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ORIGINAL ARTICLE

Plasma B-type natriuretic peptide in predicting outcomes of elective coronary artery bypass surgery

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Abstract The risks of surgery and its clinical outcome are of great importance for both patients and physicians when choosing coronary artery bypass (CABG) surgery for coronary artery disease. The purpose of the current study was to clarify the relationship between serum B-type natriuretic peptide (BNP) and patient clinical outcome. Seventy-six eligible patients who underwent CABG were enrolled into the prospective study. Venous blood samples were drawn for serum BNP and N-terminal (NT)-proBNP levels measurement on preoperative Day 1, postoperative Day 1, and postoperative Day 7. Clinical end points were: (1) intensive care unit (ICU) stay longer than 4 days postoperatively and/or hospital stay longer than 13 days postoperatively; (2) major complications and poor outcomes. Patients who had prolonged ICU stay and hospitalization had significantly higher postoperative Day 1 BNP and postoperative Day 1 NT-proBNP level ($p = 0.02$ and 0.005, respectively). Age was significantly older in patients with prolonged ICU stay and hospitalization than those without prolonged ICU stay and hospitalization ($p = 0.03$). Serum creatinine level was also significantly increased in patients with prolonged ICU stay and hospitalization ($p = 0.009$). However, age was the only remaining factor that correlated with prolonged ICU stay and hospitalization in the multivariate logistic regression model. These results suggest that research using BNP and NT-proBNP for predicting ICU stay and hospitalization in patients who have undergone CABG must adjust risk factors to present a more appropriate estimation of its clinical outcome.
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Introduction

Coronary artery disease is currently the major cause of cardiovascular-related death in the modern world as well as

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in developing countries [1]. The cost of coronary artery bypass graft (CABG) surgery has been rising, making a review of outcome and cost-effectiveness imperative. Among major adverse events, prolonged hospitalization and/or prolonged intensive care unit (ICU) stay are the most common causes of costly medical expenses other than death related to surgery. It is known that there are many factors that can affect the outcome. Therefore, preoperative factors have been grouped into a scoring system to predict the possible risk of surgical mortality and morbidity [2–4]. However, there is no gold standard prediction model for length of hospital stay, surgical complications, and outcomes [5]. Furthermore, scoring systems are often cumbersome, which means an additional predicting system is necessary. The B-type natriuretic peptide (BNP) is a neurohormone mainly secreted from cardiac ventricles by increasing ventricular wall stress and volume expansion [6]. There are several previous studies that demonstrated that serum BNP concentration significantly increased after CABG surgery and was associated with increasing postoperative mortality and cardiac events [7,8]. Furthermore, ProBNP, a serum protein comprising 108 amino acids, can be cleaved into physiologically active BNP and biologically inactive N-terminal proBNP (NT-proBNP), whose plasma concentration reflects the activity of *de novo* synthesis and may have even greater specificity to cardiac activity than BNP [9]. NT-proBNP is also more stable, which makes its measurement more reliable [10]. Studies demonstrated that NT-proBNP can be used in diagnosing left ventricular dysfunction and acute coronary syndrome [11,12]. Theoretically, the elevation of serum NT-proBNP concentration may also reflect the higher mortality and complication rates after CABG surgery. However, there were studies suggesting that several variables of general population such as female sex, old age, and impaired renal function were also significantly associated with higher BNP and NT-proBNP levels [9,13]. The variables may possibly affect the predictability by BNP and NT-proBNP levels alone. Therefore, the purposes of the current study are to assess whether BNP and NT-proBNP are correlated with postoperative complications and outcomes after adjusting for risk factors.

Methods

The study was first reviewed and approved by the hospital's ethics committee, and then written informed consent was obtained from each patient. Ninety-four patients who underwent CABG surgery of a single surgeon were enrolled into the prospective study between January 2006 and June 2007. Among the 94 patients, 10 patients with uremia, five patients with inappropriate sample collection, and three patients who underwent emergency operation were excluded from the study. The remaining 76 patients all received elective cardiac bypass surgery, including conventional CABG surgery (single aortic cross-clamping, deep hypothermia 23–25°C, and crystalloid cardioplegia) in 54 patients, off-pump CABG surgery (median sternotomy, normothermia) in 11 patients, and minimally invasive direct CABG surgery (lateral thoracotomy with short segment of 5^{th} rib resection) in 11 patients. Left ventricular ejection fractions (LVEFs) were measured by echocardiography on preoperative Day 1 and postoperative Day 7. The serum BNP and NT-proBNP levels were measured on preoperative 1 Day, postoperative Day 1, and postoperative Day 7. Venous blood samples were drawn for BNP and NT-proBNP analysis after patients rested for 30 minutes. The venous samples were placed into chilled ethylenediaminetetraacetic acid tubes and placed on ice. After centrifugation, the plasma samples were stored at −80°C until assay. During the procedure, Roche Elecsys, Roche Diagnostics, Indianapolis 1010/2010 kits and Modular analytics, Roche Diagnostics, Indianapolis E170 immunoassay analyzers were used for the quantitative determination of NT-proBNP. The Abbott AxSYM (R), Abbott Laboratories, Illinois automated immunoassay instrument system was used for BNP measurement. All data were collected afterward.

Clinical end points were: (1) ICU stay longer than 4 days postoperatively and/or hospital stay longer than 13 days postoperatively; (2) major complications and poor outcomes, including new-onset atrial fibrillation, ventricular tachycardia, ventricular fibrillation, requirement of intra-aortic balloon pump (IABP) support, unscheduled cardiac-related readmission to the hospital, and late cardiac mortality within 1 year.

Data were analyzed using SPSS software (version 11.0.0, SPSS Inc., Chicago, IL, USA) and expressed as the mean with standard deviation. Categorical variables were presented as counts and percentages. The student t test and χ^2 test were used to examine differences in continuous and categorical variables, respectively. Multivariate logistic regression analyses were used to calculate odds ratios and 95% confidence intervals, with adjustment for potential confounders such as age, sex, creatinine level, heart failure class, NYHA, and LVEF. A value of $p < 0.05$ was considered statistically significant.

Results

Patients' mean age was 64.0 ± 10.2 years, and 85.5% were male. There were 5% of patients with preoperative New York Heart Association functional class III or IV. Most patients (76.3%) had triple vessel disease or left main disease. The mean serum creatinine level was 1.2 ± 0.38 mg/dL. The mean LVEF was 61.0 ± 11.2 in preoperative evaluation and 61.6 ± 9.5 in postoperative examination. There were no significant differences between preoperative and postoperative LVEF ($p = 0.52$). Thirty-day surgical mortality and in-hospital mortality was zero.

Fig. 1 shows the BNP and NT-proBNP changes. The mean BNP was 103.8 ± 184.0 pg/mL, 361.9 ± 463.7 pg/mL, and 261.9 ± 402.4 pg/mL at preoperation, postoperative Day 1, and postoperative Day 7, respectively. There were significant differences between preoperative BNP and postoperative Day 1 BNP ($p < 0.001$), and, preoperative BNP and postoperative Day 7 BNP ($p = 0.001$). The mean NT-proBNP was 621.3 ± 1050.7 pg/mL, 2869.8 ± 3252.6 pg/mL, and 1358.5 ± 1632.3 pg/mL at preoperation, postoperative Day 1, and postoperative Day 7, respectively. The postoperative Day 1 and Day 7 NT-proBNP concentrations were significantly higher than preoperative NT-proBNP concentrations ($p < 0.001$, respectively). Linear regression with 95%

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