Troponin I, Troponin T, or Creatine Kinase-MB to Detect Perioperative Myocardial Damage After Coronary Artery Bypass Surgery*

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Study objectives: To compare cardiac troponin I (cTnI), cardiac troponin T (cTnT), and creatine kinase MB (CKMB mass) in patients with and without new Q wave on the ECG following coronary artery bypass graft (CABG) surgery.

Patients: After ethic committee's approval and informed consent, 82 patients, mean age 63±10 years, scheduled for CABG were included.

Interventions: Arterial blood samples were drawn during cardiopulmonary bypass, before, and 6, 12, 24, and 48 h after aortic cross-clamp release. cTnl, cTnT, and CKMB mass were measured. The appearance of new Q wave on the ECG performed preoperatively and 24 h postoperatively was used to assess myocardial lesion independently of biological markers.

Results: There were 69 patients without new Q wave on the ECG (group 1) and 13 with (group 2). In group 1, cTnl reached a peak of 2.1 μg/L (median, interquartile range [IQ]=2.4) at 12 h, cTnT increased progressively with a peak of 0.22 μg/L (IQ=0.2) at 48 h, and CKMB presented an earlier peak of 10 μg/L (IQ=6.2) at 6 h. Starting with the same median value, group 2 patients presented significantly higher peaks: cTnl: 17 μg/L (IQ=16) at 12 h; cTnT: 1.4 μg/L (IQ=2.3) at 12 h; and CKMB mass: 74 μg/L (IQ=61) at 6 h. Receiver operating characteristic (ROC) curves were constructed. The area under the curve was 0.90 for cTnl, 0.84 for CKMB, and 0.81 for cTnT (not significant). The best cutoff values to discriminate between group 1 and group 2 patients were determined with the ROC curves: cTnl=5 μg/L; CKMB mass=20 μg/L; cTnT=0.3 μg/L. Sensitivity, specificity, and positive and negative values for cTnl (5 μg/L) were 91%, 82%, 53%, and 98%, respectively.

Conclusions: There was little differences among cTnl, cTnT, and CKMB after CABG to diagnose myocardial damage as assessed by new Q wave on the ECG. There was a trend of cTnl to be a better discriminator than cTnT, but it did not reach statistical significance.

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Key words: coronary artery bypass surgery; creatine kinase; myocardial infarction; troponin I; troponin T

Abbreviations: CABG=coronary artery bypass graft; CK=creatine kinase; CKMB=creatine kinase MB; cTnl=cardiac troponin I; cTnT=cardiac troponin T; ROC=receiver operative characteristic

Cardiac troponin I (cTnl), troponin T (cTnT), and creatine kinase-MB (CKMB mass) are specific markers of myocardial injury and are, at present, widely used to detect perioperative myocardial dam-

age during coronary artery bypass graft (CABG) surgery. They are also of some help to compare different types and routes of delivery of cardioplegia. However, cTnT and CKMB are expressed in injured striated muscles as well, which limits their specificity. The cardiac isoform of troponin I is highly specific and allows accurate detection of myocardial damage. Therefore, cTnl dosage might help evaluate myocardial injury after CABG. The usefulness of cTnl dosages after CABG has been examined in very few studies and to our knowledge, no report compared cTnl with cTnT and CKMB in the same patients in this setting.

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The aim of this study was to compare cTnI, cTnT, and CKMB mass in patients with and without new Q wave on the surface ECG after CABG surgery.

**Materials and Methods**

**Patients**

Eighty-two patients were included in this study. Their mean (±SD) age was 63±10 years. Patients were scheduled for elective CABG surgery. They were excluded if they had a myocardial infarction or unstable angina in the previous 2 months. The ethics committee gave approval and informed consent was obtained from every patient. Myocardial protection was achieved by using a modified St. Thomas solution that was superfused directly through the coronary ostia until cardiac arrest was obtained and then reinjected every 20 min during aortic cross clamping. Standard cardiopulmonary bypass techniques with moderate hypothermia were used.

**End Point**

All patients underwent a 12-lead surface ECG preoperatively, 1 h, and 24 h postoperatively, and before hospital discharge. ECGs were assessed by an experienced cardiologist unaware of any clinical and biological information. Diagnostic criteria for “new postoperative Q wave” were new Q waves of at least 0.03 s duration or broadening of preexisting Q waves or new QS deflection in at least two leads.5

**Blood Sampling**

Serial venous blood samples were obtained immediately before anesthesia induction, before aortic declamping (0), and 6, 12, 24, and 48 h after aortic declamping. Plasma samples were stored at −70°C after centrifugation and processed in the month following collection for measurements of CKMB mass, cTnI, and cTnT.

**Analytical Methods**

cTnI was measured by a fluorometric enzyme immunoassay (Stratus; Dade International; Miami) for cTnI. This cTnI assay is an automated two-site immunoassay that utilizes two monoclonal antibodies specific for the cardiac isoform of troponin I. The mass concentration (microgram per liter) of cTnI is monitored by front surface fluorescence. According to the manufacturer’s information, the minimum detectable concentration is 0.35 μg/L. Levels of cTnI are undetectable (97.5 percentile) in apparently healthy individuals.6

Troponin T was measured by an enzyme-linked immunosorbent assay with an automated analyzer (Boehringer Mannheim; Indianapolis). The capture antibody is specific for cTnT and the detection antibody, labeled with peroxidase, has a 12% rate of cross-reactivity with skeletal muscle troponin T. The lower limit of detection of the assay is 0.035 μg/L according to manufacturer’s information, and the reference range is 0 to 0.1 μg/L.7

The serum levels of CKMB mass were measured at 25°C by an enzyme immunoassay with anti-CK-MB monoclonal antibodies (Stratus; Dade International). The limit of detection is 0.4 μg/L. The upper limit of reference range is 7 μg/L.8

**Table 1—Preoperative, Peroperative, and Postoperative Data**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Without New Q wave)</th>
<th>Group 2 (With New Q wave)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>60</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>67 (11)</td>
<td>65 (20)</td>
<td>0.7</td>
</tr>
<tr>
<td>Male, %</td>
<td>64±9.6</td>
<td>63±12</td>
<td></td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>91</td>
<td>85</td>
<td>0.4</td>
</tr>
<tr>
<td>No. of vessels with stenosis ≥75%</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>0.8</td>
</tr>
<tr>
<td>EF, %</td>
<td>2.7±0.5</td>
<td>2.7±0.4</td>
<td></td>
</tr>
<tr>
<td>Perioperative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of grafts</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>0.8</td>
</tr>
<tr>
<td>No. of IMAG</td>
<td>1.4±0.6</td>
<td>1.5±0.5</td>
<td>0.07</td>
</tr>
<tr>
<td>ECC time, min</td>
<td>67 (25)</td>
<td>76 (21)</td>
<td></td>
</tr>
<tr>
<td>ACC time, min</td>
<td>64±16</td>
<td>73±13</td>
<td></td>
</tr>
<tr>
<td>Defibrillation shocks</td>
<td>1 (1)</td>
<td>0 (2)</td>
<td>0.8</td>
</tr>
<tr>
<td>Postoperative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation, h</td>
<td>20 (5)</td>
<td>21 (8)</td>
<td>0.8</td>
</tr>
<tr>
<td>ICU stay, d</td>
<td>20.6±7.8</td>
<td>20±10.3</td>
<td></td>
</tr>
<tr>
<td>Isotropic support, %</td>
<td>1.6±1.3</td>
<td>3±2.9</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*Median (interquartile range) and mean±SD or number of patients.
ACC=aortic cross clamp; ECC=extracorporeal circulation; EF=ejection fraction; IMAG=internal mammary graft; MI=myocardial infarction.
Statistical Analysis

Continuous variables (cTnI, cTnT, CKMB values, and clinical variables) are presented as median (interquartile range, 25 to 75 percentiles width) except when stated otherwise. The Mann-Whitney test was used for comparison between group 1 and group 2. The Wilcoxon signed rank test and χ² test were used for comparisons of matched samples. The association between continuous variable was analyzed by the Spearman rank correlation test. A p value <0.05 was considered to indicate statistical significance. Receiver operative characteristic (ROC) curves were constructed and their area under the curve compared. The best thresholds for cTnI, cTnT, and CKMB were determined with the ROC curves to discriminate between patients with and without new Q wave on the ECG. Sensitivity, specificity, positive and negative predictive value, and likelihood ratio were calculated.

RESULTS

Patient Data

There were 69 patients without new Q wave (group 1) and 13 with (group 2). Preoperative, operative, and postoperative data are shown in Table 1 for the two groups. No operative death occurred and no mechanical assistance was needed in any patient. There was no significant difference between the two groups as for age, coronary lesions, number, and type of grafts. Length of stay in the ICU was significantly longer in group 2 patients.

Time Courses of cTnI, CKMB Mass, and cTnT

Among the 69 patients in group 1, the course of serial cTnI, cTnT, and CKMB mass measurements was constantly low (Fig. 1). The cTnI values before anaesthesiology induction and before the aortic cross-clamp release were <0.35 µg/L for all group 1 patients. The median peak of 2.1 µg/L was recorded at 12 h. cTnT increased progressively with a peak of 0.22 µg/L at 48 h. CKMB presented an earlier peak of 10 µg/L at 6 h. The values of cTnI, cTnT, and CKMB at 6, 12, and 24 h were significantly different from baseline (p<0.05).

In group 2 patients, cTnI, cTnT, and CKMB values were significantly higher than those of group

![Figure 2](http://journal.publications.chestnet.org/03/27/2015)

**Figure 2.** ROC curves for cTnI, cTnT, and CKMB mass. The prevalence of new Q wave was 0.16. The equation 1-specificity is represented as a straight diagonal line and indicates a worthless test. The larger the area under the ROC curve, the better the discriminative power of the test (area under the curve).

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**Table 2—Rank Correlation (Spearman Rank Correlation Test) Between cTnI at 12 and 24 h and CKMB Mass and cTnT at 12 and 24 h**

<table>
<thead>
<tr>
<th></th>
<th>MB 12</th>
<th>MB 24</th>
<th>cTnT 12</th>
<th>cTnT 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTnI 12</td>
<td>0.82</td>
<td>0.78</td>
<td>0.7</td>
<td>0.73</td>
</tr>
<tr>
<td>cTnI 24</td>
<td>0.86</td>
<td>0.84</td>
<td>0.63</td>
<td>0.75</td>
</tr>
<tr>
<td>cTnT 12</td>
<td>0.55</td>
<td>0.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnT 24</td>
<td>0.47</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All correlations are significant with p<0.001.
Table 3—Comparison of cTnI (5 μg/L), CKMB (20 μg/L), and cTnT (0.3 μg/L) for Identifying Myocardial Lesion as Indicated by the Appearance of New Q Wave on the ECG After CABG

<table>
<thead>
<tr>
<th></th>
<th>cTnI &gt;5 μg/L</th>
<th>CKMB &gt;20 μg/L</th>
<th>cTnT &gt;0.3 μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.91 (0.75–1)</td>
<td>0.82 (0.60–1)</td>
<td>0.75 (0.51–1)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.82 (0.72–0.92)</td>
<td>0.79 (0.67–0.89)</td>
<td>0.75 (0.64–0.85)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.53 (0.28–0.72)</td>
<td>0.42 (0.20–0.61)</td>
<td>0.36 (0.17–0.55)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.98 (0.94–1)</td>
<td>0.95 (0.90–1)</td>
<td>0.94 (0.87–1)</td>
</tr>
<tr>
<td>Efficiency</td>
<td>0.83 (0.74–0.92)</td>
<td>0.79 (0.69–0.88)</td>
<td>0.75 (0.65–0.85)</td>
</tr>
<tr>
<td>Likelihood ratio</td>
<td>5.6</td>
<td>4</td>
<td>2.9</td>
</tr>
</tbody>
</table>

*95% confidence limits.

1 at 6, 12, and 24 h after aortic cross-clamp release (p<0.01). Group 2 patients started with the same median value as group 1 patients (cTnI=0.35 μg/L [p=0.7]; cTnT=0.06 μg/L [p=0.8]; CKMB=3 μg/L [p=0.4]), then reached a median peak at 12 h of 17 μg/L for cTnI and 1.4 μg/L for cTnT. The median peak of CKMB mass was 74 μg/L at 6 h.

As shown in Table 2, there was a strong correlation among cTnI, cTnT, and CKMB values at any time (p<0.001, n=82).

**Diagnostic Performance of cTnI, cTnT, and CKMB Mass**

The area under the ROC curves were 0.91 (SE: 0.06) for cTnI, 0.84 (SE: 0.07) for CKMB, and 0.81 (SE: 0.07) for cTnT (p=0.1 for cTnI vs cTnT and 0.4 for cTnT vs CKMB), (Fig. 2). The best cutoff values at 12 h were 5 μg/L for cTnI, 0.3 μg/L for cTnT, and 20 μg/L for CKMB mass. The higher sensitivity and specificity were obtained with cTnI and a limit of 5 μg/L yields a 91% sensitivity, 82% specificity, 53% positive predictive value, and 98% negative predictive value (Table 3).

**DISCUSSION**

The main findings of our study were that (1) in uncomplicated postoperative CABG, cTnI values remained constantly low, contrasting with very high values when perioperative myocardial infarction occurred, and (2) there was little difference between cTnI, cTnT, and CKMB to diagnose myocardial damage after CABG as assessed by the appearance of new Q wave on the ECG.

**Troponins and CABG**

Troponins are regulatory proteins (I, C, T) located in the striated muscle. They regulate actinomyosine interactions. These proteins have a small cytosol distribution with the majority being tightly complexed to the contractile apparatus.10 Plasma levels are low in healthy patients. With acute myocardial lesion, plasma cTnI or cTnT concentration increases rapidly due to the release of the cytosolic fraction. Cell death and destruction of its contractile apparatus induce continued release of troponins for 1 week.1 cTnI is highly specific for myocardial injury,11,12 it is expressed only in the myocardium in adults, whereas CKMB and cTnT are expressed in the regenerating skeletal muscles as well.13 In patients with severe skeletal muscle damages, cTnT increases in 95% and correlated strongly with the peak activity of serum creatine kinase.14

After CABG, there is a small increase in cTnI. Dissection of the myocardium for exposure of the intramyocardial arteries, manipulation of the myocardium, and placement of the purse string sutures for cannulation cause myocardial lesions.15 These injuries may explain why cTnI was detectable just before aortic declamping and increased early. However cTnI concentrations remained low in the uncomplicated group (group 1), suggesting that lesions were minimal. This slight increase is also observed with cTnT and CKMB mass. The median values observed for peak cTnI (2.1 μg/L) and cTnT (0.17 μg/L) in patients without new Q wave were consistent with previously published data.4

**cTnI, cTnT, CKMB Mass, and Perioperative Myocardial Infarction**

Perioperative myocardial infarction is one of the major problems during CABG. Its incidence was estimated at 6.4% in the Coronary Artery Surgery Study trial.16 However, its prevalence depends on the tests and diagnostic criteria used.17 No standards are widely accepted.1 Postoperative sedation and sternotomy make clinical symptoms unreliable. Early postoperative ventricular dysfunction, as observed with echocardiography, is more likely to occur because of reversible myocardial stunning during aortic occlusion and reperfusion injury.17 Creatine kinase (CK) and CKMB are often used with no clear threshold.17 In this study, it would have been inappropriate to use CK or CKMB, a cytosolic marker, to study the diagnostic accuracy of other cytosolic markers since their release is dependent on the same
pathologic mechanisms. Since cTnI and cTnT have a cytosolic phase, we had to choose an independent means of assessing myocardial damage. The more sensitive ECG markers like ST segment depression or elevation and T-wave evolution have a low specificity in this setting. Therefore, to study a marker of myocardial lesion independent of the CK, we deliberately selected a restrictive ECG criterion, ie, the occurrence of new postoperative Q waves. In this group of patients, cTnI, cTnT, and CKMB increase to value similar to those reported on medical myocardial infarction and contrast with the low values observed in the other patients.

Limitations of This Study

Although justified, the choice of stringent ECG criteria constitutes the main limitation of this study. It has adversely affected the positive predictive accuracy of the enzyme markers. As shown by radionuclide techniques with single photon emission CT imaging, many episodes of myocardial necrosis do not result in Q-wave evolution, ie, “non-Q wave infarction.” These episodes could be responsible for an increase in cTnI and other biological indicators of myocardial necrosis and account for their low positive predictive value in this study. The ECG criteria have also restricted the power of the study and explain why the differences observed between cTnI and cTnT did not reach statistical significance.

The incidence of new or worsening Q wave appears relatively high and, given the limited number of patients, is probably explained by chance.

We did not quantify some intercurrent factors such as shed blood autotransfusion and its influence. In patients with no ECG signs of myocardial ischemia, shed blood autotransfusion significantly increases CKMB and cTnT. However, since we compared biological markers in the same patients, the influence of intercurrent factor is probably minimal.

CONCLUSION

There was little difference between cTnI, cTnT, and CKMB to diagnose perioperative myocardial damage after CABG as assessed by new Q waves on the ECG. However, and in concordance with previous data demonstrating the superiority of cTnI in other pathologic conditions, there was a trend of cTnI being a better discriminator than CKMB or cTnT. In CABG patients with the potential for concomitant myocardial and skeletal muscle injury, the high cardiospecificity of cTnI could make it a more reliable tool to diagnose perioperative myocardial infarction and to compare different cardioplegia techniques. cTnI values remained very low in most patients. Further studies to investigate the prognostic value of cTnI values >5 μg/L after CABG would be of interest.

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Clinical Investigations