

# Measurements Of Serum Cardiac Troponin T In Patients With Congestive Heart Failure

C Xue, H Yu, R Li, J Wo, J Cui, H Cheng, H Wang, Q Guan, X Suo, R Jia

## Citation

C Xue, H Yu, R Li, J Wo, J Cui, H Cheng, H Wang, Q Guan, X Suo, R Jia. *Measurements Of Serum Cardiac Troponin T In Patients With Congestive Heart Failure*. The Internet Journal of Cardiovascular Research. 2005 Volume 3 Number 1.

## Abstract

**Objectives:** To determine whether the level of serum cardiac troponin T (cTnT) was increased in patients with congestive heart failure (CHF).

**Methods:** This study consisted of 265 patients with CHF and 75 healthy people. Serum cTnT was measured by electrochemiluminescence immunoassay with Elecsys1010 automatic analyzer.

**Results** cTnT concentration was  $0.181 \pm 0.536$  ng/mL in CHF patients and  $0.003 \pm 0.001$  ng/mL in controls ( $p < 0.001$ ). Patients were categorized according to the levels of heart function and left ventricular ejection fraction (LVEF). In the first group including 105 patients with  $LVEF \leq 35\%$ , cTnT was  $0.311 \pm 0.221$  ng/mL. In the second group including 106 patients with  $LVEF > 35\%$ , cTnT was  $0.07 \pm 0.05$  ng/mL ( $p < 0.01$ ). In patients with NYHA class I-IV, cTnT values were  $0.062 \pm 0.022$  ng/mL,  $0.113 \pm 0.121$  mg/mL,  $0.191 \pm 0.231$  mg/ml, and  $0.384 \pm 0.211$  mg/mL respectively (class I vs class II  $p > 0.05$ , class II vs class III  $p < 0.01$ , class III vs class IV  $p < 0.01$ ). A negative correlation was observed between serum cTnT concentration and LVEF in 265 patients with CHF ( $r = -0.493$ ,  $p < 0.001$ )

**Conclusions** This study shows that serum cTnT was increased in patients with CHF and that the level paralleled the severity of CHF.

## INTRODUCTION

Congestive heart failure (CHF) is a clinical syndrome caused by different underlying cardiac disease. Irreversible progression of CHF is known to occur, but the underlying mechanisms remain unclear, possibly because of inadequate sensitivity of the measurements used.

Cardiac troponin T (cTnT), a tropomyosin-binding protein of the regulatory complex located on the contractile apparatus of cardiac myocytes,<sup>1</sup> is a newly developed highly sensitive and specific marker for myocardial necrosis.<sup>2</sup> Because of the high organ specificity of cTnT, increases in plasma concentration of this protein clearly indicate myocardial cell necrosis.<sup>3</sup> This study is to observe the relation between cTnT and CHF.

## PATIENTS AND METHODS

### PATIENTS

This study began on September in 1998 and finished on

August in 2001. The study group consisted of 265 consecutive patients (196 men, mean age  $56 \pm 16$  years) admitted to the Department of Cardiovascular Medicine at Binzhou People's Hospital. The diagnosis of CHF was based on the criteria of the European Society of Cardiology.<sup>4</sup>

Patients with acute myocardial infarction and unstable angina pectoris (in 60 days before blood sample was collected), cardiac surgery (in 6 months before blood sample was collected), chronic or acute decompensated pulmonary disease, end-stage renal failure, severe systemic illness, skeletal muscle diseases were excluded. Standard therapy for CHF including digoxin, diuretics, and angiotensin-converting enzyme inhibitors were used in all patients. Ischemic cardiomyopathy was diagnosed by the history of definite old myocardial infarction (98 patients) and coronary angiography (74 patients). Primary dilated cardiomyopathy (93 patients) was diagnosed by echocardiography. and coronary angiography was performed in 17 patients whose age was over 40 years old or with cardiovascular risk factor.

The characteristics of patients with CHF were summarized in Table 1.

Control population consisted of 75 healthy people (men 45, women 30, mean age 49±11years). Blood samples from patients were obtained on the first day of admission. Control blood samples from 75 healthy people were obtained at fast condition. Blood samples were allowed to clot for 30 min at room temperature and were centrifuged for 5 min. All blood samples were measured without frozen within 3 hrs after collection.

**METHODS**

Cardiac troponin T was measured by electrochemiluminescence immunoassay with Elecsys1010 automatic analyzer (Roche Company, Basel Switzerland). Inter-assay and intra-assay coefficient of variation was <4% and <7% respectively. The level of sensitivity is < 1pmol. LVEF was obtained by 2-dimensional echocardiography with HDI 3000 echocardiography.

**STATISTICAL ANALYSIS**

Data were expressed as mean ± SD. Between-group differences were compared with student t test. Relations between variables were assessed by correlations.

**Figure 1**

Table 1: The characteristics of patients with CHF

No. patients	265
Age(y)	56±18
Sex M/F	169/96
Cause of CHF	
Ischemic cardiomyopathy	172
Primary dilated cardiomyopathy	93
NYHA n (%)	
Class I	75 (28.3)
Class II	67 (25.3)
Class III	70 (26.3)
Class IV	53 (20)
Left ventricular ejection fraction	
All patients with CHF	0.30±0.01
Ischemic cardiomyopathy	0.31±0.01
Primary dilated cardiomyopathy	0.29±0.02
Class I	0.48±0.01
Class II	0.38±0.01
Class III	0.27±0.02
Class IV	0.15±0.01

**RESULTS**

In patients with CHF, the mean cTnT concentration was 0.181±0.536ng/mL, significantly higher than the healthy subjects (0.003±0.001ng/mL, P<0.001).

There were no differences in serum cTnT concentrations between patients with primary dilated cardiomyopathies and ischemic cardiomyopathies (0.175±0.21ng/mL vs 0.186±0.27ng/mL, P>0.05).

In order to evaluate the relations between serum cTnT and severity of CHF, patients were categorized according to their NYHA classes and LVEF. The mean concentrations of cTnT were 0.062±0.022ng/mL, 0.113±0.121mg/mL, 0.191±0.231mg/ml, 0.384±0.211mg/mL, respectively, in patients with NYHA class I, class II, class III, and class IV (class I vs class II, P>0.05, class II vs class III, P<0.01, class III vs class IV, P<0.01). The mean cTnT concentration was 0.311±0.221ng/mL in patients with LVEF≤35%, significantly higher than patients with LVEF>35% (0.07±0.05ng/mL, P<0.01).

There was a negative correlation between serum cTnT concentration and LVEF in the 265 patients with CHF (r=-0.493, P<0.001)

**DISCUSSION**

Previous studies have shown that patients with CHF have high levels of serum cardiac troponins. In 1995, Misson and Calzolari first reported positive serum troponin I (cutoff value = 0.1ng/mL) in 2 of 11 patients with CHF. In a further study with much more sensitive immunoenzymometric assay, the same group found that 10 of 11 patients with end stage CHF had high circulating levels of cardiac troponin I. In addition, they found a negative correlative between serum cTnT concentration and LVEF (r= -0.70, P=0.01). In 1997, they provided the first evidence for ongoing myofibrillar degradation of cardiomyocytes and increased cardiac troponin I levels in patients with advanced CHF. La Vecchia reported a similar result in 1997; they also found that the normalization of cardiac troponin I levels in circulation during hospitalization was associated with an improvement of CHF.

Both troponin T and I are subunits of troponin complex and have similar clinical significance in detecting myocytes necrosis. In our study, a much more sensitive and specific electrochemiluminescence immunoassay was used. Mean cTnT concentration was 0.003±0.001ng/mL in 75 controls. Serum cTnT concentration was 0.181±0.536ng/mL in patients with CHF, significantly higher than that in the controls (P<0.0001). The serum concentration of cTnT paralleled the severity of the disease, and had a negative correlation with LVEF in patients with CHF.

cTnT was initially used in the diagnosis of AMI with 0.1ng/mL as the upper reference limit. It is inappropriate used in the patients with CHF. This is because of the chronic low-level myocardial injury in the patients with CHF. The

prognostic value of cTnT detected by second-generation assay in patients with CHF was reported by Setsuta et al,<sup>9</sup> the discriminative value for identifying the high risk patients with CHF (cTnT $\geq$ 0.05ng/mL) was lower than discriminative value used for diagnosis of patients with AMI (cTnT $\geq$ 0.1ng/mL). In a recent study by Missov et al,<sup>10</sup> 33 patients with CHF and 47 healthy control subjects were involved. They found that cTnT was increased in patients with CHF and that the levels of serum cTnT paralleled the severity of the disease. They concluded that cTnT was a suitable candidate-marker molecule to monitor CHF from a structural perspective. Our study further demonstrated their clinical findings.

The mechanisms for the release of cTnT in CHF are not clear. Neurohormonal activation and myocardial remodeling is the main feature in the progression of CHF.<sup>11</sup> Many factors can cause myocardial remodeling: mechanical stress, angiotensin, norepinephrine, oxidative stress, inflammatory cytokines, nitric oxide, endothelin, and peptide growth factors.<sup>11</sup> Pathologically, myocardial remodeling is characterized by "...changes in the quantity and quality of the extracellular matrix, and death of cardiac myocytes by apoptosis."<sup>11</sup> Apoptosis occurs in the myocardium of patient with end-stage cardiomyopathy.<sup>12,13</sup> It may be one of the mechanisms for the release of cTnT. Reduced subendocardial coronary perfusion in severe left ventricular hypertrophy may be a mechanism of myocyte necrosis,<sup>14</sup> which may cause increased serum cTnT. Coronary artery disease was present in 68% of patients with CHF,<sup>15</sup> which causes low-level necrosis of myocytes and then elevated serum concentration of cTnT. Therefore the loss of myocytes in the patients with CHF may be the mechanism for the release of cTnT.

Ricchiuti<sup>16</sup> observed significant decrease in protein mass and concentration for troponin T and I in an experimental model of left ventricular remodeled porcine myocardium. This study further demonstrated that myofibril degradation and loss of structurally bound cardiac protein are the mechanisms for the release of cTnT.

In our study with much more sensitive and specific electrochemiluminescence immunoassay, we further demonstrated elevated serum cTnT in the patients with CHF and found a negative correlation between serum cTnT concentration and LVEF.

In summary, elevated serum cTnT in CHF may indicate

ongoing myocardial damage involved in the progression of CHF. Elevated serum cTnT in CHF is caused by multiple processes that eventually destroy the contractile apparatus. It would be interesting to know whether cTnT elevation has any diagnostic and prognostic value for CHF. Further studies are needed to elucidate the actual mechanisms and clinical significance of cTnT increases in CHF.

### CORRESPONDENCE TO

Chuncaì Xue, MD Department of Cardiology The People's Hospital of Binzhou City Shandong province, PR China 256610 Tel: +86 543-3282497 E-mail: xuehc@yahoo.com.cn

### References

1. Donnely R, Hillis WS. Cardiac troponin T. *Lancet* 1993; 341:410-411.
2. Katus HA, Looser S, Hallermayer K, et al. Development and in vitro characterization of a new immunoassay of cardiac troponin T. *Clin Chem* 1992; 38:386-393.
3. Missov E, Mair J. A novel biochemical approach to congestive heart failure: Cardiac troponin T. *Am Heart J* 1999; 138:95-99.
4. The Task Force on Heart Failure of the European Society of Cardiology. Guidelines for the diagnosis of heart failure. *Eur Heart J* 1995; 16:741-751.
5. Missov E, Calzolari C. Elevated cardiac troponin I in some patients with severe congestive heart failure [abstract]. *J Mol Cell Cardio* 1995; 27:A405.
6. Missov E, Calzolari C, Pau B. High circulating levels of circulating troponin I in human congestive heart failure. *J Am Coll Cardiol* 1996; 27(suppl A):338A.
7. Missov E, Calzolari C, Pau B. circulating troponin I in severe congestive heart failure. *Circulation* 1997; 96:2953-2958.
8. La Vecchia L, Mezzena G, Ometto R, et al. Detectable serum troponin I in patients with heart failure of nonmyocardial ischemic origin. *Am J Cardiol* 1997; 80:88-89.
9. Setsuta K, Ohtsuka T, Ogawa T, et al. Prognostic value of second generation cardiac troponin T in patients with chronic heart failure[abstract]. *J Am Coll Cardiol* 1998; 31:249A.
10. Missov E, Mair J, Innsbruck. A novel biochemical approach to congestive heart failure: Cardiac troponin T. *Am Heart J* 1999; 138:95-99.
11. Colucci WS. Molecular and cellular mechanisms of myocardial failure. *Am J Cardiol* 1997; 80:15L-25L.
12. Narula J, Haider N, Virmani R, et al. Apoptosis in myocytes in end-stage heart failure. *N Eng J Med* 1996; 335:1182-1189.
13. Olivetti G, Abbi R, Quaini F, et al. Apoptosis in the failing human heart. *N Eng J Med* 1997; 336:1131-1141.
14. Carlos H, Del Carlo, Christopher M, et al. Cardiac troponins in congestive heart failure. *Am Heart J* 1999; 138:646-653.
15. Gheorghiade M, Bonow RO. Chronic heart failure in the United States. A manifestation of coronary artery disease. *Circulation* 1998; 97:282-289.
16. Ricchiuti V, Zhang J, Apple FS. Cardiac troponin I and T alterations in heart with severe left ventricular remodeling. *Clin Chem* 1997; 43:990-995.

**Author Information**

**Chuncaai Xue, M.D.**

**Hongwei Yu, M.D.**

**Ruijie Li, M.D.**

**Jinshan Wo, M.D.**

**Jiayu Cui**

**Haibin Cheng, M.D.**

**Hongyun Wang, M.D.**

**Qinghua Guan, M.D.**

**Xiaoxia Suo, M.D.**

**Rongbo Jia, M.D.**