MAYO CLINIC

REVIEW

Myocarditis in Clinical Practice

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Abstract

Myocarditis is a polymorphic disease characterized by great variability in clinical presentation and evolution. Patients presenting with severe left ventricular dysfunction and life-threatening arrhythmias represent a demanding challenge for the clinician. Modern techniques of cardiovascular imaging and the exhaustive molecular evaluation of the myocardium with endomyocardial biopsy have provided valuable insight into the pathophysiology of this disease, and several clinical registries have unraveled the disease's long-term evolution and prognosis. However, uncertainties persist in crucial practical issues in the management of patients. This article critically reviews current information for evidence-based management, offering a rational and practical approach to patients with myocarditis. For this review, we searched the PubMed and MEDLINE databases for articles published from January 1, 1980, through December 31, 2015, using the following terms: *myocarditis*, *inflammatory cardiomyopathy*, and *endomyocardial biopsy*. Articles were selected for inclusion if they represented primary data or were review articles published in high-impact journals. In particular, a risk-oriented approach is proposed. The different patterns of presentation of myocarditis are classified as low-, intermediate-, and high-risk syndromes according to the most recent evidence on prognosis, clinical findings, and both invasive and noninvasive testing, and appropriate management strategies are proposed for each risk class.

 ■ Mayo Clin Proc. 2016;■■(■):1-11

Myocarditis is an inflammatory disease of the myocardium diagnosed using established histologic and immunohistochemical criteria (Table 1) (Figure 1).[1-3] A recently published position statement by the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases provides updated recommendations regarding the etiology, diagnosis, and therapeutic management of myocarditis.[3] However, despite the formally structured definition, myocarditis is a heterogeneous disease, characterized by extensive variability in clinical presentation and ensuing evolution.[4] This variability necessitates patient-tailored diagnostic and therapeutic management in which the advanced and often costly testing and treatments are reserved for those with the most severe and threatening clinical presentation. In fact, gaps persist between published recommendations and clinical practice, while real-world, applicable, hands-on guidelines for the practical management of the various manifestations of myocarditis are lacking.

Accordingly, this review summarizes the contemporary knowledge about myocarditis, offering a rational and practical approach for the management of this polymorphic disease. For this purpose, we searched the PubMed and MEDLINE databases for articles published from January 1, 1980, through December 31, 2015, using the following terms: *myocarditis*, *inflammatory cardiomyopathy*, and *endomyocardial biopsy*. Articles were selected for inclusion if they represented primary data or were review articles published in high-impact journals. In particular, a clinically oriented classification based on events risk is proposed. The different patterns of presentation of myocarditis are classified as low-, intermediate-, and high-risk syndromes according to the most recent evidence on prognosis, clinical findings, and both invasive and noninvasive testing, and appropriate management strategies are proposed for each risk class.

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ETIOLOGY AND EPIDEMIOLOGY

Myocarditis can be triggered by different causes: infections (ie, viruses, bacteria, parasites), autoimmune diseases, hypersensitivity, high catecholamine states, drugs, toxic

ARTICLE HIGHLIGHTS

- Myocarditis is an inflammatory disease of the myocardium characterized by great heterogeneity of presentation and evolution. The main patterns of clinical presentation are chest pain, arrhythmias, and heart failure, and disease severity may range from asymptomatic or mild self-limiting syndromes to severe life-threatening scenarios requiring intensive hemodynamic support.
- Patients presenting with chest pain and/or supraventricular arrhythmias with preserved left ventricular function typically have an excellent prognosis (low-risk syndromes). Conversely, patients presenting with heart failure and/or life-threatening arrhythmias, in particular when associated with severe left ventricular dysfunction, have a consistent probability of major clinical events in long-term follow-up, and their prognosis largely depends on the short-term response to therapy (high-risk syndromes).
- Several cases exist with intermediate characteristics between low- and high-risk syndromes (patients with mild to moderate ventricular dysfunction, frequent nonsustained ventricular arrhythmias, persistent regional wall motion and/or electrocardiographic anomalies, presence of late gadolinium enhancement). These patients merit particular attention both in the diagnostic work-up and in follow-up because their prognosis is largely unknown.
- A critical and integrated evaluation of clinical and instrumental noninvasive investigations (clinical history, electrocardiography, echocardiography, cardiac magnetic resonance imaging) is fundamental for the identification of cases of suspected myocarditis. However, the definite diagnosis of myocarditis is provided by histologic and immunohistochemical analysis of myocardial tissue samples obtained with an endomyocardial biopsy.
- The diagnostic work-up and clinical management of patients with suspected or confirmed myocarditis should be tailored on the basis of the severity of clinical presentation and response to medical therapy. Invasive diagnostic testing, such as endomyocardial biopsy, and specific therapies, like immunosuppression, should be reserved for patients presenting with major clinical syndromes (severe heart failure and/or life-threatening arrhythmias) that are refractory to conventional therapies.
- A structured follow-up is crucial in the management of patients with myocarditis. The interval between each reevaluation and the duration of the follow-up should be tailored on the basis of the severity of clinical presentation, the extent of ventricular remodeling, and subsequent risk of events.

substances, or physical agents.[5] Once other specific causes are ruled out, most cases of myocarditis observed in clinical practice are attributable to viral infections and/or immune reactions. In particular, even when no viruses are detected by serologic and polymerase chain reaction (PCR) analyses, an unrecognized viral infection remains the most probable cause of idiopathic myocarditis. These cases are presumably observed in an advanced phase (usually 3 or 4 weeks after the infection) when the immune system has already achieved a complete clearance of the virus.[5]

In consideration of the broad spectrum of clinical presentations, it is difficult to establish the actual epidemiological burden of myocarditis in the real world because its prevalence changes considerably in relationship to the population under study and to the adopted diagnostic criteria. For example, a recent epidemiological study identified myocarditis as the final diagnosis for 0.5% of all hospital admissions for cardiovascular reasons, frequently affecting a young population of mainly male patients.[6] However, previous studies detected myocarditis on endomyocardial biopsy (EMB) in 10% to 17% of patients with otherwise unexplained cardiomyopathy.[7,8] Similarly, myocarditis was found in 5% of individuals in a series of unselected and consecutive autopsies, but the disease was considered the main cause of death in only a minority.[9] In this sense, it appears that myocarditis is underdiagnosed. Yet, it is obvious that the histopathologic characterization of this condition is not always necessary and gains practical relevance only in selected cases.