Perioperative brain natriuretic peptide in off-pump coronary artery bypass

Zanxin WANG[1], MD; Degang LIANG[1], MD; Qiang FU[1], MD, PhD; Liqun JIA[1], MD; Jianlong MEN[2], MD, PhD; Minxin WEI[1], MD, PhD

[1]Dept. of Cardiovascular Surgery, Tianjin Medical University General Hospital; [2]Dept. of Clinical Laboratory, Tianjin, P. R. China.

Background — During the last decade brain natriuretic peptide (BNP) has been recognized as a useful marker for acute and chronic left ventricular dysfunction. The present study was designed to evaluate the clinical relevance of BNP before and after off-pump coronary artery bypass (OPCAB).

Methods — One hundred and twelve patients undergoing primary OPCAB were divided into two groups by preoperative BNP levels (group A, BNP ≤ 100 pg/ml and group B, BNP > 100 pg/ml). Levels of BNP and MB isoenzyme of creatine kinase (CK-MB) were measured preoperatively, 6 hours and 1 day post-operatively. Echocardiographic and clinical data were collected.

Results — Patients in group A had smaller perioperative left ventricular end-diastolic dimensions (LVEDD) and greater left ventricular ejection fractions (LVEF) compared to group B ($P < 0.05$). Levels of BNP and CKMB increased postoperatively in both groups ($P < 0.01$). However, there was no relationship between postoperative BNP and CKMB at any time point. Logistic regression analyses showed that a preoperative BNP level > 100 pg/ml was an independent risk factor for ventilation > 24 hours (odds ratio, OR = 13.33; 95% CI: 1.42-125.03) and ICU stay > 72 hours (OR = 3.01; 95% CI: 1.09-8.33).

Conclusion — The baseline BNP level correlated with preoperative ventricular function and longer durations of ventilation and hospital stay after OPCAB. BNP increased early after operation. However, postoperative BNP did not correlate with myocardial injury or clinical results after OPCAB.

Keywords: *Brain natriuretic peptide – off-pump coronary artery bypass graft surgery – myocardial injury.*

Introduction

Brain natriuretic peptide (BNP) is one of a family of structurally similar peptide hormones that also includes atrial natriuretic peptide (ANP), C-type natriuretic peptide (CNP) and urodilatin. It promotes natriuresis and diuresis, acts as a vasodilator and is an antagonist to the renin-angiotensin-aldosterone system, and therefore, improves the loading conditions of the failing heart. Both ANP and BNP are secreted by atrial and ventricular myocytes, although the major site of production of BNP is the left ventricle (LV) in response to increased wall stress. It can reflect ventricular impairment and the severity of haemodynamic decompensation in heart disease[1-5]. They also have prognostic significance[1,2,5] and may be useful in titrating pharmacotherapy in heart failure[6]. Numerous data have shown BNP as a marker of congestive heart failure and an important tool for diagnosis and risk stratification in cardiovascular disease[7,8]. De Lemos and colleagues measured the ability of plasma BNP to predict the risk of mortality, clinical heart failure and new myocardial infarction within a few days of acute coronary syndromes. Higher plasma BNP concentration may correlate with greater cardiac damage[9].

Off-pump coronary artery bypass (OPCAB) via median sternotomy may result in fewer post-operative complications and less myocardial injury[10,11]. It can reduce morbidity and mortality associated with CPB and has resulted in a greater acceptance of OPCAB procedures among the cardiovascular community. However, it is also accompanied with the inflammatory response caused by surgical trauma or reperfusion injury. Perioperative BNP release after OPCAB is not well defined. The present study was designed to evaluate perioperative BNP release and its relationship to early clinical outcome after OPCAB.

Address for correspondence: Dr. Wei, Department of Cardiovascular Surgery, Tianjin Medical University General Hospital, Tianjin, P.R. China. E-mail: minxinw@126.com

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Material and methods

Study patients

One hundred and twelve patients undergoing primary OPCAB were divided into two groups by pre-operative BNP levels (group A, BNP ≤ 100 pg/ml; group B, BNP > 100 pg/ml). The investigation was approved by the local ethics committee and informed written consent was obtained from all patients. Patients with liver or renal failure, pre-existing autoimmune disease, or severe infection were not eligible. Antiplatelet therapy was routinely stopped 5-7 days before surgery.

Anaesthesia, surgical and post-operative protocol

All patients had premedication with morphine. Anaesthetic techniques were used with sufentanyl, midazolam and vecuronium. Esmolol was given where necessary to reduce the heart rate. Standardized OPCAB was undertaken via median sternotomy with internal thoracic artery (ITA), and/or radial artery, and/or saphenous vein as conduits. Heparin (1.5 mg/kg) was administered to achieve an activated clotting time (ACT) > 300 s. A suction stabilizer (Octopus®, Medtronic Inc., Minneapolis, MN, USA) was used to stabilise the anastomotic site. Proximal anastomosis to the aorta was performed using tangential clamping. Post-operative treatment in the ICU was standardized. LVEF and LVEDD were measured by transthoracic echocardiography pre-operatively and 7 days post-operatively.

Sample collection and measurement

Venous blood samples were collected preoperatively and 6 hours and 1 day post-operatively. Plasma BNP was measured with BNP-TRIAGE® (Biosite Diagnostics, San Diego, USA) and CKMB was measured with the DGKC method by the hospital central laboratory.

Statistical analysis

Statistical analysis was performed using SPSS/Win (version 13.0). Data are presented as median (quartiles) or mean ± standard deviation as appropriate. χ^2 test was used to analyse the relationship between categorical data. The Mann-Whitney *U* test or Kruskal-Wallis test, as appropriate, were used to compare BNP or CKMB levels and different outcomes between groups. The association between two continuous variables was determined using Spearman's rank correlation. Significance was established at a P value < 0.05.

Results

All patients completed the study and there were no deaths or major complications (cerebral complications, renal and hepatic dysfunction). No significant difference was found between groups, except perioperative LVEDD and LVEF (table 1). Echocardiography showed that patients in group A had smaller pre-operative LVEDD (50 ± 5.2 mm vs. 54 ± 6.8 mm, $P = 0.021$) and higher LVEF (62 ± 7.6% vs. 55 ± 9.2%, $P = 0.001$) as compared to those in group B. Post-operative LVEDD and LVEF were not different as compared to baselines. Post-operative levels of CKMB and BNP did not correlate with any perioperative echocardiographic parameter.

BNP and CKMB increased after surgery in both groups (figure 1). BNP levels in group B were higher than those of group A. However, the change in BNP levels was not different between groups at any time points (changes of BNP (ΔBNP = BNP level minus baseline), 6 hours, group A, 32.5 [11.0-63.0] pg/ml, group B, 55.5 [2.7-143.0] pg/ml, $P = 0.475$; 1 day, group A, 168.0 [96.4-278.7] pg/ml, group B, 179.0 [75.0-432.0] pg/ml, $P = 0.799$). There was no relationship between BNP and CKMB at any time point.

Logistic regression showed that, adjusted for 11 factors (age, gender, type II diabetes mellitus, hypertension, previous MI, LVEDD, LVEF, number of diseased vessels, left main disease, number of grafts and blood loss), preoperative BNP levels > 100 pg/ml were an independent risk factor for ventilation > 24 hours (OR = 13.33; 95% CI: 1.42 ~ 125.03) and ICU stay > 72 hours (OR = 3.01; 95% CI: 1.09 ~ 8.33) (table 2).

Discussion

BNP is a member of the natriuretic peptide family with both regulatory and modulatory roles in the cardiovascular system[12]. Moreover, elevated BNP levels have been used as a diagnostic and prognostic marker in various cardiovascular diseases. Logeart and colleagues have shown that BNP was the best marker to assess prognosis of patients suffering from chronic heart failure independent from haemodynamic parameters such as LVEF or pulmonary capillary wedge pressure[13]. Additionally, BNP was suggested to be an additional factor for risk stratification of patients before cardiac surgery.

BNP correlates to preoperative cardiac function with elevated BNP being associated with ventricular dysfunction[14]. In agreement with this, our study showed that patients in group A (pre-operative BNP ≤ 100 pg/ml) had smaller preoperative LVEDD and higher LVEF as compared to those in group B (preoperative BNP > 100 pg/ml). Vinereanu and colleagues postulated that global systolic function (LVEF)

Table 1. – *Clinical data*

	Group A (n = 84) (BNP ≤ 100 pg/ml)	Group B (n = 28) (BNP > 100 pg/ml)	*P*
Age (y)	63 ± 9.3	64 ± 7.6	0.191
Gender (male/female)	58/25	18/10	0.583
Type II diabetes mellitus	26 (31%)	11 (39%)	0.442
Hypertension	57 (69%)	19 (68%)	0.936
Previous MI	21 (25%)	11 (39%)	0.160
Previous PCI	7 (8%)	1 (4%)	0.385
Preoperative LVEDD (mm)	50 ± 5.2	54 ± 6.8	0.021
Post-operative LVEDD (mm)	49 ± 4.3	51 ± 6.8	0.015
Preoperative LVEF (%)	62 ± 7.6	55 ± 9.2	0.001
Post-operative LVEF (%)	61 ± 6.6	56 ± 9.9	0.023
No. of diseased vessel	2.8 ± 0.54	2.8 ± 0.39	0.086
Left main narrowed	28 (34%)	6 (21%)	0.211
No. of grafting	2.8 ± 0.67	2.6 ± 0.78	0.192
Blood loss (ml)	423 ± 238	375 ± 162	0.217
Post-operative stay (days)	10.2 ± 4.1	8.9 ± 2.4	0.051

Data are presented as mean ± SD or numbers. MI = myocardial infarction; PCI = percutaneous coronary intervention; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction.

Table 2. – *Logistic regression analysis to assess predictors of post-operative ventilation > 1 day and ICU stay > 3 days*

	Ventilation > 24 hours	ICU stay > 72 hours
Age	0.98 (0.88 ~ 1.08)	0.99 (0.94 ~ 1.05)
Gender (male)	0.55 (0.06 ~ 5.07)	2.01 (0.75 ~ 5.43)
Type II diabetes mellitus	3.13 (0.50 ~ 19.63)	1.56 (0.57 ~ 4.24)
Hypertension	0.11 (0.01 ~ 1.00)	0.39 (0.14 ~ 1.04)
Previous MI	8.56 (0.85 ~ 85.78)	1.27 (0.43 ~ 3.72)
Preoperative LVEDD	1.07 (0.93 ~ 1.24)	1.01 (0.93 ~ 1.10)
Post-operative LVEDD	1.10 (0.97 ~ 1.25)	0.96 (0.87 ~ 1.06)
Preoperative LVEF	0.96 (0.87 ~ 1.07)	0.96 (0.91 ~ 1.02)
Post-operative LVEF	0.96 (0.88 ~ 1.07)	0.95 (0.90 ~ 1.01)
No. of diseased vessel	1.17 (0.18 ~ 7.79)	2.21 (0.63 ~ 7.79)
Left main narrowed	3.70 (0.59 ~ 23.27)	1.24 (0.44 ~ 3.44)
No. of grafting	1.23 (0.33 ~ 4.63)	1.37 (0.67 ~ 2.82)
Blood loss	0.99 (0.99 ~ 1.00)	1.00 (0.99 ~ 1.00)
BNP > 100 pg/ml	13.33 (1.42 ~ 125.03)*	3.01 (1.09 ~ 8.33)*

Data are presented as OR (95%CI); *$P < 0.05$. MI = myocardial infarction; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction.

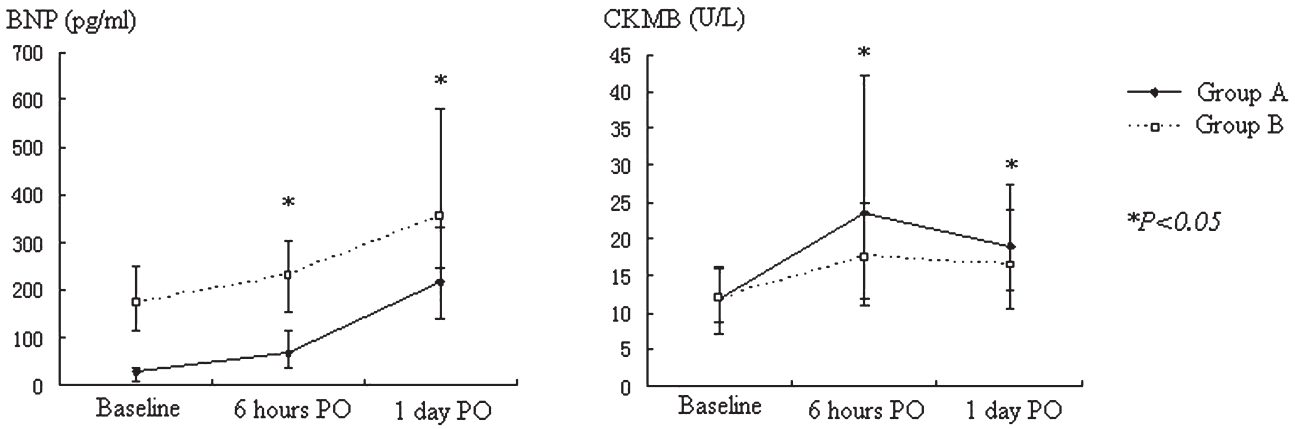

Fig. 1. – Post-operative BNP and CKMB change in different groups. Data are presented as median (quartiles). Group A: BNP ≤ 100 pg/ml; group B: BNP > 100 pg/ml. BNP = B-type natriuretic peptide; CKMB = MB isoenzyme of creatine kinase; PO = post-operative. *$P < 0.05$ as compared to baseline.

correlated to BNP levels, while LV longitudinal systolic function had a stronger correlation. The sensitivity and specificity of longitudinal systolic velocity ≤ 5.5 cm/s (mean velocity of 4 basal segments, not the annular velocity) to diagnose heart failure (defined as an elevated BNP) were 94% and 85%, respectively, while the negative predictive value was 97%[15].

BNP is secreted in response to the mechanical stretch of LV myocytes. In patients with both systolic and diastolic dysfunction, the plasma BNP level was shown to be elevated by high LV filling pressures[16]. Our study showed no relationship between perioperative BNP and CKMB, and the post-operative increase in BNP was similar between groups with different preoperative BNP levels. Post-operative increases in BNP in both groups may be caused by hypertrophy, ventricular dysfunction, wall stress or other factors rather than myocardial injury[17-19].

Previous studies have shown that BNP is a hormonal predictor of death in patients with coronary artery disease (CAD), especially in those with myocardial infarction. High BNP concentrations in patients with CAD predict a worse long-term outcome[20,21]. This study showed that, adjusted for other traditional risk factors, a preoperative BNP level > 100 pg/ml was an independent risk factor for longer ventilation time and ICU stay after OPCAB. Preoperative BNP may also provide independent information for risk prediction in patients undergoing OPCAB and support previous findings that preoperative but not intra- or post-operative BNP may be an independent risk factor for patients undergoing CABG[22,23].

The BNP level of 100 pg/ml was chosen as a cut-off based on the results of the Food and Drug Administration in the United States. This value was chosen for its 95% sensitivity in separating NYHA classes I to IV from patients who do not have heart failure. McCullough and colleagues found that, a cut-off of 100 pg/ml for BNP had a sensitivity of 90% and specificity of 73% in the setting of the evaluation of acute dyspnoea for a diagnosis of heart failure in the emergency department[24]. In a study of 1590 patients undergoing non-cardiac surgery, Dernellis and Panaretou also showed that preoperative elevated BNP was an independent biomarker of post-operative cardiac events[25]. Preoperative BNP concentration over 100 pg/ml has been shown in patients undergoing peripheral vascular surgery to identify those at increased risk of a perioperative fatal or non-fatal myocardial infarction. The present results also support that a cut-off value of 100 mg/ml might be of practical value in OPCAB.

The present research was limited to a study population with better cardiac function: preoperative LVEDD (51 ± 5.9 mm) and LVEF (60 ± 8.4%). So the influence of LVEDD and LVEF on post-operative mechanical ventilation time and duration of ICU staying might be less. Preoperative BNP value more than 100 pg/ml became an independent risk factor. Cardiac function has been confirmed to be an independent predictor of clinical outcome following CABG and is associated with mortality and morbidity. Moreover, it may influence perioperative BNP levels[26].

In summary, the present study showed that in patients undergoing OPCAB, baseline BNP levels correlated with preoperative ventricular function and longer durations of ventilation and hospital stay. BNP increased post-operatively but did not correlate with myocardial injury and clinical results.

Acknowledgements

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Conflict of interest: none declared.

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