Biomarker for the Prediction of Major Adverse Cardiac Events in Patients with Non-ST-Segment Elevation Myocardial Infarction

Ho Sun Shon\textsuperscript{a}, Jang-Whan Bae\textsuperscript{b}, Kyoung Ok Kim\textsuperscript{c}, Eun Jong Cha\textsuperscript{d}, Kyung Ah Kim\textsuperscript{d}

\textsuperscript{a}Medical Research Institute, College of Medicine, Chungbuk National University, Cheongju, Korea
\textsuperscript{b}Department of Internal Medicine, College of Medicine, Chungbuk National University, Cheongju, Korea
\textsuperscript{c}Department of Nursing, Woosong College, Daejeon, Korea
\textsuperscript{d}Department of Biomedical Engineering, College of Medicine, Chungbuk National University, Cheongju, Korea

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a well-known biomarker for the diagnosis and prognosis of heart failure, and is directly associated with myocardial dysfunction. We evaluated the prognostic value of NT-proBNP for major adverse cardiac events (MACEs) among patients with non-ST-segment elevation myocardial infarction (NSTEMI) from the Korea Acute Myocardial Infarction Registry during their mid-term follow-up period. In this paper, we analyzed NT-proBNP according to various MACE and level of NT-proBNP. We used multivariate logistic regression to determine the risk factors according to MACE type and NT-proBNP levels, and to identify the cutoff value for each MACE by using the receiver operating characteristic (ROC) curve. NT-proBNP was a significant variable among cardiac deaths ($p = 0.016$), myocardial infarction ($p = 0.000$), and coronary artery bypass grafting (CABG) ($p = 0.000$) in patients with MACE compared with those without MACE. Two-vessel coronary artery disease (CAD) ($p = 0.037$) and the maximum creatinine kinase (max-CK) ($p = 0.031$) produced significant results in repeat percutaneous coronary intervention. The area under the ROC curve was found to be statistically significant for cardiac death and CABG. NT-proBNP is a useful predictor for 12-month MACEs among patients with NSTEMI and in those with heart failure. We propose that a new index incorporating NT-proBNP, max-CK, and CAD vessel will be useful as a prognostic indicator of MACEs in the future.

**Key Words:** heart disease, cardiac biomarker, myocardial infarction, NT-proBNP

**INTRODUCTION**

Statistics Korea revealed that the mortality from cardiovascular disorders, based on the statistics on the cause of death in 2014, has increased by 38.8% in the last decade, and cardiovascular disorder was ranked second among all causes of death \[1\]. The proportion of cardiovascular deaths is continuously increasing in Korea, and the major cause is acute myocardial infarction (AMI). The Korean Myocardial Infarction Registry (KAMIR) was initiated in 2003 with a grant from the Korean Society of Cardiology, to define the characteristics of AMI and establish measures to reduce the incidence and mortality of AMI in Korea \[2\]. Substantial data support the benefit of timely primary revascularization in ST-segment elevation myocardial infarction (STEMI), with several prognostic factors already established, including rapid revascularization...
and Killip classification. However, no single useful prognostic factor to facilitate the decision for urgent revascularization in patients with non-STEMI (NSTEMI) has been identified to date. Although several multifactorial laboratory values and clinical decision criteria support the efficacy of urgent revascularization, a single useful prognostic factor is still elusive in NSTEMI [3–9].

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a useful biomarker for diagnosing, predicting the short- and long-term prognoses of, and determining the treatment strategy for heart failure (HF) [10]. Brain natriuretic peptide (BNP) is a hormone primarily secreted from the myocardium cells of the heart ventricles, unlike atrial natriuretic peptide, which is secreted from the atriums [11]. Myocardial expansion and hypoxia promote the secretion of proBNP, a precursor protein that is involved in expanding blood vessels and suppressing the secretion of aldosterone when in the forms of NT-proBNP and BNP [12,13]. This causes a diuretic effect in the kidneys; thus, it is possible to maintain homeostasis between blood pressure and water content. NT-proBNP is excreted only through the kidneys, and it is known to have a stronger negative relationship with the measured glomerular filtration rate than BNP [14,15]. In patients with acute coronary syndrome (ACS), the NT-proBNP levels measured at hospitalization for the prediction of recurrence risk suggest that both STEMI and NSTEMI can predict complications and short-term mortality in patients with ACS [16]. In Egyptian patients with ACS, the mortality rate also increased according to the level of NT-proBNP [17]. The NT-proBNP levels of patients with STEMI (p = 0.003) and NSTEMI (p = 0.002) increased after 6 months of follow-up or in case of death during hospitalization because of angina, myocardial infarction (MI), cardiogenic shock, congestive HF, or arrhythmia [18].

Studies have shown that patients with NSTEMI present with markedly higher NT-proBNP levels than patients with STEMI (1,305 [741–3,208] ng/L vs. 170 [70–424] ng/L, p < 0.001). The time to presentation from the onset of chest pain was also much longer in NSTEMI compared with STEMI (> 48 hours vs. < 6 hours, p < 0.001) [19]. Research has also revealed that the STEMI group demonstrated higher troponin-I and NT-proBNP values than the NSTEMI group [20]. However, the value of NT-proBNP measurement in patients with NSTEMI is unclear. In this study, we sought to identify the clinical value of NT-proBNP in predicting major adverse cardiac events (MACEs) among patients with NSTEMI who underwent percutaneous coronary intervention (PCI) within 24 hours of admission.

MATERIALS AND METHODS

1. Study population

The study population was derived from KAMIR. The KA-
MIR database registered 14,887 patients diagnosed as having AMI from November 2005 to January 2008 (comprising 9,222 and 5,665 patients with STEMI and NSTEMI, respectively). Our target patients were those who arrived at the hospital within 12 hours from the onset of chest pain and underwent PCI within 24 hours of admission. A total of 418 patients met these criteria. All participating cardiovascular centers achieved approval from the Institutional Review Board, and are under the regular monitoring processes.

We examined patients with NSTEMI who presented to the emergency triage within 12 hours of the onset of chest pain and underwent early PCI 12 hours from admission in KAMIR-participating hospitals from 2005 to 2008. We analyzed the clinical data including sex; age; systolic blood pressure on admission; Killip classification; echocardiographic left ventricular ejection fraction; and angiographic variables including thrombolysis in MI score, flow grade before PCI, location of the culprit lesion, and number of involved vessels. In addition, we examined the significance of laboratory results, including glucose, creatinine, initial and maximum (max) values of creatinine kinase (CK), CK-MB isoform (CK-MB), high-sensitivity C-reactive protein (hs-CRP), troponin-I, and fasting lipid profiles during admission.

2. Analysis methods

We represented continuous variables as average ± standard deviation and used PASW Statistics for Windows version 18.0 (IBM Co., Armonk, NY, USA) for data analysis. We retrospectively analyzed the factors that influenced MACE by using the chi-square test and multivariate logistic regression for statistical analysis. When using multivariate logistic regression, it is possible to incur multicollinearity. Therefore, to solve this problem, we categorized the existing data and deleted independent variables with strong linear relations [21–23]. Among patients with NSTEMI, we determined the risk factors and analyzed variables that could predict MACE in those who arrived at the hospital within 12 hours from the onset of chest pain, underwent early coronary PCI (within 12 hours), and were monitored up to 12 months. MACE was monitored for 12 months.

The relevant characteristics are shown in Figure 1 in accordance with the presence or absence of MACE, based on the data monitored for 12 months through tracking observation. MACEs included cardiac death, MI, repeat PCI (Re-PCI), and coronary artery bypass grafting (CABG). Figure 1 shows four types of MACE among patients followed for 12 months, including cardiac

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death, MI, Re-PCI, and CABG. A total of 96 MACEs occurred during the 12 months of follow-up after PCI. Cardiac death, non-fatal MI, Re-PCI, and CABG occurred in 28 (29.2%), 10 (10.4%), 33 (34.4%), and 25 (26.0%) patients, respectively.

**RESULTS**

The target subjects of this research were patients with NSTEMI. Of the patients with NSTEMI in our study population, 96 experienced MACE. The average age of the patients was 73.96 years. The clinical characteristics of the patients monitored up to 12 months are shown in Table 1. The results of the T-test, performed to calculate the average of continuous variables depending on whether the patients had MACE, showed a significant difference. Assuming equal variance, age ($p = 0.005$), hypertension ($p = 0.017$), glucose level ($p = 0.002$), max-troponin-I level ($p = 0.010$), triglyceride ($p = 0.016$), hs-CRP ($p = 0.020$), and NT-proBNP ($p = 0.001$) were statistically significant. However, the rest of the variables, such as heart rate, creatinine, max-CK, max-CK-MB, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and others proved to be statistically nonsignificant.

First, the NT-proBNP levels in patients with NSTEMI were divided into quartiles: first quartile (level 1), < 100 pg/mL; second quartile (level 2), 100–200 pg/mL; third quartile (level 3), 201–1,000 pg/mL; and fourth quartile (level 4), > 1,000 pg/mL.

Table 2 shows the risk rate from logistic regression analysis according to whether MACE occurred or not, and according to the NT-proBNP level. As a result, the odds ratio of NT-proBNP level 4 for MACE was proved dangerous at 4.3 times ($p = 0.000$; 95% confidence interval [CI], 2.01–9.91). Accordingly, as the NT-proBNP value increased, the risk rate also increased (Table 2). The results were obtained with binary logistic regression analysis by using a backward elimination method after adjusting for age, sex, and body mass index. We could not include the three covariates in this model, as they were statistically nonsignificant.

Table 3 shows how each type of MACE differed based on the NT-proBNP level. We used multivariate logistic regression for the analysis. Although the odds ratio was low, the $p$-value was statistically significant. In addition, the result showed that among the MACEs, Re-PCI and MI were statistically nonsignificant. As a result, among the MACEs, cardiac death had an odds ratio of 0.053 and 0.279 times in NT-proBNP level 2 ($p = 0.005$; 95% CI, 0.007–0.411) and level 3 ($p = 0.024$; 95% CI, 0.103–0.854), respectively. In cases of CABG, the odds ratio was $0.203, 0.068,$ and $0.226$ times in level 1 ($p = 0.017$; 95% CI, 0.055–0.748), level 2 ($p = 0.011$; 95% CI, 0.009–0.533), and level 3 ($p = 0.026$; 95% CI, 0.061–0.836), respectively. Accordingly, among patients with NSTEMI, MACE in cases of cardiac death and CABG can be used as an important biochemical indicator.

Table 4 shows the results of the significance test in the estimation of risk factors and MACE by using multivariate logistic regression analysis. According to the results, among the data
Table 1. Baseline characteristics of study patients with NSTEMI

| Characteristic                      | MACE               | p-value   |
|------------------------------------|--------------------|-----------|
|                                    | No (821)           | Yes (96)  |
| Age (y)                            | 68.7 ± 12.38       | 72.4 ± 10.76 | 0.005 |
| Gender, male                       | 536 (65.3)         | 54 (56.3)  | 0.011 |
| Body mass index (kg/m²)            | 24.65 ± 11.02      | 25.52 ± 21.23 | 0.072 |
| Medical history                    |                    |           |
| Hypertension (%)                   | 0.56 ± 0.53        | 0.64 ± 0.48 | 0.017 |
| Diabetes mellitus (%)              | 0.36 ± 0.53        | 0.29 ± 0.52 | 0.079 |
| Dyslipidemia (%)                   | 0.45 ± 0.95        | 0.40 ± 0.93 | 0.508 |
| Ischemic heart disease             | 0.19 ± 0.39        | 0.26 ± 0.44 | 0.004 |
| Smoking (pack/y)                   | 37.92 ± 59.14      | 38.39 ± 32.38 | 0.884 |
| Physical finding                   |                    |           |
| Heart rate (beat/min)              | 76.8 ± 17.5        | 79.8 ± 17.0 | 0.627 |
| Systolic BP (mmHg)                 | 129.9 ± 24.2       | 132.3 ± 22.8 | 0.262 |
| Diastolic BP (mmHg)                | 77.8 ± 14.0        | 78.4 ± 13.4 | 0.141 |
| Laboratory findings                |                    |           |
| Glucose (mg/dL)/on admission       | 158.8 ± 80.27      | 187.9 ± 112.66 | 0.002 |
| Creatinine (mg/dL)/on admission    | 1.23 ± 1.53        | 1.52 ± 1.47 | 0.100 |
| Max-CK (IU/L)                      | 667.4 ± 982.9      | 687.3 ± 1,468.5 | 0.711 |
| Max-CK-MB (ng/mL)                  | 64.9 ± 109.0       | 59.2 ± 100.0 | 0.955 |
| Max-troponin I (ng/mL)             | 17.2 ± 23.2        | 27.9 ± 75.8 | 0.010 |
| Max-troponin T (ng/mL)             | 2.03 ± 5.14        | 2.75 ± 3.66 | 0.952 |
| Total cholesterol (mg/dL)          | 182.4 ± 44.0       | 178.9 ± 53.6 | 0.234 |
| Triglyceride (mg/dL)               | 135.8 ± 100.3      | 117.5 ± 59.0 | 0.016 |
| HDL-cholesterol (mg/dL)            | 44.2 ± 16.6        | 44.8 ± 12.9 | 0.950 |
| LDL-cholesterol (mg/dL)            | 114.9 ± 44.7       | 111.4 ± 51.9 | 0.922 |
| hs-CRP (mg/dL)                     | 21.8 ± 92.8        | 7.9 ± 19.8  | 0.020 |
| NT-proBNP (pg/mL)                  | 2,198.4 ± 4,909.0  | 7,735.3 ± 10,736.2 | 0.001 |

Values are presented as mean ± standard deviation or number (%).
NSTEMI, non-ST-segment elevation myocardial infarction; MACE, major adverse cardiac event; BP, blood pressure; Max, maximum; CK-MB, creatinine kinase-muscle brain; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 2. Logistic regression according to MACE and NT-proBNP level

| NT-proBNP | MACE | OR | p-value | 95% CI for OR |
|-----------|------|----|---------|---------------|
|           | No   | Yes|         |               |
| Level 1   | 125  | 10 | 1       |               |
| Level 2   | 125  | 7  | 0.70    | 0.483         | 0.26 | 1.90 |
| Level 3   | 112  | 12 | 1.34    | 0.514         | 0.56 | 3.22 |
| Level 4   | 93   | 32 | 4.30    | 0.000         | 2.01 | 9.19 |

MACE, major adverse cardiac event; NT-proBNP, N-terminal pro-brain natriuretic peptide; OR, odds ratio; CI, confidence interval.
monitored for 12 months, when MACE was cardiac death, the estimated odds ratio of NT-proBNP was 1.00008 and the 95% CI was 1.00002–1.00015. Among patients with MACE monitored for 12 months, in those with cardiac death, the odds ratio was 1.00008 times that in patients with no MACE. This means that as NT-proBNP increased, it slightly influenced cardiac death compared with in the absence of MACE.

As a result, it can be postulated that NT-proBNP is a significant variable among cardiac deaths ($p = 0.016$), MI ($p = 0.000$), and CABG ($p = 0.000$) in patients with MACE compared with those without MACE. In addition, two-vessel coronary artery disease (CAD) ($p = 0.037$) and the max-CK ($p = 0.031$) produced significant results in Re-PCI. As a result, by setting the absence of MACE as a reference category, the most significant variable was NT-proBNP, which was shown to be statistically significant in terms of cardiac death and CABG. For a detailed analysis, the fittest cutoff value of NT-proBNP was predicted by using the receiver operating characteristic (ROC) curve for each MACE.

Table 5 shows the ROC analysis results based on each category of MACE. When MACE was cardiac death ($p = 0.0001$) or CABG ($p = 0.0019$), the area under the ROC curve (AUC) was statistically significant. In the case of cardiac deaths, the cutoff value was 1,180, with a sensitivity of 90% (95% CI, 68.3–98.5) and specificity of 66.2% (95% CI, 62.1–70.2). In the case of

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**Table 3. Multivariate logistic regression according to MACE type and NT-proBNP level**

| MACE (NT-proBNP level) | B    | SE    | OR       | $p$-value | 95% CI for OR | Lower bound | Upper bound |
|------------------------|------|-------|----------|-----------|--------------|-------------|-------------|
| **Cardiac death**      |      |       |          |           |              |             |             |
| Intercept              | −1.894 | 0.287 | 0.000    | -         | -            |             |             |
| Level 1                | −20.307 | 5,920.518 | 1.516E−9 | 0.997     | 0.000        |             |             |
| Level 2                | −2.935 | 1.044 | 0.053    | 0.005     | 0.007        | 0.411       |             |
| Level 3                | −1.216 | 0.540 | 0.297    | 0.024     | 0.103        | 0.854       |             |
| Level 4                | 0     | -     | -        | -         | -            |             |             |
| **MI**                 |      |       |          |           |              |             |             |
| Intercept              | −3.839 | 0.715 | 0.000    | -         | -            |             |             |
| Level 1                | −0.989 | 1.232 | 0.372    | 0.422     | 0.033        | 4.164       |             |
| Level 2                | −19.773 | 0.000 | 2.586E−9 | -         | 2.586E−9     | 2.586E−9    |             |
| Level 3                | −0.186 | 1.010 | 0.830    | 0.854     | 0.115        | 6.009       |             |
| Level 4                | 0     | -     | -        | -         | -            |             |             |
| **Re-PCI**             |      |       |          |           |              |             |             |
| Intercept              | −2.923 | 0.459 | 0.000    | -         | -            |             |             |
| Level 1                | −0.113 | 0.621 | 0.893    | 0.855     | 0.264        | 3.014       |             |
| Level 2                | −0.296 | 0.647 | 0.744    | 0.648     | 0.209        | 2.645       |             |
| Level 3                | −1.102 | 0.848 | 0.332    | 0.194     | 0.063        | 1.752       |             |
| Level 4                | 0     | -     | -        | -         | -            |             |             |
| **CABG**               |      |       |          |           |              |             |             |
| Intercept              | −2.135 | 0.319 | 0.000    | -         | -            |             |             |
| Level 1                | −1.595 | 0.666 | 0.203    | 0.017     | 0.055        | 0.748       |             |
| Level 2                | −2.694 | 1.053 | 0.068    | 0.011     | 0.009        | 0.533       |             |
| Level 3                | −1.485 | 0.666 | 0.226    | 0.026     | 0.061        | 0.836       |             |
| Level 4                | 0     | -     | -        | -         | -            |             |             |

MACE, major adverse cardiac event; NT-proBNP, N-terminal pro-brain natriuretic peptide; SE, standard error; OR, odds ratio; CI, confidence interval; MI, myocardial infarction; Re-PCI, repeat percutaneous coronary intervention; CABG, coronary artery bypass grafting.

*The reference category is noMACE. $^b$A floating-point overflow occurred while calculating this statistic. Therefore, the value of this statistic is set to system error. $^c$This parameter is set to zero because it is redundant.
Table 4. Risk factor estimates from multivariate logistic regression

| MACE* | B     | SE   | OR      | p-value | 95% CI for OR | Lower bound | Upper bound |
|-------|-------|------|---------|---------|---------------|-------------|-------------|
|       |       |      |         |         |               |             |             |
| Cardiac death |       |      |         |         |               |             |             |
| Intercept | −3.035 | 0.497 | -       | 0.000   | -             | -           | -           |
| NT-proBNP | 0.000  | 0.000 | 1.000081 | 0.016   | 1.000015      | 1.000147    |             |
| Max-CK | 0.000  | 0.000 | 0.999915 | 0.832   | 0.999127      | 1.000703    |             |
| [CAD_v1] | −1.273 | 0.836 | 0.279976 | 0.128   | 0.054435      | 1.439996    |             |
| [CAD_v2] | −0.638 | 0.672 | 0.528186 | 0.342   | 0.141621      | 1.969916    |             |
| [CAD_v3] | 0b    |      |         |         |               |             |             |
| MI |       |      |         |         |               |             |             |
| Intercept | −3.875 | 1.033 | -       | 0.000   | -             | -           | -           |
| NT-proBNP | 0.000  | 0.000 | 1.000153 | 0.000   | 1.000068      | 1.000239    |             |
| Max-CK | −0.002 | 0.002 | 0.997694 | 0.351   | 0.992866      | 1.002545    |             |
| [CAD_v1] | −19.099 | 0.000 | 0.000000 | -       | 0.000000      | 0.000000    |             |
| [CAD_v2] | −0.908 | 1.226 | 0.403472 | 0.459   | 0.036491      | 4.461079    |             |
| [CAD_v3] | 0b    |      |         |         |               |             |             |
| Re-PCI |       |      |         |         |               |             |             |
| Intercept | −2.690 | 0.403 | -       | 0.000   | -             | -           | -           |
| NT-proBNP | 0.000  | 0.000 | 1.000038 | 0.424   | 0.999944      | 1.000132    |             |
| Max-CK | 0.000  | 0.000 | 1.000410 | 0.031   | 1.000038      | 1.000781    |             |
| [CAD_v1] | −21.781 | 0.000 | 0.000000 | -       | 0.000000      | 0.000000    |             |
| [CAD_v2] | −1.411 | 0.675 | 0.243864 | 0.037   | 0.064944      | 0.915699    |             |
| [CAD_v3] | 0b    |      |         |         |               |             |             |
| CABG |       |      |         |         |               |             |             |
| Intercept | −2.791 | 0.532 | -       | 0.000   | -             | -           | -           |
| NT-proBNP | 0.000  | 0.000 | 1.000123 | 0.000   | 1.000065      | 1.000181    |             |
| Max-CK | −0.001 | 0.001 | 0.998612 | 0.121   | 0.996858      | 1.000368    |             |
| [CAD_v1] | 0.025  | 0.615 | 1.025292 | 0.968   | 0.307274      | 3.421133    |             |
| [CAD_v2] | −1.199 | 0.800 | 0.301380 | 0.134   | 0.062822      | 1.445838    |             |
| [CAD_v3] | 0b    |      |         |         |               |             |             |

MACE, major adverse cardiac event; OR, odds ratio; CI, confidence interval; NT-proBNP, N-terminal pro-brain natriuretic peptide; Max-CK, maximum creatinine kinase; CAD, coronary artery disease; MI, myocardial infarction; Re-PCI, repeat percutaneous coronary intervention; CABG, coronary artery bypass grafting.

*The reference category is noMACE. bThis parameter is set to zero because it is redundant.

Table 5. Receiver operating characteristic curve analysis results in each category of MACE type

| MACE | AUC | p-value | 95% CI | Cutoff value | Sensitivity | 95% CI | Specificity | 95% CI |
|------|-----|---------|-------|-------------|-------------|-------|-------------|-------|
| Cardiac death | 0.816 | 0.0001 | 0.782–0.848 | 1,180 | 90.0 | 68.3–98.5 | 66.2 | 62.1–70.2 |
| MI | 0.651 | 0.2623 | 0.610–0.690 | 930 | 80.0 | 28.8–96.7 | 58.7 | 54.5–62.8 |
| Re-PCI | 0.539 | 0.5624 | 0.497–0.581 | 516 | 61.1 | 35.8–82.6 | 55.2 | 50.9–59.4 |
| CABG | 0.716 | 0.0019 | 0.676–0.753 | 3,903 | 61.1 | 35.8–82.6 | 83.5 | 80.1, 86.5 |

MACE, major adverse cardiac event; AUC, area under the receiver operating characteristic curve; CI, confidence interval; MI, myocardial infarction; Re-PCI, repeat percutaneous coronary intervention; CABG, coronary artery bypass grafting.
CABG, the cutoff value was 3903, with a sensitivity of 61.1% (95% CI, 35.8–82.6) and specificity of 83.5% (95% CI, 80.1–86.5). When MACE were MI of Figure 2 and Re-PCI of Figure 3, the AUC was statistically nonsignificant. Figures 4 and 5 show the AUC when MACE was cardiac death and CABG [24].

**DISCUSSION**

According to existing research, the level of NT-proBNP in patients with congestive HF is related to the prognosis and determines the critical condition of HF. It is also known to be relevant to the symptoms of HF and is related to the success of treatment after hospitalization, as well as to long-term prognoses such as re-admission after discharge. It has also been shown to be related to ACS, among other diseases. In this study, we sought to determine the prognostic factors that can be applied clinically and have a high prediction rate, specifically in patients who present to the hospital within 12 hours of the onset of chest pain and who undergo PCI within 12 hours. The main purpose of this study was to determine whether NT-proBNP is a significant factor that influences the prognosis in this patient population.

Dyspnea on exertion is a common initial presentation in the emergency department and acute care settings. In real clinical situations, the distinction between dyspnea of cardiac or pulmonary (or even combined) origin is crucial for the initiation of adequate prompt treatment and long-term prognosis. BNP is a well-known circulating 32-amino-acid peptide biomarker that
has been used to differentiate dyspnea of cardiac origin from dyspnea of pulmonary origin, especially in acute care settings with limited clinical and laboratory data. Its physiological role is the integrative regulation of the renal and cardiovascular systems through the renin–angiotensin pathway. The pro-hormone of BNP is split into BNP and the inactive metabolite NT-proBNP in the ventricular cardiomyocytes. BNP and NT-proBNP are subsequently released from the ventricular myocytes into the blood in response to increased ventricular wall stress, such as pressure and volume overload. Many clinical trials have mainly assessed the diagnostic and prognostic implications in various clinical settings, focusing especially on HF and left ventricular remodeling after MI [25,26]. Furthermore, recent data also suggested that NT-proBNP is associated with myocardial necrosis, irrespective of left ventricular ejection fraction [27,28] and 6-month MACEs of AMI [29].

The main finding of our study was that the initial NT-proBNP level predicts the 12-month MACEs of patients with NSTEMI who underwent early invasive PCI, which is known to be most effective treatment strategy for NSTEMI, especially in high-risk patients. This result is consistent with our previous report on the prognostic predictive value of NT-proBNP for 6-month MACEs in patients with AMI registered in the KAMIR database. In our previous report, body mass index, severity of left ventricular systolic dysfunction (Killip class > I, in-hospital cardiogenic shock, and use of intra-aortic balloon pump), residual myocardial ischemia (previous coronary heart disease, multivessel disease), electrical instability (ventricular tachycardia or ventricular fibrillation on admission), and NT-proBNP level were independent predictors of 6-month MACEs after adjustment for clinical, angiographic, and procedural data. Compared with the previous study, this study concentrated on the disease categorization and treatment strategy. Our data focused on NSTEMI and early invasive PCI strategy. As mentioned above, this is the most effective treatment strategy for high-risk patients with NSTEMI.

In this study, max-CK and multivessel CAD were also associated with 12-month MACEs; however, NT-proBNP was still the strongest predictor. From a clinical standpoint, our findings suggest that NT-proBNP level in patients with NSTEMI could provide more reliable information than that provided by other biological markers such as troponin-I, given its potential to better define the extent of myocardial injury. Studies utilizing various statistical methods have shown that NT-proBNP is a powerful prognostic factor. Our analysis of patients with NSTEMI in this paper revealed that NT-proBNP was indeed the most powerful prognostic factor.

Some limitations of this study should be emphasized. First, our study was not a randomized and controlled study. As a result, we could not exclude the influence of many other unmeasured variables. Second, the dosage of and adherence to medications could not be assessed through our registry. Variations in the use of the appropriate medications could have led to substantial differences in MACE among our patients.

This study retrospectively analyzed MACE among patients with NSTEMI in the KAMIR database who presented to the hospital within 12 hours of the onset of chest pain and who underwent early coronary intervention (within 12 hours). The patients were followed for 12 months to determine the presence of any MACE. The significant risk factors for 12-month MACEs were NT-proBNP, max-CK, and CAD vessel. The strongest predictive factor in multivariate logistic regression was NT-proBNP. None of the other clinical and laboratory variables, including hs-CRP, troponin-I, CK, CK-MB, and BNP, showed a significant influence. Especially, the fittest cutoff value of NT-proBNP was predicted by using the AUC for each MACE. The MACEs included cardiac death, MI, Re-PCI, and CABG. When MACE was cardiac death or CABG, the AUC was found to be statistically significant. In the case of cardiac deaths, the cutoff value was 1180, with a sensitivity of 90% (95% CI, 68.3–98.5) and specificity of 66.2% (95% CI, 62.1–70.2). In the case of CABG, the cutoff value was 3,903, with a sensitivity of 61.1% (95% CI, 35.8–82.6) and specificity of 83.5% (95% CI, 80.1–86.5). Overall, NT-proBNP is a useful predictor for 12-month MACEs among patients with NSTEMI and in those with HF. We propose that a new index incorporating NT-proBNP, max-CK, and CAD vessel will be useful as a prognostic indicator of MACE in the future.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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