# Special Topics: Cardiac Markers in Myocarditis

## Cardiac Transplant Rejection and Conditions Other than Acute Coronary Syndrome

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**KEYWORDS**

• Laboratory medicine • Cardiac markers • Biomarkers • Troponin • Myocarditis
• Cardiac transplant rejection

**KEY POINTS**

- The utility of blood biomarkers of cardiac myocyte damage such as troponin T and I in the evaluation of acute coronary syndromes and heart failure is well established.
- It has long been known that cardiac biomarkers may also be elevated in conditions other than acute coronary syndromes, such as myocarditis, cardiac transplant rejection, and several other conditions.
- It is important for the clinician and laboratory to be familiar with the differential diagnosis of an elevated cardiac troponin level and to consider the laboratory value in the context of the individual patient.

### INTRODUCTION

Cardiac troponin and other markers of myocardial injury have traditionally been used to assess patients with acute coronary syndromes and more recently in patients with heart failure. However, there are other situations whereby these markers may be abnormally elevated, including myocarditis, cardiac transplant rejection, and disorders other than acute coronary syndrome or heart failure. In some cases the finding of an abnormal cardiac marker has limited diagnostic or therapeutic utility, although this is not always the case. The development and commercialization of newer so-called high-sensitivity troponins will necessitate a reassessment of the role of cardiac troponin in nonischemic cardiac injury. This article describes what is currently known about traditional markers of myocardial injury in settings other than acute coronary syndrome or heart failure.

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## MYOCARDITIS

Myocarditis is defined as an inflammatory disorder of the myocardium producing injury to cardiac myocytes.[1] In contrast to conditions whereby inflammation occurs secondary to cardiac injury of another cause (eg, infarction, cardiac surgery, or infection), in myocarditis, the inflammatory process is the primary disorder producing the myocardial damage.[1] Myocarditis can be acute, subacute, or chronic.[2] The symptoms of myocarditis are quite variable. In some cases the symptoms are mild, such as asymptomatic electrocardiographic changes, mild chest pain, fever, and sweats. In other cases more serious symptoms are observed, including arrhythmias, syncope, heart failure, and sudden death. Some patients present with findings of acute heart failure.[3] There are many causes of myocarditis. These causes include number of infectious agents, immune reactions, and miscellaneous causes as shown in **Box 1**. In the United States, viral myocarditis is the most common cause, particularly coxsackie viruses and enteroviruses.[1] In some parts of the world other infectious agents figure more prominently, such as Chagas disease in South America. The diagnosis of myocarditis is usually based on a combination of clinical, electrocardiographic, radiologic, and laboratory findings. Endomyocardial biopsy is considered the gold standard for the diagnosis of myocarditis but is usually reserved for patients with acute heart failure of unknown cause that have not responded to traditional heart failure therapy.[3] Furthermore, endomyocardial biopsy seems to be an insensitive test. Cardiac biopsies have been reported to confirm the diagnosis of myocarditis in only 25% of suspected cases.[4]

Markers of myocardial cell injury, including troponin I and T (TnI, TnT), creatine kinase, and its isoenzyme CK-MB, have been evaluated in patients with suspected myocarditis. In one study in patients from the Myocarditis Treatment Trial, TnI values were elevated in 34% of patients with myocarditis, whereas CK-MB was elevated in only 5% of patients. Elevated levels of TnI were significantly correlated with short

**Box 1**
**Selected causes of myocarditis and some examples**

*Infectious agents*

Viruses especially coxsackie viruses and enteroviruses

Bacteria: diphtheria, Lyme disease

Protozoa: Chagas disease, toxoplasmosis

Fungi

Rickettsia

Parasites: trichinosis

*Immune reactions*

Cardiac transplant rejection

Kawasaki disease, systemic lupus, sarcoidosis, polymyositis, drug allergies

*Toxins*

Cardiotoxic drugs, heavy metals

Genetic disorders with inherited immune mediated cardiomyopathies

*Other*

Giant cell myocarditis