

Serum Cardiac Troponin-T as a Prognostic Marker in Septic Shock

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Background: Cardiac troponins are markers for myocardial injury. Sepsis and septic shock can cause myocardial injury. The significance of elevated cardiac troponin T (cTnT) in septic shock was evaluated in the present study.

Material and Method: Serum levels of cTnT were measured in 40 patients with septic shock from Rajavithi Hospital during a nine-month period between December 2004 and August 2005. Patients with acute myocardial infarction were excluded by clinical presentation, electrocardiography, and measurement of creatine kinase.

Results: The levels of cardiac troponin T were elevated in 17 patients (42.5%) and not elevated in 23 patients (57.5%). There were 28 deaths (70%) and 12 patients (30%) survived and were discharged from the hospital. cTnT-positive patients had a significantly higher mortality rate (17 of 17 patients in the cTnT-positive group and 11 of 23 patients in the cTnT-negative group; $p < 0.001$).

Conclusion: Elevated cTnT levels may be a marker for severity of illness and higher mortality in patients with septic shock.

Keywords: Cardiac troponin T, Septic shock, Prognosis

J Med Assoc Thai 2008; 91 (12): 1818-22

Full text. e-Journal: <http://www.medassocthai.org/journal>

Cardiac isoforms of troponin I and troponin T are highly sensitive and specific markers for myocardial injury. The Joint Committee of the European Society of Cardiology and the American College of Cardiology recommend troponins as the standard biomarker for the diagnosis of acute myocardial infarction⁽¹⁾. Cardiac troponins are also useful prognostic markers in acute coronary syndrome⁽²⁾.

Other conditions such as sepsis^(3,4), septic shock⁽⁵⁾, acute stroke⁽⁶⁾, and pulmonary embolism⁽⁷⁾ may be associated with myocardial injury, which may lead to the elevated levels of cardiac troponins. The elevated troponin levels indicate a worse prognosis in stroke⁽⁶⁾ and pulmonary embolism^(7,8). Sepsis and septic shock can cause myocardial injury from abnormalities in coronary perfusion and microcirculation. Myocardial function is depressed in severe sepsis by myocardial

depressant factors. Cardiac troponins have been found to be elevated in septic shock and may be an adverse prognostic marker⁽⁵⁾.

The present study evaluated the prevalence of elevated cardiac troponin T (cTnT) in patients with septic shock and the prognostic value of this biomarker.

Material and Method

Patient population

The patients in the present study were hospitalized at the Department of Medicine of Rajvithi Hospital, Bangkok, Thailand. This was a prospective observational cohort study. The authors enrolled 40 patients with evidence of sepsis, septic shock, or systemic inflammatory response syndrome and multiple organ failure. Patients with unstable angina, signs of acute ischemia from the electrocardiogram (ST elevation or depression ≥ 1 mm) or elevated levels of MB fraction of creatinine kinase (CKMB) 2 times above the upper normal limit were excluded from the present study. Other

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exclusion criteria included cardiogenic pulmonary edema, history of acute coronary syndrome within the last 6 months, recent cardiothoracic trauma or surgery, cardiopulmonary resuscitation, cardioversion, evidence of endocarditis, myocarditis, and pericarditis.

Most patients had severe infections and developed septic shock within 24 hours after hospitalization. Sepsis, septic shock, and systemic inflammatory response syndrome (SIRS) are defined as follows:

1. SIRS: Two or more of the following conditions:
 - 1.1 Temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$
 - 1.2 Heart rate of > 90 beats/minute
 - 1.3 Respiratory rate of > 20 breaths/minute or partial pressure of arterial CO_2 of < 32 mmHg
 - 1.4 White blood cell count of $> 12,000$ cells/mL or $< 4,000$ cells/mL
2. Sepsis: SIRS in response to documented infection (culture or Gram stain of blood, sputum, urine, or normally sterile body fluid positive for pathogenic microorganism); or focus of infection identified by visual inspection
3. Septic shock: systolic pressure of less than 90 mmHg or a reduction of greater than 40 mmHg from the baseline blood pressure; with no response to fluid resuscitation; with organ hypoperfusion or dysfunction.

Antibiotics were initially given according to the judgment of the attending physician until the results of blood cultures were known.

All patients gave written informed consent and the present study was approved by the ethics committee of Rajvithi Hospital. The present study was funded by Rajavithi Hospital research fund.

Data collection and diagnostic investigations

All the patients were treated for septic shock with antibiotics, intravenous fluids, and vasopressors when indicated. Two blood samples were taken within a 15 minute interval for blood culture. Creatinine kinase MB isoenzyme and troponin T serum levels were measured at the medical ward with the onset of shock and 6 hours later. The levels of cTnT were determined by a qualitative immunological assay (TropT, Roche Diagnostics). An ECG was performed at the onset of shock at the medical ward and repeated 6 hours later to exclude acute coronary syndrome. Serum cTnT were defined as positive if greater than or equal to 0.1 ng/ml while levels less than 0.1 ng/ml were considered negative. At least one specimen had to be elevated to be defined as cTnT positive. The primary end point was the mortality rate in patients with elevated cTnT, in comparison with those with no elevated cTnT.

Statistical analysis

The clinical variables including sex, age, hypertension, diabetes, dyslipidemia, smoking, and alcoholic intake were documented and analyzed. The Chi-square test was used to compare the differences in categorical variables (%) and the mortality between cTnT positive and cTnT negative groups. Continuous variables were analyzed by Student's t-test. A p-value of < 0.05 was considered statistical significance different.

Results

The present study enrolled 40 patients with septic shock who matched the inclusion criteria. The mean age was 60 ± 19.7 years, with a range of 20 to 98 years. The baseline characteristics of the patients are shown in Table 1. All the patients received vasopressors including dopamine (100%), norepinephrine (12.5%), or dobutamine (7.55%). The levels of cTnT were elevated in 17 patients (42.5%) and not elevated in 23 patients (57.5%). There were 28 deaths (70%) and 12 patients (30%) survived and were discharged from the hospital. The blood culture was positive in 16 patients (40%) and negative in 24 patients (60%) (Table 2).

There were no significant differences in the frequency of baseline clinical characteristics including previous history of stroke, coronary artery disease, smoking, and alcohol intake in cTnT positive and cTnT negative groups. The cTnT positive group had a significantly higher prevalence of hypertension ($p < 0.01$) and dyslipidemia ($p = 0.05$) than the cTnT negative group (Table 1).

The cTnT positive group had a significantly higher mortality rate (17 of 17 in the cTnT positive group and 11 of 23 in the cTnT negative group, $p < 0.001$). The mean cTnT level was 0.17 ± 0.12 ng/ml on the initial evaluation and 0.19 ± 0.13 ng/ml on the second time. The mortality rate significantly increased with the increasing age and significantly decreased with patient with febrile neutropenia. The mortality rate was not increased by the site of infection or the presence of bacteremia.

Discussion

In the present study, critically ill medical patients with septic shock and elevated cardiac troponin T levels have an increased mortality rate. Troponin elevation is one of the markers of myocardial injury that is used for the diagnosis of myocardial infarction, but other conditions can cause myocardial injury. The

Table 1. The baseline characteristics and vassopressor use between cTnT positive and cTnT negative group of 40 patients with septic shock

	All patients n = 40 (%)	cTnT positive n = 17 (%)	cTnT negative n = 23 (%)	p-value
Age > 65 yrs (%)	18 (45.0)	10 (58.8)	8 (34.8)	0.23
Diabetes (%)	18 (45.0)	11 (64.7)	7 (30.4)	0.06
Hypertension (%)	26 (65.0)	16 (94.1)	10 (43.5)	<0.01
Stroke (%)	4 (10.0)	2 (11.8)	2 (8.7)	0.99
Coronary artery disease (%)	1 (2.5)	1 (5.9)	0 (0)	0.87
Smoking (%)	21 (52.5)	11 (64.7)	10 (43.5)	0.31
Alcohol (%)	14 (35.0)	6 (35.3)	8 (34.8)	0.99
Dyslipidemia (%)	20 (50.0)	12 (70.6)	8 (34.8)	0.05
Norepinephrine (%)	5 (12.5)	3 (17.6)	2 (8.7)	0.71
Dobutamine (%)	3 (7.5)	2 (11.8)	1 (4.4)	0.78
Dopamine (%)	40 (100)	17 (100)	23 (100)	NA
Positive hemoculture (%)	16 (40.0)	9 (53.0)	7 (30.4)	0.151
Sepsis due toPneumonia (%)	23 (57.5)	9 (53.0)	14 (60.9)	0.616
Sepsis due toUTI (%)	9 (22.5)	5 (29.4)	4 (17.4)	0.456

Table 2. Risk for death

	All (n = 40) (%)	Survival (n = 12) (%)	Death (n = 28) (%)	p-value
Elevated cTnT	17 (42.5)	0	17 (60.7)	<0.001
Age (years) (mean ± SD)	60 ± 19.70	47 ± 23.11	66 ± 15.12	<00.05
Positive blood culture	16 (40.0)	5 (41.7)	11 (39.3)	0.99
Pneumonia	23 (57.5)	7 (58.3)	16 (57.1)	0.99
Urinary tract infection	9 (22.5)	2 (22.5)	7 (25.0)	0.697

presence of myocardial injury probably indicates a poor prognosis whatever the cause. Troponins have been found to indicate a poor prognosis in stroke, pulmonary embolism, and sepsis. Previous studies have shown that elevated troponin levels are markers of left ventricular dysfunction in sepsis^(9,10). The duration of hypotension⁽¹¹⁾ and the maximal number of vasopressor doses administered⁽¹²⁾ were found to be correlated to cardiac troponin levels. Mehta et al⁽⁵⁾ reported that in his series of 37 patients with septic shock, troponin positive patients (9 of 16) had a higher mortality (56% vs. 24%, $p = 0.04$) compared to troponin negative patients (5 of 21). Spies et al⁽⁴⁾ also reported that in 26 patients with sepsis troponin, positive patients (15/18) had a mortality rate of 83%, whereas troponin negative patients (3 of 8) had a mortality rate of 37%, $p = 0.02$.

The diagnostic and prognostic impact of elevated cardiac troponin levels in patients with sepsis

has been established, the underlying mechanisms still require clarification. In the present study, risk factors for coronary artery disease namely hypertension and dyslipidemia were significantly more common in patients with elevated troponins. This may indicate that the endothelial function and microcirculation is abnormal in these patients and such patients may be prone to develop myocardial microinfarctions.

Conclusion

Elevated cardiac troponins may be a marker for severity of illness and higher mortality in septic shock. Significantly higher levels of cardiac troponins are found in patients with hypertension or dyslipidemia. Additional studies are needed to determine if cardiac troponins are an independent risk factor for mortality in intensive care patients without acute coronary syndrome.

Limitation

The limitations of the present study are a small sample size and lack of evaluation of the ejection fraction. Multivariate analysis was not performed because of the small sample size. Clinical prediction scores such as the APACHE II score was not calculated because it was not originally developed for individual outcome prediction in patients with septic shock⁽¹³⁾. The patients did not fit the definition⁽¹⁾ of an acute myocardial infarction but subclinical coronary artery disease could not be excluded.

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ระดับ cardiac troponin-T ในเลือดเป็นตัวบ่งชี้ถึงการพยากรณ์โรคติดเชื้อที่มีภาวะช็อก

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ภูมิหลัง: ระดับ cardiac troponin-T ในเลือดจะสูงขึ้น เมื่อกล้ามเนื้อหัวใจถูกทำลาย โรคติดเชื้อที่มีภาวะช็อกสามารถทำให้เกิดการการทำลายกล้ามเนื้อหัวใจ ระดับ cardiac troponin-T น่าจะสูงขึ้นในภาวะช็อก จากการติดเชื้อ

วัตถุประสงค์: เพื่อศึกษาถึงอุบัติการณ์ และการพยากรณ์โรคของระดับ cardiac troponin-T ในเลือดของผู้ป่วยช็อก จากการติดเชื้อ

วัสดุและวิธีการ: ทำการศึกษาผู้ป่วยช็อกจากการติดเชื้อที่รับไว้รักษาในโรงพยาบาลราชวิถี จำนวน 40 ราย ในช่วงเดือนธันวาคม พ.ศ. 2547 ถึง สิงหาคม พ.ศ. 2548 โดยเจาะหาระดับ cardiac troponin-T, ผู้ป่วยที่เป็น acute myocardial infarction จะถูกตัดออกจากการศึกษา โดยดูอาการและอาการแสดง คลื่นไฟฟ้าหัวใจ และการวัดระดับ creatinine kinase

ผลการศึกษา: ระดับ cardiac troponin-T สูงขึ้นในผู้ป่วย 17 ราย (ร้อยละ 42.5) และปกติในผู้ป่วย 23 ราย (ร้อยละ 57.5) มีผู้ป่วยเสียชีวิต 28 ราย (ร้อยละ 70) และอยู่รอดจนกลับบ้านได้ 17 ราย (ร้อยละ 30) ผู้ป่วยที่มีระดับ troponin-T สูง มีอัตราการตายสูงกว่าผู้ป่วยที่มีระดับ troponin-T ปกติ อย่างมีนัยสำคัญทางสถิติ ($p < 0.001$)

สรุป: ระดับ cardiac troponin-T ที่สูงขึ้นในผู้ป่วยช็อกจากการติดเชื้อ อาจบ่งชี้ว่าการพยากรณ์โรคไม่ดี และมีอัตราตายที่สูงขึ้น
