Evaluation of Cardiac Markers for Ruling Out Myocardial Infarction After Coronary Artery Bypass Grafting in Patients

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Background --- This study was conducted to evaluate the value of serum troponin T and creatine kinase (CK)-MB concentrations for ruling out perioperative myocardial infarction (PMI) early after cardiac surgery.

Design: Prospective study.

Setting: Recovery room of a tertiary hospital.

Patients: Twenty three patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass were included.

Methods --- Serum concentrations of troponin T and CK-MB concentrations were measured preoperatively (baseline), on arrival at the recovery room (RR), and at 0, 8, 16, and 24 h after arrival at the RR. The strength of markers studied for ruling out PMI was studied using receiver operating characteristics (ROC) curves. Based on these curves, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each marker at every time point were calculated.

Results --- PMI developed in 2 patients. On arrival at the RR, all markers were significantly increased from baseline concentrations in both patient groups. In patients with PMI, serum concentrations of troponin T and CK-MB were significantly higher than in control patients from 8, 16, and 24 hours after arrival at the RR. CK-MB concentration was the earliest marker, and its NPV reached 98.6% 8 hours after arrival at the RR. On arrival at the RR, the NPV for CK-MB concentration already reached 96.7%. Troponin T was not an early marker for ruling out PMI, with an NPV reaching 98.6% 8 hours after arrival at the RR. During the first 8 hours after arrival at the RR, sensitivity, specificity, PPV, and NPV of CK-MB exceeded that of troponin T.

Conclusion --- For ruling out PMI at the RR after CABG, CK-MB is a better marker than troponin T during the first 8 hour after arrival at the RR. Using these markers, postoperative treatment of cardiac surgical patients might be further improved. ***Phil Heart Center J 2007; 13(2):105-108.***

Key Words: CK-MB ■ Troponi T ■ Prei-operative myocardial infarction ■ coronary artery bypass grafting

In patients undergoing coronary artery bypass graft ing (CABG), early diagnosis of perioperative myo cardial infarction (PMI) is important because it remains a serious complication.[1,2] Despite many attempts to improve detection of PMI, currently, the diagnosis of PMI is still based on changes in the ECG, increased release of biochemical markers particularly creatine kinase (CK-MB), and a new regional wall motion abnormality on two-dimensional echocardiogram. Only a minority of patients (5-25% of patients undergoing CABG), however, actually experience a perioperative myocardial infarction (PMI), even in tertiary care centers currently operating on higher-risk patients. Potential causes of myocardial ischemia and infarction in the perioperative period include incomplete revascularization, diffuse atherosclerotic disease of coronary arteries, increased myocardial needs as in left ventricular hypertrophy, spasm or thrombosis of the native or bypass graft vessels, hemodynamic derangements and technical problems.[2] Possible risk factors for PMI may include emergency surgery, small coronary vessels, diffuse coronary artery disease, previous CABG, myocardial infarction (MI) in the preceding week, and failed percutaneous procedures. Previously, several biochemical markers for detection of myocardial damage have been proposed. Several studies showed that cardiac marker proteins (fatty acid-binding protein [FABP] and myoglobin) release can be used to determine myocardial tissue loss due to the surgical procedure (3). In addition, other studies showed that these proteins can be used to discriminate surgery-related myocardial injury from tissue loss caused by PMI. FABP was also shown to allow diagnosis of PMI as soon as 4 h after removal of the aortic cross-clamp.

However, next to early diagnosis, markers used for the detection of PMI should also be sensitive and specific. In this respect, FABP and myoglobin do not fulfill these recommendations. Troponin T and CK-MB have been shown to be promising candidates.[1, 4–9] As being part of

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the tropomyosin complex of myocardial tissue, troponin T is highly cardiac specific and is considered a sensitive marker of myocardial necrosis after CABG, which could improve the diagnosis of PMI in cardiac surgical patients.

In many studies, the emphasis of the diagnostic properties of biochemical markers has been on the detection rather than the ruling out of PMI. However, postoperative treatment of cardiac surgical patients could be improved in case PMI could be ruled out as early as possible after surgery. The aim of the present study was to evaluate whether Troponin T and CK-MB measurements enable a sensitive and early rule-out of PMI after surgery

Methods

Patient Selection The study group consisted of prospectively selected private patients who are to undergo "packaged" CABG with possible risk factors for PMI, between April 2006 and December 2006 at the Philippine Heart Center. An informed consent was requested from the patient and attending physician. Exclusion criteria were as follows: (1) treatment with fibrinolytics within 48 hours prior to surgery; (2) patients undergoing a concomitant valvular operation, vascular surgery, or LV aneurysmectomy; and (3) severe coagulation abnormalities. Blood Sampling Blood samples were obtained preoperatively (baseline), on arrival at the RR, and at 8, 16, and 24 h after arrival at the RR. All samples were collected in 10-mL syringe.

Myocardial Infarction Diagnosis

The criteria for definite PMI was based on the following criteria: 1) significant new Q waves (->30 msec and ->0.1 mV) in two or more contiguous leads of II, III, aVF, or two or more leads of V2 through V6, I, and VL 2) total peak CK >700 U/L with CK-MB >30 IU/L, and 3) presence of a new regional wall motion abnormality on two dimensional echocardiogram which was done exclusively for patients positive for the 1st and 2nd criteria. Diagnosis of a new wall-motion abnormality requires severe hypokinesis or akinesis in a previously normal segment. This would result in two patient groups: patients in whom PMI developed (PMI group), and patients without PMI (no-PMI group). Data Analysis All data were presented as mean + SEM. Comparisons between two variables at the same time point as well as the values from one variable between two time points were done. Receiver operating characteristics (ROC) curves were used to compare the performance of the biochemical diagnostic methods of PMI and to determine the appropriate cutoff values for the different cardiac markers. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to analyze the diagnostic value of each marker.

Results

Clinical Characteristics

There are 23 patients included in the study. The perioperative characteristics of all patients are shown in Table 1. Two patients (9.5%) showed evidence of PMI according to ECG changes, CK and CK-MB, and 2-dimensional echocardiogram. These patients had longer cardio pulmonary bypass times and a longer postoperative hospital stay than the patients without PMI.

Table 1. Clinical characteristics of Included Patients who did and did not developed Perioperative MI

Variables	No PMI N=21	PMI N=2	p-value
Age in years (mean)	62.5	65.2	NS
Male gender (%)	85	100	NS
Number of vessels anastomosed	3.8	4.0	NS
Cardiopulmonary Bypass duration in min (mean)	134	167	<0.05
Aortic cross-clamp duration in min (mean)	93	108	NS
Duration of Hospitalization Post-CABG in days (mean)	12	26	<0.05

Cardiac Marker Concentrations

Preoperative CK-MB concentrations in the no-PMI group and the PMI group were 1.7 IU/L and 1.8 IU/L respectively (Fig. 1). CK-MB concentrations in the no-PMI group slightly increased from baseline on the 8th with no significant change until the 24th hour after arrival at the recovery room (RR). In the PMI group, CK-MB concentrations showed a significant increase on the 8th hour which continued until the 24th hour after arrival at the RR. CK-MB concentration was significantly higher in the PMI group ($p<0.05$). On the 24th hour, CK-MB concentrations were 9.9 times higher in PMI patients compared to no-PMI patients. Maximal CK-MB concentration was 21 IU/L in the no-PMI group at 8 hours after arrival at the RR and 207 IU/L in the PMI group at 24 hours after arrival at the RR.

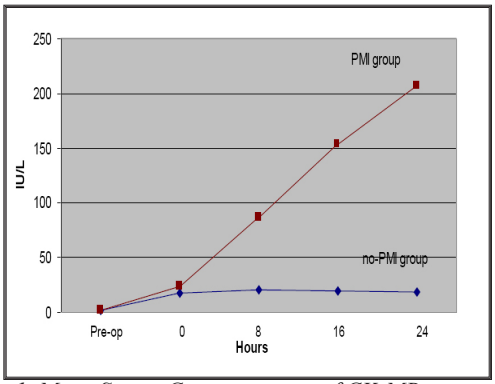

Figure 1. Mean Serum Concentrations of CK-MB

Preoperative troponin T concentrations in the no-PMI group and PMI group were 0.018 and 0.021 ng/ml, respectively (Fig. 2). Postoperative troponin T concentrations in both the no-PMI group and PMI group increased above the baseline upon arrival at the RR. However, on the 8th hour troponin T concentration for the no-PMI group was at its maximal at 0.90 ng/ml and steadily decreased until the 24th hour while the troponin T concentrations for the PMI group persistently increased until the 24th hour after arrival at the RR, at this time being 3.6 times higher than those in the no-PMI group. Thus, troponin T concentrations in the PMI group were significantly higher than in the no-PMI group from 8th hour to the 24th hour after arrival at the RR. Maximal troponin T serum concentrations were 0.9 ng/ml in the no-PMI group at 8 hours after arrival at the RR, and 3.25 ng/ml in the PMI group at 24 hours after arrival at the RR.

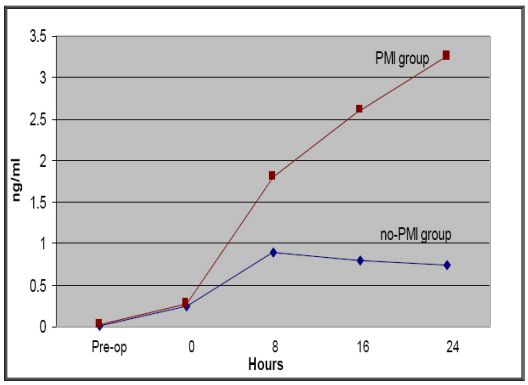

Figure 2. Mean Serum Concentrations of Troponin

Cut-off Values and Test Characteristic

The strength of correlation between standard criteria (ECG, CK with CK MB, and 2-DE) and CK-MB and troponin T concentrations was studied using ROC curves which are a plot of the true positive rate against the false positive rate for the different possible cut points of the mentioned diagnostic tests. The areas under the curve for each marker at every time point served as the measure of the test accuracy as shown in Table 2. Cut-off values were derived form the intersection of the different coordinates of the curve and the ROC curve. Corresponding cut-off values for each marker at every time points are also shown in Table 2. For each marker and at every time point, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of a single sample were calculated as shown in Table 3. Serum levels of troponin T > 1.07 ug/L 8 hours after arrival at the RR confirmed the presence of PMI with a sensitivity of 84.6%, specificity of 84.2%, PPV of 29.7%, and NPV of 98.6%. At the same time point, CK-MB concentration > 28.9 IU/L confirmed the presence of PMI with a sensitivity of 85.7%%, specificity of 86.8%, PPV of 25.6%, and NPV of 97.8%.

Table 2. Area under the ROC Curves and Optimal Cut-off values for each Marker at Every Post-operative Time Point

Hours after arrival at the RR	CK MB		Troponin T	
	AUC	Cut-off Value	AUC	Cut-off Value
0	0.74	17.9	0.59	0.25
8	0.90	28.9	0.83	1.07
16	0.88	22.2	0.91	0.75
24	0.96	292	0.94	0.81

Table 3. Test Characteristics of CK-MB Mass and Troponin T in diagnosis of Peri-operative MI post-CABG

Variables	Hours after Arrival at the RR			
	0	8	16	24
CK MB				
Sensitivity	71.4	85.7	78.6	64.3
Specificity	71.8	86.8	80.8	89.7
PPV	17.9	35.3	25.6	34.6
NPV	96.7	98.6	97.8	96.7
Troponin T				
Sensitivity	53.8	84.6	80.1	76.9
Specificity	53.3	84.2	73.7	69.5
PPV	8.2	29.7	20.0	16.4
NPV	93.7	98.6	98.4	97.5

Discussion

Peri-operative MI is a serious complication after cardiac surgery with a reported incidence of up to 25%, dependent on the criteria used to select the patient groups. (11) Several studies showed that in case CPB is used, myocardial tissue damage is unpreventable. The ideal markers for the diagnosis of PMI are those that can be used to diagnose early after cardiac surgery and should also be sensitive and specific at the same time. Troponin T and CK-MB are both promising candidates, these noted characteristics could improve the diagnosis of PMI in cardiac surgery. In this present study, we studied the value of serum troponin T and CK-MB concentrations in patients undergoing CABG.

In our study, plasma concentrations of both cardiac markers studied showed moderate elevations from preoperative values in all patients, which may signify minimal myocardial damage. This supports the study done by Fransen et al (12) that in case a patient has undergone CABG with the use of CPB, some myocardial damage occurs and is inevitable. Although the cutoff values have been reported in many studies (13-15) for patients presenting with acute chest pain, these values are not well established after cardiac surgery. Based on the data of the patients in the present study, cutoff values for each marker at every time point was obtained using the ROC

curves. In the study of Carrie et al (1), acceptable test characteristics for troponin T in CABG patients after 24 hours was shown, which increased towards the 48th hour after surgery. However, our study already showed optimal test characteristics at 8 hours after arrival at the RR for both cardiac markers. This finding can be explained by the study of Swaanenburg et al (16) which showed that the release patterns of cardiac markers after uncomplicated heart surgery depend on the type surgery (no. of vessels, ACC duration, etc.) and the circumstances during surgery (emergency, urgent, etc.) which were both not standardized in this study. Thus, our recommendation is that in future studies, the release patterns of cardiac markers for cardiac surgical procedures be determined and subsequently calculate corresponding cutoff values. In addition, the size of infarction influences the sensitivity and specificity in the early hours after MI, that is the larger the infarct the earlier the increase in cardiac markers. (9) As mentioned earlier, the test characteristics of the markers used were calculated using the ROC curves. This resulted in high values, particularly the NPV. The lowest NPV calculated for each marker was 93.7% (Table3), indicating that in the worst case, PMI can be ruled out with 93.7% certainty using any of the markers studied. Although there are higher values of sensitivity, specificity, and NPV in the CK-MB concentration in the early hours after cardiac surgery (0 and 8 hours), it can be said that both have relatively high values at all postoperative time points. This maybe explained by the fact that in our patients the "onset of symptoms", as it is usually called in acute myocardial infarction (AMI), is the same for all patients, supposing that the PMIs in the present study have a preoperative in etiology.

Conclusion

In conclusion, CK-MB concentration is a better marker than troponin T for ruling out PMI during the first 8 hours after arrival at the RR. The data of the present study showed that in patients undergoing CABG, troponin T and CK-MB concentrations should be measured during the first 8 hours after arrival at the RR, not to detect but rather to rule out or exclude PMI. Using these markers, postoperative treatment of cardiac surgical patients might be further improved.

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