Original Article

Prognostic role of NT-proBNP (N-terminal pro-brain natriuretic peptide) in patients with non-ST-segment elevation myocardial infarction: analysis based on propensity score matching and weighting

Ho Sun Shon[1], Jang Whan Bae[2], Kyoung Ok Kim[3], Eun Jong Cha[4], Kyung Ah Kim[4]*

[1]*Medical Research Institute, School of Medicine, Chungbuk National University, Cheongju 28644, Korea*
[2]*Department of Internal Medicine, College of Medicine, Chungbuk National University, Cheongju 28644, Korea*
[3]*Department of Nursing, Woosong College, Daejeon 34606, Korea*
[4]*Department of Biomedical Engineering, School of Medicine, Chungbuk National University, Cheongju 28644, Korea*

Recently, N-terminal pro-brain natriuretic peptide (NT-proBNP) has been widely used in the areas of diagnosis, monitoring treatment efficiency, and prognosis for various heart diseases, especially heart failure (HF). In this paper, we try to estimate the prognostic significance of NT-proBNP as a risk evaluation marker in Non-ST-segment Elevation Myocardial Infarction (NSTEMI) patients. We selected NSTEMI patients who underwent percutaneous coronary intervention (PCI) primarily using a drug-eluting stent within 24 h after the onset of chest pain. We compared incidences of major adverse cardiac events (MACE) including death, myocardial infarction (MI), stent thrombosis (ST), and target vessel revascularization (TVR) in two patient groups according to a high or low serum concentration of NT-proBNP, which was measured in the emergency room (ER). We intend to minimize selection bias selecting comparing groups, considering covariate of observed variables together using propensity score matching (PSM) and propensity score weighting (PSW) based on propensity score (PS) to control the difference in baseline characteristics between high- and low NT-proBNP groups. We found that as the log NT-proBNP value increases by 1 through a hazard function of COX's analysis, the risk of MACE increases by 1.312 times. This result indicated that the NT-proBNP level on ER admission can be used as a significant prognostic indicator to estimate 1 year of MACE in NSTEMI patients who were treated with PCI within 24 h after the onset of chest pain.

Key words: major adverse cardiac events, myocardial infarction, propensity score matching, propensity score weighting, NT-proBNP

Introduction

With the westernization of lifestyles, increase in the elderly population, and steep increase in the prevalence of hypertension and diabetes mellitus, incidences of ischemic heart disease are steadily increasing. In addition, because of the increased proportion of the elderly population with acute myocardial infarction (AMI), the mortality rate of this disease is also increasing. National statistics for Korea showed that the in-hospital mortality of AMI was approximately 4.5% in 2014, and an additional 5.5% of patients died within 1 year after hospital discharge. Acute coronary syndrome involves an unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). All three disease entities have a similar pathomechanism: unstable atherosclerotic plaque rupture and its associated thrombus generation in the coronary artery. Recently, the proportion of NSTEMI in AMI has been continuously increasing and was found to be approximately 50% in acute MI cases, especially in developed countries. Much data support the benefits of a timely fashioned primary revascularization for STEMI. Several types of prognostic factors have already been discussed, including rapid revascularization, Killip classification, and thrombolysis in myocardial infarction (TIMI) before percutaneous coronary intervention (PCI). However, a useful single prognostic factor that can be translated into determining the necessity of urgent revascularization for NSTEMI is still under investigation. Some multifactorial laboratories and clinical decision criteria have been developed to support the efficacy of urgent revascularization, but a useful single prognostic factor is still ambiguous for NSTEMI [1-5]. N-terminal pro-brain natriuretic

*Corresponding author: Kyung Ah Kim

Department of Biomedical Engineering, School of Medicine, Chungbuk National University, Cheongju 28644, Korea
Tel: +82-43-261-2852, Fax: +82-43-273-0848, E-mail: kimka@chungbuk.ac.kr

peptide (NT-proBNP) is secreted by an abnormal mechanical stretch in a ventricle, which increases the blood level of NT-proBNP for heart failure (HF). The blood level of NT-proBNP correlates well with the severity of systolic dysfunction of the left ventricle. A high level of NT-proBNP during treatment indicates a bad long-term prognosis for HF. NT-proBNP is a very useful biomarker for an initial diagnosis of HF. It predicts a short or long-term prognosis and determines the initial response and efficiency of treatment in HF patients [6, 7]. The value of NT-proBNP may act as an important diagnostic factor in a prospective multicenter cohort of patients hospitalized with a diagnosis of acute HF [8]. NT-proBNP has affected patients with adult congenital heart disease and plays an important role in patient management and monitoring [9]. It is also associated with cardiac arrest in infants and children younger than 3 years with heart failure due to congenital heart disease and myocardial infarction [10].

Therefore, concerns about treatment for NSTEMI patients have been increasing. In particular, an early invasive strategy with PCI for high-risk patients is known to be better than a conservative therapy method. According to the guidelines of the American College of Cardiology/American Heart Association (ACC/AHA), an early invasive strategy has been presented for high-risk NSTEMI patients. This early invasive strategy suggests performing PCI within 48 h after the onset of chest pain in NSTEMI patients. Recently, prompt treatment within 12 or 24 h has been reported to be effective at protecting the myocardium and producing a better prognosis for NSTEMI. The clinical significance of NT-proBNP in NSTEMI when treated with an early invasive strategy is still ambiguous. Therefore, we tried to find the diagnostic significance of NT-proBNP in NSTEMI patients who have undergone an early invasive strategy by using the Korean Working Group Myocardial Infarction (KorMI) database [11-19].

Some NSTEMI patients face as much danger as STEMI patients. In this study, we tried to use the value of NT-proBNP as a way to identify a small number of such patients in advance and test the role of NT-proBNP as an evaluation index that can affect the diagnosis of patients. We divided the NT-proBNP measurements into two groups and matched the variables that required adjustment by using propensity scores (PSs). We matched the variables by using propensity score matching (PSM) and propensity score weighting (PSW) and conducted a survival analysis for major adverse cardiac events (MACEs) and death according to the NT-proBNP level.

Population and Methods

Study Population

KorMI registration was initiated to find the clinical characteristics, treatment methods, and in-hospital and long-term prognoses of Korean AMI patients from 2005. This was conducted as a memorial project for the 50th-year anniversary of the Korean Society of Cardiology [20]. The KorMI registry is the second wave of registration for the KAMIR project, which operated from 2008 to 2013. The project has registered 15,533 AMI patients, including 8,382 STEMI patients and 6,711 NSTEMI patients. NSTEMI patients who underwent PCI mainly with a drug-eluting stent within 24 h after the onset of chest pain were selected from the KorMI registry and analyzed. Figure 1 shows the entire sampling procedure for the study population. First, the data were classified into 8,382 (55.5%) STEMI, 6,711 (44.5%) NSTEMI, and 440 missing values. Next, the data were classified into 4,916 (76.2%) with pain, 1,539 (23.8%) with no pain, and 256 missing values. Next, we classified the data into whether the patients received PCI within 24 h. The results showed that 2,411 (65.8%) of PCI treatments were within 24 h,
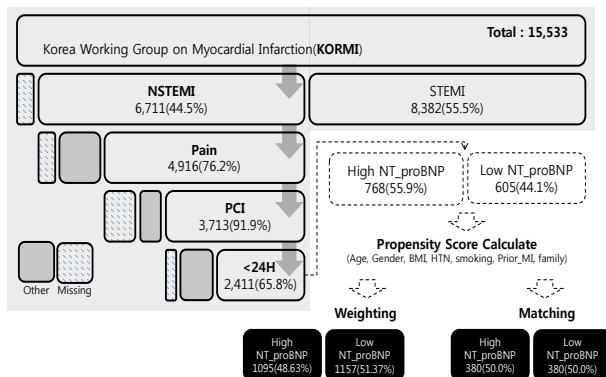

Fig. 1. Sampling procedure for the study population of NSTEMI patients.
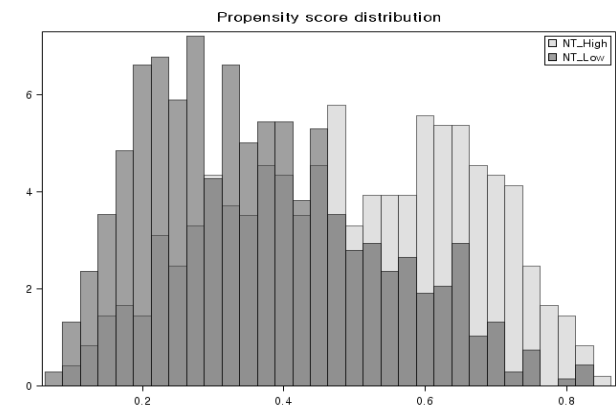

Fig. 2. Propensity score distribution of log (NT-proBNP) in two groups (high NT-proBNP & low NT-proBNP value).

1,252 (34.2%) were after 24 h, and 50 missing values. We extracted data by using two methods with PSs for the data that needed revision.

Analysis Methods

Continuous variables were expressed as the mean ± standard deviation, and categorical variables were expressed as a number and percentage. SAS ver 9.3 was used for the statistical analysis [21]. Observation studies tend to have a selection bias by their nature. In order to minimize such selection bias, confounding variables should be controlled using a matching or statistical adjustment method. When NT-proBNP, which was the marker of the study subjects, is divided into two groups, there can be a bias that leans toward one side. To resolve such an imbalance, this study used PSs. Because various variables influence the calculation of a PS, independent variables should be adjusted to test the effect of the NT-proBNP marker itself [22]. There are various ways of adjustment; when there are several variables, PS is an effective approach. PSM reduces the number of samples in each group but corrects variables better, while PSW does not correct as well as PSM but includes all of the data in analysis. In this research, we compared and analyzed the data by using PSM and PSW. These methods are based on PS and adjust the variables of the biomarker NT-proBNP. The PS represents the probability adjusted to compare two groups (e.g., therapy group vs. control group) when considering several variables observed for a subject. The PS is defined as the conditional probability for the treatment group given covariates that can be observed for the treatment group and control group. The PS is given by

$$PS = Pr(Z_i | X_i = x_i) \quad (1)$$

The PSM method is suitable when there are many control groups in contrast to a small number of treatment groups. The PS is calculated, and subjects are matched with PS values nearest to the treatment and control groups. This method is repeated until all of the treatment groups are matched. We applied the following methods. Transposing the log value of NT-proBNP forms a good normal distribution and produces quantiles such as Q1 4.4, Q2 5.7, and Q3 6.9. We divided the log value of NT-proBNP into two groups by using an arbitrary value of 6, which was very close to the median value of 5.7. Thus, we classified subjects with log (NT-proBNP) greater than 6 as the high group and subjects with log (NT-proBNP) less than 6 as the low group. To control independent variables, we matched the PSs. To verify the value of the biomarker NT-proBNP, the variables used for the PS were the age, gender, BMI, hypertension, hyperlipidemia, smoking, prior MI, and family history of cardiovascular disease.

Next, the PSW method was used. This is an estimation technique that gives weights by using the inverse of the PS value. This method is called inverse probability weighting (IPW) and can compare more than two groups. The weight of each group was defined as follows in Equations (2) and (3). To apply PSW, we classified the group with high NT-proBNP values as the treatment group and the group with low values as the control group. Then, we weighted each group [23].

$$W_t = 1/PS \text{, for treatment group} \quad (2)$$
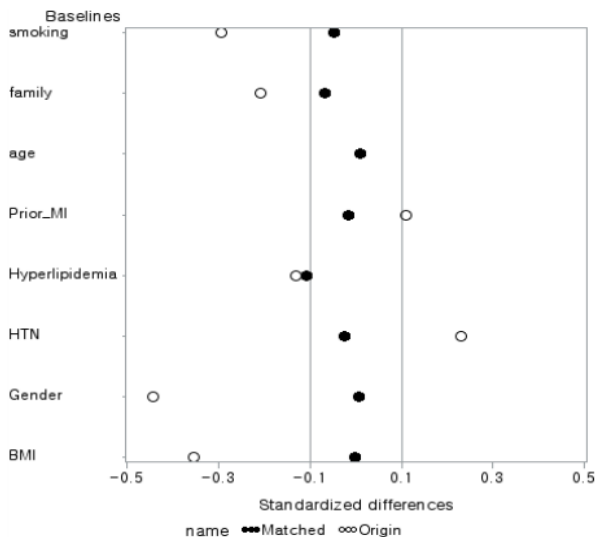$$W_c = 1/(1-PS) \text{, for control group} \quad (3)$$

Fig. 3. Standardized differences before and after the propensity score matching.
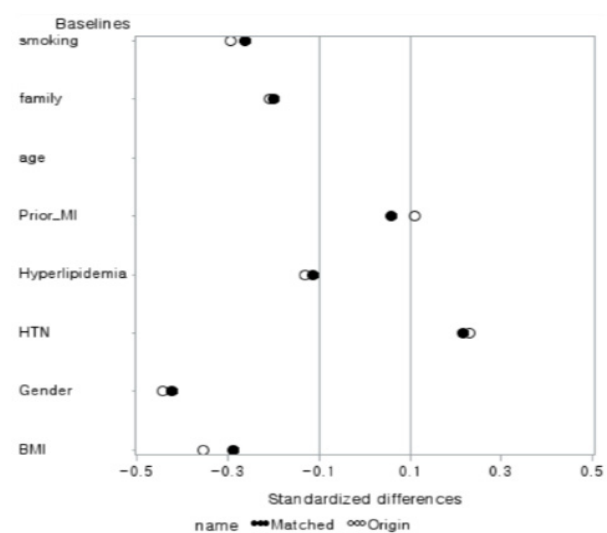

Fig. 4. Standardized differences before and after the propensity score weighting.

Table 1. Baseline characteristics of study patients

	Original Patients (N = 1373)			Patients by PSM (N = 760)			Patients by PSW (N = 1373)		
	High (768)	Low (605)		High (380)	Low (380)		High (768)	Low (605)	
	N (%) or mean ± SD		*P*-value	N (%) or mean ± SD		*P*-value	N (%) or mean ± SD		*P*-value
NT-proBNP	2,555 ± 4638.7	137 ± 110.4	<0.0001	1994.4 ± 3995.4	148.3 ± 111.2	<0.0000	2856.8 ± 7857	144.5 ± 145.6	<0.0001
Gender (Male)	387 (64.3)	638 (83.3)	<0.0001	289 (76.1)	288 (75.8)	0.932	438(57.1)	463(76.6)	<0.0000
Age (years)	67.2 ± 11.7	58.5 ± 11.4	<0.0001	63.4 ± 10.8	63.3 ± 10.5	0.892	70.5 ± 16.5	61.4 ± 15.3	<0.0001
BMI (kg/m²)	23.5 ± 3.3	24.6 ± 3	<0.0001	24 ± 3.2	24 ± 2.9	0.966	22.9 ± 4.9	24.2 ± 3.9	<0.0001
Hypertension	404 (52.6)	249 (41.2)	<0.0001	181 (47.6)	186 (48.9)	0.717	428(55.7)	272(44.9)	<0.0000
Hyperlipidemia	91 (11.9)	99 (16.4)	0.021	49 (13.4)	63 (17.2)	0.146	96(12.5)	100(16.5)	0.008
Smoking	206 (34.6)	295 (48.9)	<0.0001	150 (39.5)	159 (41.8)	0.506	239(31.1)	265(43.8)	<0.0000
Prior_MI	25 (4.1)	17 (2.2)	0.04	11 (2.9)	12 (3.2)	0.832	31(4)	19(2.9)	0.169
Family history	32 (5.7)	85 (11.5)	<0.0001	27 (7.1)	34 (8.9)	0.35	33(4.3)	57(9.3)	<0.0000
CCU_admission	461 (77.2)	602 (78.8)	0.485	291 (77.6)	288 (76.4)	0.694	603(78.6)	480(79.3)	0.719
Killip class	43 (7.6)	27 (3.8)	0.003	16 (4.5)	13 (3.7)	0.575	65(8.5)	25(4.1)	<0.0000
LV EF (%)	52.7 ± 10.9	57.1 ± 9.2	<0.0001	52.6 ± 10.2	56.7 ± 9.4	<0.0000	52.3 ± 16.5	56.5 ± 12.2	<0.0001
SBP (mmHg)	133 ± 27.4	135.6 ± 25.2	0.076	133.2 ± 26.6	133.8 ± 25.7	0.752	131.8 ± 39.6	134.5 ± 33.7	0.0796
DBP (mmHg)	79.5 ± 15.9	82.1 ± 15.7	0.003	80.4 ± 15.6	80.6 ± 15.8	0.897	78.5 ± 23.7	81.1 ± 20.7	0.0066
HR (/min)	77.2 ± 17.7	73.6 ± 14.1	<0.0001	76.6 ± 16	72.5 ± 14.1	<0.0000	77 ± 27.4	72.7 ± 18.8	<0.0001
TC (mg/dL)	184.4 ± 44.1	191.4 ± 41.8	0.003	186.1 ± 42.2	186.6 ± 38.7	0.869	183.5 ± 64.8	188.4 ± 53.7	0.0495
TG (mg/dL)	117 ± 78.3	139.7 ± 94.9	< 0.0001	120.4 ± 82.2	127. 4± 79.9	0.251	111.2 ± 106.4	134.6 ± 120.1	<0.0001
LDL-C (mg/dL)	117.5 ± 35.9	121.7 ± 36.4	0.043	119.3 ± 35.8	118.2 ± 35.1	0.669	117.7 ± 54.9	119.6 ± 46.8	0.3749
HDL-C (mg/dL)	44.1 ± 12.7	44.5 ±15.7	0.639	44.3 ± 13	45.3 ± 16.3	0.366	44.4 ± 19.1	44.9 ± 21.6	0.5957
Cr (mg/dl)	1.1 ± 1.2	0.9 ± 0.4	0.001	1.1 ± 1.3	0.9 ± 0.2	0.004	1.1 ± 1.9	0.9 ± 0.3	0.0005
FBS (mg/dL)	130.6 ± 43	131.8 ± 34.7	0.596	129.4 ± 41.9	134 ± 34.5	0.106	130.8 ± 64.8	133.3 ± 46.4	0.2765
hsCRP (mg/dL)	7.6 ± 20.7	2.8 ± 11.9	<0.0001	7.2 ± 21.2	2.2 ± 8.5	<0.0000	6.2 ± 27.9	1.9 ± 10.9	<0.0001
Maximum_CKMB	80.6 ± 134.6	95.3 ± 155	0.068	87.5 ± 145.1	90.8 ± 160.9	0.764	78.7 ± 206.8	93 ± 194.1	0.0941
Troponin I	21.4 ± 37.8	21.7 ± 35.5	0.868	21.7 ± 33.8	22.6 ± 36.9	0.75	19.2 ± 44.5	22.5 ± 46.3	0.1233
Target_LAD	271 (45.2)	345 (45)	0.94	176 (46.6)	161 (42.6)	0.272	348(45.3)	276(45.7)	0.8291
Target_LCX	164 (27.4)	210 (27.4)	0.988	105 (27.8)	100 (26.5)	0.683	203(26.4)	155(25.7)	0.69181
Target_RCA	146 (24.4)	201 (26.2)	0.432	88 (23.3)	114 (30.2)	0.033	198(25.8)	167(27.6)	0.33449
Target_LM	18 (3)	10 (1.3)	0.028	9 (2.4)	3 (0.8)	0.081	18(2.4)	5(0.9)	0.0047
Multivessel (%)	373 (62)	400 (52.4)	<0.0001	221 (58.3)	195 (51.9)	0.075	498(64.9)	322(53.3)	<0.0000
Complete_R	283 (48.8)	426 (57.6)	0.001	179 (49.3)	212 (57.5)	0.027	359(46.7)	344(56.9)	<0.0000
DES	511 (95)	621 (94.5)	0.723	321 (96.4)	298 (93.7)	0.113	732(95.3)	566(93.5)	0.082
Stent_diameter	3.1 ± 0.4	3.1 ± 0.4	0.065	3.1 ± 0.4	3.1 ± 0.4	0.531	3 ± 0.6	3.1 ± 0.6	0.006
Stent_length	24.7 ± 6.8	23.9 ± 6.6	0.074	24.7 ± 6.5	23.9 ± 6.7	0.114	24.7 ± 10.5	23.9 ± 8.8	0.060
Cilostazol	145 (25.8)	165 (22.3)	0.147	89 (24.6)	76 (20.9)	0.233	178(23.2)	125(20.7)	0.159
DC_DAPT	419 (73.3)	570 (76.2)	0.22	275 (74.9)	285 (77.2)	0.464	585(76.2)	471(77.8)	0.378
TAPT	144 (23.8)	163 (21.2)	0.255	88 (23.2)	74 (19.5)	0.215	166(21.6)	119(19.6)	0.239
DC_BB	496 (87.2)	657 (88.2)	0.577	322 (88)	324 (88)	0.978	655(86.6)	535(88.5)	0.167
DC_ACEI_ARB	470 (82.5)	642 (85.9)	0.084	305 (83.3)	314 (85.3)	0.458	628(81.8)	522(86.4)	0.004
DC_Statin	455 (80.5)	612 (82.3)	0.425	291 (80.2)	312 (85.2)	0.07	598(77.9)	494(81.7)	0.028
Nitrate	214 (38)	341 (45.9)	0.004	139 (38.4)	165 (45)	0.072	305(39.7)	277(45.8)	0.004
Nicorandil	105 (18.7)	99 (13.3)	0.008	69 (19.1)	55 (15.1)	0.152	138(18)	85(14.1)	0.014

Abbreviations: CCU admission (coronary care unit admission), LV EF (left ventricle ejection fraction), SBP (systolic blood pressure), DBP (diastolic blood pressure), HR (heart rhythm), TC (total cholesterol), TG (triglyceride), LDL-C (low-density lipoprotein-cholesterol), HDL-C (high-density lipoprotein-cholesterol), Cr (creatinine), FBS (glucose), HsCRP (high-sensitivity C-reactive protein), Maximum CK MB (maximum creatinine kinase muscle brain), Target LAD (left anterior descending), Target LCX (left circumflex), Target RCA (right coronary artery), Target LM (left main), DES (drug-eluting stent), DC_ASA (defibrillation cardioversion_acetylsalicylic acid), DC_Clopido (DC_clopidogrel), DC_DAPT (DC_dual anti-platelet therapy (= aspirin and clopidogrel)), TAPT (asprin, clopidogrel, and cilostazol), DC_BB (DC_beta blocker), DC_ACEI_ARB (DC_ACE inhibitor_angiotensin receptor blocker).
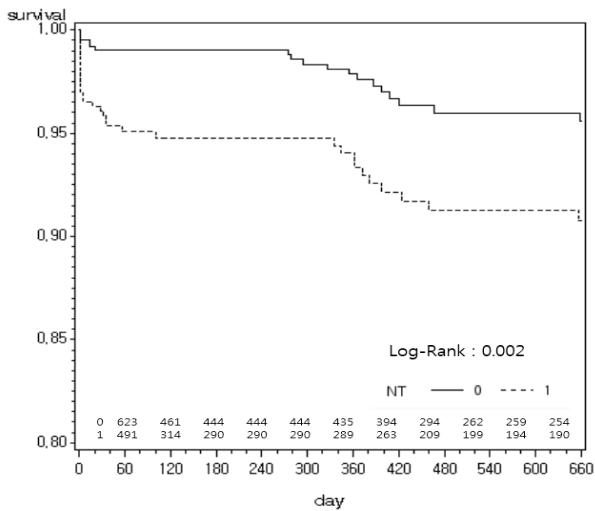
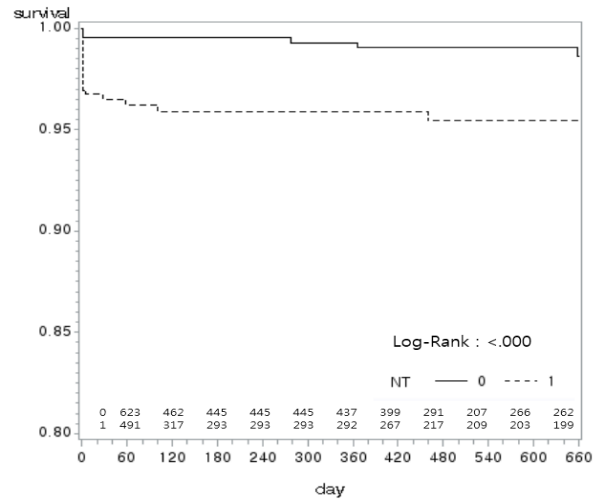**Fig. 5.** MACEs before propensity score application of NT-proBNP with Kaplan Meier method.

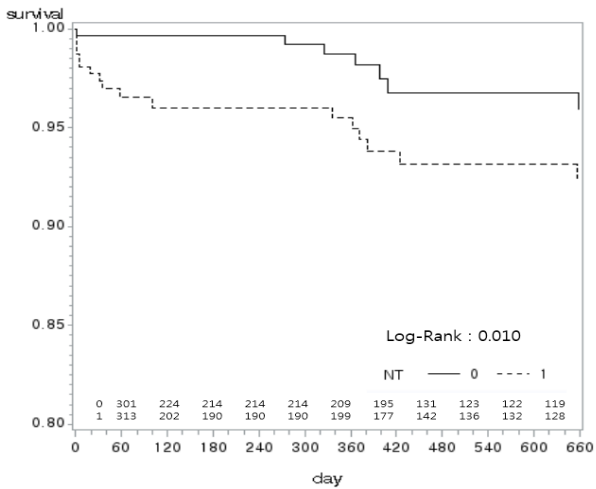**Fig. 8.** Mortality before propensity score application of NT-proBNP with Kaplan Meier method.

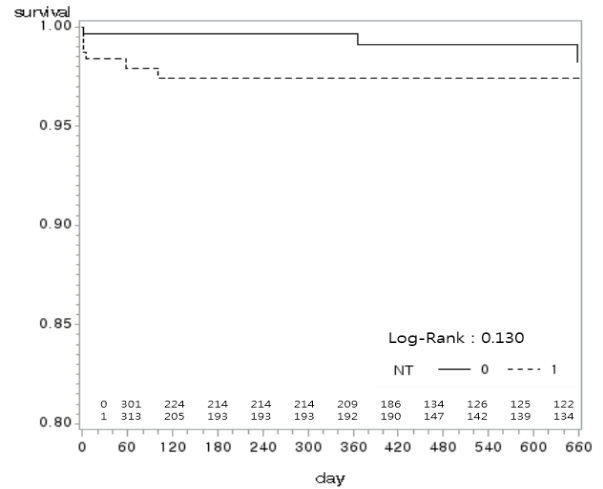**Fig. 6.** MACEs after propensity score matching of NT-proBNP with Kaplan Meier method.

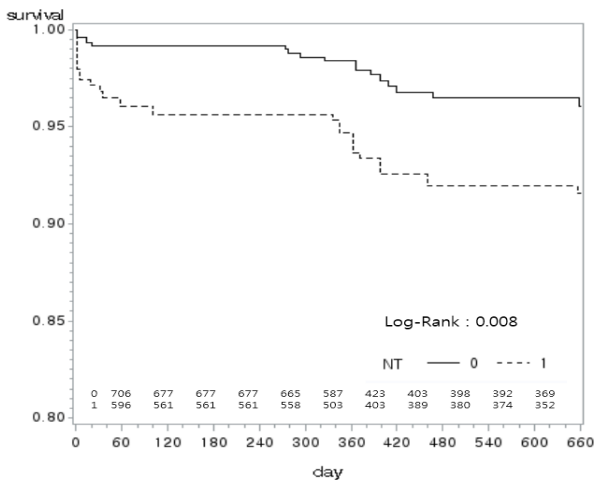**Fig. 9.** Mortality after propensity score matching of NT-proB-NP with Kaplan Meier method.

Fig. 7. MACEs after propensity score weighting of NT-proBNP with Kaplan Meier method.
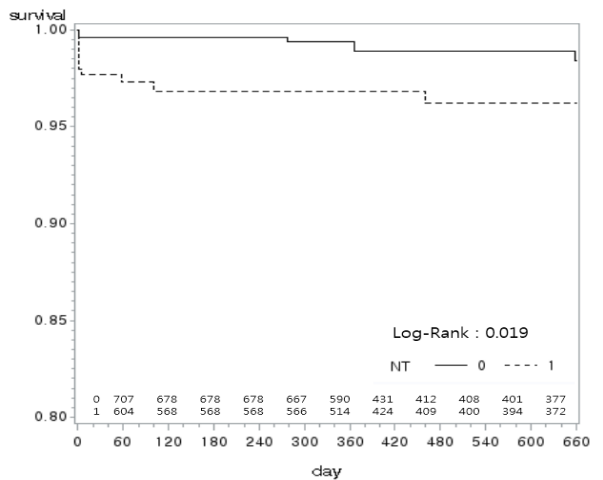

Fig. 10. Mortality after propensity score weighting of NT-proB-NP with Kaplan Meier method.

From the KorMI data, four types of MACEs were identified: death, MI, ST, and TVR. We performed Kaplan–Meier analysis on the individual MACE types and all four events. However, the number of ST, TVR, and MI events was too small to affect the survival analysis. Next, through the Cox regression, we calculated the survival function of the prediction model over time.

Results

For our experiments, we placed the NT-proBNP values into a log and classified them into two groups. Then, we revised the variables to control independent variables by PSM. Figure 2 shows the distribution nature of the log values of NT-proBNP in the two groups using PSM. In other words, it shows the distribution after the log (NT-proBNP) values were divided depending on if they were greater than 6 (NT High) and less than 6 (NT Low). We identified half of the samples where the two groups overlapped as matching. First, 1,373 patients were matched; then, the subject patients were reduced to 760.

Figure 3 shows the balance checking result for the covariate using PSM. Correction was good from 0.1 to −0.1. This means that, when the value was nearer to 0, the distribution balance between the two groups was better. There was a big imbalance when the value was nearer to 1. Figure 4 shows the balance checking result for the covariate using PSW. There was a poor distribution balance in contrast to PSM, but the advantage was that all of the samples were used. We classified the subject patients into two groups according to the initial NT-proBNP value and compared and analyzed the characteristics before and after PSM. The results showed that all of the revised variables turned out to be significant.

Table 1 presents the corrected results using PSM and PSW methods for all of the variables as baseline characteristics. When PSM was used, the accuracy of the correction increased, but the number of samples decreased. When PSW was used, even though the accuracy of the correction decreased, all of the samples could be used. For survival analysis, we compared all of the MACEs and MACES ending in mortality before and after the revision of PSM with the Kaplan–Meier method. Figures 5 and 6 show all of the MACEs before and after PSM

adjustment. Figure 7 shows the results after PSW was applied with the Kaplan–Meier method. For the MACEs, there was a significant difference in the PSW results before and after weighting. There were some differences between the two groups classified according to NT-proBNP values. Figures 8 and 9 show the mortality before and after PSM adjustment. Figure 10 shows the survival analysis results for mortality with PSW. Although there was no significant difference with PSM, as shown in Figure 9, there was a significant difference with PSW. Thus, different results may be obtained according to the sampling method. In the figure, "1" represents values when NT was greater than 6, and "0" represents values when NT was less than 6. The results of the log-rank test are expressed as *p*-values.

Then we calculated the survival function of a prediction model over time by using the Cox regression model [24, 25]. A hazard function was used to determine the conditional probability of death right after the *t* point of people who survived to the *t* point. The hazard function was used in a proportional hazard regression model and was identical to the definition of the instantaneous rate of mortality used in epidemiology. The Cox regression model represents a log risk function at the *t* point by using a linear expression of many discrimination variables at the *t* point. That is, in a Cox model with *p* discrimination variables, the values of the discrimination variable of the *i*-th characteristic are $x'_i = (x_{i1}, x_{i2}, \ldots, x_{ip})$, and the regression model coefficient is $\beta = (\beta_1, \beta_2, \cdots, \beta_p)$. The Cox regression model is represented as follows:

$$
\begin{aligned}
h_i(t) &= h_0 \, \exp(\beta x_i) \\
&= h_0 \, (t) \exp(\beta_1 x_{i1} + \beta_2 x_{i2} + \cdots \beta_p x_{ip}) \quad (4)
\end{aligned}
$$

Here, $h_0(t)$ is the baseline hazard function, and we assumed that the many discrimination values have no influence on the risk function.

Table 2 indicates that, when log (NT-proBNP) increases by 1, the risk of MACE increases by 1.312 times through the Cox hazard function. In addition, we identified the confidence interval of (1.014:1.699). These results indicate that NT-ProBNP measurements can be used to assess the predicted prognoses for NSTEMI patients and their effect on MACEs.

Table 2. Cox regression analysis of log (NT-proBNP) about propensity score matching

Parameter	Parameter Estimate	Chi-square	P>ChiSq	Hazard ratio	95% CI Low	high
Log (NTproBNP)	0.272	4.258	0.0391	1.312	1.014	1.699

Discussion

NT-proBNP is a well-known biomarker for the diagnosis, treatment efficiency, and prognosis of HF and is directly associated with the severity of systolic and diastolic myocardial dysfunctions. If the pressure of the left ventricle increases, proBNP is released from the cardiac muscle cell of the left ventricle. proBNP is separated into biologically active BNP and non-functional NT-proBNP. Physiological functions of BNP are vasodilatation, diuresis, and natriuresis. In addition, BNP is known to be an important indicator for deciding the function and estimating the prognosis of the left ventricle because the representative neurohormone is secreted from the ventricular muscle by the mechanical overload of the left ventricle in chronic HF.

Some NSTEMI patients face as much danger as STEMI patients. This study tried to use the value of NT-proBNP as a way of identifying a small number of such patients in advance and tested the role of NT-proBNP as an evaluation index that can affect the diagnosis of patients. The subjects of analysis were patients who were diagnosed with NSTEMI, had chest pain, and had PCI surgery within 24 h. In order to divide the value of NT-proBNP into two groups, PS was used to correct the bias between the groups. For analysis, the Kaplan–Meier test was used. Each MACE (all cases, ST, TVR, MI, death) was compared and analyzed using PSM and PSW to observe any differences before and after PS application. For ST, TVR, and MI, few events occurred, so survival analysis was difficult. Only the MACES of all cases and death showed significant differences in the analysis results. With the Cox regression, the analysis showed that increasing the log value of NT-proBNP by 1 raised the risk of a MACE 1.312 times. The Kaplan–Meier and Cox regression results showed that NT-proBNP can be used as an evaluation index for NSTEMI patients.

This study was limited in that the reliability of the data needs to be secured through data collection and integrated management for prospective follow-up research on prognosis of patients with AMI as well as management indices. Biochemical indices for prognosis prediction would help a clinician determine an appropriate course of treatment. Future research is needed to examine changes in the blood NT-proBNP over time among patients with acute coronary syndrome. In addition, studies on treatment plans depending on blood NT-proBNP levels need to be conducted in order to determine treatment strategies for patients with acute coronary syndrome.

Acknowledgements

ORCID

Kyung Ah Kim http://orcid.org/0000-0002-8814-6973

References

1. Kim SS, Choi HS, Jeong MH, Cho JG, Ahn YK, Kim JH, Chae SC, Kim YJ, Hur SH, Seong IW, Hong TJ, Choi DH, Cho MC, Kim CJ, Seung KB, Chung WS, Jang YS, Rha SW, Park SJ. Clinical outcomes of acute myocardial infarction with occluded left circumflex artery. J Cardio 2011;57:290–296.

2. Song Y. Analyses of studies on cardiac rehabilitation for patients with cardiovascular disease in Korea. J Korean Acad Nurs 2009;39:311–320.

3. Deedwania PC, Ahmed MI, Feller MA, Aban IB, Love TE, Pitt B, Ahmed A. Impact of diabetes mellitus on outcomes in patients with acute myocardial infarction and systolic heart failure. Eur J Heart Fail 2011;13:551–559.

4. Cho JY, Jeong MH, Choi OJ, Lee S, Jeong SY, Kim IS, Cho JS, Hwang SH, Hwang SH, Yoon NS, Moon JY, Hong YJ, Kim JH, Kim W, Ahn YK, Cho JG, Park JC, Kang JC. Predictive factors after percutaneous coronary intervention in young patients with acute myocardial infarction. Korean Circ J 2007;37:373–379.

5. Haaf P, Balmelli C, Reichlin T, Twerenbold R, Reiter M, Meissner J, Schaub N, Stelziq C, Freese M, Paniz P, Meune C, Drexler B, Freidank H, Winkler K, Hochholzer W, Mueller C. N-terminal pro B-type natriuretic peptide in the early evaluation of suspected acute myocardial infarction. Am Heart J 2011; 124:731–739.

6. Gagging HK, Mohammed AA, Bhardwai A, Rehman SU, Gregory SA, Weiner RB, Baggish AL, Moore SA, Semigran MJ, Januzzi JL Jr. Heart failure outcomes and benefits of NT-proBNP-guided management in the elderly: Results from the prospective, randomized ProBNP outpatient tailored chronic heart failure therapy (PROTECT) study. J Card Fail 2012;17:626–634.

7. Tong W, Lai H, Yang C, Ren S, Dai S, Lai S. Age, gender and metabolic syndrome-related coronary heart disease in U.S. adults, Int J Cardiol 2005;104:288–291.

8. Kang SH, Park JJ, Choi DJ, Yoon CH, Oh IY, Kang

SM, Yoo BS, Jeon ES, Kim JJ, Cho MC, Chae SC, Ryu KH, Oh BH. Prognostic value of NT-proBNP in heart failure with preserved versus reduced EF. Heart Journal 2015;101:1881–1888.

9. Baggen VJ, van den Bosch AE, Eindhoven JA, Schut AW, Cuypers JA, Witsenburg M, de Waart M, van Schaik RH, Zijlstra F, Boersma E, Roos-Hesselink JW. Prognostic Value of N-Terminal Pro-B-Type Natriuretic Peptide, Troponin-T, and Growth-Differentiation Factor 15 in Adult Congenital Heart Disease. Circulation 2017;135:264-279.

10. Iacob D, Butnariu A, Leucuţa DC, Samaşca G, Deleanu D, Lupan I. Evaluation of NT-proBNP in children with heart failure younger than 3 years old. Rom J Intern Med 2017;55:69-74.

11. Park JS, Lee HC, Lee HW, Ahn SG, Cha KS, Hong TJ, Kim SP, Kim YD, Lee SK, Kim HK, Jeong MH. Prognosis according to the timing of percutaneous coronary intervention in non-ST segment elevation myocardial infarction, based on the Korean Acute Myocardial Infarction Registry (KAMIR). Cardiol J 2011;18:421–429.

12. Bashir ME, Lee DG, Li M, Bae JW, Shon HS, Cho MC, Ryu KH. Trigger learning and ECG parameter customization for remote cardiac clinical care information system. IEEE Trans Inf Technol Biomed 2012;16:561–571.

13. Kim NY, Park IH, Jeong MH, Lee SJ, Kim DH, Lee GH, Lee MG, Sim DS, Park KH, Yoon HJ, Kim KH, Hong YJ, Kim JH, Ahn YK, Cho JG, Park JC, Kang JC. Comparison of clinical outcomes between ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction in patients younger than 40 years who underwent percutaneous coronary artery intervention. Korean J Med 2012;82:175–184.

14. Mitchell A, Misialek JR, Folsom AR, Duprez D, Alonso A, Jerosch-Herold M, Sanchez OA, Watson KE, Sallam T, Konety SH. Usefulness of N-terminal pro-brain natriuretic peptide and myocardial perfusion in asymptomatic adults (from the multi-ethnic study of atherosclerosis). Am J Cardiol. 2015;115:1341–1345.

15. Worster A, Balion CM, Hill SA, Santaguida P, Afisilsmaila, Kelvie RM, Reichert SM, McQueen MJ, Booker L, Raina PS. Diagnostic accuracy of BNP and NT-proBNP in patients presenting to acute care settings with dyspnea: A systematic review. Clin Biochem 2008;41:250–259.

16. Nilsson JC, Groenning BA, Nielsen G, Fritz-Hansen T, Trawinski J, Hildebrandt PR, Jensen GB, Larsson HB, Sondergaard L. Left ventricular remodeling in the first year after acute myocardial infarction and the predictive value of N-terminal pro brain natriuretic peptide. Am Heart J 2002;143: 696–702.

17. Castro LR, Alencar MC, Barbosa MM, Nunes MC, Cardoso JR, Ribeiro AL. NT-proBNP levels in patients with non-ST-segment elevation acute coronary syndrome. Arq Bras Cardiol 2011;97:456–461.

18. Haaf P, Balmelli C, Reichlin T, Twerenbold R, Reiter M, Meissner J, Schaub N, Stelzig C, Freese M, Paniz P, Meune C, Drexler B, Freidank H, Winkler K, Hochholzer W, Mueller C. N-terminal pro B-type natriuretic peptide in the early evaluation of suspected acute myocardial infarction. Am Heart J 2011;124:731–739.

19. Lee JH, Park HS, Chae SC, Cho Y, Yang DH, Jeong MH, Kim YJ, Kim KS, Hur SH, Seong IW, Hong TJ, Cho MC, Kim CJ, Jun JE, Park WH. Predictors of six-month major adverse cardiac events in 30-day survivors after acute myocardial infarction (from the Korea Acute Myocardial Infarction Registry). Am J Cardiol 2009; 104:182–189.

20. http://www.kormi.org/

21. http://www2.sas.com/proceedings/sugi29/165–29.

22. Olmos A, Govindasamy P. A practical guide for using propensity score weighting in R. Pract Assess Res Eval 2015;20:1–8.

23. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivar Behav Res 2011;46:399–424.

24. Patton KK, Ellinor PT, Heckbert SR, Christenson RH, DeFilippi C, Gottdiener JS, Kronmal RA. N-terminal pro-B-type natriuretic peptide is a major predictor of the development of atrial fibrillation: the Cardiovascular Health Study. Circulation 2009;120:1768–1774.

25. Zhu Q, Xiao W, Bai Y, Ye P, Luo L, Gao P, Wu H, Bai J. The prognostic value of the plasma N-terminal pro-brain natriuretic peptide level on all-cause death and major cardiovascular events in a community-based population. Clin Interv Aging 2016; 11:245–253.