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Association of cardiac enzymes with morbidity and mortality of patients undergoing coronary endarterectomy surgery

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Original Article

Abstract

BACKGROUND: The relationship between cardiac enzyme release following coronary endarterectomy (CE) and morbidity and mortality is unclear. Therefore, the present study aimed to investigate the association of cardiac enzymes with morbidity and mortality of patients undergoing CE surgery.

METHODS: This was a single-center retrospective cohort study of 475 patients who had undergone off-pump coronary artery bypass graft (OPCABG). The patients were followed up for a mean of 72.99 ± 14.60 months.

RESULTS: Among 475 patients undergoing OPCABG, 39 (8.2%) were non-survivors. Non-survivors were younger and had a fewer ejection fraction (EF). Comorbidities were similar in survivors and non-survivors. The crude Cox regression analysis showed that creatine kinase-myocardial band (CK-MB) had a protective effect against mortality, but when adjusted with age, sex, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia, smoking, family history, body mass index (BMI), left main disease (LMD), and EF, this effect disappeared. Troponin in crude and adjusted analysis did not have any significant effect.

CONCLUSION: There is no association between CK-MB and troponin and mortality in patients undergoing coronary artery bypass graft (CABG).

Keywords: Biomarkers; Coronary Artery Bypass, Off-Pump; Creatine Kinase, MB Form; Endarterectomy; Troponin

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Introduction

Coronary artery disease (CAD) is one of the major causes of death in the world, with 4.5 million deaths occurring in developing countries.[1] CAD treatment with coronary artery bypass graft (CABG) alone does not provide satisfactory results.[2] To achieve better results in diffuse CAD, surgical techniques such as coronary endarterectomy (CE) can be used.[3,4] Recently, surgeons are still unwilling to use CE in combination with CABG due to increase of mortality and myocardial infarction (MI) after surgery.[5] On the other hand, researchers recently reported good and long-term perioperative outcomes from CABG/CE, with evidence of different outcomes and with respect to coronary arteries requiring endarterectomy.[6]

MI in patients undergoing open-heart surgery is the main determinant of postoperative complications and mortality.[7] The incidence of both peri- and postoperative MI was significantly higher in the CE patients, although significant heterogeneity exists on the postoperative MI outcome.[8] Detection of MI after surgery which leads to death of myocytes is a challenging task.[7] Elevations of the biochemical markers of myocardial damage, creatine kinase-myocardial band (CK-MB), and troponin are common after CABG surgery and have been associated with increased in-hospital and short-term mortality.[9-12]

The relationship between increased postoperative concentration of troponin and

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postoperative morbidity and mortality has been well established in recent studies.[13,14]

The specific cardiac isoenzyme CK-MB is known as a susceptible indicator of cardiac muscle necrosis and it is important to measure its serum activity during postoperative CABG surgery.[15] Other cardiac enzymes such as lactate dehydrogenase (LDH) and troponin are also valuable criteria for determining the cell death rate in the heart muscle.[15] Several studies have shown that increased cardiac enzymes in the first 24 hours after CABG surgery are associated with worse prognosis.[16] Recently, several studies have been performed on the relationship of cardiac enzymes with survival in CABG patients,[7,16,17] but there is not any investigation on the changes in cardiac enzymes in patients undergoing CE. Therefore, the present study aimed to investigate the association of cardiac enzymes with morbidity and mortality of patients undergoing CE surgery.

Materials and Methods

Study type: This was a single-center retrospective cohort study on patients who underwent off-pump CABG (OPCABG) + CE in Imam Ali Hospital, Kermanshah, Iran. This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences. The patients were divided into two groups, the survivor and the non-survivor groups and analyzed according to cardiac enzyme.

Sample: With census method, we reviewed the medical records of 659 patients who had been undergoing OPCABG between March 2011 and February 2012. After exclusion of patients who had other procedures in addition to OPCABG, such as valve repair or replacement and left ventricular (LV) aneurysm resection, 475 patients met our criteria. Of these 475 patients, 69 had CE in addition to OPCABG.

Follow-up: The endpoint was all-cause mortality, which was evaluated by telephone contact after discharge for a mean follow-up of 72.99 ± 14.60 months.

Surgical procedure: All patients were operated on with median sternotomy and using the standard technique of cardiopulmonary bypass (CPB) with off-pump technique, as previously described.[18,19]

Data collection: It was conducted through analysis of medical records with a standardized form, including preoperative variables, which consisted of the following: age, gender, body mass index (BMI), diabetes mellitus (DM), hypertension (HTN), hypercholesterolemia, smoking history, family history of CAD, LV ejection fraction (LVEF), previous MI, history of arrhythmia, angina, previous CABG, and left main CAD (LMCAD). Operative data included number of vessel diseases and postoperative variables were MI, arrhythmia, low cardiac output, bleeding, blood transfusion in the intensive care unit (ICU), total length of ICU stay, and hospital mortality.

Definitions: Bleeding was considered when patients needed re-operation. Hospital mortality was defined as death occurring before discharge from the hospital and death was classified as either cardiac or non-cardiac mortality. Arrhythmia refers to postoperative atrial fibrillation (AF) or flutter, heart blockage that requires a pacemaker, and ventricular arrhythmias.

Statistical analysis: Continuous variables were presented as mean ± standard deviation (SD) and categorical variables with absolute value and percentage. Chi-square test and Student's t-test were used to compare the baseline characteristics between survivor and non-survivor patients.

A crude and adjusted Cox proportional hazards model was used to identify risk factors and protective factors relating to mortality. The results were expressed as hazard ratios (HR) with associated 95% confidence interval (CI). The results were considered to be statistically significant with a P-value of < 0.05. All analyses were performed by SPSS software (version 20, IBM Corporation, Armonk, NY, USA).

Results

The study population comprised of 475 patients with a mean age of 58.5 ± 9.5 years (range: 32 to 90 years). Distribution of demographic and clinical variables is listed in table 1. 406 patients (85.5%) underwent OPCABG and 69 (14.5%) underwent OPCABG + CE surgery. In this study, survival time was considered as the elapsed time from the time of surgery to death. The patients were followed up for a mean of 76.70 ± 0.16 months. In the OPCABG group, 32 (7.9%) patients and in the OPCABG + CE group, 7 (10.1%) patients died during the follow-up period. The long-term survival rate using nonparametric Kaplan-Meier method in OPCABG patients was 99.3% and 98.4% in OPCABG + CE patients. The risk ratio in OPCABG + CE patients was 1/2 times more than OPCABG. On the other words, CABG patients significantly had a higher survival time.

A crude and adjusted analysis was used to identify risk and protective factors relating to mortality.

Table 1. Descriptive statistics of the survivor and non-survivor patients

Variable		Survivors (n = 436)	Non-survivors (n = 39)	Total	P
Age (year)	< 50	92 (21.1)	3 (7.7)	95 (20.0)	0.001
	50-70	297 (68.1)	24 (61.5)	321 (67.6)	
	> 70	47 (10.8)	12 (30.8)	59 (12.4)	
Gender	Men	322 (73.9)	30 (76.9)	352 (74.1)	0.840
	Women	114 (26.1)	9 (23.1)	123 (25.9)	
HTN	Yes	195 (44.7)	21 (53.8)	216 (45.5)	0.310
Hyperlipidemia	Yes	147 (33.7)	9 (23.1)	156 (32.8)	0.210
Diabetes	Yes	117 (26.8)	10 (25.6)	127 (26.7)	> 0.999
Smoking	Yes	185 (42.4)	15 (38.5)	200 (42.1)	0.730
Family history	Yes	128 (29.4)	7 (17.9)	135 (28.4)	0.140
Recent MI	Yes	42 (9.6)	5 (12.8)	47 (9.9)	0.570
LMD	Yes	89 (20.4)	6 (15.4)	95 (20.0)	0.530
Bleeding after surgery	Yes	32 (7.3)	3 (7.7)	35 (7.4)	> 0.999
BMI (kg/m^2)	< 18.5	6 (1.4)	1 (2.6)	7 (1.5)	0.890
	18.5-24.9	97 (22.2)	8 (20.5)	105 (22.1)	
	25-29.9	257 (58.9)	22 (56.4)	279 (58.7)	
	> 30	76 (17.4)	8 (20.5)	84 (17.7)	
EF (%)	< 30	63 (14.4)	14 (35.9)	77 (16.2)	0.002
	30-40	85 (19.5)	9 (23.1)	94 (19.8)	
	40-50	97 (22.2)	8 (20.5)	105 (22.1)	
	> 50	191 (43.8)	8 (20.5)	199 (41.9)	
CAD (number of vessel)	1	29 (6.7)	3 (7.7)	32 (6.7)	0.840
	2	92 (21.1)	10 (25.6)	102 (21.5)	
	3	280 (64.2)	24 (61.5)	304 (64.0)	
	4	35 (8.0)	2 (5.1)	37 (7.8)	
Troponin (ng/ml)	< 0.845	26 (6.0)	4 (10.3)	30 (6.3)	0.290
	> 0.845	410 (94.0)	35 (89.7)	445 (93.7)	
CK-MB (IU/l)	< 26.5	176 (41.1)	19 (40.0)	195 (41.1)	0.310
	> 26.5	260 (58.9)	20 (60.0)	280 (58.9)	
Type of surgery	OPCABG	374 (85.8)	32 (82.1)	406 (85.5)	0.480
	OPCABG + CE	62 (14.2)	7 (17.9)	69 (14.5)	
ICU stay (hour)		39.1 ± 24.4	42.2 ± 24.5	39.4 ± 24.4	0.470

Data are presented as mean ± standard deviation (SD) or number and percentage
BMI: Body mass index; MI: Myocardial infraction; LMD: Left main disease, EF: Ejection fraction; CAD: Coronary artery disease; CK-MB: Creatine kinase-myocardial band; ICU: Intensive care unit; HTN: Hypertension

The results of the crude and adjusted analyses, using the Cox proportional hazard model, are shown in table 2.

The crude Cox regression analysis showed that CK-MB had a protective effect against mortality, but when adjusted with age, sex, DM, HTN, hyperlipidemia, smoking, family history, BMI, left main disease (LMD), and EF, this effect disappeared. Troponin in crude and adjusted analysis did not have any significant effect.

Table 2. Crude and adjusted analysis of clinical variables affecting mortality and morbidity among coronary artery bypass graft (CABG) and CABG + coronary endarterectomy (CE) patients using the Cox proportional hazard model

Variable		HR (95% CI)	P
CK-MB	Crude mode	0.86 (0.69-0.99)	0.045
	Adjusted	0.83 (0.69-1.00)	0.054
Troponin	Crude mode	1.03 (0.67-1.40)	0.850
	Adjusted	0.96 (0.70-1.48)	0.850

Data were adjusted for age, sex, diabetes, hypertension (HTN), hyperlipidemia, smoking, family history, body mass index (BMI), left main disease (LMD), and ejection fraction (EF).
HR: Hazard ratio; CI: Confidence interval; CK-MB: Creatine kinase-myocardial band

Discussion

The current study evaluated association of cardiac enzymes with morbidity and mortality of patients undergoing CE surgery. We found that there was not a significant association between troponin and CK-MB with mortality of patients undergoing OPCABG and CE; however, CK-MB had a protective effect in crude model.

Previous study reported that increase in cardiac enzyme release was associated with higher mortality,[20] but our study demonstrated that there was an independent association between cardiac enzyme release and death.

It has been reported in previous study that CK-MB is a sensitive enzyme after surgery for predicting complication. Ramsay et al. reported that increased postoperative peak CK-MB level was a stronger predictor of adverse outcomes.[11] Klatte et al.[12] and Costa et al.[21] found that CK-MB release 5 times or more was associated with an increased risk of mortality at 6 months and one year, respectively. The work by Brener et al. implied that only patients with large cardiac enzyme release (> 10 times) had an association with increased mortality.[22] Abid et al.[3] found that increased cardiac enzyme release increased mortality post-CABG.

Newall et al. reported that release of cardiac enzymes following CABG was related to one-year all-cause mortality.[20] Domanski et al. reported that increase of CK-MB or troponin levels had an independent relationship with increasing risk of mortality.[16] In our study, there was no significant difference between the groups in changes of cardiac enzyme levels and mortality.

To the best of our knowledge, this is the first study to show that there is not a relationship between cardiac enzyme and survival in CE patients. The strength of our study was that all the surgeries were performed with off-pump technique. This technique has good postoperative outcomes, so that myocyte damage is little and the cardiac enzyme release is low.[23] The limitations of the current study were retrospective design and lack of assessment of other biomarkers such as LDH for evaluation of the degree of postoperative myocardial injury after surgery. A single measurement of CK-MB after surgery added independent prognostic information to established clinical risk factors. Further studies are needed to determine whether patients with high postoperative CK-MB release may benefit from specific medical management.

Conclusion

The results of the current study showed that there was no association between CK-MB and troponin and mortality in patients undergoing CABG. It seems that these biomarkers are not valuable criteria for prediction of death.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contribution

AH, FS, AA, and SE contributed to the development of the original idea and the protocol, abstracted and analyzed the data, and prepared the manuscript.

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