Early and late Troponin T determination after elective cardiac surgery.
Two different meanings

Ann. Ital. Chir., 2011; 82: 469-474

Angelo Maria Dell'Aquila*, Stefano Matrobuoni*, Beltran Levy Praschker*,
Eduardo Alegria Barrero**, Maria Jose Iribarren***, Jesus Herreros*, Gregorio Rabago*

University of Navarra, Clinica Universitaria de Navarra, Pamplona, Spain
**Cardiovascular Surgery Department*
***Cardiology Department*
****Anesthesiology Department*

Early and late Troponin T determination after elective cardiac surgery. Two different meanings

AIM: *Although Troponins are demonstrated to be better predictors than CK-MB in quantification of myocardial damage, the relation between cut-off values for the diagnosis of perioperative myocardial infarction (PMI) and sample time is still not clear. In the present study we sought to analyse the clinical consequence of an early and late cTnt determinations after elective cardiac surgery.*
MATERIAL OF STUDY: *Data of 117 patients undergone elective open heart surgery between January 2006 and June 2007 were prospectively collected. PMI was detected on the basis of postoperative electrocardiography/echocardiography and hemodynamic state.*
RESULTS: *The in-hospital mortality was 1.7%. Eight patients (6.8%) presented PMI. Receiver-operating characteristic (ROC) analyses showed a cTnt cut-off of 1.22 mg/L (CI 0.94 to 0.99, P= 0.0001, 100% sensitivity and 96% specificity) on arrival to ICU for the diagnosis of PMI. On the second post-operative day the cut-off value was 2.8 mg/L (CI 95% 0.84 to 0.98, P= 0.0001) (sensitivity 66 % and specificity 100%). At this time the Pearson's test revealed the best correlation to ICU (P=0.008) and in-hospital (P=0.01) length of stay (LOS).*
DISCUSSION: *A better sensibility of cTnt in diagnosis of PMI in the early postoperative period has been demonstrated to be associated to an increasing specificity in the late post-operative period.*
CONCLUSIONS: *PMI must be suspected in patients with a cTnt > 1.22 mg/L. A second later assessment on the 2nd post-operative can exclude false positives and significantly predict the ICU and the in-hospital length of stay.*

KEY WORDS: Hospital length of stay, Perioperative myocardial infarction, Troponin.

Introduction

Perioperative myocardial infarction (PMI) in patients undergoing open heart surgery has been demonstrated to be a major determinant of postoperative morbidity and mortality [1-3]. The onset of a new Q-wave is associated in 25% of cases with no or minimal myocardial tissue necrosis [4]. Development of a new bundle branch block after cardiac surgery may indicate a myocardial infarction [5,6] but also has been described as effect of cold crystalloid cardioplegia, intreoperative kinking of the septum, transient perioperative ischemia and direct current defibrillation [7].
Due to limited sensitivity and specificity of CK-MB [8] in detection of perioperative myocardial necrosis, cardiac troponins have been introduced for their better sensitiv-

Pervenuto in Redazione Marzo 2011. Accettato per la pubblicazione Maggio 2011.
Per corrispondenza: Angelo Maria Dell'Aquila, Hötteweg 11, 48143, Münster, Germany (E-mail:am.dellaquila@gmail.com)

ity and specificity [9], becoming nowadays the gold standard for diagnosis of perioperative myocardial infarction [7]. In an attempt to find an optimal sampling time and a cut-off value for the detection of a critical amount of myocardial damage, a recent metanalysis [10] focused on the biochemical injury markers and mortality after coronary artery bypass grafting, concluded that troponins serve as better predictors than CK-MB but the heterogeneity of existing studies prevented the pooling of the results of troponin studies.

The present study was designed in order to highlight the rule of cTnT not only in relation to patient undergoing CABG, but in all elective cardiac patients.

Furthermore, this study provides an early and useful cTnt cut-off values in order to quantify the perioperative myocardial damage, to optimise the treatment and at the same time to predict both ICU and in-hospital length of stay.

Material and Method

Between January 2006 and June 2007, all patients scheduled for heart surgery were prospectively studied.

The study was approved by the local Committee. Patients undergoing non elective cardiac surgery, those who had suffered from an acute myocardial infarction (AMI) with ST-segment elevation within the previous 2 weeks, patients with a serum creatinine> 200 umol/L and patients younger then 40 and older then 80 year old were excluded from the study. Patient baseline characteristics analyzed included patient age, gender, New York Heart Association (NYHA) class symptoms, features of clinical presentation, type of angina, and left ventricular ejection fraction. Risk factors for ischemic heart disease, including hypertension, diabetes mellitus, smoking history, hyperlipidemia, obesity, were also compared.

The study group consisted in 117 patients, 78% were male, with a mean age of 67 years (range 44-80). Preoperative characteristics of study patients are detailed in Table I.

A standard anaesthesiological regimen was applied as follows: Premedication with Diazepam 2 mg. Anaesthesia was induced with Etomidate 0.3mg/kg of body weight, fentanyl 0.002 mg/kg, and cis-atracurio 0.2 mg/kg. After intubation, anaesthesia was maintained by controlled ventilation with oxygen (FiO2 0.5), isoflurane, fractionated doses of morphinic analgesics and muscular relaxants. Heparin was administered in order to achieve an activated coagulation time above 400 seconds.

Standard cardiopulmonary bypass (CPB) was established between ascending aortic cannulation and right atrial or bicaval cannulation using a membrane oxigenator (Cobe Apex). The perfusion temperature was maintained at 33 °C, the hematocrit was kept between 20 and 25%, pump flows were between 1.8 and 2.2 L/min per m2, and mean arterial pressure was kept between 50 and 60 mmHg. In all patients cardioprotection was achieved by antegrade cold blood cardioplegia and by retrograde cardioplegia for patients undergoing aortic valve replacement and through each bypass graft once distal anastomosis performed. Diastolic arrest was usually obtained before termination of initial infusion. The interval between two successive infusions never exceeded 20 min. Blood samples for enzymes and cTnt assays were drawn after the surgery at ICU arrival, at 8h and 36h after the procedure. cTnt was measured using a specific enzyme-linked immunosorbent assay (Elecsys 2010; Roche). A 12-lead electrocardiogram was systematically recorded on post-operative days 1, 2, 3 and at discharge. An echocardiogram was performed early in the postoperative period only in patients presenting hemodynamic instability and at the hospital discharge in all patients.

The diagnosis of PMI was made in the presence of two of the following criteria: hemodynamic instability requiring inotropic support; presence of a new Q-wave at electrocardiogram and presence of new wall abnormality at echocardiogram.

Shock was defined as a sustained impairment in cardiac index (< 1.5 l/min./m2) requiring any of the following: (>24 h) or significant need (> 2 drugs) for vasopressor therapy; intraortic baloon pump insertion. Postoperative renal failure was defined as rise in serum creatinine greater than 25% or renal dysfunction requiring initiation of temporary haemodialysis.

Postoperative major complications assessed included: PMI, shock, significant arrhythmia (new-onset of ventricular arrhythmia), respiratory failure (requiring ventilatory support for greater than 24 h), renal failure, postoperative bleeding requiring chest re-exploration, adverse neurological events, and systemic or pulmonary thromboembolism and death.

Statistical Analysis

Normal distribution of data was assessed with the Shapiro-Wilk test. Baseline and postoperative parameters were compared between two groups using a two sample *t*-test for continuous variables. Values are expressed as mean standard deviation (S.D.) or percent when appropriate.

ROC curves were used to evaluate the optimal cut-off of cTnT. These curves were constructed by sensitivity vs. specificity of the variable. Univariable followed by multivariable linear regression analyses were used in order to identify predictors of postoperative cTnt values. Clinical characteristics such as age, and medical history, as well as surgical variables such as ischemic time, bypass time, number of grafts placed, intraoperative defibrillations, and need for preoperative, intraoperative, or postoperative intraaortic balloon pump placement, were entered into the model. Variables with a value of $P<0.2$ in univariable screen were retained

for evaluation in the multivariable model; for multivariable analyses only those variables with a value of $P<0.05$ were retained statistical significant. Associations between cTnT levels and ICU length of stay, hospital length of stay were examined using bivariate correlations with Pearson analyses.
All data analyses were performed with the Statistical Package (SPSS 15.0; SPSS Inc).

Results

The study population included 54(46.2%) isolated CABG procedure, 18(15.4%) isolated aortic valve replacement, 7(5.9%) mitral valve procedure (replacement/repair), 21(17.9%) combined procedure (AVR/MVR + CABG) and 10(8.5%) patients underwent double valve procedure. (Table II)
The mean aortic cross-clamping time was 93.1± 34 min. (range 20 to 220) and the mean CPB time was 120.3 ± 44.9. The mean number of distal anastomosis were 2.86 ± 1.12 (range 1 to 5). The total in-hospital mortality was 1.7% (n=2). The in-hospital major complications were reported in 19 patients (16.2%). Five (4.3%) patients developed stoke, 1 patient (0.8%) presented

TABLE I - *Preoperative clinical data*

Characteristic	N	%
Demographics		
Patients	117	
Age	67±8.86	
Sex (F/M)	26/91	22/78
BSA	1.81± 1.6	
Cardiovascular risk factor		
Diabetes mellitus	38	32.5
Hypertension	40	34.2
Hyperlipidemia	49	42
Smoking history	51	43.6
Comorbilities		
COPD	10	8.5
PVD	7	6
Creatinine mg/dl	117	1.07±0.325
Cardiac history		
NYHA	2.52±0.545	
Previous MI	26	22.2
Previous PCI	12	10.3
Ecocardiographic data		
LV-EF > 0.51	97	83
LV-EF 0.30-0.50	14	11.9
LV-EF < 0.30	6	5.1
LVEDD	83	54.81±8.7
LVESD	83	36.7±9.2
LVEDV	83	148.1±55.2
LVESV	83	65.6±41.5

BSA= body surface area; COPD= chronic obstructive pulmonary disease; LVEDD= left ventricular end diastolic diameter; LVEDV= left ventricular end diastolic volume; LV-EF= left ventricular ejection fraction; LVESD= left ventricular end systolic diameter; LVESV= left ventricular end systolic volume; NYHA: New York Heart Association; MI: myocardial infarction; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease.

TABLE II - *Surgical procedures*

Procedure	N.	%
CABG	**54**	(46.2)
CABG plus	**21**	(17.9)
AVR	17	
MVR	3	
Aortic root replacement	1	
AVR	**18**	(15.4)
AVR plus	**5**	(4.3)
Asc. Ao replacement	3	
MVR + Asc. Ao. replacement	1	
Asc. Ao. replacement + CABG	1	
MVR	**6**	(5.1)
Double valve	**10**	(8.5)
AVR+MVR+CABG	1	
MVR+ tricuspid annuloplasty	3	
MVR + AVR	5	
MVR+AVR+ Asc. Ao replacement	1	
Others*	**3**	(2.6)

Asc. Ao replacement= ascending aorta replacement; AVR= aortic valve replacement; CABG= coronary artery by-pass grafting; MVR= mitral valve replacement.
*Includes: combined aortic valve replacement mitral replacement+ tricuspid anuloplasty (n=1); tricuspid anuloplasty (n=1); mitral valve repair (n=1).

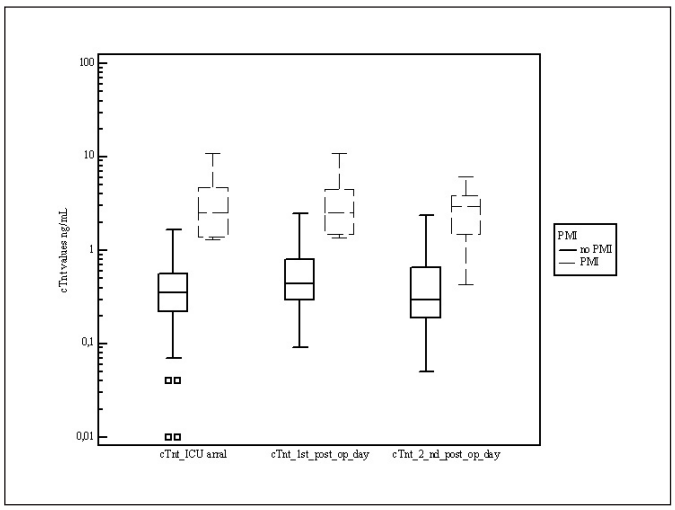

Fig. 1: Means and standard deviation of cTnT in patients with and without diagnosis of PMI at ICU arrival, on the 1st and 2nd post-operative days.
Legend: The levels of cTnt in patients presenting PMI was at all time higher than in patients without this diagnosis.

TABLE III - *Pearson's correlation test.*

	cTnt ICU arrival	cTnt 1st post op day	cTnt 2nd post. op day.
ICU stay (hours) *p*=	0,7	0,7	< 0,01
Post. op stay (days) *p*=	0,8	0,8	< 0,001

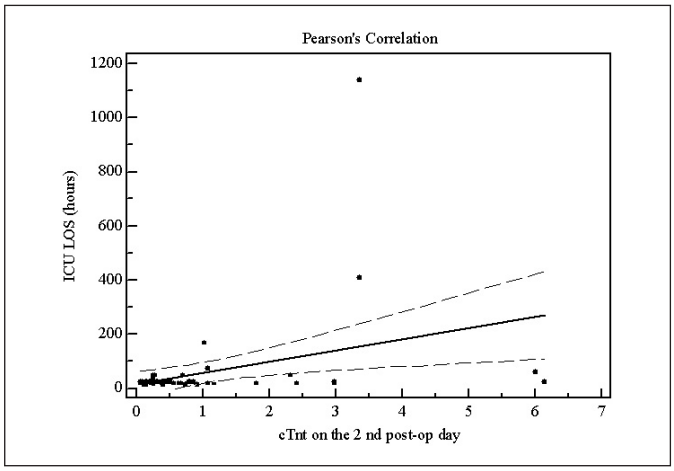

Fig. 2: Pearson's correlation
Legend: Correlation between postoperative cTnt levels on the second postoperative day and ICU LOS.

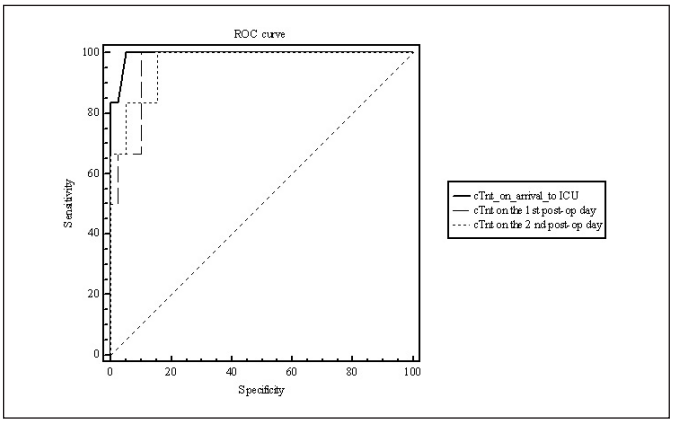

Fig. 4: ROC curve for cTnT on arrival to ICU, on the 1st and 2nd post.op day.
Legend: The highst AUC for cut-off of cTnT is on arrival to ICU.

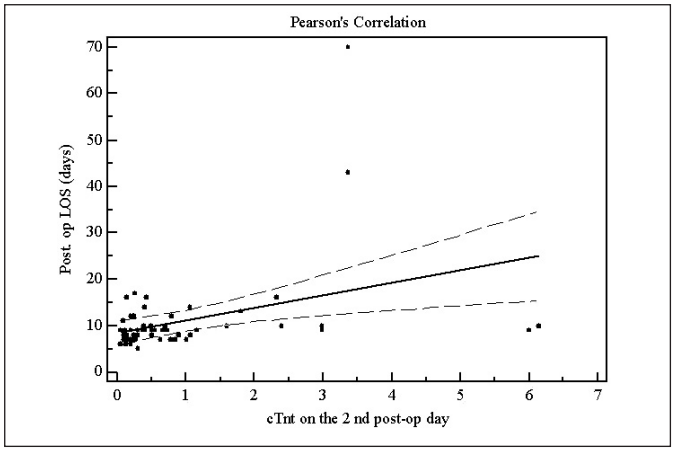

Fig. 3: Pearson's correlation
Legend: Correlation between postoperative cTnt levels on the second postoperative day and hospital LOS.

bleeding requiring chest re-exploration, 2 patients (1.7%) developed acute renal failure, 1 of them died on the postoperative day 7 from a septic shock, 2 (1.7%) patients developed major cardiac arrhythmia. Eight (6.83%) patients presented PMI, 5 of them (62.5%) had CABG procedure, 2 (25%) valvular and 1 (12.5%) combined valvular/CABG procedure. After PMI, 2 patients (1.7%) required IABP insertion and 1 patient (0.8%) required a left ventricular assist device (Levitronix) and he died from a multiorgan failure on postoperative day 21. The levels of cTnt between patients presenting PMI and patients without this diagnosis was at all time significant ($p<0.001$) (on arrival to ICU, on 1st and 2nd post-operative days) with the highest difference between means on arrival to ICU (Fig. 1).

A significant correlation was present between postoperative cTnt levels on the second postoperative day and ICU LOS (r=0.34, P=0.008) and hospital LOS (r=0.33, P=0.01). (Table III) (Figs. 2 and 3).

ROC analyses showed on arrival to ICU a cTnt cut-off value of 1.22 mg/L (CI 95% 0.94 to 0.99, P= 0.0001, 100% sensitivity and 96% specificity, AUC =0.98) and for the first post-operative day a cTnt cut-off value of 1.32 mg/L (CI 95% 0.9 to 0.99, P= 0.0001, 100% sensitivity and 96%, specificity, AUC of 0.96). A lower AUC (0.94) was observed in the second post-operative day with a cut-off value of 2,8 mg/L (CI 95% 0.84 to 0.98, P= 0.0001) with a lower sensitivity (66 %) and higher specificity (100%) (Fig. 4).

Direct predictors of postoperative cTnt values identified by multivariable linear regression analyses included previous infarction (P=0.05), previous PTCA with Stent implantation (P=0.01), number of distal anastomoses (P=0.02) and cross-clamping time (P=0.027).

Mean in-hospital LOS was 9 days for the patients without PMI and 26,8 days for the patients reporting PMI (P < 0.001) whereas mean ICU LOS was 27,4 h vs. 175,6 h respectively (P<0.001).

Discussion and commentary

The postoperative release of TnT has played an important role for prediction of short and long-term outcome following cardiac surgery [11].
The identification of patients who are at risk of developing postoperative complications as early as possible is desirable, as it allows a prompt adequate therapeutic intervention.
ECG changes can be difficult to interpret at this point due to bundle branch block, pacing, pericardial inflammation and ventricular hypertrophy. Moreover a new Q-wave is highly specific of myocardial infarction but not very sensitive, especially for the diagnosis of non-transmural infarction [12]. Echocardiogram as well, for the technical difficulty due to obstructive airway disease, mechanical ventilation, supine position, presence of pneumothorax can have a strong limitation in a ICU patient [2,13]. More sophisticated methods, such as magnetic resonance imaging or scintigraphy, are not easily applicable in the perioperative and intensive care [14]. Considering these limitations, the biochemical analysis of cardiospecific molecules have become an attractive alternative for estimation of myocardial injury.
Nowadays, troponins are considered the gold standard marker for myocardial cell injury [15]. A recent meta-analysis [10] on the biochemical injury markers and mortality after coronary artery bypass stated that troponins could be presumed to be better predictors of mortality than CK-MB because of their specificity to the myocardium. However, the authors found that absolute cut-off values varied more than sevenfold among all series analyzed. Complicating the issue, as reported by authors, few troponin studies have been published, and the heterogeneous patient populations prevented the pooling of the results. In this meta-analysis another conclusion, was that the 20- to 24-hour sample was a stronger predictor of mortality than the peak value.
Although we found a significant elevation of TnT nearly ubiquitous after cardiac surgery, we identified a cut-off value for cTnT on the arrival to ICU of 1.22 mg/L with a sensitivity of 100% and a specificity of 96% for the diagnosis of PMI with an AUC of 0.98. Mohammed et al.[16], in their prospective series of 847 CABG patients, found a cTnT cut-off > of 1.6 mg/L in the first 24 h after surgery to be a predictor of cardiac complications such as new electrocardiographic Q-wave, shock and death.
The small difference between our findings (cut-off of 1.22 mg/L) and the value identified by Mohammed et al. (1.6 mg/L) may be explained considering the use of several different forms of myocardial protection strategies employed (cold crystalloid, warm and cold blood cardioplegia). In our series only cold blood cardioplegia has been used. In another study, Leherke et al. [7] found a cut-off fo cTnT >1.26mg/L obtained 24h after surgery to be associated with a 6.3-fold higher risk for the evolution of new Q-wave. Although we found a similar cut-off, we obtained the highest AUC when the sample was drawn on arrival to ICU. During this early phase an increase of cTnt in all patients may result as a release of troponin cytosolic pool, whereas, a clinically relevant hemodynamic instability associated with relevant troponin increase may indicate a myofilaments degradation and cytosolic release with cell damage. Thus, it can be assumed that the cut-off of 1.22 mg/L can identify a "transition point" from cytosolic pool cTnt release to myofilaments degradation.
Moreover, this earlier sample time, immediately after surgery, can anticipate the diagnosis of PMI and give the clinician useful information in order to establish the best therapeutic strategy.
Another important finding of the present study is the increasing specificity of Troponins in the later post-operative period. In this setting, we found a cut-off cTnT value on the second post-operative day of 2.98 mg/L with a sensitivity of 60% and a specificity of 100% with the AUC of 0.94.
This second determination can minimize the possibility of false positive. Furthermore, this finding can also explain the best correlation between late troponin values and ICU/in-hospital LOS considering that cTnT remains elevated several days after the surgery only in the patient reporting a significant myocardial damage. This feature does not appear in "stunned myocardium" situations where the cTnT presents a rapid decrease 24h after the surgery.

Conclusion

PMI must be suspected in patients presenting a cTnT value higher than 1.22mg/L on arrival to ICU. This early determination provides a simple, inexpensive and accurate method able to identify patients with myocardial necrosis. This early assessment can also provide useful information in order to establish a prompt adequate therapeutic intervention.
Only in these patients, a second cTnT sample, drawn on the second post-operative day after the surgery, can exclude false positives and in the same time predict the ICU/in LOS.
A potential source of weakness can be the wide variety of cardiac surgical procedures. However, the aim of the study was to give the clinicians a common cut-off point for a wide range of elective cardiac surgery.

Riassunto

È risaputo che la troponina è una proteina dotata di alta sensibilità e specificità nella diagnosi dell'infarto del miocardio. Lo scopo di questo studio è stato quello di trovare un valore di riferimento (cut-off) in base al quale si può fare con molta probabilità diagnosi d'infarto mio-

cardico perioperatorio. A tale scopo, sono stati prospettivamente raccolti i dati di 117 pazienti che tra Gennaio 2006 e Giugno 2007 sono stati sottoposti ad intervento elettivo di cardochirurgia presso l'Università di Navarra (Pamplona, Spagna). La determinazione della troponina è avvenuta nell'immediato postoperatorio, in prima e seconda giornata postoperatoria. La diagnosi d'infarto del miocardio è stata ottenuta attraverso la monitorizzazione elettrocardiografica, ecocardiografica e la valutazione clinica dello stato emodinamico. Una volta avuta la diagnosi d'infarto miocardico perioparatorio, attraverso l'analisi ROC (Receiving operative curve) è stato individuato il valore di Troponina cui sono corrisposte la migliore specificità e sensibilità. Nelle prime tre ore postoperatorie questo valore di troponina è stato pari a 1.22mg/L (CI 0,94 to 0.99, P = 0.0001, con una sensibilità del 100% ed una specificità del 96%). Tale valore è in linea con recenti studi di Mohammed et al. e di Leherke et al. in cui sono stati trovati dei cut-off rispettivamente pari a 1.6 mg/L e 1.26mg/L. Tuttavia mentre in questi ultimi la misurazione è avvenuta nelle prime 24 ore post-operatorie, nel nostro studio il cut-off trovato si riferisce alle prime tre ore post-oeratorie. Ciò può avere una notevole implicazione clinica, in quanto anticipare di ore la diagnosi di infarto del miocardio potrebbe significare anticipare eventuali interventi terapeutici mirati a limitare il danno miocardico (es. contro pulsazione aortica, revisone dei graft ecc.).
Successive analisi ROC riferite a misurazioni più tardive hanno mostrato una progressiva diminuzione della sensibilità con un aumento della specificità (nella seconda giornata-postoperatoria il cut-off è stato pari a 2.8 mg/L, CI 95% 0.84 to 0.98, P = 0.0001 con una sensibilità del 66 % ed una specificità del 100%). In aggiunta a tali risultati, è stata trovata un'alta correlazione attraverso il Pearson's test tra concentrazione di Troponine e durata della degenza in unità di terapia intensiva e ospedaliera complessiva. Questo valore predittivo raggiunge la massima significatività statistica se la misurazione viene effettuata dopo la seconda giornata post-op (P = 0.008 e per la durata della degenza ospedaliera complessiva e P = 0.01 per la permanenza in unità di terapia intensiva). In conclusione si può affermare che la misurazione della Troponina nell'immediato post-operatorio permette di includere tutti i soggetti con possibile infarto miocardico perioperatorio. Mentre una successiva misurazione può esclude i falsi positivi e aggiungere un'utile informazione circa la durata della degenza in unità di terapia intensiva e della degenza ospedaliera.

References

1) Force T, Hibberd P, Weeks G, Kemper AJ, Bloomfield P, Tow D, Josa M, Khuri S, Parisi AF: *Perioperative myocardial infarction after coronary artery bypass surgery. Clinical significance and approach to risk stratification.* Circulation, 1990; 82:903-12.

2) Jain U: *Myocardial infarction during coronary artery bypass surgery.* J Cardiothorac Vasc Anesth, 1992; 6:612-23.

3) Tuman KJ: *Perioperative myocardial infarction.* Semin Thorac Cardiovasc Surg, 1991; 3:47-52.

4) Svedjeholm R, Dahlin LG, Lundberg C, Szabo Z, Kågedal B, Nylander E, Olin C, Rutberg H: *Are electrocardiographic Q-wave criteria reliable for diagnosis of perioperative myocardial infarction after coronary surgery?* Eur J Cardiothorac Surg, 1998; 13:655-61.

5) Caspi Y, Safadi T, Ammar R, Elamy A, Fishman NH, Merin G: *The significance of bundle branch block in the immediate postoperative electrocardiograms of patients undergoing coronary artery bypass.* J Thorac Cardiovasc Surg, 1987; 93:442-6.

6) Baerman JM, Kirsh MM, de Buitleir M, Hyatt L, Juni JE, Pitt B, Morady F: *Natural history and determinants of conduction defects following coronary artery bypass surgery.* Ann Thorac Surg, 1987; 44:150-53.

7) Lehrke S, Steen H, Sievers HH, Peters H, Opitz A, Müller-Bardorff M, Wiegand UK, Katus HA, Giannitsis E: *Cardiac troponin T for prediction of short- and long-term morbidity and mortality after elective open heart surgery.* Clin Chem, 2004; 50:1560-567.

8) Bonnefoy E, Filley S, Kirkorian G, Guidollet J, Roriz R, Robin J, Touboul P: *Troponin I, troponin T, or creatine kinase-MB to detect perioperative myocardial damage after coronary artery bypass surgery.* Chest, 1998; 114:482-86.

9) Alpert JS, Thygesen K, Antman E, Bassand JP: *Myocardial infarction redefined. A consensus document of the joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction.* J Am Coll Cardiol, 2000; 36:959-69.

10) Petäjä L, Salmenperä M, Pulkki K, Pettilä V: *Biochemical Injury Markers and Mortality After Coronary Artery Bypass Grafting: A Systematic Review.* Ann Thorac Surg, 2009; 87:1981-992.

11) Lasocki S, Provenchère S, Bénessiano J, Vicaut E, Lecharny JB, Desmonts JM, Dehoux M, Philip I: *Cardiac troponin I is an independent predictor of in-hospital death after adult cardiac surgery.* Anesthesiology, 2002; 97:405-11.

12) Jacquet L, Noirhomme P, El Khoury G, Goenen M, Philippe M, Col J, Dion R: *Cardiac troponin I as an early marker of myocardial damage after coronary bypass surgery.* Eur J Cardiothorac Surg, 1998; 13:378-84.

13) Swaanenburg JC, Klaase JM, DeJongste MJ, Zimmerman KW, ten Duis HJ: *Troponin I, troponin T, CKMB-activity and CKMB-mass as markers for the detection of myocardial contusion in patients who experienced blunt trauma.* Clin Chim Acta, 1998; 272:171-81.

14) Burns RJ, Gladstone PJ, Tremblay PC, Feindel CM, Salter DR, Lipton IH, Ogilvie RR, David TE: *Myocardial infarction determined by technetium-99m pyrophosphate single-photon tomography complicating elective coronary artery bypass grafting for angina pectoris.* Am J Cardiol, 1989; 63:1429-34.

15) Falahati A, Sharkey SW, Christensen D, McCoy M, Miller EA, Murakami MA, Apple FS: *Implementation of serum cardiac troponin I as marker for detection of acute myocardial infarction.* Am Heart J, 1999; 137:332-37.

16) Mohammed AA, Agnihotri AK, van Kimmenade RR, Martinez-Rumayor A, Green SM, Quiroz R, Januzzi JL Jr: *Prospective, comprehensive assessment of cardiac toponin T testing after coronary artery bypass graft surgery.* Circulation, 2009; 120:843-50.