Circulating Cardiac Troponin T in Skeletal Muscle Disease: A Reflection of Re-expression Phenomenon?

Kosit Sribhen, M.D., Dr. Med., Pusadee Luenee, M.Sc.

Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Determinations of cardiac troponin T (cTnT) and cardiac troponin I (cTnI) have replaced creatine kinase myocardial band (CK-MB) measurements as the "gold standard" biochemical methods for the detection of myocardial injury and infarction. Due to their high myocardial tissue specificity, it can can be assumed with a high probability that the troponins detected in the circulation are of cardiac origin. However, there have been several reports in recent years which showed increased serum concentrations of cTnT, but not of cTnI, in patients with skeletal muscle disorders, in whom no clinical evidence of myocardial cell damage were observed. Since cTnT isoform, in contrast to cTnI isoform, has been reported to be expressed in fetal skeletal muscle, there is the possibility that this fetal cTnT isoform is re-expressed in diseased and regenerating adult skeletal muscle. Therefore, the reported high myocardial tissue specificity of cTnT is to be questioned, and elevated cTnT concentrations found in patients with destructive skeletal muscle disease should be cautiously interpreted as biochemical evidence of myocardial cell injury.

This present review describes the physiological and pathophysiological aspects of cTnT and cTnI in health and disease, with special emphasis on the tissue expression of their isoforms in the fetal and adult hearts as well as in the fetal and adult skeletal muscles. Previous and recent data, obtained from international databases (PubMed, Scopus, Google Scholar), with reports on cardiac biomarkers in patients with acute and chronic skeletal muscle disorders are summarized and the clinical implications of these findings are also addressed and discussed.

Keywords: Cardiac troponins; expression; skeletal muscle (Siriraj Med J 2018;70: 459-465)

Physiology of cardiac troponin isoforms

Cardiac troponins, consisting of cTnT, cTnI and cTnC, represent parts / of the troponin-tropomyosin-actin complex system in the myofilament which play an important role in the regulation of muscular contraction. The molecular structures of cardiac and skeletal muscle troponin C, in contrast to those of troponin T and I, are virtually identical, which prevent the use of cTnC as a specific marker of cardiac injury. With regard to cTnT, the presence of several troponin genes as well as alternative splicing provide for the existence of multiple troponin T isoforms.[1] Human cardiac muscle contains four isoforms of cTnT: three isoforms are expressed during the fetal period and one isoform is characteristic for adult heart.[2,3] In contrast, human fetal and adult heart muscles each contains only one cTnI isoform.

In physiological condition, the embryonic isoform of cTnT is found to be expressed in human fetal skeletal

Correspondence to: Kosit Sribhen
E-mail: sipln@hotmail.com
Received 4 July 2017 Revised 6 November 2017 Accepted 10 November 2017
doi:10.14456/smj.2018.73

muscle. After birth, there is down- regulation in the production of fetal cTnT isoform, resulting in the absence of cTnT in adult skeletal muscle. In contrast, there exists no expression of cTnI either in the fetal or adult skeletal muscle.[4]

Pathophysiology of cardiac troponin isoforms

The fact that cTnT and not cTnI is physiologically expressed in both the fetal heart and skeletal muscle has led to the assumption that the fetal cTnT isoform may be re-expressed in pathological conditions of the heart, and especially in the adult skeletal muscle. In this context, several animal experimental and human clinical studies have demonstrated the existence of messenger RNA (mRNA) and protein expression of cTnT in diseased myocardial and skeletal muscle tissues, along with the presence of cTnT which increases in the absence of elevated cTnI in the peripheral circulation.

Re-expression of CK-MB and cTnT in heart diseases

Several experimental studies performed on dogs and pigs have shown that chronic myocardial ischemia induced by ligation of coronary arteries resulted in several fold increases in myocardial CK-MB content.[5,6] Since an increase in myocardial CK-B subunit mRNA in ischemic myocardium of dogs was observed,[7] it was hypothesized that CK-MB is re-expressed in diseased myocardium. In contrast to CK-MB, coronary artery occlusion did not result in increased cTnT myocardial contents.[8-10] Similar results were obtained from studies on humans with ischemic injured myocardial tissue.[8] Since increases in both mRNA of fetal cTnT[11] and fetal isoforms of cTnT[2,11,12] were observed in diseased heart muscles of animals and humans, it was assumed that chronic loss of cardiac troponin from injured myocardium is not replenished through re-expression of genes that might increase protein synthesis.[13]

Re-expression of CK-MB and cTnT in skeletal muscle diseases

The dynamics of CK-MB and cTnT alterations have also been intensively investigated in chronic skeletal muscle disorders. By using marathon runners as subjects, Apple et al.,[14,15] studied the effects of chronic long distance running on the CK-MB content of skeletal muscle. It was found that skeletal muscle CK-MB in the biopsy specimens was increased by 2-fold. Similar observation was made in patients with Duchenne muscular dystrophy.[16] Apple[13] has suggested that skeletal muscle damage and subsequent regeneration of muscle resulted in the differentiation of CK isoenzymes into the embryonic skeletal muscle formation of CK-BB and CK-MB.

The expression of cTnT isoforms in diseased skeletal muscle has been debated for several decades. Expression of mRNA of the cardiac isoforms of TnT has been found in patients with diseased human skeletal muscles such as uremic myopathy of end-stage renal disease[17] and Duchenne muscular dystrophy.[17,18] By using immunocytochemistry and immuno- blotting technique, Saggin et al.,[19] have demonstrated re-expression of cTnT in regenerating muscle fibers of rats following cold injury as well as in mature fibers after denervation. Similar results were obtained from a study by Boder et al.,[20] who reported expression of cTnT in regenerating skeletal muscles of patients with polymyositis and Duchenne muscular dystrophy. However, Ricchiuti et al.,[21] have shown that the cTnT isoform expressed in diseased skeletal muscles of chronic renal disease patients is not detected by the 2nd-generation cTnT immunoassay. These results stand in contrast to those of Jaffe et al.,[22] who found increased cTnT, but normal cTnI serum concentrations in patients with neuromuscular diseases. Western blot analyses of biopsy specimens performed on some of these patients have revealed the presence of strong immunoreactive bands, with a molecular weight similar to that of cTnT. The authors concluded that there are forms in diseased skeletal muscles that could cause increases in levels of cTnT, and these increases could reflect the re-expressed isoforms which can be detected by a more sensitive cTnT immunoassay.

Circulating CK-MB and cTnT in chronic skeletal muscle diseases

Cardiac involvement represents a common complication that confers a worse prognosis in chronic destructive myopathies.[23] It has been reported that the presence of increases in circulating CK-MB and cTnT, which may indicate myocardial involvement, is frequently associated with several chronic skeletal muscle disorders including polymyositis, dermatomyositis and muscular dystrophy.[24] Table 1 summarizes previous and recent data on the frequency of elevated cardiac biomarker levels in patients with chronic destructive skeletal muscle diseases, most of which showed no clinical evidence of acute coronary ischemic events.

In a study on 28 patients with polymyositis and several forms of muscular dystrophy, increases in the activity of CK and CK-MB were found in 86 and 100 percent of patients, respectively. Elevated cTnT, measured with the 2nd-generation immunoassay, and cTnI levels were 23 and 14 percent, respectively.[25] In a more recent study on 39 patients with polymyositis and

TABLE 1. Percentage of increased cardiac biomarkers in patients with chronic destructive skeletal muscle disorders.

Author (year)	Diagnosis	Percentage of increase			
		CK	CK-MB	cTnT	cTnI
Braun et al. (1996)	PM, DMD, BMD, LGD, FSHD	86	100	23	14
Erlacher et al. (2001)	PM, DM	nd	51	41	3
Sribhen et al. (2002)	PM, DM, DMD,	100	100	57	nd
Aggarwal et al. (2009)	PM, DM, CTDM	82 71	nd nd	64 nd	nd 2
Fisher et al. (2010)	PM, DM, IBM	100	nd	100	nd
Cox et al. (2010)	IBM	82	82	78	2
Jaffe et al. (2011)	IBM, FSHD	nd	nd	100	0

Abbreviations: BMD = Becker muscular dystrophy; DM = Dermatomyositis; DMD = Duchenne muscular dystrophy; FSHD = Facioscapulohumeral-type dystrophy; IBM = Inclusion body myositis; LGD = Limb girdle dystrophy; CTDM = Connective tissue disease-associated myositis; PM = Polymyositis; nd = not determined

dermatomyositis, increased CK-MB and cTnT were reported to be 51 and 41 percent, respectively.[26] Since there were close correlations between both cardiac biomarkers and skeletal muscle damage markers including myoglobin and myosin heavy chain, and a close relationship of cTnT with disease severity, it has been suggested that cTnT was released from skeletal muscle. By using a more sensitive and specific 3rd-generation cTnT assay, Sribhen et al.,[27] reported the frequency of cTnT increase in these patients to be 57 percent. Recent studies[22,28-30] performed on patients with inflammatory myopathies have also demonstrated that most of these patients exhibited elevated cTnT concentrations. In contrast to the cTnT results, four of the studies have found that only 0 to 3 percent of the patients displayed increased cTnI levels (Table 1).

The results from these trials have recently been confirmed by 2 studies utilizing the latest generation of cardiac troponin immunoassay. In a male patient diagnosed as having limb-girdle muscular dystrophy, Mair[31] has demonstrated chronic elevations of high-sensitivity troponin T (hs-cTnT) over several days whereas hs-cTnI was in the normal range. Echocardiography, exercise stress test and renal function were all normal. In addition, analytical interference by heterophile antibodies was ruled out. The author suggested that patients with unexplained increased cTnT with normal cTnI should be evaluated for possible, clinically still asymptomatic chronic skeletal muscle diseases. Rittoo et al.,[32] have conducted a hitherto largest study on 52 hospitalised and ambulatory patients with 20 different types of acquired and inherited neuromuscular diseases. The main finding in that study was that these patients commonly had persistent elevation of CK-MB and cTnT in the absence of electrocardiographic, echocardiographic and cTnI evidence of myocardial injury. The authors concluded that re-expressed cTnT in diseased skeletal muscle might appear to be the source of the elevated cTnT detected in the circulation of these patients.

The discordant cardiac troponin results, with the presence of increased cTnT, but normal cTnI levels, in patients with destructive skeletal muscle disorders without clinical evidence of acute coronary events, have led to the assumption that elevations of circulating cTnT found in these patients may not originate from the heart. Of interest was the observation by Kiely et al.,[33] who have

demonstrated no increase in cTnI levels in any of their 6 patients with polymyositis and dermatomyositis, despite an increase in CK-MB index. Since CK-MB showed significant correlation with skeletal muscle troponin I (sTnI) and not with cTnI, it was assumed that skeletal muscle was the source of CK-MB. In this context, it has been shown in a more recent study[34] on 129 patients with Duchenne and Becker muscular dystrophy that, although increased CK activity and cTnI concentration were found in a significant number of these subjects, there was no correlation between the two biomarkers. This can be explained by the fact that high levels of CK are usually observed in the early stage whereas cardiac involvement with release of cTnI occurs at a later stage of the disease. Since cTnI is uniquely expressed in cardiac muscle and is not expressed in other non-cardiac tissues, these results point to the usefulness of this protein as a specific biomarker to detect early stage of cardiac damage in patients with chronic destructive skeletal muscle diseases.

The patterns of cardiac biomarker release in patients with polymyositis and dermatomyositis differ significantly from those of ischemic cardiac injury. In acute coronary syndromes, there are significant rises and falls in CK-MB and cTnT levels, which return to the normal ranges within 2-3 days and 7-10 days, respectively. In contrast, the patients with inflammatory myopathies[35-37] exhibit a delayed decrease in CK-MB and relatively constant levels of cTnT when determined several days apart (Table 2). These results, thus, are not indicative of acute myocardial injury and may reflect a non-cardiac source of CK-MB and cTnT elevations.

Circulating CK-MB and cTnT in acute skeletal muscle diseases

Reports on chronic elevations of CK-MB and cTnT in the absence of cTnI increases in patients with severe acute skeletal muscle damage are rare and, to our knowledge, exist in only 3 cases in the literature. In a patient with amphetamine-related rhabdomyolysis following an intestinal operation due to intestinal herniation with bowel gangrene, Sribhen et al.,[38] observed increases in both CK-MB and cTnT without concomitant cTnI elevation in the subacute regenerating phase of the disease that persisted throughout several weeks of hospital stay. The same authors have also found chronic increases in CK-MB and cTnT, but not cTnI, from elevated baseline levels to around 7-fold the upper limit of reference ranges in a patient with chronic renal failure who developed rhabdomyolysis after limb ischemia (Fig 1, personal observation). Another patient diagnosed as having sepsis-associated rhabdomyolysis exhibited persistent increases in CK-MB and cTnT throughout their stay in the rehabilitation unit.[39] Unfortunately, measurement of cTnI was not performed. Nontheless, it was theorized in both studies that the prolonged elevations of cTnT were most likely due to re-expression of cTnT isoform in regenerating skeletal muscle.

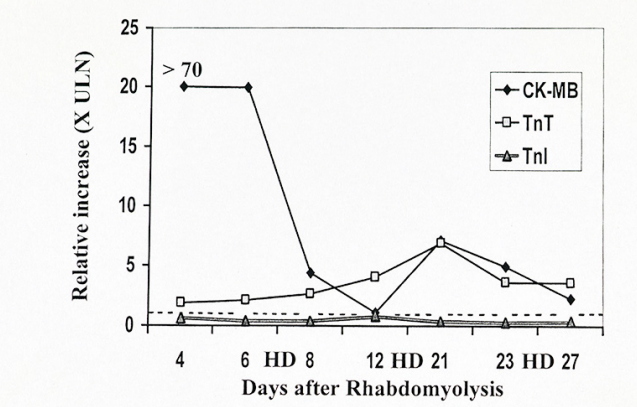
Circulating CK-MB and cTnT in cancer patients

There have been several reports of increased cardiac biomarker serum levels in cancer patients.[40-42] Even though, most of these studies have demonstrated the presence of macro CK type 1 and 2 as the non-cardiac cause of CK-MB elevation, ectopic production of CK-

TABLE 2. Serial cardiac biomarkers levels determined several days apart in patients with inflammatory myopathies.

Author (year)	Diagnosis	Cardiac biomarker levels			
		CK-MB (U/L)		cTnT (ng/ml)	
		S 1	S 2	S 1	S 2
White & Tideman (2001)	DM	243	293	0.52	0.54
Hamilton & Sharpe (2005)	DM	937	458	3.12	2.90
	PM	nd	nd	0.17	0.16
Rahim & Dave (2009)	DM	nd	nd	0.14	0.10

Abbreviations: DM = Dermatomyositis; PM = Polymyositis; S = sample; nd = not determined



CK (U/L)	161,500	80,100	15,050	529	192	272	112
CK-MB (%)	> 0.24	0.12	0.14	1.07	18.4	8.94	10.4
Creatinine	5.9	9.6	7.6	10.5	7.4	9.8	8.2

Fig 1. Patterns of cardiac biomarker release following rhabdomyolysis in a chronic renal failure patients.
Abbreviation: HD = hemodialysis. Creatinine level in mg/dl

MB by certain types of tumors has also been reported.[40] Isotalo et al.,[41] described a case of a patient with metastatic alveolar rhabdomyosarcoma in whom a series of increased concentrations of CK-MB mass and cTnT, were measured with the 2nd-generation assay, over several days. Since levels of cTnI, determined by two different immunoassays on the same blood specimens, were all in the normal ranges, a non-cardiac source of cardiac biomarkers elevations was suggested. In addition, since measurements of both CK-MB and cTnT were performed 5 months after the patient's last chemotherapy cycle, the possible toxic therapeutic effects could be ruled out. The authors theorized that rhabdomyosarcoma anaplasia leads to an immature skeletal muscle phenotype which may cause false-positive marker testing for myocardial infarction, secondary to expression of CK-MB and cTnT. Similar to these findings, persistent increases in both CK-MB and cTnT (3rd-generation assay) serum concentrations over several weeks have been found in a patient with uterine leiomyosarcoma.[42] Unfortunately, measurement of cTnI was not performed. Nevertheless, the author stated that the increases in cardiac biomarkers observed might be secondary to tumor expression of CK-MB and cTnT.

Cardiac troponins in amyotrophic lateral sclerosis

In recent years, several studies have demonstrated the presence of elevated serum cTnT concentrations in the absence of clinical evidence of an acute coronary event in amyotrophic lateral sclerosis (ALS), the most common form of motor neuron disease.[43-47] Hof et al.,[43] described a 65-year old man, diagnosed as having ALS, who presented with acute chest discomfort and nocturnal dyspnoe. Serial blood samplings have revealed slightly increased CK-MB activity and significantly elevated cTnT concentrations which persisted for several weeks. However, serum cTnI levels, determined in the same blood samples, were all in the normal ranges. Since there were no ischemic changes on electrocardiogram and the single-photon emission computed tomography (SPECT) with adenosine stimulation has shown a normal cardiac contraction and no evidence of ischemia or scarring, the initial suspicion of myocardial injury was rejected and a non-cardiac cause of cTnT elevation was assumed. Similarly, Graziani et al.[44] reported 3 cases of ALS patients with persistently high blood levels of cTnT, but normal values of cTnI in the absence of any cardiac disease. They suggested the hypothesis that non-inflammatory skeletal muscle degeneration could be the cause of re-expressed cTnT in diseased skeletal muscle and so the source of circulating cTnT. Similar observation was made in a study of ALS patients, of whom 27 (68%) patients had chronic elevations of cTnT, whereas their electrocardiographic and echocardiographic findings were negative for ischemia.[45] The study raised the possibility that cTnT originates from the atrophic skeletal muscle via re-expression of cTnT isoform.

Clinical implications for diagnosis of acute myocardial infarction

Introductions of sophisticated immunoassays for determining circulating cardiac troponins have led to cardiac biomarker testing with improved analytical sensitivity and precision. By utilizing the 99th percentile cut-off concentration that has been recommended by the international cardiology societies,[48] the diagnosis of acute coronary syndromes can be made in the early hours after the onset of symptoms, and so allowing for early risk assessment and appropriate management of the patients. The increased clinical sensitivity of the troponins, on the other hand, is associated with reduced specificity, and several conditions other than acute coronary events can cause troponin elevations.[49] These include congestive heart failure, myocarditis, stress-induced cardiomyopathy, pulmonary embolism, acute neurologic diseases (stroke, subarrhachnoid hemorrhage), sepsis and septic shock, as well as drug toxicity and drug abuse (doxorubicin, cocaine, amphetamine). Nevertheless, elevated levels of cardiac troponins found in these patients represent true-positive results indicating myocardial involvement. In contrast, increased cTnT serum concentrations in the absence of elevated cTnI found in patients with destructive skeletal muscle disorders may reflect a false-positive result, probably secondary to the re-expression of fetal cTnT isoform. Therefore, a single positive cTnT result

observed in these patients should be cautiously interpreted as biochemical evidence of cardiac involvement. In this context, it should be noted that serial measurements of cTnT which show significant rises and falls of cardiac marker points to acute coronary ischemic events, whereas chronic elevations are indicative of skeletal muscle source of cTnT. As stated by Jaffe et al.,[22] the unique specificity thought to occur for cTnT and cTnI might no longer be sustained for the current cTnT assay. The tissue specificity of cTnT could also be ensured by measuring with a sensitive cTnI assay to confirm or refute the increases in cTnT levels. Nontheless, it should be born in mind that cardiac troponin results represent only one of several criteria for the diagnosis of acute myocardial infarction and should be interpreted in conjunction with the presence of ischemic symptoms, as well as electrocardiographic, echocardiographic or other imaging results.

CONCLUSION

Measurements of cTnT and cTnI currently represent the most sensitive biochemical methods for diagnosis of myocardial injury and infarction. However, they are not disease specific, and increased cardiac troponin levels can be observed in several clinical conditions other than acute coronary syndromes. In patients with acute and chronic destructive skeletal muscle diseases, increased circulating cTnT may arise from regenerating skeletal muscle, probably as a result of re-expression of fetal cTnT isoform. In these patients, determination of cTnI levels may provide a more specific method for the early detection of myocardial involvement and a useful prognostic indicator of the diseases.

REFERENCES

1. Filatov VL, Katrukha AG, Bulargina TV, Gusev NB. Troponin: structure, properties, and mechanism of functioning. Biochemistry (Moscow). 1999;64:969-85.
2. Anderson PAW, Greig A, Mark TA, Malouf NN, Oakley AE, Ungerleider RM, et al. Molecular basis of human cardiac troponin T isoforms expressed in developing, adult and failing heart. Circ Res. 1995; 76: 681-6.
3. Adamcova M, Pelouch V. Isoforms of troponins in normal and diseased myocardium. Physiol Res. 1999; 48: 235-47.
4. Bodor GS, Porterfield D, Voss EM, Smith S, Apple FS. Cardiac troponin-I is not expressed in fetal and healthy or diseased adult human skeletal muscle tissue. Clin Chem. 1995; 41: 1710-5.
5. Sharkey SW, Murakami MM, Smith SA, Apple FS. Canine myocardial creatine kinase isoenzymes after chronic coronary artery occlusion. Circulation. 1991; 84: 333-40.
6. Hoang CD, Zhang J, Payne RM, Apple FS. Post-infarction left ventricular remodeling induces changes in creatine kinase mRNA and protein subunit levels in porcine myocardium. Am J Pathol. 1997; 151: 257-64.
7. Mehta HB, Popovic BK, Dillman WH. Comparison of creatine kinase M and B subunit mRNAs and isoenzyme activity in ischemic dog myocardium. J Mol Cell Cardiol. 1987; 19 (Suppl): 522
8. Voss EM, Sharkey SW, Gernert A, Murakami MA, Johnson RB, Hsieh CC, et al. Human and canine cardiac troponin T and CK-MB distribution in normal and diseased myocardium. Arch Pathol Lab Med. 1995; 119: 799-806.
9. Ricchiuti V, Sharkey SW, Murakami MA, Voss EM, Apple FS. Cardiac troponin I and T alterations in dogs hearts with myocardial infarction. Am J Clin Pathol. 1998; 110: 241-7.
10. Ricchiuti V, Zhang J, Apple FS. Cardiac troponin I and T alterations in hearts with severe left ventricular remodeling. Clin Chem. 1997;43:990-5.
11. Kim SH, Kim HS, Lee MM. Re-expression of fetal troponin isoforms in the postinfarction failing heart of the rat. Circ J. 2002; 66: 959-64.
12. Saba Z, Nassar R, Ungerleider RM, Oakeley AE, Anderson PWA. Cardiac troponin T isoform expression correlates with pathophysiological descriptors in patients who underwent corrective surgery for congenital heart disease. Circulation. 1996; 94: 472-6.
13. Apple FS. Tissue specificity of cardiac troponin I, cardiac troponin T and creatine kinase-MB. Clin Chim Acta. 1999; 284: 151-9.
14. Apple FS, Rogers MA, Casal DC, Sherman WM, Ivy JL. Creatine kinase MB isoenzyme adaptations in stressed human skeletal muscle of marathon runners. J Appl Physiol. 1985; 59: 149-53.
15. Apple FS, Rogers MA, Casal DC, Lewis L, Ivy JL, Lampe JW. Skeletal muscle creatine kinase MB alterations in women marathon runners. Eur J Appl Physiol. 1987; 56: 49-52.
16. Silverman LM, Mendell JR, Greumer HD. Creatine kinase isoenzymes in muscular dystrophies. Clin Chem. 1974; 20: 865-9.
17. Ricchiuti V, Apple FS. RNA expression of cardiac troponin T isoforms in diseased human skeletal muscle. Clin Chem. 1999; 45: 2129-35.
18. Messner B, Baum H, Fischer P, Quasthoff S, Neumeier D. Expression of messenger RNA of the cardiac isoforms of troponin T and I in myopathic skeletal muscle. Am J Clin Pathol. 2000; 114: 544-9.
19. Saggin L, Gorza L, Ausoni S, Schiaffino S. Cardiac troponin T in developing, regenerating and denervated rat skeletal muscle. Development. 1990; 110: 547-54.
20. Bodor GS, Survant L, Voss EM, Smith S, Porterfield D, Apple FS. Cardiac troponin T composition in normal and regenerating human skeletal muscle. Clin Chem. 1997; 43: 476-84.
21. Ricchiuti V, Voss EM, Ney A, Odland M, Anderson PAW, Apple FS. Cardiac troponin T isoforms expressed in renaldiseased skeletal muscle will not cause false-positive results by thesecondgeneration cardiac troponin T assay by Boehringer Mannheim. Clin Chem. 1998;44: 1919-24.
22. Jaffe AS, Vasile VC, Milone M, Saenger AK, Olson KN, Apple FS. Diseased skeletal muscle. A noncardiac source of increased circulating concentrations of cardiac troponin T. J Am Coll Cardiol. 2011; 58: 1819-24.
23. Gupta R, Wayangankar SA, Targoff IN, Hennebry TA. Clinical cardiac involvement in idiopathic inflammatory myopathies. A systemic review. Int J Cardiol. 2011; 148: 261-70.

24. Finsterer J, Stoellberger C, Krugluger W. Cardiac and noncardiac, particularly neuromuscular, disease with troponin-T positivity. Netherl J Med. 2007; 65: 289-95.
25. Braun SL, Pongratz DE, Bialk P, Liem S, Schlotter B, Vogt W. Discrepant results for cardiac troponin T and troponin I in chronic myopathy, depending on instrument and assay generation. Clin Chem. 1996; 42: 2039-41.
26. Erlacher P, Lercher A, Falkensammer J, Nassonov EL, Samsonov MI, Shtutman VZ, et al. Cardiac troponin and β-type myosin heavy chain concentrations in patients with polymyositis or dermatomyositis. Clin Chim Acta. 2001; 306: 27-33.
27. Sribhen K, Pussara N, Wangchaijaroenkit S, Chatchaval S. Cardiac troponin serum concentrations in patients with severe skeletal muscle damage. J Royal Coll Pathol Thai. 2002; 1: 93-6.
28. Aggarwal R, Lebiedz-Odrobina D, Sinha A, Manadan A, Case JP. Serum cardiac troponin T, but not troponin I, is elevated in idiopathic inflammatory myopathies. J Rheumatol. 2009; 36: 2711-4.
29. Fisher C, Agrawal S, Wong WM, Fahie-Wilson M, Dasgupta B. Clinical observations on the significance of raised cardiac troponin-T in patients with myositis of varying ethiologies seen in rheumatology practice. Clin Rheumatol. 2010; 29: 1107-11.
30. Cox FM, Delgado V, Verschuuren JJ, Ballieux BE, Bax JJ, Wintzen AR, et al. The heart in sporadic inclusion body myositis: a study in 51 patients. J Neurol. 2010; 257: 447-51.
31. Mair J. High-sensitivity cardiac troponins in everyday clinical practice. World J Cardiol. 2014; 6: 175-82.
32. Rittoo D, Jones A, Lecky B, Neithercut D. Elevation of cardiac troponin T but not cardiac troponin I in patients with neuromuscular diseases: Implications for the diagnosis of myocardial infarction. J Am Coll Cardiol. 2014; 63: 2411-20.
33. Kiely PD, Bruckner FE, Nisbet JA, Daghir A. Serum skeletal troponin I in inflammatory muscle disease: relation to creatine kinase, CK-MB and cardiac troponin I. Ann Rheum Dis. 2000; 59: 750-1.
34. Matsumura T, Saito T, Fujimura H, Shinno S. Cardiac troponin I for accurate evaluation of cardiac status in myopathic patients. Brain Dev. 2007; 29: 496-501.
35. White GH, Tideman PA. Increased troponin T in a patient with dermatomyositis. Clin Chem. 2001; 47: 1130-1.
36. Hamilton JS, Sharpe PC. Two cases of inflammatory muscle disease presenting with raised serum concentrations of troponin T. J Clin Pathol. 2005; 58: 1323-4.
37. Rahim KF, Dawe RS. Dermatomyositis presenting with symptomatic Dermographism and raised troponin T: a case report. J Med Case Rep. 2009; 3: 7319.
38. Sribhen K, Sirivatanaauksorn Y, Vorrakitpokatorn P, Phankingthongkum R, Opartkiattikul N. Discordant cardiac troponin results in amphetamine-related rhabdomyolysis. Siriraj Hosp Gaz. 2002; 54: 181-7.
39. Visvanathan R, Visvanathan T. A puzzling elevation of troponin T. N Zealand Med J. 2002; 115: 1-3.
40. Wu AHB, Feng YJ, Nadelman J, Acampora M, Fiedler PN. Ectopic production of creatine kinase MB: updated evaluation by mass assays. Clin Chem. 1997; 43: 2006-7.
41. Isotalo PA, Greenway DC, Donnelly JG. Metastatic alveolar rhabdomyosarcoma with increased serum creatine kinase MB and cardiac troponin T and normal cardiac troponin I. Clin Chem. 1999; 45: 1576-8.
42. Agewall S. Increases of creatine kinase MB and cardiac troponin T in serum of a patient with uterine leiomyosarcoma. Clin Chem. 2000; 46:2016-7.
43. Hof D, Jung HH, Bloch KE. Troponin T elevation in amyotrophiclateral sclerosis without cardiac damage. Amyotrophic Lateral Sclerosis. 2013; 14: 75-7.
44. Graziani A, Casmiro M, Zaninotto M, Mirici Cappa F, Lazzari I, Valenti S, et al. Serum cardiac troponin T in patients with amyotrophic lateral sclerosis without myocardial damage: case reports. Open J Clin Med Case Rep. 2017; 3: 1-5.
45. Mach L, Koneeny T, Helanova K, Jaffe AS, Sorenson EJ, Somers VK, et al. Elevation of cardiac troponin T in patients with amyotrophic lateral sclerosis. Acta Neurol Belg. 2016;116(4): 557-64.
46. Graziani A, Del Gludice E, Casmiro M, Pontone G, Lanzi A, Mirici Cappa F, et al. Elevation of troponin T in mechanical ventilated patient with amyotrophic lateral sclerosis. Case Reports Intern Med. 2015; 2: 22-5.
47. Mamo JP. Motor neurone disease presenting with raised serum troponin T. Scott Med J. 2015;60(2): e1-3.
48. Thygesen K, Alpert JS, White HD: on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Eur Heart J 2007; 28: 2525-38.
49. Sribhen K, Sribhen C. Pattern and molecular mechanisms of cardiac troponin release in conditions other than acute coronary syndromes. Siriraj Med J 2011; 63: 139-42.