Cellular and Molecular Biology

Journal homepage: www.cellmolbiol.org

Evaluating the occurrence of increased postoperative cardiac enzymes in patients with coronary atherosclerotic obstruction

Wanyi Zhang, Feng Jin, Heng Zhou*#, Wenzhi Wang*#

Department of Cardiology, Xiangyang NO.1 people's Hospital, Hubei University of Medicine, Xiangyang, Hubei441000, China

ARTICLE INFO

Original paper

Article history:
Received: October 27, 2021
Accepted: December 16, 2021
Published: January 30, 2022

Keywords:
Percutaneous Coronary Intervention; Stenting; Cardiac Enzymes

ABSTRACT

Percutaneous transluminal coronary angioplasty (PTCA) has been accepted as the elective treatment in many patients with coronary atherosclerotic obstruction. A slight increase in cardiac markers after the percutaneous coronary intervention (PCI) has been commonly reported. Some researchers have suggested that it predicts mortality and long-term complications. This study aimed to evaluate the occurrence of increased postoperative cardiac enzymes and determine the relationship between such an increase and clinical angiographic and technical variables. For this purpose, the descriptive study was performed in Hospital's cardiac ward from 2020-to 2021. One hundred twenty-two patients with stable coronary artery disease were studied for elective PTCA implanted with successful and uncomplicated stenting. Blood samples were taken from all patients to measure cardiac markers 20 hours after surgery. The normal range was CTnI ≤ 2ng/ml and CKMB ≤ 24 IU/L. Plasma levels of myocardial infarction and their relationship with clinical variables (including age, sex, risk factors for coronary artery disease, the severity of symptoms based on ccs class and previous history of acute coronary syndromes), angiographic including (lesion type, severity of stenosis) or related to the operation (operation on one or two vessels and direct stenting versus PTCA + stenting) were recorded in a questionnaire and observation sheets. The collected data were processed using descriptive statistics, frequency distribution tables, Chi-square, and student t-tests. Abnormal values of myocardial infarction were observed in 46.72% (57 patients). An increase in CTnI was observed in 39 patients (31.96%) and an increase in CKMB was seen in 31 patients (25.40%). Although the rise in CTnI exceeded the CKMB, the difference between the two was not statistically significant. The increased CTnI was significantly higher in older people, and the increase in CKMB was significantly higher in hypertensive individuals ($p = 0.01$). Based on the findings of this study, there is an increase in enzymes after successful and uncomplicated PCI selection. Increased CTnI occurs more frequently than CKMB. There is no relationship between enzyme enhancement and other clinical, angiographic, and technical variables.

DOI: http://dx.doi.org/10.14715/cmb/2022.68.1.16

Introduction

Percutaneous Coronary Intervention (PCI) as a standard procedure indicates excellent progress in treating patients with ischemic heart disease (1). Advances in technology (stents, atherectomies, and thrombectomy instruments), lateral pharmacological improvements before, during, and after surgery (Glycoprotein IIb/IIIa inhibitors), and a better understanding of early and long-term outcomes have led to widespread use of PCI for definitive treatment of the coronary arteries disease (2-4). Coronary stenting has fundamentally revolutionized interventional radiology by reducing early complications and improving long-term clinical outcomes (5, 6).

However, one of the most complex issues is myocardial infarction during or after surgery, which may be clinically apparent or asymptomatic, depending on the exact criteria of the electrocardiogram or cardiac markers (typically CKMB) (7). The latter constitutes a high percentage of cases with the increased enzyme (8). A recent analysis of studies in large groups of patients has shown that enzyme release is more common than previously thought and is also associated with prognosis (9-11). According to findings in essential databases, patients with increased cardiac markers had higher complications and cardiac mortality, independent of other predictors of mortality (12).

This study aimed to evaluate the increase in specific heart markers after successful coronary angioplasty and investigate its relationship with clinical, angiographic, and technical variables.

Materials and methods

This descriptive study was performed on selected

*Corresponding author. E-mail: 349306536@qq.com

patients with coronary angioplasty from 2020 to 2021 in the cardiovascular ward of the hospital. One hundred-twenty-two patients were studied with obstructive coronary artery disease with Cardiovascular Society (CCS) classification score ≥II angina selected for stent PCI. For all these PCI patients, direct stenting was performed based on standard techniques and in all cases with stent placement: PTCA + stenting. Sensitive CtnI and CK-MB markers were used to assess the mild myocardial injury. These markers were collected 20 hours after the operation and sent to the laboratory immediately. The CTnI was measured quantitatively by the ELISA method using specific monoclonal antibodies against TnI cardiac epitopes.

The normal range for CTnI was 2ng/ml and values greater than 2ng/ml were considered an ischemic injury. CKMB was measured enzymatically by the RA1000 autoanalyzer. The baseline values for 2Iu / L were CKMB. Preoperative enzyme levels were assumed to be normal in all patients. Acute myocardial infarction was defined based on the occurrence of pathological waves in two adjacent leads with an increase of 3% in the normal upper range of CKMB. All patients underwent electrocardiograms as usual before surgery, immediately after surgery, and the second day after surgery. Achieving more than 20% of the remaining stenosis was defined by 4Timi flow3 and the success of the angiographic procedure without major cardiac complications (death, myocardial infarction (CABG)).

Patients were studied who had an acute coronary event (unstable angina, Acute Myocardial Infarction, and Non ST elevation MI) during the two weeks before surgery and patients who were likely to have elevated preoperative enzymes. Also, Patients with postoperative major coronary events (nonfatal MI, CABG, and death) were admitted for the duration of hospitalization. Clinical characteristics of patients including age, gender, previous history of diabetes, hypertension, hyperlipidemia, smoking, family history, previous CABG or PCI, symptom severity (based on CCS Class), and history of unstable angina, NSTEMI AMI (based on history and the electrocardiogram) were collected through a questionnaire based on the objectives and hypotheses of the study, which were recorded at the time of admission for PCI.

Findings related to angiographic and operative variables were collected through operation reports and review of angiographic films or PCI. In this study, the obtained results were expressed using descriptive statistics and statistical tables and graphs. The Chi-square test was by student t-test and ANOVA for more than two groups. In this study, the minimum statistically significant level was considered $p < 0.05$.

Results and discussion

The total number of patients was 122, with a mean age of 53 ± 10 years (32 to 80 years old). The frequency distribution of clinical variables is listed in Table 1. There was a history of previous myocardial infarction in 42 patients (34.42%), a history of UA/NSTEMI in 27 patients (22.13%), and a previous history of both in eight patients (6.55%). Forty-five patients (36.9%) had no history of any of the above syndromes. Four patients (3.27%) had a history of the previous PCI, and three patients (2.45%) had a history of CABG.

Abnormal CTnI levels were found in 39 patients (31.96%) and CKMB in 31 patients (25.40%). The increase in CTnI was more significant than CKMB, but their relationship was not statistically significant. An increase in cardiac markers was found in 57 patients (46.72%). Regarding the severity of preoperative symptoms, 87 (71.31%) were in CCS Class II, and 35 (28.68%) were in III and IV.

One hundred seventy-nine lesions were observed in 122 operated patients. Out of 122 patients, 71 had stent and PTCA interventions, and 47 patients underwent direct stenting. PCI was performed in 81.14% of cases in one vessel and 18.86% in two vessels. The abnormal level of cardiac markers was not related to the number of vessels and the surgery technique (Table 1).

Patients who showed increased CKMB compared to normal after surgery had a higher mean age than those with normal enzyme levels, which was statistically significant for TnI ($p = 0.01$). In hypertensive patients, CKMB was higher than normotensive patients ($p = 0.01$). The relationship between abnormal CTnI and CKMB levels with other clinical variables was not statistically significant. The

frequency distribution of clinical variables and their relationship with the increase of enzymes are shown in Table 2. Of the 122 patients studied, 81 patients (66.39%) showed LAD (Left anterior descending), 27 patients (22.13%) had RCA (Right coronary artery), 26 (21.31%) had LCX (Left circumflex), four had diagonal, and 5 had OM (Obtius marginal). In 4 patients (3.27%), Bailout stenting was performed due to dissection or thrombosis.

Table 1. Frequency distribution of clinical variables, dependent angiography in patients

Clinical or Operation-Dependent Variable	Number	Percent
Male	79	64.75
Female	43	35.25
Diabetes	20	16.39
Hypertension	63	51.63
Hyperlipidemia	64	52.45
Smoking	37	30.32
Family history	24	19.67
STEMI	42	34.42
U/A/NSTEMI	27	22.13
CCS CLASS II	87	71.31
CCS CLASS III and IV	28	22.95
Nonspecific changes of EKG	17	13.93
Lesion type A and B1	38	31.15
Lesion type B2 and C	84	68.85
PTCA + Stenting	71	58.19
Direct stenting	47	38.52
Lesion severity up to 90%	47	38.52
Lesion severity between 90% - 100%	75	61.48
PCI in one vessel	99	81.14
PCI in more than one vessel	23	18.86

Complete obstruction was present in 13 (10.65%) patients. The type of “A” and “B1” lesion was in 38 patients (31.15%) and “B2” and “C” in 84 patients (68.85%). In 47 patients (38.52%), stenosis was less than 90%, and in 75 patients (61.48%), stenosis was 90-100%. Complex lesions and severe stenosis did not show significant enzymatic differences with more uncomplicated and less severe lesions. Seventeen patients (13.93%) had ECG changes as nonspecific ST.T changes out of the total population. In other cases, postoperative EKG did not change compared to preoperative. The difference between the increases in cardiac markers in the two groups was not significant (Tables 2).

Increased specific cardiac markers (CKMB and CtnI) are common after selective and successful PCI (13). Recent studies have shown increased cardiac markers following uncomplicated PCI with increased mortality and medium- and long-term complications (14, 15). These findings represent a standard mental error in which an excellent angiographic result is considered the best clinical outcome. Pathophysiological factors associated with myocardial injury following coronary angioplasty include transient cessation or reduction of blood flow, distal thromboembolism, lateral branch occlusion, and distal spasms due to the release of vasoactive substances and hypotension and ischemia (16).

Mild myocardial injury after successful PCI without selective complication with or without stenting is common. According to Mongiardo et al. (17), the increase in TnI after successful PCI was 40 to 45%, and in the Leonardi study (18), the increase in CKMB was 49 to 60%. In the present study, this increase was 32% and 26.3%, respectively. Drzewiecka-Gerber et al. (19) reported cardiac troponins, particularly TnI, more sensitive than CKMB for assessing the myocardial injury. In the present study, the incidence of CtnI increase was insignificantly higher than CKMB ($p = 0.01$). In Čulić's study (20), the history of MI, female sex, old age was associated with more enzymes. This study showed a negligible increase in men and a significant increase in CtnI over 57 years old ($p = 0.01$).

In limited studies, the relationship between risk factors for coronary artery disease and increased cardiac enzymes has been investigated, and no clear and proven relationship has been found (21, 22). In this study, only a history of hypertension was significantly associated with increased CKMB ($p = 0.01$).

Studies by Kini et al. (23), Gregson et al. (24), and Ben-Yehuda et al. (25) indicated that factors, such as coronary embolism during surgery, recent MI history, and minor complications like sudden transient occlusion, hypotension, saphenous vein grafts, complex lesions, extensive dissection, and preoperatively severe obstruction were associated with an increase in total CK.

The associated morphological features included thrombotic and complex lesions, saphenous vein graft lesions, and DCA. In other studies, diffuse disease, ulceration, asymmetric lesion, atherosclerotic plaque load, complex lesions, and application to multiple coronary arteries were associated with postoperative enzyme release (26-28). In some of these studies, atherosclerotic plaque loads in both lesion and basal segments and diffuse atherosclerosis were associated

with an increase in CKMB postoperatively (29-31). These findings suggest that elevated postoperative CKMB may be a marker of diffuse atherosclerosis and thus justify the adverse prognosis seen in some studies. No significant relationship was observed between lesion morphology and enzyme increase in the present study. Also, the severity of stenosis with PTCA and multi-vessel PCI did not correlate with the rise in cardiac enzymes.

Direct stenting may significantly reduce the incidence of ischemic complications associated with surgery by reducing trauma to the vessel wall and immediate dissection repair and avoiding complications associated with balloon surgery-related myocardial necrosis. In a study by Atmaca et al. (32), the use of direct stent technique compared to indirect stent has been associated with a reduction in ischemic complications during surgery and a lower increase in cardiac enzymes. A similar study by Timurkaynak et al. (33) found no significant difference between the two groups.

In this study, the increase in enzyme was higher in people who underwent stent + PTCA, although the difference between the groups was not statistically significant.

Table 2. Relationship between Tnl and CKMB with clinical variables in patients

Variable	Tnl+	Tnl-	PV	CKMB+	CKMB-	PV
Age	57 ± 11	52 ± 10	0.01	57 ± 11	53 ± 11	0.046
Male	41 (33.60%)	38 (31.14%)	0.88	34 (27.86%)	45 (36.88%)	0.092
Female	23 (18.85%)	20 (16.39%)	0.88	22 (18.03%)	21 (17.21%)	0.092
Diabetes	13 (10.65%)	22 (18.03%)	0.24	16 (13.11%)	21 (17.21%)	0.57
Hypertension	58 (47.54%)	64 (52.45%)	0.74	43 (35.24%)	79 (64.76%)	0.01
Hyperlipidemia	59 (48.36%)	63 (51.64%)	0.11	32 (26.22%)	90 (73.78%)	0.076
Smoking	25 (20.49%)	42 (34.42%)	0.11	29 (23.77%)	93 (76.23%)	0.083
CCS Class II	41 (33.60%)	81 (66.40%)	0.092	26 (21.31%)	96 (78.68%)	0.38
CCS Class III & IV	35 (28.68%)	87 (71.31%)	0.091	36 (29.50%)	86 (70.49%)	0.36
Lesion type A and B1	21 (17.21%)	17 (13.93%)	0.89	20 (16.39%)	18 (14.75%)	0.92
Lesion type B2 and C	40 (32.78%)	44 (36.06%)	0.89	41 (33.60%)	43 (35.24%)	0.92
Stenosis up to 90%	20 (16.39%)	27 (22.13%)	0.87	25 (20.49%)	22 (18.03%)	0.91
Stenosis between 90% - 100%	38 (31.14%)	37 (30.32%)	0.93	40 (32.78%)	35 (28.68%)	0.88
Single vessel-PCI	59 (48.36%)	40 (32.78%)	0.78	31 (25.40%)	68 (55.73%)	0.12
Multiple vessel-PCI	10 (8.19%)	13 (10.65%)	0.33	12 (9.83%)	11 (9.01%)	0.65
Direct Stenting	16 (13.11%)	31 (25.40%)	0.78	14 (11.47%)	33 (27.04%)	0.74
PTCA + stenting	23 (18.85%)	48 (39.34%)	0.62	20 (16.39%)	51 (41.80%)	0.63

Conclusion

This study showed that an increase in specific cardiac markers (CKMB and CTnI) after selective and seemingly successful PCI is common in patients with stable angina. In this study, a more common but insignificant increase in CTnI was observed than CKMB, indicating a higher sensitivity to CTnI. Old age is associated with abnormal TnI levels and hypertension is associated with abnormal postoperative CKMB levels. Other clinical, angiographic and technical variables were not statistically associated with abnormal postoperative enzyme levels.

Acknowledgments

None.

Conflict interest

The authors declare no conflict of interest.

References

1. Ozaki Y, Hara H, Onuma Y et al. CVIT expert consensus document on primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) update 2022. Cardiovasc Interv Ther 2022: 1-34.
2. Spadaccio C, Benedetto U. Coronary artery bypass grafting (CABG) vs. percutaneous coronary intervention (PCI) in the treatment of multivessel coronary disease: quo vadis?—a review of the evidences on coronary artery disease. Ann Cardiothorac Surg 2018; 7(4): 506.
3. Vranckx P, Lewalter T, Valgimigli M et al. Evaluation of the safety and efficacy of an edoxaban-based antithrombotic regimen in patients with atrial fibrillation following successful percutaneous coronary intervention (PCI) with stent placement: rationale and design of the ENTRUST-AF PCI trial. Am Heart J 2018; 196: 105-112.

4. Guo X, Yin B, Wang C, Huo H, Aziziaram Z. Risk assessment of gastric cancer in the presence of Helicobacter pylori cagA and hopQII genes. Cell Mol Biol 2021; 67(4): 299-305.
5. Costa F, Van Klaveren D, Feres F et al. Dual antiplatelet therapy duration based on ischemic and bleeding risks after coronary stenting. J Am Coll Cardiol 2019; 73(7): 741-754.
6. Lopes RD, Leonardi S, Wojdyla DM et al. Stent thrombosis in patients with atrial fibrillation undergoing coronary stenting in the AUGUSTUS trial. Circulation 2020; 141(9): 781-783.
7. Wungu CDK, Khaerunnisa S, Putri EAC et al. Meta-analysis of cardiac markers for predictive factors on severity and mortality of COVID-19. Int J Infect Dis 2021; 105: 551-559.
8. Rashid S, Malik A, Khurshid R, Faryal U, Qazi S. The diagnostic value of biochemical cardiac markers in acute myocardial infarction. Myocard Infract 2019; 23.
9. Jaffe AS, Lindahl B, Giannitsis E et al. ESC Study Group on Cardiac Biomarkers of the Association for Acute CardioVascular Care: A fond farewell at the retirement of CKMB. Vol 42: Oxford University Press; 2021: 2260-2264.
10. Eyyupkoca F, Karabekir E, Kiziltunc E et al. The evaluation of cTnT/CK-MB ratio is as a predictor of change in cardiac function after myocardial infarction. Heart Vessl 2021; 5(3): 113-122.
11. Aziziaram Z. C3953T genetic variation in interleukin 1β and idiopathic male infertility: a systematic review and meta-analysis. Cent Asian J Med Pharm Sci Innov 2021; 1(6): 242-249.
12. Harahap U, Margata L. The Significance of Troponin and Ck-Mb in Association with Q-Wave Myocardial Infarction. Indones J Pharm Clin Res 2018; 1(1): 11-17.
13. Hong L, Wang K, Yan W et al. High performance immunochromatographic assay for simultaneous quantitative detection of multiplex cardiac markers based on magnetic nanobeads. Theranostics 2018; 8(22): 6121.
14. Orman A, Altun MM, Benli S et al. Can Cardiac Biomarkers (Troponin-I and CK-MB) Indicate Disease Severity and Predict Mortality in Septic Newborns? 2021.
15. Monaco M, Stassano P, Di Tommaso L et al. Systematic strategy of prophylactic coronary angiography improves long-term outcome after major vascular surgery in medium-to high-risk patients: a prospective, randomized study. J Am Coll Cardiol 2009; 54(11): 989-996.
16. Valderhaug TG, Hjelmesæth J, Hartmann A et al. The association of early post-transplant glucose levels with long-term mortality. Diabetologia 2011; 54(6): 1341-1349.
17. Mongiardo A, Ferraro A, Ceravolo R et al. Mechanism of troponin and CK-MB release after percutaneous coronary interventions. J Ital Fed Cardiol 2002; 3(3): 270-274.
18. Leonardi S, Thomas L, Neely ML et al. Comparison of the prognosis of spontaneous and percutaneous coronary intervention–related myocardial infarction. J Am Coll Cardiol 2012; 60(22): 2296-2304.
19. Drzewiecka-Gerber A, Drzewiecki J, Wita K et al. Prognostic value of troponin I after elective percutaneous coronary interventions. Polish Heart J 2004; 61(8): 122-125.
20. Čulić V, Eterović D, Mirić D, Silić N. Symptom presentation of acute myocardial infarction: influence of sex, age, and risk factors. Am Heart J 2002; 144(6): 1012-1017.
21. Goktekin O, Melek M, Gorenek B et al. Cardiac troponin T and cardiac enzymes after external transthoracic cardioversion of ventricular arrhythmias in patients with coronary artery disease. Chest 2002; 122(6): 2050-2054.
22. Ramchand J, Patel SK, Srivastava PM, Farouque O, Burrell LM. Elevated plasma angiotensin converting enzyme 2 activity is an independent predictor of major adverse cardiac events in patients with obstructive coronary artery disease. PLoS One 2018; 13(6): e0198144.
23. Kini A, Marmur JD, Kini S et al. Creatine kinase-MB elevation after coronary intervention correlates with diffuse atherosclerosis, and low-to-medium level elevation has a benign clinical course: implications for early discharge after coronary intervention. J Am Coll Cardiol 1999; 34(3): 663-671.
24. Gregson J, Stone GW, Ben-Yehuda O et al. Implications of alternative definitions of peri-procedural myocardial infarction after coronary revascularization. J Am Coll Cardiol 2020; 76(14): 1609-1621.
25. Ben-Yehuda O, Chen S, Redfors B et al. Impact of large periprocedural myocardial

infarction on mortality after percutaneous coronary intervention and coronary artery bypass grafting for left main disease: an analysis from the EXCEL trial. Euro Heart J 2019; 40(24): 1930-1941.

26. Fleg JL, Stone GW, Fayad ZA et al. Detection of high-risk atherosclerotic plaque: report of the NHLBI Working Group on current status and future directions. JACC Cardiovasc Imaging 2012; 5(9): 941-955.
27. Yamagishi M, Terashima M, Awano K et al. Morphology of vulnerable coronary plaque: insights from follow-up of patients examined by intravascular ultrasound before an acute coronary syndrome. J Am Coll Cardiol 2000; 35(1): 106-111.
28. Shi X, Gao J, Lv Q et al. Calcification in atherosclerotic plaque vulnerability: friend or foe? Front Physiol 2020: 56.
29. Lanza GM, Winter PM, Caruthers SD et al. Nanomedicine opportunities for cardiovascular disease with perfluorocarbon nanoparticles. J Invasive Cardiol 2006; 15(1):33-47.
30. Willerson JT, Armstrong PW. Coronary heart disease syndromes: Pathophysiology and clinical recognition. *Coronary artery disease*: Springer; 2015: 365-407.
31. Leiner T, Bogaert J, Friedrich MG et al. SCMR Position Paper (2020) on clinical indications for cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2020; 22(1): 1-37.
32. Atmaca Y, Ertas F, Gülec S, Dincer I, Oral D. Effect of direct stent implantation on minor myocardial injury. J Invasive Cardiol 2002; 14(8): 443-446.
33. Timurkaynak T, Ozdemir M, Cengel A et al. Myocardial injury after apparently successful coronary stenting with or without balloon dilation: direct versus conventional stenting. J Invasive Cardiol 2002; 14(4): 167-170.