

Recommendations for Treatment, Lifestyle and Exercise in Myocarditis

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Overview

- Medical treatment
- Lifestyle
- Exercise

Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Identify the Cause

- Why does this patient have myocarditis

Table 1 Causes of myocarditis/inflammatory cardiomyopathy

1. Infectious myocarditis

Bacterial	<i>Staphylococcus, Streptococcus, Pneumococcus, Meningococcus, Gonococcus, Salmonella, Corynebacterium diphtheriae, Haemophilus influenzae, Mycobacterium (tuberculosis), Mycoplasma pneumoniae, Brucella</i>
Spirochaetal	<i>Borrelia</i> (Lyme disease), <i>Leptospira</i> (Weil disease)
Fungal	<i>Aspergillus, Actinomyces, Blastomyces, Candida, Coccidioides, Cryptococcus, Histoplasma, Mucormycoses, Nocardia, Sporothrix</i>
Protozoal	<i>Trypanosoma cruzi, Toxoplasma gondii, Entamoeba, Leishmania</i>
Parasitic	<i>Trichinella spiralis, Echinococcus granulosus, Taenia solium</i>
Rickettsial	<i>Coxiella burnetii</i> (Q fever), <i>R. rickettsii</i> (Rocky Mountain spotted fever), <i>R. tsutsugamuschi</i>
Viral	RNA viruses: Coxsackieviruses A and B, echoviruses, polioviruses, influenza A and B viruses, respiratory syncytial virus, mumps virus, measles virus, rubella virus, hepatitis C virus, dengue virus, yellow fever virus, Chikungunya virus, Junin virus, Lassa fever virus, rabies virus, human immunodeficiency virus-1 DNA viruses: adenoviruses, parvovirus B19, cytomegalovirus, human herpes virus-6, Epstein-Barr virus, varicella-zoster virus, herpes simplex virus, variola virus, vaccinia virus

2. Immune-mediated myocarditis

Allergens	Tetanus toxoid, vaccines, serum sickness Drugs: penicillin, cefaclor, colchicine, furosemide, isoniazid, lidocaine, tetracycline, sulfonamides, phenytoin, phenylbutazone, methyl dopa, thiazide diuretics, amitriptyline
Alloantigens	Heart transplant rejection
Autoantigens	Infection-negative lymphocytic, infection-negative giant cell Associated with autoimmune or immune-oriented disorders: systemic lupus erythematosus, rheumatoid arthritis, Churg-Strauss syndrome, Kawasaki's disease, inflammatory bowel disease, scleroderma, polymyositis, myasthenia gravis, insulin-dependent diabetes mellitus, thyrotoxicosis, sarcoidosis, Wegener's granulomatosis, rheumatic heart disease (rheumatic fever)

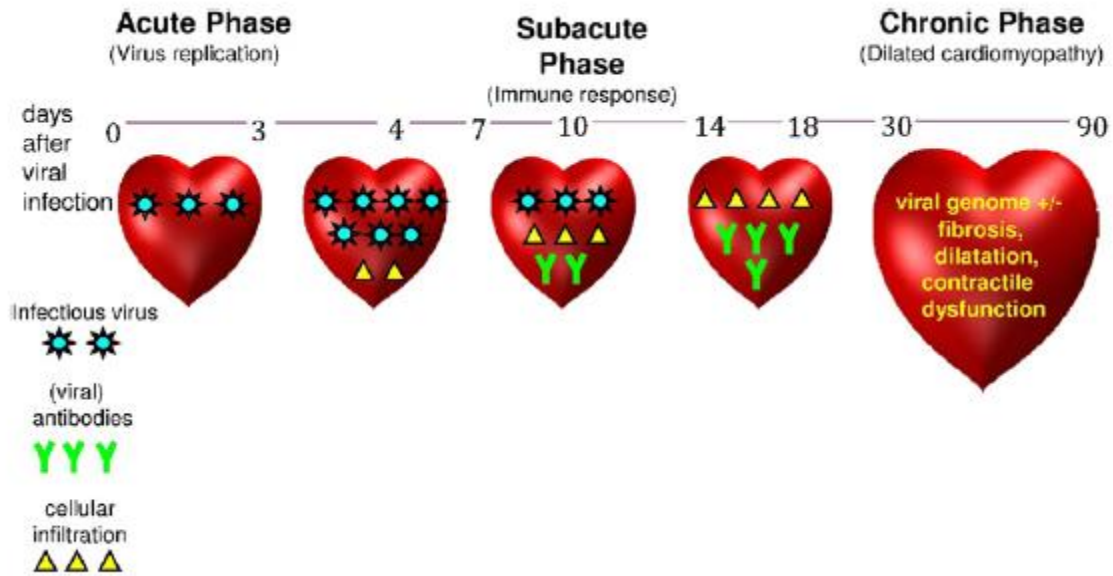
3. Toxic myocarditis

Drugs	Amphetamines, anthracyclines, cocaine, cyclophosphamide, ethanol, fluorouracil, lithium, catecholamines, hemetine, interleukin-2, trastuzumab, clozapine
Heavy metals	Copper, iron, lead (rare, more commonly cause intramyocyte accumulation)
Miscellaneous	Scorpion sting, snake, and spider bites, bee and wasp stings, carbon monoxide, inhalants, phosphorus, arsenic, sodium azide
Hormones	Phaeochromocytoma, vitamins: beri-beri
Physical agents	Radiation, electric shock

More Recent Causes

- Impact of Immune Checkpoint Inhibitors
- cardiotoxicity

Time Course



The Challenge

- Many diseases
- Think about a viral screen
- Is there a rheumatological condition ?
- Treatment of symptoms
- Treat if heart-failure or dilated cardiomyopathy
- Treatment of heart rhythm disturbances

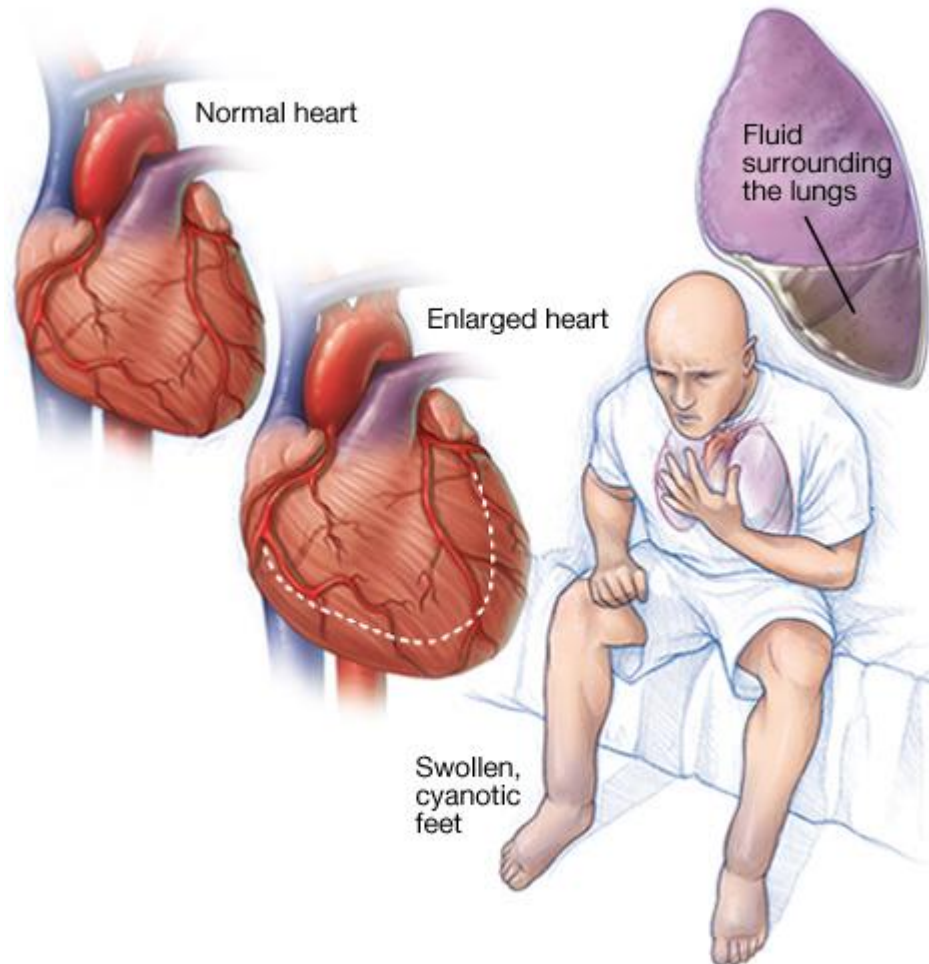
Majority of Patients

- Mild symptoms
- Conservative measures
- Pain control with colchicine
- (Occasionally with Non-steroidal drugs)
 - In experimental models have been associated with worse outcomes but ?

Depends on how severe it is and what caused it.

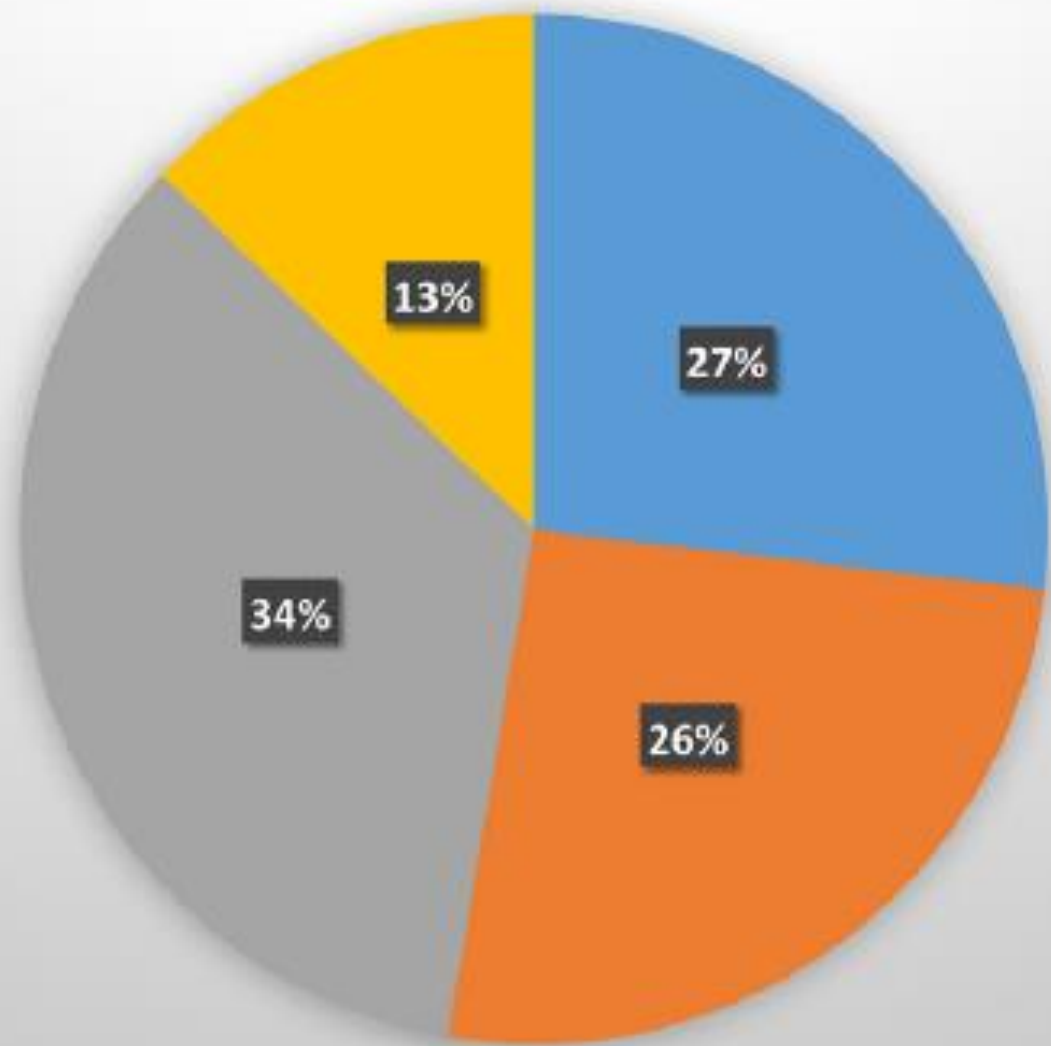
- Treatments can include:
 - Medicines – Depending on the situation, doctors can give medicines to:
 - Help you breathe better
 - Keep fluid from building up
 - Help keep the heart beating correctly
 - Stop blood clots from forming inside the body
 - Help with inflammation
 - Rest – Talk to your doctor about how much activity is right for you.
 - Oxygen – Some people need to breathe oxygen from a tank they carry with them.
 - NOT drinking alcohol, or having no more than 1 drink a day

Heart Failure



Heart-Failure

- Dilated Cardiomyopathy
 - Oxygen
 - Water tablets
 - ACE Inhibitors
 - Beta-blockers



N=210

■ Normal ■ Recover ■ Improved ■ Impaired

Is there Still Active Inflammation

- Supportive measures
- If symptoms still persist, no virus identified and reduced heart function, consider steroids or azathioprine for 12 months
- - 'immunosuppressants' in selected patients
 - Variable effect
 - Evaluation difficult as many make a spontaneous recovery

Virus-Identified

- Biopsy performed, virus has been identified
- If heart function ok, monitor
- If heart function reduced, think about antiviral therapy or interferon
- Possible role for steroids
 - May improve/stabilise heart function
 - Unclear if it changes outcomes

Viral Infection, Severe Reduction in Heart Function and Rhythm Disturbances

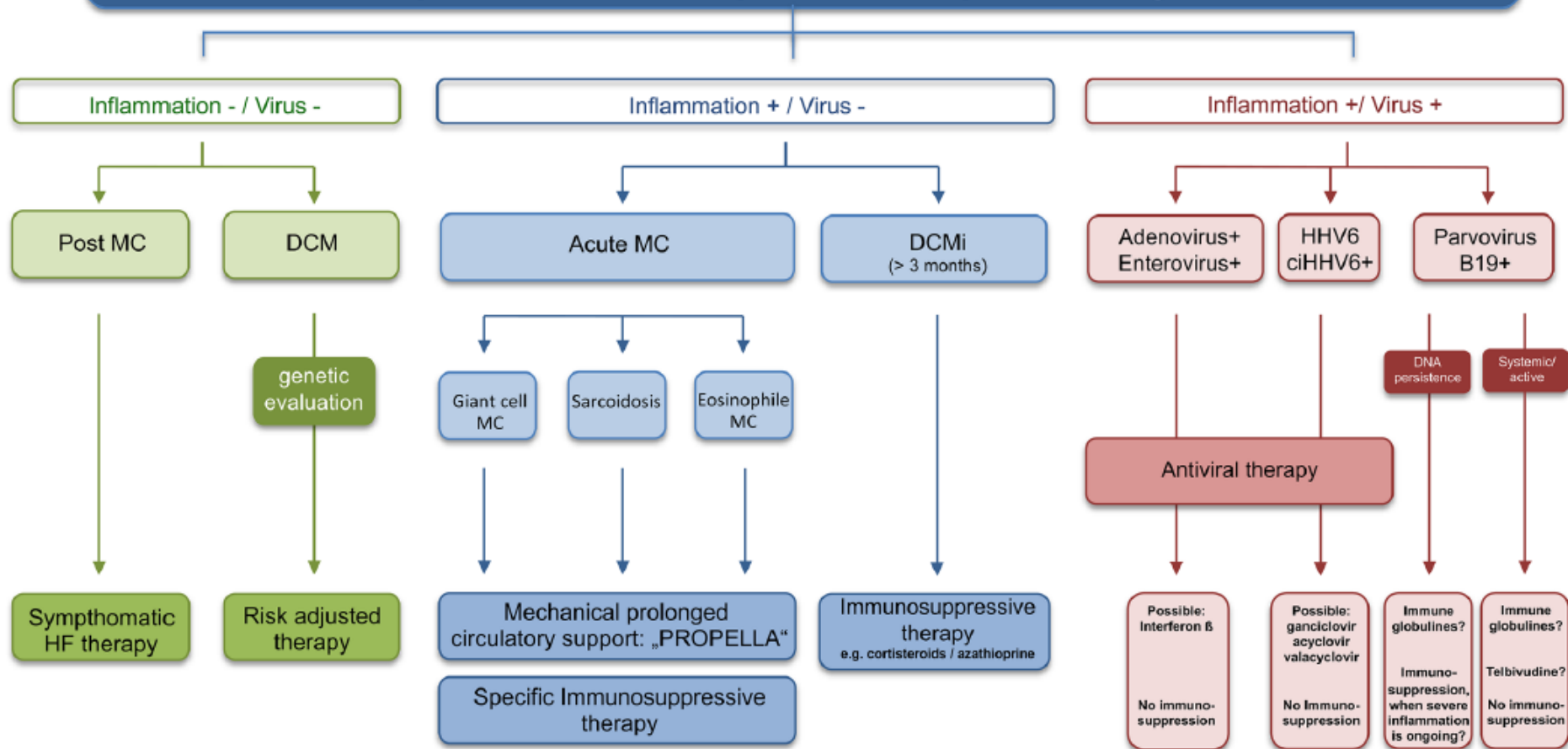
- Both fast and slow rhythm disturbances can occur
- Often resolve after the acute phase
- Often avoided if asymptomatic
- Occasionally need pacing if slow
- If severe rhythm disturbance, may need a defibrillator

Rhythm Disorders

- Very slow heart rates
 - Pacemakers



Potential therapeutic options Based on Endomyocardial Biopsy results from patients with suspected Complicated Myocarditis



Strategy	(Pre)clinical Evidence	Evidence of Target	Evidence of Therapy
IL-1 β inhibitors			
Anakinra	acute MI, ¹²⁶ acute decompensated heart failure, ¹²⁷ HFpEF, ¹²⁸ and idiopathic recurrent pericarditis fulminant myocarditis ^{129,130}	++	+++
Canakinumab	patients with previous MI and hs-CRP levels ≥ 2 mg/L (CANTOS) ¹³¹	++	+++
Colchicine	pericarditis with pericardial effluent, ^{132–135} stable coronary artery disease, ¹³⁶ and postpericardiotomy syndrome ^{137,138}	++	+++
HMGB1 inhibitors	patients suffering from acute myocarditis and troponin I-induced experimental autoimmune myocarditis ¹³⁹	++	++
S100A9 inhibitors			
Q-compounds	autoimmune disease and cancer ^{140,141} CVB3 myocarditis and DCM ^{142,143}	++	
Modulation of T cells			
Treg cells transfer	experimental model of CVB3-induced myocarditis: prophylactic ^{144,145} and therapeutic ¹⁴⁶ use	++	++
IL-2 agonists	experimental evidence in rodent MI model ¹⁴⁷	+	+
Global immunomodulation			
MSC (autologous, allogeneic, PLX)	experimental models of CVB3-induced myocarditis, ^{148–152} chronic Chagas cardiomyopathy, ¹⁵³ and autoimmune-induced DCMi ¹⁵⁴	++	+++
	trial in nonischemic DCM patients ¹⁵⁵		
CardAPs	experimental model of CVB3-induced myocarditis ¹⁵⁶	+	+
Nanocarriers	experimental autoimmune myocarditis ¹⁵⁷	+	+

Things to Avoid in the Acute Phase

- Nonsteroidal anti-inflammatory drugs generally not effective
- Heavy alcohol consumption
- Exercise
 - Especially if fever, active infection or heart-failure
 - restrict physical activity of athletes as well as non-athletes during the acute phase of myocarditis and for at least 3-6 months
 - This recommendation is based upon expert opinion.

What Should You Do About Exercise ?

- 3-6 months of abstinence from competitive sports
- After 6 months, check that no rhythm disturbance
- Check that heart function is ok
 - Treadmill test
 - Heart monitor
 - Echo or MRI scan

PREVENTION

- Vaccination ?
 - Influenza
 - Measles
 - Polio
- Genetics to identify the at-risk patient

Summary

- Treatment is geared towards:-
 - Symptoms
 - Is there heart-failure – ‘DCM’
 - Is there a rhythm disturbance
 - If poor heart function – is there still active inflammation or a virus identified