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Clinical Reviews

Diagnosis and Management of Myocarditis: An Evidence-Based Review for the Emergency Medicine Clinician

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□ **Abstract—Background: Myocarditis is a potentially fatal condition that can be misdiagnosed in the emergency department (ED) setting. Objective: The purpose of this narrative review article is to provide a summary of the background, pathophysiology, diagnosis, and management of myocarditis, with a focus on emergency clinicians. Discussion: Myocarditis occurs when inflammation of the heart musculature causes cardiac dysfunction. Symptoms may range from mild to severe and are often preceded by a viral prodrome. Laboratory assessment and an electrocardiogram can be helpful for the diagnosis, but echocardiography is the ideal test in the ED setting. Some patients may also require advanced imaging, though this will often occur during hospitalization or follow-up. Treatment is primarily focused on respiratory and hemodynamic support. Initial hemodynamic management includes vasopressors and inotropes, whereas more severe cases may require an intra-aortic balloon pump, extracorporeal membrane oxygenation, or a ventricular assist device. Nonsteroidal anti-inflammatory drugs should be avoided while intravenous immunoglobulin is controversial. Conclusion: Myocarditis is a serious condition with the potential for significant morbidity and mortality. It is important for clinicians to be aware of the current evidence regarding the diagnosis, management, and disposition of these patients. © 2021 Elsevier Inc. All rights reserved.**

□ **Keywords—myocarditis; cardiomyopathy; cardiac; emergency medicine**

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Clinical Scenarios

A. A 28-year-old female patient presents with severe shortness of breath, hypotension, and tachycardia. The patient was previously healthy and has no risk factors for pulmonary embolism. The physician initially suspects sepsis, but the patient's condition worsens after intravenous fluids and vasopressors. The physician wonders whether there is anything the physician may be missing.

B. A 14-year old male patient presents with new dyspnea on exertion and decreased exercise tolerance. The patient had previously been able to exercise without difficulty and now becomes fatigued after walking more than one block. The patient has no past medical history or relevant family history. However, the patient recalls a recent viral infection 2 weeks prior. The vital signs are notable for a heart rate of 130 beats per minute, which does not improve with intravenous fluids. The physician suspects myocarditis but is unsure how best to evaluate for this.

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Introduction

Epidemiology

Myocarditis is an inflammatory disorder of the heart that can cause significant morbidity and mortality. Overall, there are varying estimates of the incidence of myocarditis, ranging from 0.02–1.5% of the general population, based upon autopsy studies (1–5). Myocarditis can result from infectious, toxic, or autoimmune causes, with viral infection being the most common etiology (1). One study suggested that myocarditis may be present in up to 1% of all patients with acute viral infections (3). Other studies have found that acute myocarditis was the cause of death in up to 12% of autopsies among patients under 40 years of age with sudden cardiac death (6–10).

Age is a factor that influences the incidence of myocarditis. The average age of patients with giant cell myocarditis is 42 years, whereas the other forms of myocarditis range from 20–51 years (3,11,12). Myocarditis is also more common in men (2,3,13–15). This is hypothesized to occur because estrogen has a protective effect against viremia and viral infectivity of cardiomyocytes (16). Estrogen may also decrease the myocardial inflammatory response (17).

Complications of myocarditis include life-threatening dysrhythmias, heart failure, and fulminant myocarditis. Heart failure has been documented to occur in 0.5% to 4.0% of patients with myocarditis (1,18). Fulminant myocarditis is a subset of myocarditis that leads to rapidly progressing hemodynamic compromise and dysrhythmias (1). It is defined as an acute illness within 2 weeks of the onset of symptoms after a distinct viral prodrome with severe cardiovascular compromise, ventricular dysfunction, and extensive inflammatory infiltrates of lymphocytes and macrophages on histological examination (19). In the Marburg Myocarditis Registry, a collection of 1098 patients with documented myocarditis in Marburg, Germany from 1989 to 2003, only 2.5% of patients presented with fulminant myocarditis (20). The mortality rate for fulminant myocarditis is up to 20% in the first year, though the rate declines and stabilizes after approximately 3 years (21).

Given the substantial morbidity and mortality associated with this disease, it is essential that emergency physicians are aware of the diagnosis, evaluation, and management of this disease.

Methods

Authors searched PubMed for articles using the keywords "myocarditis" or "viral cardiomyopathy." The literature search was restricted to studies published in English. Authors reviewed all relevant articles and decided which studies to include for the review by consensus. When available, systematic reviews and meta-analyses were preferentially selected. These were followed sequentially by randomized controlled trials, prospective studies, retrospective studies, case reports, and other narrative reviews when alternate data were not available. A total of 147 articles were selected for inclusion in this narrative review.

Discussion

Pathophysiology and Microbiology

Myocarditis is believed to occur in three phases (22). The first phase occurs over a few days and involves the virus entering the myocytes through endothelial receptors, most notably the coxsackie-adenovirus receptor (23,24). This receptor is highly expressed in the brain and heart. Coxsackie viruses utilize the deflecting decay-accelerating factor and adenoviruses special integrins ($\alpha v\beta 3$ and $\alpha v\beta 5$) as co-receptors (24). Viruses that evade the innate immune system replicate, producing viral proteins that cause direct myocardial injury, as well as hyperactivation of the host's immune system, characterized by invasion of natural killer cells, macrophages, and T lymphocytes into the myocardium.

The second phase occurs over a few weeks to several months and involves autoimmune reactions (25). Virus-specific T lymphocytes are activated and target the host's organs by molecular mimicry (25). This leads to cardiac damage and impairment of the contractile function (25). The third phase is the chronic phase, which is characterized by myocardial remodeling and development of dilated cardiomyopathy (26).

Myocarditis has three primary histologic subtypes: lymphocytic, giant cell, and eosinophilic, with the majority consisting of lymphocytic myocarditis (1). All three forms involve direct, viral-mediated myocyte damage or immune-mediated cellular injury (27). Lymphocytic myocarditis is most frequently caused by viruses, but has also been caused by bacterial, fungal, and parasitic infections (28). Giant cell myocarditis is mediated by T-cell-induced inflammation secondary to systemic autoimmune disease (29). Eosinophilic myocarditis is poorly understood, but most cases seem to be associated with drug or allergic hypersensitivity reactions (30).

Myocarditis can be caused by a wide range of infectious and noninfectious etiologies, including bacteria, viruses, parasites, autoimmune disorders, cardiotoxins, and hypersensitivity reactions (25). Infectious etiologies are the most common, with viral infections comprising the majority of cases in Western Europe and North Amer-

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Table 1. Causes of Acute Myocarditis

Autoimmune/systemic disorders	Celiac disease, Churg-Strauss syndrome, granulomatosis with polyangiitis, inflammatory bowel disease (Crohn disease, ulcerative colitis), dermatomyositis, giant cell myocarditis, hypereosinophilic syndrome, Kawasaki disease, systemic lupus erythematosus, lymphofollicular myocarditis, rheumatoid arthritis, sarcoidosis, scleroderma, collagen-vascular diseases, thyrotoxicosis
Cardiotoxins	Anthracyclines, alcohol, arsenic, carbon monoxide, catecholamines, cocaine, cyclophosphamide, heavy metals, methysergide
Hypersensitivity reactions	Penicillin, ampicillin, cephalosporins, tetracyclines, sulfonamides, benzodiazepines, clozapine, loop and thiazide diuretics, methyldopa, smallpox vaccine, tetanus toxoid, tricyclic antidepressants, dobutamine, insect bites (e.g., scorpion, spider, bee, wasp), lithium, venomous snake bites
Infectious	Bacterial: *Chlamydia, Corynebacterium diphtheria, Legionella, Mycobacterium tuberculosis, Mycoplasma, Staphylococcus,* Group A *Streptococcus, Streptococcus pneumoniae, Bartonella, Brucellosis, Vibrio cholera, Neisseria gonorrhea, Haemophilus influenzae* Fungal: *Actinomyces, Aspergillus, Blastomyces, Candida, Nocardia Coccidioides, Cryptococcus, Histoplasmosis, Mucormycosis* Helminthic: Ascariasis, Filariasis, *Echinococcus granulosus, Trichinella spiralis*, Paragonimiasis Protozoal: Amebiasis, Leishmaniasis, *Toxoplasma gondii, Trypanosoma cruzi*, Malaria Rickettsial: *Coxiella burnetii, Rickettsia typhi* Spirochetal: *Borrelia burgdorferi, Leptospira, Treponema pallidum* Viral: Adenoviruses, Arbovirus, Echoviruses, Coxsackie B, Human Cytomegalovirus, Epstein-Barr virus, Human Herpesvirus 6, Hepatitis B Virus, Hepatitis C Virus, Human Immunodeficiency Virus, Influenza A and B virus, Parvovirus B19, Mumps, Poliomyelitis, Rabies, Varicella, Rubella, Yellow fever

ica (23). Chagas disease, caused by *Trypanosoma cruzi*, is one of the most common culprits in South and Central America, whereas Coxsackie B is one of the most common viral causes (25). Although noninfectious etiologies are less common, it is important to consider them as a potential cause, as the etiology can influence the treatment of myocarditis. Drugs can also cause myocardial inflammation by either a direct toxic effect on the heart or by inducing hypersensitivity reactions (31). Among these, anthracycline toxicity is the most common (31). Cocaine has also been increasingly implicated, but there are many other medications that can cause cardiotoxicity and can lead to myocarditis (Table 1) (32).

History and Physical Examination

The history and physical examination of myocarditis vary significantly, which can make the diagnosis challenging (33,34). The condition should be suspected in patients with evidence of heart failure or acute myocardial infarction in the absence of cardiovascular risk factors or with a recent normal angiogram (Fig. 1). Patients may present with a spectrum of signs and symptoms, ranging from mild symptoms with normal hemodynamics to cardiogenic shock and death (1,33–37).

Pediatric patients

Pediatric patients may have a viral prodrome involving respiratory or gastrointestinal symptoms (e.g., fever, malaise, myalgias, cough, vomiting, diarrhea) within 2 weeks prior to the onset of cardiac dysfunction in nearly half of cases (34,38–43). This viral prodrome is more prevalent in males (44–46). Other signs and symptoms in pediatric myocarditis cases include tachycardia (58%), chest pain (45%), lethargy (39%), new murmur (32%), fever (30%), respiratory distress (28–68%), hepatomegaly (27–36%), gastrointestinal symptoms (27%), hypotension

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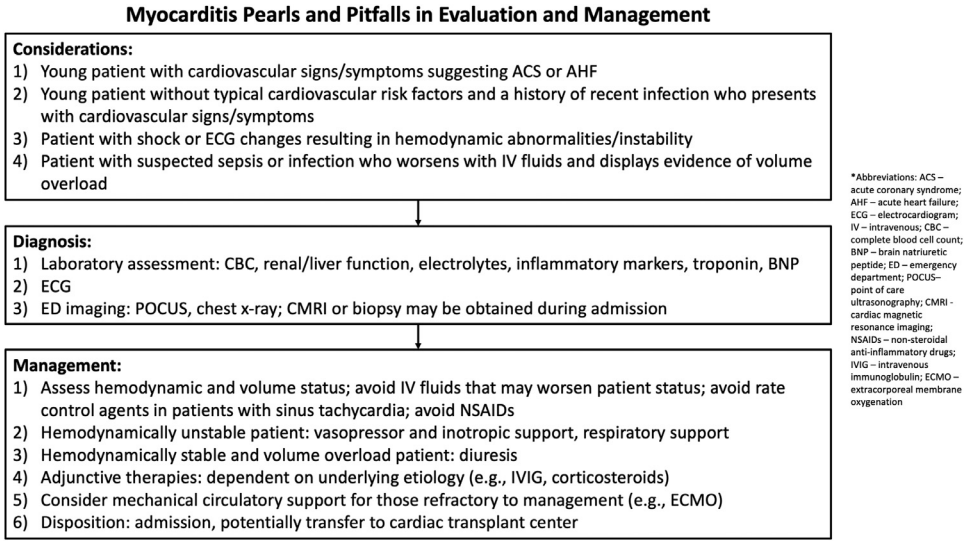

Figure 1.. Myocarditis Pearls and Pitfalls in Evaluation and Management.

(23%), and prolonged capillary refill (16%) (38,47). However, one study of 31 pediatric patients found that tachypnea was the most common sign (38). Patients may also present with symptoms of heart failure, such as dyspnea, exercise intolerance, syncope, hepatomegaly, tachycardia, and tachypnea (34,48–51). Patients with severe cardiac dysfunction may have retractions, rales, cardiac gallops, mitral or tricuspid regurgitation, and shock (34). Sudden death may be the first presentation in up to 9% of cases (10). Supraventricular or ventricular dysrhythmias may occur in 45% of patients at presentation or during hospitalization (51–55). Fulminant myocarditis is a subset of myocarditis and presents as hemodynamic instability with reduced cardiac output and poor perfusion, leading to cardiovascular collapse (55–58). Fulminant myocarditis may present rapidly, creating challenges in appropriately diagnosing and managing the disease prior to death (1,44,45,58).

Adult patients

Myocarditis can be particularly challenging to diagnose in adults, as many patients may present with subacute symptoms (35–37). Early stages of the disease in adults may present with fever, malaise, and myalgias, with one study demonstrating that 89% of adult patients experience a viral prodrome (13). Diffuse muscle tenderness is more common with myotropic viruses, such as coxsackie A (13). Additional symptoms include fatigue, chest pain, palpitations, dyspnea, or edema, frequently 1–4 weeks after a viral illness (1,44,59). One study found the most common presenting symptom in adults was dyspnea in 72%, whereas chest pain occurred in only 32% of patients (35). New or worsening heart failure symptoms may present 2 weeks to 3 months after the viral prodrome as a result of the dilated cardiomyopathy (1,44,60). Signs of right ventricular involvement include peripheral edema, hepatomegaly, and elevated jugular venous pressure, whereas left ventricular involvement is marked by pulmonary congestion and dyspnea. Severe left or right ventricular dilatation may also result in mitral or tricuspid regurgitation, leading to worsening symptoms and a new murmur (1,44,60). Fatigue and exercise intolerance may be early signs (10,61,62). As the disease advances, patients may develop life-threatening dysrhythmias or cardiogenic shock (1,44,60,61). Low systolic blood pressure or syncope is associated with an increased risk of fulminant myocarditis and worse outcomes (60,61).

Laboratory Testing

Initial assessment should include electrocardiography (ECG), complete blood count, renal and liver function, electrolytes, erythrocyte sedimentation rate, C-reactive protein, troponin, and brain natriuretic peptide (1,38,44).

The ECG may be normal or demonstrate nonspecific findings, including ST changes, atrial or ventricular ectopic beats, atrial tachycardias, atrial fibrillation, and ventricular dysrhythmias (37,54,63–65). Although the ECG has a high positive predictive value, the negative predictive value and sensitivity are low (1,44,63). Therefore, a normal ECG should not be used to exclude the diagnosis (25,60,63) ST-segment abnormalities may be present diffusely or in specific anatomic regions, and are associated with more severe forms of myocarditis (25,60,61,63).

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The ECG may also demonstrate findings consistent with pericarditis with diffuse concave ST elevations and PR depressions (61). Heart blocks including high-grade atrioventricular (AV) block can occur in Lyme disease or rheumatologic causes of myocarditis (14,34,49,51,53–55,66–68). One study of 174 biopsy-proven cases of myocarditis reported atrial fibrillation in 6%, a bundle branch block in 15%, and an AV block in 10% (14). Another study of 426 patients with acute myocarditis found that 57.5% had ST elevations, 23.5% had an abnormal ST-T segment, 4.7% had an AV block, and 14.3% had a normal ECG (44). Other findings include abnormal axis, atrial or ventricular enlargement, and decreased voltage (1,48,49,51,63). QRS prolongation > 120 ms, QTc prolongation > 440 ms, ventricular ectopy, and abnormal QRS axis have been associated with poor prognosis in acute myocarditis and are more common in the fulminant form (69,70).

The complete blood count may demonstrate eosinophilia if eosinophilic myocarditis is present. Acute phase reactants are often elevated, though this elevation is not specific. One study found that 99% of adult patients with myocarditis had an elevated erythrocyte sedimentation rate or C-reactive protein (71). However, this elevation does not seem to be associated with worse outcomes (1,38,44). Cardiac troponin levels are commonly elevated in both pediatric and adult patients with myocarditis, especially in those with symptoms for < 1 month (34,37,71–75). Troponin is more commonly elevated in those with acute myocarditis, compared with those with chronic forms of the disease (72,73). The American Heart Association and European Society of Cardiology recommend obtaining troponin to evaluate for myocarditis, though both societies state that the absence of troponin elevation should not be used to exclude myocarditis (37,76). Additionally, the troponin level should not be used as a prognostic factor, though it may reach levels comparable with myocardial infarction (37,47,76). The brain natriuretic peptide level may be elevated due to myocyte distension and reduced cardiac function and can assist in distinguishing heart failure symptoms from noncardiogenic pulmonary conditions (76–79). Over 50% of patients with myocarditis will have an elevated brain natriuretic peptide level (78). Serum aspartate aminotransferase may also be elevated in patients with myocarditis due to the muscle damage (38).

Imaging

Chest radiography is abnormal in over half of patients and can include cardiomegaly, pulmonary edema, and pleural effusions (25,38,80,81). However, a normal chest radiograph cannot be used to exclude the diagnosis.

When highly suspected, echocardiography is one of the most important tests to obtain. Echocardiography can reveal regional wall motion abnormalities and atrial or ventricular chamber dilatation (82–84). Approximately one-quarter of patients will demonstrate decreased left ventricular ejection fraction, which is associated with worse long-term outcomes (44,45). Although diffuse systolic dysfunction is the most common finding, regional or segmental dysfunction may also occur (44,45,82,85). Importantly, early stages of disease can be associated with a normal or mildly reduced ejection fraction on echocardiography (1,44,82). In contrast to left ventricular dysfunction, only 8.5% of patients had right ventricular dysfunction (41). Pericardial effusion has been noted in 26% of patients (41). Echocardiography may also reveal mitral regurgitation, tricuspid regurgitation, or intracardiac thrombi (82). If transthoracic echocardiography is not immediately available, point-of-care ultrasound may be beneficial to assess for cardiac dysfunction or pericardial effusion, though some of the above findings may require more advanced training. Point-of-care ultrasound may also be beneficial for identifying pulmonary edema in the case of a nondiagnostic radiograph (86).

Other testing modalities include cardiac magnetic resonance imaging (CMRI), cardiac catheterization, and endomyocardial biopsy, though these are not typically available or performed in the emergency department (ED) setting (57,82,87–89). CMRI is an imaging modality that provides a functional and morphological assessment of cardiac tissues (82,89–91). CMRI can visualize edema (T2-weighted imaging), hyperemia (T1-weighted imaging), and fibrosis (late gadolinium enhancement) (82,90,91). Overall sensitivity and specificity for CMRI ranges from 68–89% and 74–96%, respectively (89). CMRI sensitivity and specificity are highest in those with acute rather than chronic myocarditis (91–93).

Cardiac catheterization is indicated in patients whose presentation and ECG are indistinguishable from acute coronary syndrome. Definitive diagnosis typically includes endomyocardial biopsy (94). However, biopsy is rarely helpful and has little impact on clinical management. Moreover, if a region that is not affected undergoes biopsy, the result may be falsely negative (90,95,96). The 2010 Heart Failure Society Guideline recommends considering biopsy in those with heart failure of unknown origin (97). Other guidelines recommend biopsy in those with new-onset heart failure within 2 weeks and hemodynamic instability irrespective of left ventricular dilatation, heart failure of 2 weeks to 3 months in duration with a dilated left ventricle, ventricular dysrhythmias, and high-grade atrioventricular block; or symptoms that are unresponsive to therapy within 1–2 weeks (59,98).

Sagar et al. proposed a more practical means of diagnosing myocarditis incorporating history, physical exam-

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Table 2. Three-Tier Classification System for Diagnosing Myocarditis

Classification	Criteria
Possible subclinical acute myocarditis	No cardiovascular symptoms but at least one of the following: elevated cardiac biomarkers, ECG findings suggesting cardiac injury, abnormal cardiac function on echocardiogram, or CMRI
Probable acute myocarditis	Cardiovascular symptoms and at least one of the following: elevated cardiac biomarkers, ECG findings suggesting cardiac injury, abnormal cardiac function on echocardiogram, or CMRI
Definite myocarditis	Histological or immune-histological evidence of myocarditis

Adapted from Sagar et al. (99).
ECG = electrocardiogram; CMRI = cardiac magnetic resonance imaging.

ination, laboratory, and echocardiographic findings into a three-tier classification system (99). This system can be used in the ED for "possible" or "probable" diagnosis, but "definite" requires histological or immunohistological evidence (Table 2) (99).

Management

Hemodynamic support

The goals of therapy for myocarditis are based on the patient's hemodynamic and volume status, which may include inotropic support, afterload reduction, diuresis, and ventilatory support. It is important to assess the patient's volume status and avoid excessive intravenous fluids that can worsen symptoms (100,101). In patients who are hemodynamically unstable, vasopressors are recommended. Norepinephrine can provide vascular tone, as well as cardiac contractility and inotropy due to its combined alpha and beta agonism (102). Epinephrine has predominantly inotropic effects at low doses (0.01–0.05 μg/kg/min i.v.), though with escalation, vasoconstrictive properties predominate with adrenergic agonism, increasing not only afterload but also the risk of tachycardias and dysrhythmias in acute decompensated heart failure (103). In a multinational study evaluating inotropes and vasopressors in cardiogenic shock, epinephrine was associated with an increase in 90-day mortality as well as worsening renal and cardiac markers (104). Similarly, a recent meta-analysis demonstrated a threefold increase in short-term mortality with epinephrine use in cardiogenic shock (105). Therefore, norepinephrine combined with an inotropic agent is preferred over epinephrine monotherapy in these patients (105).

For patients with normal blood pressure but depressed ejection fraction, inotropic support is recommended with agents such as dobutamine or milrinone. If initiating an inotrope, providers should be prepared to administer a vasopressor due to the risk of hypotension. Milrinone serves as an afterload reduction agent, with the additional benefit of dilating pulmonary vasculature and improving hemodynamics in acute decompensated heart failure; however, this agent has a long half-life and is more dysrhythmogenic than dobutamine (106–108). One study of pediatric patients that administered a loading dose of 50 ug/kg over 5 min reported an increase in cardiac index by 18%, with a decrease in the mean arterial pressure by 12%, highlighting both the inotropic potency and the risk of hypotension from this medication (109). Among the two agents, dobutamine may be preferable due to its lower risk of side effects and shorter half-life (110,111).

Although angiotensin-converting enzyme inhibitors and beta-blockers prevent ventricular remodeling and relieve vasospasm after myocarditis, they should only be administered once the patient is hemodynamically stable, likely after hospital admission (112,113). In patients with evidence of volume overload, diuretics (e.g., furosemide) may assist in returning to a euvolemic state with careful monitoring of hemodynamic status (114).

Respiratory support

Noninvasive positive pressure ventilation provides pulmonary support while reducing left ventricular afterload and therefore, left ventricular wall tension (90). This should be considered early in the management of patients with myocarditis who have pulmonary edema with respiratory distress. Patients with respiratory failure at presentation or those who fail noninvasive ventilation measures should be intubated. In addition to respiratory support and afterload reduction, intubation may also decrease the oxygen consumption of the myocardium and respiratory muscles (115). However, intubation in patients with myocardial dysfunction can be challenging, particularly given their tenuous hemodynamics. Optimizing preintubation hemodynamics and preload will help mitigate these risks. In patients with a normal or low blood pressure, a lower dose of etomidate or ketamine (i.e., etomidate 0.1 mg/kg i.v. or ketamine 0.1–0.3 mg/kg i.v.) is recommended to reduce the risk of further hemodynamic compromise during induction (19,116,117).

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Clinicians should consider having vasopressors immediately available in case the blood pressure acutely lowers.

Adjunctive therapies

Additional agents remain controversial and vary in efficacy based on the underlying etiology. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided, as NSAIDs may worsen mortality in myocarditis patients (44). For adult patients with idiopathic acute myocarditis, neither corticosteroids nor intravenous immunoglobulin (IVIG) have demonstrated improved outcomes (118,119). In a trial of 111 biopsy-confirmed adult patients with acute myocarditis from any etiology, prednisone with either azathioprine or cyclosporine did not decrease transplant-free survival or improve left ventricular ejection fraction as compared with placebo (13). Two retrospective studies of IVIG in pediatric patients with acute decompensated myocarditis also demonstrated no benefit in clinical outcome (120,121). However, in a subset of adult patients with acute myocarditis secondary to Parvovirus B19 and a high viral load, high-dose IVIG at 2 g/kg was found to improve their New York Heart Association functional class and left ventricular ejection fraction (122). Additionally, IVIG has demonstrated benefit, specifically in pediatric acute decompensated myocarditis, improving left ventricular function and decreasing the number of fulminant dysrhythmias (123). Although IVIG has demonstrated short- and long-term benefit in some studies, others have demonstrated equivocal findings (124–126). Therefore, further randomized controlled trials are needed to further characterize the role of IVIG before it can be recommended for routine use.

For patients with myocarditis from giant cell or eosinophilic myocarditis, corticosteroids are the foundation of treatment to correct the underlying condition. When given in conjunction with immunosuppressants (e.g., cyclosporine, sirolimus, muromonab), patients with giant cell myocarditis receiving corticosteroids have increased transplant-free survival (27,127). In contrast, although in vitro data suggested a potential benefit, there are no data to suggest that antiviral agents (e.g., ribavirin) improve outcomes in vivo (128–130).

Mechanical circulatory support

Mechanical circulatory support (e.g., intra-aortic balloon pump, extracorporeal membrane oxygenation, ventricular assist device) should be considered in patients with refractory hypotension despite vasopressors and inotropic support (131,132). Intra-aortic balloon pump (IABP) allows for ventricular support by increasing systolic blood pressure while offloading afterload and myocardial oxygenation demands (132). In a trial of adult acute decompensated myocarditis patients, IABP deployed within the first 24 h of presentation decreased mortality compared with deployment after 24 h 133. However, this may be inadequate in isolation and may require further escalation to extracorporeal membrane oxygenation (ECMO) in refractory cases (131,132).

Among pediatric patients hospitalized with myocarditis, one study reported the use of ECMO in 20% of patients, with 80% surviving to discharge, and 60% of these patients having full myocardial recovery (134). A separate study of pediatric myocarditis cases from the Extracorporeal Life Support Organization registry reported a 61% survival-to-discharge rate using multicenter data from 1995–2006 (135). In adult myocarditis patients requiring ECMO, 46–85% of patients survived to discharge (131,136–141). Survival was correlated with the precannulation left ventricular function, as well as the overall improvement in left ventricular function (136,137). One study found that pediatric patients with fulminant myocarditis receiving ECMO had slightly better outcomes than adults (71% vs. 61% survival) (131). In those who respond to ECMO, left ventricular improvement will usually be seen within the first week, whereas those on ECMO for more than 2 weeks or with evidence of dysrhythmia, end-organ damage, or need for dialysis tend to have worse outcomes and higher mortality (142,143).

In contrast to ECMO, ventricular assist devices (VADs) allow for single-ventricle support. VADs are increasingly used in pediatric myocarditis, as they allow for bridging to transplantation (144). One study demonstrated a 27% mortality and a 67% successful transplant rate (144). Decisions regarding which therapeutic option is best for a given patient will often be made in concert with a cardiologist or cardiothoracic surgeon, so it is important to involve them early in the care of critically ill patients who are refractory to vasopressors and inotropes.

Disposition

All patients with acute myocarditis should be admitted. Patients with hypotension or receiving i.v. vasopressors or inotropes should be admitted to an intensive care unit. Among patients with acute myocarditis, 50% will recover fully, 30% will decompensate, and 20% will require transplantation (37). One retrospective review found that New York Heart Association class III or IV, histological signs of inflammation, late gadolinium enhancement (especially in a septal distribution), and ejection fraction $< 40\%$ were associated with increased rates of death or cardiac transplantation (145). Therefore, patients with these findings may benefit from transfer to the nearest cardiac transplant center (145). Patients with worsening clinical decompensation or evidence of fulminant myocarditis should be transferred to facilities with ECMO or LVAD capabilities, as these are often required in refractory cases (142,146,147).

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Conclusion

Myocarditis is a potentially fatal condition, wherein inflammation of the heart musculature causes cardiac dysfunction. Symptoms may vary from mild to severe and are often preceded by a viral prodrome. Laboratory assessment and an ECG can assist with the diagnosis, but echocardiography is the ideal test in the ED setting. Some patients may also require advanced imaging, though this will often occur during hospitalization or follow-up. Treatment is primarily focused on respiratory and hemodynamic support. Initial hemodynamic management often includes vasopressors and inotropes, though more severe cases may require an IABP, ECMO, or an VAD. NSAIDs should be avoided while IVIG is controversial. It is important for emergency clinicians to be aware of the diagnosis and management of acute myocarditis.

Clinical Bottom Line

A. The physician performs a point-of-care ultrasound examination of the heart and lungs, noting markedly limited cardiac activity and diffuse B lines consistent with pulmonary edema. The physician stops the intravenous fluids, initiates diuretics, and starts an inotropic agent. The physician also contacts the vascular surgery team for consideration of ECMO.

B. The physician obtains an electrocardiogram, chest radiograph, and laboratory testing, including a troponin. The physician then performs a point-of-care cardiac ultrasound and identifies diffusely decreased cardiac activity consistent with myocarditis. The physician gives the patient a diuretic, consults Cardiology, and admits the patient for further evaluation and management.

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ARTICLE SUMMARY

1. Why is this topic important?

Myocarditis is a condition with the potential for significant morbidity and mortality, which may be misdiagnosed in the emergency department.

2. What does this review attempt to show?

This review summarizes the background, pathophysiology, diagnosis, and management of myocarditis.

3. What are the key findings?

Myocarditis symptoms can range from mild to severe and are often preceded by a viral prodrome. Laboratory assessment and electrocardiogram can be helpful in diagnosis, but echocardiography is the ideal test. Treatment can include vasopressors, inotropes, intra-aortic balloon pump, extracorporeal membrane oxygenation, or a ventricular assist device.

4. How is patient care impacted?

By understanding the current evidence regarding the diagnosis, management, and disposition of patients with myocarditis, clinicians can better identify and treat these patients.

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