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Review

Brief Version of Chinese Society of Cardiology Guidelines on the Diagnosis and Treatment of Adult Fulminant Myocarditis

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Abstract: Fulminant myocarditis is an acute and severe diffuse inflammatory disease of the heart with a high mortality rate. Its pathogenesis is driven by overactivation of the innate immunity and inflammatory storms. Based on China's practical experience, the clinical guidelines for the management of the disease recommend adoption of a "life support-based comprehensive treatment regimen" which comprises mechanical circulatory support and immunomodulatory therapy at optimized doses of glucocorticoids and immunoglobin rather than immunosuppression to improve survival rates and long-term prognosis. The application experience of this treatment regimen in China provides evidence upon which the guidelines are formulated. This regimen emphasizes the importance of early identification, diagnosis, prediction, and treatment in patients with fulminant myocarditis. This is a brief introduction of the guidelines.

Keywords: fulminant myocarditis; diagnosis; treatment; guidelines; life support-based comprehensive treatment regimen; immunomodulatory therapy; cytokine storm; overactivation of innate immunity

1. Introduction

Myocarditis is a type of myocardial inflammation and damage caused by various pathogens. Fulminant myocarditis is a severe and unique type that is characterized by rapid onset and rapid progression. Patients may experience hemodynamic instability, such as the collapse of cardiac pumping function, circulatory system failure, and arrhythmia. Fulminant myocarditis is associated with high mortality rates. The ever-increasing number of basic and clinical studies, and reports of treatment experience in China, especially after the release of the Chinese expert consensus statement in 2017, have provided solid evidence that China's treatment regimen has reduced in-hospital mortality from over 50% to approximately 5% and prolonged the prognosis of patients. The Chinese Society of Cardiology believes it is their responsibility to promote expert consensus on these guidelines. This upgrade aims to effectively guide the clinical diagnosis and treatment of fulminant myocarditis in China and globally. The upgraded guidelines focus on strengthening the training of medical personnel, particularly in the aspects of early identification, diagnosis, prediction, and treatment of diseases.

2. Methods

The evidence in this guide was obtained by searching and screening relevant literature from Chinese and foreign medical electronic databases (including PubMed and Wanfang Medical Literature Library). The recommendations in this guide are divided into the following categories.

Type I: This evidence indicates that specific treatments or procedures are beneficial, useful, effective, or have gained widespread consensus.

Type II: This evidence suggests that the treatment or strategy may be useful but has yet to be fully confirmed, or the evidence of its usefulness or effectiveness needs to be stronger.

Category IIa: The weight of evidence tends to support its usefulness and practicality.

Class IIb: Evidence or expert opinion deems its usefulness and effectiveness poor.

Category III: This evidence or broad consensus suggests that surgical treatment is ineffective and may be harmful in certain situations.

The level of evidence sources is as follows:

Level A: Evidence is based on data from multiple randomized clinical trials or meta-analyses.

Level B: Evidence is based on data from a single randomized or non-randomized study.

Level C: Evidence from expert consensus, case studies, or nursing standards.

3. Epidemiology of Fulminant Myocarditis

Currently, the true epidemiological status of fulminant myocarditis remains unclear. The available data on the incidence rates are mainly derived from death statistics for myocarditis and acute myocarditis. A Finnish study reviewed deaths from myocarditis and found that the incidence rate of fatal myocarditis was 4.6/1 million person-years [1], and the mortality rate of fulminant myocarditis in the acute phase was approximately 50% [2]. Accordingly, fulminant myocarditis is estimated to be approximately 9.2/1 million person-years. In addition, data from a global disease burden study conducted from 1990 to 2017 showed that the age-standardized incidence rate of myocarditis was approximately 23.2/1 million person-years. The incidence of myocarditis varies across regions worldwide. The incidence rate of myocarditis in the Asia-Pacific region is approximately 45.6/1 million person-years, whereas that in China it is 30 – 40/1 million person-years [3,4]. However, the proportion of fulminant myocarditis in myocarditis varies in different studies. According to a large multicenter study, fulminant cardiomyopathy accounts for approximately 10% of myocarditis cases [5,6]. Overall, the average incidence rate of fulminant myocarditis is estimated to be 9–23/1 million person-years. In China, the annual incidence of fulminant myocarditis among adults aged >14 years is approximately 30,000–50,000 in the general population.

4. Etiology and Pathophysiology of Fulminant Myocarditis

The pathogenic factors (infectious and noninfectious factors) of fulminant myocarditis are similar to those of acute and chronic myocarditis. Among them, viral infection is the most common cause of myocarditis, and other factors include allergens and checkpoint inhibitors. In recent years, several viruses has been identified to contribute to fulminant myocarditis; such as influenza viruses (types A and B), COVID-19, and dengue, which caused earlier pandemics [7]. In fulminant myocarditis with high viral load or viral replication in myocardial tissue, immunosuppressive agents are prohibited [8, 9]. The most important update of concept is that innate immunity is overactivated by various pathogens, causing rapid release of many inflammatory factors or cytokines by immune cells and phenotype-changed cardiomyocytes, forming a so-called "inflammatory storm," which injures the heart [10]. This intense inflammatory response is considered a key factor leading to the rapid onset, progression, severity, and high mortality rate in fulminant myocarditis [11,12].

Pathology of Fulminant Myocarditis and Its Clinical Relationship

Fulminant myocarditis is characterized by widespread infiltration of inflammatory cells into myocardial tissue, accompanied by significant myocardial cell death, characterized by more than 50 inflammatory cells per square millimeter under a microscope [13]. Infiltrating inflammatory cells can be divided into lymphocyte, eosinophilic, giant cell myocarditis, and cardiac sarcoidosis types, the most common of which is the lymphatic type, which constitutes over 90% of the cases. Histologically, it is characterized by patchy infiltration of T lymphocytes and macrophages in the myocardium, accompanied with myocardial cell necrosis or degeneration [14]. Giant cell myocarditis is characterized by extensive infiltration of white blood cells, mainly myeloid cells (macrophages), which differs from other forms of myocarditis in which T cells are commonly detected. This type of myocarditis has a poor prognosis, and survivors are prone to developing

dilated cardiomyopathy [15–17]. The histological manifestation of eosinophilic myocarditis is a patchy interstitial infiltration of eosinophils. This form of myocarditis is typically observed in systemic diseases associated with peripheral eosinophilia (such as primary idiopathic eosinophilia, hypersensitivity to drugs, parasitic infections, allergic diseases, and autoimmune diseases). Cardiac sarcoidosis is a systemic disease of unknown etiology that typically affects the lungs and intrathoracic lymph nodes. Histologically, cardiac nodules are characterized with extensive infiltration of macrophages, leading to chronic inflammation and tissue damage caused by fiber substitutes [18].

5. Clinical Evaluation of Fulminant Myocarditis

5.1. History Taking

Comprehensive evaluation of the medical history and physical examination are crucial for establishing the diagnosis. It is necessary to carefully understand whether the patient has symptoms of upper respiratory tract infection or diarrhea, inquire about the history of drug or food allergies, whether they have taken drugs known to cause toxic to the heart, and whether they have ingested toxins such as aconitum, snake bile, and fish bile. Clinicians should also inquire whether one has been infected with dengue fever in an endemic area or related travel experiences. In addition, some noncardiac diseases should not be ignored (immune-mediated systemic diseases). In recent years, COVID-19 and influenza have become common causes of death.

5.2. Symptoms: No Specific

5.2.1. Symptoms of Prodrome

The initial symptoms are often not specific and are not the main complaints of patients seeking medical treatment or having a fever, such as cold or tiredness, or little diarrhea. However, they provide major clues for diagnosing myocarditis. Common symptoms include fatigue and appetite [19–22].

5.2.2. Manifestations of Myocardial Damage

Abnormal hemodynamics are a significant feature of fulminant myocarditis. Most patients experience dizziness and weakness, which is usually caused by hypotension or shock and may sometimes even cause fainting or loss of consciousness. In addition, some patients may experience emergencies such as acute left heart failure, cardiogenic shock, and severe arrhythmia [23,24].

5.2.3. Involvement of other Tissues and Organs

In the early stages of fulminant myocarditis, most patients do not experience significant damage to liver or kidney function. Damage or multiple organ failure is usually caused by delayed or inappropriate treatment, and/or a long-term shock state [25].

5.3. Physical Signs: No Specificity

5.3.1. Vital Signs

Abnormal blood pressure, respiratory rate, and heartbeat rhythm are signs of hemodynamic instability, which are common in fulminant myocarditis and can be used as indicators for evaluating disease severity [26].

5.3.2. Cardiac-Related Signs

Pulsation at the apex of the heart often appears weakened or disappears; when perceived, but the boundary of the heart is not enlarged. On auscultation, the heart sound appears low and dull, and a third heart-sound gallop rhythm is often heard [27]. Most patients have a rapid heart rate; however, some have a normal or slow heart rate (bradycardia). Arrhythmias, including atrial and ventricular premature beats, tachycardia, and ventricular fibrillation, are common, and some patients may present with complete AVB requiring temporary PM implantation.

5.4. Laboratory Examination

5.4.1. Routine Blood Test

In fulminant myocarditis, patients' routine blood test results may vary depending on the type of pathogen and their immune responses.

5.4.2. Markers of Myocardial Injury: hs-cTnI/T

In most fulminant myocarditis cases, high-sensitivity troponin I/T (hs-cTnI/T) and troponin I (cTnI/T) are significantly elevated. Changes in the levels of these biomarkers influence the treatment efficacy. Therefore, continuous monitoring of hs cTnI or cTnI as a biomarker for measuring cardiac injury is recommended in fulminant myocarditis [19] (I, B). The combination of marked cTnI and soluble suppression of tumorigenicity-2 (sST2) elevation can facilitate diagnosis.

5.4.3. BNP or NT-proBNP

B-type natriuretic peptide (BNP) and N-terminal B-type (pro-BNP) are sensitive indicators of cardiac function in patients with fulminant myocarditis [28]. It is recommended to dynamically monitor the levels and changes in NT-proBNP in the plasma to evaluate the degree of cardiac dysfunction and the developmental trend of the disease in patients with fulminant myocarditis [16] (I, B).

5.4.4. Liver and Kidney Function, Electrolyte, Acid-base Balance

The degree of liver and kidney dysfunction has a significant impact on the prognosis of patients with fulminant myocarditis [29, 30]. Therefore, regular and dynamic monitoring of liver and kidney function indicators is recommended (I, C).

Maintaining electrolyte and acid-base balance in the blood is crucial for managing such patients, especially in controlling serum potassium concentrations within the 4.0 to 5.0 $mmol \cdot L^{-1}$ (I, A).

Continuous monitoring of blood oxygen saturation and periodic dynamic monitoring of arterial blood gas and blood pH values are also recommended for patients with fulminant myocarditis to evaluate the condition and guide treatment (I, A) [31,32].

5.4.5. Coagulation Function Tests

Regular and continuous monitoring of coagulation function is recommended. Shock and inflammatory storms may inhibit the synthetic function of hepatocytes, thereby increasing the risk of coagulation abnormalities or disseminated intravascular coagulation (DIC) in patients (I, A).

5.4.6. Detection of Inflammatory Factors or Cytokines

For patients suspected of fulminant myocarditis, routine and continuous monitoring is recommended to track changes in plasma levels of inflammatory factors, including various cytokines, particularly soluble ST2 (sST2) [33]. Markedly elevated sST2 level combined with increased cTnI level may indicate a diagnosis of fulminant myocarditis. Thus, monitoring these indicators is crucial for disease diagnosis, treatment effectiveness assessment, and prognosis evaluation (I, B). In patients with fulminant myocarditis, procalcitonin (PCT) levels are often markedly elevated, which is related to the infiltration of inflammatory cells, myocardial injury, and inflammatory storm in the heart. However, this does not necessarily indicate the presence of a bacterial infection [34] (IIb).

5.5. Special Examination for Fulminant Myocarditis

5.5.1. Electrocardiogram

Almost all patients with fulminant myocarditis have electrocardiogram abnormalities, including marked low-voltage, significant broadening of the QRS wave, elevated ST-segment like acute myocardial infarction, lower T-wave, ST segment depression, and arrhythmias, as the electrocardiogram may experience rapid

changes; therefore, continuous electrocardiogram monitoring should be implemented [27] (I, B).

5.5.2. Echocardiography

Echocardiography plays a crucial role in the rapid diagnosis of fulminant by assessing the severity of the condition, guiding the development and adjustment of treatment strategies, evaluating treatment effectiveness and prognosis, and conducting subsequent follow-ups. Therefore, it is recommended that all patients with fulminant myocarditis undergo routine echocardiography, especially for those with hemodynamic instability that requires dynamic monitoring (I, B) [35,36]. The ventricular global longitudinal strain (GLS) is also better for assessing cardiac function and hemodynamic changes, including lactic myocardial contraction.

5.5.3. Chest CT or X-ray

Most patients have small or slightly enlarged but powerless heart shadows and bilateral pulmonary congestion [37].

5.5.4. Coronary Angiography

It is recommended that all patients with fulminant myocarditis undergo coronary angiography at an early stage, regardless of whether there are high-risk factors for coronary atherosclerosis [27,37] to differentiate acute myocardial infarction from fulminant myocarditis. Both result in acute and severe myocardial injury, but because the treatment strategies and prognosis of these two diseases are fundamentally different, immediate treatment is required. During coronary angiography, the use of contrast agents should be minimized as much as possible [35] (I A).

5.5.5. Cardiac Magnetic Resonance

Cardiac magnetic resonance imaging (CMRI) combined with elevated levels of cardiac troponin has gradually replaced myocardial biopsy as a noninvasive diagnostic method for myocarditis because it can help differentiate acute myocardial infarction. This technology has been applied in clinical studies of myocarditis in recent years, especially in low-risk patients (I, A) [5]. However, because it takes a long time to complete in a narrow space with noise and requires special experience to read the results, it is not easy to perform this test at an early stage.

5.5.6. Endomyocardial Biopsy

Pathological analysis of myocardial endometrial biopsies (EMB) has always been the gold standard for diagnosing myocarditis[38,39]. The histological diagnostic criteria for fulminant myocarditis are described in the Pathology section [40,41]. In addition to directly confirming myocardial tissue inflammation and diagnosing myocarditis, EMB can guide subsequent treatment [42–44]. Therefore, EMB is strongly recommended for fulminant myocarditis (I, B). Additionally, immunohistochemical staining for inflammatory cell classification may be performed to identify the classes of infiltrating cells.

5.6. Diagnostic Criteria

Fulminant myocarditis is diagnosed through clinical, pathological, and etiological approaches. The most important step is to make a clinical diagnosis as soon as possible to initiate the correct treatment regimen and save patients. For patients with some prodromes, such as fever, tiredness, respiratory infections like cold or diarrhea, and subsequent chest pain or discomfort, ECG examination, serum levels of hs-cTnI/cTnI and BNP/NT pro-BNP, as well as cytokines, especially sST2 levels, should be tested. If severe hemodynamic instability and arrhythmia occur rapidly after the patient presents with prodromal symptoms, the levels of hs-cTnI/cTnI and BNP/NT pro-BNP are markedly elevated, accompanied by significant ECG abnormalities. Moreover, echocardiography examination may show diffuse movement disorder of the left ventricular walls, a significant decrease in left ventricular ejection fraction, weakened left ventricular long axis strain, and a significant increase in inflammatory factor levels, which can be clinically diagnosed as fulminant myocarditis after acute myocardial ischemia (AMI). Stress cardiomyopathy is excluded immediately via coronary

angiography and a potent stress history, respectively. Markedly elevated levels of sST2 and high hscTnI/cTnI and BNP/NT pro-BNP will help diagnose fulminant myocarditis and differentiate acute myocardial infarction (AMI).

5.7. Diagnostic Map

The diagnosis of fulminant myocarditis involves three aspects: (1) clinical diagnosis, including proposed diagnosis (clinical manifestations, electrocardiogram, cardiac biomarkers, cardiac ultrasound, and inflammatory factor screening), and confirmed diagnosis (coronary angiography to exclude acute myocardial infarction, EMB or CMRI), and (2) etiological diagnosis (etiological and toxin testing such as viral and other microbe tests can help identify the cause), and (3) pathologic diagnosis based on endomyocardial biopsy or autopsy. For timely emergency treatment, a swift clinical diagnosis is paramount. Therefore, these three aspects should be assessed concurrently, rather than following a rigid, sequential order. Early coronary angiography should be performed to rule out acute myocardial infarction; EMB and inflammatory factors can help confirm the diagnosis.

(1) Clinical diagnosis: patients suspected of fulminant myocarditis with prodromal symptoms, clinical manifestations, and signs of upper respiratory or digestive tract infections, as well as elevated electrocardiogram and troponin levels, should undergo echocardiography, coronary angiography, and CMRI as soon as possible to clarify the possibility of fulminant myocarditis.
(2) Etiological diagnosis: patients with fulminant myocarditis can seek the cause through pathogen microbiology, autoimmune antibody, and toxin testing.
(3) Pathological diagnosis: if the patient can tolerate EMB, it can be performed simultaneously with coronary angiography. Each type manifests as fulminant myocarditis. The myocarditis histotype has an independent and crucial prognostic value.

5.8. Differential Diagnosis

Fulminant myocarditis should be distinguished from AMI, bacterial septic cardiomyopathy, common (nonfulminant) acute myocarditis, stress cardiomyopathy, viral pneumonia, and severe arrhythmias.

6. Treatment of Fulminant Myocarditis

6.1. Acute Phase Treatment of Fulminant Myocarditis

6.1.1. Patient bedside Monitoring

ECG Blood Pressure Oxygen Saturation Monitoring: Continuous ECG monitoring can detect possible arrhythmias in patients with fulminant myocarditis. Blood pressure monitoring, whether through non-invasive or invasive methods, can accurately determine whether a shock has occurred. Blood oxygen saturation monitoring relies on finger pulse oximeters and arterial blood gas analysis. For patients with peripheral circulation damage, arterial blood gas analysis to monitor oxygen partial pressure and saturation is more accurate (I, A). In patients with fulminant myocarditis supported by VA extracorporeal membrane oxygenation (ECMO), right upper limb oxygen saturation can more accurately reflect the overall oxygenation level (I, B).

Invasive Blood Pressure Monitoring: Invasive blood pressure monitoring is more accurate than noninvasive and is particularly suitable for critically ill patients with an unstable hemodynamic status (I, A).

Central Venous Pressure: In patients with shock, a central venous pressure exceeding 15 mmHg may indicate right ventricular dysfunction or fluid overload.

Pulse Wave Indicator Continuous Cardiac Output (PICCO) Hemodynamic Monitoring: The hemodynamic parameters provided by Pulse Wave Indicator Continuous Cardiac Output (PICCO) technology enhance the accuracy of bedside patient assessment, which is particularly useful for guiding clinical decision-making in patients with hypotension (I, B).

6.1.2. Principles of Rescue

For patients with fulminant myocarditis, we emphasize the adoption of a “Life support-based

comprehensive treatment regimen", which allows early identification, diagnosis, prediction, and rescue principles. The core contents include the following:

(i) Mechanical circulatory support: mechanical circulation equipment should be used to maintain the stability of blood circulation and ensure adequate perfusion of organs; additionally, if patients have respiratory distress or a rapid or slow respiratory rate, mechanical respiratory support should be immediately administered because it will help reduce the cardiac effort load.
(ii) Immunomodulatory therapy: this is a fundamental treatment measure for severe cardiac inflammation, and we recommend using sufficient doses of both glucocorticoids and immunoglobulins to regulate the immune system and fight inflammation rather than immune suppression treatment using cytotoxic agents.
(iii) Neuraminidase inhibitors are used to alleviate myocardial injury.
(iv) Other treatment measures: if patients have respiratory distress or a rapid or slow respiratory rate, mechanical respiratory support should be administered immediately because it will help reduce the cardiac effort load. Blood purification treatment should also be performed, and if necessary, a temporary pacemaker should be implanted.

6.1.3. Treatment Methods

Life support therapy is the preferred treatment for fulminant myocarditis as it improves patient survival. This treatment includes interventions including those that provide mechanical circulatory support and, when necessary, respiratory support.

Mechanical Circulatory Support: Under comprehensive systemic therapy, mechanical circulatory support has been identified as the preferred treatment strategy that reduces cardiac load and promotes functional recovery [21,45]. Mechanical circulatory support includes intra-aortic balloon pumps (IABP) [46], ECMO [19, 35, 47, 48], Impella [49], and other cardiac-assistive device applications [50]. Other forms of mechanical support therapy include mechanical ventilation therapy to improve hypoxemia, reduce respiratory burden, relieve breathing difficulties, and assist in cardiac function recovery (I, A), as well as continuous renal replacement therapy (CRRT), which optimizes the hemodynamic state of septic shock patients by clearing inflammatory mediators (IIa, C) [51,52]. In our practice, we preferentially recommend using IABP because it raises blood pressure and lowers cardiac afterload. Its use alone raises systolic blood pressure over 20 mm Hg and reduces the vasoactive agent dose, and it may be sufficient to maintain circulation in most patients when started early. It is recommended that patients with fulminant myocarditis who exhibit early signs of shock, such as hypotension and an increased heart rate, immediately undergo IABP. If IABP alone is insufficient to correct the shock and heart failure, ECMO should be performed. If patients have deep shock, severe arrhythmias such as ventricular tachycardias, ventricular fibrillation, and ECMO must be immediately used, IAPB should be added because IABP and ECMO can have synergistic effects by reducing cardiac afterload and preload, respectively. Applying Impella alone or combined with VA-ECMO for circulatory support in patients with fulminant myocarditis extends the support time and improves long-term prognosis [53–55]. The tandem heart as a biventricular assist system has also been reported in case reports of circulatory support in fulminant myocarditis [56]. Mechanical circulatory support must be combined with immunomodulatory therapy, as described below.

Immunomodulatory Therapy: The commonly used immunomodulatory therapy are glucocorticoids and immunoglobulins to sever etiological connections, reduce inflammation and edema, combat shock, and alleviate clinical symptoms, thereby saving lives and enhancing cure rates. The specific suggestions are as follows.

(1) Sufficient glucocorticoid doses should be administered as early as possible. Once a clinical diagnosis is established, glucocorticoid therapy should be initiated immediately. Intravenous 200–500 mg (or 3–8 mg/kg) methylprednisolone is often administered daily. After continuous treatment for 3-5 days, methylprednisone should be gradually decreased according to conditions (usually starting from a left ventricular EF value greater than 40%). The treatment is changed to oral prednisone 20–40 mg/d before discharge, and treatment is maintained for ~3 months or longer. In the subsequent treatment process, it is necessary to decide whether to halt treatment or adjust the medication regimen based on the patient's symptoms, cardiac function status, and drug tolerance (I, A).

(2) Early IV administration of sufficient immunoglobulins. It is recommended that patients start receiving intravenous immunoglobulin as soon as possible after admission, with a starting dose of 20 g per day for 3 to 5 days and a total dose of approximately 2 g kg^{-1} (I, A) [57–59].

Antiviral Therapy and Neuraminidase Inhibitors: Although viral infection is still considered the most common cause of myocarditis, many patients do not have direct evidence of viral infection. Therefore, no antiviral drugs are recommended, except for anti-influenza virus drugs or anti-COVID-19 drugs, when viral pathogens are identified. Neuraminidase inhibitors can alleviate heart damage by inhibiting the elevated activity of neuraminidase during acute myocardial injury [60, 61]. It is recommended that patients with fulminant myocarditis routinely use oseltamivir phosphate capsules or receive intravenous injections of piperamivir [49] (IIa, C).

7. Treatment and Follow-Up of the Convalescent Phase of Fulminant Myocarditis

7.1. Rehabilitation Period Treatment

7.1.1. Assessment and Classification

Patients with fulminant myocarditis require regular and comprehensive evaluations before discharge. Discharged patients can be divided into three categories based on the results of these evaluations: healed myocarditis, healing myocarditis, and persistent myocarditis [5].

7.1.2. Pharmacotherapy

It is recommended that all patients take angiotensin-converting enzyme inhibitors, β Receptor blockers, and trimetazidine; oral prednisone application is suggested for 3 months. For patients with cardiac arrhythmia, standardized drug treatment should be administered according to the corresponding guidelines (I, C) [62, 63]. For patients with myocarditis who have received standard anti-HF treatment but whose heart failure symptoms have not been relieved, myocardial biopsy is necessary to gain a deeper understanding of the pathological types of myocarditis (I, C). Glucocorticoids or immunosuppressive therapy may help improve the clinical symptoms of giant cell myocarditis patients after discharge [64,65] (I, B).

7.1.3. Nonpharmacologic Interventions

For patients with giant cell myocarditis, it is recommended to install an implantable defibrillator (ICD) to prevent sudden death (I, C). If the heart function of patients with chronic myocarditis cannot be improved through drug therapy, long-term mechanical circulation support therapy should be considered (I, C).

7.1.4. Exercise-Based Cardiac Rehabilitation

Before starting the cardiac rehabilitation program, all patients should undergo a comprehensive re-examination to assess the risk of sudden death related to exercise (I, B). Moderate-to-high-intensity exercise is not recommended for patients with myocardial inflammation, scars, or persistent left ventricular dysfunction, as suggested by CMRI [27]. Moderate-to-high-intensity exercise is also not recommended for all patients with fulminant myocarditis who have been discharged for 3–6 months. [21] (III, B). Six months after the acute phase, exercise-based cardiac rehabilitation can be initiated (IIa, C). The exercise plan should start at a low intensity, and the patient's clinical symptoms and other biomarkers should be regularly monitored during cardiac rehabilitation (I, C).

7.2. Long-Term Follow-Up

Approximately one-quarter of discharged patients experience cardiac dilation, heart failure, or arrhythmia during the one-year follow-up period [66, 67]. All patients with fulminant myocarditis should undergo long-term follow-up monitoring after discharge (I, C) [68]. Monthly follow-up is recommended for the first three months and then every three months thereafter. The major symptoms include palpitations, shortness of breath, ECG, echocardiography examination, CMR, cTnI, BNP or NT-proBNP levels, and sST2 levels, which help to assess the inflammatory status.

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