Original Article

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The Relationship between Troponin I Level and Severity of Liver Cirrhosis

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ABSTRACT

Background: Troponin I is a biological marker specifically derived from the cardiac muscle and is used to make a diagnosis of myocardial injury in clinical practice. Cirrhotic cardiomyopathy is a new entity recently reported in patients with advanced cirrhosis. Elevation of troponin I is accepted to be a marker of cirrhotic cardiomyopathy.

Objective: To determine the relationship between troponin I level and the severity of cirrhosis and other parameters.

Methods: Seventy-nine cirrhotic patients without established cardiovascular diseases were enrolled consecutively to the study between 1 January 2011 and 31 December 2011. The demographic and laboratory data were obtained. Sera were collected for measurement of troponin I levels by chemiluminescent microparticle immunoassay (CMIA). Univariate analysis was performed. Correlation of troponin I level and the severity of cirrhosis (Child-Pugh and MELD score) were analyzed by Pearson correlation test. *P*-value less than 0.05 was defined as statistical significance.

Result: Forty patients (50.6%) were male. Mean age was 60.8 ± 9.2 years. The etiologies of cirrhosis were alcohol (39.2%) and non-alcohol (60.8%) related. Mean troponin I level was 0.0064 ± 0.013 ng/mL. Child class A, B, and C were found in 40 (50.6%), 34 (43%), and 5 (6.3%) patients, respectively. From univariate analysis, the factors significantly associated with decompensated cirrhosis (defined by Child B or Child C group) were lower blood pressure, hyponatremia, elevation of troponin I level, prolonged QTc interval, and male gender. There was a significant correlation between troponin I level and serum potassium (r = 0.24, $p = 0.035$), and Child-Pugh score (r = 0.28, $p = 0.013$). Mean troponin I levels in Child class A, B and, C were 0.0028 ± 0.005, 0.0100 ± 0.018, and 0.0098 ± 0.007 ng/mL ($p = 0.004$), respectively.

Conclusion: Serum troponin I level increases with more advanced stages in cirrhotic patients. This may lead to the possibility that cirrhotic cardiomyopathy is more common in end stage liver diseases. The use of serum troponin I to detect cirrhotic cardiomyopathy in clinical practice requires further study.

Key words : Troponin I, cirrhotic cardiomyopathy, liver cirrhosis

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INTRODUCTION

Hemodynamic change in cirrhotic patients was characterized by hyperdynamic heart reflected by increase in cardiac output, and heart rate, and decrease in systemic vascular resistance[1]. From the 2005 World congress of gastroenterology in Montreal, the definition of cirrhotic cardiomyopathy is a cardiac dysfunction in cirrhotic patients characterized by impaired contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease[2]. This condition can be diagnosed by the evidence of systolic or diastolic dysfunction with some supportive evidences such as abnormal electrophysiology, chronotropic response, prolonged QTc interval, increased BNP, pro-BNP, or troponin I[2]. Nearly one third of the patients with cirrhosis have evidence of cardiomyopathy[3]. Furthermore, more than 80% of patients with end stage of liver disease have parasympathetic or sympathetic dysfunction characterized by abnormal response of heart rate or blood pressure to physical activity[4].

Troponin is a complex consisting of troponin I, T, and C protein which is essential for the process of the calcium-mediated regulation of skeletal and cardiac muscle contraction[5]. Troponin T contains the binding site for tropomyosin and troponin C. The troponin I is the inhibitor of actomyosin ATPase that inhibits muscle contraction. The binding of calcium to troponin C abolishes the inhibitory action of troponin on actin filaments. Because troponin C isoform in cardiac and skeletal muscles cannot be distinguished, therefore, it is not specific to the cardiac injury[6]. Troponin I and troponin T isoforms are dissimilar to the other isoforms and specific to the cardiac muscle[7-12]. The CK-MB assays are not specific for the heart muscle. It is also expressed in the skeletal muscle, the gastrointestinal tract and the uterus of the pregnant woman[14]. Therefore, the troponin assays are more specific to the cardiac muscle and have been used to diagnose the cardiac injury since their first introduction in the early nineties.

Interestingly, Pateron *et al*. found that there were 10 out of 32 cirrhotic patients without previous cardiac disease who have elevated troponin I level from their study which was correlated with lower stroke volume index and ventricular mass index[14]. In patients with acute liver failure, Parekh *et al*. showed that the elevation of troponin I level was associated with higher mortality rate and more severe of coma[15]. Watt *et al*. showed that the elevation of troponin I level can predict patients and graft survival in patients after liver transplantation[16]. And the recent study by Coss E *et al*., serum troponin I level before liver transplantation is associated with post-transplant cardiovascular events[17].

However, there are still small data about the relationship of serum troponin I level and the severity of liver cirrhosis and its correlation with other clinical parameters in cirrhotic patients. So the aim of this study is to determine the relationship between troponin I level and the severity of cirrhosis and other parameters. Of note, cardiac troponin I isoform is used in this study because it is less interfered by renal insufficiency than cardiac troponin T[16,18].

MATERIALS AND METHODS

Study patients

Seventy-nine cirrhotic patients who visited the liver clinic at Ramathibodi hospital from 1 January to 31 December 2011 were enrolled in the cross-sectional study. The inclusion criteria was cirrhotic patients older than 18 years; liver cirrhosis was diagnosed by clinical, imaging, transient elastography, and/or liver biopsy. The exclusion criteria were the history of cardiac diseases (such as acute coronary syndrome, congestive heart failure, arrhythmia, valvular heart disease, post cardiac surgery, myocarditis, pericarditis, post percutaneous coronary intervention, post radiofrequency ablation, pacemaker implantation, and implantable cardioverter defibrillator shock), non-cardiac condition that may have elevated serum cardiac troponin I level (such as hypertensive crisis, pulmonary embolism, COPD, rhabdomyolysis, sepsis, acute stroke, subarachnoid hemorrhage, amyloidosis, post chemotherapy, seizure, diabetic ketotic acidosis, electrical trauma), hepatocellular carcinoma, pregnancy, taking medications that effect the QT interval, active alcoholic, and patients who denied to participate the study. Patient data including age, sex, height, weight, body mass index, systolic blood pressure, diastolic blood pressure, pulse rate, causes of cirrhosis, grading of ascites, and hepatic encephalopathy, severity of cirrhosis, underlying disease and current medication were obtained. The study protocol was approved by the hospital ethics committees.

Laboratory tests

Blood samples were obtained for complete blood count, prothrombin time, INR, blood urea nitrogen, creatinine, electrolyte, calcium, magnesium, phosphate, liver biochemistry test, lipid profile, fasting blood sugar and troponin I. Sera were store at -80oc and collected for measurement of troponin I levels by chemiluminescent microparticle immunoassay (CMIA). The assay was performed by biochemist blinded to the patient data.

Statistical Analysis

Results were presented in mean ± SD. Univariate analysis was performed with *t*-test, non-parametric, or Exact tests where appropriate. Correlation of troponin I level and parameters including the severity of cirrhosis (Child-Pugh and MELD score) was analyzed by Pearson correlation test. Kruskal-Wallis test was used for comparing troponin I level among 3 groups of cirrhosis according to Child-Pugh classification. *P*-value less than 0.05 was defined as statistical significance. All statistic analyses were performed using PASW version 18.

RESULTS

Forty patients (50.6%) were male. Mean age was 60.8 ± 9.2 years. The etiologies of cirrhosis were alcohol (39.2%), hepatitis C virus (22.8%), hepatitis B virus (21.5%), NASH (8.9%), autoimmune liver disease (5.1%), Wilson disease (1.3%), and HBV-HCV coinfection (1.3%). Child class A, B and C were found in 40 (50.6%), 34 (43%) and 5 (6.3%) patients, respectively.

By univariate analysis, the factors significantly associate with decompensated cirrhosis (defined by Child B plus Child C group) were lower systolic blood pressure (p = 0.025), lower diastolic blood pressure (p = 0.004), hyponatremia (p <0.001), elevation of troponin I level (p = 0.015), prolonged QTc interval (p <0.001), and male gender (p = 0.002).

Mean troponin I level in this study population was

Table 1. Clinical and laboratory data in compensated and decompensated cirrhotic patients.

	Compensated cirrhosis (n = 40)	Decompensated cirrhosis (n = 39)	Univariate analysis *p*-value
Age*(years)	62 (8.8)	59.6 (9.6)	0.252
Sex: male#	13 (32.5)	27 (69.2)	0.002
SBP*(mmHg)	129.2 (18.7)	119.1 (20.2)	0.025
DBP*(mmHg)	74.8 (10.2)	66.7 (13.6)	0.004
MELD score*	8.7 (1.8)	13 (2.8)	<0.001
Creatinine* (mg/dL)	0.9 (0.2)	1 (0.3)	0.134
Sodium* (mmol/L)	138.8 (2.9)	135.6 (3.8)	<0.001
Potassium* (mmol/L)	4.1 (0.3)	4.1 (0.5)	0.959
Magnesium* (mg/dL)	2.1 (0.4)	1.8 (0.2)	0.001
Troponin I* (ng/mL)	0.0028 (0.005)	0.0100 (0.17)	0.015
QTc interval* (ms)	427.2 (22.4)	456.2 (22.5)	<0.001

*mean (SD); #n (%)

Table 2. QTc interval in cirrhotic patients.

Child-Pugh classification	Mean (ms)	Standard deviation (ms)	Min (ms)	Max (ms)
A	427.16	22.43	384	479
B	456.37	23.42	423	499
C	454.00	11.53	442	465
Total	**440.63**	**26.63**	**384**	**499**

(p <0.001)

Table 3. Serum troponin I level in cirrhotic patients.

Child-Pugh classification	Mean (ng/mL)	SD (ng/mL)	Min (ng/mL)	Max (ng/mL)
A	0.0028	0.005	0	0.0028
B	0.0100	0.018	0	0.0910
C	0.0098	0.007	0	0.0210
Total	**0.0064**	**0.013**	**0**	**0.0910**

($p = 0.004$)

Table 4. The correlation between troponin I level (ng/mL) with clinical and laboratory parameters.

	SBP (mmHg)	DBP (mmHg)	Na (mmol/L)	K (mmol/L)	Corrected Ca (mg/dL)	Mg (mg/dL)	MELD	Child score	QTc (msec)
r	0.025	-0.086	-0.062	0.239	0.161	-0.190	0.219	0.279	0.198
p-value	0.831	0.455	0.588	0.035	0.161	0.098	0.052	0.013	0.098

0.0064 ± 0.013 ng/mL and the levels in Child class A, B and C, respectively were 0.0028 ± 0.005, 0.0100 ± 0.018, and 0.0098 ± 0.007 ng/mL ($p = 0.004$). By Pearson's correlation coefficient, the troponin I level significantly correlate with serum potassium (r = 0.24, $p = 0.035$), and Child-Pugh score (r = 0.28, $p = 0.013$) (Table 1).

Discussion

Serum troponin I level has been used for making the diagnosis of myocardial injury. Elevated troponin I could be found in cirrhotic patients who had no history of cardiac disease and was related to lower stroke-volume index and left ventricular mass[14]. It could increase in acute liver failure and was associated with more advanced hepatic coma (grade III or IV) and death rate[15]. In liver transplant patients, the pre-transplant elevation of troponin I level could predict the post-transplant patient mortality, graft loss[16], and cardiovascular events[17]. In our study, we found that elevated troponin I level was associated to the more severity of cirrhosis according to Child-Pugh score and serum potassium of cirrhotic patients. We hypothesize that decompensated cirrhotic patients may have some degree of myocardial injury more than the other. Therefore, troponin I was increased in parallel to the worsening of liver cirrhotic status. Aldosterone antagonist is usually required in patients with decompensated cirrhotic. Thus, hyperkalemia-related to aldosterone antagonist was correlated with the elevation of troponin I level.

Conclusion

Elevated troponin I is one of addition criteria to diagnose cirrhotic cardiomyopathy. It is associated to the severity of cirrhosis and serum potassium in our study.

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