Journal of Current and Advance Medical Research
July 2021, Vol. 8, No. 2, pp. 85-89
http://www.banglajol.info/index.php/JCAMR ISSN
(Print) 2313-447X
ISSN (Online) 2413-323X
NLM Catalog ID 101673828
DOI: https://doi.org/ 10.3329/jcamr.v8i2.57430

ORIGINAL ARTICLE

Predictors of Post-Operative Acute Kidney Injury in relation with N-Terminal Pro-B-Type Natriuretic Peptide Level among Patients Undergoing Mitral Valve Replacement

Md. Tanvir Hossain[1], Asraful Hoque[2], Tasmin Rubayath[3], Romena Rahman[4], Abu Shadat Mohammad Saem Khan[5], Md. Noor-E-Elahi Mozumder[6], Md. Monzur Hossain[7], Imran Ahmed[8], Muhammad Asif Ahsan Chowdhury[9], Wahida Salam[10]

[1]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [2]Associate Professor, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [3]Medical Officer, Department of Clinical Pathology; Dhaka Medical College Hospital; Dhaka, Bangladesh; [4]Assistant Professor, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [5]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [6]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [7]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [8]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [9]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [10]Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

[**Received on:** 1 February 2021; **Accepted on:** 20 March 2021; **Published on:** 1 July 2021]

Abstract

Background: The N-terminal Pro-B-type natriuretic peptide (NT-proBNP) level can be utilized as post-operative prediction models suring cardiac surgery. **Objective:** The objective was to find out the predictors of post-operative acute kidney injury in relation with N-Terminal Pro-B-Type natriuretic peptide level among mitral valve replacement patients. **Methodology:** This cross-sectional study was conducted in the Department of Cardiac Surgery at National Institute of Cardiovascular Diseases, Dhaka, Bangladesh from January 2018 to December 2019. Patients with the age of more than or equal to 18 years with both sexes who were underwent mitral valve replacement were selected as study population. Patients were divided into two groups based on pre-operative NT-proBNP level. Post-operatively patients were observed on the basis of post-operative serum creatinine. **Results:** A total number of 100 patients were recruited for this study of which 50 cases were in group A and the rest of 50 cases were in the group B. Elevated NT-proBNP was the most powerful and independent pre-operative variable in predicting post-operative AKI development (OR 0.999, 95% CI 0.998-1.00) **Conclusion:** In conclusion elevated NT-proBNP is the most powerful and independent pre-operative variable in predicting post-operative acute kidney injury. [*Journal of Current and Advance Medical Research, July 2021;8(2):85-89*]

Keywords: acute kidney injury; N-terminal Pro-B-type natriuretic peptide; mitral valve replacement

Correspondence: Dr. Md. Tanvir Hossain, Assistant Register, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Sher E Bangla Nagar, Dhaka-1207, Bangladesh; **Email:** tanvir67678@gmail.com; **Cell no.:** +8801715122705
Cite this article as: Hossain MT, Hoque A, Rubayath T, Rahman R, Khan ASMS, Mozumder MNEE, Hossain MM, Ahmed I, Chowdhury MAA, Salam W. Predictors of Post-Operative Acute Kidney Injury in relation with N-Terminal Pro-B-Type Natriuretic Peptide Level among Patients Undergoing Mitral Valve Replacement. J Curr Adv Med Res 2021;8(2):85-89
Funding: This study has been performed without any funding from outside else.
Conflict of Interest: There was no conflict of interest to any of the authors.
Contributions to authors: All authors involved from protocol preparation up to manuscript writing & revision.

Introduction

Mitral valve is most commonly affected in rheumatic heart disease followed by aortic valve in a percentage of 56.7% and 6% respectively in Bangladesh[1]. Isolated mitral stenosis (MS) accounts for about 25% of all cases and an additional 40% have mixed mitral stenosis and regurgitation[2]. Other than rheumatic heart disease, mitral regurgitation (MR) also caused by ischemic heart disease, degeneration, chronic annular calcification and congenital causes such as a valve cleft. Mitral stenosis, as well as regurgitation in advanced condition requires surgical interventions. Following mitral valve replacement (MVR), post-operative morbidities like arrhythmia, heart failure, acute kidney injury are commonly seen. Postoperative heart failure (PHF) remains the major cause of mortality after MVR[3-4].

Natriuretic peptides (NP) are hormones, which are mainly secreted from the heart and have important natriuretic and kaliuretic properties. There are four different groups of NPs identified till date which are atrial natriuretic peptide (ANP), B type natriuretic peptide, C type natriuretic peptide, dendroaspis natriuretic peptide[5]. The amino-terminal pro–B-type natriuretic peptide (NT-proBNP) are predominantly synthesized and released constitutively from ventricular cardiac myocytes. The prime stimulus for synthesis and release of BNP is myocyte stretch secondary to transmural distending pressure. So measurement of brain natriuretic peptide (BNP) has become a potent diagnostic aid for identifying patients with systolic or diastolic dysfunction with valvular heart disease. For excretion, NT-proBNP is reliant on the kidney[6].

In patients with increased ventricular wall stress, NT-proBNP rises more than BNP. Despite being equally used for the diagnosis of heart failure, there are major differences including the plasma half-time, which is about 20 minutes for BNP and 25-70 minutes for NT-proBNP. Because of its longer half-life, a higher sensitivity to detect early stage of LV dysfunction has been proposed for NT-proBNP[7]. The purpose of the present study was to find out the predictors of post-operative acute kidney injury in relation with N-Terminal Pro-B-Type natriuretic peptide level among patients undergoing mitral valve replacement.

Methodology

This was a comparative cross-sectional study. The study was conducted in the Department of Cardiac Surgery at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from January 2018 to December 2019 for a period of two years. Patients with the age of more than or equal to 18 years with both sexes who were underwent mitral valve replacement after meeting the selection criteria and were admitted in the Department of Cardiac Surgery at NICVD, Dhaka, Bangladesh were selected as study population. Patients were divided into two groups on the basis of pre-operative NT-proBNP level. Patients who had NT-proBNP level less than or equal to 900 pg/mL were included in group A and patients who had more than or equal to 900 pg/ml NT-proBNP level were included in the group B. Patients with Mitral valve replacement perform with concomitant other valve surgery and procedures for congenital heart diseases, as well as coronary artery and great vessel surgery, previous history of opened or closed mitral commissurotomy, patients with severe left ventricular systolic dysfunction (LVEF $\leq$ 30%), patients with preoperative renal dysfunction (serum creatinine more than 1.4 mg/dl), severe respiratory dysfunction and BMI $\geq$ 30 kg/m^2 were excluded from this study. Purposive sampling method was applied for this study. A standardized semi-structured questionnaire was developed in English. The questionnaire was developed using the selected variables according to the specific objectives. The questionnaire contained questions related to socio-demographic characteristics, preoperative, peroperative and postoperative parameters. All relevant data were recorded in a data collection sheet. After selection of the patients, informed written consent from all patients was obtained for this study. NT-proBNP was measured on admission using Beckman coulter (automated immunology analyzer, Access 2) at NICVD and total study population was categorized into two groups according to cutoff value of NT-proBNP level. Sociodemographic and clinical history of each patient was taken and recorded by researcher. According to schedule, patients were taken to the operating room. Peripheral venous catheterization and central venous catheterization in the internal jugular vein and arterial line were done aseptically. Standard anesthetic techniques of induction and maintenance were followed for all procedures. All patients were operated through a median sternotomy approach. Cardiopulmonary bypass was established with appropriate aortic, superior & inferior vena caval cannulation. Heart was arrested in diastole by giving antegrade cardioplegia after applying aortic cross clamp. Then heart was opened by giving appropriate incision and appropriate prosthetic mitral valve used (mechanical/tissue). Per-operatively, cardiopulmonary bypass time and

cross clamp time was documented. After completion of surgery all patients were transferred to intensive care unit (ICU) intubated and ventilated. All patients received inotrope support and other medication as per hospital protocol. Patients were extubated as soon as they met the standard criteria. Post-operatively patients were observed on the basis of ICU stay, mechanical ventilation time, usage of inotrope, hospital stay. Post-operative serum creatinine was measured. All the patients were categorized according to NYHA functional class at the time of discharge. After meeting the discharge criteria, the patients were discharged from the hospital. Statistical analysis was conducted using Statistical Package for Social Science (SPSS) version 23.0 for windows software. Comparisons between groups were made with descriptive and inferential statistics. Observations were recorded as statistically significant if a p-value is ≤0.05. Ethical clearance for the study was taken from the concerned departmental academic and technical committee and also from the institutional review board.

Results

A total number of 100 patients were recruited for this study of which 50 cases were in group A and the rest of 50 cases were in the group B. Among the study population mean age in group A was 52.78± 7.192 years and in group B was 54.70± 6.929 years. Highest percentage of patients from both group A and group B belonged to 50 to 59 years which were 40% and 42% cases respectively. There was no significant differences between the two groups of patients regarding age (p=0.177) (Table 1).

Table 1: Comparison of age between two groups

Age Group	Group A	Group B
40 to 49 Years	18 (36.0%)	13 (26.0%)
50 to 59 Years	20 (40.0%)	21 (42.0%)
≥60 years	12 (24.0%)	16 (32.0%)
Total	**50(100.0%)**	**50(100.0%)**
Mean±SD	52.8±7.192	54.7±6.929

Statistical analysis was done by Student's t-test to compare between groups p value=0.177

Pre and post-operative renal status distribution: Among the study population, there were no significant differences between two groups of patients in distribution pre-operative renal status (serum creatine level) as p value >0.05 but there were highly significant differences in post-operative serum creatinine level distribution in both groups after 24 and 48 hours of operation (p value <0.001). AKI developed more in group B (28.0%) compared to group A (4.0%) with highly statistical significance (p value <0.001) (Table 2).

Table 2: Comparison of Pre and Post-Operative Renal Status between Two Groups

Renal status	Group A	Group B	P value
Pre-operative S. creatinine	1.1±0.07	1.3 ±0.04	0.186
Post-operative Serum creatinine After			
• 24 hours	1.2±0.08	1.5 ±0.25	0.001
• 48 hours	1.3±0.18	1.6 ±0.35	0.001
AKI developed	2(4.0%)	14(28.0%)	0.001

Chi-square test (χ^2) and Student's t-test were performed to compare both groups when appropriate;

Pearson co-efficient correlation test for preoperative predictor and postoperative outcomes: Pearson co-efficient correlation model shows highly significant moderately strong positive association of preoperative NT-proBNP with post-operative serum creatinine after 48 hours (r value 0.595) (Table 3).

Table 3: Correlation of Post-Operative Serum Creatinine with NT-proBNP

NT-proBNP vs	r value	P value
Post-operative serum creatinine (after 48 hours)	0.595*	<0.001

Pearson's correlation was done to measure the level of significance; **Correlation is significant at the 0.01 level

Analysis of predictors of AKI following mitral valve replacement: Multivariate logistic regression analysis to determine the independent predictors of developing post-operative AKI shows that elevated NT-proBNP (>900 pg/ml) was the most powerful and independent pre-operative variable in predicting post-operative AKI development (OR 0.999, 95% CI 0.998-1.00; p value 0.009) (Table 4).

Table 4: Logistic Regression Analysis of predictors of developing post-operative Acute Kidney Injury (AKI)

Predictors	OR (95.0% CI)	P value
NT-proBNP	0.99(0.99 to 1.00)	0.009
NYHA functional class	0.68(0.26 to 1.77)	0.428
LVEDDi	0.90(0.59 to 1.38)	0.633
LVEF	1.01(0.80 to 1.26)	0.958

Discussion

NT-proBNP is a key cardiovascular hormone mainly secreted from ventricular cardiac myocytes in response to increased transmural wall tension due to ventricular stress, hypertrophy or volume overload[8]. Its level is frequently increased in patients with an impaired left ventricular function and there is a body of information suggesting that the plasma NT-proBNP level is a sensitive predictor for the occurrence of future congestive heart failure events[9]. Little is known about the pre-operative level of NT-proBNP in patients with mitral valve disease undergoing cardiac surgery and its potential relationship with early post-operative outcome.

This study was done to evaluate the correlation between raised pre-operative NT-proBNP level and acute kidney injury as in-hospital surgical outcomes after mitral valve replacement. Total 100 patients who underwent mitral valve replacement following isolated mitral valve disease, irrespective of their race, ethnic group and age were included in this prospective observational study after careful history taking, examination and appropriate investigations fulfilling inclusion and exclusion criteria and categorized into two groups. In group A 50 patients who had NT pro-BNP ≤ 900 pg/ml and in group B 50 patients who had NT-proBNP > 900 pg/ml.

In comparison of two groups, among the study population there had no significant differences between group A and group B regarding age (p value >0.05). These demographic and anthropometric characteristics of this study are consistent with different prospective studies across the world[9-10] which also reports female predominance along with similar characteristics.

In terms of postoperative outcome, AKI developed more in group B (28%) compared to group A (4%) with highly statistical significance (p value <0.001). Several other investigators have focused on the predictive value of NT-proBNP on surgical outcome. Filsoufi et al[9] found significant relation of NT-proBNP level with post-operative outcome like ICU stay, length of hospital stay, ventilation duration and inotropic use. In a series of 200 patients, Palazuelos et al[11] reported a pre-operative higher NT-proBNP level used as a predictor for the post-operative complications and one-year mortality after valve surgery. They also demonstrated an association between the elevated post-operative peak level of NT-proBNP and prolonged hospital stay and mortality. Finally, Cuthbertson et al[12] measured the pre- and post-operative proBNP levels in 146 patients undergoing cardiac surgery including mitral valve surgery.

Multivariate logistic regression analysis showing pre-operative elevated NT-proBNP as independent risk factor for post-operative renal dysfunction (OR .999, 95% CI .998-1.000, p value 0.009). Perreas and colleagues[10] also found that preoperative elevated NT-proBNP level was associated with postoperative morbidity after mitral valve replacement in a multivariate analysis.

In a cohort study of Perreas et al[10], mortality rate was 5.3% cases. Maganti et al[4] found 4.89% cases in hospital mortality among study patients undergoing cardiac surgery due to post-operative heart failure, neurologic deficit, post-operative renal/lung failure and sepsis. But in this study, there was no post-operative MI, lung failure, sepsis, neurological deficit and no mortality. This lack of significance may be due to the small sample size.

Conclusion

In conclusion there are no significant differences between two groups of patients in distribution pre-operative renal status; however, there are highly significant differences in post-operative serum creatinine level distribution in both groups after 24 and 48 hours of operation. In addition to that moderately strong positive correlation of preoperative NT-proBNP with post-operative serum creatinine after 48 hours is found which is highly significant. Furthermore, the elevated NT-proBNP is the most powerful and independent pre-operative variable in predicting post-operative AKI development. Further large scale study should be conducted.

References

1. Islam AM, Majumder AA. Rheumatic fever and rheumatic heart disease in Bangladesh: a review. Indian heart journal. 2016;68(1):88-98
2. Walker BR, Colledge NR, Ralston SH, Penman ID. Davidson's principles & practice of Medicine, 22nd edition. Edinburgh, Scotland. Churchill Livingstone Elsevier, 2014;37-39
3. Nozohoor S, Nilsson J, Lührs C, Roijer A, Algotsson L, Sjögren J. B-type natriuretic peptide as a predictor of postoperative heart failure after aortic valve replacement. Journal of cardiothoracic and vascular anesthesia. 2009;23(2):161-5
4. Maganti M, Badiwala M, Sheikh A, Scully H, Feindel C, David TE, Rao V. Predictors of low cardiac output syndrome after isolated mitral valve surgery. The Journal of thoracic and cardiovascular surgery. 2010;140(4):790-6
5. Pandit K, Mukhopadhyay P, Ghosh S, Chowdhury S. Natriuretic peptides: Diagnostic and therapeutic use. Indian

journal of endocrinology and metabolism. 2011;15(Suppl4):S345-S353
6. Bergler-Klein J, Gyöngyösi M, Maurer G. The role of biomarkers in valvular heart disease: focus on natriuretic peptides. Canadian Journal of Cardiology. 2014;30(9):1027-34
7. Januzzi JL, van Kimmenade R, Lainchbury J, Bayes-Genis A, Ordonez-Llanos J, Santalo-Bel M, Pinto YM, Richards M. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. European heart journal. 2006;27(3):330-7
8. Richards AM. N-terminal B-type natriuretic peptide in heart failure. Heart failure clinics. 2018;14(1):27-39
9. Filsoufi F, Rahmanian PB, Salzberg S, Harbou KV, Bodian CA, Adams DH. B-Type Natriuretic Peptide (BNP) in Patients Undergoing Mitral Valve Surgery. Journal of cardiac surgery. 2008;23(6):600-5
10. Perreas K, Samanidis G, Dimitriou S, Athanasiou A, Balanika M, Smirli A, Antzaka C, Politis K, Khoury M, Michalis A. NT-proBNP in the mitral valve surgery. Critical pathways in cardiology. 2014;13(2):55-61
11. Palazuelos J, Alonso MÁ, Montón PC. Prognostic implications of baseline NT-proBNP before cardiac surgery. The Journal of thoracic and cardiovascular surgery. 2016;152(1):252-3
12. Cuthbertson BH, Croal BL, Rae D, Gibson PH, McNeilly JD, Jeffrey RR, Smith WC, Prescott GJ, Buchan KG, El-Shafei H, Gibson GA. N-terminal pro-B-type natriuretic peptide levels and early outcome after cardiac surgery: a prospective cohort study. British journal of anaesthesia. 2009;103(5):647-53