Case Report

Evaluation of Cardiac Biomarkers after Percutaneous Balloon Mitral Commissurotomy

Hamid Reza Sanati[1], MD; Mohammad Javad Alemzadeh-Ansari[1], MD; Ali Zahedmehr[1]*, MD; Ali Azarshab[1], MD; Ata Firouzi[1], MD; Farshad Shakerian[1], MD; Reza Kiani[1], MD

ABSTRACT

Background: Rheumatic heart disease is the major cause of cardiovascular death in children and young adults in developing countries.

Objectives: In the present study, we investigated the changes in cardiac biomarker levels before and after percutaneous balloon mitral commissurotomy (PMC).

Methods: Patients with severe mitral stenosis undergoing elective PMC were prospectively enrolled. The blood sample was taken for the measurement of cardiac biomarkers (CKMB and CTnI) before and then 6 hours and 12 hours after PMC. The maximum level of the biomarkers after the procedure was determined for analysis.

Results: Of a total of 56 patients (mean age =44.0±14.1 y), 91.1% were female. Except for 1 patient, all the other patients had cardiac biomarkers before the procedure in normal ranges. The serum levels of CTnI and CKMB increased significantly after the procedure. The patients who underwent complex septostomy had a significantly higher rise in CKMB (9.4±9.34 IU/L vs. 3.17±12.39 IU/L; P=0.03) and CTnI (0.15±0.20 µg/L vs. 0.07±0.12 µg/L; P=0.002).

Conclusions: The serum levels of CTnI and CKMB increased significantly following the procedure, especially in patients who underwent complex septostomy. ***(Iranian Heart Journal 2016; 17(1): 64-70)***

Keywords: ■Creatine kinase MB ■Troponin I ■Percutaneous balloon mitral commissurotomy

[1] Department of Cardiovascular Intervention, Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, I.R. Iran

***Corresponding Author:** Ali Zahedmehr, MD
Email: arashzahedmehr@yahoo.com **Tel:** 02123922108

Received: November 30, 2015 **Accepted:** May 1, 2016

Rheumatic heart disease is a chronic manifestation of rheumatic carditis, which is a major burden in developing countries. It causes about 250,000 premature deaths every year worldwide and is the major cause of cardiovascular deaths in children and young adults in developing countries.[(1)] Percutaneous balloon mitral commissurotomy (PMC) has established itself as the procedure of choice for suitable patients suffering from

severe symptomatic rheumatic mitral stenosis (MS) with excellent immediate and long outcomes.[2-5] A recent long follow-up study showed that more than one-third of patients treated with successful PMC still exhibit a good clinical status after 20 years.[6]

Although PMC is a relatively safe procedure, it has some adverse procedural complications which can lead to mortality in rare cases. Most of the adverse complications relevant to PMC occur during the process of interatrial septum puncture, manipulation of the Inoue balloon catheter in the left atrium, and commissurotomy of the mitral valve with the Inoue balloon catheter. During the Brockenbrough puncture, the Brockenbrough needle could penetrate the adjacent structures and enter the ascending aorta or the postatrium pericardial space. Also, the Inoue catheter or guide wires, while being manipulated in the cardiac chambers, might perforate the vulnerable structures such as the left atrial appendage, pulmonary veins, or left ventricular apex.[3]

Myocardial damage by any mechanism could influence the cardiovascular outcomes. An increase in the level of cardiac biomarkers is associated with increased motility, even in the general population.[7,8] The association between an increase in cardiac biomarkers and mitral valve surgery has been established in previous studies.[9-12] Our literature review failed to yield any research on myocardial damage after PMC. We, therefore, conducted this observational study for the first time to evaluate cardiac biomarker levels before and after PMC.

METHODS

From July 2010 to September 2011, all consecutive patients with severe MS undergoing elective PMC were prospectively enrolled. Demographic data—including age, gender, and risk factors were collected and recorded. Transesophageal echocardiography was done for all the patients before PMC. After light sedation, PMC was performed via the femoral approach with a 9-F sheath in the vein and a 6-F sheath in the artery. Right heart catheterization was performed. Additionally, right atriography was done, and mitral commissurotomy was performed using a Brockenbrough needle through the transseptal approach. If it succeeded in reaching into the left atrium at the first attempt or easily passing through the fossa ovalis, it was defined as a simple septostomy procedure; however, if more than 1 attempt was needed to reach into the left atrium, it was defined as a complex septostomy procedure. Successful PMC was defined as achieving mitral valve area (MVA) >1.5 cm^2 or 1cm^2/m^2 without significant complications. The blood sample was taken for the measurement of cardiac biomarkers (CKMB and CTnI) before and then 6 and 12 hours after PMC. The upper limit of cardiac biomarkers was determined as 24 IU/L for CKMB and 0.01 µg/L for CTnI. The maximum level of the biomarkers after the procedure was determined for analysis.

Prior to study enrollment, all the participants were approached and written informed consent was obtained. The study protocol and related materials were approved by the local research ethics committee.

Statistical Analysis

The continuous variables are expressed as means ± SDs. Also, the continuous variables were compared using the Student *t*-test or the Mann–Whitney U-test, as appropriate. The discrete variables are expressed as frequencies and percentages and were compared using the chi-square test or the Fisher exact test, as required. All P values <0.05 were considered statistically significant. The statistical analyses were conducted using SPSS, version 13.1 (SPSS Inc., Chicago, IL).

RESULTS

During the study period, a total of 56 patients (mean age =44.0±14.1 y) with documented severe MS were entered in our study and

subjected to PMC. The majority of them were female (91.1%), and only 5 (8.9%) patients were male. Seven (13.7%) of the female patients were pregnant and necessary precautions were taken for fetal protection from radiation. The patients' cardiac biomarkers before the procedure were within normal ranges; the exception was 1 patient with a high level of CKMB (38 IU/L) and CTnI within the normal range (Table 1).

Table 1. Baseline characteristics of 56 patients undergoing percutaneous balloon mitral commissurotomy

Female (n, %)	51 (91.1%)
Pregnant (n, %)	7/51 (13.7%)
Age (y)	44.0 ± 14.1
Risk factors	
Hypertension (n, %)	5 (8.9%)
Diabetes mellitus (n, %)	5 (8.9%)
Cardiac biomarkers	
CTnI (IU/L)	0.001 ± 0.01
CKMB (µg/L)	13.56 ± 3.87

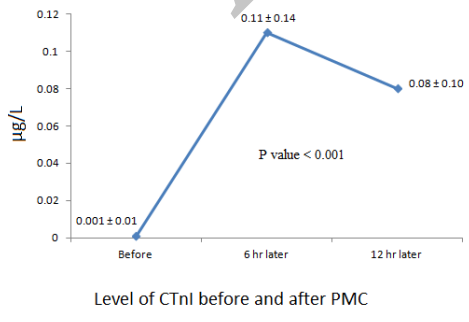
Mean MVA and also mean transmitral valve gradient before and after the procedure are illustrated in Table 2. Although coronary angiography was performed for 20 patients (35.7%) based on their history and noninvasive testing, this modality did not change the decision to perform PMC. Also, significant coronary artery disease was not found in any of the patients. Simple and complex septostomy was done for 34 and 22 patients, respectively. The PMC was performed successfully in the majority of the patients. Iatrogenic atrial septal defect occurred in 7 (12.5%) patients, 6 of whom had undergone complex septostomy. Tamponade occurred in 3 patients, who underwent conservative management without need for open surgery.

Table 2. Findings related to PMC

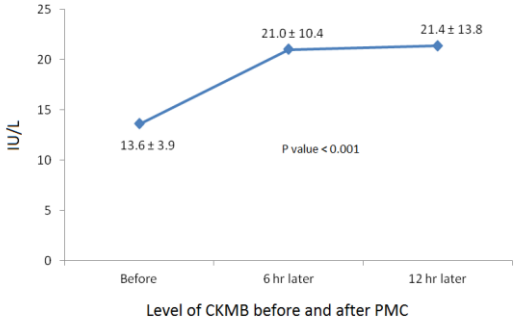
PMC score by echocardiography		8.6 ± 0.18
Balloon size (mm)		26 or 28
MVA (cm^2)	Before PMC	0.9 ± 0.16
	After PMC	1.7 ± 1.8
Mean gradients (mm Hg)	Before PMC	11.5 ± 4.8
	After PMC	1.7 ± 2.6
Septostomy	Simple	34 (60.7%)
	Complex	22 (39.3%)

PMC, Percutaneous balloon mitral commissurotomy; MVA, Mitral valve area

After the procedure, an increase in CKMB was observed in 16 (28.6%) patients, while an increase in CTnI was detected in 33 (58.9%). The maximum increase in the level of CKMB (70 IU/L) was seen in 1 patient with a high level of CKMB at baseline. The changes in the levels of the cardiac biomarkers after the procedure are depicted in Figure 1. The serum level of CKMB and CTnI rose significantly at 6 hours and 12 hours compared to the baseline value (P<0.001); however, no significant changes between the 2 samples after the procedure were seen in CKMB (P=0.76) and CTnI (P=0.09) levels. There was no significant association between mean rises in CKMB or CTnI and gender, presence of risk factors, balloon size, number of balloon inflations, and echocardiographic score of the valve (Table 3).



Level of CTnI before and after PMC



Level of CKMB before and after PMC

Figure 1. Serum levels of CTnI and CKMB increased significantly after the procedure.

Table 3. Relation between raise in CKMB and CTnI and different factors

		N	Mean Rise in CKMB (IU/L)	P value	Mean Rise in CTnI (µg/L)	P value
Gender	Female	51	5.54 ± 11.91	0.61	0.11 ± 0.15	0.70
	Male	5	6.40 ± 9.01		0.15 ± 0.15	
Risk factors	Yes	10	7.0 ± 8.0	0.68	0.10 ± 0.14	0.62
	No	46	5.32 ± 12.32		0.12 ± 0.15	
Balloon size	26 mm	25	5.04 ± 8.55	0.73	0.15 ± 0.16	0.14
	28 mm	31	6.09 ± 13.72		0.09 ± 0.13	
Number of balloon inflations	1	2	0	0.95	0.15 ± 0.02	0.70
	2	17	6.94 ± 8.92		0.14 ± 0.12	
	3	28	5.11 ± 14.09		0.12 ± 0.18	
	4	7	5.86 ± 10.01		0.04 ± 0.08	
	5	2	6.50 ± 9.19		0.09 ± 0.05	
Percutaneous balloon mitral commissurotomy score by echocardiography	7	6	11.67 ± 28.58	0.69	0.11 ± 0.01	0.76
	8	14	5.36 ± 9.03		0.09 ± 0.08	
	9	26	4.92 ± 7.23		0.15 ± 0.19	
	10	7	2.57 ± 6.80		0.08 ± 0.08	
	11	3	8.00 ± 13.85		0.13 ± 0.14	

Interestingly, the patients who underwent complex septostomy had a significantly higher rise in CKMB and CTnI (Fig. 2). Also, the patients with a significant rise in cardiac biomarkers were more in the complex septostomy group than in the simple septostomy group. A significant rise in CKMB was observed in 12 patients with complex septostomy and 4 patients with simple septostomy (54.5% vs. 11.8%; P<0.001). Also, a significant rise in CTnI was observed in 21 patients with complex septostomy and 12 patients with simple septostomy (95.5% vs. 35.3%; P<0.001). The serial ECG of the patients showed no evidence of myocardial ischemia, also none of them experienced ischemic pain manifestations.

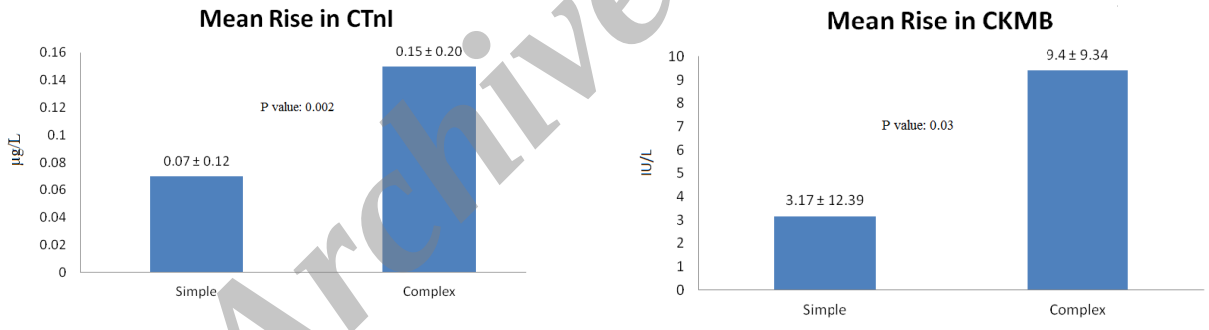


Figure 2. Mean rise in CTnI and CKMB was significantly higher in the patients undergoing complex septostomy.

DISCUSSION

The importance of increase in cardiac biomarkers in patients without coronary artery disease is an issue that always has been discussed. In this study, significant increase in cardiac biomarkers was observed in patients after PMC. This increase did not associate with coronary artery disease. About 36% of patients with suspected coronary artery involvement underwent coronary angiography before PMC. Significant coronary artery disease was not found in any of them. This finding suggested that the increase in cardiac biomarkers was secondary to direct myocardial damage during PMC.

According to the current guidelines, serum troponin has more sensitivity and specificity than CKMB.[13] Elevated cardiac troponin is used for the diagnosis and risk stratification of high-risk patients with acute coronary syndromes[14-16], as well as those undergoing cardiac and even noncardiac surgery.[12,17,18] However, the role of cardiac biomarkers after

PMC in the evaluation of myocardial damage and detection of high-risk patients remains less clear. In our study, increase in cardiac biomarkers significantly occurred in the patients with complex septostomy procedures, although these changes did not associate with other factors—including demographic, mitral valve morphology, and other procedural factors such as balloon size or number of balloon inflations. About 39% of the patients needed complex septostomy, and 54.5% of these patients had a rise in CKMB and 95.5% had a rise in CTnI. Regarding the type of septostomy, there were more patients with a rise in CTnI than were patients with a rise in CKMB. That is because CTnI is more sensitive than CKMB secondary to myocardial damage. Previous studies have documented that cardiac troponin is more sensitive and specific for myocardial damage,[14,17] which is concordant with our findings.

The association between cardiac biomarkers elevations, especially troponin, and mortality is known predominately within the first days of surgery—regardless of the surgical type. The association between all levels of troponin and postoperative mortality has been confirmed in previous studies.[18,19] Interestingly, preoperative troponin elevations are significantly associated with postoperative myocardial infarction and long-term mortality after surgery.[20-22] Accordingly, a failure to detect increased troponin with the current standard of care can lead to irreversible cardiovascular complications and even increase in mortality.[18] Nonetheless, larger studies are needed for the evaluation of the association between cardiac biomarkers elevations and the outcome of patients undergoing PMC.

Limitations

The impact of elevated cardiac biomarkers after PMC on early and late in-hospital complications needs to be evaluated by larger studies with long-term follow-up. Our relatively small sample size might have rendered our study underpowered for certain comparisons such as the association between elevated cardiac biomarkers and other factors such as balloon size or number of balloon inflations. Other cardiac biomarkers such as CTnT may be more sensitive for the detection of myocardial damage. Hence, more studies are needed to assess myocardial damage after PMC by newer cardiac biomarkers.

REFERENCES

1. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. The Lancet. 2012;379(9819):953-64.

2. Iung B, Garbarz E, Michaud P, Helou S, Farah B, Berdah P, et al. Late Results of Percutaneous Mitral Commissurotomy in a Series of 1024 Patients Analysis of Late Clinical Deterioration: Frequency, Anatomic Findings, and Predictive Factors. Circulation. 1999;99(25):3272-8.

3. Nobuyoshi M, Arita T, Shirai S-i, Hamasaki N, Yokoi H, Iwabuchi M, et al. Percutaneous balloon mitral valvuloplasty a review. Circulation. 2009;119(8):e211-e9.

4. Farhat MB, Ayari M, Maatouk F, Betbout F, Gamra H, Jarrar M, et al. Percutaneous balloon versus surgical closed and open mitral commissurotomy seven-year follow-up results of a randomized trial. Circulation. 1998;97(3):245-50.

5. Multicenter experience with balloon mitral commissurotomy. NHLBI Balloon Valvuloplasty Registry Report on immediate and 30-day follow-up results. The National Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry Participants. Circulation. 1992 Feb;85(2):448-61.

6. Tomai F, Gaspardone A, Versaci F, Ghini AS, Altamura L, De Luca L, et al. Twenty year follow-up after successful percutaneous balloon mitral valvuloplasty in a large contemporary series of patients with mitral stenosis. International journal of cardiology. 2014;177(3):881-5.

7. de Lemos JA, Drazner MH, Omland T, Ayers CR, Khera A, Rohatgi A, et al. Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. Jama. 2010;304(22):2503-12.

8. Saunders JT, Nambi V, de Lemos JA, Chambless LE, Virani SS, Boerwinkle E, et al. Cardiac troponin T measured by a highly sensitive assay predicts coronary heart disease, heart failure, and mortality in the Atherosclerosis Risk in Communities Study. Circulation. 2011;123(13):1367-76.

9. Nesher N, Alghamdi AA, Singh SK, Sever JY, Christakis GT, Goldman BS, et al. Troponin after cardiac surgery: a predictor or a phenomenon? The Annals of Thoracic Surgery. 2008;85(4):1348-54.

10. Croal BL, Hillis GS, Gibson PH, Fazal MT, El-Shafei H, Gibson G, et al. Relationship between postoperative cardiac troponin I levels and outcome of cardiac surgery. Circulation. 2006;114(14):1468-75.

11. Swaanenburg JC, Loef BG, Volmer M, Boonstra PW, Grandjean JG, Mariani MA, et al. Creatine kinase MB, troponin I, and troponin T release patterns after coronary artery bypass grafting with or without cardiopulmonary bypass and after aortic and mitral valve surgery. Clinical chemistry. 2001;47(3):584-7.

12. Januzzi JL, Lewandrowski K, MacGillivray TE, Newell JB, Kathiresan S, Servoss SJ, et al. A comparison of cardiac troponin T and creatine kinase-MB for patient evaluation after cardiac surgery. Journal of the American College of Cardiology. 2002;39(9):1518-23.

13. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, et al. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2014;64(24):e139-e228.

14. Sivaranjani N, Venkataraman D, Elango G, Rao SV. Evaluation of cardiac specific Troponin T as a specific and sensitive biomarker over Creatine Kinase-MB in Acute Myocardial Infarction patients-A correlation analysis study. International Journal of Biomedical Research. 2014;5(2):121-3.

15. Hicks KA. Circulating Cardiac Troponins as Specific Biomarkers of Myocardial Damage: Clinical Considerations. Pathophysiology and Pharmacotherapy of Cardiovascular Disease: Springer; 2015. p. 193-209.

16. Fathil M, Arshad MM, Gopinath SC, Hashim U, Adzhri R, Ayub R, et al. Diagnostics on acute myocardial infarction: Cardiac troponin biomarkers. Biosensors and Bioelectronics. 2015;70:209-20.

17. Søraas CL, Friis C, Engebretsen KVT, Sandvik L, Kjeldsen SE, Tønnessen T. Troponin T is a better predictor than creatine kinase-MB of long-term mortality after coronary artery bypass graft surgery. American heart journal. 2012;164(5):779-85.

18. Beattie WS, Karkouti K, Tait G, Steel A, Yip P, McCluskey S, et al. Use of clinically based troponin underestimates the cardiac injury in non-cardiac surgery: a single-centre cohort study in 51,701 consecutive patients. Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2012;59(11):1013-22.

19. Levy M, Heels-Ansdell D, Hiralal R, Bhandari M, Guyatt G, Yusuf S, et al. Prognostic value of troponin and creatine kinase muscle and brain isoenzyme measurement after noncardiac surgery: a systematic review and meta-analysis. Anesthesiology. 2011 Apr;114(4):796-806.

20. Thielmann M, Massoudy P, Neuhäuser M, Tsagakis K, Marggraf G, Kamler M, et al. Prognostic value of preoperative cardiac troponin I in patients undergoing emergency coronary artery bypass surgery with non–ST-elevation or ST-elevation acute coronary syndromes. Circulation. 2006;114(1 suppl):I-448-I-53.

21. Nagele P, Brown F, Gage BF, Gibson DW, Miller JP, Jaffe AS, et al. High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. American heart journal. 2013;166(2):325-32. e1.

22. Abukhudair W, Porqueddo M, Ahmed N, Hafed A, Ashmeg A, Yousef TB. Troponin level before coronary artery bypass graft surgery is associated with increased mortality rate. Journal of the Saudi Heart Association. 2013;25(2):169.