Histopathological Dallas criteria,[31] in addition to immunohistological staining to detect $CD3^+$ T cells and $CD68^+$ macrophages, are required to identify specific histological subtypes of myocarditis and to differentiate from phenocopies [e.g. arrhythmogenic right ventricular cardiomyopathy (ARVC)].[32,33] New quantitative criteria are presently required, since the ESC criteria of ≥14 leucocytes/mm^2 including ≥7 $CD3^+$ T cells/mm^2 have been questioned by cardiopathologists.[10] In addition, molecular analysis of EMB and blood [including assessment of viral deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) in peripheral leucocytes and in plasma] using quantitative polymerase chain reaction (PCR) is necessary to identify the aetiopathogenesis of myocarditis and allow targeted therapies (antiviral or immunosuppressive/immunomodulatory), if clinically useful.[10,32,34] Examples are given in *Section 5.9.1*.

3.3.2. Diagnostic criteria for pericarditis

Pericarditis is an inflammatory pericardial syndrome with or without pericardial effusion (PEff). The definite clinical diagnosis can be made with a clinical presentation and more than one additional criterion (*Table 4*). The main presenting symptom is usually chest pain (85%–90% of cases), which is typically sharp and pleuritic, improves by sitting up and leaning forward, and is exacerbated by inspiration, lying down, and deglutition, due to increased attrition between inflamed pericardial layers. Dyspnoea can be reported by the elderly, or right HF signs and symptoms in the case of pericarditis with constriction. Arrhythmic presentations are rare and are usually associated with atrial fibrillation (AF). Additional criteria include a pericardial friction rub (≤33% of cases), which is a superficial scratchy or squeaking sound, caused by friction between the two inflamed pericardial layers. Electrocardiogram changes have been historically reported as a typical hallmark of AP; however, the pericardium is electrically silent, so ECG changes imply concomitant inflammation of the myocardium, warranting investigation for concurrent myocarditis.[35] On imaging, new or worsening PEff (up to 60% of cases), which is generally mild, might be detected. As pericarditis classically manifests with an inflammatory syndrome, elevated laboratory markers of inflammation, such as C-reactive protein (79%–90%),[36] erythrocyte sedimentation rate (ESR), and neutrophilic leucocytosis,[37,38] can provide additional supportive criteria. The inflamed pericardium is neovascularized and contrast-enhanced on computed tomography (CT) and CMR. Cardiovascular magnetic resonance is superior for tissue characterization and can reveal pericardial oedema and/or pericardial late gadolinium enhancement (LGE), providing additional imaging criteria for the diagnosis.

3.4. Aetiology of myocarditis and pericarditis

Myocardial and pericardial diseases share mostly similar aetiologies (see Supplementary data online, *Table S1*). The aetiology of IMPS can be either infectious or non-infectious. These can trigger IMPS in a genetically predisposed individual by inflammatory/autoimmune mechanisms. However, the prevalence of each aetiology and the impact of the causative agent on the clinical course, prognosis, and therapeutic approach may differ between the two entities.[1,10]

3.4.1. Aetiology of myocarditis

The most common infectious aetiology is presumed to be viral.[10,39,40] Enteroviruses, adenoviruses, parvovirus B19 (B19V) and some herpesviruses [Epstein–Barr virus (EBV), human herpesvirus 6 (HHV-6)], as well as influenza and coronaviruses, are the most common viruses associated with myocarditis (Supplementary data online, *Table S1*). Non-cytotoxic viruses trigger myocarditis indirectly by activating the immune system.[41,42] Bacterial infection with *Borrelia* species [Lyme carditis (LC)] and parasitic infections, such as *Trypanosoma cruzi* [Chagas disease (CD)], are additional important aetiologies in specific regions of the globe.

However, several non-infectious aetiologies should be recognized, including systemic diseases, autoimmune (or likely autoimmune) disorders [systemic lupus erythematosus (SLE), systemic sclerosis (SSc), rheumatoid arthritis (RA), eosinophilic granulomatosis with polyangiitis (EGPA), hypereosinophilic syndrome (HES)], immune-mediated forms [such as LM, giant-cell myocarditis (GCM), eosinophilic myocarditis (EM), and cardiac sarcoidosis (CS)], inflammatory bowel disorders, drugs and toxic reactions (including ICI-associated myocarditis, see *Section 9.6.1.1*) and chest radiation, as well as genetic conditions such as inherited CMP (see *Section 5.3*);[10,39] see Supplementary data online, *Table S1*.[10]

3.4.2. Aetiology of pericarditis

The aetiology largely depends on the epidemiological background, patient population, and clinical setting.[1,10] Idiopathic or viral pericarditis is the most frequent aetiology in developed countries, ranging from 50% in inpatient settings to >80% in outpatient settings.[43–48] Tuberculosis (TB) is responsible for about 70% of all cases, especially in human immunodeficiency (HIV)-infected patients, in regions where the disease is endemic. An increasing number of cases are related to interventional procedures and surgery [post-cardiac injury syndrome (PCIS)] due to the increased number of procedures performed and the ageing population.[49] Other common causes include systemic inflammatory/autoimmune diseases and cancer (especially lung and breast cancer or lymphomas and leukaemia) (see Supplementary data online, *Table S1*).[1]

About 5%–15% of patients with recurrence have genetic mutations, sometimes related to a monogenic autoinflammatory disease, mainly familial Mediterranean fever (FMF) and tumour necrosis factor receptor-associated periodic syndrome (TRAPS).[50,51] A genetic predisposition and an autoinflammatory/immune-mediated pathogenesis are also suspected in patients with multiple recurrences. For additional information see Supplementary data online, *Tables S2* and *S3*.[50–52]

4. Clinical presentation of inflammatory myopericardial syndrome

The term IMPS includes a spectrum of inflammatory diseases from isolated myocarditis to isolated pericarditis through a combination of both. IMPS should be used as an umbrella term during the initial diagnostic work-up until the final diagnosis is made. One of the major challenges for the diagnosis of IMPS is recognition itself, therefore the TF highlighted red flags (*Table 6*). These symptoms and signs should suggest IMPS. The red flags for IMPS are mainly clinical signs, accompanied by serological and/or imaging biomarkers, and are not equivalent to the risk. Red flags for IMPS are warning signs, aiming to raise the awareness of the disease. If there is a suspicion of IMPS, staging based on the risk assessment should be performed (*Table 7*).