Original Article

Association of Preoperative and Postoperative Brain Natriuretic Peptide Hormone with Morbidity in Adult Patients Undergoing Coronary Artery Bypass Graft Surgery

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Abstract

Background: Brain natriuretic peptide (BNP) is a cardiac hormone, which its levels as a marker of morbidity in patients undergoing coronary artery bypass grafting (CABG) is still controversial. This study aimed to investigate the relationship between the pre- and postoperative BNP changes and morbidity in adult patients undergoing CABG.

Methods and materials: In this descriptive-analytical study, 50 patients were enrolled underwent elective CABG at the heart center of Rajaei hospital, Tehran, Iran, from September 2016 to May 2017. To determine the serum levels of BNP, blood samples were sent to laboratory at 24 hours before and 24 hours after induction of anesthesia. Duration of intubation, intensive care unit (ICU) stay, and ejection fraction and serum creatinine were considered. Data were analyzed with SPSS Version 22 software and significance level was 5%.

Results: Of patients, 33 (66%) were male and 17 (34%) were female. The mean age ± SD of patients was 61±9 (range 36-82 years). Mean ± SD preoperative BNP level was 919.81±2264.22 pg/ml and postoperative BNP level was 2951.22±4291.27 pg/ml. A significant correlation between pre and postoperative BNP levels and the amount of creatinine, surgical time and length of stay in ICU was not observed. The ejection fraction was correlated with pre and postoperative BNP levels.

Conclusion: Serum levels of BNP at 24 hours before and after cardiac surgery could be a good biomarker for prediction and early diagnosis of heart failure in adults.

Keywords: B- natriuretic peptide, coronary bypass surgery, morbidity

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Introduction

Open heart surgery is a common therapeutic intervention to management and treatment of heart disease that aims to increase the survival and improve the quality of life of these patients (1). Like all other

surgeries, this surgery is accompanied by complications that may affect the patient's recovery and health (2). Rate of morbidity in patients undergoing coronary artery bypass grafting (CABG) surgery has not been clearly reported (3-5). Hence, several studies have been conducted to identify prognosis in recovery and to reduce the mortality and morbidity rate after this high risk Surgery (6-9). Study on changes in levels of cardiac biomarkers has been considered in recent years for detecting prognosis of patients after open heart surgery (10, 11). Brain natriuretic peptide (BNP) is a type of heart biomarker or hormone that has been introduced as an indicator of the diagnosis, progression and outcome of treatment in congestive heart failure, acute cerebrovascular accidents and hypertension (12-14). The biomarker is a neuro-hormonal agent that is released by the ventricular myocardium, especially in conditions of increased afterload and ventricular dilation (15). Brain natriuretic peptide, which its bioactive form is N-terminal pro-BNP, has diuretic, natriuretic, vasodilatory, anti-renin-angiotensin-aldosterone characteristics and inhibitory activity on the sympathetic system (14, 16, 17). Concentration of the hormone remains constant after it has increased in the blood, significantly in human plasma, which is easily detectable (14). Normal serum level of N-terminal pro-BNP is less than 300 pg/ml, which increases by aging (15, 18). Level of the hormone affected in several physiological and pathological conditions such as ventricular hypertrophy, left ventricular dysfunction, atrial fibrillation, severe hypertension, aortic stenosis, congestive heart failure, myocardial infarction, pulmonary hypertension, pregnancy hypertension and chronic renal failure (14,19-21). However, BNP as a predictor of cardiovascular events, side effects, and mortality in patients undergoing CABG had been associated with controversial results (22-24). In order that, elevated BNP levels in the early hours after cardiac surgery could be associated with longer hospitalization and higher mortality (25), while Bill et al. (2004) did not report any relationship between BNP levels and ejection fraction, myocardial infarction as an effective factor in morbidity (26). On the other hand, most of these studies examined the relationship between BNP level before and after surgery with patients' morbidity, but relation to determinants of morbidity is less studied.

Regarding the controversial results of previous studies, as well as the evaluation and comparison of BNP levels before and after operation with morbidity, in this study, association of this hormone before and after surgery with factors that can affect the process of recovery and health is examined. Our hypothesis was that preoperative BNP can be like post-operative BNP as a determinative factor in estimating the morbidity of patients after CABG. Therefore, patients with possible post-operative complications can be recognized. The aim of this study was to determine the relationship between pre and post-operative BNP hormone and morbidity in adult patients undergoing CABG surgery.

Methods

In the descriptive-analytic study, patients undergoing elective CABG surgery in the range of 21-89 years who referred to Shahid Rajaie's Heart Center, Tehran, Iran (from September 2016 to May 2017) included the study. Informed consent was obtained from the patients by expressing purpose of the study. All patients who had an emergency or re-operation, as well as simultaneous valve operation, patients with inotrope therapy before surgery and preoperative hematocrit less than 25 were excluded. Sampling was done in convenience method and the sample size was determined according to similar studies. BNP levels were measured in two steps based on samples, which were sent to laboratory at 24 hours before and after surgery. A blood sample (5ml) was collected after that the patient positioned at supine for 15 minutes, and was poured into a tube containing potassium EDTA. Then, serum NT-pro BNP was measured by ELISA with Biomedica Slovakia s.r.o kit (SK-1204) and accurately> 95%.

Demographic and clinical data was collected for pre-operative (24 hours before surgery) and postoperative (24 hours after operation) using a questionnaire. This information includes age, sex, body mass index, underlying illness, history of smoking, ejection fraction (EF), creatinine (Cr), blood urea nitrogen (Bun), glomerular filtration rate before and after surgery, The time of aortic clamp, time of cardiopulmonary bypass, surgical time, number of grafts, duration of intubation and duration of patient's stay in intensive care unit (ICU) were completed.

These patients were considered as morbidity factors:

- low cardiac output (need for inotrope for more than 24 hours or balloon pump placement)
- myocardial infarction (MI: ECG findings and increased cardiac enzymes)
- atrial fibrillation (AF; More than 10 minutes during ICU hospitalization)
- renal failure (Cr>3 or need to dialysis)
- long term intubation (more than 48 hours)
- long term ICU hospitalization (more than 4 days)

SPSS version 20 software using Kolmogrov-Smirnov test (for determination of normality), paired t-test (in parametric data) and dependent Wilcoxon (in nonparametric data) and correlation tests analyzed data. A significant level of 5% was considered.

Results

In this study, 50 patients were evaluated. Of them 33 (66%) were male and 17 (34%) were female. Mean±SD age of patients was 61±9 with a range of 36-82. Most patients (54%, n= 27) were overweight and 21 (42%) people were normal weight and two (4%) were obese. Hypertension had the highest frequency of all comorbidities (60%, n=30). Diabetes mellitus (36%, n=18) and renal failure (4%, n=2) were in the next ranks. Smokers were 19 (38%). Table 1 shows the parameters measured before and after the operation. There was a significant difference between serum creatinine and BNP before and after surgery.

Mean ± SD duration of: surgery was 228.90 ± 43.08, aortic clamp was 48.87 ± 18.17, cardiopulmonary bypass was 90.16 ± 28.21, intubation (hours) was 12.14 ± 4.95 and admission to ICU (day) was 3.28 ± 0.6. Relationship between BNP before and after surgery with sex, smoking and underlying diseases was investigated, which no significant relationship was found (Table 2).

Tables 3 and 4 show correlation between BNP before and after surgery and the variables considered for morbidity (postoperative ejection fraction, postoperative creatinine, duration of intubation, hospitalization in ICU, surgery; aortic clamping and pump times). Among these variables, only ejection fraction had a significant correlation with BNP at both times, before and after the operation.

Discussion

Efforts to identify and assess risks of preoperative and postoperative heart surgery to reduce morbidity and mortality studied. Evaluation of BNP as a criterion in recognition of morbidity in patients undergoing cardiac surgery has been investigated in several studies (18, 20, 26). However, advantage of present study is to examine the level of BNP and its relationship with determinants of morbidity in both

Table 1: Parameters measured before and after the operation.

Variables	Before operation SD± Mean	After operation SD± Mean	P value
Hemoglobin (gr/dl)	1.64 ± 13.73	1.71±13.48	0. 242
Hematocrit (%)	4.79±41.11	4.24±40.81	0.259
Ejection fraction (%)	41.93±11.85	40.81±10.41	0.234
Bun (mg/dl)	6.34±17.51	6.7±17.30	0.421
Creatinine (mg/dl)	0.22 ±0.989	0.31 ± 1.08	0.028
Glomerular filtration rate (ml/min/1.73 m2)	26.05 ±78.84	30.46 ± 76.40	0.448
BNP	919.81± 2364.22	2951.22 ±4291.27	0.000

Table 2: Relationship of mean serum BNP levels before and after surgery with clinical and demographic variables.

Variables		number	BNP1 (pg/ml)	BNP2 (pg/ml)	P value
Gender	female	17	1592.274	5203.411	0.237
	male	33	632.463	1873.939	0.235
Diabetes	+	18	1410.958	4583.611	0.310
	_	32	700.55	2298.93	0.125
Smoking	+	19	461.321	1993.210	0.236
	_	31	1262.96	3816.03	0.237
Hypertension	+	28	1342.623	3213.928	0.237
	_	22	499.67	1667.10	0.236
Kidney disease	+	3	1725.875	2015.25	0.199
	_	47	939.32	3073.00	0.238
Arrhythmia	+	1	85.4	1088	---
	_	49	976.15	3037.75	0.238

before and after cardiac surgery. Open heart surgery is a complex procedure which can lead to morbidity in patients, therefore examining association of BNP in preoperative conditions may be a suitable method to

Table 3: Correlation between preoperative BNP and clinical variables.

Variables		Before surgery	P value
Ejection fraction	50	-0.380	0.006
Creatinine	50	0.114	0.430
Duration of intubation	50	0.108	0.466
Length of ICU hospitalization	50	0.220	0.879
Duration of surgery	50	0.111	0.414
Duration of aortic clamping	50	0.211	0.770
Duration of pump	50	0.151	0.485

predict the complications.

Table 4: Correlation between postoperative BNP and clinical variables

Variables		after surgery	P value
Ejection fraction	50	-0.416	0.003
Creatinine	50	0.068	0.641
Duration of intubation	50	0.044	0.760
Length of ICU hospitalization	50	0.218	0.128
Duration of surgery	50	0.113	0.421
Duration of aortic clamping	50	0.224	0.811
Duration of pump	50	0.131	0.428

In different studies relationship between preoperative BNP serum levels and postoperative morbidity was investigated (22, 27-29), and in some other studies postoperative serum levels of BNP have been considered (30-32). Only in a study, predictive value of BNP serum level before and after operation with morbidity was compared (33). Results of our study showed that postoperative serum BNP levels increased by 3 times in comparison with preoperative CABG after surgery. Increased BNP after surgery has been shown in numerous studies, which can be due to changes in the preload and afterload. In present study, there was a reverse and significant correlation between preoperative and postoperative BNP values and EF after surgery, so that an increased BNP levels was observed in reduced EF. In addition, the relationship between BNP before and after surgery and postoperative creatinine, duration of intubation and duration of ICU stay were observed, however this relationship was not significant. The FDA has approved measuring the NT-proBNP test for the diagnosis of heart failure (14). ProBNP is the most sensitive marker for heart failure or mild cardiac failure (20).

Bosseau et al. showed that although BNP is not a specific hormone for cardiac function, but it can be used as a marker for the diagnosis of congestive heart failure (34). In the study of Hussain et al. BNP levels also had a significant relationship with left ventricular ejection fraction (35). Fox et al concluded that preoperative BNP could be a predictor of post-operative complications, mortality and morbidity (33). In our study, preoperative BNP had a significant correlation with EF after surgery alone. This may be due to the difference in the normal range in the two studies, low sample size in our study and the difference in the factors affecting the BNP level, such as the sex of women and age, which was observed in Fox et al study. Limitations of this study were the low sample size; lack of BNP repeated examination during surgery to determine the rate of BNP increase and the mortality rate of patients.

Conclusion

BNP level can be affected by various factors, but its relationship with EF decreases is significant, which can be used to diagnose the congestive heart failure in patients after open heart surgery. Patients with high levels of BNP before or after surgery may need extra attention due to probable reduced ejection fraction.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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