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REVIEW

# Management of pericarditis and myocarditis: Could heart-rate-reducing drugs hold a promise?

## Prise en charge des péricardites et myocardites: les médicaments bradycardisants sont-ils prometteurs?

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Heart rate

**Summary** Rest is usually recommended in acute pericarditis and acute myocarditis. Given that myocarditis often leads to hospitalization, this task seems easy to carry out in hospital practice; however, it could be a real challenge at home in daily life. Heart rate-lowering treatments (mainly beta-blockers) are usually recommended in case of acute myocarditis, especially in case of heart failure or arrhythmias, but level of proof remains weak. Calcium channel inhibitors and digoxin are sometimes proposed, albeit in limited situations. It is possible that rest or even heart rate-lowering treatments could help to manage these patients by preventing heart failure as well as by limiting ''mechanical inflammation'' and controlling arrhythmias,

*Abbreviations:* CRP, C-reactive protein; ESC, European Society of Cardiology; HF, heart failure; HR, heart rate; LV, left ventricular; NSAID, non-steroidal anti-inflammatory drug; PROBE, prospective randomized open blinded endpoint.

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especially life-threatening ones. Whether heart rate has an effect on inflammation remains unclear. Several questions remain unsolved, such as the duration of such treatments, especially in light of new heart rate-lowering treatments, such as ivabradine. In this review, we discuss rest and heart-rate lowering medications for the treatment of pericarditis and myocarditis. We also highlight some work in experimental models that indicates the beneficial effects of such treatments for these conditions. Finally, we suggest certain experimental avenues, through the use of animal models and clinical studies, which could lead to improved management of these patients.


**MOTS CLÉS**
Péricardite ;
Myocardite ;
Bêta-bloquants ;
Inflammation ;
Fréquence cardiaque

**Résumé** Le repos est généralement recommandé en cas de péricardite ou de myocardite aiguë. Compte tenu que la survenue d'une myocardite conduit généralement à l'hospitalisation, le repos est facile à obtenir dans cette situation; c'est parfois au contraire un vrai défi dans la vie quotidienne. Les traitements bradycardisants (principalement les bêta-bloquants) sont habituellement recommandés en cas de myocardite aiguë, en particulier en cas d'insuffisance cardiaque ou d'arythmies, mais le niveau de preuve reste bas. Les inhibiteurs calciques, voire les digitaliques ont été proposés dans certaines indications limitées. Il est possible que le repos, voire des traitements bradycardisants puissent aider au traitement de ces patients en empêchant l'insuffisance cardiaque ou encore en limitant une « inflammation mécanique » et en contrôlant les arythmies, en particulier celles menaçantes. Que la fréquence cardiaque puisse avoir un effet sur le niveau d'inflammation n'est pas établi. Plusieurs questions restent non résolues, comme la durée des traitements, ou encore l'intérêt des nouveaux bradycardisants, comme l'ivabradine. Dans cette revue, sont discutés le repos et les différents traitements bradycardisants dans le traitement des péricardites et myocardites. Certaines études expérimentales sur le sujet montrent l'intérêt d'une telle approche dans divers modèles. Enfin, nous proposons des pistes fondamentales ou cliniques pour améliorer la prise en charge de ces patients.


## Introduction

Acute pericarditis and acute myocarditis are often difficult to distinguish; they constitute a continuum, with frontier forms named ''myopericarditis''. Acute pericarditis is diagnosed in case of two of the following elements: typical chest pain or pericardial rub; typical electrocardiogram; pericardial effusion (often on echocardiography); and biological inflammatory syndrome. On the other hand, acute myocarditis involves myocardium with biomarker elevation (mainly troponin) and left ventricular (LV) dysfunction.

Acute pericarditis is rather frequent with an annual incidence estimated at 27.7 new cases per 100,000 inhabitants in Europe [1]. About 5% of all patients with non-ischaemic chest pain who are admitted to emergency departments could have pericarditis [2]. The causes of pericarditis vary, with most common causes including viral or bacterial infections of the pericardium [3]. Most patients are young, with a heavy cost to society, especially due to hospitalizations.

Myocarditis is less common than pericarditis. The main difficulty in the assessment of this condition is the wide spectrum of possible clinical presentations, ranging from acute fulminant forms to late dilated cardiomyopathies. A broad range of pathological processes are involved and many classifications have been proposed [4,5]. Epidemiological studies are lacking and real incidences and prevalences are not well established [6]. Prospective post-mortem data suggested that myocarditis could be implicated in the sudden death of young adults at rates of 8.6—12% [7,8]. Up to 15% of pericarditis could be considered as myopericarditis, including cardiac enzyme elevation, wall motion abnormalities, arrhythmias and conduction disturbance [9]. The introduction of hypersensitive dosages of cardiac enzymes, such as high-sensitivity troponin, should increase the prevalence of this diagnosis; the value of these sorts of biomarkers in these clinical settings has to be investigated.

Main guidelines for acute pericarditis were published by the European Society of Cardiology (ESC), in 2004 [3]. Diagnosis is consensually defined. Hospitalizations are recommended in the worst cases and treatments include non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin, other anti-inflammatory drugs and colchicine. Although rest is highly recommended, this is difficult to obtain in this young population and the means of achieving it are lacking. Importantly, there are many problems associated with the management of this disease, including different procedures in different centres (despite guidelines), hospitalization, choice of drugs and duration of treatment. Relief of symptoms is the immediate goal for the physician, but the high risk of recurrences and even the aim of controlling the inflammatory process deserve to be considered. Guidelines for the management of myocarditis are patchier, especially for heart rate (HR)-controlling treatments.

However, HR-controlling treatments may exert several beneficial effects. HR is a well-established risk-marker for various cardiovascular diseases [10,11], including coronary artery disease [12,13] and heart failure (HF) [14,15]. Sinus tachycardia is almost invariably observed in myopericarditis [3,16], even in the absence of other contributing