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Comparison between creatine kinase MB, heart-type fatty acid-binding protein, and cardiac troponin T for detecting myocardial ischemic injury after cardiac surgery

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ABSTRACT

Background: Heart-type fatty acid-binding protein (H-FABP) is a cytoplasmic protein and is released form necrotic cardiac myocytes, as well as ischemic cardiac myocytes. In this study, we compared creatine kinase MB (CK-MB), H-FABP, and cardiac troponin T (cTnT) after coronary artery bypass grafting (CABG), heart valve surgery, or septal defect surgery to evaluate the difference in detecting myocardial injury between three markers.
Methods: A total of 69 patients (CABG, 32; valve surgery, 27; and septal defect surgery, 10) were prospectively enrolled. Blood samples were taken at specific intervals.
Results: Mean amount ($AUC_{0\text{-}72h}$) of CK-MB and cTnT released for 72 h in the patients with valve surgery were 2446 h·ng/ml and 93.2 h·ng/ml, which were significantly larger than those in the patients with CABG or septal defect surgery ($p < .05$). Mean amount ($AUC_{0\text{-}72h}$) of H-FABP released for 72 h in the patients with CABG was 1939 h·ng/ml, which was significantly larger than that in the patients with septal defect surgery (700.1 h·ng/ml) ($p < .05$).
Conclusion: H-FABP would be a more useful marker for detecting myocardial ischemic injury than CK-MB and cTnT. CK-MB and cTnT would be more sensitive to myocardial injury with surgical trauma than with ischemic injury in the patients with cardiac surgery.

1. Introduction

Cardiac troponins are a very specific marker for myocardial infarction (MI) [1,2] and currently the measurement of cardiac troponin T (cTnT) or troponin I (cTnI) is the gold standard in laboratory diagnosis of MI [3]. As cardiac troponin increases begin 2 to 4 h after acute MI, it is difficult to diagnose acute MI early by using cardiac troponins [4]. Early diagnosis of acute MI and early intervention improve the prognosis [5,6].Consequently, many studies have been conducted to detect early diagnostic marker for acute MI [7–9]. Heart-type fatty acid-binding protein (H-FABP) is one of these markers.

H-FABP is a small cytoplasmic protein (15 kDa) and 2–10 times more expressed in cardiac muscle than in skeletal muscle [10–12]. It is rapidly released into the circulation following myocardial injury and detected at high concentrations in blood within 1 h of myocardial injury [13,14]. H-FABP has been considered as an early marker for acute myocardial infarction (MI) [15,16]. However, H-FABP has not yet been widely used in clinical laboratories.

The majority of cardiac troponins is bound to myofilaments and so cardiac troponins are mainly released from necrotic cardiac myocytes [17]. In comparison, H-FABP is a cytoplasmic protein and is released form necrotic cardiac myocytes, as well as ischemic cardiac myocytes [18–20]. As myocardial infarction (MI) is more common after coronary artery bypass grafting (CABG) than after septal defect surgery [21–26], so the comparison of blood concentrations between cTnT and H-FABP after CABG and spetal defect surgery would be useful to understand difference between both markers.

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2. Materials and methods

2.1. Patients

A total of 74 patients who had cardiac surgery with cardiopulmonary bypass (CBP) and aortic cross-clamping (ACC) at the Department of Thoracic & Cardiovascular Surgery of St. Vincent's Hospital, Korea, between December 2008 and November 2009 were enrolled in this prospective study. Among these patients, five were excluded due to complications (two deaths, one hypertension, one arrhythmia, and one reoperation). Of the 69 patients, 32 (46.4%) underwent CABG, 27 (39.1%) underwent valve surgery, and the remaining 10 (14.5%) underwent septal defect surgery. After the operation, blood samples were taken at specific intervals. All subjects provided informed written consent and this study was approved by St. Vincent's Hospital Institutional Review Board.

2.2. Measurements of cardiac biomarkers

Blood concentrations of the cardiac biomarkers were measured just before cardiac surgery, just after, and at 3, 6, 12 h, and 1 d, 2, 3, 4, 5, 6, and 7 d after cardiac surgery was completed. In addition, the measurement of cTnT was continued until the concentration was normalized. The amounts of the biomarkers released from injured myocardium were calculated by using the area under the concentration-time curve (AUC) just after the surgery to a certain time. The cardiac biomarkers measured in this study were cardiac troponin T (cTnT), CK-MB and H-FABP. cTnT and CK-MB were measured using electrochemiluminescence immunoassays on the Elecsys 2010 analyzer (Roche Diagnostics). Reference ranges of CK-MB and cTnT were < 6.7 ng/ml and 0.1 ng/ml, respectively. The limit of quantitation of cTnT was 0.013 ng/ml. H-FABP was measured using the HiSens h-FABP turbidometric immunoassay (Genematrixbio), which uses latex particles coated with a monoclonal anti-H-FABP antibody. It provided a minimum detection limit of 0.1 ng/ml and a within-run precision of 4.8% at 2.5 ng/ml. This turbidometric immunoassay was performed using the Hitachi 7600 chemistry analyzer, with a reference range of < 6.2 ng/ml.

2.3. Half-lives of cardiac biomarkers

Half-lives of CK-MB, cTnT and H-FABP were calculated by using the non-compartment model. The maximum concentration (C_{max}) and the time to Cmax (t_{max}) were obtained by visual inspection of the result. The sampling time to reach C_{max} was considered to be time zero. The area under the concentration-time curve from time zero to a certain time ($AUC_{0\text{-}t}$) and the area under the concentration-time curve from time zero to infinity ($AUC_{0\text{-}\infty}$) were calculated using the linear trapezoidal method. The mean resident time (MRT) was calculated from $AUMC_{0\text{-}\infty}/AUC_{0\text{-}\infty}$, where $AUMC_{0\text{-}\infty}$ is the area under the first-moment curve of the concentration-time curve from time zero to infinity. The elimination rate constant (k_e) was calculated as 1/MRT and each half-life ($t_{1/2}$) was calculated as $0.693/k_e$ [27].

Glomerular filtration rate (GFR) was calculated using the MDRD study equation as follows [28]:

$$\text{GFR (ml/min/1.73m}^2) = 186 \times [\text{serum creatinine (mg/dL)}]^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}).$$

Study patients were divided into 3 groups depending on the level of GFR ($<60, 60 - < 90, \geq 90$ ml/min/1.73m^2).

2.4. Statistics

Continuous data were expressed as mean ± SD and compared using Student's *t*-test. Non-normally distributed continuous data were compared using Mann-Whitney *U* test. Multiple linear regression was used to explain the relationship between the amount of the biomarker released after cardiac surgery and age, GFR, CPB time, ACC time, length of hospitalization, and length in the intensive care unit. The relationship between the amount of the biomarker and type of surgery was analyzed using Student's *t*-test or Mann-Whitney *U* test. A $p < .05$ was considered statistically significant. The statistical analysis was performed using SPSS software, ver 13.0.

Table 1
Patients' characteristics.

	CABG	Valve surgery	Septal surgery	*p*
n	32	27	10	
Age	63.9 ± 7.1	59.5 ± 10.9	40.1 ± 14.7	< 0.05[a]
Sex(M/F)	20/12	12/15	3/7	
CPB time (min)	175.5 ± 64.3	187.7 ± 56.5	93.0 ± 51.0	< 0.05[a]
ACC time (min)	138.3 ± 56.8	139.8 ± 50.8	69.6 ± 33.9	< 0.05[a]
Hospitalization at ICU (d)	17.2 ± 13.7	12.8 ± 8.8	6.3 ± 4.7	< 0.05[a]

[a] *p* values between septal surgery and the other two groups.

3. Results

A total of 69 patients included 32 patients with CABG, 27 patients with valve surgery, and 10 patients with septal defect surgery (Table 1). CPB times in the patients with CABG, valve surgery, and septal defect surgery were 175.5 ± 64.3 min, 187.7 ± 56.5 min, and 93.0 ± 51.0 min, respectively. ACC times in the patients with CABG, valve operation, and septal defect surgery were 138.3 ± 56.8 min, 139.8 ± 50.8 min, and 69.6 ± 33.9 min, respectively. The patients with septal defect surgery had a significantly shorter time of CPB and ACC than did the other two patient groups ($p < .05$). There was no significant difference in the CPB and ACC time between the patients with CABG and those with valve surgery. The lengths in the intensive care unit (ICU) for the patients with CABG and those with valve surgery were not significantly different (17.2 ± 13.7 d and 12.8 ± 8.8 d, respectively), but these were significantly longer than those for the patients with septal defect surgery (6.3 ± 4.7 d) ($p < .05$).

The times to reach the maximum concentration in the blood of CK-MB, H-FABP and cTnT after the cardiac operation was completed were 3.78 ± 5.82 h, 5.60 ± 8.58 h and 6.75 ± 11.05 h, respectively (Table 2). CK-MB concentrations showed an increase until the 3 h time point and then decreased to baseline on the 4th day after the cardiac operation (Fig. 1). cTnT concentrations showed an increase until the 6 h time point and then decreased. H-FABP concentrations showed two types of pattern. Among 69 patients, 29 (42.0%) patients had H-FABP concentrations showing initially decrease and then increase with a peak 24 h after the cardiac operation. The other 40 patients had H-FABP concentrations showing a continuous decrease after the cardiac operation. Among 32 patients with CABG, 16 (50%) showed the biphasic distribution of H-FABP. Twelve (44.4%) of 27 patients with valve surgery and one (10%) of 10 patients with septal surgery showed the biphasic distribution of H-FABP after surgery.

Of the 69 patients, 37 had a GFR of ≥ 90 ml/min/1.73m^2, 24 had a GFR of 60 to < 90 ml/min/1.73m^2, and 8 had a GFR of < 60 ml/min/1.73m^2 (Table 3). In the 37 patients with a GFR of ≥ 90 ml/min/1.73m^2, the half-life of CK-MB was 19.7 ± 3.9 h which was significantly shorter than those of cTnT (49.6 ± 17.7 h) and H-FABP (25.7 ± 9.1 h) ($P < .05$). CK-MB showed no significant difference in half-life according to renal function. However, cTnT and H-FABP showed a significant increase of half-life with the decrease of GFR ($p < .05$).

Multiple linear regression showed that the amounts of H-FABP and cTnT released after the cardiac surgery was significantly associated

Table 2
Concentrations of three biomarkers after cardiac surgery in 69 patients (mean ± SD).

Time	CK-MB (ng/ml)	H-FABP (ng/ml)	cTnT (ng/ml)
Pre-operation	2.8 ± 2.7	3.6 ± 6.3	0.05 ± 0.16
0 h after surgery	55.4 ± 50.0	46.1 ± 45.2	1.39 ± 1.50
3 h	53.9 ± 41.4	40.4 ± 47.2	1.40 ± 1.42
6 h	50.7 ± 39.7	40.5 ± 51.3	1.41 ± 1.40
9 h	46.4 ± 38.8	40.1 ± 51.9	1.31 ± 1.32
12 h	42.6 ± 35.6	45.0 ± 57.3	1.27 ± 1.41
1d	29.5 ± 21.7	42.1 ± 45.5	1.02 ± 1.09
2d	14.8 ± 10.6	31.0 ± 36.1	0.77 ± 0.73
3d	8.2 ± 8.0	18.0 ± 21.1	0.70 ± 0.63
4d	5.2 ± 4.3	14.1 ± 29.1	0.67 ± 0.65
5d	4.9 ± 9.5	10.1 ± 26.3	0.62 ± 0.77
6d	4.2 ± 6.2	9.4 ± 28.8	0.51 ± 0.91
7d	3.7 ± 2.9	8.7 ± 29.0	0.43 ± 0.92
p	< 0.05[a]	< 0.05[b]	< 0.05[c]

[a] Comparison using paired sample *t*-test between the following groups: pre-op vs 0 h after surgery; 3 vs 6 h; 6 vs 9 h; 9 vs 12 h; 12 h vs 1 d; 1 vs 2 d; 2 vs 3 d; 3 vs 4 d.

[b] Comparison using paired sample *t*-test between the following groups: pre-op vs 0 h after surgery; 0 h after surgery vs 3 h; 12 vs 1 d; 1 vs 2 d; 2 vs 3 d; 4 vs 5 d; 6 vs 7 d.

[c] Comparison using paired sample *t*-test between the following groups: pre-op vs 0 h after surgery; 6 vs 9 h; 12 h vs 1 d; 1 vs 2 d; 2 vs 3 d; 5 vs 6 d; 6 vs 7 d.

with GFR and CPB time (Table 4). In addition, CPB time was also significantly associated with the amount of CK-MB. However, age, ACC time, and length of hospitalization were not associated with the amount of each marker.

Table 3
Half-life (h) of cardiac markers according to renal function.

GFR (ml/min/1.73m^2)	Half-life (h)			*p*
	CK-MB	cTnT	H-FABP	
< 60 (*n* = 8)	20.2 ± 6.6	63.3 ± 21.7	36.8 ± 9.7	< 0.05
60- < 90 (*n* = 24)	21.8 ± 3.2	56.7 ± 20.3	34.7 ± 7.9	< 0.05
≥90 (*n* = 37)	19.7 ± 3.9	49.6 ± 17.7	25.7 ± 9.1	< 0.05
Total (11.8–186.3)	20.4 ± 4.1	53.6 ± 19.4	30.0 ± 9.9	< 0.05
p	*NS*	< 0.05	< 0.05	

As GFR increased the concentrations of H-FABP and cTnT released after the cardiac surgery, the relationship between the amount of the three biomarkers and type of surgery was analyzed by using 61 patients with GFR of ≥60 ml/min/1.73m^2 (Table 5). The mean amount ($AUC_{0\text{-}72h}$) of CK-MB and cTnT released for 72 h in the patients with valve surgery were 2446 h·ng/ml and 93.2 h·ng/ml, which were significantly larger than those in the patients with CABG or septal defect surgery ($p < .05$) (Table 2). There was no significant difference in the amount of CK-MB and cTnT between the patients with CABG and those with septal defect surgery. In contrast, the mean amount ($AUC_{0\text{-}72h}$) of H-FABP released for 72 h in the patients with valve surgery was 2229 h·ng/ml, which was similar to that in the patients with CABG (1939 h·ng/ml), which was significantly larger than that in the patients with septal defect surgery (700 h·ng/ml) ($p < .05$).

4. Discussion

Our data showed that the amounts of CK-MB, cTnT and H-FABP

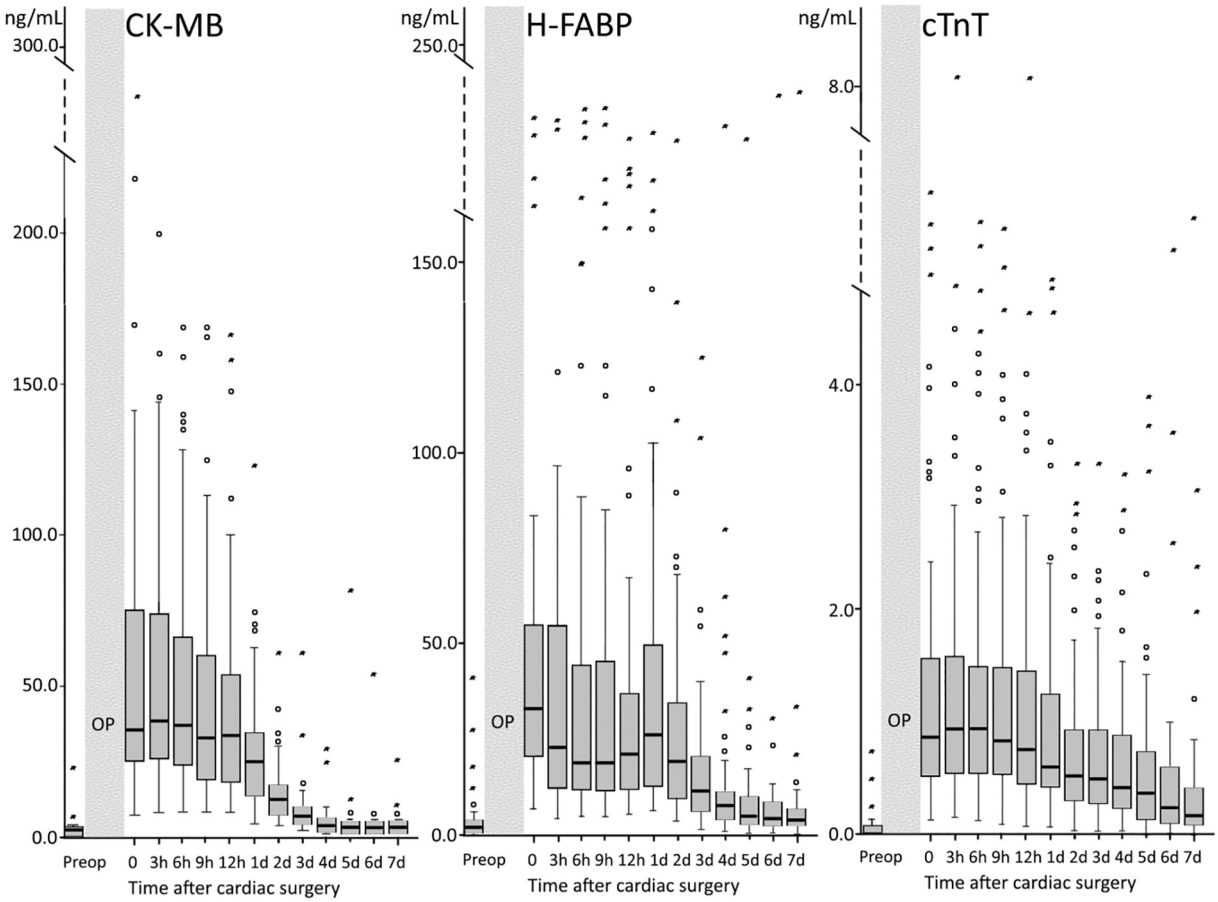

Fig. 1. Release kinetics of CK-MB, H-FABP and cTnT after cardiac surgery. The median is shown as a line in the box. Circles (°) indicate suspect outliers and asterisks (*) indicate very suspect outliers in box plot.

Table 4
Relationship between the amounts of three biomarkers and age, GFR, CPB time, ACC time, length of hospitalization, and length in the intensive care unit using multiple linear regression.

	CK-MB ($AUC_{0\text{-}72h}$)		H-FABP ($AUC_{0\text{-}72h}$)		cTnT ($AUC_{0\text{-}72h}$)	
	β	*p*	β	*p*	β	*p*
Age	−0.014	0.926	0.038	0.763	−0.119	0.375
GFR	0.062	0.649	−0.442	0.000	−0.243	0.057
CPB time	0.679	0.071	0.613	0.060	0.878	0.012
ACC time	−0.403	0.276	−0.441	0.170	−0.534	0.118
Length of hospitalization	0.012	0.935	0.133	0.299	0.116	0.392
Length in ICU	−0.140	0.347	0.008	0.949	−0.210	0.126

β = Standardized coefficients.

Table 5
Area under the concentration-time curve according to the type of cardiac operation in 61 patients (GFR ≥ 60).

AUC	CABG	Valve surgery	Septal surgery	*p*
CK-MB (h·ng/ml)				
$AUC_{0\text{-}24h}$	710 ± 631	1527 ± 860	762 ± 302	< 0.05
$AUC_{0\text{-}48h}$	1098 ± 943	2145 ± 1122	1064 ± 366	< 0.05
$AUC_{0\text{-}72h}$	1263 ± 1067	2446 ± 1259	1216 ± 419	< 0.05
$AUC_{0\text{-}96h}$	1423 ± 1108	2623 ± 1328	1309 ± 446	< 0.05
p[a]	< 0.05	< 0.05	< 0.05	
H-FABP (h·ng/ml)				
$AUC_{0\text{-}24h}$	858 ± 991	1024 ± 981	347 ± 238	< 0.05
$AUC_{0\text{-}48h}$	1526 ± 1587	1793 ± 1511	574 ± 320	< 0.05
$AUC_{0\text{-}72h}$	1939 ± 1796	2229 ± 1757	700 ± 368	< 0.05
$AUC_{0\text{-}96h}$	2336 ± 2237	2452 ± 1876	762 ± 398	< 0.05
p[a]	< 0.05	< 0.05	< 0.05	
cTnT (h·ng/ml)				
$AUC_{0\text{-}24h}$	19.5 ± 13.8	43.1 ± 38.9	15.7 ± 12.2	< 0.05
$AUC_{0\text{-}48h}$	34.4 ± 27.6	70.7 ± 60.7	29.1 ± 20.9	< 0.05
$AUC_{0\text{-}72h}$	45.6 ± 40.3	93.2 ± 76.0	41.4 ± 29.9	< 0.05
$AUC_{0\text{-}96h}$	58.0 ± 57.8	113.7 ± 89.3	50.6 ± 37.1	< 0.05
p[a]	< 0.05	< 0.05	< 0.05	

[a] Comparison using paired sample *t*-test.

released after valve surgery for a specific time period were about 2 times larger than those in the patients with septal defect surgery. Valve surgery needs longer operating time and is more invasive than septal defect surgery. This finding indicated that repeated surgical trauma caused direct myocyte damage and release of cardiac markers. In addition, all of our patients underwent cardiac surgery with cardiopulmonary bypass (CPB) which resulted in myocardial ischemic injury [29–31]. In our study, CPB time for valve surgery was about twice as long as that for septal defect surgery. This finding also suggests that ischemia-reperfusion injury is also a major cause of increase in the cardiac markers.

Ischemia-reperfusion injury (IRI) is common in cardiac surgery with CPB. During cardiac surgery with CPB, the heart is isolated from the circulation which results in myocardial ischemia [30]. The restoration of blood flow to the ischemic myocardium results in oxidative stress and oxidative damage of myocytes which could lead to myocardial infarction and cardiac arrhythmias [32,33]. IRI is also common in orthopedic surgery with tourniquet, organ transplantation, percutaneous coronary intervention, and CABG without CPB [34–36]. In our study, the amounts of CK-MB and cTnT released after CABG were similar to those after septal defect surgery. This finding was not the same as expected. As the patients with CABG had coronary artery stenosis and longer duration of CPB compared with septal defect surgery, more severe IRI would be occurred in the patents with CABG. This data indicated that CK-MB and cTnT did not properly represent IRI in the patients with CABG. In contrast, the amounts of H-FABP after CABG were about three times larger than those after septal defect surgery. These findings suggested that H-FABP would be a more useful marker for detecting myocardial ischemic injury than CK-MB and cTnT. Our result was similar to the study of Muehlschlegel et al. that H-FABP was a superior independent predictor of postoperative mortality and ventricular dysfunction after CABG than CK-MB and cTnI [37]. The study of Malik et al. also showed that Heart-type fatty-acid–binding protein was a more rapid marker of perioperative myocardial damage than CK-MB in the patients with CABG [31]. The study of Thielmann et al. also told that H-FABP was a sensitive and rapid biomarker that detected MI reliably at 1 h after CABG, much earlier than cTnI [38].

MI is common after CABG [39]. MI is more common after CABG than after valve surgery [38,40]. However, our data showed that the amounts of CK-MB and cTnT released after CABG were half those after valve surgery, but the amounts of CK-MB and cTnT released after valve surgery were about two times larger than after septal defect surgery. This finding indicated that CK-MB and cTnT would be more sensitive to myocardial injury with surgical trauma than with ischemic injury in the patients with cardiac surgery.

Our study showed that H-FABP and cTnT were affected by renal function, as in other studies [41–43]. This finding suggests that a different cutoff of H-FABP for myocardial infarction should be applied to the patients with renal disease.

This study has a few limitations. First, our data are from a relatively small sample size and from one center. Further larger cohort studies would be desirable to confirm the difference between cTnT and H-FABP for detecting myocardial ischemic injury after cardiac surgery. Second, H-FABP concentrations released after cardiac surgery showed the biphasic distribution in the twenty nine of 69 patients in this study. The biphasic distribution occurred more frequently in the patients with CABG than the other two groups. However, we did not perform long-term follow-up of the patients showing the biphasic distribution of H-FABP after cardiac surgery.

In conclusion, H-FABP would be a more useful marker for detecting myocardial ischemic injury than CK-MB and cTnT. CK-MB and cTnT would be more sensitive to myocardial injury with surgical trauma than with ischemic injury in the patients with cardiac surgery.

References

[1] H.A. Katus, S. Looser, K. Hallermayer, A. Remppis, T. Scheffold, A. Borgya, U. Essig, U. Geuss, Development and in vitro characterization of a new immunoassay of cardiac troponin T, Clin. Chem. 38 (3) (1992) 386–393.
[2] E.M. Ohman, P.W. Armstrong, R.H. Christenson, C.B. Granger, H.A. Katus, C.W. Hamm, M.A. O', G.S. Hanesian, N.S. Wagner, F.E. Harrell Kleiman Jr., R.M. Califf, E.J. Topol, Cardiac troponin T levels for risk stratification in acute myocardial ischemia. GUSTO IIA investigators, N. Engl. J. Med. 335 (18) (1996) 1333–1341.
[3] M.F. Fathil, M.K. Md Arshad, S.C. Gopinath, U. Hashim, R. Adzhri, R.M. Ayub, A.R. Ruslinda, M.N.M. Nuzaihan, A.H. Azman, M. Zaki, T.H. Tang, Diagnostics on acute myocardial infarction: Cardiac troponin biomarkers, Biosens. Bioelectron. 70 (2015) 209–220.
[4] A.S. Jaffe, L. Babuin, F.S. Apple, Biomarkers in acute cardiac disease: the present and the future, J. Am. Coll. Cardiol. 48 (1) (2006) 1–11.
[5] S.R. Mehta, C.B. Granger, W.E. Boden, P.G. Steg, J.P. Bassand, D.P. Faxon, R. Afzal, S. Chrolavicius, S.S. Jolly, P. Widimsky, A. Avezum, H.J. Rupprecht, J. Zhu, J. Col, M.K. Natarajan, C. Horsman, K.A. Fox, S. Yusuf, Early versus delayed invasive

intervention in acute coronary syndromes, N. Engl. J. Med. 360 (21) (2009) 2165–2175.
[6] M. O'Donoghue, W.E. Boden, E. Braunwald, C.P. Cannon, T.C. Clayton, R.J. de Winter, K.A. Fox, B. Lagerqvist, P.A. McCullough, S.A. Murphy, R. Spacek, E. Swahn, L. Wallentin, F. Windhausen, M.S. Sabatine, Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction: a meta-analysis, JAMA 300 (1) (2008) 71–80.
[7] Y. Kawai, M. Yoshida, K. Arakawa, T. Kumamoto, N. Morikawa, K. Masamura, H. Tada, S. Ito, H. Hoshizaki, S. Oshima, K. Taniguchi, H. Terasawa, I. Miyamori, K. Kishi, T. Yasuda, Diagnostic use of serum deoxyribonuclease I activity as a novel early-phase marker in acute myocardial infarction, Circulation 109 (20) (2004) 2398–2400.
[8] M. Rubini Gimenez, R. Twerenbold, T. Reichlin, K. Wildi, P. Haaf, M. Schaefer, C. Zellweger, B. Moehring, F. Stallone, S.M. Sou, M. Mueller, K. Denhaerynck, T. Mosimann, M. Reiter, B. Meller, M. Freese, C. Stelzig, I. Klimmeck, J. Voegele, B. Hartmann, K. Rentsch, S. Osswald, C. Mueller, Direct comparison of high-sensitivity-cardiac troponin I vs. T for the early diagnosis of acute myocardial infarction, Eur. Heart J. 35 (34) (2014) 2303–2311.
[9] H. Katus, A. Ziegler, O. Ekinci, E. Giannitsis, W.G. Stough, S. Achenbach, S. Blankenberg, M. Brueckmann, P. Collinson, D. Comaniciu, F. Crea, W. Dinh, G. Ducrocq, F.A. Flachskampf, K.A.A. Fox, M.G. Friedrich, K.A. Hebert, A. Himmelmann, M. Hlatky, D. Lautsch, B. Lindahl, D. Lindholm, N.L. Mills, G. Minotti, M. Mockel, T. Omland, V. Semjonow, Early diagnosis of acute coronary syndrome, Eur. Heart J. 38 (41) (2017) 3049–3055.
[10] J.A. Kragten, F.A. van Nieuwenhoven, M.P. van Dieijen Visser, P.H. Theunissen, W.T. Hermens, J.F. Glatz, Distribution of myoglobin and fatty acid-binding protein in human cardiac autopsies, Clin. Chem. 42 (2) (1996) 337–338.
[11] J. Storch, A.E. Thumser, The fatty acid transport function of fatty acid-binding proteins, Biochim. Biophys. Acta 1486 (1) (2000) 28–44.
[12] J.F. Glatz, J. Storch, Unravelling the significance of cellular fatty acid-binding proteins, Curr. Opin. Lipidol. 12 (3) (2001) 267–274.
[13] F.A. Van Nieuwenhoven, A.H. Kleine, W.H. Wodzig, W.T. Hermens, H.A. Kragten, J.G. Maessen, C.D. Punt, M.P. Van Dieijen, G.J. Van der Vusse, J.F. Glatz, Discrimination between myocardial and skeletal muscle injury by assessment of the plasma ratio of myoglobin over fatty acid-binding protein, Circulation 92 (10) (1995) 2848–2854.
[14] Y. Kim, H. Kim, S.Y. Kim, H.K. Lee, H.J. Kwon, Y.G. Kim, J. Lee, H.M. Kim, B.H. So, Automated heart-type fatty acid-binding protein assay for the early diagnosis of acute myocardial infarction, Am. J. Clin. Pathol. 134 (1) (2010) 157–162.
[15] S.P. Kabekkodu, S.R. Mananje, R.P. Saya, A Study on the Role of Heart Type Fatty Acid Binding Protein in the Diagnosis of Acute Myocardial Infarction, J. Clin. Diagn. Res. 10 (1) (2016) Oc07–10.
[16] A.K. Pyati, B.B. Devaranavadagi, S.L. Sajjannar, S.V. Nikam, M. Shannawaz, Sudharani, Heart-Type Fatty Acid Binding Protein: a Better Cardiac Biomarker than CK-MB and Myoglobin in the early Diagnosis of Acute Myocardial Infarction, J. Clin. Diagn. Res. 9 (10) (2015) Bc08–11.
[17] S. Agewall, E. Giannitsis, Troponin elevation in coronary ischemia and necrosis, Curr. Atheroscler. Rep. 16 (3) (2014) 396.
[18] A. Vupputuri, S. Sekhar, S. Krishnan, K. Venugopal, K.U. Natarajan, Heart-type fatty acid-binding protein (H-FABP) as an early diagnostic biomarker in patients with acute chest pain, Indian Heart J. 67 (6) (2015) 538–542.
[19] H.M. Azzazy, M.M. Pelsers, R.H. Christenson, Unbound free fatty acids and heart-type fatty acid-binding protein: diagnostic assays and clinical applications, Clin. Chem. 52 (1) (2006) 19–29.
[20] K. Tambara, M. Fujita, S. Miyamoto, K. Doi, K. Nishimura, M. Komeda, Pericardial fluid level of heart-type cytoplasmic fatty acid-binding protein (H-FABP) is an indicator of severe myocardial ischemia, Int. J. Cardiol. 93 (2–3) (2004) 281–284.
[21] F.G. Bakaeen, D. Chu, R.F. Kelly, W.L. Holman, M.E. Jessen, H.B. Ward, Perioperative outcomes after on- and off-pump coronary artery bypass grafting, Tex. Heart Inst. J. 41 (2) (2014) 144–151.
[22] D.J. Lapar, I.K. Crosby, J.B. Rich, E. Fonner Jr., I.L. Kron, G. Ailawadi, A.M. Speir, A contemporary cost analysis of postoperative morbidity after coronary artery bypass grafting with and without concomitant aortic valve replacement to improve patient quality and cost-effective care, Ann. Thorac. Surg. 96 (5) (2013) 1621–1627.
[23] A.G. van Boxtel, S. Bramer, M.A. Soliman Hamad, A.H. van Straten, Perioperative serum aspartate aminotransferase level as a predictor of survival after coronary artery bypass grafting, Ann. Thorac. Surg. 94 (5) (2012) 1492–1498.
[24] A. Bordalo, A. Nobre, R. Pereira, A. Lemos, M. Mendes, F. Pereira, C. Serpa, J. Cravino, Perioperative myocardial infarction in coronary bypass surgery: characterization of risk factors, clinical pictures and prognosis, Revista portuguesa de cirurgia cardio-toracica e vascular 18 (1) (2011) 11–21.
[25] H.B. Ward, R.F. Kelly, L. Thottapurathu, T.E. Moritz, G.C. Larsen, G. Pierpont, S. Santilli, S. Goldman, W.C. Krupski, F. Littooy, D.J. Reda, E.O. McFalls, Coronary artery bypass grafting is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery, Ann. Thorac. Surg. 82 (3) (2006) 795–800 (discussion 800-1).
[26] H. Cubero-Gallego, M. Lorenzo, M. Heredia, I. Gomez, E. Tamayo, Diagnosis of perioperative myocardial infarction after heart valve surgery with new cut-off point of high-sensitivity troponin T and new electrocardiogram or echocardiogram changes, J. Thorac. Cardiovasc. Surg. 154 (3) (2017) 895–903.
[27] A.A. Nava-Ocampo, A. Pastrak, T. Cruz, G. Koren, Pharmacokinetics of high doses of cyanocobalamin administered by intravenous injection for 26 weeks in rats, Clin. Exp. Pharmacol. Physiol. 32 (1–2) (2005) 13–18.
[28] A.S. Levey, J.P. Bosch, J.B. Lewis, T. Greene, N. Rogers, D. Roth, A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group, Ann. Intern. Med. 130 (6) (1999) 461–470.
[29] P. Chivasso, G.A. Guida, D. Fudulu, V.D. Bruno, R. Marsico, H. Sedmakov, M. Zakkar, F. Rapetto, A.J. Bryan, G.D. Angelini, Impact of off-pump coronary artery bypass grafting on survival: current best available evidence, Journal of thoracic disease 8 (Suppl. 10) (2016) S808–s817.
[30] S. De Hert, A. Moerman, Myocardial injury and protection related to cardiopulmonary bypass, Best Pract. Res. Clin. Anaesthesiol. 29 (2) (2015) 137–149.
[31] V. Malik, S.C. Kale, U.K. Chowdhury, L. Ramakrishnan, S. Chauhan, U. Kiran, Myocardial injury in coronary artery bypass grafting: On-pump versus off-pump comparison by measuring heart-type fatty-acid-binding protein release, Tex. Heart Inst. J. 33 (3) (2006) 321–327.
[32] N.L. Halladin, Oxidative and inflammatory biomarkers of ischemia and reperfusion injuries, Danish medical journal 62 (4) (2015) B5054.
[33] J.L. Kristeller, A. Jankowski, T. Reinaker, Role of corticosteroids during cardiopulmonary bypass, Hosp. Pharm. 49 (3) (2014) 232–236.
[34] B. Dorweiler, D. Pruefer, T.B. Andrasi, S.M. Maksan, W. Schmiedt, A. Neufang, C.F. Vahl, Ischemia-Reperfusion Injury : Pathophysiology and Clinical Implications, European journal of trauma and emergency surgery : official publication of the, European Trauma Society 33 (6) (2007) 600–612.
[35] C.H. Moller, L. Penninga, J. Wetterslev, D.A. Steinbruchel, C. Gluud, Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease, The Cochrane Database Syst. Rev. (3) (2012) (Cd007224).
[36] F. Jiang, J. Yang, L. Zhang, R. Li, L. Zhuo, L. Sun, Q. Zhao, Rosuvastatin reduces ischemia-reperfusion injury in patients with acute coronary syndrome treated with percutaneous coronary intervention, Clin. Cardiol. 37 (9) (2014) 530–535.
[37] J.D. Muehlschlegel, T.E. Perry, K.Y. Liu, A.A. Fox, C.D. Collard, S.K. Shernan, S.C. Body, Heart-type fatty acid binding protein is an independent predictor of death and ventricular dysfunction after coronary artery bypass graft surgery, Anesth. Analg. 111 (5) (2010) 1101–1109.
[38] M. Thielmann, S. Pasa, T. Holst, D. Wendt, D.S. Dohle, E. Demircioglu, V. Sharma, H. Jakob, Heart-Type Fatty Acid Binding Protein and Ischemia-Modified Albumin for Detection of Myocardial Infarction after Coronary Artery Bypass Graft Surgery, Ann. Thorac. Surg. 104 (1) (2017) 130–137.
[39] B.H. Bulkely, G.M. Hutchins, Myocardial consequences of coronary artery bypass graft surgery. The paradox of necrosis in areas of revascularization, Circulation 56 (6) (1977) 906–913.
[40] Y. Okamura, Y. Takeuchi, A. Gomi, M. Nagashima, H. Mori, J. Hattori, Clinical evaluation of perioperative myocardial infarction as a complication of valve replacement Kyobu geka, The Japanese journal of thoracic surgery 42 (12) (1989) 1012–1015.
[41] N. Nayashida, S. Chihara, E. Tayama, K. Akasu, E. Kai, T. Kawara, S. Aoyagi, Influence of renal function on serum and urinary heart fatty acid-binding protein levels, J. Cardiovasc. Surg. 42 (6) (2001) 735–740.
[42] D.P. Bathia, D.R. Carless, K. Viswanathan, A.S. Hall, J.H. Barth, Serum 99th centile values for two heart-type fatty acid binding protein assays, Ann. Clin. Biochem. 46 (2009) 464–467 Pt 6.
[43] T. Niizeki, Y. Takeishi, N. Takabatake, Y. Shibata, T. Konta, T. Kato, S. Kawata, I. Kubota, Circulating levels of heart-type fatty acid-binding protein in a general Japanese population: effects of age, gender, and physiologic characteristics, Circulation journal 71 (9) (2007) 1452–1457.