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Original Research Article

Association of pre-operative N-terminal pro–B-type natriuretic peptide level on early outcomes of off-pump coronary artery bypass grafting

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ABSTRACT

Background: Off-pump coronary artery bypass grafting (OPCABG) is considered safer than traditional on-pump coronary artery bypass grafting (CABG) due to its avoidance of a heart-lung machine. This study was aimed to evaluate role of pre-operative N-terminal pro–B-type natriuretic peptide (NT-pro-BNP) level in patients undergoing OPCABG.
Methods: A comparative cross-sectional study was carried out in the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD) from January 2022 to December 2023. Continuous data were analyzed by Student's t-test and categorical data by Chi-square and Fisher's exact test. A $p \leq 0.05$ was considered statistically significant.
Results: Our study shows that the incidence of arrhythmia was significantly higher in group A (NT-pro-BNP≥348 pg/ml) than group B (NT-pro-BNP<348 pg/ml). Post-operative arrhythmia occurred only in 9 (18%) patients in group B but in group A 19 (38%) patients developed arrhythmia ($p<0.001$). Incidence of postoperative low cardiac output syndrome (LCOS) was significantly higher in group A (NT-pro-BNP≥348 pg/ml). Group A patients experienced notably extended mechanical ventilation time (9.77±4.87 versus 6.39±2.13 hours; $p<0.001$), prolonged ICU stay (7.01±5.12 versus 4.87±2.98 days; $p=0.005$), and extended postoperative hospital stay (12.56±5.40 versus 7.08±4.15 days; $p<0.001$) compared to group B. No significant difference was observed between the two groups in regards to demographics and associated risk factors.
Conclusion: Our current study illustrated that elevated preoperative NT-pro-BNP levels (≥348) were linked to an increased occurrence of postoperative complications such as low cardiac output syndrome and arrhythmia.

Keywords: Pre-operative, NT- Pro-BNP, Early outcomes, CABG

INTRODUCTION

Coronary artery disease (CAD) is the most prevalent health issues and pose a significant burden of disease, contributing to approximately 32% of global fatalities.[1] Cardiovascular diseases (CVD) hold the foremost position as the primary cause of death globally. According to estimates in Bangladesh CAD being responsible for 30% of these deaths.[2] According to the World Health Organization (WHO), 17.7 million people died from CVDs in 2023, representing 31% of all global deaths, a number that is expected to grow.[3] Now a days, coronary artery bypass grafting (CABG) has become the preferred revascularization strategy for multivessel CAD.[4] The off-pump coronary bypass (OPCAB) was first developed in

the 1960s in which the anastomoses are performed on the beating heart and has recently seen a resurgence in popularity.[5] Off-pump coronary artery bypass grafting (OPCABG) allows for myocardial revascularization without the need for cardiopulmonary bypass (CPB).

OPCABG is associated with several risks for postoperative cardiac events. A variety of multifactorial risk indexes have been described to help delineate preoperative risk assessment of patients undergoing cardiac surgery. Natriuretic peptide hormones, a family of vasoactive peptides with many favorable physiological properties, have emerged as important candidates for development of diagnostic tools and therapeutic agents in cardiovascular disease.[6] N terminal B-type natriuretic peptide (NT-pro-BNP) is a member of this family that is synthesized by ventricular myocytes in response to ventricular dysfunction and wall-stress. It modulates plasma volume and myocardial stretch through its actions as a diuretic, a renin-angiotensin-aldosterone system (RAAS) antagonist, and as an inhibitor of sympathetic outflow and vasoconstrictor production.[7] Most of the multivariable risk indices for preoperative assessment use ejection fraction as a major factor in their calculations of risk, and studies have shown that low ejection fraction alone is one of the best independent predictors of postoperative morbidity and mortality.[8] Therefore, it seems logical that preoperative NT-pro-BNP could be capable of predicting postoperative outcomes because it has been shown to correlate with ejection fraction and ventricular dysfunction.

Cardiac biomarkers play a crucial role in identifying patients at higher risk.[9] Considering the longer half-life of NT-pro-BNP compared to B-type natriuretic peptide (BNP), NT-pro-BNP emerges as a reliable candidate for risk assessment and prognostication. Its extended duration of detection makes it a valuable biomarker in predicting outcomes and complications associated with cardiac surgery.[10] If the risks can be predicted prior to surgery, a lot of change in the patient management could be possible to bypass the predicted adverse outcomes. The measurement of NT-pro-BNP serum concentration has low cost, is easily performed and highly available, and has good reproducibility.[11] As the utilization of OPCABG gains prominence for its perceived advantages in reducing complications, understanding the relationship between pre-operative NT-Pro-BNP levels and early postoperative outcomes becomes pivotal. This research aims to contribute valuable insights into risk stratification and management strategies, providing a foundation for optimizing patient selection and enhancing the overall efficacy of OPCABG procedures.

METHODS

This comparative cross-sectional study was conducted between 01 January 2022 to 31 December 2023 at the Department of Cardiac surgery, National Institute of Cardiovascular Diseases (NICVD), Sher-E-Bangla Nagar, Dhaka, Bangladesh. The study was carried out on the patients who underwent cardiac isolated OPCABG at Department of Cardiac Surgery, NICVD after fulfilling the inclusion and exclusion criteria.

Inclusion criteria

All adult (18-65 years) patients undergoing isolated OPCABG surgery were included in the study.

Exclusion criteria

Patients of age >65 years and <18 years, preoperative conversion to OPCABG, combined procedures, patient with known CKD, patient undergoing emergency surgery, VEF<35%, redo cardiac surgery, and self-withdrawal of patient willfully/who did not give consent were excluded.

Patients were divided into two groups on the basis of preoperative NT-pro-BNP level. Cut off value for NT-pro-BNP was 348 pg/ml.

Group A

50 patients who met the inclusion criteria within the study period and who had preoperative NT-pro-BNP level ≥348 pg/ml.

Group B

50 patients who met the inclusion criteria within the study period and who had preoperative NT-pro-BNP level <348 pg/ml.

An ethical approval was taken from ethical committee of NICVD to conduct the study. Meticulous history and detailed clinical examination were performed and recorded in predesigned structured data sheet. Demographic data e.g., age, sex, height and weight were recorded. Sampling for NT-pro-BNP was done 24 hours before surgery and plasma levels were analyzed using electro-chemoiluminescence immunoassay on a Roche Elecsys 2022 automated platform (Roche Diagnostics, Basel, Switzerland). All patients were monitored up to their discharge from hospital for incidence of arrhythmia, postoperative myocardial infraction and low cardiac output syndrome. Clinical outcome in terms of mechanical ventilation time, ICU stay, Postoperative hospital stays and any mortality was also observed up to they were discharged from hospital.

Statistical analyses were performed using windows-based computer software devised with statistical packages for social sciences (SPSS-27) (SPSS Inc, Chicago, IL, USA). Descriptive and inferential statistical methods were applied to analyze data. In descriptive statistics, continuous data was summarized by mean±SD and categorical data was summarized into frequency distribution and percentage. To make comparison between groups and draw conclusions on data, several inferential statistics were used including Chi-square or Fisher's exact

test for qualitative data and unpaired t-test for quantitative data. All comparison were made here between preoperative NT-pro-BNP ≥348 pg/ml and <348 pg/ml group. To assess performance of preoperative NT-pro-BNP as a biomarker in early postoperative outcomes, receiver operating characteristic (ROC) curve was generated, area under the curve (AUC) was calculated, along with its 95% CI. For all analytic tests, the statistical significance threshold was set at 5% and a p≤0.05 was considered statistically significant.

RESULTS

Total 100 patients CAD who underwent OPCABG were enrolled in this study. Among them 50 patients (group A) with pre-operative NT-pro-BNP >348 pg/ml and other 50 patients (group-B) with pre-operative NT-pro-BNP <348 pg/ml. Majority patients were between 30-49 years of age which was 58% in group A and 66% in group B. The mean age was 49.82±8.44 in group A and 50.15±9.39 in group B. Male patients were predominant in both groups (group A-72% and group-B-78%). Out of 100 patients, 55 patients had hypertension (52% in group A versus 58% in group B), 43 patients had dyslipidemia (46% in group A versus 40% in group B), 30 patients had DM (26% in group A versus 34% in group B) and 43 patients were smokers (40% in group A versus 46% in group B). But these differences in findings were statistically not significant between the two groups (p>0.05) (Table 1).

Table 1: Demographic characteristics of the patients.

Variables	Group A (n=50) (%)	Group B (n=50) (%)	P value
Age (mean±SD)	49.82±8.44	50.15±9.39	0.349
Sex			
Male	36 (72)	39 (78)	0.488
Female	14 (28)	11 (22)	
Co-morbidities			
Smoking	20 (40)	23 (46)	0.175
DM	13 (26)	17 (34)	0.382
Hypertension	26 (52)	29 (58)	0.546
Dyslipidemia	23 (46)	20 (40)	0.544

Patients in group A had significantly higher NT-pro-BNP level in the preoperative period (448.35±233.98 versus 291.66±57.78, p<0.001). Most of the patients from both groups had triple vessel disease on coronary angiogram (Table 2). There was no statistically significant difference between the two groups regarding the duration of surgery (4.25±0.76 hours versus 4.33±0.68 p=0.312).

Patients in group A compared to group B had significantly longer mechanical ventilation time (6.11±3.84 versus 9.98±1.23 hours; p<0.001), longer length of ICU stay (4.01±2.12 versus 9.87±2.98 days; p<0.001) and postoperative hospital stay (7.56±2.4 versus 13.0±4.95 days; p<0.001). There was one in hospital mortality, which was from group B. There was three in hospital mortality, which was from group A (0.312). The difference was not statistically significant. Post-operative arrhythmia was more in group A (54% versus 18%) and statistically the difference was significant (p<0.001) (Table 3).

Table 2: Pre-operative variables of the study population.

Variables	Group A (n=50) (%)	Group B (n=50) (%)	P value
Preoperative serum NT-pro-BNP (pg/ml)	448.35± 233.98	291.66± 57.78	<0.001
Preoperative LVEF	51.28± 7.96	53.22±7.08	0.100
Number of diseased vessels			
1	1 (2)	2 (4)	
2	2 (4)	2 (4)	0.354
3	41 (82)	43 (86)	
≥4	6 (12)	3 (6)	

Table 3: Outcome comparison of outcome between two groups.

Variables	Group A (%)	Group B (%)	P value
Mean duration of surgery (hours)	4.25± 0.76	4.33± 0.68	0.312
Mean mechanical ventilation time (hours)	9.77± 4.87	6.39± 2.13	<0.001
Mean ICU stay (days)	7.01± 5.12	4.87± 2.98	0.005
Mean hospital stay (days)	12.56± 5.40	7.08± 4.15	<0.001
Postoperative arrhythmia (n)	27 (54)	9 (18)	<0.001
Postoperative myocardial infarction (n)	7 (14)	4 (8)	0.352
Postoperative low cardiac output syndrome (n)	19 (38)	8 (16)	0.023
In hospital mortality (n)	3 (6)	1 (2)	0.312

Receiver operative characteristic (ROC) curve analysis revealed an area under the curve (AUC) of 0.851, indicating preoperative NT-pro-BNP had an excellent diagnostic accuracy for predicting postoperative arrhythmia. At our preset cutoff value of 348, preoperative NT-pro-BNP could optimally predict post-OPCAB arrhythmia with 87.5% sensitivity, 90.9% specificity. Besides, NT-pro-BNP had an excellent diagnostic accuracy for predicting postoperative low cardiac output syndrome (LCOS) too. At our preset cutoff value of 348, preoperative NT-Pro-BNP could optimally predict post-

OPCAB LCOS with 93.8% sensitivity, 88.6% specificity (Table 4).

Table 4: Specificity and sensitivity of NT-pro BNP for diagnosing post-operative arrhythmia and LCOS at cut off point of 348 pg/ml.

Variables	AUC	95% CI	Sensitivity (%)	Specificity (%)	P value
Post-operative arrhythmia	0.851	0.721 - 0.981	87.5	90.9	<0.001 s
Post-operative LCOS	0.881	0.785 - 0.978	93.8	88.6	<0.001 s

s: Statistically significant

DISCUSSION

Over the course of two years, 100 individuals diagnosed with CAD underwent OPCABG surgery. Group A consisted of 50 patients with preoperative NT-pro-BNP ≥348 pg/ml, while group B comprised the remaining 50 patients with preoperative NT-pro-BNP <348 pg/ml. The mean age of the patients in group A (preoperative NT-pro-BNP ≥348 pg/ml) and group B (preoperative NT-pro-BNP <348 pg/ml) was 49.82±8.44 years and 50.15±9.39 years, respectively. However, in comparable studies, Fawzy et al reported mean ages of 49.22±11.4 years in high NT-pro-BNP group and 50.77±9.6 years in low preoperative NT-pro-BNP group.[12] Matsuura et al reported ages of 53.50± 6.33 in high NT-pro-BNP group and 55.62±5.92 years in low NT-pro-BNP group.[13] The variation could arise from the diverse composition of Bangladesh's population. Distribution of patients according to gender was also not significantly different between the two groups (p=0.488). More than half of the patients had history of smoking, diabetes mellitus, hypertension and dyslipidemia. The percentage of these comorbidities was also almost similar in between two groups which coincides with previous studies.[14,15]

Preoperative NT-pro-BNP was 448.35±233.98 pg/ml versus 291.66±57.78 pg/ml for group A and B respectively (p<0.05). Provenchere et al showed that preoperative mean NT-pro-BNP level was 362.78±97.98 pg/ml in their study population.[16] Incidence of postoperative low cardiac output syndrome (LCOS) was significantly higher in group A (NT-pro-BNP ≥348 pg/ml). Among 27 patients who developed postoperative LCOS, majority 19 (38%) belonged to group A. Only 8 (16%) patients who developed postoperative LCOS fell in group B (NT-pro-BNP<348 pg/ml) yielding a p=0.023. These results show similarities with the study conducted by Fellahi et al.[17] The incidence of arrhythmia was significantly higher in group A (NT-pro-BNP ≥348 pg/ml) than group B (NT-pro-BNP <348 pg/ml). Post-operative arrhythmia occurred only in 9 (18%) patients in group B but in group A 27 (54%) patients developed arrhythmia which was statistically significant (p<0.001).

Group A patients experienced notably extended mechanical ventilation time (9.77±4.87 versus 6.39±2.13 hours; p<0.001), prolonged ICU stay (7.01±5.12 versus 4.87±2.98 days; p=0.005), and an extended postoperative hospital stay (12.56±5.40 versus 7.08±4.15 days; p<0.001) compared to group B. Jogia et al reported low to modest correlations between preoperative NT-pro-BNP levels and prolong the need for postoperative mechanical ventilation, ICU stay and hospital stay.[18] On the other hand, Liu et al found no significant differences in ventilation time in patients with high versus low preoperative NT-pro-BNP levels which showed dissimilarity with our study.[19] Our study showed no significant differences between two groups regarding postoperative MI. This is similar to the reports by Eliasdottir et al.[20]

The ROC curve for preoperative NT-pro-BNP yielded an AUC of 0.851 (p<0.001) in predicting postoperative arrhythmia achieving a sensitivity of 87.5% and specificity of 90.9% at the set cutoff value of 348 pg/ml. Besides, AUC of the ROC curve for preoperative NT-pro-BNP was 0.881 (p<0.001), indicating preoperative NT-pro-BNP had an outstanding potential to be used as a predictor of post OPCAB LCOS having a sensitivity of 93.8% and 88.6% specificity at our preset cut off value of 348 pg/ml. Our results are comparable to those by Fawzy et al, Matsuura et al, and Holm et al.[12,13,21]

This study had some limitations. The sample size was small which was conducted in a single centre over a short period of time. Besides, sampling was not randomized. Further studies on larger and more diverse populations are warranted to compare predictive ability of preoperative NT-pro-BNP to current multivariable risk indexes and to evaluate potential for integration of this tool into preoperative evaluation.

CONCLUSION

Our current study illustrated that elevated preoperative NT-pro-BNP levels (≥348) were linked to an increased occurrence of postoperative complications such as low cardiac output syndrome and arrhythmia. In the future, physicians may be able to use these quantitative cut-off values in their decision to delay heart surgery in order to further “tune up” the patient.

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