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# Sports and inflammatory heart diseases

## Abstract

Regular and moderate training reduces the individual cardiovascular risk in the long term. Nevertheless, physical activity may impose a considerable risk of sudden cardiac death on patients with heart diseases. This is particularly the case with myocarditis and pericarditis, which often affect younger people. So far, there is no evidence that sports by itself increase individual susceptibility to inflammatory heart diseases. In patients with symptomatic or asymptomatic cardiac inflammation, however, physical activity is clearly pro-arrhythmic and might even promote myocarditis progression. From these points of view, all patients with cardiac inflammation, in particular if they are involved in competitive sports, need clear recommendations regarding their physical training.

## Zusammenfassung

Regelmässiges und angemessenes Training vermindert das individuelle kardiovaskuläre Risiko langfristig. Gleichwohl kann körperliche Belastung eine beachtliche Gefahr für einen herzerkrankten Patienten darstellen und zum plötzlichen Herztod führen. Dies ist vor allem bei Myokarditis und Perikarditis der Fall, an welchen oft jüngere Menschen erkranken. Soweit ist nicht erwiesen, dass Sport die Anfälligkeit auf entzündliche Herzerkrankungen erhöht. Bei Patienten mit symptomatischen oder asymptomatischen Herzentzündungen wirkt körperliche Belastung jedoch proarrhythmisch und kann zudem zur Myokarditisprogression führen. So betrachtet, benötigen alle Patienten mit entzündlichen Herzerkrankungen, insbesondere Leistungssportler, klare Empfehlungen in Bezug auf ihr individuelles Training.

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## Epidemiology

Myocarditis denotes inflammation of the heart muscle and often results from viral infections and their associated immune responses. Patients may develop heart failure and/or arrhythmias but are not necessarily symptomatic. Nevertheless, the disease can progress to dilated cardiomyopathy, a common cause of heart failure in young patients. Myocarditis incidence approaches 13 cases/10<sup>5</sup> per year in Europe. Prevalence, however, is most likely much higher, given the fact that many patients show minimal symptoms only. Interestingly, sex hormones are supposed to affect considerably the extent of viremia, as well as the severity of inflammatory responses [16,26] and may explain male predominance [1].

Pericarditis denotes inflammation of the fibrous sac surrounding the heart. Epidemiologic studies on pericarditis are rare. An Italian observational study reported an incidence of up to 27.7 cases/10<sup>5</sup> per year [28]. Acute pericarditis accounts for up to 5% of non-ischemic chest pain presentations in emergency departments [27]. Myopericarditis means that the inflammation not only involves the pericardium but also the heart muscle to some extent. Perimyocarditis refers to a predominant cardiac inflammation that also involves the pericardium. Not surprisingly, myocarditis and pericarditis share many etiologic agents, in particular viruses, but we do not know yet, how genetic and environmental factors dictate the development of either one or the other disease phenotype [14,13].

## Impact of sports on cardiac inflammation

Myocarditis has been considered an important cause of sudden death in young competing athletes accounting for 5–22% of the incidents [17,18,4,6]. This is mainly due to the fact, that coronary heart disease, the major cause of cardiac death in the overall population, has a rather low prevalence in the young and active population. Accordingly, myocarditis accounted for 13% and 15% of sudden cardiac death cases in an athletic and non-athletic popu-

lation aged 12 to 35 years, respectively [5]. There is, however, no evidence, that athletes are more susceptible to cardiac inflammation, neither for myocarditis nor pericarditis compared to healthy controls.

Nevertheless, sports infer a considerable risk of sudden death on patients already suffering from symptomatic or asymptomatic myocarditis. This is mainly due to electrical instability of the inflamed heart. From an immunological point of view, exercise during early phases of myocarditis may also promote viral replication within cardiomyocytes, cytolysis and local tissue inflammation [9,10,7].

## Clinical picture, diagnostic approach, and prognosis of inflammatory heart diseases

Both, myocarditis and pericarditis are often preceded by flu-like or gastrointestinal complaints but the clinical course is highly variable. Depending on the extent and dynamics of myocardial inflammation, symptoms of heart failure, chest pain, and/or arrhythmias may develop within days to weeks in patients with myocarditis. Chest pain is a major symptom of acute pericarditis, but affected patients may also present with fatigue only, or with dyspnea in case of extensive pericardial effusion, for example. The clinical picture of myocarditis and pericarditis is identical in athletes and the general population.

Diagnostic work-up with ECG, echocardiography and coronary angiography is often mandatory to exclude other major heart diseases. Cardiac MRI is on the way to become a helpful diagnostic tool in the future, mainly because it may increase the sensitivity of heart muscle biopsies. A definite diagnosis of myocarditis, however, still requires the histological and/or immunohistochemical detection of inflammatory cells within the myocardium [15]. At the moment, heart muscle biopsies are only considered in selected patients, such as those with rapidly progressive heart failure or persistently severely impaired ejection fraction after exclusion of coronary arterial disease and/or valvular heart disease.

A diagnosis of pericarditis integrates clinical judgement, ECG analysis, laboratory findings, and echocardiography. The fact that Troponin I and T levels can be transiently elevated in up to 50% of the patients with pericarditis underscores the importance to actively exclude the acute coronary syndrome in patients with presumed pericarditis. Additional tests such as MRI, CT-scan, or pericardial biopsy are almost never necessary.

Prognosis is variable in patients with myocarditis. Many patients recover completely, but progression to end stage heart failure is not uncommon. Interestingly, patients with fulminant myocarditis have an excellent long-term prognosis if they survive the initial stage of severe heart failure. In contrast, patients with acute myocarditis have a remarkable mortality on follow-up [22]

The prognosis of pericarditis is usually favourable and relevant arrhythmias are very rare. If ventricular arrhythmias are present in patients with presumed pericarditis, these findings strongly suggest significant inflammation of the myocardium, i.e. perimyocarditis. Although generally self-limited, potential complications of pericarditis include recurrent pericarditis (up to 20% of the patients), cardiac tamponade, and constriction (< 1% of the cases) [25,29]. Of note, there are no data regarding the impact of competitive sports on the development of these complications.

### Treatment principles in patients with inflammatory heart diseases

Patients with myocarditis and heart failure should be treated with diuretics, beta-blocking agents (e.g. bisoprolol, carvedilol), angiotensin-converting enzyme inhibitors (or angiotensin receptor antagonists, if necessary), and aldosterone antagonists if feasible [1,3]. We avoid digoxin in these patients, because it increased mortality in animal models of viral myocarditis [21]. Patients with persistently impaired cardiac function should be evaluated for an implantable cardiac defibrillator (ICD), and/or cardiac re-synchronization therapy defibrillator (CRT-D) treatment. Some patients with histologically proven myocarditis but undetectable viral genomes in heart muscle biopsies might take advantage of immunosuppressive treatment with prednisone and azathioprine [8]. Competitive sports are not recommended in patients with ongoing myocarditis and worsening heart failure. Patients with stable end-stage heart failure, however, may take advantage of regular physical activity, if they are protected by an ICD (or CRT-D).

Acute pericarditis is treated with non-steroidal anti-inflammatory drugs according to the up-dated guidelines of the European Society of Cardiology [20]. Adding colchicines to the treatment regimen shortens the disease course and reduces the frequency of recurrences [12,11]. Steroids on the other hand are strongly discouraged as they may promote recurrent pericarditis.

### Recommendations for athletes suffering from inflammatory heart diseases

Practicing cardiologists are frequently asked to give recommendations on exercise programs and sport participation in patients suffering from inflammatory heart diseases. Recommendations for competitive sports and leisure-time physical activities are both based on consensus documents of expert panels of the European Society of Cardiology and the sports cardiology section of the European Association of Cardiovascular Prevention and Rehabilitation [23,24]. Based on the different cultural, social, and legal backgrounds in the U.S. the Bethesda Conference #36 (consensus conference of the American College of Cardiology Foundation and other relevant organizations) issued slightly different US cardiovascular recommendations for competitive sports [19]. Regarding inflammatory heart diseases, however, European and US guidelines are identical. For patients with myocarditis or myopericarditis, it is strongly recommended to avoid any competitive and leisure time sport activity for six months. Three months are recommended for patients with pericarditis. These recommendations are inde-

pendent of age and gender. After full recovery, but not before 6 respectively 3 months after diseases onset, a clinical re-assessment is mandatory (Table 1). Sport activity can only be granted if left ventricular function has recovered, inflammatory serum markers have returned to normal and if the patient is free from arrhythmias [2,4].

Lesion	Recommendation	Re-evaluation	Eligibility	Follow-up
Myocarditis	No competitive sports for 6 months	History, PE, ECG, ECHO, ET, Holter	All competitive sports if no symptoms, normal LV function, no arrhythmias.	6 months
Myopericarditis	No competitive sports for 6 months	History, PE, ECG, Echo, ET, Holter	All competitive sports if no symptoms, normal LV function, no arrhythmias.	6 months
Pericarditis	No competitive sports for 3 months	History, PE, ECG, Echo, ET	All competitive sports if no symptoms, and normal inflammatory markers at re-evaluation	6 months

Table 1: Recommendations for participation in competitive sports

ECG = electrocardiogram; ECHO = echocardiography; EF= ejection fraction, LV=left ventricle; PE = physical examination; ET = exercise testing; Holter = 24-h ECG monitoring.

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### References

- Blauwet L.A., Cooper L.T. (2010): Myocarditis. *Prog Cardiovasc Dis.* 52: 274–88.
- Caforio A.L., Keeling P.J., Zachara E., et al. (1994): Evidence from family studies for autoimmunity in dilated cardiomyopathy. *Lancet.* 344: 773–7.
- Cooper Jr. L.T. (2009): Myocarditis. *NEJM.* 360: 1526–1538.
- Corrado D., Basso C., Rizzoli G., et al.(2003): Does sports activity enhance the risk of sudden death in adolescents and young adults? *J. Am. Coll. Cardiol.* 42: 1959–1963.
- Corrado D., Basso C., Pavei A., et al. (2006): Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA.* 296: 1593–1601.
- Drory Y., Turetz Y., Hiss Y., et al.(1991): Sudden unexpected death in persons less than 40 years of age. *Am. J. Cardiol.* 68: 1388–1392.
- Friman G., Wesslen L. (2000): Special feature for the Olympics. Effects of exercise on the immune system: infections and exercise in high performance athletes. *Immunol. Cell. Biol.* 78: 510–522.
- Frustaci A., Russo M.A., Chimenti C. (2009): Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study. *Eur. Heart J.* 30: 1995–2002.
- Gatmaitan B.G., Chason J.L., Lerner A.M. (1970): Augmentation of the virulence of murine coxsackievirus B3 myocardiopathy by exercise. *J. Exp. Med.* 131: 1121–1136.
- Ilback N.G., Fohlman J., Friman G.(1989): Exercise in cox-sackie B3 myocarditis: effects on heart lymphocyte subpopulations and the inflammatory reaction. *Am. Heart J.* 117: 1298–1302.

- 11 Imazio M., Bobbio M., Cecchi E. et al. (2005): Colchicine as first choice therapy for recurrent pericarditis: results of the CORE (Colchicine for recurrent pericarditis) trial. *Arch. Intern. Med.* 165(17): 1987–1991.
- 12 Imazio M., Bobbio M., Cecchi E. et al. (2005): Colchicine in addition to conventional therapy for acute pericarditis: results of the COPE (Colchicine for acute Pericarditis (COPE) trial. *Circulation.* 112: 2012–2016.
- 13 Imazio M., Trincheri R. (2008): Myopericarditis: Etiology, management and Prognosis. *Int. J. Cardiol.* 127 (1): 17–26.
- 14 Imazio M., Cecchi E., Demichelis B. (2008): Myopericarditis versus viral or idiopathic acute pericarditis. *Heart.* 94: 498–501.
- 15 Kindermann I., Kindermann M., Kandolf R. et al. (2008): Predictors of outcome in patients with suspected myocarditis. *Circulation.* 118: 639–648.
- 16 Lyden D.C., Olszewski J., Feran M. et al. (1987): Coxsackievirus B-3-induced myocarditis. Effect of sex steroids on viremia and infectivity of cardiocytes. *Am. J. Pathol.* 126: 432.
- 17 Maron B.J., Shirani J., Poliac L.C., et al. (1996): Sudden death in young competitive athletes: clinical, demographic, and pathological profiles. *JAMA.* 276: 199–204.
- 18 Maron B.J. (2003): Sudden death in young athletes. *N. Engl. J. Med.* 349: 1064–1075.
- 19 Maron B.J., Zipes D.P. (2005): 36th Bethesda Conference: eligibility recommendations for competitive athletes with cardiovascular abnormalities. *J. Am. Coll. Cardiol.* 45: 2–64.
- 20 Maisch et al. (2004): Guidelines on the Diagnosis and management of pericardial diseases executive summary; Task force on the diagnosis and management of pericardial diseases of the European society of cardiology. *Eur. Heart J.* 25: 587.
- 21 Matsumori A., Igata H., Ono K. et al. (1999): High doses of digitalis increase the myocardial production of proinflammatory cytokines and worsen myocardial injury in viral myocarditis: a possible mechanism of digitalis toxicity. *Jpn. Circ. J.* 63: 934–940.
- 22 McCarthy R.E. 3<sup>rd</sup>, Boehmer J.P., Hruban R.H., et al. (2000): Long-term outcome of fulminant myocarditis as compared with acute (non-fulminant) myocarditis. *N. Engl. J. Med.* 342: 690.
- 23 Pelliccia A., Fagard R., Bjornstad H.H., et al. (2005): Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur. Heart J.* 26: 1422–1445.
- 24 Pelliccia A., Corrado D., Bjornstad H.H., et al. (2006): Recommendations for participation in competitive sport and leisure-time physical activity in individuals with cardiomyopathies, myocarditis and pericarditis. *Eur. J. Cardiovasc. Prev. Rehabil.* 13: 876–885.
- 25 Permanyer-Miralda et al. (1985): Primary acute pericardial disease: a prospective series of 231 consecutive patients. *Am. J. Cardiol.* 56: 623.
- 26 Schwartz J., Sartini D., Huber S. (2004): Myocarditis susceptibility in female mice depends upon ovarian cycle phase at infection. *Virology.* 330: 16.
- 27 Spodick D.H. (2001): Myopericarditis/Perimyocarditis. In the Pericardium. Marcel Dekker, Inc. New York; 114.
- 28 Spodick D.H. (2003): Acute cardiac tamponade. *N. Engl. J. Medicine.* 349: 684.
- 29 Zayas et al. (1995): Incidence of specific etiology and role of method for specific etiologic diagnosis of primary acute pericarditis. *Am. J. Cardiology.* 75: 378.