Myocarditis

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Definition

- Myocarditis is an inflammatory disease of the myocardium caused by different infectious and noninfectious triggers.

- Dilated Cardiomyopathy & Heart Failure are the most significant long term morbidity.

Etiology

Table 1 Causes of myocarditis

Viruses/disorders	Bacteria/disorders	Cardiotoxins	Hypersensitivity
Adenovirus*	*Chlamydia*	Ethanol*	Cephalosporins
Coxsackievirus B*	Cholera	Anthracycline drugs*	Clozapine
Cytomegalovirus*	*Mycoplasma*	Arsenic	Diuretics
Epstein–Barr virus	*Neisseria*	Carbon monoxide	Insect bites
Hepatitis C virus	*Salmonella*	Catecholamines	Lithium
Herpes simplex virus	*Staphylococcus*	Cocaine*	Snake bites
HIV*	*Streptococcus*	Heavy metals	Sulfonamides
Influenza virus	Tetanus	Copper	Tetanus toxoid
Mumps	Tuberculosis	Mercury	Tetracycline
Parvovirus B19		Lead	
Poliovirus	**Spirochetal**		**Systemic disorders**
Rabies	Leptospirosis	**Protozoa**	Hypereosinophilia
Rubella	Lyme disease	Chagas disease	Kawasaki disease
Varicella zoster virus	Relapsing fever	Leishmaniasis	Sarcoidosis
Yellow fever	Syphilis	Malaria	Wegener granulomatosis

*Frequent cause of myocarditis.

- Viruses are the most common agents.
- The spectrum of viruses shifted from *coxsackievirus B* to *adenovirus* in the late 1990s.
- Adenoviral infections can be much more virulent than coxsackievirus and can cause extensive cell death without comparable inflammatory response.

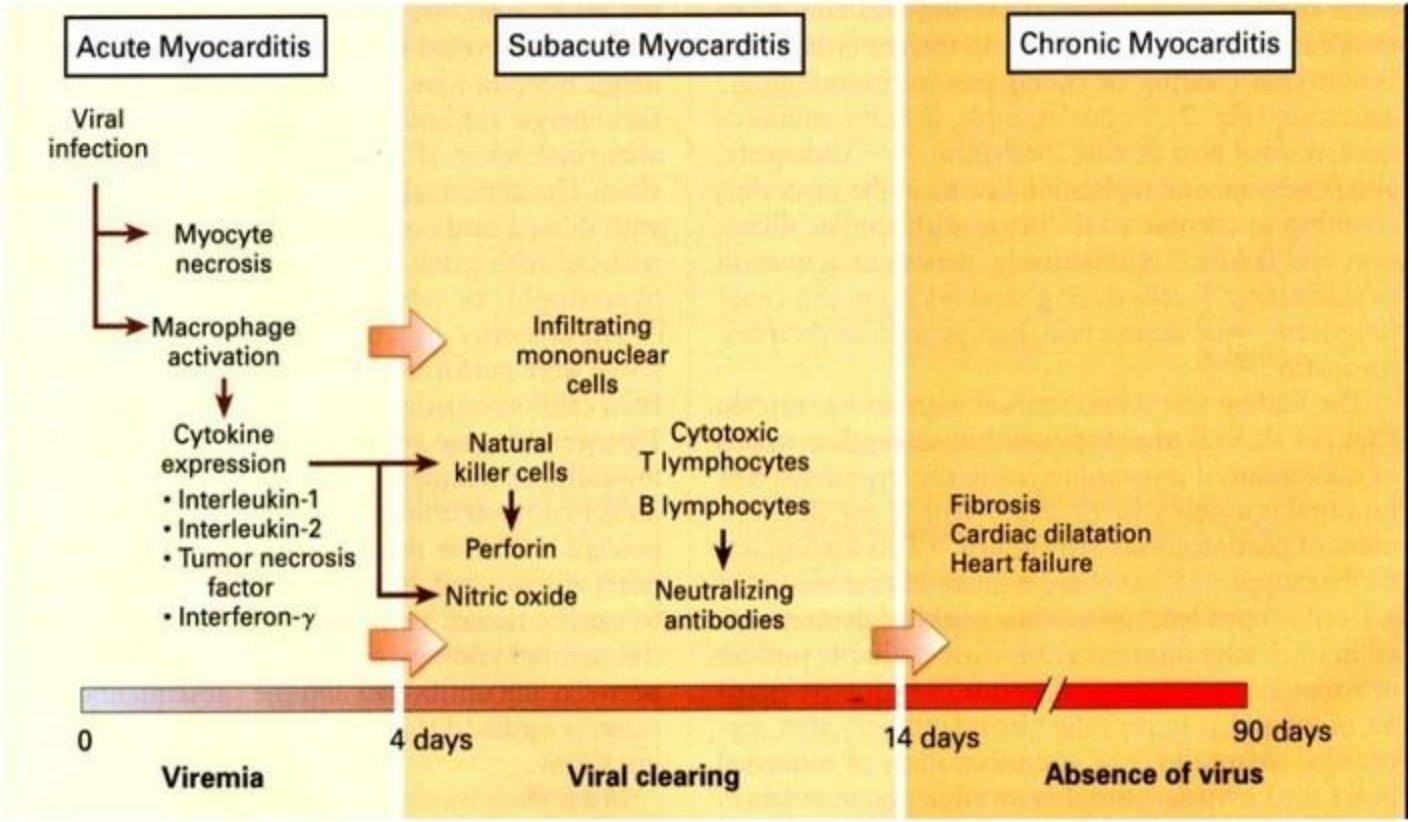
Statistics

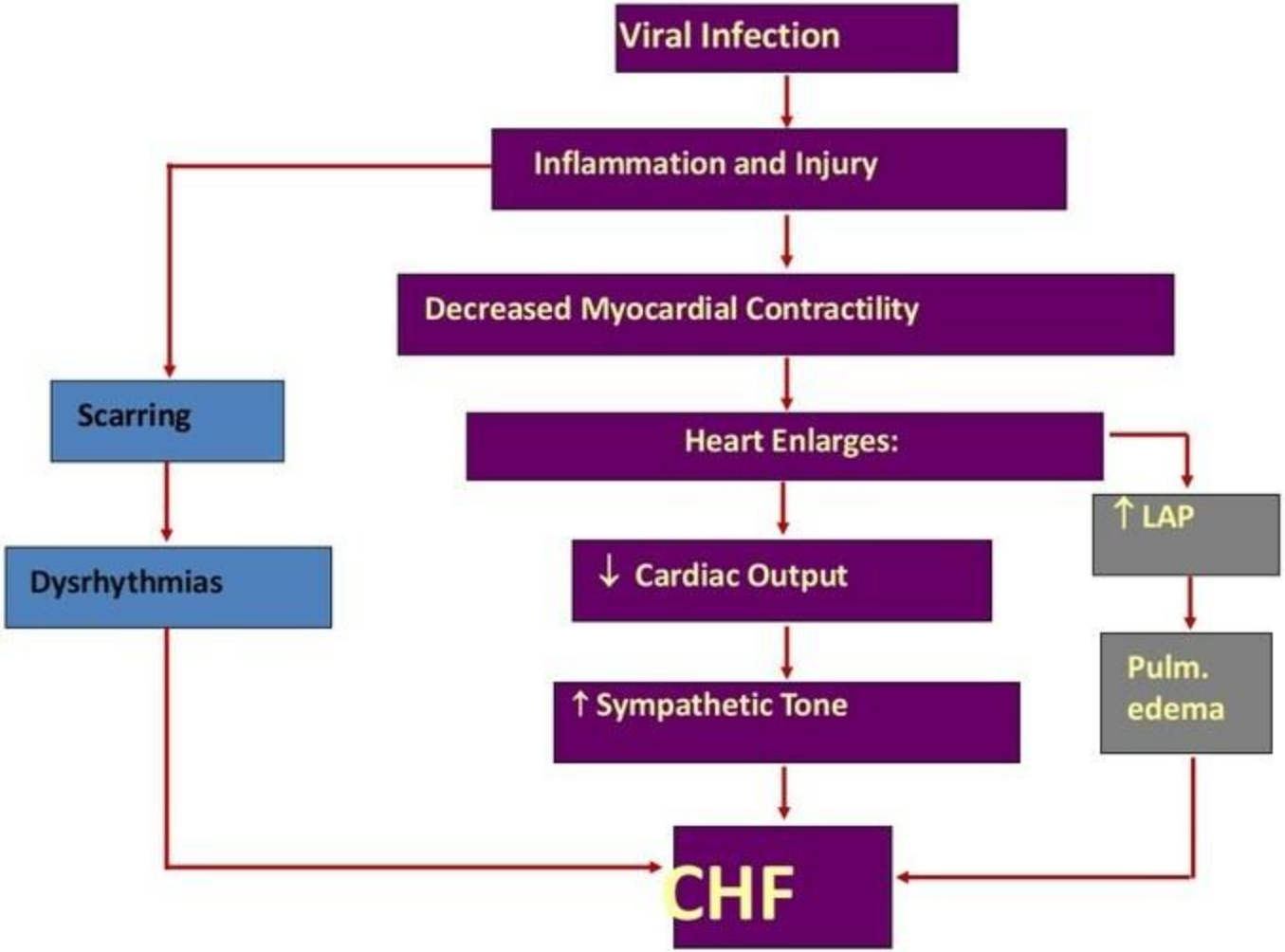
- Bowles & coworkers analyzed biopsy specimens from 624 patients with PCR and found overall viral positivity was 38% (239/624).

- On analysis,22.8% tested positive for adenovirus, 13.6% for enterovirus and 1% for parvovirus.

Bowles et al, JACC 42:466,2003

Pathophysiology




Viral Infection
Inflammation and Injury
Decreased Myocardial Contractility
Scarring
Heart Enlarges:
↑ LAP
Dysrhythmias
↓ Cardiac Output
Pulm. edema
↑ Sympathetic Tone
CHF

Clinical Features

- Acute Viral Myocarditis often presents with Heart Failure with preceding fever & myalgias.
- Chest Pain(due to Pericarditis or myocardial injury & destruction)
- Palpitations(due to Arrhythmia's)

- Rapid progressions from a febrile respiratory syndrome to Cardiogenic Shock(discharged from Urgent care settings for Viral illness)

- **Sudden death** (in young adults, myocarditis causes up to 20% of all cases of sudden death).

Important types of Myocarditis

1. ***Chagas Diseases***

- Most common Infective cause.
- Endemic in Rural areas of South & Central America
- Chronic infection leads to Conduction system anomaly, AF, Ventricular Tachyarrhythmia.
- Treatment- HF medications & benznidazole-Nifurtimox.

2.Granulomatous Myocarditis

- ***Sarcoidosis***
- Rapid onset HF & ventricular Tachyarrhythmia's
- Conduction block
- ***Giant cell Myocarditis***
- Typically with Rapidly progressive HF & ventricular Tachycardia
- Diffuse Granulomatous lesion surrounded by extensive inflammatory infiltrate in endomyocardial biopsy

Diagnosis

- **ECG**- changes widely variable & non-specific-

1. Non specific ST segment & T wave changes
2. Sinus tachycardia
3. Ventricular arrhythmia's
4. AV conduction defects

Cardiac Biomarkers

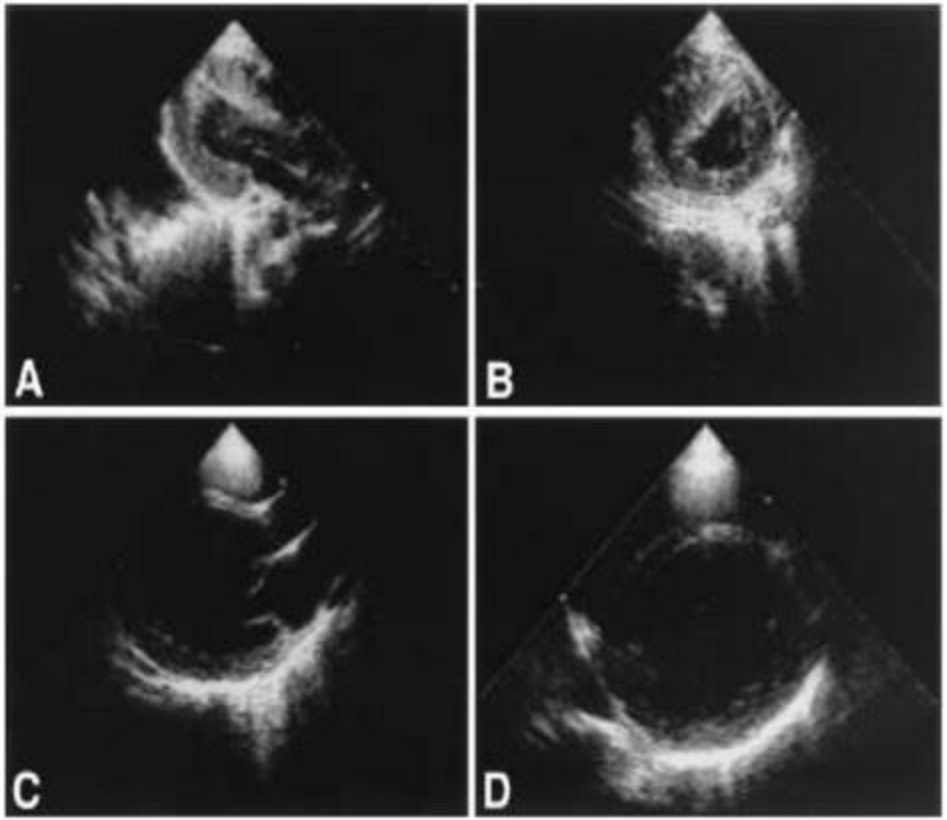
- Cardiac Troponins more sensitive than CPK-MB.

- Largely nonspecific

Echocardiography

- Rule out non-inflammatory cardiac disease such as valve disease and to monitor changes in cardiac chamber size, wall thickness, ventricular function, and pericardial effusions.

- Global ventricular dysfunction, regional wall motion abnormalities may occur in myocarditis.



Fulminant Myocarditis

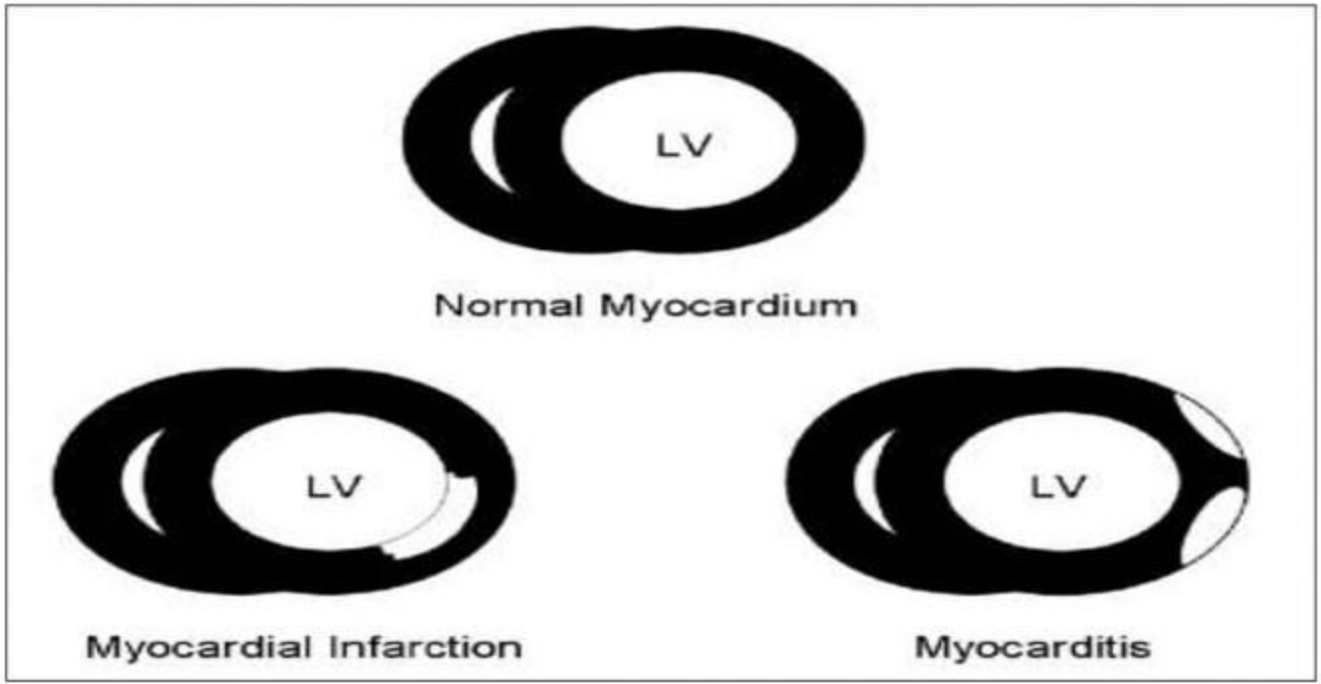
Acute Myocarditis

MRI of Heart

MRI is emerging as an important tool for the diagnosis and follow-up of patients with acute myocarditis

MRI can also play a role in discriminating **myocarditis** from **myocardial infarction**, which can help in the evaluation of acute chest pain.

In myocarditis the infiltrates are characteristically located in the mid-wall and tend to spare the sub-endocardium,whereas in infarction, the sub-endocardium is involved first.



Gold Standard

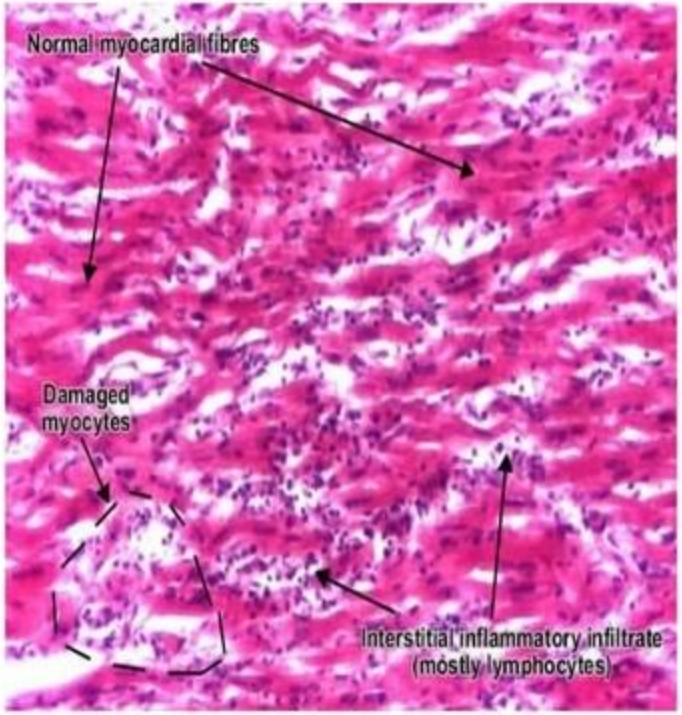
- ***Endomyocardial Biopsy(Dallas Criteria)***
- At least 5 separate biopsy specimens

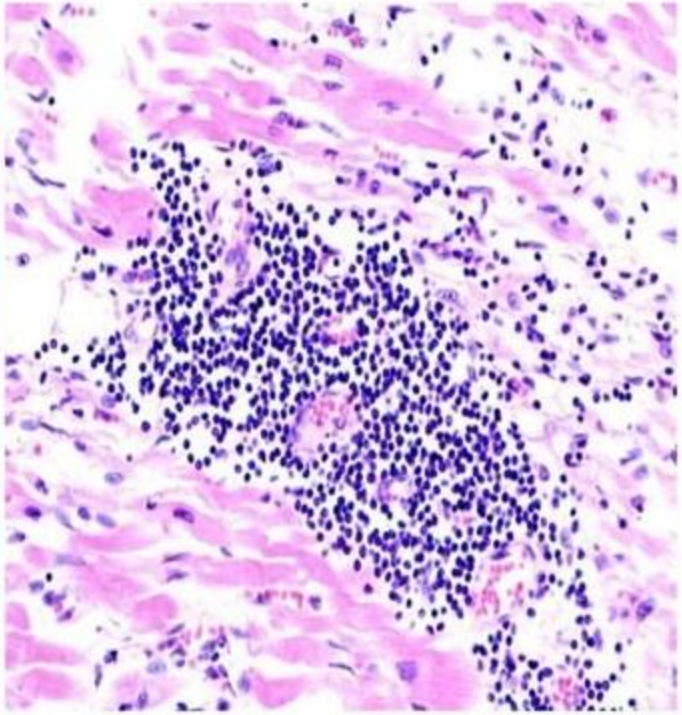
- First Biopsy- Myocyte necrosis or degeneration or both associated with an inflammatory infiltrate adjacent to the degenerating or necrotic myocyte.

Subsequent Changes

- Ongoing(persisting) Myocarditis with or without fibrosis
- Resolving(healing) Myocarditis with or without Fibrosis
- Resolved(healed) Myocarditis with or without Fibrosis

Histological Picture





- *Chow and McManus* demonstrated that with a single EMB sample, histologic myocarditis could be demonstrated in only 25% of cases. Even with 5 random samples, correct diagnosis by classic Dallas criteria could be reached in only about 2/3rd of subjects.

Clinical Classification

1. Possible subclinical Acute Myocarditis

- ❑ Typical Viral syndrome without cardiac symptoms with one or more of following-
- Elevated Cardiac Biomarkers
- ECG findings suggestive of Acute Injury
- Reduced LVEF
- Abnormality in Cardiac Imaging

2. Probable Acute Myocarditis

- Previous criteria accompanied by Cardiac symptoms.

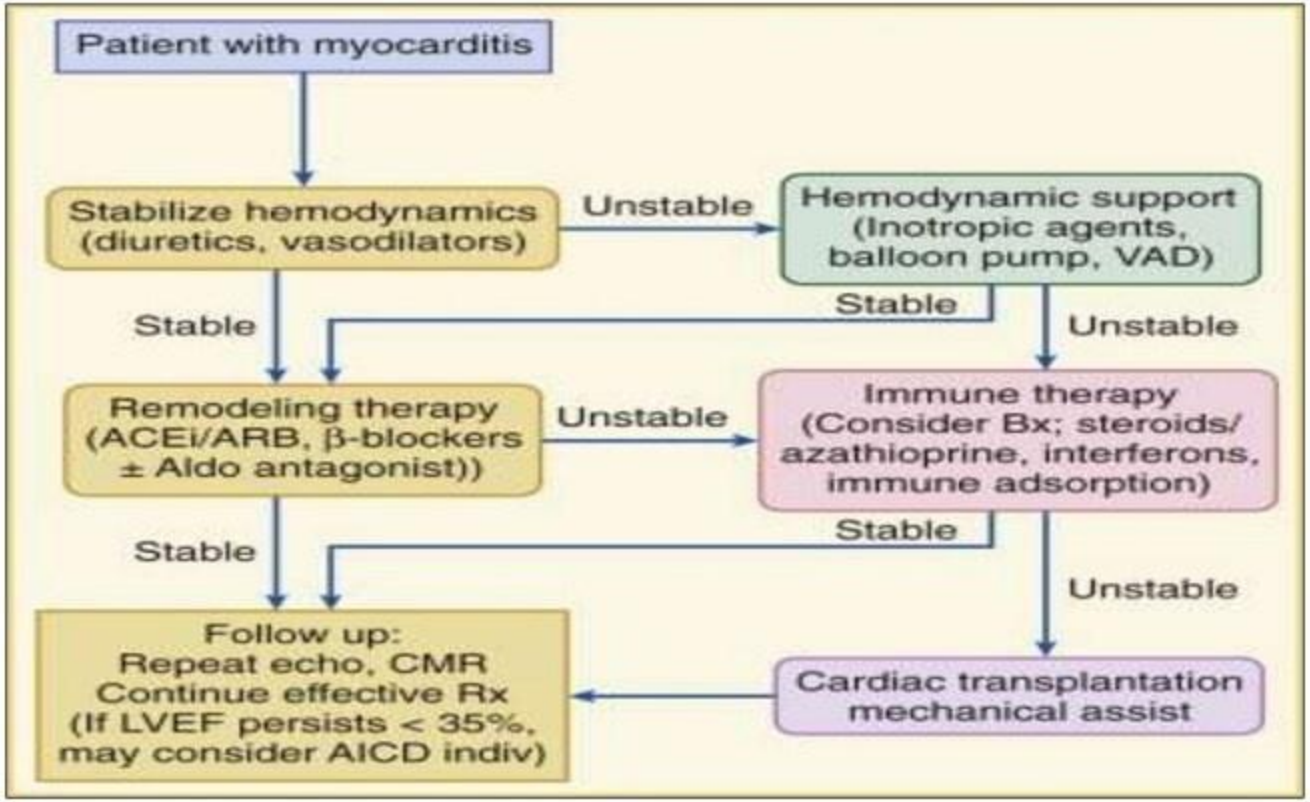
3. Definite Myocarditis

- Previous criteria plus histological evidence

Treatment

- The core principles of treatment in myocarditis are optimal care of arrhythmia and of heart failure
- Patients with LV dysfunction or symptomatic HF should follow current HF therapy guidelines, including diuretics and ACE inhibitors or ARBs

Management Algorithm



Immunosuppresion

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A CLINICAL TRIAL OF IMMUNOSUPPRESSIVE THERAPY FOR MYOCARDITIS

JAY W. MASON, M.D., JOHN B. O'CONNELL, M.D., AHVIE HERSKOWITZ, M.D., NOEL R. ROSE, M.D., PH.D., BRUCE M. MCMANUS, M.D., PH.D., MARGARET E. BILLINGHAM, M.D., THOMAS E. MOON, PH.D., AND THE MYOCARDITIS TREATMENT TRIAL INVESTIGATORS*

111 patients of myocarditis and LVEF < 45% were randomly assigned to conventional therapy alone or combined with 24 weeks of immunosuppressive therapy

Abstract *Background. Myocarditis is a serious disorder, and treatment options are limited. This trial was designed to determine whether immunosuppressive therapy improves left ventricular function in patients with myocarditis.*

Methods. We randomly assigned 111 patients with a histopathological diagnosis of myocarditis and a left ventricular ejection fraction of less than 0.45 to receive conventional therapy alone or combined with a 24-week regimen of immunosuppressive therapy. Immunosuppressive therapy consisted of prednisone with either cyclosporine or azathioprine. The primary outcome measure was a change in the left ventricular ejection fraction at 28 weeks.

Results. In the group as a whole, the mean (±SE) left ventricular ejection fraction improved from 0.25±0.01 at base line to 0.34±0.02 at 28 weeks (P<0.001). The mean change in the left ventricular ejection fraction at 28 weeks did not differ significantly between the group of patients who received immunosuppressive therapy (a gain of 0.10; 95 percent confidence interval, 0.07 to 0.12) and the control group (a gain of 0.07; 95 percent confidence interval, 0.03 to 0.12). A higher left ventricular ejection fraction at base line, less intensive conventional drug therapy at base line, and a shorter duration of disease, but not the treatment assignment, were positive independent predictors of the left ventricular ejection fraction at week 28. There was no significant difference in survival between the two groups (P=0.96). The mortality rate for the entire group was 20 percent at 1 year and 56 percent at 4.3 years. Features suggesting an effective inflammatory response were associated with less severe initial disease.

Conclusions. Our results do not support routine treatment of myocarditis with immunosuppressive drugs. Ventricular function improved regardless of whether patients received immunosuppressive therapy, but long-term mortality was high. (N Engl J Med 1995;333:269-75.)

- C Hia W Yip & S Quek(2012) concluded that Immunosuppression doesn’t significantly change the outcome.
- Frustaci et all(dept. of Cardiology,Catholic Univ. Rome,2014) concluded that Active Lymphocytic Myocarditis those with circulating autoAb & no Viral Genome can benefit from Immunosuppression.

The New England Journal of Medicine

IDIOPATHIC GIANT-CELL MYOCARDITIS — NATURAL HISTORY AND TREATMENT

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ABSTRACT

Background Idiopathic giant-cell myocarditis is a rare and frequently fatal disorder. We used a multicenter data base to define the natural history of giant-cell myocarditis and the effect of treatment.

Methods We identified 63 patients with idiopathic giant-cell myocarditis through journal announcements and direct mailings to cardiovascular centers worldwide.

Results The patients consisted of 33 men and 30 women with an average age of 42.6 years; 88 percent were white, 5 percent were black, 5 percent were Southeast Asian or Indian, and 2 percent were Middle Eastern. Most presented with congestive heart failure (47 patients, or 75 percent), ventricular arrhythmia (9 patients, or 14 percent), or heart block (3 patients, or 5 percent), although in some cases the initial symptoms resembled those of acute myocardial infarction (4 patients). Nineteen percent had associated autoimmune disorders. The rate of survival was worse than among 111 patients with lymphocytic myocarditis in the Myocarditis Treatment Trial ($P<0.001$); among our patients, the rate of death or cardiac transplantation was 89 percent, and median

survival was only 5.5 months from the onset of symptoms. The 22 patients treated with corticosteroids and cyclosporine, azathioprine, or both therapies survived for an average of 12.3 months, as compared with an average of 3.0 months for the 30 patients who received no immunosuppressive therapy ($P=0.001$). Of the 34 patients who underwent heart transplantation, 9 (26 percent) had a giant-cell infiltrate in the transplanted heart and 1 died of recurrent giant-cell myocarditis.

Conclusions Giant-cell myocarditis is a disease of relatively young, predominantly healthy adults. Patients usually die of heart failure and ventricular arrhythmia unless cardiac transplantation is performed. Despite the possibility of fatal disease recurrence, transplantation is the treatment of choice for most patients. (N Engl J Med 1997;336:1860-6.)

- These studies suggest that immunosuppression is having a doubtful value in the routine treatment of acute lymphocytic myocarditis.

- But,transplant-free survival in patients with giant-cell myocarditis may be prolonged with a combination of cyclosporine and corticosteroids