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Log-transformed B-type natriuretic peptide as a prognostic predictor in patients undergoing cardiovascular surgery

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Abstract

Objective: This study was performed to explore the association between circulating B-type natriuretic peptide (BNP) and other mortality-related factors in patients undergoing cardiovascular surgery.

Methods: In this observational study, multilevel linear regression analysis and multilevel survival analysis were performed to measure the log-transformed BNP (lnBNP) value at four time points in 197 patients with 788 repeated data measurements. Effects of the interaction between the time points and the two intervention groups (cardiac surgery and vascular surgery) were also investigated. Six models were evaluated to identify the best fit for the data. Stata/MP® version 14.2 (Stata Corp., College Station, TX, USA) was used to analyze the two-level variance component model fitting.

Results: There were significant differences in the fixed-effect parameters of lnBNP, such as the time point, age, body mass index, emergency operation, prognostic nutritional index, and estimated glomerular filtration rate. According to the multilevel survival analysis for all-cause death and vascular death, lnBNP significantly differed and was a common prognostic marker.

Conclusion: As lnBNP increased by 1 point, all-cause death increased 2.07 times and vascular death increased 3.10 times. lnBNP is an important prognostic predictor and quantitative biochemical marker in patients undergoing cardiovascular surgery.

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Introduction

B-type natriuretic peptide (BNP) is a cardiac biomarker that is secreted mainly from the left ventricle in response to volume expansion.[1,2] BNP is reportedly a reliable marker for the diagnosis and prognosis in patients with heart failure.[3–5]

Some studies have shown that an elevated postoperative BNP concentration is independently associated with postoperative cardiovascular complications.[6] The European Society of Cardiology and European Society of Anaesthesiology guidelines for preoperative cardiac risk assessment have recommended consideration of preoperative BNP measurement in patients undergoing high-risk noncardiac surgery.[7] Cagini et al.[8] reported that postoperative BNP elevation is the strongest independent predictor of cardiopulmonary complications after thoracic surgery. Mitchell and Webb[9] reported that preoperative and postoperative measurements of BNP can help to predict postoperative cardiac dysfunction and adverse outcomes in patients undergoing cardiac surgery. Several reports have revealed that the BNP level is an important biomarker in surgery; however, a limitation of BNP is the skewness of its distribution.[10,11] The BNP value must be log-transformed before analysis to achieve a normal distribution. However, few reports have focused on the natural logarithmic transformation of BNP (lnBNP) values in patients undergoing cardiovascular surgery. Therefore, in this study, we examined postoperative survival according to the lnBNP values, physiological findings, nutritional status, and blood biochemistry parameters of patients undergoing cardiovascular surgery.

Materials and methods

Data source

Patients who underwent cardiac surgery or vascular surgery from 2009 to 2017 were included in this observational study at Kanazawa Medical University Himi Municipal Hospital. Measurements were recorded at four time points: admission, discharge, 1 month after discharge, and >1 month after discharge. Measurements soon after surgery were excluded to reduce the effect of the surgical intervention on the BNP level. The timing of all-cause death and vascular death was examined. The anonymity of all patients was maintained, and the study was conducted in accordance with the principles of the Declaration of Helsinki. This study protocol was approved by the Ethics Committee of Kanazawa Medical University Himi Municipal Hospital, Toyama Prefecture, and written informed consent was obtained from each patient (approval number 102).

Study variables

We examined the physiological findings, medical history, nutritional status, and blood biochemistry parameters of patients who underwent cardiac or vascular surgery. Each physiological finding, nutritional

status, and blood biochemistry parameter was measured at the four above-mentioned time points. The patients were divided into two groups: those who underwent cardiac surgery that required cardiopulmonary bypass and those who underwent vascular surgery (abdominal aortic aneurysm open repair, endovascular aneurysm repair, or thoracic endovascular aortic repair). The nutritional status was assessed using the prognostic nutritional index (PNI), which was calculated using the serum albumin and total lymphocyte count as follows: $\text{PNI} = (10 \times \text{albumin}) + (0.005 \times \text{total lymphocyte count})$.[12] We used the lnBNP values to meet the demands of a normal distribution.

Statistical analysis

Continuous variables between the two groups (cardiac surgery and vascular surgery) were compared using Student's t-test and the Wilcoxon rank sum test. Categorical variables were compared using Fisher's exact two-tailed test (Table 1). Because the data were multilevel, linear modeling was used to assess the association between the response variable (lnBNP) and explanatory variables (fixed-effect parameters, random-effect parameters (patient-level variables)). The random effect was considered a random parameter of both slope and intercept. Multilevel linear regression analysis was used to identify the marker that might be associated with lnBNP, namely right cardiac failure.

The following equation was used to assess the random effect on time:

$$\text{lnBNP} = \beta_0 + \beta_1 \text{time}_{ij} + \mu_{0j} + \mu_{1j}\text{time}_{ij} + \varepsilon_{ij},$$

where i = one of the four time points (admission, discharge, 1 month after discharge, or >1 month after discharge); j = 1, 2, … 197 patients; and β_0 = a constant term.

The random effects, μ_{0j} and μ_{1j}, indicate the random intercept and random slope, respectively, and ε_{ij} denotes the overall error term. Six models were used to determine the best fit for the data (Table 2). We calculated the proportional change in variance (PCV) compared with the change in the null model (model 0) as the benchmark. We used an identity matrix to model the within-patient error correlation structure because of the two-level variance component model fitting. Interpatient reliability was estimated using an intraclass correlation coefficient (ICC). The models were assessed for the accuracy of the PCV of the predictors, Akaike's information criterion, and the Bayesian information criterion.

Model 1 was the same as the null model with the addition of the time point, patient group, interaction, and findings on admission as covariates to account for compositional differences between patients. Model 2 was the same as Model 1 with the addition of the medical history to account for background differences between patients. Model 3 was the same as Model 2 with the addition of physiological findings to account for measurable status differences between patients.

Model 4 was the same as Model 3 with the addition of the PNI to account for nutritional status differences between patients. Model 5 was the same as Model 4 with the addition of blood biochemistry parameters to account for blood status differences between patients. A variable in the same dataset was centered by subtracting patient means that were designated "group mean centering."

The end of follow-up was defined as either the day of patient death or the last day that the patient was known to be alive.

While it is reasonable to assume the independence of patients, we would not want to assume that the timing of death within each patient is independent. The models were created to assess the correlation by assuming that death was the result of a patient-level effect. We estimated the

Table 1. Baseline characteristics of patients undergoing the two interventions in the present study

Variables		Cardiac surgery			Vascular surgery			P-value[*1]
		Patients (n)	Mean or %	SD	Patients (n)	Mean or %	SD	
Findings on admission								
Baseline age	Years	127	71.0	10.7	70	77.8	9.1	<0.001
Sex	Male, n, %	78	61.4		53	75.7		0.042
Smoking	Yes, n, %	58	45.7		49	70.0		0.001
Emergency operation	Yes, n, %	23	18.1		6	8.6		0.07
Physiological findings								
Baseline body mass index	kg/m^2	126	22.8	3.5	68	22.4	3.8	0.43
Systolic blood pressure	mmHg	127	126.0	21.1	70	124.1	17.4	0.515
Diastolic blood pressure	mmHg	127	71.6	14.3	70	68.9	12.7	0.193
Pulse rate	bpm	127	77.6	14.5	70	71.4	11.3	0.002
Cardiothoracic ratio	%	127	57.9	8.0	69	52.8	5.5	<0.001
Medical history								
Hypertension	Yes, n, %	86	67.7		63	90.0		0.002
Dyslipidemia	Yes, n, %	43	34.1		29	41.4		0.31
Diabetes mellitus	Yes, n, %	37	29.1		15	21.4		0.24
Cardiac disorder	Yes, n, %	57	44.9		26	37.1		0.29
Respiratory dysfunction	Yes, n, %	7	5.5		18	25.7		<0.001
Digestive disorder	Yes, n, %	18	14.3		8	11.4		0.57
Kidney disorder	Yes, n, %	35	27.6		21	30.0		0.72
Cerebrovascular disease	n, %	30	23.8		23	32.9		0.17
Nutritional status								
Prognostic nutritional index		121	45.9	6.8	66	44.8	7.4	0.34
Blood biochemistry								
Estimated glomerular filtration rate	$mL/min/1.73m^2$	126	61.1	26.1	70	59.8	24.4	0.73
Aspartate aminotransferase	IU/L	127	27.8	25.9	70	20.9	8.3	0.032
Alanine aminotransferase	IU/L	127	23.6	29.3	70	17.9	11.7	0.12
Alkaline phosphatase	IU/L	117	256.1	88.8	67	262.9	91.6	0.62
γ-Guanosine triphosphate	IU/L	127	42.3	39.9	69	32.1	27.1	0.06
Total bilirubin	mg/dL	124	0.71	0.48	69	0.60	0.38	0.09
Total protein	g/dL	126	6.8	0.6	69	6.9	0.7	0.39
Median BNP (IQR)	pg/mL	127	124.3	45.8–379.4[†]	70	71.5	39.3–189.4[†]	<0.001[*2]
Log-transformed BNP	l	127	4.9	1.5	70	4.4	1.1	0.025
Inverse-transformed BNP as above	pg/mL	127	128.0	99.5–164.7[‡]	70	79.0	60.6–103.1[‡]	

SD, standard deviation; BNP, B-type natriuretic peptide; IQR, interquartile range.
Comparison of patients treated with cardiac surgery with those treated with vascular surgery was performed by *[1]the paired t-test or Fisher's exact two-tailed test or *[2]the Wilcoxon rank sum test. [†]25% to 75% percentile, [‡]95% confidence intervals

hazard ratio (HR) and standard error for all-cause death and vascular death by applying a multilevel parametric proportional hazard regression model with a Weibull distribution. A two-sided P-value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed using Stata/MP® version 14.2 (Stata Corp., College Station, TX, USA).

Results

In total, 197 patients were included in this study. The patients were categorized into

Table 2. Estimated log-transformed BNP from multilevel linear regression

		Model 0		Model 1		Model 2		Model 3		Model 4		Model 5	
		Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE
Fixed-effect parameters (2a)													
Time point	Admission			Reference		Reference		Reference		Reference		Reference	
	Discharge			−0.27	0.09**	−0.26	0.09**	−0.34	0.10**	−0.43	0.11**	−0.39	0.11**
	1 month after discharge			−0.29	0.10**	−0.26	0.10**	−0.24	0.11**	−0.24	0.11**	−0.22	0.11**
	>1 month after discharge			0.09	0.12	0.11	0.12	0.10	0.12	0.10	0.12	0.05	0.12
Intervention groups	Vascular surgery			−0.39	0.18**	−0.34	0.17*	−0.26	0.16	−0.23	0.17	−0.21	0.17
Interaction	Admission × vascular surgery			Reference		Reference		Reference		Reference		Reference	
	Discharge × vascular surgery			−0.02	0.15	−0.03	0.15	−0.13	0.16	−0.17	0.16	−0.24	0.17
	1 month × vascular surgery			0.42	0.17**	0.40	0.17*	0.28	0.17	0.27	0.17	0.21	0.18
	>1 month × vascular surgery			0.03	0.19	0.004	0.19	−0.01	0.19	−0.06	0.19	−0.10	0.19
Findings on admission													
Baseline age	1 year			0.16	0.04**	0.13	0.04**	0.11	0.03**	0.10	0.03**	0.09	0.03**
Sex	Female			0.30	0.21	0.33	0.19*	0.09	0.18	0.08	0.18	0.04	0.18
Smoking	Yes			0.14	0.20	−0.06	0.18	−0.08	0.17	−0.09	0.16	−0.11	0.16
Emergency operation	Yes			0.87	0.22**	0.78	0.20**	0.55	0.20**	0.51	0.20**	0.50	0.19**
Medical history													
Hypertension	Yes					−0.13	0.17	−0.07	0.16	−0.08	0.15	−0.08	0.15
Dyslipidemia	Yes					−0.19	0.15	−0.10	0.14	−0.09	0.14	−0.07	0.14
Diabetes mellitus	Yes					0.21	0.17	0.14	0.16	0.17	0.15	0.18	0.15
Cardiac disorder	Yes					0.44	0.15**	0.36	0.14**	0.35	0.13**	0.33	0.13**
Respiratory dysfunction	Yes					0.48	0.22**	0.39	0.20**	0.42	0.19**	0.48	0.19**
Digestive disorder	Yes					0.17	0.20	0.17	0.18	0.17	0.18	0.15	0.18
Kidney disorder	Yes					0.59	0.16**	0.60	0.15**	0.55	0.14**	0.44	0.16**
Cerebrovascular disease	Yes					0.16	0.16	0.02	0.15	0.02	0.14	0.03	0.14
Physiological findings													
Body mass index	1 kg/m^2							−0.06	0.02**	−0.05	0.02**	−0.05	0.02**
Systolic blood pressure	5 mmHg							0.02	0.02	0.02	0.02	0.03	0.02
Pulse rate	10 bpm							−0.001	0.006	−0.001	0.006	−0.003	0.006
Cardiothoracic ratio	5%							0.30	0.04**	0.28	0.04**	0.28	0.04**
Nutritional status													
Prognostic nutritional index										−0.08	0.03**	−0.07	0.03**

(continued)

Table 2. Continued

		Model 0		Model 1		Model 2		Model 3		Model 4		Model 5	
		Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE	Coeff.	SE
Blood biochemistry													
Estimated glomerular filtration rate	10 mL/min/1.73 m^2											−0.039	0.020**
Aspartate aminotransferase	10 IU/L											0.004	0.005
Alkaline phosphatase	10 IU/L											0.0001	0.0033
γ-Guanosine triphosphate	10 IU/L											0.008	0.008
Total bilirubin	1 mg/dl											−0.012	0.063
Intercept		4.57	0.08**	4.21	0.36**	3.87	0.36**	4.23	0.33**	4.28	0.33**	4.38	0.34**
Random-effect parameters (2b)													
Individual-level variance	Slope variance	0.034	0.013	0.041	0.012	0.036	0.011	0.020	0.009	0.015	0.009	0.008	0.009
	Intercept variance	1.031	0.137	0.784	0.113	0.566	0.090	0.443	0.074	0.426	0.073	0.435	0.073
	Residual variance	0.548	0.042	0.495	0.038	0.507	0.039	0.487	0.037	0.501	0.039	0.505	0.040
Z-score		7.5		6.9		6.3		5.9		5.8		6.0	
Intraclass correlation coefficient		65.3%		61.3%		52.7%		47.6%		46.0%		46.3%	
Proportional changes in variance (%)		–		24.0%		45.2%		57.1%		58.7%		57.8%	
Model fit statistics (2c)													
Log likelihood		−1021.9		−982.0		−946.5		−828.9		−813.2		−784.3	
AIC		2051.8		1994.1		1938.9		1711.8		1682.4		1634.6	
BIC		2070.0		2062.5		2043.4		1832.1		1806.6		1780.0	

BNP, B-type natriuretic peptide; Coeff., coefficient; SE, standard error; AIC, Akaike's information criterion; BIC, Bayesian information criterion
**$P < 0.05$, *$P < 0.10$

two groups based on the type of surgery: cardiac surgery requiring cardiopulmonary bypass (n = 127) and vascular surgery (abdominal aortic aneurysm open repair, n = 47; endovascular aneurysm repair, n = 19; and thoracic endovascular aortic repair, n = 4) (Table 1). We found statistically significant differences at baseline in age, sex, smoking status, pulse rate, cardiothoracic ratio, history of hypertension and respiratory dysfunction, or aspartate aminotransferase and lnBNP levels. When considering Models 1 to 5 in greater detail, the following parameters were significantly associated with lnBNP: the time point at discharge, the time point at 1 month after discharge, baseline age, emergency operation, history of cardiac disorder and respiratory dysfunction, kidney disorder, physiological findings of body mass index and cardiothoracic ratio, PNI, and estimated glomerular filtration rate. Stable coefficients were established regardless of the model (Table 2a). Models 2 to 5 showed no significant correlation between the extent of lnBNP and the intervention groups.

All Z-scores were >2, and significant differences were found between the individual data. Additionally, both the variance of intercept (1.031) and the variance of slope (0.034) were significant at an individual level, as shown in Table 2, indicating notable variance between individuals. Furthermore, the higher the ICC, the greater the influence on intraindividual variability. The ICC of Model 0 was relatively high at 65.3%, as shown in Table 2; the extent of lnBNP was dependent upon the patients. In Models 1-5, the ICC tended to be lower than that in Model 0 but retained a more than relatively high score of 45.0%. The PCV in Models 1 to 5 improved from 24.0% to 58.7%, and the data suggested that about 60% of the variance between patients (the cause of interobserver variability) could explain the explanatory markers of Model 5 (Table 2b). The PCV in Model 4 was the highest (58.7%) (Table 2b), and the fitting values of the variance error in Model 5 were the lowest (log likelihood, −784.3; Akaike's information criterion, 1634.6; Bayesian information criterion, 1780.0) (Table 2c).

We performed a multilevel survival analysis including all-cause and vascular death to obtain a model that included significant markers of a multilevel univariate analysis for validation of Model 5 in Table 2. We further evaluated the association between the developmental events of death and the significant markers from the multilevel univariate survival analysis results (baseline age, smoking, emergency operation, kidney disorder, body mass index, diastolic blood pressure, cardiothoracic ratio, PNI, estimated glomerular filtration rate, alanine aminotransferase, alkaline phosphatase, γ-guanosine triphosphate, total bilirubin, and lnBNP). The multivariate multilevel survival analysis results revealed significant differences in the smoking status (HR = 4.87), emergency operation (HR = 8.26), PNI (HR = 1.46 per 1-point increase), and lnBNP (HR = 2.07 per 1-point increase) in the model of all-cause death and in only lnBNP (HR = 3.10 per 1-point increase) in the model of vascular death (Table 3).

Discussion

In this study, we observationally examined postoperative survival according to the lnBNP values, physiological findings, nutritional status, and blood biochemistry parameters of patients undergoing cardiovascular surgery and found that lnBNP is a prognostic predictor in these patients. Moreover, the multilevel survival analysis revealed that the lnBNP value was a significant prognostic factor for all-cause death and vascular death. Our findings suggest that the lnBNP value could be a very

Table 3. Multilevel analysis of two outcomes related to survival data

		Univariate analysis				Multivariate analysis (n = 188)					
		All-cause death				All-cause death			Vascular death		
Variable	Reference or per increased	Patients (n)	HR	SE	P-value	HR	SE	P-value	HR	SE	P-value
Strategy for therapeutic intervention											
Vascular surgery	Cardiac surgery	196	0.60	0.30	0.31	2.02	1.32	0.28	1.54	1.45	0.65
Findings on admission											
Sex	Male	196	0.57	0.28	0.26						
Baseline age	5 years	196	1.28	0.15	0.028	1.27	0.21	0.15	1.01	0.24	0.98
Smoking	Yes	196	2.48	1.14	0.047	4.87	2.98	0.009	5.77	5.20	0.052
Emergency operation	Yes	196	46.5	24.5	<0.001	8.26	6.34	0.006	7.33	7.99	0.07
Medical history											
Hypertension	Yes	196	2.75	1.55	0.07						
Dyslipidemia	Yes	195	0.75	0.35	0.54						
Diabetes mellitus	Yes	196	1.51	0.74	0.40						
Cardiac disorder	Yes	196	1.23	0.56	0.64						
Respiratory dysfunction	Yes	196	1.10	0.81	0.90						
Digestive disorder	Yes	195	0.53	0.39	0.39						
Kidney disorder	Yes	196	7.13	3.32	<0.001	1.50	0.93	0.52	1.96	1.79	0.46
Cerebrovascular disease	Yes	195	0.88	0.47	0.81						
Physiological findings											
Body mass index	1 kg/m^2	193	0.85	0.04	0.001	1.01	0.07	0.87	1.02	0.11	0.89
Systolic blood pressure	10 mmHg	193	0.98	0.12	0.84						
Diastolic blood pressure	10 mmHg	193	0.57	0.10	0.001	1.16	0.28	0.55	0.99	0.36	0.99
Pulse rate	5 bpm	193	1.01	0.01	0.59						
Cardiothoracic ratio	5%	195	1.43	0.15	0.001	1.00	0.18	0.98	1.16	0.27	0.52
Nutritional status											
Prognostic nutritional index		193	2.02	0.37	<0.001	1.46	0.28	0.046	1.45	0.43	0.21
Blood biochemistry											
Estimated glomerular filtration rate	10 mL/min/ $1.73m^2$	194	0.66	0.06	<0.001	1.03	0.13	0.83	1.14	0.18	0.41
Aspartate aminotransferase	10 IU/L	195	1.02	0.00	<0.001						
Alanine aminotransferase	10 IU/L	195	1.03	0.01	0.002	0.99	0.01	0.35	0.94	0.07	0.41
Alkaline phosphatase	10 IU/L	193	1.02	0.00	<0.001	1.01	0.01	0.53	1.02	0.02	0.33
γ-Guanosine triphosphate	10 IU/L	195	1.04	0.01	<0.001	1.02	0.04	0.67	1.00	0.07	0.98
Total bilirubin	1 mg/dl	195	1.33	0.07	<0.001	0.73	0.12	0.058	0.59	0.17	0.073
Total protein	1 g/dl	195	0.21	0.04	<0.001						
Log-transformed BNP	1	196	1.98	0.21	<0.001	2.07	0.52	0.004	3.10	1.20	0.004

HR, hazard ratio; SE, standard error; BNP, B-type natriuretic peptide

important prognostic predictor in patients undergoing cardiovascular surgery. This study was a multilevel analysis in which four iterative measurements were considered and five models were examined. Compared with the null model, Models 3 to 5 were able to improve the error between individuals by approximately 60%. This allowed for highly accurate prediction, which is considered clinically beneficial. This study is the first to involve conduction of a multilevel analysis using the lnBNP value and surgical operation.

BNP is the gold standard marker in the diagnosis and prognosis of heart failure.[3,5,13] However, some studies have showed that the BNP level might be limited by its skewed distribution.[10,11] Therefore, we used the natural lnBNP to meet the demands of a normal distribution.

BNP is a strong independent predictor of perioperative and long-term cardiovascular and cardiopulmonary complications following noncardiac surgical procedures.[6,8,14] The postoperative serum concentration of BNP is an independent predictor of mortality in patients undergoing cardiac surgery.[15] In the present study, lnBNP was similarly predictive of the patients' prognosis. As lnBNP increased by 1 point, all-cause death increased by 2.07 times and vascular death increased by 3.10 times; lnBNP was especially associated with a high risk of all-cause death and vascular death. Additionally, in patients undergoing emergency surgery, all-cause death and vascular death represent a risk of onset of 8 to 9 times. This suggests that postoperative follow-up is very important in patients who have undergone an emergency operation.

The prognostic factors in cardiac surgery are troponin and BNP.[16,17] The survival analysis in the present study showed that lnBNP, smoking, emergency operation, and PNI were prognostic factors in patients undergoing cardiovascular surgery. Smoking and an emergency operation have been reported as risk factors for surgery[18–20] and regulated prognostic factors; these results are consistent with the findings of our study, in which they were also prognostic factors. The PNI was also recently shown to be a predictive marker for postoperative complications in patients with some malignant tumours.[21–23] Our findings suggest that the PNI is a significant prognostic factor for all-cause death in patients undergoing cardiovascular surgery. The present study is likely to be the first to report this finding in patients undergoing cardiovascular surgery.

The lnBNP value was significantly related to laboratory variables reflective of disease severity and to systolic and diastolic myocardial dysfunction, suggesting that the lnBNP concentration may be a quantitative biomarker of myocarditis in patients with Kawasaki disease.[11] Yang and Bao[24] reported that lnBNP was an independent determinant of pulmonary systolic artery pressure. Mentias et al.[25] reported that a higher lnBNP level was significantly associated with increased mortality in asymptomatic patients with mitral regurgitation and a preserved left ventricular ejection fraction. Oikawa et al.[26] reported that multiplying lnBNP and the ratio of the mitral inflow early- and late-diastolic filling velocities is a useful parameter for detecting elevated pulmonary capillary wedge pressure regardless of the left ventricular ejection fraction. Zhou et al.[27] reported that lnBNP is an independent risk factor for contrast-induced acute kidney injury in patients with acute myocardial infarction. Therefore, we suggest that the lnBNP level is a useful marker that is simple and easy to implement in the clinical setting, not only in patients undergoing surgery but also in those with heart disease. The clinical value of lnBNP for various disease is expected to be revealed in future research.

This study has some limitations. First, this was an observational study. Second, the observation period was short and the number of patients was small. However, this study is the first multilevel analysis among longitudinal observational studies in cardiovascular surgery. Third, this study had biases due to the patients' backgrounds. Therefore, further studies with longer observation periods and larger sample sizes but without bias due to the patients' backgrounds are necessary. Multicenter research is needed to validate these findings. Fourth, a preoperative

serum BNP assay was not performed in this study because of the biases resulting from the patients' backgrounds. Finally, we did not analyze cardiac surgery and vascular surgery separately and did not perform non-discrimination between valve surgery and myocardial revascularization in cardiac surgery. Redfors et al.[28] reported that in the EXCEL trial, an elevated baseline BNP level in patients with left main coronary artery disease undergoing revascularization was independently associated with long-term mortality. Therefore, each type of surgery should be separately analyzed in future studies.

In conclusion, as the lnBNP level increased by 1 point, all-cause death increased 2.07 times and vascular death increased 3.10 times. The lnBNP value was correlated with survival. Therefore, lnBNP is an important prognostic predictor and quantitative biochemical marker in patients undergoing cardiovascular surgery.

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