Comparison between Cardiac Troponin I and Troponin T in the Diagnosis of Acute Myocardial Infarction

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Abstract

Background: Accurate measurement of cardiac troponin is important as an aid in the diagnosis of acute myocardial infarction (AMI). The Architect® new troponin I (cTnI) assays are a fully automated chemiluminescent microparticle immunoassay (CMIA). The assays, a two-step sandwich format with a highly specific monoclonal antibody, claim to provide more sensitivity than the conventional troponin T (cTnT) assay in the diagnosis of AMI patients. Moreover, the Architect® cTnI assay is suppose to be free from renal failure interferences and to provide excellent precision in the low concentration range. The aim of this study was to compare the reliability of the two cardiac specific troponin assays; namely the new Architect® cTnI and conventional cTnT assay in aiding in decision making of suspected AMI patients. We also compared the correlation of both assays in patients without AMI that have chronic kidney disease.

Methods: The diagnostic study was conducted in the Emergency Department of the Ramathibodi hospital during a six month period in 2006-2007. Eligible patients had to be at least 30 years old with chest pain lasting more than 20 minutes that was suspected to be myocardial in origin with the onset occurring within 3 to 72 hours. Cardiac troponin assays were tested together with other general blood chemistries. The final diagnosis and clinical data were later obtained from their medical records.

Results: Of the 87 included patients, one third (29, 33.3%) had AMI. The quantitative assays for both cTnI and cTnT were detected in 20 (68.9%) patients with AMI. In regards to the cTnI assay, the provisional cut-off point from the manufacturer (0.032 ng/ml) showed a sensitivity of 82.8% and a specificity of 79.3% (positive predictive value = 0.67, negative predictive value = 0.90). While in the cTnT assay at the cut-off point of 0.03 ng/ml, a sensitivity and specificity of 69.0% and 89.7% (PPV = 0.77, NPV = 0.85) respectively were shown. The area under the curve of troponin I was 0.87 while that of troponin T was 0.84 (p = 0.44). In patients without AMI who had chronic kidney disease (CKD) serum cTnI and cTnT concentrations were more likely to increase in association with more severe CKD.

Conclusion: Although the recently developed cTnI assay claims to have more sensitivity for the diagnosis of AMI patients, our study demonstrated no significant differences between cTnI and cTnT in the diagnosis of AMI. The concern in patients with chronic kidney disease who might have false positive results from the tests, both serum cTnI and cTnT concentrations were similarly increased with increasing severity of CKD.

Keywords: Acute myocardial infarction, Cardiac troponin, Chronic kidney disease

Introduction

Cardiovascular disease (CVD) is the one leading cause of morbidity and mortality in Thailand. In 2002 World Health Organization (WHO) reported about 280,000 Thai people died from CVD. Thus, proper triage of the Emergency Department (ED) patients with chest pain will not only reduce morbidity and mortality but will also decrease health care expenditures. The Joint European Society of Cardiology/American College of Cardiology Committee current guideline redefines MI and supports the use of cardiac troponin (cTn) as a preferred marker for myocardial injury(1). Accordingly, cardiac troponin (cTn) is regarded as the most sensitive and specific marker in
aiding in the diagnosis of myocardial infarction. In the past, there were no fundamental differences between troponin T (cTnT) and troponin I (cTnI) testing (2-7). In a recent report it was shown that some assays had superior clinical performance compared with other troponin assays with similar analytic sensitivities and performances (8). With the accumulating knowledge of the presence in blood of many different forms of troponins and interfering factors in the form of autoantibodies, we postulated that the assay configuration with respect to epitope specificity of the antibodies determines the clinical performance, possibly because different forms and molecular complexes of troponins are identified by the assays (8). It appears that epitope 41–49 is critical.

Recently, the ARCHITECT Stat troponin I which is a chemiluminescent microparticle immunoassay was developed. It is a two-step sandwich configured with monoclonal antibodies for both the microparticles and the acridinium-derivative conjugate. It includes a monoclonal antibody directed toward epitope 41-49. This method provides an increase in sensitivity for the diagnosis of acute myocardial infarction (AMI) patients. Moreover, controversy about increasing troponin levels in patients without acute coronary syndrome (ACS) but who have chronic kidney disease is an issue. The Architect cTnI assay is suppose to be free from interferences due to renal failure and also provide excellent precision in the low concentration range.

Our objective was to compare the accuracy between cTnI (Architect stat troponin I) and cTnT (Elecys TnT Roche diagnostics) in the diagnosis of patients suspected of myocardial infarction (MI) as well as in patients without AMI that have chronic kidney disease.

Methods
Study design

The diagnostic study was conducted at a single center in the ED of the Ramathibodi hospital during a six month period in 2006-2007. Eligible patients had to be at least 30 years old with chest pain lasting more than 20 minutes suspected to be myocardial in origin and occurring within 3 to 72 hours of presentation. This study was approved by the Ethics committee. The patients had to give informed consent. We excluded the patient who had angina with an established precipitating cause (e.g. Anemia or Tachydysrhythmia).

The final diagnosis and clinical data of these patients were obtained later from their medical records.

Blood samples were obtained on arrival in the Emergency Department and sent to the chemistry laboratory. The physician collected the clinical data. Management and disposition of the patient were determined by the attending physician. Attending physicians and investigators did not have access to the results of the cardiac marker from the core laboratory. ECG was interpreted by 2 cardiologists unaware of any results.

A final diagnosis of AMI was established according to the presence of two out of three criteria (Thai Acute Coronary Syndrome registry)

ST-segment Elevation Myocardial Infarction (STEMI):
angina pain > 20 minutes combined with one of the following criteria:

1. ECG: New or presumed new ST-segment elevation in 2 or more contiguous leads with the cutoff points greater than or equal to 0.2 mV in leads V1, V2, or V3, or greater than or equal to 0.1 mV in other leads or new left bundle branch block
2. Elevation of creatine kinase (CK) or creatine kinase MB (CKMB) level ≥ 2 times of the upper normal limit

(Notes: typical elevation of ECG as STEMI without angina pain can be diagnosed as STEMI)

Non-ST segment Elevation Myocardial Infarction (NSTEMI): criteria for diagnosis:

1. Angina pain ≥ 20 minutes and/or symptoms of dyspnea
2. Elevation of CK or CKMB level ≥ 2 times of the upper normal limit
3. EKG: ST depression or inverted T wave

The definition of chronic kidney disease were from the National Kidney Foundation of the United States through its Kidney Disease Outcomes Quality Initiative (K/DOQI) program (9) and National Health and Nutrition Examination Survey (NHANES) (10)
**Stage 1** disease is defined by a normal glomerular filtration rate (GFR) (greater than 90 mL/min per 1.73 m²) and persistent albuminuria (2.8 percent of the total United States population)

**Stage 2** disease is a GFR between 60 to 89 mL/min per 1.73 m² and persistent albuminuria (2.8 percent)

**Stage 3** disease is a GFR between 30 and 59 mL/min per 1.73 m² (3.7 percent)

**Stage 4** disease is a GFR between 15 and 29 mL/min per 1.73 m² (0.13 percent)

**Stage 5** disease is a GFR of less than 15 mL/min per 1.73 m² or end-stage renal diseases.

**Laboratory analysis**

Blood samples were collected in an EDTA-coated tube and assayed with ARCHITECT® STAT Troponin-I (Abbot Diagnostic’s division, Germany) for the cTnI level while the cTnT level was assayed with Elecsys TnT (Roche diagnostics, Switzerland). The ESC/ACC guideline for the cut-off value of cTnI for AMI uses a 10% coefficient variation (CV) at 0.032 ng/mL while the cut-off value of cTnT uses a 10% CV at 0.03 ng/mL.

Blood samples for CK-MB were also collected in EDTA coated tubes and were analyzed by CK-MB Immuno (Abbot Diagnostic’s division, Germany). The upper reference limit (URL) was 24 U/L. The cutoff limit for AMI was greater than or equal to two times the upper normal limit.

**Statistical analyses**

Continuous variables are presented as mean ± SD or median with 25th and 75th percentiles. Discrete variables are expressed as frequencies and percentages. Sensitivity and specificity were obtained cross-sectionally. Exact 95% CIs for binomial proportions were calculated for sensitivity and specificity. P value ≤ 0.05 was considered significant. The area and standard error of the ROC curve were calculated for cTnI and for cTnT to evaluate the relationship between concentrations of each of these markers for sensitivity and specificity for the diagnosis of MI by use of SPSS 11.5. The area under the curve for cTnI and cTnT were compared by STATA 8. The relationship between cTnI and cTnT in chronic kidney disease patients without AMI were compared by the Kolmogorov-Smirnov test.

**Results**

Of 87 included patients, one third (29, 33.3%) had AMI. Seven patients had STEMI while 22 patients had NSTEMI. Of the fifty-five patients without AMI, two thirds had CKD stage ≥ 3. Table 1 illustrates the demographic characteristics of the patients between the two groups. Most of the demographic data were comparable between the two groups, with the exception of more smokers in the AMI group.

The over all accuracies of cTnI and cTnT in the discrimination of patients with or without AMI were evaluated by ROC analysis (Figure 1). The areas under ROC curves for cTnI was larger at 0.88 (95%CI 0.78 - 0.97) compared with cTnT, which had a ROC area of 0.84 (95% CI 0.79 – 0.89) with p = 0.44. Regarding cTnI, the provisional cut-off point from the manufacturer (0.032 ng/ml) showed a sensitivity of 82.8% and a specificity of 79.3% (positive predictive value or PPV = 0.67, negative predictive value or NPV = 0.90). Whereas cTnT, at the cut-off point 0.03 ng/ml, showed a sensitivity and specificity of 69.6% and 89.7% (PPV = 0.77, NPV = 0.85) respectively. Five of 29 (17.2%) patients found to be negative by both assays to cTn developed coronary syndromes. False positive results were seen in 9 patients. These patients were diagnosed with conditions such as congestive heart failure (3), CKD ≥ 3 (5) and bronchitis (1).

![ROC for cTnI and cTnT](image_url)
We classified the patients without AMI into 5 groups (CKD 1-5) according to glomerular infiltration rate and determined the value of cTnI and cTnT in each group. The median value at each stage is shown in Figure 2.

From our study, patients with chronic kidney disease without AMI, both serum cTnI and cTnT concentrations were more likely to increase in the presence of more severe CKD (Figure 2). At the 10% CV cutoff value for cTnI false positives were 12/58 (20.7%), whereas for cTnT false positives were 6/58 (10.3%), respectively.

### Table 1. Demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>AMI (N = 29)</th>
<th>Non-AMI (N = 58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>64.62 ± 12.66</td>
<td>64.12 ± 11.71</td>
<td>0.85</td>
</tr>
<tr>
<td>Gender, Male/Female</td>
<td>20/9</td>
<td>36/22</td>
<td>0.53</td>
</tr>
<tr>
<td>Symptom duration at arrival to ED, mean ± SD, h</td>
<td>13.24 ± 15.58</td>
<td>18.77 ± 15.11</td>
<td>0.15</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>51.7</td>
<td>41.4</td>
<td>0.36</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>75.9</td>
<td>69</td>
<td>0.5</td>
</tr>
<tr>
<td>Dyslipidemia, %</td>
<td>72.4</td>
<td>56.9</td>
<td>0.16</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>37.9</td>
<td>17.9</td>
<td>0.042</td>
</tr>
<tr>
<td>Prior MI/CABG, %</td>
<td>48.3</td>
<td>39.7</td>
<td>0.44</td>
</tr>
<tr>
<td>CKD ≥ 3, %</td>
<td>62</td>
<td>65.55</td>
<td>1.00</td>
</tr>
<tr>
<td>CVA, %</td>
<td>13.8</td>
<td>12.1</td>
<td>0.82</td>
</tr>
<tr>
<td>PVD, %</td>
<td>3.4</td>
<td>0</td>
<td>0.15</td>
</tr>
<tr>
<td>Heart rate, mean ± SD, bpm</td>
<td>84.86 ± 20.64</td>
<td>82.86 ± 16.76</td>
<td>0.10</td>
</tr>
<tr>
<td>SBP, mean ± SD, mmHg</td>
<td>144.79 ± 34.21</td>
<td>139.40 ± 27.58</td>
<td>0.12</td>
</tr>
<tr>
<td>DBP, mean ± SD, mmHg</td>
<td>80.45 ± 19.91</td>
<td>78.48 ± 14.51</td>
<td>0.08</td>
</tr>
</tbody>
</table>

### Discussion

Myocardial salvage in cases of an acute coronary event (MI/ACS) is time dependent, and the greatest potential benefit exists in the first few hours of ACS (11). MI is more likely in patients with elevated cTnI than in those with normal values (11), and mortality of patients with elevated troponin I or T is significantly increased (odds ratio= 3:1) compared to that of patients with a negative test (12). Clinical judgment supported by troponin tests has been demonstrated to be more predictive than clinical judgment alone (12).

Comparisons of the sensitivities and specificities of troponin I and T for the diagnosis of acute MI have been made. In the past, there was no fundamental difference between cTnT and cTnI testing (2-4, 6-7). In a recent report it was shown that some assays had superior clinical performance compared with other troponin assays with similar analytic sensitivities and performances (8). Recently, Abbott Diagnostics redesigned their cTnI assay and included in their Architect assay a monoclonal antibody against epitope 41-49 in the heart-specific N-terminal region of the troponin molecule. This seemed to be more
From our study as shown in Figure 2, serum cTnI and cTnT concentrations were more commonly increased in the presence of more severe CKD. The cut off value from the manufacture may cause false positive results in 20.7%, 10.3% for cTnI and cTnT, respectively. However, elevated cTnT identify a subgroup of ESRD patients who have poor survival and a high risk of cardiac death despite being asymptomatic. These findings suggest that cTnT is a promising risk stratification tool and may help frame therapeutic decisions. The clinical interpretation of elevated cTnI levels, however, remain unclear, largely because of the lack of standardization of assays (19).

The limitation of our study was too small of a sample size that was performed in a single center. So a larger study should be done. This may show differences in sensitivity and specificity for the diagnosis of AMI which would benefit patients to receive the best treatment and risk stratification.

In conclusion, although recently developed cTnI seems to have more sensitivity for diagnosing the AMI patient our study showed that there were no significant differences between cTnI and cTnT in the diagnosis of AMI. As concerns, patients with chronic kidney disease, who might have false positive results from the test, both serum cTnI and cTnT concentrations were similarly increased as the severity of CKD increased.

References


การศึกษาเปรียบเทียบระหว่างการคัดเลือกทดสอบโปรตีน (cTnI) และ การคัดเลือกโปรตีน (cTnT) ในการวินิจฉัยผู้ป่วยที่มีภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน

อริยลักษณ์ เจริญพหุชิตร ผศ.น. ปิยะรัต ศรีราชา ผศ.น. อร.น., ดุษฎี เลิศวรรณ์ ผศ.น. อร.น., สมลักษณ์ วรรณวงศ์ วท.น.เพทยิ

วิทยาศาสตร์

บทคัดย่อ

วัตถุประสงค์: ตามแนวคิดในการตรวจสอบการคัดเลือกทดสอบโปรตีนในเคี้ยวเอ็นบทบาทสำคัญในการช่วยวินิจฉัยผู้ป่วยที่มีภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน ไปในงานเรียน Architect® เป็นวิธีการตรวจหาการคัดเลือกทดสอบโปรตีน (cTnI) ในเคี้ยวเอ็นบทบาท โดยการใช้ chemiluminescent microparticle immunoassay (CMIA) ส่งผลถึงผลแบบ is two-step sandwich format การตรวจคัดเลือกการคัดเลือกที่ผู้มีภาวะกลั้มเนื้อหัวใจตายเฉียบพลันมากกว่าการตรวจหาการคัดเลือกทดสอบโปรตีน (cTnT) ที่ใช้กันโดยทั่วไป นอกจำกนั้นการตรวจหาการคัดเลือกทดสอบโปรตีน (cTnI) ซึ่งมีผลกระทบจากภาวะได้รับกระตือรนั้น การศึกษามีวัตถุประสงค์เพื่อเปรียบเทียบความไวและความแม่นยำของการใช้การคัดเลือกทดสอบโปรตีนที่ผลิตจากองค์การในการช่วยวินิจฉัยผู้ป่วยที่มีภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน รวมทั้งการศึกษาความสัมพันธ์ของการคัดเลือกทดสอบโปรตีนที่ผลิตจากองค์การกับผู้ป่วยที่มีภาวะได้รับกระตือรนั้น ๆ

วิธีการศึกษา: วิธีการตรวจหาการคัดเลือกทดสอบโปรตีน (cTnI) และการคัดเลือกทดสอบโปรตีน (cTnT) ในเคี้ยวเอ็นของผู้ป่วยที่มารับการรักษาที่แผนกภักดีรวมเวลาในช่วง 6 เดือนระหว่าง พ.ศ. 2549-2550 ผู้ป่วยทั้งหมดมีการศึกษาจะต้องมีอายุอย่างน้อย 30 ปี มีอาการเจ็บป่วยที่คลาสคลินิกมากกว่ากระตือรนั้นเริ่มต้นโดยถูกส่งเข้าพยาบาลเป็นเวลาอย่างน้อย 20นาที และอยู่ในช่วง 3-72 ชั่วโมงหลังเกิดอาการ และทำการเก็บเชื้อวัคซีนโลหิตและข้อมูลทางคลินิกจากวิทยาศาสตร์ของผู้ป่วยในภายหลัง

ผลการศึกษา: มีผู้ป่วยขึ้นร่วมการศึกษาทั้งสิ้นจำนวน 87 คนทั้งในของผู้ป่วย (29,33.3%) ถูกวินิจฉัยว่าภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน และตรวจหาการคัดเลือกทดสอบโปรตีนที่ผลิตจากองค์การทั้งหมดจำนวน 20 คน (68.9%) จากที่ค่า cut-off ของคัดเลือกทดสอบโปรตีน (cTnI) ที่ 0.032 ng/ml พบว่ามี sensitivitityเท่ากับ 82.8% และ specificity เท่ากับ 79.3% (positive predictive value เท่ากับ 0.67, negative predictive value เท่ากับ 0.90) ในขณะที่การใช้คัดเลือกทดสอบโปรตีน (cTnT) ที่ค่า cut-off เท่ากับ 0.031 ng/ml พบว่ามี sensivitity เท่ากับ 69.0% และ specificity เท่ากับ 89.7% (positive predictive value เท่ากับ 0.77, negative predictive value เท่ากับ 0.85) ตามที่เป็น Area under the curve ของการคัดเลือกทดสอบโปรตีน (cTnI) เท่ากับ 0.87 และ Area under the curve ของการคัดเลือกทดสอบโปรตีน (cTnT) มีค่าเท่ากับ 0.84 (p = 0.44). ในผู้ป่วยโรคโลหิตแข็งรั้งที่ไม่ได้รับการวินิจฉัยว่าภาวะกลั้มเนื้อหัวใจตายเฉียบพลันรวมทั้งหมดพบว่า ระดับของการคัดเลือกทดสอบโปรตีนที่ผลิตจากองค์การไม่มีผลต่อกลับมันความรุนแรงของการตายเฉียบพลัน

สรุป: ไม่พึงมีความแตกต่างระหว่างการใช้การคัดเลือกทดสอบโปรตีน (cTnI) และการคัดเลือกทดสอบโปรตีน (cTnT) ในภาวะวินิจฉัยผู้ป่วยที่มีภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน ผู้ป่วยโรคโลหิตแข็งรั้งที่ถูกวินิจฉัยว่าภาวะกลั้มเนื้อหัวใจตายเฉียบพลัน พบไม่มีผลต่อกลับมันความรุนแรงของการตายเฉียบพลันเรื่อง