Postoperative Increase in B-Type Natriuretic Peptide Levels Predicts Adverse Outcome After Cardiac Surgery

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Objective: **To evaluate the prognostic implication of changes in postoperative B-type natriuretic peptide (BNP) concentrations in patients undergoing cardiopulmonary bypass for cardiac surgery.**

Design: **A retrospective analysis of prospectively collected clinical data.**

Setting: **Cardiothoracic surgery and an intensive care unit (ICU) in a university hospital.**

Participants: **The present study included a total of 407 consecutive patients undergoing cardiac surgery.**

Interventions: **None.**

Measurements and Main Results: **BNP concentrations were measured on admittance to the ICU (D0) and at day 1 after surgery. Patients were divided into quintiles according to their BNP level on admittance to the ICU. The predictive value of absolute changes in BNP levels during the first 24 hours postoperatively was analyzed with Kaplan-Meier estimates of survival and Cox multivariate proportional analysis. Prognostic factors for impaired midterm survival included elevation of the BNP level (HR, 7.3/ log10^{x}; 95% confidence interval, 1.8-29, $p = 0.005$). The BNP levels of patients undergoing isolated valve surgery or valve and concomitant CABG surgery were significantly higher ($p = 0.012$ and $p = 0.032$, respectively) than those undergoing isolated coronary artery bypass graft surgery. Patients in higher quintiles required ventilation for a longer time ($p < 0.001$), and prolonged inotropic support ($p < 0.001$). The mean plasma BNP concentration of 172 pg/mL (median, 64; interquartile range, 172) on arrival at the ICU had a sensitivity of 75% and a specificity of 74% for predicting 1-year mortality.**

Conclusions: **Elevated BNP levels on admittance to the ICU and postoperatively increasing BNP levels are associated with adverse postoperative outcome and are predictive of impaired late survival. Sequential postoperative BNP monitoring facilitates the early identification of patients at an increased risk of heart failure and may be used as an adjunct for clinical decision making and optimized patient management.**

KEY WORDS: cardiac surgery, natriuretic peptides, BNP, heart failure, mortality, intensive care unit

HEART FAILURE after cardiac surgery is a serious condition that worsens the prognosis of the patient,[1] and thus early diagnosis and appropriate treatment are crucial. Levels of B-type natriuretic peptide (BNP) routinely are monitored postoperatively at many centers for cardiac surgery as an indicator of poor myocardial recovery or the risk of heart failure.[2,3] Several studies have shown that cardiac natriuretic hormones are reliable indices of left ventricular dysfunction[4,5] and progressive heart failure.[6] An increase in the secretion of BNP previously has been reported to occur after cardiac surgery and has been suggested to be secondary to preoperative native valve disease, heart failure,[5,7] and the intraoperative duration of ischemia.[8,9] However, it is difficult to evaluate the clinical value of BNP after cardiac surgery because the duration of cardiopulmonary bypass (CPB) is likely to influence the postoperative release of BNP.[10] Furthermore, the secretion pattern and the increase in the concentration of BNP also may depend on the type of surgery.[10] Finally, although it has not previously been shown, BNP release theoretically may also result from incomplete myocardial protection and intraoperative reperfusion injury.

Previous studies have focused mainly on BNP secretion before and during CPB[11] and on the precursor of BNP (NT-proBNP).[12-14] It remains to be determined whether the measurement BNP or NT-proBNP offers any advantage over the other in a preoperative[15] or postoperative clinical setting.[5,16,17] However, the clinical impact and long-term prognostic value of an increasing postoperative BNP level have not been evaluated sufficiently. In a small study by Hutfless et al,[18] an increase to peak levels of BNP was associated with prolonged hospital stay as well as impaired survival at 1 year. The dynamics of plasma BNP concentration with its variations during the postoperative period after cardiac surgery remain poorly understood. Thus, the objective of the present study was to determine whether an increase in postoperative plasma BNP concentration predicts impaired survival and to evaluate the relation between early BNP release and adverse postoperative outcome.

METHODS

Samples of blood for plasma BNP concentration analysis were taken from 407 patients between January and August 2007 after cardiac surgery at the Department of Cardiothoracic Surgery at Lund University Hospital. The spectrum of surgical interventions included isolated coronary artery bypass graft (CABG) surgery (n = 283), isolated valve replacement (aortic valve replacement [AVR], n = 45; mitral valve replacement [MVR], n = 18), and valve surgery with concomitant CABG surgery (AVR and CABG, n = 45; MVR and CABG, n = 16). Exclusion criteria were aortic dissection, surgery on the ascending aorta, aortic root or arch, double-valve procedures, and procedures including deep hypothermia with circulatory arrest. CPB was performed under mild hypothermia (34°C) in all types of surgery, and myocardial protection was achieved by intermittent anterograde or combined (anterograde plus retrograde) cold blood cardioplegia. Pre-, peri-, and postoperative variables were collected prospectively and entered into the department's computerized cardiac surgery database. The study protocol was approved by The Ethics Committee for Clinical Research at Lund University.

Postoperative blood samples (5 mL) were obtained immediately on admittance to the intensive care unit ICU (D0) and on the first post-

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operative day (D1). These postoperative time points were chosen in accordance with previous reports showing that peak BNP values remain unchanged up to 6 hours after cardiac surgery[3] and with reports showing that a single 24-hour BNP value is a significant predictor of cardiac dysfunction[8] and is associated with short-term and long-term adverse outcome in cardiac surgical patients.[3] Samples were obtained daily from patients showing increasing BNP levels until the peak concentration was reached. No further samples were taken from patients showing a decline in BNP level on the first postoperative day (D1 <D0). The samples were collected in a tube containing potassium EDTA, and the BNP level was analyzed immediately using a point-of-care device (Triage; Biosite Diagnostics, San Diego, CA).

The primary endpoint was the predictive value of the absolute change in BNP level (log-transformed) between baseline (D0) and the first postoperative day (D1). Low-cardiac-output syndrome was defined as the need for postoperative inotropic support (dobutamine or levosimendan with or without additional norepinephrine infusion) for more than 24 or 48 hours. Myocardial infarction was diagnosed by electro-

Table 1. Patient Characteristics and Type of Surgical Procedure

	CABG n (283)	CABG + AVR n (45)	AVR n (45)	CABG + MVR n (16)	MVR n (18)
Preoperative variables					
Age (y)	68 ± 10	74 ± 8	68 ± 15	67 ± 8	61 ± 13
Female	63 (22)	14 (31)	19 (42)	4 (25)	7 (39)
Atrial fibrillation	13 (5)	5 (11)	5 (11)	2 (13)	1 (6)
NYHA III/IV	115 (41)	22 (49)	21 (47)	12 (75)	10 (56)
LVEF 30%-50%	73 (26)	15 (33)	10 (22)	2 (13)	2 (11)
LVEF <30%	38 (14)	3 (7)	3 (7)	7 (44)	0
Diabetes mellitus	72 (26)	6 (14)	8 (18)	3 (19)	0
Recent MI	123 (44)	6 (13)	1 (2)	5 (31)	0
Hemoglobin (g/L)	134 ± 16	133 ± 15	133 ± 18	129 ± 18	138 ± 14
COPD	25 (9)	5 (11)	2 (5)	1 (6)	1 (6)
Creatinine (μmol/L)	91 ± 33	96 ± 31	89 ± 26	93 ± 28	90 ± 55
PVD	32 (11)	10 (22)	4 (9)	3 (19)	1 (6)
PHT	2 (1)	0	4.5 (2)	8 (50)	6 (33)
Redo surgery	9 (3)	1 (2)	8 (18)	1 (6)	2 (11)
Emergency surgery	27 (10)	3 (7)	0	3 (19)	0
Endocarditis	0	1 (2)	3 (7)	0	2 (11)
Neurologic dysfunction	5 (2)	1 (2)	3 (7)	0	1 (6)
Critical preoperative state	14 (5)	0	0	3 (19)	0
Higgins score	3 ± 3	4 ± 3	3 ± 2	8 ± 6	5 ± 2
Additive EuroSCORE	5 ± 3	8 ± 3	6 ± 4	9 ± 7	6 ± 2
Logistic EuroSCORE	7 ± 10	13 ± 15	10 ± 12	23 ± 29	7 ± 6
Operative variables					
LCOS >48 h	28 (10)	9 (20)	6 (14)	6 (38)	4 (22)
Levosimendan (Simdax)*	22 (8)	7 (16)	5 (11)	8 (50)	2 (11)
MI perioperatively	9 (3)	2 (4)	0	0	0
CVI peri-/postoperatively	2 (1)	2 (4)	1 (2)	1 (6)	1 (6)
CPB (min)	81 ± 26	145 ± 27	108 ± 26	184 ± 47	141 ± 71
Cross-clamping time (min)	47 ± 15	104 ± 20	73 ± 21	110 ± 32	105 ± 57
Postoperative variables					
OFB (L)	3.4 ± 1.5	4.5 ± 2.1	3.8 ± 1.2	4.1 ± 2.1	3.9 ± 1.2
IABP	9 (3)	1 (2)	0	4 (25)	0
Creatinine (peak) ICU (μmol/L)	96 ± 54	108 ± 72	98 ± 55	118 ± 42	78 ± 22
AF	82 (29)	21 (47)	14 (31)	6 (38)	6 (33)
BNP (D0) pg/mL (median, IQR)	56 (130)	89 (232)	107 (286)	294 (444)	97 (147)
BNP (D1) pg/mL (median, IQR)	155 (216)	262 (444)	214 (283)	627 (1,177)	166 (161)
Log_{10} BNP	1.9 ± 0.5	2.2 ± 0.4	1.9 ± 0.6	2.3 ± 0.5	1.9 ± 0.5
Time on ventilation (h) (median, IQR)	7 (7)	8 (8)	6 (6)	15 (64)	8 (11)
LOS ICU (h) (median, IQR)	22 (6)	23 (39)	23 (5)	48 (123)	22 (150)
Perioperative bank blood (U) (median, IQR)	0 (1)	0 (2)	0 (2)	2 (5)	0 (2)
Postoperative bank blood (U) (median, IQR)	0 (2)	2 (4)	0 (2)	3 (9)	0 (3)
Postoperative platelets (U)	0 (0)	0 (0)	0 (0)	0 (2)	0 (0)

NOTE. Values are expressed as number (%), median (IQR), or mean (± standard deviation).

Abbreviations: NYHA, New York Heart Association Classification; LVEF, left ventricular ejection fraction; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; PHT, pulmonary hypertension (p_{syst} >60 mmHg); LCOS, low coronary output syndrome; TnI, cardiac troponin I; OFB, operative fluid balance; IABP, intra-aortic balloon pump; LOS ICU, length of stay in the intensive care unit.

Hemoglobin level <110 g/L.

*Treatment with levosimendan infusion peri-/postoperatively.

cardiogram (left bundle-branch block, Q-wave) and cardiac enzymes. Postoperative atrial fibrillation was defined as one or more episodes of supraventricular tachyarrhythmia after cardiac surgery monitored by continuous telemetry electrocardiography in patients with no previous history of AF. Postoperative renal failure was defined as a serum creatinine level exceeding 200 μmol/L or the need for dialysis. The length of stay in the ICU refers to the number of days in the ICU before the patient was moved to the ward.

Postdischarge survival data were obtained from the National Board of Health and Welfare (Socialstyrelsen, Sweden) or, if available, from patient records. The total number of patient years during follow-up was 820 years, with a mean of 2.0 $\pm$ 0.4 (interquartile range [IQR], 0.2 years). Follow-up was performed in April 2009 and was 100% complete.

Categoric variables were expressed as percentages, and continuous variables were expressed as mean $\pm$ standard deviation or medians and IQRs. Categoric data were compared using the chi-square test or Fisher exact test when the expected frequency was less than 5. Continuous variables were tested for normal distribution using the Kolmogorov-Smirnov test. The Student t test was used to evaluate continuous variables. Continuous variables not following a normal distribution were log transformed for analysis but for descriptive purposes are presented in their nonlogarithmic format as mean $\pm$ standard deviation. The study cohort was divided into quintiles according to the BNP level on arrival at the ICU, and the characteristics of patients in the different quintiles and different postoperative outcomes were compared using the chi-square test for trend or analysis of variance, depending on the nature of the data. Stepwise Cox proportional hazards analysis was used for risk adjustment and to identify independent risk factors for overall mortality after cardiac surgery. The inclusion criterion for the full model for each outcome was $p < 0.2$, and the limit for stepwise backward elimination was $p < 0.1$. The proportional hazards assumption for the Cox model was assessed by the analysis of Schoenfeld residuals versus time showing no violation of the assumption of proportionality because none of the variables selected for the final model showed a characteristic pattern of association of its effect over time in the graphic analysis of Schoenfeld residuals. The discriminatory ability of plasma BNP concentration to predict mortality was determined by the coordinates of the receiver operating characteristic (ROC) curve to obtain maximum sensitivity and minimal loss of specificity. The Kaplan-Meier method was used to analyze and plot the survival of groups with different increased levels of BNP. The log-rank test was used to compare differences between stratified groups. Statistical significance was defined as $p < 0.05$, and analysis was performed with the SPSS statistical software package (SPSS 17.0; SPSS Inc, Chicago, IL).

RESULTS

Patient characteristics and surgical procedure are presented in Table 1. The median BNP level (D0) for the entire population was 64 pg/mL (IQR, 171; mean, 172 $\pm$ 284) and showed a nonnormal distribution (Kolmogorov-Smirnov $p < 0.001$). The observed overall 30-day mortality rate was 1.5% (6/407). The mortality rate for each procedure studied was 1.1% (3/283) for isolated CABG surgery, 0% (0/45) for isolated AVR and isolated MVR (0/18), 4.4% (2/45) for AVR with concomitant CABG surgery, and 6.3% (1/16) for MVR with concomitant CABG. There was no significant trend toward an increase in 30-day mortality among patients in the higher quintiles ($p = 0.22$). The plasma BNP concentration of patients undergoing isolated valve surgery or valve and concomitant CABG surgery

Table 2. BNP Quintiles and Peri-/Postoperative Course

Quintile	1	2	3	4	5	p Value
N	88	78	80	79	82	
BNP (D0) (pg/mL)	1-19	20-43	44-98	99-240	>240	
Mean $\pm$ SD	12 $\pm$ 4	30 $\pm$ 6	69 $\pm$ 16	160 $\pm$ 42	590 $\pm$ 409	
Median (IQR)	11 (7)	29 (10)	68 (28)	155 (74)	442 (347)	
Min-max BNP (pg/mL)	5-19	20-43	44-99	100-238	240-2,200	
Perioperative MI	1 (1)	1 (1)	1 (1)	3 (4)	5 (6)	0.198
LCOS 48 h	1 (1)	8 (10)	7 (9)	13 (17)	24 (29)	<0.001
Dobutamine >48 h	0	5 (5)	4 (5)	6 (8)	17 (21)	<0.001
Norepinephrine >48 h	1 (1)	8 (10)	7 (9)	12 (15)	23 (28)	<0.001
Levosimendan (Simdax)	0	3 (4)	3 (4)	9 (11)	29 (35)	<0.001
IABP (postoperatively)	0	1 (1)	1 (1)	1 (1)	9 (11)	<0.001
30-day mortality	0	0	2 (3)	1 (1)	3 (4)	0.22
Postoperative AF	13 (15)	20 (26)	27 (34)	31 (39)	38 (46)	<0.001
OFB (L)	3.4 $\pm$ 1.2	3.4 $\pm$ 1.3	3.7 $\pm$ 1.7	3.9 $\pm$ 1.3	3.6 $\pm$ 2.2	0.29
Postoperative bank blood (U)	0.7 $\pm$ 1.5	1.1 $\pm$ 1.4	1.2 $\pm$ 1.7	2.1 $\pm$ 2.5	2.6 $\pm$ 3.5	<0.001
Postoperative FFP (median, IQR)	0 (0)	0 (1)	0 (2)	0 (0)	1.5 (7)	<0.001
Postoperative platelets (U) (median, IQR)	0 (0)	0 (0)	0 (0)	0 (0)	0 (1)	0.009
Creatinine (peak) (μmol/L)	78 $\pm$ 22	96 $\pm$ 45	100 $\pm$ 60	95 $\pm$ 40	119 $\pm$ 82	<0.001
Time on ventilator (h) (median, IQR)	5 (5)	7 (5)	6 (5)	9 (10)	8 (14)	<0.001
LOS ICU (h) (median, IQR)	21 (5)	22 (5)	22 (7)	23 (23)	27 (68)	<0.001
Valve surgery	22 (25)	19 (24)	18 (23)	30 (38)	35 (43)	0.012
Valve and CABG surgery	8 (9)	11 (14)	9 (11)	12 (15)	21 (26)	0.032

NOTE. Values are expressed as number (%), mean ($\pm$ standard deviation), or median (IQR); p value for difference between groups. Statistical method: 1-way analysis of variance.

Abbreviations: NYHA, New York Heart Association Classification; LVEF, left ventricular ejection fraction; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; PHT, pulmonary hypertension (p_{syst} >60 mmHg); LCOS, low coronary output syndrome; TnI, cardiac troponin I; OFB, operative fluid balance; IABP, intra-aortic balloon pump; LOS ICU, length of stay in the intensive care unit.

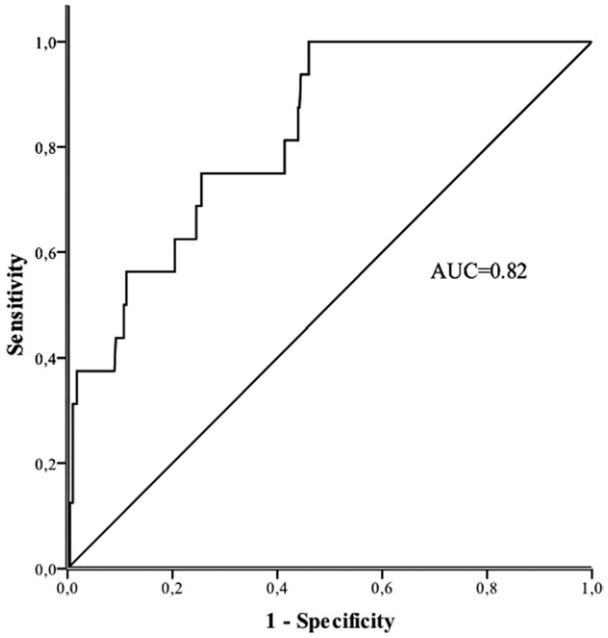

Fig 1. ROC curve for the BNP level on arrival at the ICU, which was used to predict mortality within 1 year of cardiac surgery (AUC = 0.823; 95% CI, 0.74-0.91).

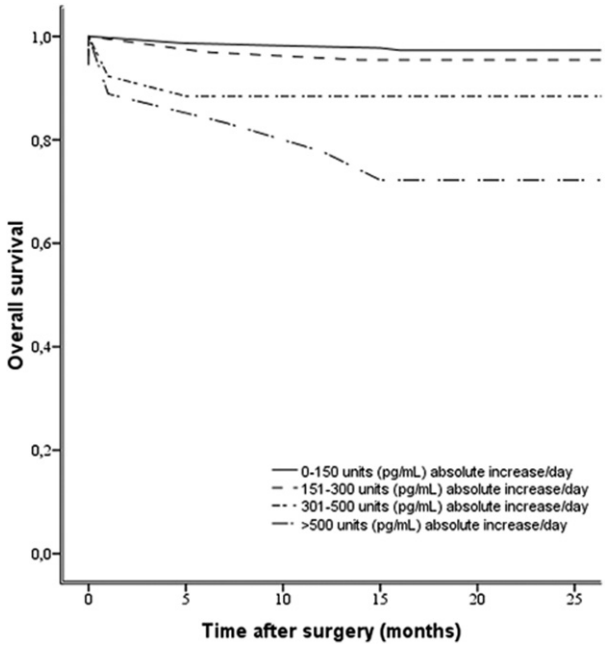

Fig 2. Results of Kaplan-Meier analysis showing long-term survival of patients stratified into 4 groups based on the increase in BNP level on the first postoperative day compared with that on admittance to the ICU (BNP 0-150 *v* 151-300, log-rank $p = 0.46$; BNP 0-150 *v* 301-500, log-rank $p = 0.015$; 1-150 *v* >500, log-rank $p < 0.001$).

were significantly higher ($p = 0.012$ and $p = 0.032$, respectively) than in those undergoing isolated CABG surgery. Patients in higher quintiles required a longer period of ventilation ($p < 0.001$) and prolonged inotropic support ($p < 0.001$). The relationship between adverse outcome and BNP is presented for each quintile in Table 2.

A cutoff BNP level (D0) of 88 pg/mL had a sensitivity of 81% and a specificity of 59% for predicting 1-year mortality (area under the curve [AUC] = 0.82; 95% confidence interval [CI] 0.74-0.91), whereas the mean plasma BNP concentration of 172 ± 284 pg/mL (median, 64; IQR, 172) had a sensitivity of 75% and a specificity of 74% (Fig 1). The plasma BNP concentration at D1 showed an AUC of 0.89 (95% CI, 0.83-0.95) for 1-year mortality. For patients undergoing isolated CABG surgery, a BNP (D0) level of 172 pg/mL had a sensitivity of 80% and a specificity of 79% in predicting 1-year mortality (AUC, 0.84; 95% CI, 0.75-0.93). For patients undergoing AVR, with or without concomitant CABG surgery, the BNP (D0) level of 172 pg/mL had a sensitivity of 60% and a specificity of 67% in predicting 1-year mortality (AUC, 0.75; 95% CI, 0.53-0.97). The number of patients undergoing MVR with or without concomitant CABG surgery was limited; however, the AUC for the prediction of 2-year mortality was 0.77 (95% CI, 0.53-1.0).

The mean increase in BNP level from D0 to D1 in 333 patients was 163 ± 213 pg/mL (increase in $\log_{10}$ BNP of 2.0 ± 0.5; median, 99; IQR, 135), whereas the remaining 74 patients showed a mean decrease in BNP of 73 ± 212 pg/mL (median, 4; IQR, 83). Kaplan-Meier analysis, presenting the overall survival in patients stratified into 4 groups based on the increase in BNP between admittance to the ICU and the first postoperative day (D1-D0), is shown in Figure 2 (BNP 0-150 *v* 151-300 pg/mL, log-rank $p = 0.46$; BNP 0-150 *v* 301-500 pg/mL, log-rank $p = 0.015$; BNP 1-150 *v* >500 pg/mL, log-rank $p < 0.001$). Prognostic factors for decreased long-term survival determined by Cox proportional hazards analysis are presented in Table 3. Because of the nonnormal distribution of plasma BNP concentration on arrival at the ICU, the absolute change between D0 and D1 was evaluated in a logarithmic fashion. Log_{10} of the absolute difference in BNP D0-D1 showed a hazard ratio of 7.3 for an increase of 10^x, where x represents the logarithmic difference in BNP concentration between admittance to the ICU and postoperative day 1.

DISCUSSION

The main finding of the present study was that an increase in BNP level during the first postoperative day is an independent predictor of late mortality after cardiac surgery. Of all the risk factors evaluated in the present study, an increasing value of $\log_{10}$ BNP showed the highest hazard ratio (7.3) for late mortality. Moreover, postoperative complications, especially prolonged requirement for inotropic support, were significantly more frequent in patients presenting with a high postoperative BNP on admittance to the ICU. The present results suggest that the postoperative BNP release pattern and changes reflect early and late clinical outcome.

Information concerning cardiac function is often desirable in the period after cardiac surgery because complex surgery in combination with prolonged CPB and insufficient myocardial protection could lead to postoperative deterioration of myocardial performance. Echocardiographic evaluation is an accessi-

Table 3. Cox Multivariate Proportional Hazards Regression Analysis of Prognostic Factors Influencing Long-term Survival After Cardiac Surgery

	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*p* Value	HR	95% CI	*p* Value
Age (y)*	1.1	1.04–1.15	0.001			
Age ordinal (per 10 years)	2.0	1.3–3.2	0.002	2.2	1.2–4.3	0.014
Female sex	1.1	0.46–2.64	0.83			
Atrial fibrillation	3.0	1.03–8.8	0.043			
NYHA III/IV	3.4	1.4–8.0	0.007			
Diabetes mellitus	1.7	0.7–4.0	0.21			
Recent MI	3.8	1.7–8.7	0.001			
Hemoglobin (g/L)	0.97	0.94–0.99	0.002			
COPD	3.0	1.1–8.0	0.028			
Creatinine (μmol/L)	1.01	1.006–1.018	<0.001	1.01	1.001–1.02	0.036
Ejection fraction <50%	1.2	0.5–2.8	0.71			
Ejection fraction <30%	5.1	2.3–11	<0.001			
PVD	4.4	1.9–9.9	<0.001			
Redo surgery	2.6	0.8–8.7	0.12			
Emergency surgery	4.0	1.6–10.1	0.003	4.4	1.4–14	0.014
Neurologic dysfunction preoperatively	3.7	0.9–16	0.077	6.6	1.1–39	0.037
Critical preoperative state	5.2	1.8–15	0.002			
IABP preoperatively	1.4	0.2–10	0.74			
Valve surgery	1.5	0.7–3.4	0.29			
Valve and CABG surgery	2.3	0.96–5.5	0.063			
BNP $\log_{10}$ absolute difference D1-D0	8.5	2.9–25	<0.001	7.3	1.8–29	0.005
BNP (D0) (pg/mL)*	1.002	1.001–1.002	<0.001			
Intraoperative bank blood transfusion	5.1	2–13	0.001			
EuroSCORE (logistic)	1.05	1.04–1.06	<0.001			
Higgins score	1.3	1.2–1.4	<0.001			
CPB (min)	1.01	1.004–1.02	<0.001			
Cross-clamping time (min)	1.006	0.99–1.02	0.26			

NOTE. There were no patients with the risk factors pulmonary hypertension or endocarditis among those who were deceased at follow-up.

Abbreviations: NYHA, New York Heart Association Classification; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; LCOS, low coronary output syndrome; TnI, cardiac troponin I; IABP, intra-aortic balloon pump; HR, hazard ratio.

*Not included in multivariate analysis.

ble and noninvasive method, but it might be technically challenging, leading to suboptimal image quality. Furthermore, the preoperative assessment of the left ventricular function might not reflect the postoperative ventricular performance because of myocardial stunning. Therefore, there is a need for a point-of-care method of analysis in the ICU setting. An elevated BNP per se may indicate postoperative heart failure and serve as a diagnostic tool for the early identification of patients at risk, allowing the instigation of appropriate therapeutic management.

B-type natriuretic peptides have a well-documented clinical value in providing powerful diagnostic as well as prognostic information. In addition to systolic and diastolic left ventricular dysfunction,[19] BNP is elevated in a broad spectrum of cardiovascular diseases, including acute coronary syndromes, valvular heart disease, acute and chronic right ventricular failure, and left and right ventricular hypertrophy secondary to arterial or pulmonary hypertension.[5,20-22] Therefore, BNP also may be of clinical value when identifying patients at risk of left ventricular impairment and increased mortality after cardiac surgery. However, understanding of the dynamics of BNP release after cardiac surgery remains unclear. Although previous studies have described the prognostic value of plasma BNP concentration after cardiac surgery, the focus has been on preoperative BNP levels before CPB.[23] Furthermore, the sample size has either been relatively small[10] or all male.[18] Morimoto et al[8] investigated the variation in plasma BNP concentration before and during CPB and showed that plasma concentrations of BNP become markedly elevated after cardiac surgery with CPB, reflecting the acute state of the left ventricle. In a study by Hutfless et al,[18] ROC curve analysis was performed to evaluate whether a postoperative increase to a maximum BNP could discriminate between survivors and nonsurvivors at 1 year. The authors reported an AUC of 0.76, but the potential confounding effects of pre- and intraoperative variables were not statistically evaluated. The results of the present study suggest that the intensity of neurohumoral activation, based on serial evaluation of plasma BNP concentration, can add prognostic information regardless of pre- or perioperative levels.

The postoperative release of BNP differed significantly among the surgical categories (Table 3). Plasma BNP concentration was significantly more elevated in patients undergoing combined surgery compared with patients undergoing isolated CABG or valve surgery, whereas CABG surgery was associated with the lowest postoperative plasma BNP concentration. The present findings are similar to those of a previous study by Berendes et al,[2] showing different secretion patterns of BNP after various kinds of cardiac surgery. In addition, the present

authors found that a prolonged length of stay in the ICU, the need for inotropic support (pharmacological and mechanical), and prolonged ventilation were more frequent in patients with elevated plasma BNP concentration on admittance to the ICU. The relation between elevated postoperative plasma BNP concentration and postoperative cardiac and respiratory complications may be explained by excess fluid and stunning of the myocardium.[2] The postoperative pattern of BNP secretion depends on the type of surgery, and the level of BNP also seems to be increased after prolonged surgical procedures.

Previous reports have suggested a threshold of 80 pg/mL for the diagnosis of preoperative heart failure,[24] whereas few studies have evaluated the clinically applicable BNP level for diagnostic guidance in the postoperative setting. Hutfless et al[18] showed that a preoperative plasma BNP concentration exceeding 385 pg/mL could indicate poor late survival. However, no multivariate analysis was performed in this relatively small, all-male population. Provenchere et al[3] suggested that a BNP level of 352 pg/mL, approximately 4 times higher than the threshold found in the present study, predicted late mortality. However, in their study, no discrimination was made between the type of surgery, and no multivariate analysis was performed. In the present study, the authors found that a BNP threshold of 88 pg/mL (D0) had the best discriminatory ability to predict 1-year mortality (AUC = 0.82). Berendes et al[10] previously have shown that patients undergoing CABG surgery show a peak increase in plasma BNP concentration during the first 24 postoperative hours. BNP is not stored in intracellular vesicles, and a delay in secretion pattern may explain the low threshold measured on admittance to the ICU in the present study. This low threshold may lead to an unnecessarily aggressive therapeutic approach and is therefore probably of limited clinical value. The discriminatory ability of BNP to predict 1-year mortality was fairly good for patients undergoing isolated CABG surgery (AUC = 0.85), but less favorable for patients after AVR (AUC = 0.76). The ROC analysis for patients having undergone MVR was not significant, probably because of the small number of patients evaluated.

This study is limited by its retrospective and observational design although BNP was sampled in a prospective fashion. Furthermore, a larger patient population, known preoperative plasma BNP concentration, and longer follow-up may provide relevant information.

In conclusion, the present study has shown that an increasing postoperative BNP level is associated with adverse postoperative outcome and is predictive of impaired long-term survival. Thus, sequential postoperative BNP monitoring may facilitate early identification of patients at increased risk of postoperative heart failure and late death. Therefore, the present authors support the clinical use of BNP as a supplement for predicting adverse cardiac outcome in order to optimize postoperative patient management.

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