ORIGINAL CONTRIBUTION

Cardiac Troponin I vs EuroSCORE: Myocardial Infarction and Hospital Mortality

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ABSTRACT

Perioperative myocardial infarction is the most common cause of morbidity and mortality in cardiac surgery. It occurs in 8% to 35% of patients. The primary aim of this prospective study was to determine the level of cardiac troponin I that indicates perioperative myocardial infarction in patients undergoing coronary artery bypass. A secondary goal was to establish the best independent predictor of hospital death. There were 180 consecutive patients undergoing isolated coronary artery bypass surgery enrolled in this study. Values of cardiac troponin I > 12.9 $ng \cdot mL^{-1}$ at 8 hours postoperatively predicted perioperative myocardial infarction with a sensitivity of 100% and a specificity of 93.2%. Compared to patients who survived, those who suffered hospital death were significantly older (74 ± 7 vs 63 ± 10 years), had significantly higher levels of cardiac troponin I at 24 hours (9 ± 17 vs 27.3 ± 16 $ng \cdot mL^{-1}$) and 48 hours (6.9 ± 19 vs 30.3 ± 24 $ng \cdot mL^{-1}$) postoperatively, and a significantly higher EuroSCORE (9 ± 2 vs 4 ± 3). At 8 hours postoperatively, cardiac troponin I led to an earlier diagnosis of perioperative myocardial infarction, while EuroSCORE was the strongest independent predictor of hospital death.

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INTRODUCTION

The incidence of perioperative myocardial infarction (PMI) varies from 8% to 35%.[1–6] While electrocardiogram (EKG) and echocardiogram changes do not allow early diagnosis of small or non-transmural infarcts, troponin levels may reflect myocardial damage.[7] Cardiac troponin I (cTnI) is a well-recognized marker of acute myocardial infarction, but there is no established cut-off value of plasma cTnI for the diagnosis of PMI.[8] Indeed, it is necessary that each cardiac center establishes its own cut-off level for the diagnosis of myocardial damage.[9] Cardiac troponin I is the inhibitory subunit of troponin, part of the thin-filament cardiac contractile apparatus, troponin-tropomyosin complex.[10] Cardiac troponin I is highly specific for myocardial tissue and is not expressed in human skeletal muscle at any stage of development or after trauma and regeneration, and it is not detectable in healthy subjects.[1,11,12] Previous studies have demonstrated a significant release of this marker after cardiac surgery, peaking at 8–24 hours postoperatively, suggesting that cTnI might provide early diagnosis of PMI.[3,7,10–12] The specificity of cTnI has been confirmed in various conditions, such as myocardial infarction, contusion, myocarditis and renal failure.[13] We investigated the clinical significance of specific cardiac biomarkers after coronary artery bypass grafting (CABG), and their relationship to postoperative course and hospital mortality. We hypothesized that monitoring cTnI levels during and after CABG might help to identify patients at risk of PMI. We further hypothesized that the European System for Cardiac Operative Risk Evaluation (EuroSCORE) might be an important predictor of hospital mortality in patients undergoing CABG.[14] Thus this study aimed to confirm and extend previous observations on

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the predictive value of cTnI for PMI and to establish the best independent predictor of hospital mortality in patients undergoing CABG.

Patient and Methods

The local ethics committee approved the study, and all patients gave their informed consent. From March to October 2005, 180 consecutive patients (mean age, 63.0 ± 9.9 years) undergoing isolated CABG were prospectively enrolled, and sequential measurements of biological cardiac markers were obtained. Exclusion criteria included active infection, malignancy, uncontrolled diabetes, hepatic disease, cardiogenic shock, recent (72 hours) percutaneous angioplasty failure, a ventricular pacemaker, reoperation, combined coronary and valvular operations, and acute coronary syndrome. All patients were assessed by EuroSCORE, which is a system for predicting mortality in cardiac surgical patients on the basis of objective risk factors.[9] This identifies 3 types of risk factors: patient-related factors are age over 60 years, sex, chronic pulmonary disease, extracardiac arteriopathy, neurological dysfunction, previous cardiac surgery, serum creatinine > 200 μmol·L^{-1}, active endocarditis and critical preoperative state; cardiac factors are unstable angina on intravenous nitrates, reduced left ventricular ejection fraction, recent myocardial infarction, and pulmonary systolic pressure > 60 mm Hg; operation-related factors are emergency, anything other than isolated CABG, thoracic aorta surgery and surgery for post-infarct septal rupture. The scoring system was applied to classify patients into 3 risk groups: low risk (EuroSCORE 1–2), medium risk (EuroSCORE 3–5) and high risk (EuroSCORE 6+).

Radial and pulmonary arterial catheters were introduced under local anesthesia. After standard general anesthesia, a median sternotomy was performed, followed by routine aortic and right atrial cannulation. Cardiopulmonary bypass (CPB) was carried out using membrane oxygenators and moderate systemic hypothermia. Myocardial protection was achieved by antegrade mild hypothermic (32°C) blood cardioplegia, repeated every 15 min. Heparin 3.0 mg·kg^{-1} was administered, and the activated clotting time was maintained > 400 sec during the procedure. Heparin was neutralized with protamine in a ratio of 1:3 within 10 min after the end of CPB. During the operation, aortic cross clamping time, CPB time and number of grafts were recorded for all patients. Intraoperative quality control of the bypass vessels was conducted using a probe of 1.0 or 1.5 mm in diameter, which was introduced inside the vessel during distal anastomosis.

After surgery, all patients were followed up in the intensive care unit (ICU). Blood samples for creatine kinase (CK) activity and cTnI determination were drawn 15 min after aortic cross clamping, 15 min after cross clamp release, on ICU admission, 8 hours after ICU admission and 24 and 48 hours postoperatively. Total CK activity was quantified with an Abbot AxSym (MEIA) system (Abbott Park, IL, USA), with an upper normal limit of 174 IU·L^{-1}. Creatine kinase-MB activity was quantified with an Elecsys 2010 (Roche, Nutly, NJ, USA), with an upper limit of 3.77 ng·mL^{-1}. Cardiac troponin Iwas assayed by Abbot AxSym (MEIA) system which has an upper normal limit of 0.04 ng·mL^{-1}. An EKG was performed on each patient on arrival in the ICU, and on each of the next 5 days. Postoperative echocardiography was carried out within 4 days after surgery, using a transthoracic Acuson Sequoia C256 system (Acuson Corporation, Mountain View, CA, USA) with a 3V2C probe. Perioperative myocardial infarction was defined by EKG criteria of newly developed Q-waves or left bundle branch block, ST changes or new onset of regional wall hypokinesia on echocardiography, assessed by cardiologists blinded to the biochemical markers.

Continuous variables are expressed as mean ± standard error of the mean, and categorical data as proportions. Comparisons of continuous variables were made with Student's unpaired *t* test, and categorical variables were compared with chi-squared tests or Fisher's exact test. Variables with a p value < 0.05 were consecutively subjected to a multivariate logistic regression model to assess the independent impact of each risk factor on PMI and hospital mortality. A forward stepwise procedure was used with a p value < 0.05 to enter, and a p value > 0.1 to eliminate variables. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit statistic and residual analysis. Receiver-operating characteristic curve analysis was used to identify the optimal cut-off value for significant multivariate predictors of PMI. All statistical analyses were performed with SPSS statistical package version 13.0 (SPSS, Inc., Chicago, IL, USA).

Results

Table 1 shows the demographic, clinical, peri and post surgical characteristics of 180 patients who underwent CABG. Electrocardiographic or echocardiographic evidence of PMI was observed in 19 (10.5%) patients. No differences were noted in cTnI concentration between patients with or without PMI during the operation, however, those with PMI had a higher plasma cTnI concentration at ICU admission to 48 hours postoperatively (Table 2). While CK-MB was higher in patients who had PMI at aortic declamping to 48 hours postoperatively (Table 3), and CK was elevated early from 15 min after cross clamping and at all other time points (Table 4). Peak cTnI and CK-MB were observed at 24 and 48 hours postoperatively. Risk of hospital death was higher in patients with PMI than those without PMI (15% vs 0.6%, p = 0.0001). On multivariate

Table 1. **Peri and Postoperative Data in Patients with and without PMI**

Time	PMI (n = 19)	No PMI (n = 161)	p Value
Age (years)	66 ± 10	63 ± 10	NS
Weight (kg)	60 ± 18	65 ± 15	NS
Female sex	10.5%	17.8%	NS
Diabetes mellitus	37.5%	32.2%	NS
NYHA class I–II	10	106	NS
NYHA class III–IV	9	55	NS
Hypertension	15	150	NS
Ejection fraction (%)	54 ± 8	53 ± 7	NS
Creatinine clearance ($mL \cdot min^{-1}$)	88 ± 24	80 ± 25	NS
Plasma creatinine ($mg \cdot dL^{-1}$)	1.22 ± 0.39	1.05 ± 0.32	NS
COPD	6.3%	8.5%	NS
EuroSCORE	5 ± 3	4 ± 3	NS
CPB time (min)	105 ± 34	109 ± 30	NS
Aortic cross clamp time (min)	76 ± 37	83 ± 27	NS
No. of grafts per patient	3 ± 1	3 ± 1	NS
Ventilation (hours)	8 ± 4	9 ± 15	NS
ICU stay (days)	2 ± 1	2 ± 1	NS
Ward stay (days)	10 ± 3	9 ± 3	NS

COPD = chronic obstructive pulmonary disease, CPB = cardiopulmonary bypass, ICU = intensive care unit, NYHA = New York Heart Association, PMI = perioperative myocardial infarction.

Table 2. **Cardiac Troponin I Levels ($ng \cdot mL^{-1}$) in Patients with and without PMI**

Time	PMI (n = 19)	No PMI (n = 161)	p Value
15 min after cross clamping	0.7 ± 0.6	0.4 ± 1.3	> 0.05
15 min after declamping	2.0 ± 1.7	1.0 ± 2.4	> 0.05
ICU admission	11.60 ± 9.90	2.29 ± 3.42	< 0.0001
8 hours postoperatively	35.59 ± 19.39	4.13 ± 4.69	< 0.0001
24 hours postoperatively	47.05 ± 27.63	4.80 ± 7.49	< 0.0001
48 hours postoperatively	40.29 ± 45.38	3.34 ± 6.63	< 0.001

ICU = intensive care unit, PMI = perioperative myocardial infarction.

Table 3. **Creatine Kinase-MB Levels ($ng \cdot mL^{-1}$) in Patients with and without PMI**

Time	PMI (n = 19)	No PMI (n = 161)	p Value
15 min after cross clamping	5 ± 3	4 ± 3	> 0.05
15 min after declamping	27 ± 78	10 ± 7	0.007
ICU Admission	73.41 ± 203.04	19.47 ± 13.24	0.001
8 hours postoperatively	71.49 ± 83.49	23.53 ± 25.00	< 0.0001
24 hours postoperatively	131.5 ± 260.9	21.3 ± 38.8	< 0.0001
48 hours postoperatively	71.74 ± 168.28	12.19 ± 24.11	< 0.0001

ICU = intensive care unit, PMI = perioperative myocardial infarction.

Table 4. **Creatine Kinase Levels (IU·L^{-1}) in Patients with and without PMI**

Time	PMI (n = 19)	No PMI (n = 161)	p Value
15 min after cross clamping	103 ± 75	79 ± 47	< 0.047
15 min after declamping	233 ± 140	221 ± 144	> 0.05
ICU admission	458 ± 200	403 ± 259	> 0.05
8 hours postoperatively	942 ± 473	729 ± 718	> 0.05
24 hours postoperatively	1,241 ± 670	843 ± 821	< 0.039
48 hours postoperatively	1,971 ± 3,300	689 ± 717	< 0.0001

ICU = intensive care unit, PMI = perioperative myocardial infarction.

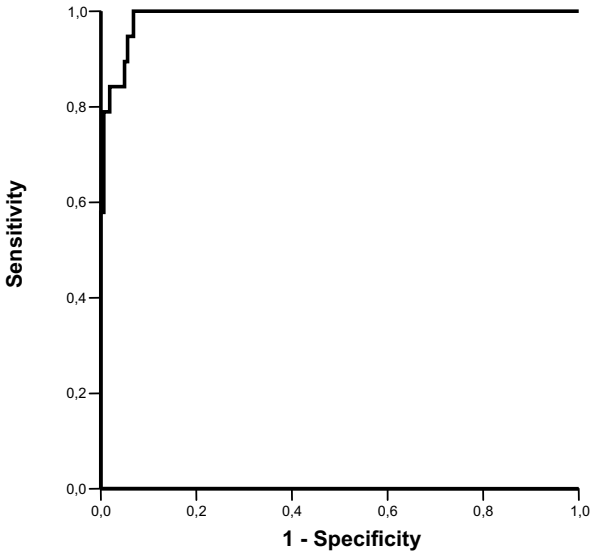

Figure 1. Receiver-operating characteristic curve analysis showed that cardiac troponin I at 8 hours postoperatively > 12.91 ng·mL^{-1} confirmed the presence of perioperative myocardial infarction with a sensitivity of 100% and a specificity of 93.2% (area under the curve = 0.98).

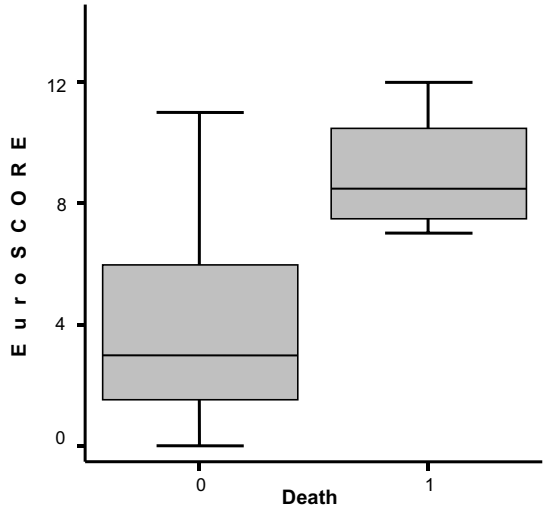

Figure 2. EuroSCORE in patients who suffered hospital mortality (1) and those who survived (0).

analysis, the only independent predictor of PMI was plasma cTnI level at 8 hours postoperatively (odds ratio = 15.4; $p < 0.0001$). Model fit was adequate (Hosmer-Lemeshow test: $\chi^2 = 2.38$, df = 8, $p = 0.967$). As shown in Figure 1, cTnI > 12.9 ng·mL^{-1} at 8 hours postoperatively predicted PMI with a sensitivity of 100% and specificity of 93.2%. Compared to patients who survived, those who suffered hospital death had higher levels of cTnI at 24 hours (9 ± 17 vs 27.3 ± 16 ng·mL^{-1}; $p = 0.039$) and 48 hours postoperatively (6.9 ± 19 vs 30.3 ± 24 ng·mL^{-1}; $p = 0.019$), higher CK at 48 hours postoperatively (3,177 ± 3,928 vs 776 ± 1,192 IU·L^{-1}; $p < 0.0001$), higher EuroSCORE (9 ± 2 vs 4 ± 3; $p = 0.001$; Figure 2), and higher incidence of PMI (75% vs 9.6%; $p = 0.0001$), and they were older (74 ± 7 vs 63 ± 10 years; $p = 0.032$). On multivariate analysis, the only independent predictor of hospital mortality was EuroSCORE (odds ratio = 4.191; $p < 0.025$; Homer-Lemeshow test: $\chi^2 = 0.447$, df = 7, $p = 1$).

Discussion

The main result of this study is that plasma cTnI at 8 hours after the end of cardiac surgery proved a good marker for early diagnosis of PMI, while EuroSCORE is the best predictor of hospital mortality. Numerous clinical studies have demonstrated that a significant rise of cardiac biomarkers, such as cTnI and cardiac enzymes (CK, CK-MB), occurs after cardiac surgery.[2,11,12,15,16-18] In a recent study by Selvanayagam and colleagues[19] aimed at evaluating reversible and irreversible myocardial injury in patients undergoing off-pump or on-pump CABG, a similar incidence and magnitude of new irreversible myocardial injury was documented in both groups, despite a greater release of cTnI after on-pump CABG. Dissection of the myocardium to expose intramyocardial arteries, aortic cross clamping, manipulation of the myocardium, left atriotomy for mitral valve replacement, aortotomy to expose the aortic valve and placement of pursestring sutures for cannulation cause myocardial lesions. These injuries might explain why cTnI increases early.

We demonstrated that at 8 hours postoperatively, cTnI is the best predictor of PMI after CABG among all biomarkers evaluated. The cut-off value of cTnI > 12.91 ng·mL^{-1} at 8 hours post-CABG indicated PMI with a sensitivity of 100% and a specificity of 93%. Elevated cTnI is associated with a cardiac cause of hospital death. In our patients, the incidence of PMI after myocardial surgery was 10.5%. This agrees with previously reported risks of acute myocardial necrosis after CABG of 3% to 35%.[4,12] Plasma cTnI concentrations increased in all patients after CPB, which may make it difficult to interpret the data, but the increase was smaller in those without complications, underscoring the need for an optimal cut-off value of cTnI.

Interpretation of EKG data is hampered by pericardial involvement, and changes in heart position might cause EKG changes without graft occlusion. Chest pain as an indicator of reocclusion after CABG (compared to angioplasty) is a dubious parameter due to surgical trauma. Elevated concentrations of biochemical markers may also be related to suboptimal cardioplegia, extracorporeal circulation, surgical trauma and other factors.[8] Noninvasive discrimination between graft occlusion and PMI is difficult. In the near future, new noninvasive imaging techniques, such as contrast echocardiography or ultra-high-speed magnetic resonance imaging might overcome some of the limitations associated with angiography. Most Q-waves appearing after coronary surgery are not associated with major myocardial tissue damage, and a correlation with cTnI concentration is necessary to confirm the diagnosis of PMI. Furthermore, some episodes of myocardial necrosis do not result in Q-wave evolution (non-Q-wave infarction). Postoperative rhythm disturbances, pacing and pericardial inflammation commonly interference with EKG interpretation, and new Q-waves have been found to reflect unmasking of old MI in some patients.[19] Thus monitoring a specific and sensitive biomarker of myocardial damage is necessary.

Cardiac troponin I was long considered the only independent predictor of hospital mortality; however, EuroSCORE was the only independent predictor of hospital mortality in our series. We speculate that the lack of predictive power of cTnI for hospital mortality was at least in part due to the fact that patients who presented with high cTnI levels were considered as high risk and treated more aggressively to reduce the expected high incidence of adverse outcomes. The most common adverse outcomes in patients undergoing CABG are hemodynamic instability, prolonged intubation time, pulmonary and renal disease. EuroSCORE has been shown to work well to predict 30-day mortality in many European countries and in the United States, and compares favorably with The Society of Thoracic Surgeons risk stratification algorithm. Previous reports confirm our hypothesis that cTnI is a valuable marker to detect acute myocardial necrosis, but it has a poor ability to predict long-term outcome. It was surprising to observe that EuroSCORE is a better predictor of hospital mortality than cTnI, as the biochemical factor should be more sensitive than EuroSCORE, which is an algorithm system. Our study was a single-center experience, so further studies are clearly warranted. Another limitation is that repeat angiography to determine graft status was not performed. Investigations in a larger population are needed to confirm these data.

We found the cut-off value of cTnI of 12.91 ng·mL^{-1} at 8 hours postoperatively was useful for diagnosis of PMI during cardiac surgery. The peak cTnI level after open heart surgery offers a potentially reliable, inexpensive and easy method to detect clinical outcomes and thus provide better patient care, reduce hospital costs and aid in quality improvement. Furthermore, the only independent predictor of hospital mortality was found to be the EuroSCORE.

References

1. Alyanakian MA, Dehoux M, Chatel D, Seguret C, Desmonts JM, Durand G, et al. Cardiac troponin I in diagnosis of perioperative myocardial infarction after cardiac surgery. J Cardiothorac Vasc Anesth 1998;12:288–94.
2. Bonnefoy E, Filley S, Kirkorian G, Guidollet J, Roriz R, Robin J, et al. Troponin I, troponin T, or creatinine kinase-MB to detect perioperative myocardial damage after coronary artery bypass surgery. Chest 1998;114:482–6.
3. Jacquet L, Noirhomme P, El Khoury G, Goenen M, Philippe M, Col J, et al. Cardiac troponin I as an early marker of myocardial damage after coronary bypass surgery. Eur J Cardiothorac Surg 1998;13:378–84.
4. Fellahi JL, Léger P, Philippe E, Arthaud M, Riou B, Gandjbakhch I, et al. Pericardial cardiac troponin I release after coronary artery bypass grafting. Anesth Analg 1999;89:829–34.
5. Benoit MO, Paris M, Silleran J, Fiemeyer A, Moatti N. Cardiac troponin I: its contribution to the diagnosis of perioperative myocardial infarction and various complications of cardiac surgery. Crit Care Med 2001;10:1880–6.
6. Carrier M, Pellerin M, Perrault LP, Solymoss BC, Pelletier LC. Troponin levels in patients with myocardial infarction after coronary artery bypass grafting. Ann Thorac Surg 2000;69:435–40.
7. Crescenzi G, Bove T, Pappalardo F, Scandroglio AM, Landoni G, Aletti G, et al. Clinical significance of a new Q wave after cardiac surgery. Eur J Cardiothorac Surg 2004;25:1001–5.
8. Jaffe AS, Ravkilde J, Roberts R, Naslund U, Apple FS, Galvani M, et al. It's time for a change to a troponin standard. Circulation 2000;102:1216–20.
9. Babuin L Jaffe AS, Troponin: the biomarker of choice for the detection of cardiac injury. CMAJ 2005;173:1191–202.
10. Higgins JP, Higgins JA. Elevation of cardiac troponin I indicates more than myocardial ischemia [Review]. Clin Invest Med 2003;26:133–47.
11. Sadony V, Körber M, Albes G, Podtschaske V, Etgen T, Trösken T, et al. Cardiac troponin I plasma levels for diagnosis and quantisation of perioperative myocardial damage in patients undergoing coronary artery bypass surgery. Eur J Cardiothorac Surg 1998;13:57–65.

12. Adams JE 3rd, Sicard GA, Allen BT, Bridwell KH, Lenke LG, Dávila-Román VG, et al. Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. N Engl J Med 1994;10:670–4.
13. McDonough JL, Labugger R, Pickett W, Tse MY, MacKenzie S, Pang SC, et al.Cardiac troponin I is modified in the myocardium of bypass patients. Circulation 2001;103:58–64.
14. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9–13.
15. Greenson N, Macoviak J, Krishnaswamy P, Morrisey R, James C, Clopton P, et al. Usefulness of cardiac troponin I in patients undergoing open-heart surgery. Am Heart J 2001;141(3) 447–55.
16. Gensini GF, Fusi C, Conti AA, Calamai GC, Montesi GF, Galanti G, et al. Cardiac troponin I and Q-wave perioperative myocardial infarction after coronary artery bypass surgery. Crit Care Med 1998;12:1986–90.
17. Newman MF. Troponin I in cardiac surgery: marking the future. Am Heart J 2001;141:325–6.
18. Thielmann M, Massoudy P, Marggraf G, Knipp S, Schmermund A, Piotrowski J, et al. Role of troponin I, myoglobin, and creatinine kinase for the detection of early graft failure following coronary artery bypass grafting. Eur J Cardiothorac Surg 2004;26:102–9.
19. Selvanayagam JB, Petersen SE, Francis JM, Robson MD, Kardos A, Neubauer S, et al. Effects of off-pump versus on-pump coronary surgery on reversible and irreversible myocardial injury: a randomized trial using cardiovascular magnetic resonance imaging and biochemical markers. Circulation 2004;109:345–50.