INTRODUCTION

The cardiac troponins I, T, and C (cTnI, cTnT, and cTnC) are thin filament-associated regulatory proteins of the heart muscle. They are crucial to the interaction between actin and myosin and occur at regular intervals of 38 nm along the tropomyosin molecule. Cardiac troponin I (“I” for inhibition) is uniquely expressed in the myocardium and is a potent inhibitor of the process of actin-myosin cross-bridge formation. The molecular weight is 24,000 D. Cardiac troponin I has been investigated extensively in people and has been found to be a very sensitive serum marker of physical or metabolic myocardial injury, myocardial ischemia, or necrosis with a cardiac specificity of 100%. Cardiac troponin T (“T” for tropomyosin binding) has a molecular weight of 37,000 D and binds the troponin complex to tropomyosin. The cardiac specificity of serum cTnT is less than 100% because it may be re-expressed in skeletal muscle during regeneration processes after trauma and may also be elevated in renal disease or acute pulmonary thromboembolism. Cardiac troponin C (“C” for calcium) binds to calcium and starts, therefore, the crossbridge cycle. However, it has not gained any diagnostic significance yet. As with cTnI, approximately 95% of cTnT in man and dogs is myofibril bound and about 5% is cytosolically dissolved. Mechanisms for an elevation in circulating cardiac troponins include an increase of myocyte membrane permeability (initial release of the cytosolic troponin pool) or cell necrosis (release of myofibril-bound troponins). Four to six hours after acute myocardial cell injury, the cardiac troponin concentration in blood increases in a biphasic pattern. A rather low initial elevation is followed by a more pronounced release of structurally bound cardiac troponins depending on severity of the lesion. Plasma half-life of cardiac troponins is approximately two hours, and elimination mainly occurs via the reticuloendothelial system (cTnI and cTnT) and renal loss (cTnT). Troponins from cardiac muscle and slow-and fast-twitch skeletal muscle are products of different genes with unique amino acid sequences. Thus, recently developed monoclonal antibodies to cTnI have no and to cTnT only minor cross-reactivity with skeletal muscle isoforms. Cardiac troponins are phylogenetically highly preserved proteins with a more than 95% total structural agreement between mammals. Therefore, established human serologic tests for troponin analysis may be used reliably in pets as well. In normal dogs and cats, serum cTnT is less than 0.1 ng/ml and serum cTnI is less than 0.5 ng/ml. The cut-off level of serum cardiac troponins to separate significant from non-significant myocardial cell injury in people is 0.1 ng/ml for cTnT and 2.0 ng/ml for cTnI.

Myocardial cell injury, manifested anatomically as inflammation (endomyocarditis, myocarditis, perimyocarditis), acute degeneration, apoptosis, or necrosis or hemodynamically as transient or permanent cardiac contractile dysfunction, is a frequent consequence of physical myocardial trauma (cardiac contusion), cardiomyopathy, metabolic (diabetes mellitus, renal insufficiency, pancreatitis) or toxic myocardial damage (anthracyclines, catecholamines, bacterial endotoxins, tumor necrosis factor), myocardial ischemia (tachycardia-induced, pathologic hypertrophy with small vessel disease, arterosclerosis) or infarction. Diagnostic sensitivity of electrocardiography (ECG) or echocardiography to diagnose minor myocardial injury is poor. However, early diagnosis of myocardial injury may be important from a therapeutic and prognostic perspective.

MYOCARDIAL CONTUSION

Myocardial contusion (i.e., necrosis, fiber fragmentation, or hemorrhage) has been reported in dogs and cats with blunt chest trauma. Vehicular impact, kicks of horses, falls, pivot window trauma, and cardiac resuscitative procedures may cause direct damage to the heart. Fractures of the bony structures of the chest wall are not necessary accompaniments of cardiac injury in any of these situations. ECG alterations (Q-wave and ST-T abnormalities) and echocardiographically detectable regional wall motion abnormalities have been considered to detect cardiac contusion, however, their diagnostic sensitivity or specificity are rather low. In studies in 33 dogs and 31 cats with blunt chest trauma, done by the authors, 55 % of dogs and 64 % of cats had serologic evidence of relevant myocardial injury. Correlation between serum levels of cardiac troponins and ECG abnormalities as well as prognosis have also been shown in these animals.

CANINE DILATED CARDIOMYOPATHY

Progression of dilated cardiomyopathy is structurally characterized by cellular degeneration, multiple foci of myocardial cell death, and replacement fibrosis. Recent studies have shown that myofibrilolysis-associated elevation of circulating cardiac troponins relates to pathophysiology, clinical signs, decreased ejection fraction, and prognosis in people with progressive myocardial failure. Analysis of cTnT or cTnT may identify latent or progressive myocardial damage and patients who are at increased risk of cardiac events. In a study with 22 dogs with DCM, 12 (55 %) had biochemical evidence of ongoing myocardial cell injury (unpublished data).
FELINE HYPERTROPHIC AND RESTRICTIVE CARDIOMYOPATHY

In feline cardiomyopathy, abnormal myocardial growth and small vessel disease leading to ischemia and myocardial or endomyocardial fibrosis, or progressive endomyocarditis may be characteristic features. In clinical situations, myocardial cell injury may only be detected using serum cardiac troponins as markers of myocardial damage. In a cohort of 22 cats with cardiomyopathy, 16 (73 %) had elevated cardiac troponin levels. Very high values (above 50 ng/ml) resembled acute myocardial infarction in some animals. There was also a relationship between biochemically detectable cardiac injury and ECG abnormalities and prognosis in cats with HCM.

MYOCARDITIS

In dogs and cats with clinically suspected myocarditis (fever, sudden onset of a murmur or an arrhythmia without echocardiographic evidence of structural myocardial disease), the definitive diagnosis has to be established by the demonstration of myocytolysis and lymphocytic infiltrates in endomyocardial biopsy or post mortem specimens. However, endomyocardial biopsy is invasive and has a rather low diagnostic yield. Studies in people and mice have shown, that the sensitivity, specificity, and positive predictive value of increased concentrations of circulating cTnI or cTnT for the diagnosis of acute myocarditis are high. In addition, the analysis of serum troponins may be particularly helpful to exclude relevant myocardial inflammation as shown in 21 dogs with suspected myocarditis (unpublished data).

PERICARDITIS

Recent reports in people suggest that significant elevations of serum cTnI may be observed in acute pericarditis. Subepicardial myocarditis, to be suspected from ST-segment elevations on ECG, may be present in most patients with acute pericarditis causing superficial myocardial cell injury. Moreover, cardiac troponin analysis in pericardial effusion fluid may be helpful in discriminating inflammatory from neoplastic pericardial disease.

GASTRIC DILATATION VOLVULUS SYNDROME (GDV)

Acute myocardial degeneration, myocardioctyolysis, and myocardial necrosis have been reported in dogs with GDV caused by reperfusion injury, electrolyte and acid-base abnormalities, cytokines, catecholamines, toxins, hypoxia, and autonomic dysbalance. Life-threatening ventricular dysrhythmias and depressed myocardial performance may be the result. The definitive diagnosis of myocardial lesions in GDV is restricted to histopathologic findings. However, there is a close relationship between serum cTnI elevations, ECG abnormalities, histologically proven myocardial necrosis, and prognosis in GDV. In a study with 85 dogs with gastric torsion performed by the authors, 58 dogs (68 %) had increased levels of circulating cardiac troponins. Ventricular arrhythmias and survival could be predicted from serial cTnI and cTnT determinations.

ANTHRACYCLINE-INDUCED CARDIAC DAMAGE

Chemotherapy with anthracyclines (e.g. doxorubicin) is well known to cause dose-dependent cardiotoxicity resulting in myocardial dysfunction, arrhythmias, and congestive heart failure. Elevations of cTnI and cTnT in people and animals undergoing chemotherapy with anthracyclines may reliably suggest the occurrence of myocardial damage and may predict the development of systolic ventricular dysfunction.

FURTHER READING


**KEY WORDS**
Cardiac troponin I, cardiac troponin T, myocardial contusion, cardiomyopathy, myocarditis, gastric dilatation volvulus syndrome