhancement sequences are heavily T1 weighted and so can be used to evaluated pericardial anatomy. With normal inversion times set to null the myocardium, in the late phase, normal pericardium appears black (arrows)

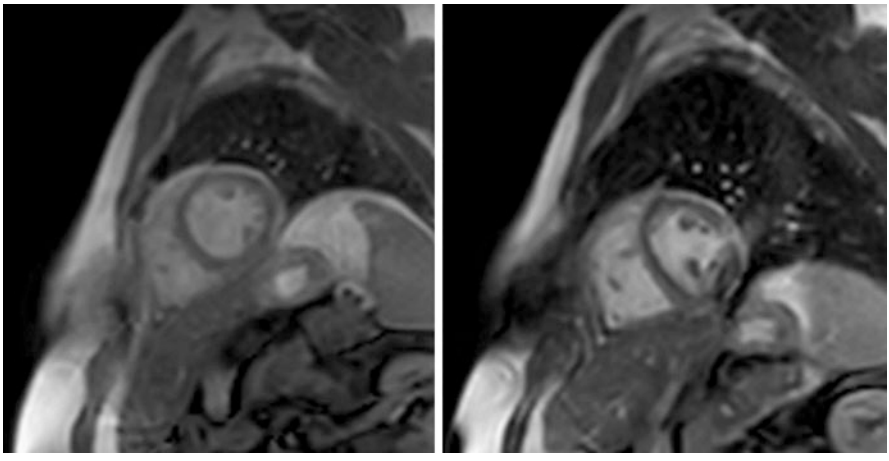


Fig. 6.7 Real-time free-breathing short-axis cine in a patient with pericardial constriction demonstrating increased interventricular interdependence. At end-expiration (left) the left ventricle is circular with the septum convex to the left. During inspiration (note the position of the dome of the diaphragm), as RV filling increases, and LV filling falls, the interventricular septum is displaced towards the left

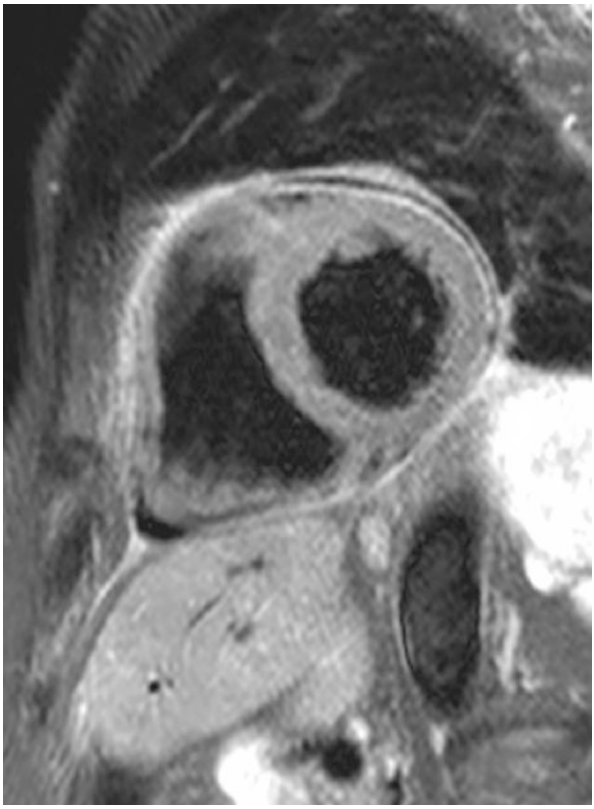


Fig. 6.8 Mid-ventricular short-axis T2-Weighted spin echo sequence in a patient with acute pericarditis. There is hyperintensity of the visceral and parietal pericardium reflecting pericardial inflammation and increased interstitial water content

dysfunction or biochemical evidence of necrosis which may point to the presence of a limited amount of myocarditis (myopericarditis) or to myocarditis being the dominant pathology (peri-myocarditis) [25] (see also Chap. 7/Myocarditis).

The acutely inflamed pericardium may be thickened. There may be an associated exudative effusion; however, the absence of this does not exclude active pericarditis as particularly in the early phases, the amount of fluid production can be balanced by resorption resulting in little or no new fluid accumulation. The pericardium may be high signal on T2W spin echo sequences, whereas healthy pericardium is not normally clearly seen (Figs. 6.8 and 6.9). Late enhancement sequences may reveal contrast uptake by the pericardium as inflammation causes expansion of the pericardial interstitium (Fig. 6.10). The pericardium is normally relatively avascular and does not readily enhance in the late phase with conventionally chosen inversion times. Although enhancement can signify inflammation [31], it can sometimes persist even after acute inflammation has settled owing to neovascularisation of the pericardium itself in response to chronic inflammation. This may suggest potential responsiveness to anti-inflammatory interventions to prevent the emergence of constriction [32]. Observational data has also suggested that CMR may be useful to

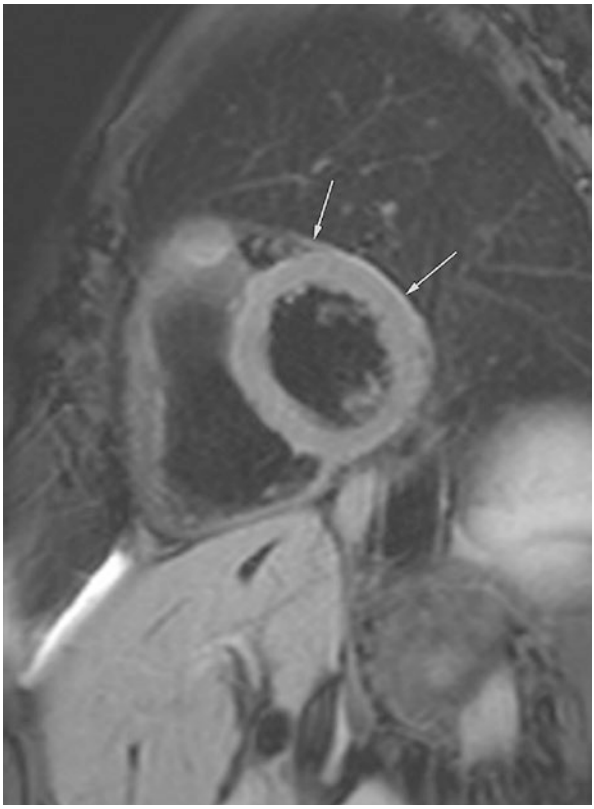


Fig. 6.9 Mid-ventricular short-axis T2-Weighted short-tau inversion recovery sequence in a patient with recovering pericarditis. The pericardium appears high signal (white arrows)

objectify response to therapy and guide the tapering of steroids in patients with recurrent pericarditis [33].

6.6.3 CMR and Pericardial Effusions

A pericardial effusion is the excess accumulation of fluid in the pericardial space as a result of pericardial fluid production exceeding resorption or the addition of extrinsic fluid to the pericardial space. As with pleural effusions, the aetiologies can be classified under two principal umbrellas: transudative and exudative. In both the latter situations, the fluid originates from the serosal pericardial layers. Fluid can also enter the pericardial space from extrinsic sources, e.g., blood from trauma, aortic dissection, or surgery giving rise to a haemopericardium and chyle from injury to the thoracic duct giving rise to chylopericardium.

Transudates occur due to an alteration in the balance of hydrostatic forces most commonly through impaired venous drainage. Normal pericardial venous drainage occurs into the superior vena cava via the azygos system. As a result, chronic elevations of systemic venous pressure, e.g., chronic right heart failure, tricuspid regurgitation, pulmonary hypertension, can give rise to transudative effusions. Increased

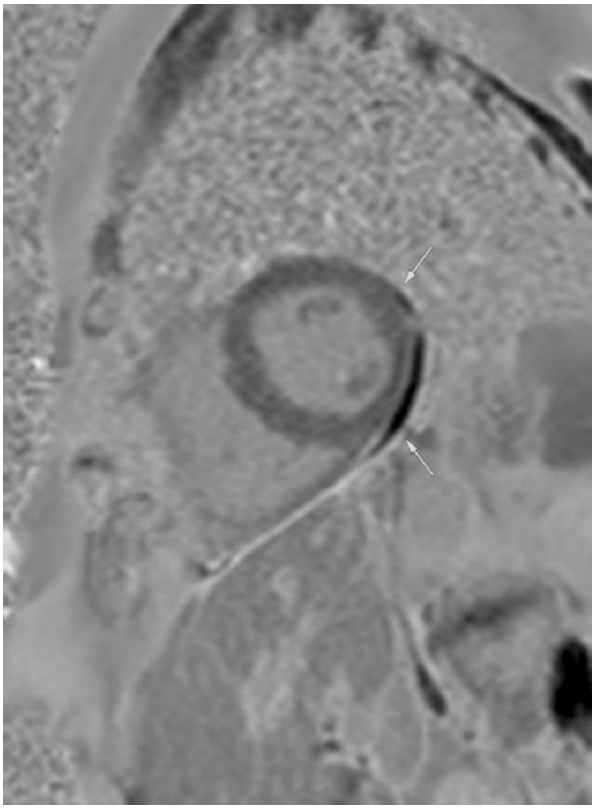


Fig. 6.10 Mid-ventricular short-axis late gadolinium enhancement sequence with phase-sensitive inversion recovery reconstruction in a patient with recovering pericarditis. The pericardium appears high signal/enhanced in contrast to the normal pericardium in Fig. 6.5. There is a thin rim of pericardial fluid next to the lateral wall which is black reflecting the comparatively long T1 of water

fluid shift can also occur in conditions such as nephrotic syndrome and in other states of systemic fluid overload. By definition, the protein content of transudates relative to their water content is low.

Exudates in contrast develop as a result of serosal pericardial inflammation or pericarditis and have a relatively high protein content. Their differential diagnosis therefore closely reflects that of pericarditis.

Echocardiography remains the first modality of choice for the diagnosis and evaluation of pericardial effusions. Especially where there is a clinical concern about haemodynamic instability or potential cardiac tamponade, it is rarely advisable to transfer the patient to the confines of the MR-environment. However, outside of this scenario, CMR can add considerable value by allowing: (1) rapid evaluation of the presence, size, and location of effusions, particularly if loculation is present, thereby guiding drainage; (2) detecting concomitant pericarditis and/or myocardial injury (see section on Pericarditis above); and (3) where diagnostic pericardiocentesis is not planned, evaluation of effusion signal characteristics in the wider clinical context may help with classification of the effusion as an exudate or transudate.

The haemodynamic importance of a pericardial effusion is determined not only by its size/volume but by its rate of formation or accumulation. A small but rapidly

developing effusion gives little time for the pericardium to stretch and accommodate the additional fluid and so can produce more significant effects than larger effusions that develop more slowly. The grading of effusion size (measured in end-diastole on b-SSFP cine sequences) is therefore somewhat moot, but in general, effusions ≤1 cm are considered small, 1–2 cm moderate, and > 2 cm in depth large [34]. The usual approaches to percutaneous drainage are sub-xiphoid or transapical. A description of the depth of the effusion at these potential access sites can therefore be helpful to referrers. The presence of loculation and complex septation of the effusion may point towards the need for a surgical approach.

On balanced SSFP sequences which have strong T1 and T2 weighting, pericardial fluid is usually high signal. It can usually be readily differentiated from pericardial fat which is also high signal by its greater intensity and uniformity. Native T1 sequences are also very helpful to clearly distinguish fat from fluid. If doubt persists however, heavily T1-weighted sequences such as those acquired for LGE imaging can be helpful, particularly where a phase-sensitive inversion recovery reconstruction is used. With conventional inversion times (designed to null the myocardium), on the latter, fat appears bright/high signal, whereas fluid is near black or signal void owing to its long T1 (Fig. 6.10). Balanced SSFP cine sequences can be used to evaluate the impact of an effusion on right ventricular filling in diastole and to look for right atrial or RV outflow tract compression.

The signal characteristics of an effusion can be used to help classify it. Transudates have a high water content relative to protein and so appear high signal on T2-weighted sequences and low signal on T1-weighted imaging. The presence of an exudate can sometimes be inferred by fibrin strands seen oscillating over the surface of the visceral pericardium, and the presence of pericardial thickening, which is usually absent with transudative effusions, particularly if this is seen on T2-weighted sequences (Fig. 6.11). Exudates tend to have more heterogeneous signal characteristics and by

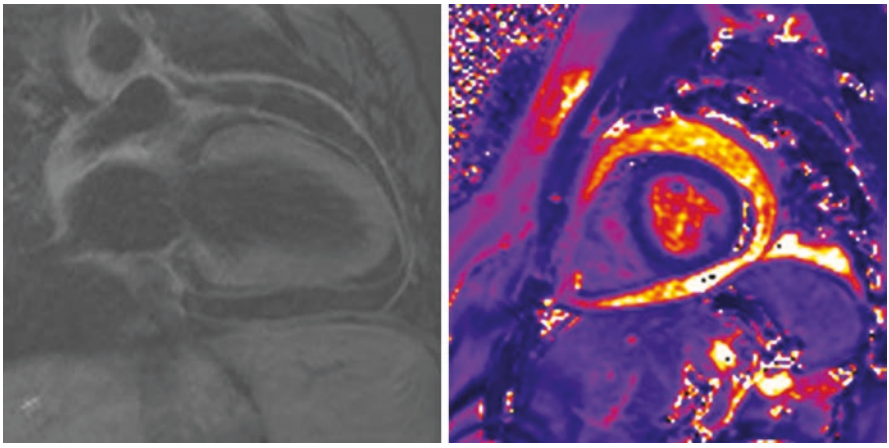


Fig. 6.11 T2W-short tau inversion recovery sequence (left) depicting pericardial high signal with an associated exudative global pericardial effusion. T2-maps (right) confirm pericardial inflammation and reveal heterogeneous T2 signal in the resulting pericardial effusion

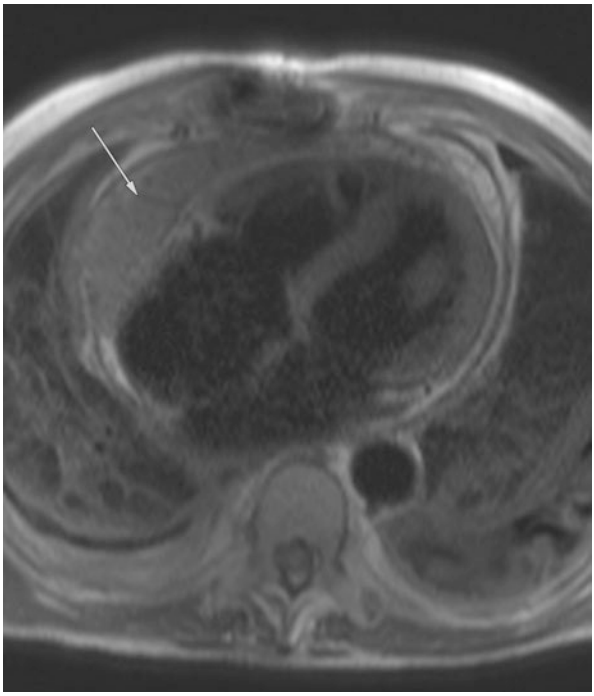


Fig. 6.12 Axial Half-Fourier Acquisition Single-Shot Turbo Spin Echo (HASTE) sequence in a patient post mitral and tricuspid valve repair. Note the susceptibility artefact from the sternotomy wires. The pericardium is markedly thickened. There is a collection overlying the right atrium and right ventricle which is of intermediate signal intensity suggesting a serosanguinous exudate (arrow). There are bilateral pleural effusions and signs of pulmonary congestion

virtue of their high protein content relative to water, appearing intermediate or lower signal on T1 and T2-weighted sequences (Figs. 6.12, 6.13, 6.14). Chylous effusions are rare but owing to their lipid rich content, tend to be high signal on T1-weighted sequences. Native T1 mapping techniques may become another straightforward approach to differentiate between transudative effusions (low in protein with very high native T1 values similar to cerebrospinal fluid), exudative effusions (elevated protein with native T1 values lower than CSF but higher than ventricular blood pool) and haemopericardium (native T1 values similar to ventricular blood pool).

6.6.4 CMR and Pericardial Constriction

This is an important and underdiagnosed complication of acute and chronic inflammatory pericardial syndromes. It occurs as a result of thickening and fibrosis of the visceral and/or parietal pericardium which often also undergoes dystrophic calcification but this can also occur without pericardial thickening [26]. These changes reduce the normal compliance of the pericardium, rendering it rigid and inelastic. This causes the pericardium to become a barrier to normal cardiac filling. Pericardial constriction should be considered in the differential diagnosis of any patient with signs and symptoms of heart failure but normal ejection fraction, particularly where right-sided features predominate. Suspicion should also be heightened in any patient

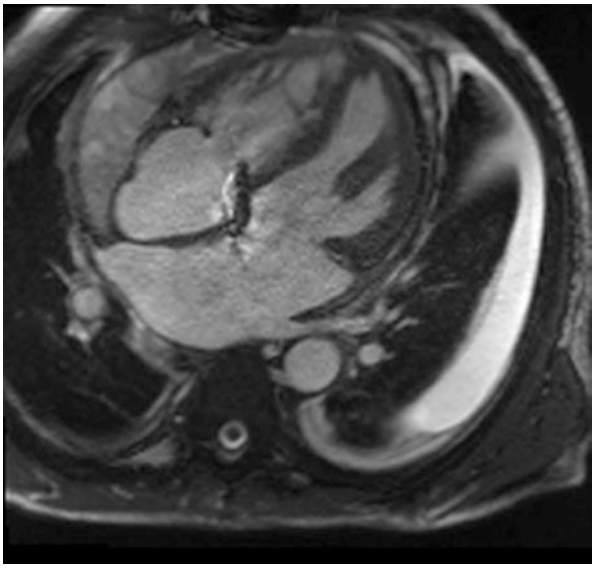


Fig. 6.13 Balanced steady-state free precession sequence in the four-chamber orientation for patient described in Fig. 6.12. Note the heterogeneous signal in the collection in contrast to the left pleural effusion which is brighter and more uniform in signal intensity suggesting a lower protein content

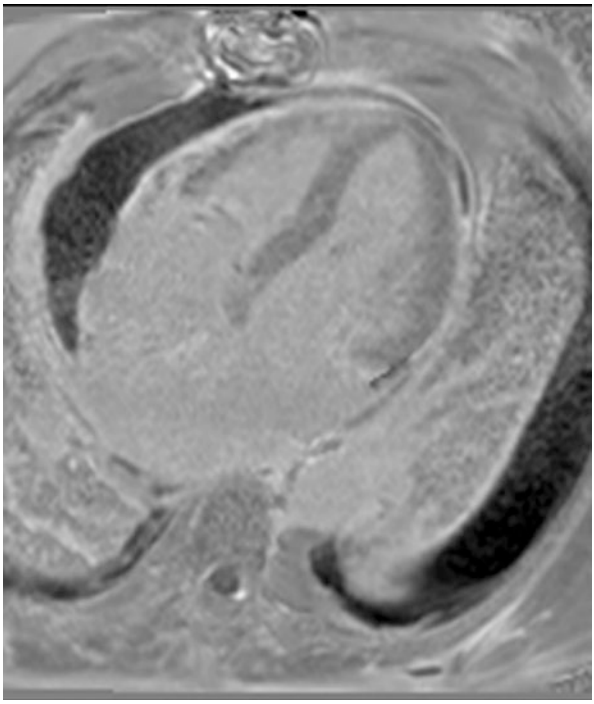


Fig. 6.14 Four chamber late gadolinium enhancement sequence with phase-sensitive inversion recovery reconstruction for patient in Fig. 6.12. The inflamed pericardium enhances with contrast and is high signal. The anterior pericardial collection is low signal but has a heterogeneous texture which is less evident in the more water rich left pleural effusion

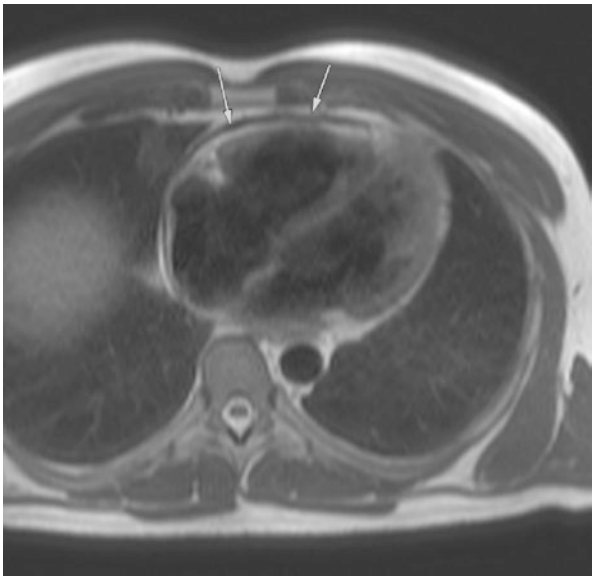


Fig. 6.15 Axial Half-Fourier Acquisition Single-Shot Turbo Spin Echo (HASTE) sequence in a patient with constrictive pericarditis. There is marked anterior pericardial thickening

with a history of previous cardiac surgery or previous pericarditis due to a predisposing condition. Viral myocarditis can be but seldom is complicated by constriction; however, suppurative processes such as tuberculosis and other purulent bacterial infections pose a particular risk [35].

CMR can play a valuable role in non-invasive diagnosis [36]. Scout sequences may reveal signs of chronically elevated right-sided filling pressures and congestion. The superior and inferior vena cava may be dilated, together with the hepatic tributaries of the latter. There may be evidence of ascites. The patient's resting heart rate may be increased to preserve cardiac output as a means of compensating for the limited stroke volume. In chronic constriction, the atria are often enlarged. T1W-spin echo sequences may reveal pericardial thickening (Figs. 6.15 and 6.16), which can be significant and accompanied by areas of signal void where dystrophic calcification has occurred. However, it is important to note that normal pericardial thickness does not exclude a diagnosis of constriction and when present, can also be very localised. Approximately 20% of patients with constriction have an apparently normal pericardial thickness of 2 mm or less and the problem appears to be simply increased stiffness [26]. This may reflect altered pericardial compliance in the setting of acute inflammation (potentially signifying transient constriction) [37] or simply that current imaging techniques lack sufficient spatial resolution to accurately measure true pericardial thickness which physiologically is ~1 mm rather than 2 mm, a 50% relative difference.

On occasions, fibrosis and calcification of the visceral pericardium can directly alter the geometry of the right ventricle hinting at the presence of constriction. Tagging sequences can be used to demonstrate a failure of relative slippage between the myocardium and the surrounding pericardium. On SSFP cine

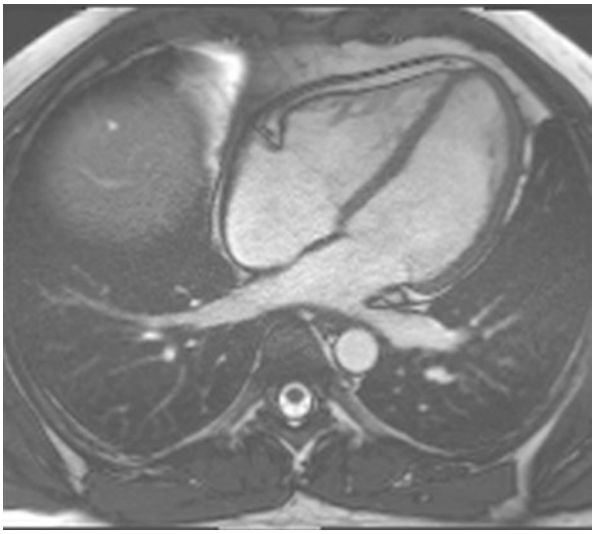


Fig. 6.16 Four chamber balanced steady-state free precession cine in a patient with pericardial constriction at early diastole. Note the increased pericardial thickness and the loss of the normal concavity of the LV septum in early diastole

sequence, biventricular size and systolic function are usually normal. In particular, RV long axis motion is either normal or increased, in contradistinction to the situation with primary restrictive cardiomyopathies which may mimic constriction clinically. Rarely, the two pathologies can coexist particularly where concurrent pericardial and right ventricular injury have occurred, e.g., radiotherapy-induced pericarditis and right ventricular injury. On occasions, it may be possible to see exaggerated early septal bounce which suggests increased interventricular dependence.

Under normal circumstances, the RV fills slightly earlier than the left ventricle (LV). As the RV blood volume increases during early diastole, the RV simply expands within the normally unrestricted pericardial space to readily accommodate the additional ingress of systemic venous return with no impact on LV filling. The septum may move at most slightly towards the left as the intracavitary pressure in the LV is usually close to that of the RV. However, with pericardial constriction, filling of the RV is limited by the rigid and non-compliant pericardium. Thus, as RV filling increases abruptly, the pressure transiently rises abruptly displacing the septum leftward (Fig. 6.16). As the LV eventually fills and intracavitary pressure increases, the septum is pushed back to its normal position giving rise to an exaggerated early septal bounce.

Increased ventricular interdependence can be demonstrated by observing septal motion usually in a basal or mid-ventricular short-axis view during free inspiration and expiration (Fig. 6.7) [38]. As the diaphragm descends, there is a fall in intrathoracic pressure which increases systemic venous return to the RV. At the same time, the fall in intrathoracic pressure commensurately reduces pulmonary venous return directly and by increasing pulmonary venous capacitance. Only a small portion of the pulmonary veins are within the pericardial sac, therefore the impact of the fall in intrapleural pressure on the pulmonary veins is significant. In the setting of constriction, this again forces the septum to displace towards the LV cavity as LV volumes

fall and RV pressures and volumes rise. Usually, two or three respiratory cycles are sufficient to demonstrate the phenomenon. Breath holds should be avoided as these may engender a Valsalva response if prolonged and performed at end-inspiration. Similarly, the phenomenon will not be seen in patients who are anaesthetised or receiving positive pressure ventilation as the latter increases rather than decreases intrapleural/intrathoracic pressure during inspiration.

Increased ventricular interdependence can also be seen in other settings where RV compliance is reduced directly, e.g., RV infarction, or indirectly through increased pericardial pressure, e.g., pericardial tamponade. However, these two circumstances are usually readily distinguished from constriction clinically by their acuity or from the history alone. Patients with suspected cardiac tamponade should not be subjected to CMR.

Late gadolinium enhancement imaging can play a valuable role in the evaluation of patients with suspected pericardial constriction. It may disclose the presence of myocardial disease, particularly in the setting of restrictive cardiomyopathy where imaging is being used to differentiate the latter from constriction. Where both pathologies are present, e.g., radiation-induced pericardial and RV disease, the presence of RV injury and fibrosis may highlight a subgroup of patients that may not respond to pericardial stripping surgery. Patients with increased signal on T2W-STIR sequences and prominent late enhancement may constitute an important subgroup that may potentially respond to anti-inflammatory treatments [32]. Similarly, simply the presence of pericardial late enhancement itself may signify the presence of neovascularisation of the pericardium and on-going organising pericarditis which may merit a trial of medical therapy targeting inflammation before considering pericardiectomy in patients who are symptomatic but not end-stage [39] (Fig. 6.17).

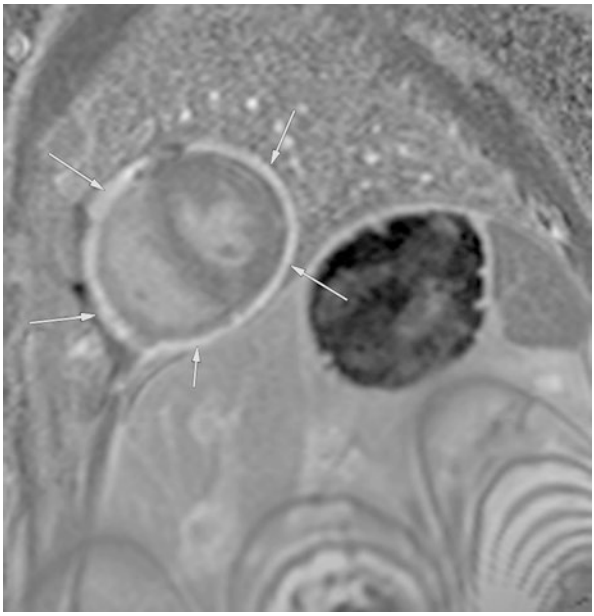


Fig. 6.17 Mid-ventricular short-axis late gadolinium enhancement sequence with phase-sensitive inversion recovery in a patient with pericardial constriction. Note the marked thickening and enhancement of the pericardium (arrows). This enhancement may highlight a subgroup of patients who may respond to medical therapy focussed on treating inflammation

CMR can therefore also be used to monitor response to such therapeutic trials [40], particularly where there is an underlying systemic autoimmune rheumatic disease (where alternative indications for immunosuppression may coexist) or there is clinical concern about concomitant myocardial involvement where again CMR may play a valuable role in diagnosing cardiac involvement and response to treatment.

6.6.5 Constrictive–Effusive Pericarditis

In this setting, there is the combined presence of features of pericardial constriction and a concomitant pericardial effusion [30]. The presentation can mimic cardiac tamponade, but usually atrial pressures remain elevated (assuming the absence of any primary RV failure) despite drainage of any associated effusion and the features of constriction persist post-drainage [41]. The phenomenon may represent an intermediate phase in the evolution of acute pericarditis to chronic constriction. In addition to identifying features of constriction, CMR can be of value in highlighting the presence of active/on-going inflammation (signified by increased pericardial signal on T2W-STIR imaging and enhancement in the late phase after gadolinium injection).

6.7 Molecular Imaging

Molecular imaging with 2-deoxy-2-[^{18}F]-fluoro-D-glucose (^{18}FDG) and positron emission tomography (PET) can study the entire heart revealing focal or diffuse patterns of inflammation and appears an appealing tool for the non-invasive diagnosis of the disease. Glucose is a normal metabolic substrate of myocardium and when the clinical question is the detection of an increased focal augmentation of myocardial glucose metabolism caused by an inflammatory process, the metabolic activity of the normal myocardium may disturb clinical interpretation of the images. Therefore, long fasting, a fatty meal or fractionated/unfractionated heparin administration before ^{18}FDG injection has been proposed to suppress physiological myocardial radiotracer uptake, a crucial requirement to identifying inflammation of the pericardial layers [42–44].

In infective pericarditis or myopericarditis, ^{18}FDG-PET/CT has been less used than echocardiography, cardiovascular magnetic resonance, or diagnostic CT (Figs. 6.18 and 6.19). Dong and colleagues studied 15 patients with acute tuberculous (n = 5) or idiopathic pericarditis (n = 10) [45]. Radiotracer uptake measured by using standardized uptake value (SUV) was more increased in both pericardium and mediastinal and supraclavicular lymph nodes affected by tuberculosis than in idiopathic lesions. Thus, the authors concluded that the degree of ^{18}FDG uptake is useful for differentiating acute tuberculous from idiopathic pericarditis. Moreover, ^{18}FDG PET can be more sensitive than CT in assessing lymph nodes involvement. Sathekge et al. reported a greater number of lymph nodes detected by dual phase ^{18}FDG-PET/CT than CT (18 sites vs 9) in nine patients affected by tuberculosis [46].

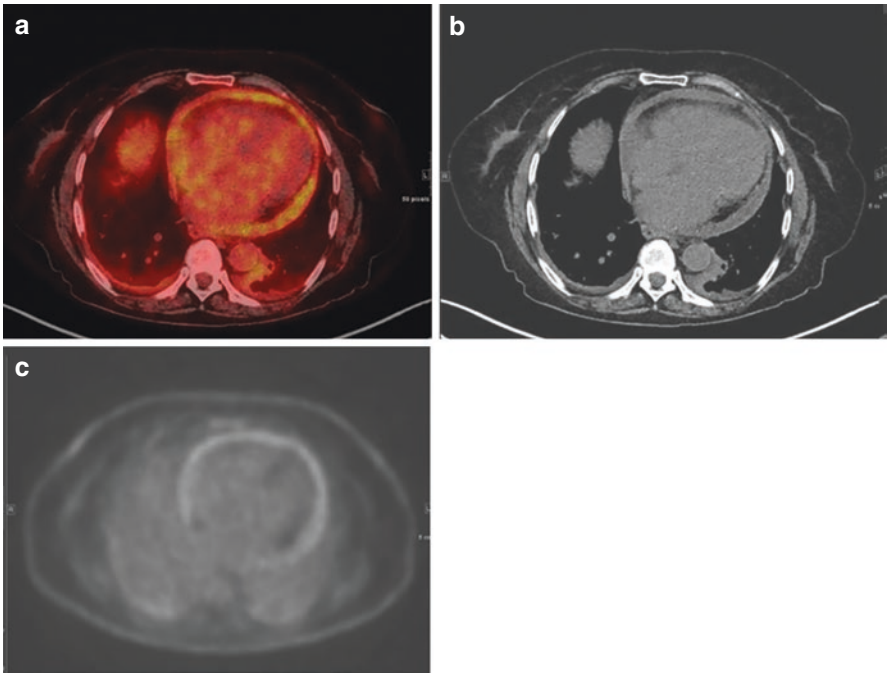


Fig. 6.18 Representative images of a 78 year-old woman diagnosed with pericarditis. Patient underwent a 72h dietary preparation prior to the investigation in order to suppress the physiological myocardial glucose metabolism. Fused PET/CT images (**a**) show a diffuse, moderately increased FDG uptake within the pericardium, corresponding to a moderate pericardial effusion as seen on CT images (**b**). The extent of the hypermetabolism, consistent with an infective pericarditis, is more evident on PET images (**c**), wherein the absence of myocardial uptake can be demonstrated, which can rule out a concomitant myocarditis

Recently, Chang et al. prospectively studied 16 patients with constrictive pericarditis [47]. ^{18}FDG-PET/CT was performed at enrolment and at follow-up (after 3 months of steroid therapy). Using a SUV_{max} cut-off value of 3.0, the sensitivity and specificity of ^{18}FDG-PET/CT for predicting responders were 100% and 71%, respectively. These data are encouraging, but further studies are needed to establish the clinical utility of the technique in this field. On the other hand, theoretically, and as for other malignant diseases, ^{18}FDG-PET/CT could be used for the diagnosis of primary and metastatic pericardial lesions and for disease staging. Pericardial effusion of neoplastic aetiology can be a manifestation of pericardial mesothelioma [48] or associated with breast cancer, lung cancer, Hodgkin's lymphoma, and sarcoma. Sarcoma and lymphoma also can present as constrictive pericarditis. In the presence of a pericardial effusion, a whole body ^{18}FDG-PET/CT scan could be helpful to find or exclude other malignant lesions, and to identify the origin of the neoplasm of which pericardial effusion is a primary or secondary manifestation (paraneoplastic syndrome). High accumulation of ^{18}FDG in mediastinal or other lymph nodes can be used to speculate about malignancy or infective disease [49] although differentiation between benign and malignant pericardial disease remains challenging.

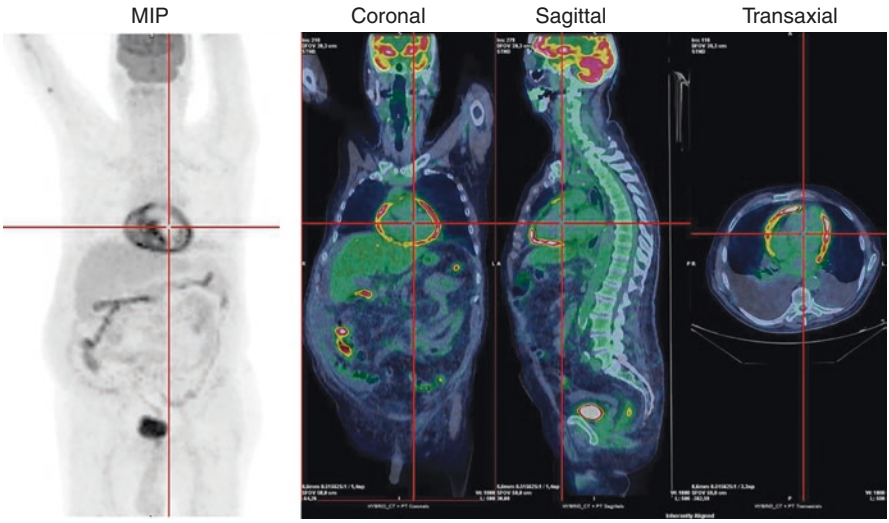


Fig. 6.19 PET/CT imaging in pericarditis. 1-month after a febrile prodromal syndrome followed by persistent asthenia and worsening dyspnoea, a 67 year old patient was admitted with atrial fibrillation. Serologic findings and echocardiographic/CMR images were suggestive of incessant pericarditis. PET/CT scan confirmed the diagnosis revealing diffuse uptake of ^{18}FDG in the pericardial layers without myocardial involvement and associated large bilateral pleural effusions

6.8 Basics of Treatment

A detailed description of treatment of pericarditis is outside the framework of this book. To give a brief summary, anti-inflammatory therapy is the cornerstone of acute pericarditis: Non-steroidal anti-inflammatory drugs are recommended based on clinical experience [2]. The benefit of colchicine is well established in both acute and recurrent pericarditis [30]. Systemic corticosteroids have been used mostly as second- or third-line treatments. Recently, IL-1 blockers (i.e., anakinra) have proven beneficial in recurrent pericarditis [50]. In purulent pericarditis, a rare but potentially life-threatening disease, specific antimicrobial therapy according to the causative agent is indicated [51]. The indication of pericardiectomy should always be based on a multi-disciplinary heart-team approach when patients remain highly symptomatic and all medical therapies are deemed ineffective.

6.9 Conclusion

Pericarditis can be considered a relatively uncommon, often self-limiting disease. However, if not promptly diagnosed and treated, it tends to relapse, become chronic, and lead to re-hospitalisation. Diagnosis and differential diagnosis remain challenging because the accessibility of pericardial fluid and tissue is limited and pericardiocentesis is not without risk. Therefore, high levels of clinical suspicion and multimodal imaging are necessary for the correct management of patients and to prevent or diagnose long-term complications.

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